A

2 × 2 Table

► Contingency Table

2 & 7 Test

► Ruff 2&7 Selective Attention Test

3MS

► Modified Mini-Mental State Examination

5-HTP

► L-Tryptophan

5-Hydroxytryptophan

► L-Tryptophan

6MWD

► Six-Minute Walk Test

6MWT

► Six-Minute Walk Test

7-Item BBS-3P

► Berg Balance Scale

15 Item Test

► Rey 15 Item Test

504 Plan

M. J. Holcomb[1], David E. Macintosh[2]
[1]Ball State University
Muncie, IN, USA
[2]Ball State University
Muncie, IN, USA

Definition

A 504 Plan refers to Section 504 of the *Rehabilitation Act of 1973* (Public Law 93-112) and the *Americans with Disabilities Act of 1990* (Public Law 101-336), which makes it illegal to exclude anyone from a federally funded program or activity based on a disability. Section 504, a federal civil rights law, specifically prohibits discrimination against individuals with disabilities, within any school system or other recipient of federal financial assistance. The definition of *recipient* is a broad one, as it can include not only schools but also states (including their Departments of Education) or counties, agencies, institutions, or other organizations that benefit from Federal funds, directly or indirectly.

Current Knowledge

A 504 plan documents accommodations for qualified students which will allow them to have opportunities similar

Jeffrey S. Kreutzer, John DeLuca, Bruce Caplan (eds.), *Encyclopedia of Clinical Neuropsychology*, DOI 10.1007/978-0-387-79948-3,

to those of their peers. An *Individualized Education Plan* (IEP) is not a 504 plan because IEPs only cover an inclusive list of students with disabilities. A 504 plan covers a far wider range of conditions, including both those that actually limit one or more major life activities (the criterion for *disability* under IDEA) and those that do not limit a major life activity but are perceived as limiting by the recipient of funding. Thus, individuals who are not eligible for special education services under IDEA may nonetheless be eligible for accommodations under Section 504. While both laws require provision of a free appropriate public education, a comprehensive evaluation is not required to obtain services under the provisions of Section 504. While IDEA provides for comprehensive evaluation at the expense of the school district, this is not the case for services requested under Section 504.

In sum, the purpose of 504 legislation is to *level the playing field* for those who don't require the significant level of accommodation and/or assistance needed by those who meet criteria for an IEP under IDEA. Examples of conditions that may qualify for 504 services include asthma, diabetes, eating disorders, ADHD, depression, and conduct disorder.

Cross References

- ▶ Accommodations
- ▶ Americans with Disabilities Act (1990)
- ▶ IDEA
- ▶ Rehabilitation Act of 1973

References and Readings

Smith, T. E. C., & Patton, J. R. (1998). *Section 504 and the public schools.* Austin: TXL Pro-Ed.

AACN Practice Guidelines

Robert L. Heilbronner
Chicago Neuropsychology Group
Chicago, IL, USA

Synonyms

Practice development; Practice guidelines

Historical Background

The American Board of Clinical Neuropsychology (ABCN) is a specialty board within the American Board of Professional Psychology (ABPP). For those seeking board certification in clinical neuropsychology, ABCN is the board responsible for overseeing the examination process. The American Academy of Clinical Neuropsychology (AACN) is the organization for those awarded board certification by the ABCN. In 2007, AACN produced the first set of practice guidelines, which were intended to "...facilitate the continued systematic growth of the profession of clinical neuropsychology, and to help assure a high level of professional practice."

Current Knowledge

Given the recent growth of clinical neuropsychology, coupled with the American Psychological Association's focus on Evidence-Based Practice, the AACN established (AACN, 2007) guidelines for the practice of neuropsychological assessment and consultation. The guidelines are intended to provide standards for competence and professional conduct within the practice of neuropsychology by describing the "most desirable and highest level of professional conduct" for clinical neuropsychologists providing clinical neuropsychology services. It is important to note that the guidelines are fully compatible with the current APA (2002) Ethical Principles of Psychologists and Code of Conduct (EPPCC) as well as the Criteria for Practice Guideline Development and Evaluation (2002) and Determination and Documentation of the Need for Practice Guidelines (2005). The AACN practice guidelines include recommendations for the practice of clinical neuropsychology and they are not to be regarded as mandatory standards. The guidelines detail consideration of ethical and clinical issues as well as specific methods and procedures for the practice of neuropsychology.

There are several major areas of emphasis in the guidelines. They include: (1) Definitions; (2) purpose and scope; (3) education and training; (4) work settings; (5) ethical and clinical issues (e.g., informed consent, patient issues in third party assessments, test security; underserved populations/cultural issues; and (6) methods and procedures (e.g., review of records, measurement procedures, test administration and scoring, and interpretation).

References and Readings

American Psychological Association. (2002). Criteria for practice guideline development and evaluation. *American Psychologist, 57*, 1048–1051.

American Psychological Association. (2002) Ethical principles of psychologists and code of conduct. *American Psychologist, 57*, 1060–1073.

American Psychological Association. (2005). Determination and documentation of the need for practice guidelines. *American Psychologist, 60*, 976–978.

Committee on Ethical Guidelines for Forensic Psychologists. (1991). Specialty guidelines for forensic psychologists. *Law and Human Behavior, 15*, 655–665.

The AACN practice guidelines can be found on the AACN's Web site (www.theaacn.org) and are also published in the AACN's journal: *The Clinical Neuropsychologist, 21*, 209–231.

AAMD ABS: 2

► AAMD Adaptive Behavior Scales

AAMD Adaptive Behavior Scales

Crista A. Hopp[1], Ida Sue Baron[2]
[1]Inova Fairfax Hospital for Children
[2]Inova Fairfax Hospital for Children
Falls Church, VA, USA

Synonyms

AAMD ABS: 2; AAMR ABS-RC: 2; AAMR ABS-S: 2

Description

The American Association for Mental Deficiency Adaptive Behavior Scales (AAMD ABS) is a revised edition (1993) of the original assessments that were published in 1969. The American Association for Mental Retardation (AAMR) (formerly known as the American Association for Mental Deficiency) has changed its name to American Association on Intellectual and Developmental Disabilities (AAIDD). Therefore, *intellectual disabilities* have replaced *mental retardation* as the terminology of choice. The behavior scales have been published in two versions, the Adaptive Behavior Scales-Residential and Community, 2nd edition (ABS-RC: 2) and the Adaptive Behavior Scales-School, 2nd edition (ABS-S: 2). Current versions are a comprehensive compilation of the past versions. These assessments seek to develop an estimate of adaptive behaviors in two scales defined with personal independence and maladaptive behaviors in individuals with intellectual disabilities. Items are rated with a yes/no response, on a 0–3 scale, or by frequency. Historically, the ABS-RC: 2 was used in institutions, but it is now also used in community settings, whereas the ABS-S: 2 was designed for use in school settings.

For both the ABS-RC: 2 and the ABS-S: 2, the assessment can be administered by either of two approaches. In one method, the assessment is completed by a professional or paraprofessional trained to use the scales. In the second method, the assessment is administered by someone familiar with the individual being evaluated. Interpretation of results must be completed by an individual with formal training in psychometrics and these scales.

The ABS-S: 2 enables an appraisal of an individual's ability to cope with challenges they encounter in their school, and aids in the diagnosis of intellectual disabilities at ages 3–21. There are nine subscales in the first part of the assessment, measuring personal independence and responsibility of daily living: independent functioning, physical development, economic activity, language development, numbers and time, prevocational/vocational activity, self-direction, responsibility, and socialization. The second part of the assessment, which addresses behavioral domains, consists of seven subscales: social behavior, conformity, trustworthiness, stereotyped and hyperactive behavior, self-abusive behavior, social engagement, and disturbing interpersonal behavior.

The ABS-S: 2 was normed on 2,074 students with intellectual disabilities and 1,254 of their peers without intellectual disabilities. Administration takes place in an interview format with either a parent or teacher and may vary from 20 min to 2 h, dependent on the rater. Scoring is completed by hand. Raw scores are converted into percentiles, standard scores, and age equivalents for each subdomain. Five factors can be derived: Personal self-sufficiency, community self-sufficiency, personal social responsibility, social adjustment, and personal adjustment. Percentiles, factor standard scores, and age equivalents are then reported based on factor scores.

The ABS-RC: 2 is also useful for the assessment of personal development and social behavior in individuals with intellectual disabilities, but it has been developed for individuals aged 18–79. Like the ABS-S: 2, the assessment has two parts, but there are more subscales in each part.

The first part has ten subscales: independent functioning, physical development, economic activity, language development, numbers and time, domestic activity, prevocational/vocational activity, self-direction, responsibility, and socialization. The second part contains eight subscales: social behavior, conformity, trustworthiness, stereotyped and hyperactive behavior, sexual behavior, self-abusive behavior, social engagement, and disturbing interpersonal behavior. The ABS-RC: 2 was normed on a sample of 4,000 adults with intellectual disabilities, and administration times vary between 15 and 40 min, depending on the informant's knowledge of the individual being assessed. Raw scores are recorded and then converted to standard scores and percentiles. The subscales yield the same five-factor scales as the ABS-S: 2.

Historical Background

The AAMD first published the ABS in 1969 in response to the definition of mental retardation that was enlarged in 1959 to include adaptive behavior. The ABS-S: 2, first published in 1969 by Nihira, Foster, Shellhaas, and Leland, was revised and standardized in 1974 by Lambert, Windmiller, and Cole and again in 1981 by Lambert and Windmiller. The second and current edition was published in 1993. The ABS-RC:2 were also first published in 1969 by Nihira, Foster, Shellhaas, and Leland. It was revised in 1974, and again in 1993. The goals of the revisions have been to improve the reliability of the interviewer in differentiating between individuals with intellectual disabilities who are institutionalized and those living in the community. Previously, these individuals had been classified at different adaptive behavior levels according to the AAIDD.

Psychometric Data

The authors of the ABS-S: 2 report three types of reliability: internal consistency, stability, and interscorer. Internal consistency is reported to range from 0.79 to 0.98, while measures of stability range from 0.82 to 0.97. For Part I, interscorer reliability ranges from 0.95 to 0.98 whereas it is 0.96 to 0.99 for Part II. Authors report criterion validity in Part 1 moderately correlated with the ABS and the Vineland Adaptive Behavior Scales, although Part II was not significantly related to either (Lyman, 2007).

The ABS-RC: 2 reports an internal consistency ranging from 0.81 to 0.97. Concerning discriminant validity, adaptive behavior as measured in Part II was not related to the Vineland Adaptive Behavior Scale and Adaptive Behavior Inventory (ABI), other measures of maladaptive behaviors.

Clinical Uses

The ABS: 2 assesses the status of individuals with intellectual disability, emotional maladjustment, autism, or developmental disability. It enables a professional to assess strengths and weaknesses of an individual in adaptive areas, document progress, and assess the effectiveness of intervention/school programs. The manual cautions that the examiner should interview a significant informant or the instrument should be administered by that significant informant. If an informant is unable to provide needed information, then another informant needs to be interviewed. Whereas the ABS is a standard assessment used in determining adaptive and maladaptive behavior, its psychometric properties are limited, especially compared to other measures such as the Vineland Adaptive Behavior Scales.

Whereas a strength of the ABS-S: 2 is that it was normed on students with and without intellectual disabilities, the ABS-RC: 2's standard scores and percentile ranks were not compared to individuals without intellectual disabilities. Therefore, this assessment may not meet the criteria to make a diagnosis of mental retardation according to the AAMR requirements.

Cross References

► Vineland Adaptive Behavior Scales

References and Readings

Aiken, L. (1996). *Assessment of intellectual functioning.* Switzerland: Burkhauser.

Bracken, B., & Nagle, R. (2007). *Psychoeducational assessment of preschool children.* New York: Routledge.

Hogg, J., & Langa, A. (2005). *Assessing* Adults with Intellectual Disabilities. Malden, MA: Blackwell.

Lyman, W. (2008). Test review In N. Lambert, K. Nihira, & H. Lel (1993). AAMR Adaptive behavior scales: school. *Assessment for Affective Intervention, 33*, 55–57.

Reynolds, C., & Fletcher-Janzen, E. (2007). *Encyclopedia of special education, a reference for the education of children, adolescents, and adults with disabilities and other exceptional individuals* (3rd ed., Vol. 1). Hoboken, NJ: Wiley.

AAMR ABS-RC: 2

► AAMD Adaptive Behavior Scales

AAMR ABS-S: 2

► AAMD Adaptive Behavior Scales

ABAS

► Adaptive Behavior Assessment System – Second Edition

Abasia

Douglas I. Katz
Braintree Rehabiltation Hospital
Braintree, MA, USA
Boston University School of Medicine
Boston, MA, USA

Definition

This refers to an inability to walk. Abasia may be caused by a variety of conditions including weakness, spasticity, cerebellar incoordination, and movement disorders of various types.

Cross References

► Ataxia
► Spastic Gait

ABAS-II

► Adaptive Behavior Assessment System – Second Edition

Abbreviated Injury Scale

Edison Wong
Center for Pain & Medical Rehab
Fitchburg, MA, USA

Synonyms

Organ injury scale

Definition

The Abbreviated Injury Scale (AIS) is an anatomical scoring system first introduced in 1969. It has been revised and updated against survival data so that it now provides a reasonably accurate way of ranking the severity of injury.

Injuries are ranked on a scale of 1–6, with 1 being minor, 5 severe, and 6 an unsurvivable injury (Table 1). This represents the "threat to life" associated with an injury and is not meant to represent a comprehensive measure of severity. The AIS is not a linear scale, in that the difference between AIS1 and AIS2 is not the same as that between AIS4 and AIS5. Organ Injury Scales of the American Association for the Surgery of Trauma are mapped to the AIS score for calculation of the Injury Severity Score.

Current Knowledge

The latest incarnation of the AIS score is the 2005 revision. AIS is monitored by a scaling committee of the Association for the Advancement of Automotive

Abbreviated Injury Scale. Table 1 AIS scores and their definition of injury severity

AIS Score	Injury
1	Minor
2	Moderate
3	Serious
4	Severe
5	Critical
6	Unsurvivable

Medicine and has been adopted by the American Association for the Surgery of Trauma since its publication in the *Journal of Trauma* in 1985.

References and Readings

Copes, W. S., Sacco, W. J., Champion, H. R., & Bain, L. W. (1989). *Progress in characterizing anatomic injury.* Proceedings of the 33rd Annual Meeting of the Association for the Advancement of Automotive Medicine, pp. 205–218.

Greenspan, L., McClellan, B. A., & Greig, H. (1985). Abbreviated injury scale and injury severity score: A scoring chart. *The Journal of Trauma, 25*, 60–64.

Moore, E. E., Shackford, S. R., Pachter, H. L., McAninch, J. W. Browner, B. D., Champion, H. R., et al. (1989). Organ injury scaling: Spleen, liver, and kidney. *The Journal of Trauma, 29*, 1664–6.

Yentis, S. M., Hirsch, N. P., & Smith, G. B. (2004). *Anaesthesia and intensive care A-Z.* New York: Butterworth & Heinemann.

Ability Focused

► Flexible Battery

Ablation

Edison Wong
Center for Pain and Medical Rehab
Fitchburg, MA, USA

Synonyms

Resection

Definition

Ablation is the removal or destruction of an anatomical structure by means of surgery, disease, or other physical or energetic process. Ablation is employed as a treatment of various medical conditions and includes recent advances in technology. Surgical ablation of neuronal pathways to the globus pallidus or thalamus has been used historically to treat parkinsonism. Interventional pain experts use radiofrequency ablation of nerves in the spine to treat chronic back pain. Gamma radiation or "gamma knife surgery" is used to excise brain tumors when traditional surgical ablation is too destructive to neighboring tissues. Even with sophisticated neurosurgical techniques, ablation of any type in the nervous system may still produce unwanted motor, sensory, or cognitive-behavioral impairments.

Cross References

► Commissurotomy
► Craniotomy
► Gamma Knife
► Hemispherectomy
► Lobectomy
► Lobotomy
► Pallidotomy
► Prefrontal Lobotomy
► Radiosurgery
► Temporal Lobectomy

References and Readings

Krayenbuhl, H., Wyss, O. A., & Yasargil, M. G. (1961). Bilateral thalamotomy and pallidotomy as treatment for bilateral parkinsonism. *Journal of Neurosurgery, 18*, 429–444.

Lord, S. M., & Bogduk, N. (2002). Radiofrequency procedures in chronic pain. *Best Practice & Research. Clinical Anaesthesiology, 16*, 597–617.

Lunsford, L. D., Flickinger, J. C., & Steiner, L. (1988). The gamma knife. *JAMA, 259*, 2544.

Shah, R. V., Ericksen, J. J., & Lacerte, M. (2003). Interventions in chronic pain management. 2. New frontiers: Invasive nonsurgical interventions. *Archives Physical Medicine and Rehabilitation, 84*, S39–44.

Abnormal Brain Growth

► Microcephaly

Abnormal Walking

► Gait Disorders

Aboulia

► Abulia

ABS

► Agitated Behavior Scale

Absence Epilepsy

Jeffrey B. Titus[1,2], Rebecca Kanive[1]
Michael Morrissey[1]
[1]St. Louis Children's Hospital
St. Louis, MO, USA
[2]Washington University School of Medicine
St. Louis, MO, USA

Synonyms

Petit mal epilepsy; Psychomotor seizures; Pyknoleptic petit mal (childhood absence epilepsy)

Definition

Absence epilepsy is a form of idiopathic generalized epilepsy that is characterized by seizures that involve sudden arrest in activity, awareness, and responsiveness, and may include some mild motor features. Typical absence seizures usually last less than 10 s and end as abruptly as they start. Patients have no recollection of the event and often return immediately to their previous activity with little or no post-ictal alterations in functioning. Generalized spike-and-wave discharges on EEG are required for the diagnosis and are strongly correlated with the clinical events.

Categorization

Childhood absence epilepsy (CAE).
Juvenile absence epilepsy (JAE).

Epidemiology

Incidence reports of absence epilepsy range from 49 to 98 per 100,000. Among children with epilepsy, 2–8% have been estimated to have CAE. The incidence of JAE has not been well-studied. Estimates suggest that JAE accounts for up to 20% of absence epilepsy cases; however, this may be an underestimation. It has been suggested that JAE may be as common as juvenile myoclonic epilepsy (JME), though this has not been well-established. CAE is typically considered to be more common in females.

CAE is associated with a strong family history of seizures. There is strong concordance among identical twins, and multiple genes likely account for transmission. Siblings of patients with CAE have about a 10% chance of having seizures, and about one-third of patients with CAE have a family member with epilepsy. Nevertheless, the causal influences of CAE are believed to be multifactorial, depending on both genetic and nongenetic factors. Causal factors in JAE have not been well-studied but may be similar to what is found in CAE.

Natural History, Prognostic Factors, Outcomes

Typical age of onset in CAE is between 3 and 8 years, but rare cases of onset prior to 3 years of age have been reported. Onset of JAE is considered to be between 10 and 17 years. Because onset of CAE has been reported in cases as old as 10 or 11 years, there is clear overlap between CAE and JAE. EEG and clinical findings are often useful in differentiating CAE from JAE in older children and younger adolescents. It is unusual for a child to exhibit features of CAE after the age of 11 years.

Outcomes in CAE and JAE are generally favorable. Most patients with CAE experience remission of seizures by mid-adolescence, with only a small proportion experiencing absence seizures into adulthood. About 40% of patients with CAE also exhibit generalized tonic–clonic seizures. They often emerge around the time of puberty, are relatively easy to control, and more commonly persist into adulthood than absence seizures. Tonic–clonic seizures

Absence Epilepsy. Table 1 Clinical features of CAE and JAE

	CAE	JAE
Incidence	2–8% (of children with epilepsy)	Unknown
Age of onset	3–8 years	10–17 years
Seizure frequency	Multiple per day	One or fewer per day
Response to treatment	Good	Good
Seizure freedom	Expected	Less common
Treatment duration	Through mid-adolescence	Often through adulthood

are more common in JAE and occur in about 80–90% of cases. Some patients with JAE also exhibit myoclonic seizures, but they are typically mild and infrequent. While most patients with CAE become seizure-free in adolescence, seizure outcome in JAE is not well known.

CAE is considered to be a benign childhood epilepsy because of relatively good seizure control and functional outcomes. Seizure control is less common in JAE, but functional outcomes may be similar. Further research is needed to examine this. Tonic–clonic seizures are believed to be a marker for poorer seizure outcome in both CAE and JAE. Functional outcomes in CAE are thought to be most heavily influenced by psychosocial factors, such as family adjustment, support systems, educational attitudes, and stigma toward the condition. Cognitive and/or behavioral side effects from antiepileptic drug (AED) therapy may also limit outcomes.

Neuropsychology and Psychology of Absence Epilepsy

Cognitive functioning in CAE is traditionally considered "benign," because children typically present with normal intelligence and exhibit no significant impairments in functional outcomes. However, more recent research has found evidence that patients with CAE are prone to having cognitive deficits and psychosocial problems, and they are more likely to receive special education services and display low academic achievement. While patients with poor seizure control exhibit the greatest difficulties, cognitive and behavioral problems are also experienced by patients with good seizure control. Unfortunately, limited information is known about cognitive and psychological functioning in JAE.

Patients with CAE do not have a characteristic cognitive profile. Cognitive difficulties have been reported in multiple domains, including attention, memory, and visual-spatial processing. A recent study by Caplan et al. (2008) revealed the presence of subtle cognitive impairments in children with CAE. When compared with controls, they found that children with CAE (ages 6.7–11.2 years) had significantly lower intelligence, as measured by the *Wechsler Intelligence Scale for Children* – Revised/Third Edition. While, as a group, children with CAE performed in the average range, they were below the performance of a control group. Similar differences were noted on verbal and visual intellectual tasks. The difference in performance IQ (PIQ) was less robust, but still significant, between children with CAE and controls. Among their sample of 69 children with CAE, 27% demonstrated overall intelligence at least one standard deviation below the mean. Similar rates were found for VIQ and PIQ. Their spoken language quotient (SLQ), as measured by various versions of the Test of Language Development, was average, but it was also lower than controls. A high percentage of children with CAE performed at least one standard deviation below the mean on language measures.

In addition to finding a higher rate of cognitive limitations, Caplan et al. (2008) confirmed that children with CAE also experience emotional and behavioral comorbidities. Among the 69 children with CAE in their sample, 30% had a diagnosis of attention-deficit/hyperactivity disorder (ADHD), with 52% of those children diagnosed as ADHD-inattentive type. Moreover, about 29% of their samples were diagnosed with a form of internalizing psychopathology. Among those children, 75% were diagnosed with anxiety, 20% with depression, and 5% with both anxiety and depression. After controlling for IQ and demographic variables, children with CAE were found to have significantly higher ratings on scales of the Child Behavior Checklist (CBCL) that assess attention problems, somatic problems, social problems, withdrawal, and thought problems. The authors discovered that children with lower intelligence had greater social problems, and females in the CAE sample were almost six times more likely to be diagnosed with an anxiety disorder. In addition, children with CAE were more likely to be diagnosed with ADHD or anxiety if they had more frequent seizures or a longer duration of illness.

Evaluation

Children and adolescents with CAE and JAE typically present with no focal neurological abnormalities on examination. The presence of absence seizures is a defining feature of absence epilepsy, and hyperventilation or light stimulation can be highly effective at eliciting an event. In CAE, absence seizures occur multiple times per day, but, in JAE, they are more rare and may only occur once per day.

Absence seizures can be either typical or atypical, and discrimination between the two types is usually done off of EEG findings. While typical absence seizures are characterized by clearly delineated episodes of activity arrest and impaired consciousness for less than 10 s, atypical absence seizures are associated with less abrupt onset and termination, and they may more commonly involve various semiological phenomena. Atypical absence seizures often last for more than 10 s and cannot be elicited by hyperventilation or light stimulation. Tonic

seizures are also frequently present in children with atypical absence seizures.

Typical absence seizures can be subdivided into simple and complex. Simple typical absence seizures constitute about 90% of cases and may involve only minor motor mannerisms (e.g., mild eyelid fluttering). Patients with complex typical absence seizures display more involvement of motor features, such as automatisms or decreased or increased muscle tone. Loss of consciousness may also be longer.

Complex partial seizures can often mimic absence seizures, particularly when their expression is limited. Typical absence seizures can be distinguished from complex partial seizures because they are briefer, more frequent, and have no post-ictal impairment. EEG characteristics and the presence of various seizure types often distinguish atypical absence seizures from complex partial epilepsy.

When considering the presence of absence seizures, it is important to consider whether the episodes can be accounted for by variations in attention. This is especially important when considering the high rate of attention problems in children with epilepsy. Attempting to determine the degree of responsiveness during the episodes often helps with making the differential diagnosis; however, this can be difficult to determine when episodes are very brief. Moreover, it is not uncommon for patients to have both absence seizures and attention problems. Therefore, a child's ability to respond during an episode cannot be used to rule-out the presence of absence seizures. Sometimes a neuropsychological assessment can be helpful in differentiating between absence seizures and episodes of inattention. If the examiner has experience with absence seizures, the neuropsychological assessment can provide multiple hours of one-on-one observation and interaction that might provide opportunities to observe the episodes and attempt to elicit responses. This can also be helpful if mental fatigue tends to elicit more events.

On EEG, absence seizures are characterized by paroxysmal bursts of high amplitude 3–4 Hz spike and slow waves that are superimposed on a normal background. The bursts vary in length (3–10 s), and the clinical absence is time-locked to the burst period. This activity (clinical and electrographic) can be provoked during a routine EEG recording using the hyperventilation activation procedure.

Treatment

Response to AED therapy in CAE and JAE is good, and valproic acid is often considered the drug of first choice. Ethosuximide has also been recommended and may be more appropriate for younger patients. In rare cases of more difficulty in controlling seizures, polytherapy may be needed. In patients with CAE, a seizure-free period of 2 years is often recommended prior to discontinuation of therapy; however, this should be determined on a case-by-case basis. Patients with JAE will require longer treatment and may continue on AEDs indefinitely. In adolescent patients, it is important to educate about the increased risk of seizures with poor medication compliance, alcohol consumption, or sleep deprivation.

Cross References

- ▶ Petit Mal Seizure
- ▶ Juvenile Myoclonic Epilepsy (JME)

References and Readings

Aicardi, J. (1998). *Diseases of the nervous system in childhood.* London: Mac Keith.

Berkovic, S. F., & Benbadis, S. (2001). Childhood and juvenile absence epilepsy. In E. Wyllie (Ed.), *The treatment of epilepsy: Principles and practice* (3rd ed. pp. 485–490). Philadelphia, PA: Lippincott Williams & Wilkins.

Caplan, R., Siddarth, P., Stahl, L., Lanphier, E., Vona, P., Gurbani, S., Koh, S., Sankar, R., & Shields, W. D. (2008). Childhood absence epilepsy: Behavioral, cognitive, and linguistic comorbidities. *Epilepsia, 49*(11), 1838–1846.

Absence Seizure

Kenneth Perrine
Northeast Regional Epilepsy Group
Hackensack, NJ, USA
Weill-Cornell College of Medicine
New York, NY, USA

Synonyms

Petit mal seizure; Psychomotor seizures

Definition

An *absence* (usually pronounced with a French accent as "ab-SAWNS") *seizure* is a type of generalized seizure caused by a large burst of electrical discharges that

begins in broad, bilateral brain regions simultaneously (as opposed to a *partial seizure*). During an absence seizure, the patient will lose interaction with the environment, stare blankly ("zone out"), and perhaps blink the eyes. There is no true loss of consciousness or motor functions. The seizure is typically short in duration (only several seconds), and patients often resume their ongoing activity without realizing even that they had a seizure (but will be amnestic for anything occurring during the episode). There are no postictal problems after the end of the seizure. Although no first aid is required, the patient should be protected from doing anything dangerous during the episode (e.g., cooking, crossing the street) but the episodes are often so brief that intervention is difficult.

Current Knowledge

The cause of absence seizures is unknown. Patients with absence seizures typically have no positive neuroimaging findings, but usually have bursts of 3-per-s bilaterally synchronous spike/wave epileptiform activity on a routine EEG (even when not having a seizure). Absence seizures can be differentiated clinically from complex partial seizures, in which there is a similar disruption of consciousness and "zoning out," by the duration of the episode. Absence seizures last only a few seconds, while complex partial seizures usually last 1–1.5 min. Absence seizures typically begin in childhood, respond well to medication, and often remit spontaneously by adulthood. Common medications for absence seizures include divalproex/valproate sodium (Depakote), ethosuximide (Zarontin), and lamotrigine (Lamictal). Although the frequency of absence seizures can approach dozens per day, only mild (at worst) neuropsychological deficits are typically shown if the absence episodes occur without other seizure types. They do not have a dramatic impact on academic performance. However, absence seizures may occur with other seizure types in serious disorders such as Lennox-Gastaut syndrome, in which case there is considerable cognitive dysfunction and a worse prognosis.

Cross References

► Epilepsy

References and Readings

Engel, J., & Pedley, T. A. (Eds.). (2008). *Epilepsy: A comprehensive textbook* (2nd ed.). New York: Lippincott Williams & Wilkins.
www.epilepsyfoundation.org

Abstract Reasoning

David Hulac
University of South Dakota
Vermillion, SD, USA

Synonyms

Logical reasoning

Definition

The neuropsychological construct of abstract reasoning refers to an individual's ability to recognize patterns and relationships of theoretical or intangible ideas. Abstract reasoning is contrary to concrete reasoning whereby an individual recognizes patterns in information obtained through the immediate senses. When thinking abstractly, an individual must analyze and synthesize information without the aid of empirical information. Frequently, abstract reasoning requires an individual to apply concrete information to other scenarios that may not directly relate to that person's experience.

Abstract reasoning is most closely related to rational thought as opposed to empirical thought. While using deductive reasoning, a purely rational thinker does not look to determine the accuracy of a premise, but seeks only to understand the relationship between the premises. An example of deductive reasoning, which requires abstract reasoning, may go like this:

1. Premise 1: Egypt is located in South America.
2. Premise 2: The Sphinx lies in Egypt.
3. Conclusion: The Sphinx is located in South America.

Empirically and concretely, it is obvious that Egypt is not in South America, but in Africa. To complete the syllogism, however, the thinker must ignore the concrete distortion, and instead focus on the two premises and understand if the conclusion logically flows.

Common measures of abstract reasoning include the Similarities, Picture Concepts, and Matrix Reasoning subtests of the Wechsler scales. During a mental status exam, abstract reasoning is measured by asking a subject to describe the meanings of proverbs or to describe word similarities.

Abstract reasoning, most commonly understood as being a function of the left hemisphere of the brain, is a precursor for using and understanding language and

mathematics. Individuals who struggle with abstract reasoning benefit when an instructor uses examples to make the concept more concrete. Frequently, children with learning disabilities have difficulty with these abstract subjects, but achieve greater success in courses with more concrete subject matters such as social studies and science.

References and Readings

Goldstein, G. (2004). Abstract reasoning and problem solving in adults. In M. Hersen (Ed.), *Comprehensive handbook of psychological assessment, Vol. 1: Intellectual and neuropsychological assessment* (pp. 293–308). Hoboken, NJ: Wiley.

Abulia

Irene Piryatinsky
Butler Hospital and Alpert Medical School of Brown University
Providence, RI, USA

Synonyms

Aboulia; Apathy; Athymia; Loss of psychic self-activation; Psychic akinesia

Definition

Abulia refers to a lack of will, drive, or initiative. The word is derived from the Greek "αβουλία," meaning "non-will." It should be distinguished from an inability to actually *perform* the activity due to cognitive or physical disability. Abulia is manifested by the lack of motivation, spontaneity, and initiation. Some research indicates that abulia occurs because of malfunction of the brain's dopamine-dependent circuitry, especially bilateral lesions in the medial frontal lobes, basal ganglia, and their connections. The following criteria have been suggested for the diagnosis of abulia: (1) decreased spontaneity in activity and speech; (2) prolonged latency in responding to queries, directions, and other stimuli; and (3) reduced ability to persist with a task.

Cross References

▶ Action-Intentional Disorders
▶ Adynamia
▶ Avolition

References and Readings

Berrios, G. E., & Grli, M. (1995). Abulia and impulsiveness revisited: A conceptual history. *Acta Psychiatrica Scandinavica, 92*(3), 161–167.

Caplan, L. R., Schmahmann, J. D., Kase, C. S., Feldmann, E., Baquis, G., Greenberg, J. P., et al. (1990). Caudate infarcts. *Archives of neurology, 47*(2), 133–143.

Drubach, D. A., Zeilig, G., Perez, J., Peralta, L., & Makley, M. (1995). Treatment of abulia with carbidopa/levadopa. *Journal of Neurologic Rehabilitation, 9*, 151–155.

Egnelborghs, S., Marien, M. A., Pickut, B. A., Verstraeten, M. A., & De Deyn, P. P. (2000). Loss of psychic self-activation after paramedian bithalamic infarction. *Stroke, 31*, 1762–1765.

Forstl, H., & Sahakian, B. A. (1991). A psychiatric presentation of abulia: Three cases of frontal lobe ischaemia and atrophy. *Journal of the Royal Society of Medicine, 84*, 89–91.

Kumral, E., Evyapan, D., & Balkir, K. (1999). Acute caudate vascular lesions. *Stroke, 30*, 100–108.

Laplande, D. N. A., Sauron, B., de Billy, A., & Dubois, B. (1992). Lesions of the basal ganglia due to disulfiram neurotoxicity. *Journal of Neurology, Neurosurgery & Psychiatry, 55*, 925–929.

Litvan, I., Paulsen, J. S., Mega, M. S., & Cummings, J. L. (1998). Neuropsychiatric assessment of patients with hyperkinetic and hypokinetic movement disorders. *Archives of Neurology, 55*, 1313–1319.

Powell, J. H., Al-Adawi, S., Morgan, J., & Greenwood, R. J. (1996). Motivation deficits after brain injury: Effects of bromocriptine in 11 patients. *Journal of Neurology, Neurosurgery & Psychiatry, 60*, 416–421.

Abusive Head Trauma

▶ Shaken Baby Syndrome (SBS)

ACA

▶ Anterior Cerebral Artery

Academic Ability

▶ Academic Competency

Academic Competency

Todd Van Wieren
Indiana University of Pennsylvania
Indiana, PA, USA

Synonyms

Academic ability; Academic performance; Educational productivity

Definition

The multidimensional characteristics of a learner – including skills, attitudes, and behaviors – that factor into their academic success. These characteristics can be separated and considered in one of two primary domains: academic skills or academic enablers (DiPerna & Elliot, 2000; Elliot & DiPerna, 2002). Academic skills are both the basic and complex skills (e.g., reading, writing, calculating, and critical thinking) needed to access and interact with content-specific knowledge. Academic enablers, however, are the attitudes and behaviors (e.g., interpersonal skills, motivation, study skills, and engagement) that a learner needs in order to take advantage of education.

Cross References

► Academic Skills
► Learning

References and Readings

Edl, H. M., Jones, M. H., & Estell, D. B. (2008). Ethnicity and english proficiency: Teacher perceptions of academic and interpersonal competence in European American and Latino students. *School Psychology Review, 37*(1), 38–45.

Elliot, S. N., & DiPerna, J. C. (2002). Assessing the academic competence of college students: Validation of a self-report measure of skills and enablers. *Journal of Postsecondary Education and Disability, 15*(2), 87–100.

DiPerna, J. C., & Elliot, S. N. (2000). *The academic competence evaluation scales (ACES college)*. San Antonio, TX: The Psychological Association.

Hutto, L. (2009). *Measuring academic competence in college students: a review of research and instruments.* Saarbrücken Germany: VDM Verlag.

Ma, L., Phelps, E., Lerner, J. V., & Lerner, R. M. (2009). Academic competence for adolescents who bully and who are bullied. *The Journal of Early Adolescence, 29*(6), 862–897.

Shapiro, E. S. (2008). From research to practice: promoting academic competence for underserved students. *School Psychology Review, 37*(1), 46–51.

Academic Performance

► Academic Competency

Academic Skills

Christina Zafiris
University of Northern Colorado
Greeley, CO, USA

Definition

Academic skills refer to a student's ability to perform age-appropriate school activities related to writing, reading, and mathematical problem-solving. Additionally, academic skills refer to the information learned which is relevant to school success. Having solid academic skills improves academic progress throughout one's school experience. Many of the academic skills a child learns are acquired in the school setting. However, pre-academic skills may be obtained in the child's environment prior to the start of formal schooling. This may be achieved by exposure to mathematics (such as adding and subtracting objects at home), coloring, and reading with and to the child.

Cross References

► Academic Competency
► Educational Testing
► Learning
► Reading

References and Readings

Burchinal, M. R., Peisner-Feinberg, E., Pianta, R., & Howes, C. (2002). Development of academic skills from preschool through second grade: Family and classroom predictors of developmental trajectories. *Journal of School Psychology, 40*(5), 415–436.

Christian, K., Morrison, F. J., & Bryant, F. B. (1998). Predicting kindergarten academic skills: Interactions among child care, maternal education, and family literacy environments. *Early Childhood Research Quarterly, 13*(3), 501–521.

Shapiro, E. S. (2004). *Academic skills problems: Direct assessment and intervention* (3rd ed.). New York: Guilford Press.

Acalculia

Natalie Wahmhoff, Elaine Clark
University of Utah
Salt Lake City, UT, USA

Synonyms

Acquired dyscalculia; Dyscalculia; Mathematics disability

Definition

Acalculia, most simply, is the inability to perform mathematical tasks. These difficulties can stem from other deficits or can exist independently. Acalculia deficits can be global or selective and manifest in a wide variety of number processing and calculation abilities.

Categorization

Generally, authors have agreed on two major distinctions: primary and secondary acalculia (Growth-Marnat, 2000). Primary acalculia occurs when mathematical deficits are fundamental and are present independently of other deficits. Deficits in primary acalculia include poor estimation, number comparison abilities, and difficulty understanding procedural rules and numerical signs. In primary acalculia, these deficits will exist regardless of whether tasks are presented in an oral or written format (Adila & Rosselli, 2002).

The secondary acalculias are due to primary deficits in other areas. *Aphasic acalculia* occurs in patients with Wernicke's and Broca's aphasia. Patients with Broca's aphasia have problems when translating word representations of numbers (three hundred and forty-five) to their numeral form (345). They may also read numbers with morphological errors (15 is read as 50) (Ardila & Rosselli, 2002; Basso, Burgio, & Caporali, 2000). When the secondary acalculia stems from Wernicke's aphasia, deficits are more severe. Reading and writing of numbers often have semantic errors, and poor verbal memory often impacts the calculation abilities of these patients (Grafman & Rickart, 2000).

Alexic acalculia is the inability to read number and correlations with the inability to read text. People with this type of acalculia may focus only on beginning digits (538 is read as 53). For those with alexic acalculia, mental calculation abilities exceed written calculation abilities (Ardila & Rosselli, 2002).

Agraphic acalculia is the inability to write numbers. Like aphasic acalculia, agraphic acalculia correlates with Broca's and Wernicke's aphasia. In Broca's aphasia, acalculia deficits manifest as omissions, substitutions, and order reversal. In Wernicke's aphasia, difficulties are especially evident when required to write quantities when they are orally dictated. Those with Wernicke's aphasia also tend to make paralexias and paragraphias (Ardila & Rosselli, 2002; Growth-Marnat, 2000).

Frontal acalculia deficits occur in conjunction with attention difficulties, perseveration, and impairment of more complex math concepts (Dehaene, Cohen, & Changeux, 1998). Difficulties are most apparent with multistep operations, algorithms, and when planning is required. While complex concepts are difficult for patients with frontal acalculia, more basic math concepts are usually maintained (Ardila & Rosselli, 2002).

Spatial acalculia impacts written mathematical tasks more than mental math tasks. A difficulty with writing numbers is quite apparent in these cases and manifest in several ways. Writing on only one side of the page, inability to write numbers in a straight line, and general disorganization are some of the deficits that impact math performance (Basso, Burgio, & Caporali, 2000). Patients with spatial acalculia often forget where to place remainders and carried numbers, despite understanding the basic division and multiplication functions. Math procedure signs are often undetected or switched (add instead of subtract).

Epidemiology

Acalculia can result from stroke, tumors, and trauma. It is also seen in patients with degenerative dementia (Ardila & Rosselli, 2002).

Prognostic Factors and Outcomes

There is noted variability in prognosis for acalculia, ranging from no recovery to full recovery. For primary acalculia, improvement is limited. In the case of secondary acalculias, recovery from the primary deficit, such as aphasia, alexia, and agraphia, occur, the corresponding acalculia deficits tend to improve as well.

Neuropsychology and Psychology of Acalculia

Primary acalculia is associated with left posterior parietal lesions. More specifically, damage to the left angular and supramarginal gyri occurs with primary acalculia (Grafman & Rickart, 2000). It is suggested that there are separate neuropathways for rote number knowledge and semantic number knowledge.

Neuroimaging techniques reveal that several brain areas are active when performing calculations and also that the pattern differs according to what type of calculation is done (Dehaene, Cohen, & Changeux, 1998). This occurs to the many abilities that calculation often requires, including verbal, spatial, executive functioning, and memory. The areas most associated with calculation are the upper cortical surface and anterior aspect of the left middle frontal gyrus, the bilateral supramarginal and angular gyrus, the left dorsolateral prefrontal and premotor cortices, Broca's area, inferior parietal and left parietal cortex, and the inferior occipitotempral regions (Ardila & Rosselli, 2002).

It is important to keep in mind that damage to the right hemisphere and the frontal lobes also impact the occurrence of acalculia, especially when it is a secondary acalculia.

Evaluation

The arithmetic section of the Wide Range Achievement Test (WRAT) has often been used to test operational skills. The Key Math, which is designed for children and adolescents, tests more targeted and specific abilities that are suggested for an acalculia assessment (Grafman & Rickart, 2000). Many authors have suggested experimental batteries that target specific functions and include error analysis. These batteries often assess skills in the following areas: number recognition, number writing, number transcoding, quantification, magnitude estimation, basic arithmetic operations, calculation fact verification, multicolumn calculations, magnitude comparison, fractions, algebra, and numeric knowledge. When possible, these skills should be assessed in both written and oral form (Ardila & Rosselli, 2002; Grafman & Rickart, 2000).

Treatment

Some authors have suggested beginning rehabilitation with an error analysis if it was not completed during the assessment. This will provide explicit areas to target during rehabilitation (Grafman & Rickart, 2000). Long-term rehabilitation programs should begin simply and progressively work toward more complex tasks. With secondary acalculia, focusing rehabilitation on the primary deficit may significantly improve the secondary acalculia deficits (Ardila & Rosselli, 2002).

Cross References

- ▶ Agraphia
- ▶ Alexia
- ▶ Aphasia
- ▶ Gerstmann's Syndrome
- ▶ Spatial Dyscalculia

References and Readings

Ardila, A., & Rosselli, M. (2002). Acalculia and dyscalculia. *Neuropsychology Review, 12*, 179–231.

Ardila, A., Matute, E., & Inozemtseva, O. (2003). Progressive agraphia, acalculia, and anomia: a single-case report. *Applied Neuropsychology, 10*, 205–214.

Basso, A., Burgio, F., & Caporali, A. (2000). Acalculia, aphasia, and spatial disorders in left and right brain-damaged patient. *Cortex, 36*, 265–280.

Dehaene, S., Cohen, L., & Changeux, J. P. (1998). Neuronal network models of acalculia and prefrontal deficits. In R. W. Parks, D. S. Levine, & D. L. Long (Eds.), *Fundamentals of neural network modeling: neuropsychology and cognitive neuroscience* (pp. 233–255). Cambridge, MA, USA: MIT.

Grafman, J., & Rickart, T. (2000). Acalculia. In M. J. Farah & T. E., Fienberg (Eds.), *Patient based approaches to cognitive neurosciences: issues in clinical and cognitive neuropsychology.* Cambridge, Massachusetts: MIT.

Growth-Marnat, G. (Ed.). (2000). *Neuropsychological assessment in clinical practice.* New York: Wiley.

Scruggs, T. E. & Mastropieri, M. A. (2000). Acalculia. In *Encyclopedia of special education* (2nd ed., Vol. 1, p. 27). New York: Wiley.

ACC

▶ Anterior Cingulate Cortex

Accelerated Hypertension

▶ Hypertensive Encephalopathy

Acceleration Injury

Beth Rush
Mayo Clinic
Jacksonville, FL, USA

Synonyms

Acceleration–deceleration injury

Definition

Traumatic injury to the brain resulting from high-speed acceleration of the brain within the skull cavity in the direction of inertial force.

Current Knowledge

During acceleration injury, movement of the head is unrestricted. One of the most common scenarios resulting in acceleration injury is a high-speed motor vehicle accident. Primary brain injury results from brain tissue and brain structures compressing against one another in the force of inertia. This may result in bruising, hemorrhage, and shearing of the underlying tensile strength of white matter connections deep within the brain. Secondary injury may occur hours or even days after the inciting traumatic event. Secondary effects of injury can include decreased cerebral blood flow, edema, hemorrhage, increased intracranial pressure, and biochemical changes that may cause excitotoxicity and more extensive damage to the surrounding brain structures and their associated connections.

Theoretical models of linear acceleration injury now address the heterogeneity of effects that can result from such biomechanical injuries. Although diffuse brain damage may result from this type of injury, a key factor that predicts the extent of damage following acceleration injury is the area of initial impact. Given that the structure and projection pathways of the brain have varying densities and tensile strengths within different regions of the brain, the point of impact is most likely the key in determining the extent of damage that takes place and the likelihood and course of recovery that is possible following injury.

Patients sustaining acceleration injury may experience headache, photophobia, phonophobia, nausea, and dizziness immediately following injury onset. On neuropsychological evaluation, patients with acceleration injuries are more likely to demonstrate a diffuse, rather than focal, profile of cognitive impairment when cognitive impairment is present. The lateralization of cognitive impairment that is typically observed in focal brain injury is relatively uncommon following acceleration injury. A diffuse profile of cognitive impairment in acceleration injury is due to the disruption of white matter tracts that are responsible for efficiency and coordination of communication between functional brain injuries. As such, a patient with acceleration injury may demonstrate cognitive slowing, executive dysfunction, and problems with simple and complex attention as a consequence of his/her brain injury.

Cross References

▶ Biomechanics of Injury
▶ Deceleration Injury
▶ Diffuse Axonal Injury

References and Readings

Bayly, P. V., Cohen, T. S., Leister, E. P., Ajo, D., Leuthardt, E. C., Genin, G. M. (2005). Acceleration-induced deformation of the human brain. *Journal of Neurotrauma, 22*(8), 845–856.

Sabet, A. A., Christoforou, E., Zatlin, B., Genin, G. M., & Bayly, P. V. (2008). Deformation of the human brain induced by mild angular head acceleration. *Journal of Biomechanics, 41*(2), 307–315.

Acceleration–deceleration Injury

▶ Acceleration Injury
▶ Deceleration Injury

Accessory Cuneate Nucleus

John E. Mendoza
Tulane University Medical Center
New Orleans, LA, USA

Synonyms

Lateral cuneate nucleus

Definition

Nucleus in the dorsolateral portion of the medulla that receives sensory information likely from touch, pressure, and stretch receptors in the upper extremities. It gives rise to the *cuneocerebellar tract* which enters the cerebellum via the inferior cerebellar peduncle. The accessory cuneate nucleus is thought to be the equivalent of the dorsal nucleus of Clarke in the lumbar, thoracic, and lower cervical cord which is the source of the dorsal spinocerebellar tract. These nuclei and tracts provide unconscious (as opposed to "conscious") sensory feedback to the cerebellum in its regulation of individual muscles. Lesions of this nucleus might be expected to produce cerebellar type symptoms of the ipsilateral upper extremity (i.e., ataxia/incoordination of movement), but it is relatively small and isolated lesions are likely to be extremely rare.

Accident Claims

► Personal Injury

Accident Neurosis

► Compensation Neurosis

Accommodations

Jacob T. Lutz[1], David E. McIntosh[2]
[1]Bell State University
Muncie, IN, USA
[2]Bell State University
Muncie, IN, USA

Synonyms

Reasonable accommodations

Definition

In order to provide students with disabilities the free, appropriate public education mandated by IDEA 2004 and Section 504 of the Rehabilitation Act of 1973, changes typically must be made to a child's educational curriculum or environment. These accommodations include changes in the method of presentation of material, classroom seating location, availability of an interpreter for those with hearing impairment, response format, testing time allowed, setting, or other reasonable steps that do not significantly alter the content of educational material or the validity of tests. To be eligible to receive accommodations, students must be identified as having a disability consistent with the guidelines presented in IDEA 2004 or Section 504 of the Rehabilitation Act of 1973.

Accommodations may also be required in the workplace under the Americans with Disabilities Act. These could include installation of a ramp to permit wheelchair access, flexible working hours, or provision of TTY machines.

Cross References

► 504 Plan, Americans with Disabilities Act

References and Readings

Education, 34 C.F.R. §104.
Individuals with Disabilities Education Improvement Act of 2004, 20 U.S. C. § 1400 et seq.
Rehabilitation Act, 29 U.S.C. § 794.

Accumbens Nucleus

► Nucleus Accumbens

Acetylaspartic Acid

► *N*-Acetyl Aspartate

A

Acetylcholine

JoAnn T. Tschanz[1], Katherine Treiber[2]
[1]Utah State University
Logan, UT, USA
[2]University of Massachusetts Medical School
Worcester, MA, USA

Definition

Acetylcholine has been identified as a neurotransmitter substance since the mid-1920s. It is the neurotransmitter substance present at the neuromuscular junction and also innervates structures of the parasympathetic and sympathetic nervous systems (Feldman, Meyer, & Quenzer, 1997; Iversen, Iversen, Bloom, & Roth, 2009). In the brain, cholinergic neurons have a wide distribution. Projections emanate from the basal forebrain in the medial septal nucleus and terminate in the hippocampus and limbic cortex. Among other areas receiving cholinergic input are the neocortex, olfactory bulbs, amygdala, neostriatum (caudate nucleus and putamen), the hypothalamus, and various regions in the brain stem (Feldman et al., 1997).

Acetylcholine is synthesized from the precursors Acetyl CoA and choline in a chemical reaction involving the catalytic enzyme, choline acetyltransferase (ChAT). The presence of this enzyme has been used as a marker to locate cholinergic neurons. Acetylcholine degradation (the primary mode of removal from synapses) is accomplished by the activity of a group of enzymes known as cholinesterases. Acetylcholinesterase is the primary enzyme that breaks down acetylcholine in the synapse. Thus, to enhance cholinergic function, a number of substances have been developed that inhibit the activity of this enzyme (Iversen et al., 2009).

Based on differences in the agonists that stimulate cholinergic receptors, two receptor subtypes have been identified, nicotinic and muscarinic. Nicotinic receptors are stimulated by nicotine, are excitatory, and show a rapid response to stimulation. Muscarinic receptors are stimulated by muscarine, have either excitatory or inhibitory effects, and show a slower response to stimulation. Further subtypes exist within the nicotinic and muscarinic classes (Feldman et al., 1997; Iversen et al., 2009).

Acetylcholine is involved in a number of behavioral processes. As a neurotransmitter substance at the neuromuscular junction, it acts on motor neurons of the spinal cord and cranial motor nerve nuclei, playing an important role in the contraction of skeletal muscles. Studies also suggest a role in cortical arousal, REM sleep, and cognitive functions such as attention, learning, and memory. Its presence in cardiac and smooth muscles, organs, and salivary, tear, and sweat glands affect autonomic functions (Feldman et al., 1997).

Current Knowledge

Applications

Dysfunction in the cholinergic system has been implicated in a number of clinical conditions including Alzheimer's disease (AD), diffuse Lewy body dementia (Londos, Brun, Gustafson, & Passant, 2003), Huntington's disease, and myasthenia gravis (Iversen et al., 2009). Recent work also suggests a reduction in cholinergic activity in Parkinson's disease that may appear relatively early in the course of the condition (Shimada et al., 2009). Acetylchoinesterase inhibitors are used in the palliative treatment of AD and myasthenia gravis. Cholinergic or anticholinergic compounds are also used as a muscle relaxant for surgery, treatment of parkinsonism, glaucoma, urinary retention, and in nonclinical applications such as insecticides in agriculture and neurotoxins (and their antidotes) in warfare (Feldman et al., 1997; Iversen et al., 2009). Much research is being conducted to develop agents with greater receptor subtype specificity to better address clinical conditions.

Cross References

▶ Alzheimer's Disease
▶ Anticholinesterase Inhibitors
▶ Cholinesterase Inhibitors

References and Readings

Feldman, R. S., Meyer, J. S., & Quenzer, L. F. (1997). Acetylcholine. In *Principles of neuropsychoparhmacology* (pp. 246–249). Sunderland, MA: Sinauer Associates.

Iversen, L. L., Iversen, S. D., Bloom, F. E., & Roth, R. H. (2009). Acetylcholine. In *Introduction to neuropsychopharmacology* (pp. 128–149). New York: Oxford University Press.

Londos, E., Brun, A., Gustafson, L., & Passant, U. (2003). Lewy body dementia. Clinical challenges in diagnosis and management. In K. Iqbal & B. Winblad (Eds.), *Alzheimer's disease and related*

disorders: Research advances (pp. 133–142). Bucharest, Romania: Ana Asian International Academy of Aging.
Shimada, H., Hirano, S., Shinotoh, H., Aotsuka, A., Sato, K., Tanaka, N., et al. (2009). Mapping of brain acetylcholinesterase alterations in Lewy body disease by PET. *Neurology, 73*, 273–278.

Acetylcholinergic System

► Cholinergic System

Acetylcholinesterase Inhibitors

► Anticholinesterase Inhibitors
► Cholinesterase Inhibitors

ACHE Inhibitors

► Anticholinesterase Inhibitors

AchEIs

► Anticholinesterase Inhibitors
► Cholinesterase Inhibitors

Achromatopsia

Sophie Lebrecht, Michael J. Tarr
Brown University
Providence, RI, USA

Synonyms

Acquired achromatopsial; Color agnosia; Color blindness; Cortical color blindness

Short Description or Definition

Following damage to the ventral medial region of the occipital lobe, known as the "color center" of the brain (Bartels & Zeki, 2000), patients lose the ability to perceive color, and therefore experience the world as varying shades of gray. This disorder is termed cerebral achromatopsia. The loss of color vision in these patients cannot be explained by the photoreceptors typically damaged or absent in patients with other types of color blindness.

Categorization

Cerebral achromatopsia results from bilateral damage to the V4/V4α region of the color center. If patients experience complete ablation of V4, they lose color vision in their entire visual field. However, if patients experience unilateral damage to V4, hemi-achromatopsia ensues, where patients only lose color vision in the contralateral half of their visual field. In less extreme cases, known as dyschromatopsia, patients lose the ability to perceive selective colors and/or color constancy. These neuropsychological disorders, which are the result of damage to the cerebral cortex, should not be confused with congenital achromatopsia, which occurs as a malfunction of the cone photoreceptors.

Epidemiology

Cerebral achromatopsia arises following brain damage to V4/V4α located in the ventral medial region of the occipital lobe, typically caused by a tumor, a hemorrhage, or some sort of brain trauma. Due to the low incidence rate of cerebral achromatopsia, it is difficult to provide a reliable estimate of its prevalence. However, it seems safe to say that it is extremely rare. A review of the documented cases showed that of the 27 cases reported, 3 patients recovered, 3 partially recovered, and 21 showed no recovery (Bartels & Zeki, 2000).

Natural History, Prognostic Factors, Outcomes

The first cases of cerebral achromatopsia were reported by Verrey (1888). In response to these patients, Verrey introduced the concept of a "color center" in the brain. Continued research confirmed the existence of a cortical region devoted to color processing. Almost a century later, Meadows demonstrated a correlation between the cortical regions sensitive to color, and the damaged cortical regions in achromatopsic patients (Meadows, 1974).

Neuropsychology and Psychology of Achromatopsia

The region of damage in the visual field of achromotopsic patients, V4/V4α, is organized retinotopically; therefore, damage to a particular region of V4 results in a loss of color vision at the corresponding location in the visual field. For example, if damage to V4 occurs in the *left* hemisphere, the patient will lose color vision in the *right* half of their visual field. Because V4 is located in the vicinity of the fusiform gyrus and the lingual gyrus, known to process faces (Kanwisher et al., 1997), the comorbity between achromatopsia and prospoagnosia is extremely high (Bouvier & Engel, 2006). In addition, patients with achromatopsia also have a higher incidence of spatial and shape deficits. It has been noted that patients with complete achromatopsia cannot even imagine color, which means they cannot dream in color or use color during mental imagery. This absence of color vision often leaves patients with no appetite for foods, which appear gray, and no desire for intimacy, as flesh appears gray. An insightful case study of a color-blind painter describes these experiences in detail (Sacks, 1995).

Evaluation

Cerebral achromatopsia can be diagnosed using a range of color vision tests. The simplest test is an explicit color-naming task that requires patients to name the color of individual flash cards. The most common test for color blindness is the Ishihara plates test. These plates contain isoluminant colored dots of varying sizes that together create the perception of a number embedded in noise. In order to perceive the number, patients must be able to distinguish between the different colored dots. Another widely-used test is the Farnsworth-Maunsell 100 Hue test, in which patients are required to order colored caps based on gradual shifts in hue from light to dark. Patients with color blindness are unable to perform this task. Rarely, a diagnosis is made using a Nagel Anomaloscope. This apparatus is typically used to determine whether a patient is a monochromat or a diachromat; however, some experimenters/practitioners use it in the study of cerebral achromatopsia.

Treatment

There is a period of spontaneous recovery for neurovisual lesions, which typically lasts 3 months post-lesion, but can occur for up to a year. With regard to the treatment and diagnosis of cerebral achromatopsia, experimenters report that some patients are not conscious of the absence of color vision. This phenomenon has been explained by the ablation of a color module leaving patients without even the concept of color post-lesion. This symptom of achromatopsia should be noted when addressing patients, because pushing a patient to describe a condition they are not aware of could be distressing for the patient.

Cross References

► Scotoma

References and Readings

Bartels, A., & Zeki, S. (2000). The architecture of the color centre in the human visual brain: New results and a review. *The European Journal of Neuroscience, 12*(1), 172–193.

Bouvier, S. E., & Engel, S. A. (2006). Behavioral deficits and cortical damage loci in cerebral achromatopsia. *Cerebral Cortex (New York, N.Y.: 1991), 16*(2), 183–191.

Kanwisher, N., McDermott, J., & Chun, M. M. (1997). The fusiform face area: A module in human extrastriate cortex specialized for face perception. *Journal of Neuroscience, 17*(11), 4302–4311.

Meadows, J. C. (1974). Disturbed perception of colors associated with localized cerebral lesions. *Brain: A Journal of Neurology, 97*(4), 615–632.

Sacks, O. W. (1995). *An anthropologist on mars: Seven paradoxical tales.* New York: Vintage Books.

Verrey, D. (1888). Hémiachromatopsie Droite Absolue. Conversation Partielle De La Perception Lumineuse Et Des Formes. Ancien Kyste Hémorrhagique De La Partie Inférieure Du Lobe Occipital Gauche. *Archives d'ophtalmologie, 8*, 289–300.

Werner, J. S., & Chalupa, L. M. (2004). *The visual neurosciences.* Cambridge, MA: MIT Press.

ACoA

► Anterior Communicating Artery

Acoustic Aphasia

► Pure Word Deafness

Acoustic Neuroma

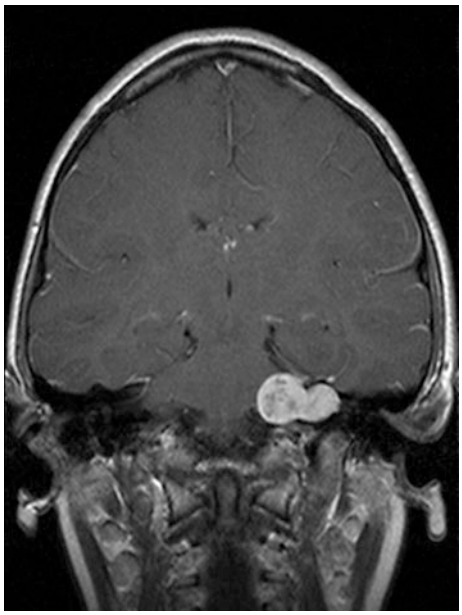
Ethan Moitra
Drexel University
Morgantown, WV, USA

Synonyms

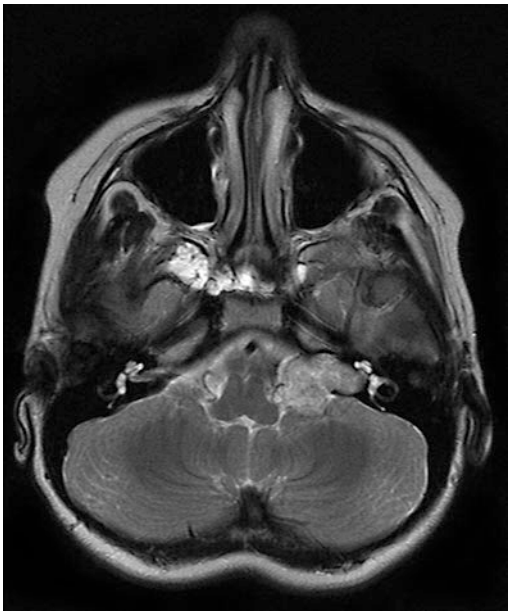
Neurolemmoma; Vestibular schwannoma

Definition

A benign tumor of the Schwann cells occurring near the cerebellopontine angle of the brain stem. Typically, it arises from the vestibulocochlear or eighth cranial nerve, which connects the brain to the inner ear. It is commonly associated with neurofibromatosis type 2 and often occurs bilaterally. Tumor growth is usually slow and may result in some hearing loss or deafness, tinnitus, vertigo, and vestibular dysfunction. Most acoustic neuromas are diagnosed in patients between the ages 30 and 60. Etiology is unknown. Treatment options include radiosurgery and microsurgical removal.



Acoustic Neuroma. Figure 1 Courtesy Carol Armstrong. Children's Hospital of Philadelphia and the University of Pennsylvania Medical School, Department of Neurology



Acoustic Neuroma. Figure 2 Courtesy Carol Armstrong. Children's Hospital of Philadelphia and the University of Pennsylvania Medical School, Department of Neurology

Cross References

- ▶ Radiosurgery
- ▶ Radiotherapy

References and Readings

Jørgensen, B. G., & Pedersen, C. B. (1994). Acoustic neuroma. Follow-up of 78 patients. *Clinical Otolaryngology, 19*, 478–484.

Acquired Achromatopsial

- ▶ Achromatopsia

Acquired Dyscalculia

- ▶ Acalculia

Acquired Epileptic Aphasia

► Landau–Kleffner Syndrome

Acquired Immunodeficiency Syndrome (AIDS)

C. Michael Nina
William Paterson University
Wayne, NJ, USA

Short Description or Definition

Acquired immunodeficiency syndrome or AIDS is a disease caused by infection with the human immunodeficiency virus or HIV. HIV is a viral pathogen that attacks CD4+ T cells (thymus originating lymphocyte cells with cluster determinant 4 + surface receptor sites) of the human body's immune system. These CD4+ T cells (also called T4 or T helper cells) play a central signaling role in the human immune response. In addition, HIV also causes damage to the central nervous system. The exact cause of this damage is unclear at this time, but it is believed to be caused either by the "Trojan horse" model or neuroinflammation model. In the Trojan horse model, immune system cells known as macrophages conceal and convey HIV into the brain, where they can disrupt supportive brain cells such as astrocytes and microglia. In the neuroinflammation model, the body's over stimulated immune system causes an increased production of CD14+ CD16+ monocytes which flood the brain, causing inflammation and damage to brain cells and structures.

AIDS is the name given to the end stage of HIV infection when the body's ability to fight off microorganisms is compromised, resulting in debilitating or fatal diseases, which are known as "opportunistic infections." An individual with HIV infection receives a formal diagnosis of AIDS when the individual has at least one opportunistic infection or when the individual's CD4+ T cell count is below 200 per mm^3 of blood (normal count is typically 500–1,500 per mm^3).

In the absence of anti-HIV or antiretroviral drug therapy, progression to AIDS can take an average of 8–12 years for adults and adolescents, and 3 years from birth in prenatally infected children. A quarter of a century after the first deaths from AIDS were identified, the AIDS pandemic has killed approximately 25 million people worldwide. UNAIDS, a joint program of the United Nations and the World Health Organization, estimates that globally, in 2007, 33.2 million people lived with HIV, 2.5 million became newly infected, and 2.1 million died from AIDS. In North America alone, 1.3 million lived with HIV, 46,000 became newly infected, and 21,000 died from AIDS; and approximately, 500,000 have already died from AIDS.

Categorization

Differentiation between a diagnosis of HIV or AIDS depends on CD4+ T cell count and presence of opportunistic infections.

Etiology/Epidemiology

In 1981, the US Centers for Disease Control and Prevention (CDC) began receiving reports about unusual cases of *Pneumocystis carinii* pneumonia (PCP) and Kaposi's sarcoma in young gay men and PCP in injection drug users. These diseases were not typically seen in individuals with healthy immune systems. In early 1982, similar disease patterns were seen in blood transfusion recipients, hemophiliacs, and heterosexual partners of those already infected. In late 1982, the CDC officially named this disease pattern as acquired immune deficiency syndrome or AIDS. In 1984, a previously unknown human retrovirus was discovered in the blood of individuals with AIDS by teams in the US and France. In 1986, the retrovirus was named as HIV.

Retroviruses have an RNA (ribonucleic acid) genome, and use an enzyme called reverse transcriptase to convert their RNA into DNA (deoxyribonucleic acid), in order to

Acquired Immunodeficiency Syndrome (AIDS). Table 1 Differentiation between human immunodeficiency virus (HIV) infection and acquired immunodeficiency syndrome (AIDS) in individuals infected with HIV

Symptom	Diagnosis
CD4+ T cell count of 200 or higher per mm^3/blood	HIV infection
CD4+ T cell count below 200 per mm^3/blood	AIDS
Presence of one or more opportunistic infection	AIDS

replicate, which is done in the nucleus of infected cells. HIV is a member of the lentivirus group of retroviruses which also includes simian immunodeficiency virus. Lentiviruses typically have longer incubation periods and greater genetic complexity than other retroviruses.

In 1985, a second strain of the virus was discovered, which was designated as HIV-2. The original strain of the virus was designated as HIV-1. HIV-1 is much more common throughout the world, while HIV-2 is more common in certain parts of Africa alone. Also, HIV-2 appears to be milder than HIV-1, with a slower progression to AIDS. Since its establishment in humans, HIV-1 has undergone mutation of its genome and there are now three groups of HIV-1.

How HIV is transmitted tends to vary worldwide depending upon the geographic region. In the United States, approximately 45% of current cases of HIV infection were obtained through male–male sexual contact (men who have sex with men or MSM), 22% were through injecting drug users (IDU), and 5% were through individuals who were both MSM and IDU. Approximately, 27% of cases were through male–female sexual contact. Transmission rates have been changing though, with new cases of infection in older white MSM decreasing. Transmission rates have been increasing in African–American and Latino MSM and younger white MSM due to increases in high-risk sexual practices; approximately, 50% of new cases are in African–American MSM. Rates of transmission are also increasing in women, primarily due to heterosexual contact with MSM and IDU. In Africa, transmission is primarily due to male–female sexual contact. In Eastern Europe, transmission is primarily in IDU or male–female sexual contact. In Southeast Asia, transmission is primarily through contact with commercial sex workers.

Natural History, Prognostic Factors, Outcomes

HIV is not transmitted through casual contact, such as touching. It can be transmitted when the bodily fluids of infected individuals – primarily blood, semen, vaginal fluid, or breast milk – comes into contact with the bloodstream or mucosal tissues of uninfected individuals. Transmission can occur through:

1. Unprotected sexual contact (anal, vaginal, or oral) with an individual infected with HIV
2. Sharing needles or syringes with HIV-infected individuals
3. Transfusion of infected blood or other bodily incorporation of infected blood
4. A fetus or infant exposed to HIV before or during birth or through breast feeding

The natural progression of HIV infection can be divided into three stages: primary infection, clinical latency, and symptomatic disease stage. The symptomatic disease stage is further divided into early and late stages, with AIDS being equated with the late-symptomatic disease stage. After a person is initially infected with HIV, a primary or acute infection stage commences, in which HIV replicates up to ten billion copies of itself daily; high levels of HIV in the blood or viraemia is evident. Approximately, 2–4 weeks after exposure, nearly 70% of those newly infected will experience an acute illness, which has symptoms similar to influenza or mononucleosis, including fever, fatigue, muscle weakness, headache, ocular pain, sensitivity to light, sore throat, diarrhea, and lymphadenopathy. This illness is due to the temporary reduction of CD4+ T cells; it lasts for approximately 2 weeks and then resolves spontaneously. It is during this stage that the individual typically first begins to produce antibodies to HIV, which is designated as seroconversion.

Serological testing of blood can reliably detect HIV antibodies 2–6 months after seroconversion. Testing typically begins with an enzyme-linked immunosorbent assay (ELISA) or test that looks for antibodies to HIV. A second positive ELISA is needed in order to confirm the result. This would then be followed by the Western Blot Procedure to confirm the presence of at least two specific HIV antigen groups. A diagnosis of HIV infection is given after a positive Western Blot test follows two positive ELISA tests. If HIV is confirmed, additional tests for plasma viral RNA (viral load) and CD4+ T cell counts are then typically completed, in order to assess the state of the immune system and disease prognosis. Higher viral load counts are typically related to faster disease progression. Lower CD4+ T cell counts are typically related to greater clinical vulnerabilities.

After the acute illness disappears, the individual enters the clinical latency stage in which symptoms are typically absent, other than possibly chronic lymphadenopathy. This stage lasts an average of 10 years. During the clinical latency stage, HIV continues to replicate and attack CD4+ T cells, which in turn continues to counter attack.

As the immune system becomes more compromised, individuals eventually enter the early symptomatic disease stage, when a variety of symptoms begin to manifest, including lymphadenopathy, lack of energy, diarrhea,

unintentional weight loss, chronic low-grade fever and sweats, frequent rashes or fungal infections, headaches, or short-term memory loss.

Finally, individuals enter the late stage of the symptomatic disease stage or AIDS when the person has at least one opportunistic infection or when the individual's CD4+ T cell count is below 200 per mm^3 of blood. The most common opportunistic infections are PCP, Kaposi's sarcoma, HIV wasting syndrome, and HIV encephalopathy (also known as dementia due to HIV disease or AIDS dementia complex).

Psychological and Neuropsychological Correlates of HIV Infection

As HIV infection progresses, various psychological and neuropsychological complications involving both the central as well as peripheral nervous systems can become evident. During primary infection, reports of headaches and aseptic meningitis are common. During the clinical latency stage, an acute inflammatory demyelinating neuropathy (similar to Guillain-Barre syndrome; characterized by progressive muscle weakness) can occasionally develop. During the early symptomatic disease stage, peripheral neuropathy is common. This is characterized by spontaneous pain (dysesthesia), pain due to light touches or changes in temperature (hyperesthesia), and weakness and wasting in arms/legs (distal atrophy).

It is during the late symptomatic disease stage or AIDS that most major neuropsychological complications develop, and can include:

1. HIV encephalopathy (HIV dementia)
2. Opportunistic infections
   (a) Viral (Cytomegalovirus; Herpes Simplex I and II; Herpes Zoster; JC virus, a polyomavirus or papovavirus which causes PML [progressive multifocal leukoencephalopathy])
   (b) Fungal/Protozoan (Toxoplasmosis, Cryptococcus, Candida, Mycobacterium)
3. Lymphomas
   (a) Primary central nervous system lymphomas
   (b) Systemic (metastatic) lymphomas. (The most common systemic lymphomas are: Hodgkin's; immunoblastic; Burkitt's; and non-Hodgkin's, which is particularly prevalent.)

HIV encephalopathy is the term used to describe the pathological features of encephalitis of the brain due to HIV, while HIV dementia (also known as AIDS dementia complex) is used to describe the clinical syndrome. This syndrome is characterized by behavioral, cognitive, and motor declines and difficulties (Table 2). Initial symptoms typically manifest as cognitive difficulties (loss of concentration and mild deficits in memory) with motor and behavioral difficulties frequently occurring. (This early stage is often labeled as HIV-associated minor cognitive motor disorder.) Later symptoms include partial paralysis, incontinence, and severe cognitive impairment. Death usually occurs within 1–6 months after onset of severe symptoms. Individuals who are coinfected with hepatitis C or were IDU, typically display worse symptoms faster. As HIV-infected individuals live longer, it is estimated that 50–75% of all patients with AIDS will evidence some form of HIV dementia.

Acquired Immunodeficiency Syndrome (AIDS). Table 2 HIV dementia symptoms

Behavioral difficulties
Depression
Apathy, anhedonia, social withdrawal
Personality changes, including spontaneous sudden and strong emotions
Cognitive difficulties
Confusion
Short-term memory lapses
Loss of concentration
Motor difficulties
Lack of muscular coordination
Tremors
Muscle weakness
Loss of balance

While HIV can be present in any part of the brain, HIV is particularly common in the basal ganglia and central white matter (and to a lesser extent in neocortical gray matter, the brainstem, and the cerebellum) in individuals not receiving antiretroviral therapy or highly active antiretroviral therapy (HAART) (see below). In individuals on HAART, there is evidence of greater inflammation in the hippocampus and surrounding entorhinal and temporal cortex.

Treatment

While there is no cure or vaccine for HIV or AIDS at this time, there are currently four different classes of

antiretroviral drugs that interfere with the ability of HIV to replicate: reverse transcriptase inhibitors (nucleoside and non-nucleoside types); protease inhibitors; entry/fusion inhibitors; and integrase inhibitors. In 1987, the US Food and Drug Administration (FDA) approved Azidothymidine (AZT, also known as Zidovudine), the first nucleoside-reverse transcriptase inhibitor (NRTIs). Saquinavir, the first protease inhibitor was approved in 1995. Nevirapine, the first non-nucleoside-reverse transcriptase inhibitor was approved in 1996. Enfuvirtide, the first fusion inhibitor was approved in 2003. Maraviroc, the first entry inhibitor, and Reltegravir, the first integrase inhibitor, were approved in 2007.

In 1996, combination drug therapy or HAART began. Three or more drugs are used in combination in order to counter the development of drug resistance by HIV. Strict adherence to medication intake schedules is required. Not only is this schedule difficult to follow for many individuals, HAART often produces unpleasant and toxic side effects, including stomach problems and lipodystrophy. If followed correctly, HAART typically and drastically reduces viral load, often to undetectable levels in the blood, which allows the immune system to rebound. Antiretroviral drug therapy and treatments for opportunistic infections have greatly increased life expectancy of those with HIV infection, but due to the presence of HIV in cells that remain out of reach of antiretroviral drugs, eradication of HIV from the human body is unattainable at this time.

Cross References

► Dementia
► Encephalitis
► Meningitis

References and Readings

Bartlett, J., & Finkbeiner, A. (2006). *The guide to living with HIV infection, developed at the John Hopkins AIDS clinic* (6th ed.). Baltimore: Johns Hopkins University Press.

Portegies, P., & Berger, J. (Eds.). (2007). *HIV/AIDS and the nervous system: Handbook of clinical neurology.* Amsterdam: Elsevier.

Pratt, R. (2003). *HIV & AIDS: A foundation for nursing and healthcare practice.* London: Arnold Publishers.

Sande, M., & Volberding, P. (Eds.). (1999). *The medical management of AIDS* (6th ed.). Philadelphia: Saunders.

Stine, G. (2005). *AIDS update 2005.* San Francisco: Pearson/Benjamin Cummings.

UNAIDS. (2007). *UNAIDS Annual Report 2007: Knowing your epidemic.* Retrieved June 15, 2008 from http://data.unaids.org/pub/Report/2008/jc1535_annual_report07_en.pdf

Weeks, B. S., & Alcamo, I. E. (2006). *AIDS: The biological basis* (4th ed.). Sudbury, MA: Jones and Bartlett Publishers.

Acquisition of Knowledge

► Learning

Action Tremor

Anna DePold Hohler[1], Marcus Ponce de Leon[2]
[1]Boston University Medical Center
Boston, MA, USA
[2]William Beaumont Army Medical Center
El Paso, TX, USA

Synonyms

Intention Tremors

Definition

Action tremor is a rhythmic, oscillatory, and involuntary movement of the limb that is seen with movement of an extremity. It may be seen in isolation with a cerebellar lesion or associated with other tremor types such as the postural tremor of essential tremor or the rest tremor of Parkinson's disease.

Cross References

► Essential Tremor
► Parkinson's Disease

References and Readings

Fahn, S., & Jankovic, J. (Eds.). (2007). Tremors: Diagnosis and treatment. In *Movement disorders* (pp. 451–479). Philadelphia: Churchill Livingstone Elsevier.

Action-Intentional Disorders

Kenneth M. Heilman
The Malcom Randall Veterans Affairs Hospital
Randall Veteran's Affairs Medical Center
Gainesville, FL, USA

Synonyms

Abulia; Akinesis; Hypokinesis; Motor impersistence (These terms are not fully synonymous with action-intentional disorders, but comprise important elements of the syndrome and are often used when describing specific these elements.)

Definition

In the absence of weakness, patients can have a disability with initiating (akinesia, hypokinesia, abulia) or sustaining actions (impersistence), inhibiting irrelevant actions (defective response inhibition), and stopping an action when the task has been completed (motor perseveration).

Current Concepts

The motor system allows humans to interact with their environment and alter themselves as well as others. The human corticospinal motor system together with the motor units and muscles can mediate an almost infinite number of movements and thus the human motor system needs to be guided by at least two major types of programs: *praxic* and *intentional*. The praxic programs provide the corticospinal system with the knowledge of *how* to make skilled movements (spatial and temporal aspects of movements) and the intentional programs provide the corticospinal system with information about *when* to move. In this section, we will discuss disorders of the intentional, or "when," systems. When interacting with environmental stimuli or the self, there are four "when" questions that must be addressed: these are (1) when to move, (2) when to persist at a movement or movements, (3) when to end a movement or a series of movements, and (4) when not to move. The inability to initiate a movement in the absence of a corticospinal or motor unit injury is called *akinesia*. Some patients are able to move after a delay and we call this *hypokinesia*. *Motor impersistence* is when a patient cannot sustain a movement or a series of movements that are needed to complete a task. The inability to stop a movement or an action program when it is no longer required is called *motor perseveration* and the inability to withhold a response to a sensory stimulus is called *defective response inhibition*.

These motor intentional disorders are parallel to disorders of sensory attention, akinesia being akin to unawareness, impersistence being the motor parallel of decreased vigilance, motor perseveration being parallel to failures of extinction or habituation, and defective response inhibition being similar to distractibility. There are also cognitive defects that mirror four types of intentional motor disorders mention above, but these will not be discussed here.

In the next section, we briefly describe each of these intentional disorders, including subtypes of each category and in the final section we briefly discuss the possible pathophysiology.

Clinical Manifestations

Akinesia

An organism might fail to initiate a movement for many reasons, but comprehension, attentional, perceptual, sensory, and motor disorders that lead to a failure of movement initiation should not be termed *akinesia*. In contrast to these disorders, akinesia is caused by a failure of the systems that are responsible for activating the motor system.

There are three methods by which akinesia can be distinguished from extreme weakness. Certain forms of akinesia are present under certain sets of circumstances and absent in others. Thus, using the behavioral method, if it can be demonstrated that a patient makes movements in one set of circumstances (e.g., a motionless left hand is brought over to the right side of the body and the patient is able to now move this hand) and not in the other, this failure to move is related to an akinesia. If the akinesia is not limited to a set of circumstances then the clinician may have to depend on brain imaging, or physiological techniques such as magnetic stimulation of the motor cortex to demonstrate that the brain lesion did not involve the motor system and thus the failure to move is not caused by weakness.

There are at least three subtypes of akinesia: (1) *Body part*: Akinesia may involve the eyes, the neck and head, a limb, or the total body; (2) *Action space:* Akinesia of the limbs, eyes, or head may depend on where in space the body part is moved or in what direction it is moved.

The former is called *spatial akinesia* (e.g., a hand that does not move in left hemispace, but does move in right body-centered hemispace) and the latter is called *directional akinesia* (e.g., a horizontal gaze palsy where patients cannot move their eyes to the left); (3) *Stimulus–response conditions*: Some patients, such as those with Parkinson's disease, are impaired in spontaneously initiating a movement, but in response to a stimulus often have no trouble initiating a movement. We call this *endogenously evoked akinesia (endo-evoked)*. Patients who fail to move to an imperative stimulus but will move spontaneously we call *exogenously evoked akinesia.* A patient may have both exo-evoked and endo-evoked akinesia, which we term *mixed or global akinesia.*

Hypokinesia

A milder defect in the intentional motor ("when") systems might not induce a total inability to initiate a response (i.e., akinesia), but rather these patients' intentional deficit might be manifested by a delay in initiating a response. We call this delay *hypokinesia.* The hypokinesias may also be subtyped into body part (e.g., limb or eyes) and action space (e.g., directional and hemispatial).

Motor Extinction

Patients with *sensory extinction* are able to detect single stimuli on either side of their body, but when presented with two stimuli one on each side of their body they remain unaware of contralesional stimuli. *Motor extinction* is a form of akinesia or hypokinesia where a patient who is without sensory extinction is asked to respond by moving the hand (or hands) that was (were) touched. The examiner then delivers stimuli to the right, left, and both hands and patients with motor extinction are aware that both hands have been touched, but either fail to lift the contralesional hand to simultaneous stimuli or lift it after a delay.

Motor Impersistence

The inability to sustain a motor act or a series of motor acts that are required to complete a goal is called *motor impersistence.* Like akinesia, impersistence can be associated with various *body parts* including the limbs, eyes, neck, eyelids (e.g., keep your eyes closed for until I tell you to open them), jaw, and tongue. Patients can even demonstrate impersistence in activities such as walking. Like akinesia, it may also be *directional* (e.g., inability to maintain leftward gaze) or hemispatial (inability to maintain dorsiflexion of the wrist in left space with the left arm, but able to do so in right space).

Defective Response Inhibition

Not all stimuli require a response and sometimes a response might interfere with goal-oriented behavior. *Defective response inhibition* is defined as responding when no response of that body part is required. It can be seen in a variety of body parts and might also be directional and perhaps hemispatial.

There are several forms of defective response inhibition. One means of testing for this disorder is to use the *crossed response task.* A blindfolded patient is instructed to raise the hand opposite to that touched. Patients with defective response inhibition will often raise the touched hand first. This type of defective response inhibition may be termed *motor* (*limb* or *eye directional*) *response disinhibition.* These can be either contralesional or bilateral. The eye directional defective response inhibition has also been called a *visual grasp.* There are some patients, however, who have a perceptual disorder and when stimulated on one side (e.g., left hand) feel that they were stimulated on the other (e.g., right hand). This phenomenon is called *allesthesia* and it should not be confused with defective crossed response inhibition.

Patients with defective response inhibition may also fail on the types of go–no-go tasks described by Luria. For example, the patient may be instructed to put up two fingers when the examiner puts up one finger and to put up no fingers if the examiner puts up two fingers. If the patient mimics the examiner such that when the examiner puts up one finger, the patient puts up one finger and when the examiner puts up two fingers, the patient puts up two fingers, the patient has *echopraxia.*

Motor Perseveration

When a patient incorrectly repeats a prior response or when a patient continues to perform the same act when the goal of the act has been completed, it is called

motor perseveration. In one type of motor perseveration, when the task requirements have changed the patient is unable to switch to a different motor program and incorrectly repeats the movements. Luria (1965) calls this *inertia of program action* and Sandson and Albert (1987) call this *recurrent perseveration.* In the second type, the patient continues to perform movements even though the task is completed. Luria (1965) called this *efferent perseveration*; however, Sandson and Albert (1987) call this *continuous perseveration.*

Pathophysiology of Intentional Disorders

Intentional motor disorders are often associated with bilateral hemispheric lesions, but when these disorders are caused by a unilateral hemispheric lesion they are more commonly associated with right than left-hemisphere lesions. The intentional disorders that have been reported to be induced by primarily right-hemisphere lesions include akinesia (e.g., left-sided limbs, leftward arm movements, and even left horizontal gaze), hypokinesia (slowed reaction times), motor impersistence of the left-sided limbs, left-sided gaze), and motor (continuous) perseveration. Many of the intentional defects associated with right-hemisphere dysfunction, however, are not just limited to the left limbs. For example, patients with a right-hemisphere lesion are more often abulic, have slowed reaction times of their right hand, and have motor impersistence of eye closure. These clinical studies suggest that the right hemisphere may be dominant for intentional control of the motor systems. Studies with normal subjects provide further evidence for right-hemisphere intentional dominance. The anatomic and physiological basis for this dominance is not entirely understood.

Studies of patients with focal lesions and studies of monkeys suggest that the frontal lobes may play a critical role in mediating intentional activity. The most important areas of the frontal lobes appear to be the medial and lateral frontal lobes. The frontal cortex has strong projections to the striatum. The lateral portion of the frontal lobe projects to the caudate. The premotor cortex projects to the putamen and the cingulate gyrus projects to the ventral striatum. The striatum projects to the pars reticularis of the substantia nigra and the globus pallidus. The globus pallidus projects to specific thalamic nuclei and these thalamic nuclei project back to the frontal cortex. Just as injury of the frontal lobes can induce intentional deficits, injuries, or diseases that injure the basal ganglia, the substantia nigra (e.g., Parkinson's disease), portions of the thalamus, as well as the white matter connections can also induce intentional deficits.

Future Directions

Disorders of intention have received considerably less neuroscientific study than have disorders of sensory selective attention. There is a need for additional experimental and clinical neuropsychological studies of these disorders. Furthermore, assessment batteries are needed that will facilitate the assessment of the subtypes of motor intention disturbances and which may provide additional quantitative data for experimental analysis and normative comparison between patient groups and health individuals.

Cross References

- ▶ Attention
- ▶ Directional Hypokinesis
- ▶ Impersistence
- ▶ Neglect Syndrome

References and Readings

Heilman, K. M., Valenstein, E, Rothi, L. J. G., & Watson, R. T. (2004). Intentional motor disorders and apraxia. In W. G. Bradley, R. B. Daroff, G. M. Fenichel, & J. Jankovic (Eds.), *Neurology in clinical practice: Principles of diagnosis and management.* (pp. 117–130). Phila Penn: Butterworth Heineman.

Heilman, K. M., Watson, R. T., & Valenstein, E. (2003). Neglect and related disorders. In K. M. Heilman, & E. Valenstein (Eds.), *Clinical neuropsychology, (*4th ed., pp. 296–346). New York: Oxford University Press.

Heilman, K. M. (2004). Intentional neglect. *Frontiers in Bioscience, 9*, 694–705.

Luria, A. R. (1965). Two kinds of motor perseveration in massive injury to the frontal lobes. *Brain, 88*, 1–10.

Sandson, J., & Albert, M. L. (1987). Varieties of perseveration. *Neuropsychologia, 22*, 715–732.

Activa®

- ▶ Deep Brain Stimulator (Parkinsons)

Active Limb Activation

Sarah A. Raskin
Trinity College
Hartford, CT, USA

Synonyms

Limb activation

Definition

Active limb activation is a rehabilitation technique for individuals with unilateral neglect. In a series of studies, Robertson and North (1992, 1993, 1994) and others (Mattingly, Robertson, & Driver, 1998) have demonstrated that moving the upper or lower extremity on the affected side can reduce neglect symptoms. The effect is seen only with active movement, as opposed to passive movement, and only when the limb is moved in the effected hemispace. However, the limb need not be observed visually. It should be noted that the effect has not been demonstrated universally (e.g., Brown, Walker, Gray, & Findlay, 1999).

Cross References

- ► Attention Training
- ► Behavioral Inattention Test
- ► Cognitive Rehabilitation
- ► Neglect Syndrome

References and Readings

Brown, V., Walker, R., Gray, C., & Findlay, J. (1999). Limb activation and the rehabilitation of unilateral neglect: Evidence of task-specific effects. *Neurocase, 5*, 129–142.

Mattingly, J., Robertson, I., & Driver, J. (1998). Modulation of covert visual attention by hand movement: Evidence from parietal extinction after right hemisphere damage. *Neurocase, 4*, 245–253.

Robertson, I., & North, N. (1992). Spatio-motor cueing in unilateral left neglect: The role of hemispace, hand and motor activation. *Neuropsychologia, 30*, 553–563.

Robertson, I., & North, N. (1993). Active and passive activation of left limbs: Influence on visual and sensory neglect. *Neuropsychologia, 31*, 293–300.

Roberson, I., & North, N. (1994). One hand is better than two: Motor extinction of left hand advantage in unilateral neglect. *Neuropsychologia, 32*, 1–11.

Active Memory

► Short-Term Memory

Activities of Daily Living (ADL)

Angela K. Troyer
Baycrest Centre for Geriatric Care
Toronto, Ontario, Canada

Synonyms

Adaptive functions; Functional abilities

Definition

Activities of daily living (ADLs) are self-care activities that are important for health maintenance and independent living. ADLs comprise a broad spectrum of activities, traditionally classified as basic and instrumental ADLs (BADLs and IADLs, respectively). BADLs, also called physical or self-maintenance ADLs, are life-sustaining self-care activities such as feeding, grooming, bathing, dressing, toileting, and ambulation. IADLs are more complex activities that are necessary for independent living, such as using the telephone, preparing meals, shopping, managing finances, taking medications, arranging appointments, and driving. These activities are important for participating in one's usual work, social, or leisure roles.

Historical Background

The evolution of the concept of ADLs is reflected in the development of instruments to measure these abilities (McDowell & Newell, 1996). Measures of BADLs were first developed in the 1940s and 1950s, primarily out of the needs to assess fitness for military duty in World War II and to determine the required levels of care for institutionalized older adults and those with chronic illnesses. These early measures include the PULSES profile, the Barthel Index, and the Katz Index of ADL, among others. Later, in the 1960s and 1970s, there was increased interest in caring for older and disabled individuals in the community, and this spawned the need for tools to

measure IADLs that are important for independent living. Some of the first of these measures were Lawton and Brody's IADL Scale and the Disability Interview Schedule.

Current Knowledge

ADLs are of interest across various health disciplines. Current knowledge in this area is based on research conducted by psychologists, occupational therapists, nurses, psychiatrists, neurologists, and social workers, among others.

Relevance to Neuropsychology

For the neuropsychologist, an understanding of the patient's level of independence in ADLs, and in particular IADLs, is of interest for several reasons. The diagnosis of a number of cognitive and mental disorders requires an appraisal of the patient's functional ability (American Psychiatric Association, 2000). For example, impairment in adaptive or functional ability is a diagnostic criterion for mental retardation and for schizophrenia. Impaired daily functioning is also required for the diagnosis of dementia and is one of the defining differences between dementia (in which IADLs are impaired) and mild cognitive impairment (in which IADLs are intact or minimally affected).

Increasingly, the evaluation of daily functioning is also used to identify appropriate treatments for cognitive and mental disorders. In particular, an important part of determining the effectiveness of behavioral or pharmacological interventions is measuring the impact of the intervention on the patient's daily functional ability, in addition to cognitive or affective outcomes.

Assessment of ADLs

Assessment of ADLs can be accomplished in a number of ways. *Real-world observation* of the patient in his or her own home provides relevant, objective information about daily function. However, this method is obviously time and labor intensive, and there are practical limits to the number of behaviors that can be observed within a given time period. An alternative is the use of *performance-based measures,* which require the patient to complete functional tasks – such as preparing a meal, using the telephone, or making personal financial transactions – that are presented in a standardized way in the laboratory or clinic. A number of such instruments have been developed to measure single or multiple functional domains. Tests include the Direct Assessment of Functional Status, the Independent Living Scales, the Structured Assessment of Independent Living Skills, the Medication Management Abilities Assessment, and many others.

The use of questionnaires administered either on paper or by interview allows the sampling of a large number of behaviors in a short period of time. *Self-report questionnaires* may be appropriate for use with cognitively-normal or mildly impaired populations. In the evaluation of dementia and other cognitive disorders, however, self-reported abilities may be difficult to interpret because of disease-related decreases in self-awareness. The use of *informant-based questionnaires* avoids this limitation, although informants can also be biased in their reports and may not always be available. Nevertheless, this is one of the most common methods for measuring IADLs, and a large number of informant-based questionnaires exist, such as the Lawton-Brody IADL Scale, the Bristol ADL Scale, and the ADL questionnaire.

The choice of which particular method of assessment to be used will depend, in addition to practical considerations such as time, on the purpose of the assessment. Real-word observations and performance-based measures provide information about what the person is *capable of doing*. Questionnaires, on the other hand, measure what the individual is *actually doing* in his or her day-to-day life.

Future Directions

Although there are a large number of relevant instruments that have been developed to assess ADLs, they vary in terms of how well their psychometric properties have been characterized. Systematic literature reviews (e.g., Moore, Palmer, Patterson, & Jeste, 2007; Sikkes, de Lange-de Klerk, Pijnenburg, Scheltens, & Uitdehaag, 2009) indicate that, for many of these measures, there is a need for better theoretical justification of the content of the instrument, additional information about test validity and reliability, indication of what constitutes a meaningful change over time, information about the relation between test performance and actual real-world functioning, and the development of comprehensive normative data.

Cross References

- ▶ Adaptive Behavior
- ▶ Basic Activities of Daily Living (B-ADL)
- ▶ Functional Status

► Instrumental Activities of Daily Living (I-ADL)
► Lawton-Brody iADL Scale

References and Readings

American Psychiatric Association. (2000). *Diagnostic and statistical manual of mental disorders* (4th ed., text revision). Washington, DC: Author.

Law, M., Baum, C., & Dunn, W. (Eds.). (2001). *Measuring occupational performance: Supporting best practice in occupational therapy.* Thorofare, NJ: Slack.

Lawton, M. P., & Brody, E. M. (1969). Assessment of older people: Self-maintaining and instrumental activities of daily living. *Gerontologist, 9*, 179–186.

McDowell, I., & Newell, C. (1996). *Measuring health: A guide to rating scales and questionnaires* (2nd ed.). New York: Oxford.

Moore, D. J., Palmer, B. W., Patterson, T. L., & Jeste, D. V. (2007). A review of performance-based measures of functional living skills. *Journal of Psychiatric Research, 41*, 97–118.

Sikkes, S. A. M., de Lange-de Klerk, E. S. M., Pijnenburg, Y. A. L., Scheltens, P., & Uitdehaag, B. M. J. (2009). A systematic review of Instrumental Activities of Daily Living scales in dementia: room for improvement. *Journal of Neurology, Neurosurgery, and Psychiatry, 80*, 7–12.

Strauss, E., Sherman, E. M. S., & Spreen, O. (2006). *A compendium of neuropsychological tests* (3rd ed.). New York: Oxford.

Activities of Daily Living Questionnaire

Jessica Fish
Medical Research Council Cognition & Brain Sciences Unit
Cambridge, UK

Synonyms

ADLQ

Description

The activities of daily living questionnaire (ADLQ) was developed to measure the functional abilities of people with dementia. It is an informant-rated questionnaire and should be completed by the patient's primary caregiver. It consists of 28 items covering both basic and instrumental activities of daily living, organized into six subscales: self-care activities; household care; employment and recreation; shopping and money; travel; and communication. The informant rates the subject's competence in each area according to a set of four descriptions of different competence levels; scores range from 0 to 3 where higher scores indicate greater impairment. A fifth response option, "don't know/has never done" is also available, and if this option is selected, the item is excluded from scoring. Scores from individual items are summed (with adjustment for any items marked "don't know/has never done") to form subscale scores and then transformed to a percentage impairment total score. Scores of 0–33% are classified as no/mild impairment, those of 34–66% as moderate impairment, and those of 67–100% as severe impairment.

Historical Background

The first reported use of the ADLQ was in a longitudinal study looking at cognitive test performance and daily functioning in patients with Alzheimer's disease (Locascio, Growdon, & Corkin, 1995). However, the development and psychometric properties of the measure were first reported in Johnson, Barion, Rademaker, Rehkemper, and Weintraub (2004). Since then, a Chinese version has been developed and evaluated (ADLQ-CV; Chu & Chung, 2008), and it has been used in several studies involving people with non-Alzheimer's dementia.

Psychometric Data

Johnson et al. (2004) collected ADLQ data from the primary caregivers of 140 people with dementia of various types (Alzheimer's disease, vascular/mixed, and fronto-temporal/primary progressive aphasia). The scale was completed twice, with a 1 year interval between completions. Evidence of convergent validity was in the form of correlations with global severity ratings (clinical dementia rating $r = 0.5$ and 0.55 for first/second ratings, respectively; MMSE $r = -0.42$ and -0.38 for first and second ratings, respectively). Further evidence of its validity came from the finding that scores declined significantly over the year-long interval between testings, as would be expected in people with degenerative conditions. A subgroup of 28 participants took part in a test–retest reliability study, with a 2–8 week interval between testings (mean 25.6 days, SD 12.2). Correlations between first and second ratings for the six subscales were high, between 0.86 and 0.92, with the exception of the employment subscale, which correlated at 0.65. Kappa scores for 25% of scale

items were 0.42–0.60 (classified as "moderate"), for 54% of scale items were 0.61–0.80 (classified as "good"), and for 21% of scale items 0.81–1.0 (classified as "very good"). The validity of the ADLQ was investigated via correlations between 29 participants' scores on the ADLQ and the record of independent living (RIL), another ADL measure. In line with Johnson et al.'s predictions, there were significant correlations between the ADLQ and the "activities" and "communication" subscales of the RIL, but not the "behavior" subscale of the RIL.

Chu and Chung (2008) conducted a study examining the psychometric properties of a Chinese translation of the ADLQ (ADLQ-CV), with 125 caregivers of people with moderate Alzheimer's disease. The ADLQ-CV was shown to have good internal consistency ($\alpha = 0.81$), test–retest reliability at a 2-week interval (intra-class correlation (ICC) = 0.998), and inter-rater reliability (ICC = 0.997, for primary and secondary caregiver ratings). Correlations with the disability assessment for dementia were strong ($r = 0.92$), suggesting that it is a valid measure. A factor analysis also confirmed that the ADLQ-CV has a six-factor structure, following the six proposed subscales.

Clinical Uses

The ADLQ may be used to assist in the diagnosis of dementia, in decision making regarding necessary intervention and/or assistance, and in monitoring change over time or in response to treatment.

Cross References

- ► Alzheimer's Disease Cooperative Study ADL Scale
- ► Bristol Activities of Daily Living Scale
- ► Disability Assessment for Dementia
- ► Lawton-Brody ADL Scale

References and Readings

Chu, T. K. C., & Chung, J. C. C. (2008). Psychometric evaluation of the Chinese version of the activities of daily living questionnaire (ADLQ-CV). *International Psychogeriatrics, 20*, 1251–1261.

Johnson, N., Barion, A., Rademaker, A., Rehkemper, G., & Weintraub, S. (2004). The activities of daily living questionnaire: A validation study in patients with dementia. *Alzheimer's Disease and Associated Disorders, 18*, 223–230.

Locascio, J. J., Growdon, J. H., & Corkin, S. (1995). Cognitive test performance in detecting, staging, and tracking Alzheimer's disease. *Archives of Neurology, 52*(11), 1087–1099.

Activity Restrictions, Limitations

Brian Yochim
University of Colorado at Colorado Springs
Colorado Springs, CO, USA

Definition

This idea refers to restrictions prescribed by clinicians who treat patients with recent strokes, head injuries, or other neurological conditions, after a neurological event has left the patient with deficits in important areas of functioning. Patients are often restricted from driving, cooking, managing finances, or completing other instrumental activities of daily living after a neurological event. The activities of focus must be tailored to the patient and can range from restrictions in playing professional sports to restrictions in managing small amounts of cash.

Current Knowledge

Rehabilitation professionals encounter patients whose injuries have left them with deficits both in physical and cognitive realms. Strokes and traumatic brain injuries can cause physical impairments in walking, swallowing, use of an arm and/or leg, communication, and other important skills. Injuries can also lead to cognitive deficits in memory, executive functioning, social functioning, language, visuospatial skills, attention, and/or processing speed. These basic deficits in turn lead to impaired functioning in everyday life. Rehabilitation professionals must assess patients' abilities to complete these daily activities and often must place restrictions on what activities patients can continue to complete. If patients are deemed to be unable to drive, for example, clinicians must follow appropriate legal and ethical channels to protect the patient and public.

These limitations in activities can lead to difficulties in adjustment for the patient, which can sometimes result in depressed mood and other affective symptoms. This notion is related to the Activity Restriction Model of Depressed Affect (Williamson & Shaffer, 2000), which has been studied as one etiology of depressive symptoms among older adults.

Cross References

- ► Instrumental Activities of Daily Living (IADLs)
- ► Recommendation

References and Readings

Greenwood, R. J., Barnes, M. P., McMillan, T. M., & Ward, C. D. (Eds.). (2003). *Handbook of neurological rehabilitation* (2nd ed.). New York: Psychology Press.

Mills, V. M., Cassidy, J. W., & Katz, D. I. (Eds.). (1997). *Neurologic rehabilitation: A guide to diagnosis, prognosis, and treatment planning.* Malden, MA: Blackwell Science.

Williamson, G. M. & Shaffer, D. R. (2000). The activity restriction model of depressed affect: Antecedents and consequences of restricted normal activities. In G. M. Williamson, D. R. Shaffer, & P. A. Parmelee (Eds.), *Physical illness and depression in older adults: A handbook of theory, research, and practice.* New York: Kluwer Academic/Plenum Publishers.

Activity Therapy

► Recreational Therapy

Actus Reus

Moira C. Dux
University of Maryland Medical Center/Baltimore VA
Baltimore, MD, USA

Definition

Actus reus is Latin for "guilty act." Under most circumstances, a crime consists of at least two factors. The first factor is the physical conduct or act associated with the crime, which is known as the "actus reus." In order for an individual to be convicted of a crime, it must be demonstrated beyond a reasonable doubt, that the defendant committed the physical act of the crime, or the "actus reus." However, it must concurrently be established that the defendant also possessed "mens reas," which translates to "guilty mind" referring to the mental element of the crime. Thus, a conviction necessitates, beyond reasonable doubt, establishment of an illegal act coupled with a particular mental state (e.g., intent, knowledge, recklessness, or negligence). Description of the actus reus is typically classified into one of three categories: commissions, omissions, and/or commonwealth. Commission refers to an affirmative act; omission refers to a failure to act; and commonwealth refers to a state of affairs, or circumstances. Commissions and omissions necessitate causation; commonwealth does not always require voluntariness and instead the actus reus is viewed in light of the severity of the offense.

Cross References

► Insanity
► Insanity Defense
► Mens Rea

References and Readings

Melton, G. B., Petrila, J., Poythress, N. G., & Slobogin, C. (1997). *Psychological evaluations for the courts: A handbook for mental health professionals and lawyers.* New York: Guilford.

Acute Brain Failure

► Delirium

Acute Brain Syndrome

► Metabolic Encephalopathy

Acute Cerebrovascular Attack

► Stroke

Acute Confusional State

► Delirium
► Metabolic Encephalopathy

Acute Coronary Syndrome

► Myocardial Infarction

Acute Encephalopathy

► Delirium
► Toxic-Metabolic Encephalopathy

Acute Febrile Polyneuritis

► Guillain–Barré Syndrome

Acute Infective Polyneuritis

► Guillain–Barré Syndrome

Acute Inflammatory Demyelinating Polyradiculoneuropathy (AIDP)

► Guillain–Barré Syndrome

Acute Lymphoblastic Leukemia

Jacqueline L. Cunningham
The Children's Hospital of Philadelphia
Philadelphia, PA, USA

Synonyms

ALL

Definition

Acute lymphoblastic leukemia (ALL) is a form of cancer of the white blood cells (leukocytes). ALL is the most common type of childhood leukemia, and is distinguished from chronic lymphoblastic leukemia (CLL) and acute myeloid (or myelogenous) leukemia, which are more prevalent in adults.

Current Knowledge

Symptoms

ALL is characterized by the rapid proliferation of immature blood cells (lymphoblasts), which crowd out mature, functional cells. It is associated with the enlargement of lymphoid tissue in areas including the lymph nodes, spleen, bone marrow, and lungs, and with increased lymphocytic cells circulating in blood and in various tissues and organs. Persons afflicted will experience weakness and fatigue, anemia, unexplained fever and infections, weight loss, or loss of appetite.

Pathophysiology

Cancer, including ALL, is caused by damage to DNA.

Treatment

The earlier the ALL is detected, the more effective is its treatment. The goal is to induce a lasting remission, considered to be a prevalence of less than 5% of lymphoblasts in bone marrow. Advances made in the ability to match the genetic properties of the blast cells to treatment options, in association with the availability of new drugs and improvements made in bone marrow and stem cell transplantation, have changed the prognosis for ALL from a zero to a 75% survival rate over the past 40 years.

Most (if not all) patients with a childhood history of ALL have brain atrophy. Whereas atrophy is associated with treatment-effects of cranial irradiation therapy and intrathecal chemotherapy (usually methotrexate), it can also occur as a result of the condition, itself, rather than as an outcome of treatment, as it appears to cause atrophy of the brain, which is not specific to certain brain tissues (Lucy Rorke, MD, personal communication). Nonetheless, the strongest detrimental impacts on cognition are attributable to treatment-effects and their damaging influence on the biological substrates of core neurocognitive abilities, including executive functions and information processing. Such impacts disrupt the secondary abilities, i.e., those that are acquired and knowledge-based. The main approaches to alleviating neurocognitive effects of treatment include cognitive remediation, pharmacology, and ecological alterations in the classroom.

Cross References

- ▶ Acute Myelogenous Leukemia
- ▶ Leukemia
- ▶ Neoplasms

References and Readings

Butler, R. W., & Mulhern, R. K. (2005). Neurocognitive interventions for children and adolescents surviving cancer. *Journal of Pediatric Psychology, 30*, 65–78.

Crosley, C. J., Rorke, L. B., Evans, A., & Nigro, M. (1978). Central nervous system lesions in childhood leukemia. *Neurology, 28*, 678–685.

Prassopoulos, P., Carouras, D., Golfinopoulos, S., Evlogias, N., Theodoropoulos, V., & Panagiotou, J. (1996). Quantitative assessment of cerebral atrophy during and after treatment in children with acute lymphoblastic leukemia. *Investigational Radiology, 12*, 749–754.

Pui, Ching-Hon (2003). *Treatment of acute leukemias: New directions for clinical research*. New York: Humana Press.

Acute Myelogenous Leukemia

Jacqueline L. Cunningham
The Children's Hospital of Philadelphia
Philadelphia, PA, USA

Synonyms

Acute myeloid leukemia; AML

Definition

Acute myelogenous leukemia (AML) is a form of cancer of the white blood cells (leukocytes). It is a relatively rare cancer that occurs more commonly in adults than in children, with more men affected than women. The median age at diagnosis is 63 years.

Current Knowledge

Symptoms

Acute forms of leukemia are characterized by the rapid proliferation of immature blood cells which rapidly crowd out mature, functional cells. In AML, the cell type is granuloid, whose cancerous change disrupts its normal ability to form red cells, some types of white cells, and platelets. Resulting symptoms are anemia, easy bruising and bleeding, and disruption to the body's ability to resist infection. Impaired cognition and fatigue are also strongly associated with AML. Whereas impairments in these areas have been attributed to effects of chemotherapy, recent research by Meyers, Albitar, and Estey (2005) has identified differing cytokine levels present prior to chemotherapy as also contributing to these symptoms.

Pathophysiology

The malignant cell in AML is the myeloblast, a mutated and immature cell in the granulocytic series, which undergoes combinations with other mutations, to produce a leukemic clone of cells. Because the process contributes to much diversity and heterogeneity in cell differentiation, the diagnosis of AML can be challenging. It remains important, however, since the chromosomal structure of the leukemic cells is the disease's most critical prognostic factor.

Treatment

Treatment in AML consists primarily of chemotherapy, with the goal of achieving remission. Without postremission (consolidation) therapy, almost all patients eventually relapse. Neurocognitive and neuropsychiatric symptoms are highly prevalent in patients with cancer and cause significant impairments in their ability to function. Whereas such impairments are known to be associated with aggressive cancer treatment, they are additionally attributed to biologic mechanisms underlying the cancer itself. Recent research (Meyers et al., 2005) on AML has made linkages between cytokine-immunologic activation and factors including cognitive functioning, significant fatigue, and quality of life in AML patients studied *prior* to the initiation of treatment.

Cross References

- ▶ Acute Lymphoblastic Leukemia
- ▶ Leukemia
- ▶ Neoplasms

References and Readings

Meyers, C. A., Albitar, M., & Estey, E. (2005). Cognitive impairment, fatigue, and cytokine levels in patients with acute myelogenous leukemia or myelodysplastic syndrome. *Cancer, 104*, 788–793.

Pui, C.-H. (2003). *Treatment of acute leukemias: New directions for clinical research*. New York: Humana Press.

Acute Myeloid Leukemia

► Acute Myelogenous Leukemia

Acute Radiation Somnolence

Jacqueline L. Cunningham
The Children's Hospital of Philadelphia
Philadelphia, PA, USA

Definition

Acute radiation somnolence is a relatively transient and benign effect of cranial irradiation. It is manifested as sleepiness occurring during irradiation used to treat brain tumors. It occurs in both children and adults and usually affects daily functioning during the course of treatment. Although it is self-limiting, and resolves with medication and with the termination of irradiation, symptoms can be upsetting to patients. Nursing intervention which focuses on preparation through counseling and education serves to alleviate distress. Acute radiation somnolence is usually treated with steroids.

Cross References

► Radiation Oncology
► Radiotherapy

References and Readings

Brady, L. W., Heilmann, H. P., Molls, M., & Schlegel, W. (2006). *New techniques in radiation oncology*. New York: Springer.

Acute Respiratory Distress Syndrome

Dona EC Locke
Mayo Clinic
Scottsdale, AZ, USA

Synonyms

Adult respiratory distress syndrome; Respiratory distress syndrome

Definition

Acute respiratory distress syndrome (ARDS) is the presence of pulmonary edema in the absence of volume overload or depressed left ventricular function, and is characterized by the development of sudden breathlessness within hours to days of an inciting event. ARDS is not a specific disease; instead, it is a type of severe, acute lung dysfunction that is associated with a variety of diseases and trauma.

Historical Background

In the past, ARDS signified adult respiratory distress syndrome to separate this from infant respiratory distress syndrome seen in premature infants. However, this type of pulmonary edema can also occur in children, so ARDS has gradually evolved to mean acute rather than adult.

Current Knowledge

ARDS typically develops within 12–48 h after the inciting event, although, in rare instances, it may take up to a few days. Persons developing ARDS are critically ill, often with multi-system organ failure. It is a life-threatening condition; therefore, hospitalization is required for prompt management.

ARDS is associated with severe and diffuse injury to the alveolar-capillary membrane (the air sacs and small blood vessels) of the lungs. Fluid accumulates in some alveoli of the lungs, while some other alveoli collapse. This alveolar damage impedes the exchange of oxygen and carbon dioxide, which leads to a reduced concentration of oxygen in the blood. Low levels of oxygen in the blood cause damage to other vital organs of the body such as the kidneys.

The 1994 American–European Consensus Committee defines ARDS as the acute onset of bilateral infiltrates on chest radiography, a partial pressure of arterial oxygen (PaO_2) to fraction of inspired oxygen (FIO_2) ratio of less than 200 mmHg and a pulmonary artery occlusion pressure of less than 18, or the absence of clinical evidence of left arterial hypertension.

The mortality rate is approximately 30–40%. Death usually results from multi-system organ failure rather than lung failure alone.

Causes: A number of clinical conditions are associated with the development of ARDS.

- Sepsis and the systemic inflammatory response syndrome (SIRS) are the most common conditions associated with the development of ARDS.
- Severe traumatic injury (especially multiple fractures), severe head injury, and pulmonary contusion are strongly associated with the development of ARDS. In traumatic injury, factures of the long bones can cause ARDS through fat embolism. In severe brain injury, ARDS is thought to develop owing to a sudden discharge of the sympathetic nervous system, which then leads to acute pulmonary hypertension and injury to the pulmonary capillary bed. In pulmonary contusions, ARDS develops through direct trauma to the lung.
- Multiple blood transfusions are an independent risk factor for ARDS. The risk is independent of the reason for the transfusion or the coexistence of trauma. The incidence of ARDS increases with the number of units of blood transfused. If the patient has pre-existing abnormal liver functioning or a coagulation abnormality, the risk is further increased.
- Near drowning can be another cause of ARDS. Development of ARDS is slightly more common with salt-water than with fresh-water. Aspiration leads to an osmotic gradient that favors movement of water into airspaces of the lung. Aspiration may be visible with chest radiography, although the chest radiograph may be normal early in the course of the disease.
- Smoke inhalation is another possible cause of ARDS. Smoke inhalation causes lung tissue damage from direct heat, toxic chemicals, and particulate matter carried into the lung. Patients with smoke inhalation initially may be asymptomatic, but patients with airway burns, exposure to toxic fumes, or exposure to carbon monoxide should be monitored closely for the development of ARDS, even if the symptoms are initially absent.
- Overdoses of narcotics, tricyclic antidepressants, and other sedatives have been associated with the development of ARDS. Overdoses of tricyclic antidepressants are the most common. This risk is independent of the risk from concurrent aspiration.

Medical Treatment for ARDS:

- People with ARDS require hospitalization and treatment in an intensive care unit.
- There is no specific treatment for ARDS, but rather, treatment is primarily supportive using a mechanical respirator and supplemental oxygen.
- Diuretics can be given to eliminate fluid from the lungs. However, fluids are often given via IV to provide nutrition and prevent dehydration, but fluids must be carefully monitored to avoid fluid accumulation in the lungs.
- Antibiotic therapy may be administered to treat infection, which is often the underlying cause of ARDS.
- Corticosteroids may sometimes be given late in the process of ARDS or if the patient is in shock. If the patient is in shock, drugs to counteract low blood pressure caused by shock may be administered.
- If the patient is experiencing anxiety, this can be treated with anti-anxiety medications.

Respiratory therapists may see these patients to provide inhaled drugs to decrease inflammation and provide respiratory comfort.

Because of the acute and medically serious nature of ARDS, it would be unlikely for neuropsychological exam to be requested when a person is acutely ill with ARDS. Mortality with ARDS is 30–40% and the person would typically be treated in an Intensive Care Unit. If the person survives, outpatient neuropsychological evaluation could be requested and results may show memory deficits related to the hypoxia as well as neuropsychological deficits related to the underlying medical cause for ARDS (e.g., severe TBI, near drowning, sepsis, medication overdose).

Cross References

- ▶ Anoxia
- ▶ Hypoxia

References and Readings

Bernard, G. R., Artigas, A., Brigham, K. L., Charlet, J., Falke, K., Hudson, L, Lamy M., Legall, J. R., Morris, A., & Spragg, R. (1994). Report of the American-European consensus conference on ARDS: Definitions, mechanisms, relevant outcomes and clinical trial coordination. *Intensive Care Medicine, 20,* 225–232.

ADA

► American's with Disabilities Act of 1990

Adaptation

► Tachyphylaxis

Adaptive Behavior Assessment System – Second Edition

Thomas Oakland
University of Florida
Gainesville, FL, USA

Synonyms

ABAS; ABAS-II

Description

The Adaptive Behavior Assessment System – Second Edition (ABAS-II; Harrison & Oakland, 2003) provides an assessment of adaptive behavior and skills for persons from birth through age 89. Five forms are available: parent/primary caregiver form (for ages 0–5), teacher/day-care provider form (for ages 2–5), parent form (for ages 5–21), teacher form (for ages 5–21), and an adult form (for ages 16–89). Its standardization sample is large (>4,000) and representative of US data from 1999 to 2000 with respect to gender, race/ethnicity, and parental education, and it is proportional to individuals with disabilities. Forms are available in French-Canadian and Spanish. The scales have been adapted for use in Sweden and Taiwan, with plans for extensions to the Czech Republic, Denmark, Germany, Romania, and Spain.

Historic Background

The ABAS (Harrison & Oakland, 2000) preceded the development of the ABAS-II. The ABAS was developed to be a measure of adaptive behavior consistent with current definitions (e.g., those promulgated by the American Psychiatric Association's (2000) Diagnostic and Statistical Manual of Mental Disorders and the American Association on Intellectual and Developmental Disabilities' (AAIDD, 1992) models of adaptive behavior) that underscored the importance of ten skill areas: communication, community use, functional academics, health and safety, home or school living, leisure, self-care, self-direction, social, and work skills. The ABAS norm groups were large and included persons 5 through 89. The ABAS was revised shortly after its publication in response to two issues: a need for the downward extension of the ABAS for younger children and a change in the concept of adaptive behavior embodied in AAIDD's 2002 definition, one that emphasized the importance of three domains (e.g., conceptual, social, and practical).

The ABAS-II is the only scale of adaptive behavior consistent with models of adaptive behavior advocated by the AAIDD's 1992 and 2002 definitions and the American Psychiatric Association's (2000) Diagnostic and Statistical Manual of Mental Disorders. Scaled scores for 11 adaptive skill areas are provided (Table 1). Ten skill area scores combine to produce standard scores in their respective domains: conceptual (communication, functional academics, and self-direction), social (social skills and leisure), and practical (self-care, home or school living, community use, health and safety, and work for adults); motor skills are assessed for young children. A General Adaptive Composite Score is derived from the skill scores.

Item Data

All items are scored on a four-point scale: 0 (cannot perform the behavior), 1 (can perform the behavior yet does not), 2 (performs the behavior sometimes), and 4 (performs the behavior most or all of the time). This feature is consistent with the World Health Organization's International Classification of Functioning (Mpofu & Oakland, 2010) effort to distinguish activities and performance.

Respondents may indicate that they guessed. Data from subtests with more than three guesses should not be used. The ABAS-II's scoring and reporting system informs clinicians of interventions likely to promote the development of selected behaviors associated with critical items.

Adaptive Behavior Assessment System – Second Edition. Table 1 Adaptive skills and three adaptive domains

Adaptive skills	
Communication	Speech, language, and listening skills needed for communication with other people, including vocabulary, responding to questions, and conversation skills
Community use	Skills needed for functioning in the community, including use of community resources, shopping skills, and getting around in the community
Functional academics	Basic reading, writing, mathematics, and other academic skills needed for daily, independent functioning, including telling time, measurement, as well as writing notes and letters
Home living	Skills needed for basic care of a home or living setting, including cleaning, straightening, property maintenance and repairs, as well as food preparation and performing chores
Health and safety	Skills needed for protection of health and to respond to illness and injury, including following safety rules, using medicines, and showing caution
Leisure	Skills needed for engaging in and planning leisure and recreational activities, including playing with others, engaging in recreation at home, and following rules in games
Self-care	Skills needed for personal care including eating, dressing, bathing, toileting, grooming, and hygiene
Self-direction	Skills needed for independence, responsibility, and self-control, including starting and completing tasks, keeping a schedule, following time limits, following directions, and making choices
Social	Skills needed to interact socially and get along with other people, including having friends, showing and recognizing emotions, assisting others, and using manners
Work	Skills needed for successful functioning and holding a part-time or full-time job in a work setting, including completing work tasks, working with supervisors, and following a work schedule
Motor skills[a]	Basic fine and gross motor skills needed for locomotion, manipulation of the environment, and the development of more complex activities such as sports, including sitting, pulling up to a standing position, walking, fine motor control, and kicking
Three domains and associated skill areas	
Conceptual	Includes communication, functional academics, self-direction, and health and safety skills
Practical	Includes social skills and leisure skills
Social	Includes self-care, home/school living, community use, health and safety, and work skills

[a]Although fine and gross motor development is not included as one of the ten skills identified by the American Association on Intellectual and Developmental Disabilities, it is included in some scales of adaptive behavior.

Psychometric Data

Scaled scores generally range from 40 to 120. Consistent with all measures of adaptive behavior, the ABAS-II is more sensitive to the assessment of adaptive behavior and skills at the lower than the higher ranges. Cut scores are not provided by disability category; instead, reliance is placed on diagnostic standards established by state and national authorities.

The ABAS-II demonstrates suitable psychometric qualities. Internal consistency is high, with reliability coefficients of 0.85–0.99 for the General Adaptive Composite, three adaptive behavior domains, and skill areas. Test–retest reliability coefficients are in the 0.80s and 0.90s for the General Adaptive Composite, three domains, and skill areas (Harrison & Oakland, 2003). Inter-rater reliability coefficients (e.g., between teachers, day-care providers, and parents) range from the 0.60s to the 0.80s for the skill areas and are in the 0.90s for the General Adaptive Composite. Its construct validity is strong as displayed through factor analyses (Harrison & Oakland, 2003; Wei, Oakland, & Algina, 2008). Its concurrent validity with the Vineland Adaptive Behavior Scales – Classroom Edition's Adaptive Behavior Composite is high, $r = 0.82$ (Harrison & Oakland, 2003). See reviews by Burns (2005), Meikamp and Suppa (2005), and Rust and Wallace (2004) for additional details.

Clinical Uses

Measures of adaptive behavior have been most important in assessment of persons with mental retardation (now

referred to as intellectual disabilities by AAIDD). The ABAS-II is useful in this diagnosis as well as in intervention planning and monitoring for this and other disorders.

The ABAS-II also may assist in promoting an understanding of the impact on a person's daily life activities of other disorders (e.g., those often diagnosed first during infancy or early childhood include autism, disorders of attention, communication, conduct, elimination, feeding and eating, learning, motor skills, and pervasive developmental disorders; Harman, Smith-Bonahue, & Oakland, 2009; Oakland & Harrison, 2008). The ABAS-II is useful with children and adolescents who display disorders including attention deficit/hyperactivity, acquired brain injury, auditory or visual impairment, autism, developmental delays, emotional/behavioral disorders, learning disabilities, and physical impairments (Ditterline, Banner, Oakland, & Becton 2008; Harrison & Oakland, 2003; Oakland & Harrison, 2008).

Adults diagnosed with such disorders as anxiety, acute stress or adjustment disorder, bipolar disorder, depression, mood disorders, psychosis, Parkinson's, postpartum depression, substance abuse, schizophrenia, and sleep disturbance may display impairments in their functional daily living skills. Older adults diagnosed with Alzheimer's type dementia and other cognitive and neuropsychological disorders with late-life onset often display impairments in their functional daily living skills. Although data from the ABAS-II may not be crucial in the diagnosis of some of these disorders, ABAS-II data will promote an understanding of their impact on daily living skills. The ABAS-II is used in the assessment of mental retardation among death row inmates in light of the 2002 US Supreme Court Atkins decision (Olley & Cox, 2008).

Cross References

- ► Activities of Daily Living
- ► Activity Restrictions and Limitations
- ► Adaptive Behavior
- ► Intellectual Disabilities

References

American Association on Intellectual and Developmental Disabilities. (1992). *Definitions, classifications, and systems of supports* (9th ed.). Washington, DC: American Association on Mental Retardation.

American Association on Intellectual and Developmental Disabilities. (2002). *Mental retardation: Definition, classification, and systems of support* (10th ed.). Washington, DC: American Association on Mental Retardation.

American Psychiatric Association. (2000). *Diagnostic and statistical manual of mental disorders* (4th ed., text revision). Washington, DC: American Association on Mental Retardation.

Burns, M. K. (2005). Review of the adaptive behavior assessment system – second edition. In R. Spies & B. Plake (Eds.), *The sixteenth mental measurements yearbook*. Lincoln, NE: Buros Institute of Mental Measurements.

Ditterline, J., Banner, D., Oakland, T., & Becton, D. (2008). Adaptive behavior profiles of students with disabilities. *Journal of Applied School Psychology, 24*, 191–208.

Harman, J., Smith-Bonahue, T., & Oakland, T. (2009). Assessment of adaptive behavior development in young children. In E. Mpofu & T. Oakland (Eds.). *Rehabilitation and Health Assessment: Applying ICF Guidelines*. New York: Springer.

Harrison, P. & Oakland, T. (2000). *Adaptive behavior assessment system*. San Antonio, TX: Harcourt Assessment.

Harrison, P. & Oakland, T. (2003). *Adaptive behavior assessment system – second edition*. San Antonio, TX: Harcourt Assessment.

Meikamp, J., & Suppa, C. H. (2005). Review of the adaptive behavior assessment system – second edition. In R. Spies & B. Plake (Eds.), *The sixteenth mental measurements yearbook*. Lincoln, NE: Buros Institute of Mental Measurements.

Mpofu, E. & Oakland, T. (2010). *Assessment in rehabilitation and health*. Upper Saddle River, NJ: Merrill.

Oakland, T. & Harrison, P. (2008). *Adaptive behavior assessment system-II: Behavior assessment system-II: Clinical use and interpretation*. New York: Elsevier

Olley, J. G., & Cox, A. (2008). Assessment of adaptive behavior in adult forensic cases: The use of the ABAS-II. In T. Oakland, & P. Harrison, (Eds.), *Adaptive behavior assessment system-II: Clinical use and interpretation*. Boston: Elsevier

Rust, J. O. & Wallace, M. A. (2004). Test review: Adaptive behavior assessment system – second edition. *Journal of Psychoeducational Assessment, 22*, 367–373.

Wei, Y., Oakland, T., & Algina, J. (2008). Multigroup confirmatory factor analysis for the parent form, ages 5–21, of the adaptive behavior assessment system-II. *American Journal on Mental Retardation. 113*, 178–186.

Adaptive Functions

- ► Activities of Daily Living (ADL)

ADD

- ► Attention Deficit, Hyperactivity Disorder
- ► Minimal Brain Dysfunction

Addiction

- ► Substance Abuse Disorders

Adelaide Activities Index

► Frenchay Activity Index

Adenoma

Ethan Moitra
Drexel University
Morgantown, WV, USA

Definition

A benign tumor of glandular origin. There are three types of adenomas: tubular (most common; tube-like structure), villous (least common; most likely to become cancerous; ruffled structure), and tubulovillous (blend of tubular and villous structures). Adenomas do not metastasize, though they can develop into malignancies known as adenocarcinomas. The tumor may occur throughout the endocrine system, including the pituitary gland.

Pituitary adenomas occur at a much higher incidence in adults than in children. Because their invasiveness is local, they are almost always benign and can be difficult to detect. There is the secreting and the nonsecreting type. Clinical symptoms come from the endocrine dysfunction or from mass effect, and include headaches, hypopituitarism, and visual loss (caused by compression in the optic chiasm). Treatment of pituitary adenomas includes correction of electrolyte dysfunction, replacement of pituitary hormones, surgical resection, and radiotherapy.

Cross References

► Pituitary Adenoma

References and Readings

Mazzaferri, E. L., & Saaman, N. A. (Eds.) (1993). *Endocrine tumors.* Boston: Blackwell Scientific Publications.

ADHD

► Attention Deficit, Hyperactivity Disorder
► Minimal Brain Dysfunction

ADHD, Combined

► Attention Deficit, Hyperactivity Disorder
► Minimal Brain Dysfunction

ADHD, Predominantly Hyperactive-impulsive Type

► Attention Deficit, Hyperactivity Disorder
► Minimal Brain Dysfunction

ADHD, Predominantly Inattentive Type

► Attention Deficit, Hyperactivity Disorder
► Minimal Brain Dysfunction

ADI-R

► Autism Diagnostic Interview, Revised

ADLQ

► Activities of Daily Living Questionnaire

Admissibility

Moira C. Dux
University of Maryland Medical Center/Baltimore VA
Baltimore, MD, USA

Definition

Admissibility of evidence refers to any testimonial, documentary material, or other form of tangible evidence that can be considered by the trier of fact, most typically a judge or a jury, in the context of a judicial or administrative proceeding. In order for evidence to be admissible, it must be relevant, non-prejudicial, and possess some indicia of reliability. For example, if

evidence consists of a witness testimonial, it must be established that the witness is credible and that he/she has knowledge of that which he/she is declaring. For neuropsychologists, a central issue is the admissibility of one's data and opinions. Rules 401, 402, and 702–705 from Article VII of the Federal Rules of Evidence (FRE) relate to "Opinions & Expert Testimony." Perhaps of most relevance to psychologists is rule FRE 702 which states, "If scientific, technical, or other specialized knowledge will assist the trier of fact to understand the evidence or to determine a fact in issue, a witness qualified as an expert by knowledge, skill, experience, training or education, may testify thereto in the form of an opinion or otherwise." In other words, the expert should possess some form of knowledge that a typical judge or juror would not be expected to know or understand. Rule 703 states, "The facts or data in the particular case upon which an expert bases an opinion or inference may be those perceived by or made known to the expert at or before the hearing. If of a type reasonably relied upon by experts in the particular field in forming opinions or inferences upon the subject, the facts or data need not be admissible in evidence in order for the opinion or the inference to be admitted. Facts or data that are otherwise inadmissible shall not be disclosed to the jury by the proponent of the opinion or inference unless the court determines that their probative value in assisting the jury to evaluate the expert's opinion substantially outweighs their prejudicial effect."

Several important cases have addressed the admissibility of scientific testimony. In the case of *Frye v. United States* (1923), the *Frye* standard was established which stated that: only scientific methods and concepts with "general acceptance" within a particular field are admissible. In the more recent case of *Daubert v. Merrell Dow* (1993), it was determined that scientific testimony has to abide by two criteria, the testimony must be: (a) scientifically valid and (b) relevant to the case at hand.

Cross References

► Daubert v. Merrell Dow Pharmaceuticals (1993)

References and Readings

A complete list of the Federal Rules of Evidence is available at: http://judiciary.house.gov/media/pdfs/printers/108th/evid2004.pdf.

Greiffenstein, M. F. (2009). Basics of forensic neuropsychology. In J. Morgan, & J. Ricker (Eds.). *Textbook of clinical neuropsychology.* New York: Taylor & Francis.

Jenkins v. United States, 307 F. 2d 637 (1962).

Kaufmann, P. M. (2008). Admissibility of neuropsychological evidence in criminal cases: Competency, insanity, culpability, and mitigation. In R. Denney, & J. Sullivan (Eds.). *Clinical neuropsychology in the criminal forensic setting.* New York: Guilford.

Admissibility of Psychological Evidence

► *Jenkins v. U.S. (1962)*

Admissibility of Psychological/ Neuropsychological Evidence

► Baxter v. Temple (2005)

Adoption Studies

Rohan Palmer[1], Martin Hahn[2]
[1]University of Colorado
Boulder, CO, USA
[2]William Paterson University
Wayne, NJ, USA

Definition

Adoption studies typically compare pairs of persons, e.g., adopted child and adoptive mother or adopted child and biological mother to assess genetic and environmental influences on behavior.

Current Knowledge

Design

Familial resemblance of behaviors is due to genetic and/or common familial environmental influences. Adoption studies provide a direct test of the role of both factors. This is possible by drawing comparisons between families that share genetic and environmental influences and

families that share only genetic or environmental factors. Adoption creates two types of families. The "genetic family" consists of pairs of genetically related individuals who do not share a common family environment (e.g., biological parent and adopted-away child). The similarity between these pairs of relatives provides a direct estimate of genetic effects on behaviors. The second type family is the "environmental family," which is made up of pairs of individuals who are not genetically related but who share a common family environment (e. g., adoptive parent and adopted child). The similarity between pairs of relatives from an "environmental family" indicates the presence of environmental influences on behavior. Adoption studies utilize either parent–offspring pairs or sibling pairs. Because data on biological parents and siblings of adoptees are sometimes rare, comparison between "genetic-plus-environmental" families (i.e., intact families) and adoptive families also provides evidence of genetic and environmental influences.

Relevance to Neuropsychology

The Colorado Adoption Project has been collecting longitudinal data on biological and adoptive parents and their biological or adopted children for over 30 years (Petrill, Plomin, DeFries, & Hewitt, 2003). In one set of analyses from that project reported by Plomin, Fulker, Corley, and DeFries (1997), parent–offspring correlations were calculated for children aged 3–16 years. The results of the analyses show increasing correlations across those ages between biological parents and their adopted-away children on such special cognitive abilities as verbal skills and perceptual speed. Correlations between adoptive parents and adopted children remained about zero across those ages. The authors interpret the results to indicate that heritability increases for those special cognitive abilities with age and that the role of shared environment is low or nonexistent.

Today, adoption study data are used to assess the genetic and environmental influence on a variety of clinical outcomes that include drug addiction (Young, Rhee, Stallings, Corley, & Hewitt, 2006) and age of sexual initiation (Bricker et al., 2006), to name a few.

Cross References

► Twin Studies

References and Readings

Bricker, J. B., Stallings, M. C., Corley, R. P., Wadsworth, S. J., Bryan, A., Timberlake, D. S., et al. (2006). Genetic and environmental influences on age at sexual initiation in the Colorado adoption project. *Behavior Genetics, 36*, 820–832.

Petrill, S. A., Plomin, R., DeFries, J. C., & Hewitt, J. K. (2003). *Nature, nurture, and the transition to early adolescence.* Oxford: Oxford University Press.

Plomin, R., Fulker, D. W., Corley, R., & DeFries, J. C. (1997). Nature, nurture, and cognitive development from 1 to 16 years: A parent-offspring adoption study. *Psychological Science, 8*, 442–447.

Young, S. E., Rhee, S. H., Stallings, M. C., Corley, R. P., & Hewitt, J. K. (2006). Genetic and environmental vulnerabilities underlying adolescent substance use and problem use: General or specific? *Behavior Genetics, 36*, 603–615.

ADOS

► Autism Diagnostic Observation Schedule

Adrenal Hormones

► Minimal Brain Dysfunction

Adrenaline

► Epinephrine

Adrenergic Agonists

► Catecholamines

Adrenocorticotropic Hormone

David J. Libon
Drexel University, College of Medicine
Philadelphia, PA, USA

Definition

Adrenocorticotropic hormone (ACTH) is produced by the anterior pituitary gland and is a component of the

hypothalamic-pituitary-adrenal axis. The release of ACTH is associated with the biological response to stress. The production of ACTH from the pituitary gland stimulates the adrenal glands to produce cortisol. The ACTH stimulation test is a common procedure used to assess the integrity of the adrenal glands. This test is used to identify a number of medical conditions including adrenal insufficiency, Addison's disease, and related medical conditions (Melmed & Kleinberg, 2008).

Cross References

► Hypothalamus

References and Readings

Melmed, S., & Kleinberg, D. (2008). Anterior pituitary. In H. M. Kronenberg, S. Melmed, K. S. Polonsky, & P. R. Larsen (Eds.), *Williams textbook of endocrinology* (11th edn.). Philadelphia, PA: Saunders Elsevier.

Adult Respiratory Distress Syndrome

► Acute Respiratory Distress Syndrome

Advanced MS

► Secondary-Progressive Multiple Sclerosis

Advanced Progressive Matrices

Victoria M. Leavitt
Kessler Foundation Research Center
West Orange, NJ, USA

Synonyms

APM

Description

First developed in the 1940s as an additional form of the Raven's progressive matrices, the advanced progressive matrices (APM) were developed to test intellectual efficiency in people with greater than average intellectual ability, and to differentiate clearly between people of superior ability. A nonverbal test of inductive reasoning, the APM contains 48 items, presented as one set of 12 (Set I), and another of 36 (Set II). As in the standard version of the test (SPM), items are presented in black ink on a white background, and become increasingly difficult as progress is made through each set. Although it is an untimed task, some clinicians administer the APM under time constraints. Set II can be used without a time limit to assess the examinee's total reasoning capacity. In this case, the examinee would first be shown the problems of Set I as examples to explain the principles of the test, and would then be given approximately 1 h to complete the task. Alternately, Set I can be given as a short practice test followed by Set II as a speed test. In this case, 40 min is the time limit most commonly given for Set II.

Historical Background

The APM was designed in the 1940s to assess nonverbal abstract conceptualization skills of individuals for whom the standard version was too easy; that is, those achieving a raw score of 50 or above on the SPM. For children over 10 years of age with high intellectual functioning, the APM may be the appropriate version to ensure an adequate ceiling (Mills, Ablard, & Brody, 1993). For additional information about the historical background of the original test, please refer to the entry for Raven's Progressive Matrices.

Psychometric Data

Norms for adolescents (ages 12–16.5) and adults (18–68+; Sets I and II) for untimed (ages 12–70+) and timed (ages 17–28) versions are provided for North America (Raven, Raven Court, 1998).The reliability of the test is considered good, with high internal consistency of APM Set II, and split-half reliability coefficients varying between 0.83 and 0.87 (Strauss, Sherman, & Spreen, 2006). Set I, as it has only 12 items, yields lower figures. Reliability of the original 48-item version was found to be high for adults and children aged 11.5 years+ (>0.80); for younger

children, it was only reasonably reliable (0.76). Overall, Set II scores increased by three points on retest (Raven et al., 1998).

Clinical Uses

The SPM and CPM have been found to be sensitive to a variety of neurological and neuropsychiatric conditions (► Raven's Progressive Matrices). The APM, designed for use with higher functioning individuals, may be more appropriately employed for assessing an individual's capacity for decision-making or strategic planning at the management level in the workplace or in a higher education setting.

Cross References

► Colored Progressive Matrices
► Raven's Progressive Matrices
► Standard Progressive Matrices

References and Readings

Mills, C. J., Ablard, K. E., & Brody, L. E. (1993). The Raven's progressive matrices: Its usefulness for identifying gifted/talented students. *Roeper Review, 15*, 183–186.

Raven, J. C. (1965, 1994). *Advanced progressive matrices sets I and II.* Oxford: Oxford Psychologists Press.

Raven, J., Raven, J. C., & Court, J. H. (1996). *Progressive matrices: A perceptual test of intelligence. Individual form.* Oxford: Oxford Psychologists Press. (Original work published 1938)

Raven, J., Raven, J. C., & Court, J. H. (1998). *Raven manual: Section 4. Advanced progressive matrices.* Oxford: Oxford Psychologists Press Ltd.

Raven, J., Raven, J. C., & Court, J. H. (2003). *Manual for Raven's progressive matrices and vocabulary scales. Section 1: General overview.* San Antonio, TX: Harcourt Assessment.

Strauss, E., Sherman, E. M. S., Spreen, O. (Eds.). (2006). *A compendium of neuropsychological tests* (3rd ed.). NY: Oxford University Press.

Advocacy

Amy J. Armstrong
Virginia Commonwealth University
Richmond, VA, USA

Synonyms

Advocate; Support

Definition

The process of supporting or acting on behalf of a cause; facilitating equal community access and participation of individuals or groups that have typically been socially and/or economically marginalized. There are several types of advocacy to include:

Systems Advocacy: the process in which any system (public, private, community based) is made more responsive to the needs of the individual served by the system. This process may include increasing awareness of services and resources available within a community; identifying unmet needs of individuals; identifying existing barriers that impede access to community services and resources; developing strategies to eliminate legislative, regulatory, social and economic barriers that may impede access to one's community supports and resources.

Individual Advocacy: the process of increasing awareness of unmet needs and procuring rights or benefits on behalf of another individual or group of individuals.

Self-Advocacy: the process of empowering an individual to rely upon him or herself to make his/her own choices and decisions in order to direct the course of his/her life. The People First movement of the 1970s was a progenitor of self-advocacy as a civil rights movement. The independent living movement also fostered self-advocacy and provided a foundation for self-advocacy activism.

Cross References

► Americans with Disabilities Act
► Independent Living

References and Readings

Dell Orto, A. E., & Marinelli, R. P. (Eds.) (1995). *Encyclopedia of disability and rehabilitation.* New York: MacMillian Publishing.

Test, D., Fowler, C. H., Wood, W. M., Brewer, D. M., & Eddy, S. (2005). Conceptual framework of self-advocacy for students with disabilities. *Remedial and Special Education, 26*, 43–54.

Wehmeyer, M. L. (2004). Self-determination and the empowerment of people with disabilities. *American Rehabilitation, 28*, 22–29.

Advocate

► Advocacy

Adynamia

Irene Shulova-Piryatinsky
Butler Hospital
Providence, RI, USA

Synonyms

Asthenia

Definition

Adynamia refers to a general weakness and lack of energy evident through lack of verbal or overt behavior due to a disease or neurological conditions. It can manifest as lethargy, loss of strength, weakness in extremities, and difficulty initiating activities or completing tasks. Adynamia can be observed after trauma to the frontal lobes, multiple sclerosis, and other conditions. In language, verbal adynamia (lack of spontaneity of speech) is seen with lesions of the medial frontal lobes and refers to difficulty in initiation and maintenance of language output.

Cross References

- ▶ Abulia
- ▶ Apathy
- ▶ Transcortical Motor Aphasia

References and Readings

Berrios, G. E. (2008). Classic text no. 76: 'Asthenia' by A. Dechambre (1865). *History of Psychiatry, 19*(4), 490–501.

Caplan, D. (1987). *Neurolinguistics and linguistic aphasiology: An introduction.* New York: Cambridge University Press.

Affect

Joel W. Hughes
Kent State University
Kent, OH, USA

Synonyms

Affect display

Definition

Affect is the display and experiencing of emotion. It includes positive dimensions such as joy, interest, and contentment, as well as negative dimensions of emotion such as disgust, fear, and anger. Affect is a very rapid response to internal (e.g., thoughts, memory) or external stimuli (e.g., other people). It is different from mood, in that it is more momentary and observable by others, whereas mood is longer-lasting and constitutes a symptom that patients may report (e.g., depression). Affect can be observed from facial expression, gestures, posture, and speech (e.g., word choice, tone, rate).

Cross References

- ▶ Affective Disorder
- ▶ Emotions
- ▶ Mood Disorder

References and Readings

Batson, C. D., Shaw, L. L., & Oleson, K. C. (1992). *Differentiating affect, mood and emotion: Toward functionally-based conceptual distinctions. Emotion.* Newbury Park, CA: Sage.

Blechman, E. A. (1990). *Moods, affect, and emotions.* Hillsdale, NJ: Lawrence Erlbaum Associates.

Ekman, P. (1993). An argument for basic emotion. *Cognition and Emotion, 6*, 169–200.

Affect Display

- ▶ Affect

Affective Disorder

Joel W. Hughes
Kent State University
Kent, OH, USA

Synonyms

Emotional disorder; Mood disorder

Short Description or Definition

Affective disorder is a mental disorder predominantly characterized by altered mood that results in a significant impairment in social, occupational, or other important area of functioning. Affective disorders include depressive disorders such as major depressive disorder, minor depressive disorder, and dysthymia, as well as manic disorders such as bipolar disorder and cyclothymic disorder. Affective disorders may be primary or caused by medical conditions or substances.

Categorization

Mania and depression seem to anchor the ends of an emotional and behavioral continuum, an observation that dates from ancient times. In Hippocrates' humoral theory, mania resulted from an excess of yellow bile, and depression to an excess of black bile. In the early twentieth century, German psychiatrist Emil Kraepelin described affective disorders as belonging to a manic–depressive form of psychosis, which he differentiated from *dementia praecox*. The term "manic depression" was replaced by more contemporary language, including major depressive disorder and bipolar disorder in the twentieth century, and, for example, major depressive disorder was first incorporated into the third edition of the Diagnostic and Statistical Manual (DSM-III).

Depressive disorders include major depressive disorder and dysthymic disorder. Diagnosis of major depressive disorder is made on the basis of symptoms, as there is no physiological test that reliably diagnoses depression. Major depressive disorder requires at least 2 weeks of depressed mood and/or loss of interest in usually pleasurable activities (anhedonia). In addition, at least four of the following seven symptoms must also be present; significant weight gain or loss or appetite changes, sleep disturbance (e.g., early morning awakening with difficulty returning to sleep), observable disturbances in psychomotor speed (increased or diminished), loss of energy or excessive fatigue, feelings of low self-worth or inappropriate guilt, cognitive changes such as the subjective experience of difficulty concentrating, and thinking about or planning suicide.

Dysthymia is similar to major depressive disorder, although the depression must be chronic (i.e., two or more years of depressed mood), and during the first 2 years of the dysthymia, there must not have been an episode of major depression or a period of longer than 2 months with no symptoms.

Bipolar disorder is diagnosed when there is a "manic" mood disturbance characterized by markedly expansive, elevated, or irritable mood, lasting at least 1 week. The mood disturbance must be accompanied by additional symptoms such as grandiosity, excessive risky behavior such as sexual behavior or irresponsible spending, and decreased need for sleep. A "mixed" episode denotes mood disturbances that are characterized by both manic and depressive symptoms. A "hypomanic" episode is a less-pronounced elevation of mood that would not qualify as a true manic episode. Bipolar disorders follow a course in which periods of elevated mood alternate with periods of depression, and are categorized according to the nature of these episodes. For example, Bipolar I involves alternating manic and depressive episodes; in Bipolar II, there are alternating hypomanic and depressive episodes; cyclothymic disorder involves alternating hypomanic and depressive episodes that do not meet full criteria for major depression.

Epidemiology

Affective disorders are very common. At any one time, approximately 10% of the adult population, or nearly 20 million Americans, have a depressive illness. Rates of depression are even higher in patients with comorbid medical conditions, and, for example, about 30% of patients with cardiac disease have clinically significant depression. Bipolar disorder is much less common than unipolar depression, occurring in between 2% and 4% of the population (including Bipolar I, Bipolar II, and cyclothymic disorder). While depression is twice as common among women as men, bipolar is equally common in men and women.

Natural History, Prognostic Factors, and Outcomes

Affective disorders often start in adolescence. For example, the onset of Bipolar disorder is typically 15–24 years of age. However, the most likely ages for a first major depressive episode are 30–40 years of age. Depressive disorders often remit spontaneously, but recurrence is common, and about 15% of individuals experiencing an initial major depressive episode will develop chronic recurrent depression. The bipolar disorders are highly heritable, and research continues to determine genetic risk markers for bipolar disorder. Brain imaging studies also suggest that a broad risk for unstable moods may underlie

bipolar disorder, but more research is warranted. The causes of depression are not fully understood, but appear to involve the interaction of genetic and environmental factors such as stress and disruptions in interpersonal relationships. Thus, in addition to female gender, risk factors for depression include severe life stress such as traumatic events and loss of significant relationships. Depression is associated with shorter life expectancy from suicide and other causes of death. For example, depression increases risk of cardiac disease, as well as risk of mortality among individuals with cardiac disease.

Neuropsychology and Psychology of Affective Disorder

Depression is common in neurological conditions such as stroke and traumatic brain injury (Robinson, 2006; Rosenthal, Christensen, & Ross, 1998). Even without an obvious neurologic insult, individuals with alterations in executive control, memory, and emotion regulation are at increased risk for depression. Furthermore, individuals with depression often show neuropsychological deficits in the absence of neurological conditions. The neuropsychological deficits specified in the diagnostic criteria for depression include difficulty concentrating and making decisions. Thus, depressed patients often exhibit deficits in executive control, memory, and processing speed. For bipolar disorder, distractibility is typically present, as well as impaired decision making reflected in the criterion relating to distractibility of excessive involvement in activities that present significant risk of negative consequences. Current neuropsychological theories of depression emphasize the frontal lobes and basal ganglia, including abnormalities in neural circuitry involving the prefrontal cortex, mesiotemporal cortex, striatum, amygdala, and thalamus (Chamberlain & Sahakain, 2006). These areas may also be implicated in bipolar disorder, as they appear to underlie mood symptoms and treatment effects.

Evaluation

Assessment of affective disorders focuses on self-report instruments and clinical interviews. Neuropsychological testing may reveal deficits in executive function, attention psychomotor slowing, and biases in the processing of emotional stimuli. Specifically, depressed individuals have exaggerated responses to negative feedback, including rumination. Neuropsychological evaluations in depression and bipolar disorder are used frequently in research, as tests with broad clinical utility in the context of assessing or treating affective disorders have not been widely disseminated.

Treatment

Depression is often treated with medication and/or psychotherapy. A large number of medications are available to treat depression, including selective serotonin reuptake inhibitors, which typically have relatively milder side effects and lower risks than older drugs such as monoamine oxidase inhibitors. Treatment of bipolar disorders requires pharmacotherapy. In contrast to major depressive disorder, bipolar cannot be successfully treated by psychotherapy alone.

Cross References

► Depressive Disorder

References and Readings

Allen, L. B., McHugh, R. K., & Barlow, D. H. (2008). Emotional disorders: A unified protocol. In D. H. Barlow (Ed.), *Clinical handbook of psychological disorders: A step-by-step treatment manual* (4th ed.) (pp. 216–249). New York: Guilford Press.

American Psychiatric Association (2000). *Diagnostic and statistical manual of mental disorders* (4th ed.). Text Revision. Washington, DC: American Psychiatric Association.

Chamberlain, S. R., & Sahakain, B. J. (2006). The neuropsychology of mood disorders. *Current Psychiatry Reports, 8*, 458–463.

Clark, L., Chamberlain, S. R., & Sahakian, B. J. (2009). Neurocognitive mechanisms in depression: Implications for treatment. *Annual Review of Neuroscience, 32*, 57–74.

Robinson, R. (2006). *The neuropsychiatry of stroke* (2nd ed.). New York: Cambridge University Press.

Rosenthal, M., Christensen, B., & Ross, T. (1998). Depression following traumatic brain injury. *Archives of Physical Medicine and Rehabilitation, 79*, 90–103.

Affective Spectrum Disorders

► Unexplained Illness

Afferent

John Bigbee
Virginia Commonwealth University
Richmond, VA, USA

Synonyms

Sensory

Definition

Afferent is an anatomical term that indicates functional directionality. In nervous tissue, afferent is often used synonymously with sensory information when it refers to nerves carrying impulses from peripheral receptors toward the central nervous system. Afferent can also be used in general to refer to any connection coming into a structure within the nervous system. The opposite direction of conduction is efferent.

Afferent Paresis

Maryellen Romero
Tulane University Health Sciences Center
New Orleans, LA, USA

Definition

A deficit in the ability to perform voluntary movements due to loss of kinesthetic feedback. The primary and secondary motor cortices have extensive inputs from the somatosensory areas in the parietal lobes. Following lesions to this latter area, particularly the post-central gyrus or to the lemniscal system which provides proprioceptive information to it, motor difficulties may be observed either in the limbs or in speech production. Although the muscles involved in such activities are not weak per se, the loss of sensory information results in a disruption of motor control and an imprecise excitation of muscle groups required to execute specific, voluntary fine-motor responses.

Cross References

▶ Lemniscal System

References and Readings

Luria, A. L. (1976). *The working brain: An introduction to neuropsychology.* New York: Perseus Books Group.

Age Decrements

Sandra Banks
Allegheny General Hospital
Pittsburgh, PA, USA

Synonyms

Age-associated cognitive decline

Definition

The concept of age decrements in neuropsychology refers to a decline in cognitive performance due to normal aging rather than due to an extraneous or internal event that is known to negatively affect cognitive performance, such as a traumatic brain injury, stroke, psychiatric symptoms, and extensive drug use history.

Current Knowledge

Variability in the performance of aging individuals adds complexity to the determination of specific age decrements on neuropsychological tests. It is generally thought that individuals are more likely to retain "crystallized" knowledge (e.g., that which is practiced, overlearned, and skill-based) than "fluid" knowledge (e.g., problem-solving). As there are factors that heighten the risk for age decrements, protective factors may counteract the risk. For instance, higher levels of education and positive health status may slow down the rate of cognitive decline that would otherwise occur with increasing age.

One concept that illustrates age decrements is Age-Associated Memory Impairment (AAMI), which pertains to age-related decline in performance specifically in terms of memory.

Cross References

► Cognitive Reserve
► Memory Impairment

References and Readings

Lezak, M. D. (2004). *Neuropsychological assessment* (4th Ed.). New York: Oxford University Press.

Age Equivalent

► Mental Age

Age-associated Cognitive Decline

► Age Decrements
► Mild Cognitive Impairment

Age-Associated Memory Impairment (AAMI)

► Benign Senescent Forgetfulness

Agenesis of Corpus Callosum

John E. Mendoza
Tulane University Medical Center
New Orleans, LA, USA

Definition

A developmental defect in which either all or part of the corpus callosum fails to develop.

Current Knowledge

Agenesis can result from various etiologies, including genetic predisposition, chromosomal abnormalities, or intrauterine trauma, such as infection. When present, this condition is commonly associated with other neuroanatomical anomalies, metabolic disturbances, and/or neurobehavioral deficits. The latter might include mental retardation, seizures, motor deficits, and psychiatric disturbances. However, some patients may be relatively asymptomatic, the callosal defect being discovered only serendipitously late in life. The latter is more likely to occur when the agenesis is not accompanied by other neurological or metabolic defects. Whereas "disconnection syndromes" are routinely present following surgical commissurotomy for intractable epilepsy, they are generally not present with agenesis.

References and Readings

Aicardi, J., Chevrie, J.-J., & Baraton, J. (1987). Agenesis of the corpus callosum. In P. J. Vinken, G. W. Bruyn, & H. L. Klawans (Eds.), *Handbook of clinical neurology* (Vol.50, pp. 149–173). New York: Elsevier.

Marszal, E., Jamroz, E., Pilch, J., Kluczewska, E., Jablecka, H., & Krawczyk, R. (2000). Agenesis of the corpus callosum: Clinical description and etiology. *Journal of Child Neurology, 15*, 401–405.

Zaidel, E., & Iacoboni, M. (2003). *The parallel brain: The cognitive neuroscience of the corpus callosum*. Cambridge, MA: MIT Press.

Ageusia

Maryellen Romero
Tulane University Health Sciences Center
New Orleans, LA, USA

Definition

Ageusia is the loss of the sense of taste. The disorder should be distinguished from a disruption in the ability to perceive *flavor*, which requires a combination of olfactory, gustatory, and somatosensory functions. Frequently, complaints of ageusia are often explained by olfactory

dysfunction rather than a disruption in taste perception, *per se.* The majority of taste receptors (buds) are located on the tongue and this information is carried by the VIIth (anterior two thirds) and IXth (posterior third) cranial nerves, with other taste receptors (cranial nerve X) located in other regions of the mouth and throat. These taste fibers enter the solitary nucleus (rostral portion) in the upper medulla and from there second-order neurons travel to the ventral posterior medial nuclei of the thalamus. Thalamic projections carrying this gustatory information then project to the post-central gyrus in the region of the parietal operculum and to the underlying insular cortex where the sensation of taste is likely experienced.

Lesions of the VIIth nerve can result in loss of taste in the ipsilateral anterior two thirds of the tongue which is more readily assessable to clinical testing than lesions of the IXth or Xth nerves. However, total loss of taste (ageusia) is seldom seen as a result of structural lesions because of the multiple and bilateral pathways involved. Ageusia (or hypogeusia) is more likely to result from more systemic problems such as treatments for cancer (radiation, chemotherapy), certain types of influenza, diabetes, or certain medications. Taste acuity (hypogeusia) can decline with age and may contribute to the anorexia and weight loss often seen in elderly persons. The prognosis in acquired ageusia is often correlated directly with the expected course of the illness or injury causing the dysfunction.

Cross References

► Taste

References and Readings

Cerf-Ducastel, Van de Moortele, P.-F., MacLeod, P. Le Bihan, D., & Faurion, A. (2001). Interaction of gustatory and lingual somatosensory perceptions at the cortical level in the human: A functional magnetic resonance imaging study. *Chemical Senses*, May 1, *26*(4), 371–383.

Doty, R. L., & Kimmelman, C. P. (1992). Lesser20R.P. Smell and taste and their disorders. In A. K. Asbury, G. M. McKhann, & W. I. McDonald (Eds.), *Diseases of the nervous system* (2nd ed., pp. 390–403). Philadelphia, PA: W.B. Saunders.

Wilson-Pauwek, L., Akesson, E., & Stewart, P. (1988). *Cranial nerves: Anatomy and clinical comments.* Philadelphia, PA: B.C. Decker.

Aggravating Factors

Robert L. Heilbronner
Chicago Neuropsychology Group
Chicago, IL, USA

Definition

Refers to any relevant circumstances in correspondence with the evidence presented during the trial that, from the perspective of the jurors, makes the harshest penalty appropriate. By contrast, mitigating factors refer to evidence regarding the defendant's character or circumstances related to the crime that would provide foundation for a juror to vote for a lesser sentence.

Historical Background

In 1972, the U.S. Supreme Court considered the death penalty to be a cruel and an unusual punishment because the manner in which capital sentences were decided in Georgia was capricious (Furman v. Georgia, 1972). This decision discontinued death penalty litigation in the USA at that time because none of the states had a system that was substantially different. In 1976 (*Gregg v. Georgia*), the Court accepted as constitutional Georgia's rewrite of their statute which included a capital sentencing process that required presentation before a judge or jury of aggravating and mitigating factors. It required at least one or ten specified aggravating circumstances to be established beyond reasonable doubt to impose the death penalty. Some examples include: whether the crime (murder) was particularly cruel and atrocious, if more than one victim was murdered, whether the murder occurred during the commission of a felony, etc.

Current Knowledge

Laws regarding how aggravating or mitigating factors should be weighed by jurors vary based on state laws. Neuropsychological assessments in death penalty cases typically focus on mitigating factors, such as neuropsychological or neurobehavioral impairments, as there is an increased body of evidence demonstrating a preponderance of neurocognitive deficits in violent criminals. Neuropsychological assessment with respect to aggravating factors is less common and typically addresses increased risk of future dangerousness.

Cross References

► Mitigating Factors

References and Readings

Denney, R. L. (2005). Criminal responsibility and other criminal forensic issues. In G. Larrabee (Ed.), *Forensic neuropsychology: A scientific approach.* New York: Oxford University Press.

Furman v. Georgia, 408 U.S. 238 (1972).

Gregg v. Georgia, 49 L.Ed.2d. 859 (1976).

Melton, G. B., Petrila, J., Poythress, N. G., & Slobogin, C. (2007). *Psychological evaluations for the courts: A Handbook for mental health professionals and lawyers. (*3rd ed.). New York: Guilford Press.

Agitated Behavior Scale

Daniel N. Allen
University of Nevada
Las Vegas, Nevada, USA

Synonyms

ABS

Description

The agitated behavior scale (ABS) was designed to evaluate agitation and other problematic behaviors that commonly occur during the acute recovery phase following traumatic brain injury (Corrigan, 1989). The ABS is composed of 14 items that represent a number of commonly occurring problematic behaviors such as short attention span, impulsivity, uncooperativeness, violence, and angry outbursts. Information that assists in completing the ABS, including descriptions of the behaviors and ratings for each item, as well as examples, is available with the author (Corrigan). Each item is rated on a 1–4-point scale based on intensity of the behavior or frequency of its occurrence. Additionally, when assigning ratings, the degree to which the behavior interferes with functional behavior is also considered. If the behavior is absent a rating of 1 is assigned. When the behavior is present a rating of 2 or greater is assigned, with a rating of 4 indicating that the behavior is present to an extreme degree. A total score is derived by summing across all 14 items (range 14–56) with scores less than 22 in the normal range, scores of 22–28 indicating mild agitation, 29–35 moderate agitation, and 35–56 severe agitation. Subscale scores can also be calculated for disinhibition, aggression, and lability although it appears that ABS primarily measures a single construct (Bogner et al., 2000), so that the total score may be most appropriate when interpreting test results.

Current Knowledge

The ABS is often used to perform serial assessments to track changes in agitation that occur as a natural part of the recovery process and as a result of treatment. Although designed with traumatic brain injury in mind, the ABS has also been used to assess agitation in other populations, such as patients with progressive dementia (Corrigan, Bogner, and Tabloski, 1996; Tabloski, McKinnon-Howe, and Remington, 1995). No differences have been found between males and females with brain injury on the total score or the subscale scores (Kadyan et al., 2004). Internal consistency estimates range from 0.74 to 0.92 (Bogner et al., 1999; Corrigan, 1989), with interrater reliability of 0.92 for the total score, and with comparable reliabilities of 0.90, 0.91, and 0.73 for the disinhibition, aggression, and lability scores, respectively. Subscale to total score correlations range from 0.43 to 0.55. The construct validity of the ABS has been supported by factor-analytic studies that demonstrated the presence of three factors representing disinhibition, aggression, and lability (Corrigan and Bogner, 1994). ABS scores account for a substantial portion of the variance (from 36% to 62%) in independent observations of agitation (Corrigan, 1989) and are able to predict changes in cognition (Corrigan and Mysiw, 1988), which provides additional support for its validity. Thus, there is evidence that the ABS is a highly practical measure with sound psychometric properties that allow for serial assessment of agitation in populations with brain injury.

Cross References

► Post-traumatic Confusional State
► Traumatic Brain Injury

References and Readings

Bogner, J. A., Corrigan, J. D., Bode, R. K., & Heinemann, A. W. (2000). Rating scale analysis of the Agitated Behavior Scale. *Journal of Head Trauma Rehabilitation, 15*, 656–659.

Bogner, J. A., Corrigan, J. D., Stange, M., & Rabold, D. (1999). Reliability of the Agitated Behavior Scale. *Journal of Head Trauma Rehabilitation, 14*, 91–96.

Corrigan, J. D. (1989). Development of a scale for assessment of agitation following traumatic brain injury. *Journal of Clinical and Experimental Neuropsychology, 11*, 261–277.

Corrigan, J. D. & Bogner J. A. (1994). Factor structure of the Agitated Behavior Scale. *Journal of Clinical and Experimental Neuropsychology, 16*, 386–392.

Corrigan, J. D. & Mysiw, W. J. (1988). Agitation following traumatic head injury: equivocal evidence for a discrete stage of cognitive recovery. *Archives of Physical Medicine and Rehabiltation, 69*, 487–492.

Kadyan, V., Mysiw, W. J., Bogner, J. A., Corrigan, J. D., Fugate, L. P., & Clinchot, D. M. (2004). Gender differences in agitation after traumatic brain injury. *American Journal of Physical Medicine & Rehabilitation, 83*, 747–752.

Agitation

Paul D. Newman
Drake Center
Cincinnati, OH, USA

Synonyms

Posttraumatic agitation

Definition

Agitation is an *excess* of one or more behaviors that occur during the course of delirium when cognition is impaired. The behaviors most often in excess during agitation include aggression, akathisia, disinhibition, and/or emotional lability. Specific examples of agitated behavior may include pacing, hand wringing, pulling at tubes or restraints, inappropriate verbalizations, excessive crying or laughter, etc.

Agitation is often conceptualized to result from an inability to cope with overstimulation. Stimulation may be internal (e.g., pain or hallucinations) or external (e.g., noise, light, or conversation). One's ability to cope with stimulation may be viewed as a threshold. Adverse changes to the brain's typical functioning have the potential to lower this threshold. Thus, individuals with traumatic brain injury or dementia may become agitated at lower levels of stimulation than noninjured individuals.

Current Knowledge

There was no consensus on the definition of agitation within the greater health-care profession for many years. Clinicians in neuro-rehabilitation were using the term in the early 1980s to describe a pattern of behavior observed during recovery from traumatic brain injury. The development of the Agitated Behavior Scale by Corrigan and associates in the late 1980s to measure this brain-injury-related behavior led to a more refined definition of the term. The term is not limited to just traumatic brain injury as agitation can manifest in any setting in which an individual experiences delirium and impaired cognition (e.g., dementia).

The importance of the concept of agitation and its measurement was vital to the establishment of the now accepted viewpoint that recovery from agitation is preceded by improvement in cognition. Or conversely, interventions that decrease arousal and/or cognition can lead to a worsening of agitation.

Cross References

▶ Agitated Behavior Scale
▶ Behavior Management
▶ Deescalation
▶ Dementia
▶ Frustration Tolerance
▶ Post-traumatic Confusional State
▶ Traumatic Brain Injury

References and Readings

Corrigan, J. D. (1989). Development of a scale for assessment of agitation following traumatic brain injury. *Journal of Clinical and Experimental Neuropsychology, 69*, 261–277.

Sandel, M. E., & Bysiw, W. J. (1996). The agitated brain injured patient. Part 1: Definitions, differential diagnosis, and assessment. *Archives of Physical Medicine and Rehabilitation, 77*, 617–623.

Smith, M., Gardner, L. A., Hall, G. R., & Buckwalter, K. C. (2004). History, development, and future of the progressively lowered stress threshold: A conceptual model for dementia care. *Journal of the American Geriatric Society, 52*, 1755–1760.

Agnogenic Medial Arteriopathy

▶ Cadasil

A

Agnosia

Anastasia Raymer
Old Dominion University
Norfolk, VA, USA

Definition

Agnosia is a failure to recognize a sensory stimulus that is not attributable to dysfunction of peripheral sensory mechanisms or to other cognitive impairments associated with brain damage (Bauer & Demery, 2003). Agnosia is often described as a percept that is "stripped of its meaning." The individual can respond to the presence of the stimulus, but has difficulty processing the perceptual information in sufficient detail to make sense of and meaningfully recognize it. The stimulus can be recognized through other sensory modalities.

Current Knowledge

Agnosia can occur in any perceptual modality, though it is most commonly reported to affect the visual modality (Farah, 1990). Multi-modality forms of agnosia also have been described (Feinberg, Rothi, and Heilman, 1986). Lesions associated with agnosia will vary across sensory modalities, usually affecting bilateral post-Rolandic cortical sensory regions or disconnecting incoming pathways from one hemisphere to the other (Bauer & Demery, 2003).

Different forms of agnosia have been described that depend upon how much incoming information can be processed. Some forms (e.g., apperceptive agnosia) are associated with disruption at early stages of perceptual processing. The person cannot copy or match an incoming percept to a like stimulus and may make perceptual confusions, yet can conjure up some perceptual information from memory (e.g., visual imagery tasks) or answer questions about perceptual attributes of a stimulus. In other forms of agnosia (e.g., associative agnosia), the person can copy or match percepts, but is not able to conjure up information about perceptual characteristics of a stimulus from memory and also has difficulty appreciating the meaningfulness of a percept, its category, context, associated objects and actions. In either case, accurate processing through that perceptual modality is disrupted.

Cross References

▶ Apperceptive Visual Agnosia
▶ Associative Visual Agnosia
▶ Auditory Agnosia
▶ Pure Word Deafness
▶ Tactile Agnosia
▶ Visual Object Agnosia

References and Readings

Bauer, R. M., & Demery, J. A. (2003). Agnosia. In K. M. Heilman & E. Valenstein (Eds.), *Clinical neuropsychology* (4th ed., pp. 236–295). New York: Oxford University Press.

Farah, M. J. (1990). *Visual agnosia*. Cambridge, MA: MIT Press.

Feinberg, T. E., Rothi, L. J. G., & Heilman, K. M. (1986). Multimodal agnosia after unilateral left hemisphere lesion. *Neurology, 36*, 864–867.

Riddoch, M. J., & Humphreys, G. W. (2001). Object recognition. In B. Rapp (Ed.), *The handbook of cognitive neuropsychology* (pp. 45–74). Philadelphia, PA: Psychology Press.

Agonist

▶ Receptor Spectrum

Agonist Spectrum

▶ Receptor Spectrum

Agrammatic Aphasia

▶ Agrammatism

Agrammatic Speech

▶ Telegraphic Speech

Agrammatism

Lyn Turkstra[1], Cynthia K. Thompson[2]
[1]University of Wisconsin-Madison
Madison, WI, USA
[2]Northwestern University
Evanston, IL, USA

Synonyms

Agrammatic aphasia

Definition

Agrammatism refers to language production that is lacking in grammatical structures. The basic signs of agrammatism are short phrase length, simplified syntax, errors and omissions of main verbs, and omission or substitution of grammatical morphemes such as plural markers or functors (Saffran, Berndt, & Schwartz, 1989). There may also be errors in tense, number, and gender, and difficulty in producing sentences with movement of grammatical elements, such as passive sentences, Wh- questions, and complex sentences (Benedet, Christiansen, & Goodglass, 1998; Caplan & Hanna, 1998; Goodglass, 1997; Faroqi-Shah & Thompson, 2004). Spoken and written production typically shows similar error patterns. Typically, individuals with agrammatic aphasia also show impaired comprehension of grammatical structures, particularly noncanonical semantically reversible sentences (e.g., "the boy was kicked by the horse"; Berndt, Mitchum, & Haendiges, 1996; Caramazza & Zurif, 1976).

Historical Background

Historically, agrammatism was thought of as a syndrome typically associated with nonfluent aphasia (Goodglass, 1997). More recent studies (e.g., Dick et al., 2001) have shown that features of agrammatism are present in the production of many individuals with various forms of aphasia, as well as in normal speakers under stressful conditions, and agrammatism is not attributable to any single site of lesion.

Current Knowledge

The underlying mechanisms of agrammatism have been debated in the literature over the past several decades. Some authors have argued that agrammatism reflects an *underlying impairment* in language representation and/or processing (Grodzinsky 1986, 1990, 1995; Zurif, Swinney, Prather, Solomon, & Bushell, 1993), while others contend that they represent the speaker's *strategic adaptation* to an underlying language processing impairment that is not specific to grammar (Kolk & Heeschen, 1990; also see discussion in Beeke, Wilkinson & Maxim, 2007). Consistent with the processing deficit view, individuals with agrammatic aphasia show problems computing syntactic structures in real time (Dickey, Choy, & Thompson, 2007; Swinney, Prather, & Love, 2000; but see Blumstein et al., 1998) and also may have deficits that impact both production and comprehension, although not always the same structures (Dickey, Milman, & Thompson, 2008). Also, the structures that typically are impaired in agrammatic aphasia are similar across many languages. In support of the adaptation view, there is evidence that the grammatical structures used by individuals with agrammatic aphasia vary as a function of the task. For example, individuals with agrammatic aphasia may produce more complex sentences on standardized language tests, in which grammatical completeness is the focus, than in conversational interactions, in which the message and interaction are the focus and the communication partners are co-constructing a dialog (Beeke, Maxim, & Wilkinson, 2008).

There is evidence of treatment efficacy for interventions aimed improvement of underlying representation/processing impairments and deficits in adaptation. Verb as Core (Loverso, Prescott, & Selinger, 1986), Mapping Therapy (Schwartz, Saffran, Fink, & Myers, 1994), and Treatment of Underlying Forms (TUF; Thompson, Shapiro, Kiran, & Sobecks, 2003; Thompson, 2008) focus treatment on verbs and verb argument structure, training patients to map form to meaning in both simple and complex sentences. Notably, TUF results in strong generalization from complex to simple structures by controlling the lexical and syntactic variables of sentences trained (see Thompson & Shapiro, 2007, for review). Various approaches to treatment of grammatical morphology, such as deficits in verb tense and agreement, also have been shown to be efficacious (Faroqi-Shah, 2008; Friedmann, Wenkert-Olenik, & Gil, 2000; Mitchum & Berndt, 1994; Weinrich, Boser, & McCall, 1999).

Cross References

▶ Aphasia
▶ Grammar

A

► Nonfluent Aphasia
► Paragrammatism
► Syntax
► Telegraphic Speech

References and Readings

Beeke, S., Maxim, J., & Wilkinson, R. (2008). Rethinking agrammatism: Factors affecting the form of language elicited via clinical test procedures. *Clinical Linguistics and Phonetics, 22*(4–5), 317–323.

Beeke, S., Wilkinson, R., & Maxim, J. (2007). Individual variation in agrammatism: A single case study of the influence of interaction. *International Journal of Language and Communication Disorders, 42*(6), 629–647.

Benedet, M. J., Christiansen, J. A., & Goodglass, H. (1998). A cross-linguistic study of grammatical morphology in Spanish- and English-speaking agrammatic patients. *Cortex, 34*(3), 309–336.

Berndt, R. S., Mitchum, C. C., & Haendiges, A. N. (1996). Comprehension of reversible sentences in "agrammatism": A meta-analysis. *Cognition, 58*(3), 289–308.

Blumstein, S. E., Byma, G., Kurowski, K., Hourihan, J., Brown, T., & Hutchinson, A. (1998). On-line processing of filler-gap construction in aphasia. *Brain and Language, 61*, 149–168.

Caplan, D., & Hanna, J. E. (1998). Sentence production by aphasic patients in a constrained task. *Brain and Language, 63*(2), 184–218.

Caramazza, A., & Zurif, E. B. (1976). Dissociation of algorithmic and heuristic processes in language comprehension: Evidence from aphasia. *Brain and Language, 3*(4), 572–582.

Dick, F., Bates, E., Wulfeck, B., Utman, J. A., Dronkers, N., & Gernsbacher, M. A. (2001). Language deficits, localization, and grammar: Evidence for a distributive model of language breakdown in aphasic patients and neurologically intact individuals. *Psychological Review, 108*(4), 759–788.

Dickey, M. W., Choy, J., & Thompson, C. K. (2007). Real-time comprehension of wh-movement in apahsia: Evidence from eyetracking while listening. *Brain and Language, 100*, 1–22.

Dickey, M. W., Milman, L. H., & Thompson, C. K. (2008). Judgment of functional morphology in agrammatic aphasia. *Journal of Neurolinguistics, 21*(1), 35–65.

Faroqi-Shah, Y., & Thompson, C. K. (2004). Semantic, lexical, and phonological influences on the production of verb inflections in agrammatic aphasia. *Brain and Language, 89*(3), 484–498.

Faroqi-Shah, Y. (2008). A comparison of two theoretically-driven treatments of verb inflections in agrammatic aphasia. *Neuropsychologia, 46*, 3088–3100.

Friedmann, N., Wenkert-Olenik, D., & Gil, M. (2000). From theory to practice: Treatment of agrammatic production in hebrew based on the tree pruning hypothesis. *Journal of Neurolinguistics, 13*, 250–254.

Grodzinsky, Y. (1986). Language deficits and syntactic theory. *Brain and Language, 27*, 135–159.

Grodzinsky, Y. (1990). *Theoretical perspectives on language deficits.* Cambridge, MA: MIT Press.

Grodzinsky, Y. (1995). A restrictive theory of agrammatic comprehension. *Brain and Language, 50*, 27–51.

Goodglass, H. (1997). Agrammatism in aphasiology. *Clinical Neuroscience, 4*(2), 51–56.

Kolk, H. H. J., & Heeschen C. (1990). Adaptation symptoms and impairment symptoms in Broca's aphasia. *Aphasiology, 4*, 221–231.

Loverso, F. L., Prescott, T. E., & Selinger, M. (1986). Cuing verbs: A treatment strategy for aphasic adults. *Journal of Rehabilitation Research, 25*, 47–60.

Mitchum, C., & Berndt, R. (1994). Verb retrieval and sentence construction: Effects of targeted intervention. In M. J. Riddoch & G. Humphreys (Eds.), *Cognitive neuropsychology and cognitive rehabilitation.* Hove, Sussex: Erlbaum.

Saffran, E. M., Berndt, R. S., & Schwartz, M. F. (1989). The quantitative analysis of agrammatic production: Procedure and data. *Brain and Language, 37*(3), 440–479.

Schwartz, M. F., Saffran, E. M., Fink, R. B., & Myers, J. L. (1994). Mapping therapy: A treatment programme for agrammatism. *Aphasiology, 8*, 19–54.

Swinney, D., Prather, P., & Love, T. (2000). The time course of lexical access and the role of context: Converging evidence from normal and aphasic processing. In Y. Grodzinsky, L. P. Shapiro, & D. Swinney (Eds.), *Language and the brain: Representation and processing.* New York: Academic Press.

Thompson, C. K., & Shapiro, L. P. (2007). Complexity in treatment of syntactic deficits. *American Journal of Speech and Language Pathology, 16*, 30–42.

Thompson, C. K., Shapiro, L. P., Kiran, S., & Sobecks, J. (2003). The role of syntactic complexity in treatment of sentence deficits in agrammatic aphasia: The complexity account of treatment efficacy (CATE). *Journal of Speech, Language and Hearing Research, 42*, 690–707.

Weinrich, M., Boser, K. I., & McCall, D. (1999). Representation of linguistic rules in the brain: Evidence from training an aphasic patient to produce past tense verb morphology. *Brain and Language, 70*, 144–158.

Zurif, E., Swinney, D., Prather, P., Solomon, J., & Bushell, C. (1993). On-line analysis of syntactic processing in Broca's and Wernicke's aphasia. *Brain and Language, 45*, 448–464.

Agranular (Motor Cortex)

► Primary Cortex

Agraphia

Pélagie M. Beeson[1,2], Steven Z. Rapcsak[1,2,3]
[1]Department of Speech, Language, & Hearing Sciences
[2]Department of Neurology
[3]Southern VA Health Care System, The University of Arizona
Tucson, AZ, USA

Synonyms

Written language disorders

Short Description or Definition

Agraphia is the term applied to acquired disorders of spelling or writing caused by neurological damage in individuals with normal premorbid literacy skills. There are several different agraphia profiles that variously result from impairments of spelling knowledge, sound-to-letter correspondences, letter-shape information, or motor control for handwriting. Although agraphia can occur in relative isolation, it often co-occurs with acquired impairments of reading (alexia) and spoken language (aphasia).

Categorization

Several distinct forms of acquired agraphia occur that reflect specific combinations of impaired and preserved spelling and writing abilities following damage to certain brain regions. Spelling difficulties can result from damage to *central* linguistic processes supported by the language-dominant hemisphere in a manner analogous to acquired impairments of reading (► alexia). Agraphia can also result from disruption of *peripheral* processing components that guide the selection and production of appropriate letter shapes.

Common central agraphia syndromes

- *Phonological agraphia* refers to an impaired ability to manipulate the sound system of the language (phonology) which manifests as a disproportionate difficulty with the spelling of nonwords (e.g., *flig*, *merber*) compared with real words.
- *Deep agraphia* is characterized by a marked impairment of spelling ability for nonwords, as seen in phonological agraphia, but with the additional hallmark feature of semantic errors (e.g., *car* for *vehicle)*.
- *Surface agraphia* (also called lexical agraphia) is characterized by relatively preserved ability to spell nonwords and regularly spelled words in the face of marked impairment of spelling words with irregular sound–letter correspondences, such as *choir*.

Common peripheral agraphia syndromes

- *Allographic agraphia* is an impairment of written spelling due to errors in letter selection.
- *Apraxic agraphia* is an impairment of the selection and implementation of graphic motor programs necessary to move the hand to form letter shapes.
- *Micrographia* is the production of abnormally small letters due to defective control of the force, speed, and amplitude of handwriting movements.

Epidemiology

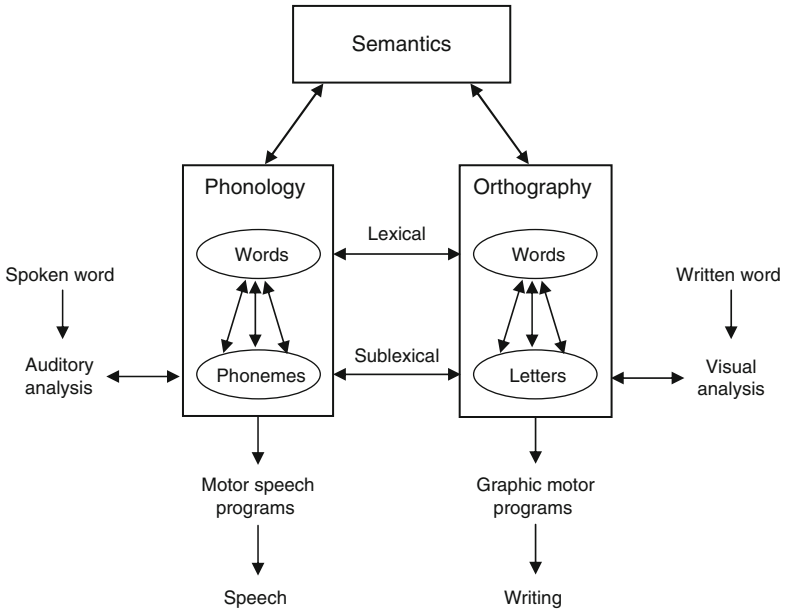
Agraphia is commonly observed following damage to the language-dominant left hemisphere. Although it is most frequently caused by stroke, agraphia can follow any kind of focal damage to the brain regions critical for implementing the various cognitive operations necessary for normal spelling and writing. Agraphia is also observed in individuals with neurodegenerative disorders, including those with primary progressive aphasia/semantic dementia or Alzheimer's disease. The specific agraphia profile reflects the region of cortical damage or atrophy.

Natural History, Prognostic Factors, Outcomes

The prognosis for recovery from agraphia depends on the etiology of the lesion and the extent of the underlying brain damage. Agraphia following stroke or traumatic brain injury tends to show some spontaneous recovery in the first months after brain damage occurs, but residual impairments often persist. Additional improvements may be achieved with behavioral treatment directed toward strengthening the weakened cognitive processes that support spelling or motor control for writing. In individuals with neurodegenerative disorders, progressive worsening of the spelling impairment is observed along with the gradual deterioration of other language and cognitive functions.

Neuropsychology and Psychology of Agraphia

Written words are typically produced in response to activation of a concept in the semantic system. The motivation to write a word may be driven by the desire to convey a message, or in response to an auditory stimulus, as in the context of writing a word to dictation. As depicted in the cognitive model of single-word processing in Fig. 1, the word meaning (semantics) and the phonological word form (phonology) both provide access to spelling knowledge (orthography). In literate adults, the spellings of familiar words are easily recalled as whole words from one's spelling vocabulary (i.e., orthographic lexicon). In contrast to this *lexical* approach, spellings can be assembled on the basis of the knowledge of sound-to-letter correspondences using a *sublexical* processing strategy as depicted in Fig. 1. A sublexical approach is often employed when one is unsure about the spelling of a



Agraphia. Figure 1 A cognitive model indicating the component processes involved in spelling and writing

word, or when required to spell an unfamiliar word or a nonword, such as *glope*. Spelling via sound–letter correspondences is likely to yield correct responses for regularly spelled words, such as *drive*, but over-reliance on the sublexical route will result in phonologically plausible errors for irregularly spelled words, such as *kwire* for *choir*. Thus, according to a dual-route model as depicted in Fig. 1, only the lexical route can deliver correct spellings for irregularly spelled words. The final stages of writing require translation of abstract spelling knowledge into letter shapes and selection and implementation of the graphic motor programs for the appropriate handwriting movements. The various agraphia syndromes reflect specific impairments to these component processes necessary for spelling and writing.

Phonological/Deep Agraphia

Phonological agraphia is characterized by difficulty in the generation of spellings on the basis of sound-to-letter correspondences. This problem is particularly evident during clinical evaluation when an individual is asked to generate plausible spellings for nonwords. The disproportionate difficulty in spelling nonwords compared to familiar words gives rise to an exaggerated *lexicality effect* (Henry, Beeson, Stark, & Rapcsak, 2007; Rapcsak et al., 2009). According to a dual-route model (Fig. 1), poor nonword spelling in phonological agraphia is attributable to damage to the sublexical route, while the better preserved real-word spelling by these patients reflects the residual functional capacity of the lexical and semantic routes. There is evidence to suggest that phonological agraphia reflects a central impairment of phonological processing ability that is also apparent on reading tasks; however, the spelling impairment is typically of greater severity due to the fact that spelling is a harder task than reading (Rapcsak et al., 2009). Although spelling accuracy for words (both regular and irregular) is better preserved than spelling of nonwords, performance is often degraded to some extent relative to premorbid performance. Due to the reliance on lexical processing with limited sublexical input, real word spelling is typically influenced by lexical-semantic variables such as word frequency (high > low), imageability (concrete > abstract), and grammatical class (nouns > verbs > functors). Deep agraphia includes all of the characteristic features of phonological agraphia, but it is distinguished from the latter by the production of semantic errors (e.g., *husband* written as *wife*). In essence, deep agraphia can be considered a more severe form of phonological agraphia.

Like phonological/deep alexia, phonological/deep agraphia is typically encountered in patients with aphasia syndromes characterized by phonological impairment including Broca's, conduction, and Wernicke's aphasia. In such cases, there is damage to a network of *perisylvian* cortical regions involved in speech production/perception and phonological processing including Broca's area,

precentral gyrus, insula, Wernicke's area, and supramarginal gyrus (Fig. 2). The contribution of these regions to phonological processing skills is evident from lesion studies, but also in functional imaging studies of healthy individuals when they perform a variety of written and spoken language tasks requiring phonological processing (Jobard et al., 2003; Vigneau et al., 2006; Rapcsak et al., 2009). In individuals with deep agraphia, the left hemisphere damage tends to be more extensive than that associated with phonological agraphia, and it has been hypothesized that the right hemisphere may be responsible for the characteristic deep agraphia profile (Rapcsak, Beeson, & Rubens, 1991).

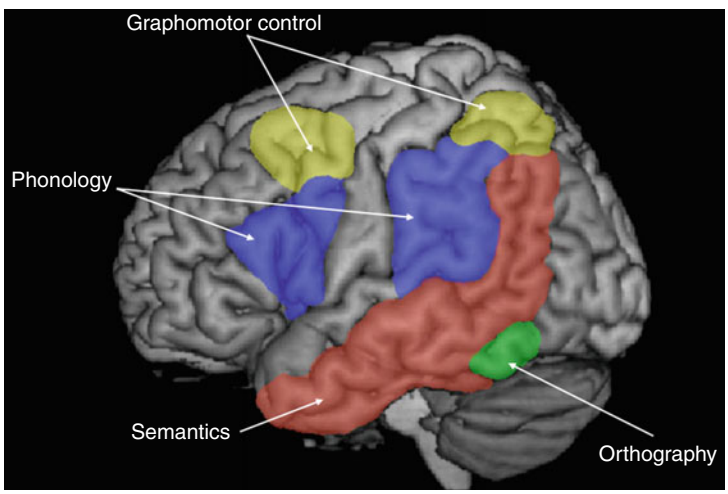
Surface Agraphia

Surface agraphia is characterized by difficulty in spelling irregular words, which contain atypical sound-to-letter correspondences. Regular words are spelled with significantly better accuracy, thus yielding a *regularity effect*. Nonword spelling is relatively preserved. In a manner analogous to surface alexia, a dual-route theory attributes surface agraphia to dysfunction of the lexical spelling route (Fig. 1). Specifically, it has been suggested that the spelling disorder results from damage to the orthographic lexicon (Rapcsak & Beeson, 2004). The loss of word-specific orthographic knowledge prompts reliance on a sublexical phoneme–grapheme conversion strategy that produces phonologically plausible regularization errors on irregular words, a finding that is most pronounced on low frequency items (e.g., *yot* for *yacht*). Surface agraphia may also result from damage to central semantic representations as observed in individuals with semantic dementia (Graham, Patterson, & Hodges, 2000). The reduction in the ability to process lexical-semantic information in such individuals results in overreliance on sublexical spelling procedures and regularization errors. As expected, it is not uncommon to observe co-occurance of surface alexia and agraphia in individuals with semantic dementia (Graham et al., 2000).

Surface agraphia, like surface alexia, is typically associated with *extrasylvian* brain pathology (Fig. 2). Focal lesions that give rise to surface agraphia have been documented in the left inferior occipito-temporal cortex (Rapcsak & Beeson, 2004). This region includes a portion of the fusiform gyrus known as the visual word form area that has been shown to be engaged in healthy adults during reading (Cohen et al., 2002) and spelling tasks (Beeson et al., 2003) and may represent the neural substrate of the orthographic lexicon. Surface agraphia has also been described following focal damage to posterior middle/inferior temporal gyrus and angular gyrus (Rapcsak & Beeson, 2002) and in patients with left anterior temporal lobe atrophy (Graham et al., 2000). In these cases, the spelling deficit may reflect damage to a distributed extrasylvian cortical network involved in semantic processing (Fig. 2).

Allographic Agraphia

Allographic agraphia refers to a disturbance of the ability to activate or select appropriate letter shapes for the abstract orthographic representations generated by central spelling routes. This impairment of handwriting



Agraphia. Figure 2 Cortical regions involved in spelling and writing

is characterized by letter selection errors that often include the substitution of physically similar letter forms (e.g., *b* for *h*). The allographic difficulty may be specific to letter case (upper vs. lower) or style (print vs. cursive). When allographic agraphia occurs in isolation, oral spelling is preserved, as well as the ability to correctly arrange component letters that make up a word (i.e., anagram spelling) and typing. Allographic agraphia is often associated with damage to left temporo-parieto-occipital regions.

Apraxic Agraphia

Apraxic agraphia is characterized by poor letter formation in handwriting that is not attributable to allographic disorder or sensorimotor, cerebellar, or basal ganglia dysfunction. The difficulty arises at the level of motor programming for the skilled movements of the hand so that the spatiotemporal aspects of writing are disturbed. Individual letters are often difficult to recognize, and may simply appear to be meaningless scrawls. Lesions associated with apraxic agraphia have been noted in the hemisphere contralateral to the dominant hand. Thus, in right-handed individuals, the damage typically involves the left superior parietal lobe in the region of the intraparietal sulcus, the dorsolateral premotor cortex just anterior to primary motor cortex for the hand, or the supplementary motor area (Fig. 2).

Nonapraxic Disorders of Motor Execution

In addition to apraxic agraphia, there are several additional disorders of motor execution that affect the ability to form legible letter shapes. These writing difficulties include disturbances of the regulation of movement force, speech, and amplitude. Micrographia (the production of small letters with reduced legibility) is a common example that is associated with the basal ganglia pathology in Parkinson disease. Cerebellar pathology can also result in poor handwriting due to irregular and disjointed hand movements. Handwriting difficulty is also associated with damage to primary sensorimotor cortex and/or associated corticospinal tracts that cause hemiparesis of the dominant hand. When the hemiparesis is marked, individuals typically shift to writing with the nondominant hand. Improvement in graphomotor control of the nondominant hand is apparent with practice and often provides a fully functional substitute; however, the automaticity of motor movements is rarely comparable to the premorbidly dominant hand.

Evaluation

Evaluation of individuals with acquired agraphia is structured so that the status of all the relevant component processes involved in spelling and writing are examined. Controlled word lists for such assessment can be found in the literature (e.g., Beeson & Henry, 2008) or in commercially available test batteries (e.g., Kay, Lesser, & Coltheart, 1992). A comprehensive battery should include regularly and irregularly spelled words as well as nonwords. The evaluation should allow the clinician to identify the nature of the functional impairment and to locate the level of breakdown with reference to a cognitive model of normal spelling. It is equally important to document relatively spared abilities and the use of compensatory strategies by the patient, as this information is helpful in planning treatment.

Treatment

Several behavioral treatment approaches have shown positive outcomes in the rehabilitation of agraphia (for a recent review see Beeson & Henry, 2008). In general, treatment is directed toward strengthening impaired processes and training the use of compensatory strategies necessary to bypass the functional deficit. Because written spelling tasks inherently involve reading, behavioral treatments for spelling can also serve to strengthen reading. However, given that spelling is often significantly more impaired than reading, it is not uncommon to address spelling at a lexical level while treating reading at the text level (Beeson & Rapcsak, 2006).

Cross References

- ▶ Alexia
- ▶ Aphasia
- ▶ Phonological/Deep Alexia
- ▶ Pure Alexia
- ▶ Surface Alexia

References and Readings

Beeson, P. M., & Henry, M. L. (2008). Comprehension and production of written language. In. R. Chapey (Ed.), *Language intervention strategies in adult aphasia* (5th ed., pp. 654–688). Baltimore, MD: Wolters Kluwer/Lippincott, Williams & Wilkins.

Beeson, P. M., & Rapcsak, S. Z. (2002). Clinical diagnosis and treatment of spelling disorders. In A. E. Hillis (Ed.), *Handbook on adult language disorders: Integrating cognitive neuropsychology, neurology, and rehabilitation* (pp. 101–120). Philadelphia: Psychology Press.

Beeson, P. M., & Rapcsak, S. Z. (2006). Treatment of alexia and agraphia. In J. H. Noseworthy (Ed.), *Neurological Therapeutics: Principles and Practice* (2nd ed., pp. 3045–3060). London: Martin Dunitz.

Beeson, P. M., Rapcsak, S. Z., Plante, E., Chargualaf, J., Chung, A., Johnson, S. C., et al. (2003). The neural substrates of writing: A functional magnetic resonance imaging study. *Aphasiology, 17*, 647–665.

Cohen, L., Lehéricy, S., Chochon, F., Lemer, C., Rivaud, S., & Dehaene, S. (2002). Language-specific tuning of visual cortex? Functional properties of the Visual Word Form Area. *Brain, 125*, 1054–1069.

Graham, N. L., Patterson, K., & Hodges, J. R. (2000). The impact of semantic memory impairment on spelling: evidence from semantic dementia. *Neuropsychologia, 38*, 143–163.

Henry, M. L. Beeson, P. M., Stark, A. J., & Rapcsak, S. Z. (2007). The role of left perisylvian cortical regions in spelling. *Brain and Language, 100*, 44–52.

Jobard, G., Crivello, F., & Tzourio-Mazoyer, N. (2003). Evaluation of the dual route theory of reading: A metaanalysis of 35 neuroimaging studies. *NeuroImage, 20*, 693–712.

Kay, J., Lesser, R., & Coltheart, M. (1992). *Psycholinguistic assessments of language processing in Aphasia* (*PALPA*). East Sussex, England: Lawrence Erlbaum Associates.

Rapcsak, S. Z., & Beeson, P. M. (2000). Agraphia. In L. J. G. Rothi, B. Crosson, & S. Nadeau (Eds.), *Aphasia and language: Theory and practice* (pp. 184–220). New York: Guilford.

Rapcsak, S. Z., & Beeson, P. M. (2004). The role of left posterior inferior temporal cortex in spelling. *Neurology, 62*, 2221–2229.

Rapcsak, S. Z., Beeson, P. M., Henry, M. L., Leyden, A., Kim, E. S., Rising, K., et al. (2009). Phonological dyslexia and dysgraphia: cognitive mechanisms and neural substrates. *Cortex, 45*(5), 575–591.

Rapcsak, S. Z., Beeson, P. M., & Rubens, A. B. (1991). Writing with the right hemisphere. *Brain and Language, 41*, 510–530.

Tainturier, M.-J., & Rapp, B. (2001). The spelling process. In B. Rapp (Ed.), *The handbook of cognitive neuropsychology* (pp. 233–262). Philadelphia: Psychology Press.

Vigneau, M., Beaucousin, V., Hervé, P. Y., Duffau, H., Crivello, F., Houdé, O., et al. (2006). Meta-analyzing left hemisphere language areas: phonology, semantics, and sentence processing. *NeuroImage, 30*, 1414–1432.

Ahylognosia

John E. Mendoza
Tulane University Medical Center
New Orleans, LA, USA

Definition

Inability to determine by touch alone certain physical properties of an object such as its texture, density (weight), or resistance to pressure, with difficulties in perceiving size or shape is referred to as amorphognosia. While perhaps seeming a bit artificial, according to Bauer and Demery (2003), the distinction between ahylognosia and amorphognosia apparently traces back to 1935 when a French neurologist, Delay, divided astereognosis into two subtypes of deficits: amorphognosia, which was defined as a difficulty in recognizing the size or shape of an object by touch, and ahylognosia, which was described as a failure to differentiate the "molecular qualities" of an object, such as its density, weight, thermal conductivity, or roughness. Delay also defined a third type of astereognosis, tactile asymboly, which was characterized as the inability to identify an object by touch in the absence of amorphognosia and ahylognosia. These same distinctions were followed by Critchley (1969) and continue to be used by more recent authors (Bauer & Demery, 2003). Hecaen and Albert (1978) in their book, Human Neuropsychology, attempted to explain these distinctions by suggesting that ahylognosia was "the loss of the capacity to differentiate structural components of objects, resulted from impairment of intensity analyzers." By contrast, amorphognosia, was thought to reflect "the loss of the capacity to differentiate forms, resulted from impairment of the analyzers of extent." Because determining any of these qualities requires discriminatory judgments, in the absence of more elementary tactual defects, such disturbances suggest pathology involving the somatosensory areas of the parietal lobe.

Cross References

► Amorphognosis
► Astereognosis
► Tactile Agnosia

References and Readings

Bauer, R. M., & Demery, J. A. (2003). Agnosia. In K. Heilman, & E. Valenstein (Eds.), *Clinical Neuropsychology*, (4th ed., pp. 236–295). New York: Oxford University Press.

Critchley, M. (1969). *The parietal lobes*. New York: Hafner Publishing Co.

Delay, J. (1935). *Les astereognosis. Pathologie due Toucher, Clinque, Physiologie, Topographie*. Paris: Masson.

Hecaen, H., & Albert, M. L. (1978). *Human neuropsychology (Chapter 6, Disorders of somesthesis and somatognosis)*. New York: Wiley.

Akathisia

Anna DePold Hohler[1], Marcus Ponce de Leon[2]
[1]Boston University Medical Center
Boston, MA, USA
[2]William Beaumont Army Medical Center
El Paso, TX, USA

Synonyms

Restlessness

Definition

Akathisia is a syndrome characterized by unpleasant sensations of inner restlessness that manifests itself with an inability to sit still or remain motionless.

Current Knowledge

It is most often seen as a side effect of medications, mainly neuroleptic antipsychotics. Patients may have difficulty describing their symptoms, leading to a misdiagnosis of anxiety and worsening of the condition upon treatment with neuroleptic antipsychotic agents. Several medications have been used to treat the condition, including benztropine and beta-blocking agents. Withdrawal of the offending agent is often most effective. It may be seen with Parkinson's disease.

Cross References

► Parkinson's Disease
► Tardive Dyskinesia

References and Readings

Kumar, A., & Calne, D. (2004). Approach to the patient with a movement disorder and overview of movement disorders. In R. L. Watts, & W. C. Koller (Eds.), *Movement disorders* (2nd ed., p. 9). New York: McGraw-Hill.

Akelaitis, Andrew John Edward ("A.J.") (1904–1955)

Michael J. Larson, Joseph E. Fair
Brigham Young University
Provo, UT, USA

Major Appointments

- Dr. A.J. Akelaitis began his career as an assistant professor in the Department of Medicine, Division of Psychiatry, at the University of Rochester School of Medicine and Dentistry. At the same time, he also held appointments at the clinics of the Strong Memorial and Rochester Municipal Hospitals in Rochester, New York. He left these appointments to serve in the Navy during World War II. Following his service in the war, Dr. Akelaitis worked as an Assistant Professor of Neurology at the New York Medical College and Assistant Professor of Clinical Medicine in Neurology at Cornell University Medical College. He also served as the attending neuropsychiatrist at Mount Vernon (New York) Hospital and on the staff of the Bellevue Hospital and the New York Hospital.

Major Honors and Awards

- Dr. Akelaitis was a Fellow of the American Psychiatric Association. He was specialty certified by the American Board of Psychiatry and Neurology and held membership appointments in the American Medical Association, the New York State Medical Society, the New York Society for Clinical Psychiatry, and the New York Neurological Society.

Landmark Clinical, Scientific, and Professional Contributions

- Dr. A.J. Akelaitis is best known for his observations of patients who underwent sectioning of the corpus callosum (i.e., "split-brain" patients). Beginning in the late 1930s, the neurosurgeon Dr. William P. van Wagenen pioneered surgical sectioning of the corpus callosum for the treatment of intractable epilepsy (Mathews, Linskey, & Binder, 2008). Dr. Akelaitis worked closely with Dr. van Wagenen and performed

pre and postoperative tests of cognitive and neurological functioning on many of these individuals. According to Akelaitis' reports, patients who underwent callosotomy surgery largely did not show lasting changes in cognitive, intellectual, or motor functioning, although their seizure activity was consistently alleviated. For nearly two decades, Akelaitis' reports of largely normal functioning after callosotomy perpetuated the generally accepted belief that sectioning the corpus callosum did not impact cognitive or motor functioning in humans.

- Despite his reports of few neurological changes following callosotomy, Akelaitis noted periodic cases with hemiplegia and praxic disturbances. He was slow, however, to include the sectioning of the corpus callosum in his explanations for these changes; rather, he attributed the symptoms to unintended operative damage to adjacent cortical areas. In some cases, postoperative symptoms were seen as exacerbations of precallosotomy characteristics or were attributed to preexisting and/or postoperative psychological or behavioral factors. Further, many of the symptoms observed by Akelaitis were transient and consequently not considered to be conclusively linked with callosal sectioning (Sauerwein & Lassonde, 1996).
- Several factors most likely influenced Akelaitis' reports of minimal neurological changes following callosotomy surgery. First, the majority of patients Akelaitis observed did not have complete callosotomies, nor were neurosurgical procedures well standardized at the time. Of the 28 patients he studied, only one third were reported to have undergone "complete" callosal sectioning, with the remainder "nearly complete" or "partial" sectioning (Bogen, 1995). The patients with only partially sectioned callosal fibers undoubtedly continued to have interhemispheric transmission, thereby contributing to Akelaitis' findings of generally intact functioning. Next, emerging research at the time reported no cognitive changes following sectioning of the corpus callosum. For example, Walter Dandy stated in 1936 that when "the corpus callosum is split longitudinally. . . no symptoms follow its division. This simple experiment at once disposes of the extravagant claims to the functions of the corpus callosum" (see Zaidel, Iacoboni, Zaidel, & Bogen, 2003). Finally, Akelaitis lacked the technologies, such as the tachistoscope used by his successors, to present stimuli to one visual field. Such technology would possibly have given him insight into the specialization of the two hemispheres and interhemispheric transfer of information via the corpus callosum (Mathews, Linskey, & Binder, 2008).
- Despite his contributions as one of the first individuals to study neurological functioning following callosotomy, Akelaitis has been criticized for employing insensitive or inadequate testing procedures. However, reviews of his cases have confirmed that his patients did exhibit what are now considered typical symptoms, although his explanations for these manifestations, while consistent with much of the research of the time, were often inadequate (Sauerwein & Lassonde, 1996). In the 1950s and 1960s, researchers including Roger Sperry, Michael Gazzaniga, Norman Geschwind, Edith Kaplan, and Joseph Bogen began to publish articles involving callosotomies in animals and humans, which contradicted many of Akelaitis' findings. This sparked renewed interest in the function of the corpus callosum and eventually earned Sperry the Nobel Prize in 1981.
- Through the course of his short career, Dr. Akelaitis made significant contributions toward research on the corpus callosum and advanced the treatment of intractable epilepsy. He also published articles regarding the psychiatric aspects of myxedema (severe hypothyroidism), hereditary and vascular cerebral atrophy, lead encephalopathy, acute demyelinating processes (multiple sclerosis), and Pick's disease.

Short Biography

Andrew John ("A.J.") Akelaitis was born in Baltimore, Maryland, on July 11, 1904. He studied medicine at Johns Hopkins University and received his M.D. in 1929. In the early 1930s, he practiced clinical neurology in Rochester, New York. He subsequently became an Assistant Professor of Medicine at the University of Rochester School of Medicine and Dentistry. Dr. Akelaitis joined the Navy during World War II where he served with distinction at the rank of Commander. He married the former Victoria Chesno. The couple had one son, Andrew, and a daughter, Lillian. Akelaitis died at the New York Hospital on November 24, 1955 at the young age of 51.

Cross References

- ▶ Corpus Callosum
- ▶ Epilepsy
- ▶ Split Brain

References and Readings

Akelaitis, A. J. (1941). Psychobiological studies following section of the corpus callosum: A preliminary report. *American Journal of Psychiatry, 97*, 1147–1157.

Akelaitis, A. J. (1941). Studies on the corpus callosum. II. The higher visual functions in each homonymous field following complete section of the corpus callosum. *Archives of Neurology and Psychiatry, 45*, 788–796.

Akelaitis, A. J., Risteen, W. A., Herren, R. Y., & Van Wagenen, W. P. (1942). Studies on the corpus callosum. III. A contribution to the study of dyspraxia and apraxia following partial and complete section of the corpus callosum. *Archives of Neurology and Psychiatry, 47*, 971–1008.

Akelaitis, A. J. (1944). Studies on the corpus callosum. IV. Diagonistic dyspraxia in epileptics following partial and complete section of the corpus callosum. *American Journal of Psychiatry, 101*, 594–599.

Akelaitis, A. J. (1944). Study on gnosis, praxis, and language following section of corpus callosum and anterior commisure. *Journal of Neurosurgery, 1*, 94–102.

Bogen, J. (1995). Some historical aspects of callosotomy for epilepsy. In A. G. Reeves & D. W. Roberts (Eds.), *Epilepsy and the corpus callosum 2* (pp. 107–121). New York: Plenum Press.

Gazzaniga, M. S. (1995). Principles of human brain organization derived from split brain studies. *Neuron, 14*, 217–228.

Gazzaniga, M. S. (2005). Forty-five years of split-brain research and still going strong. *Nature Reviews: Neuroscience, 6*, 653–659.

Mathews, S., Linskey, M., & Binder, D. (2008). William P. van Wagenen and the first corpus callosotomies for epilepsy. *Journal of Neurosurgery, 108*, 608–613.

Sauerwein, H. C., & Lassonde, M. (1996). Akelaitis' investigations of the first split-brain patients. In C. Code, C.-W. Wallesh, Y. Joanette, & A. R. Lecours (Eds.), *Classic cases in neuropsychology* (pp. 305–317). Hove, East Sussex: Psychology Press.

Zaidel, E., Iacoboni, M., Zaidel, D., & Bogen, J. (2003). The callosal syndromes. In K. M. Heilman & E. Valenstein (Eds.), *Clinical neuropsychology* (pp. 347–403). New York: Oxford University Press.

Akinesia

► Akinesis

Akinesis

Douglas I. Katz
Braintree Rehabilitation Hospital
Braintree, MA, USA
Boston University School of Medicine
Boston, MA, USA

Synonyms

Akinesia; Akinetic

Definition

Akinesis is an absence or paucity of movement, resulting from an abnormal motor control. It is a problem that may occur in Parkinson's disease when patients develop freezing or inability to initiate movement. It may also occur as a result of a paralyzed muscle, such as with an anesthetic nerve block.

Cross References

► Action-Intentional Disorders
► Akinetic Mutism
► Bradykinesia
► Parkinson's Disease

Akinetic

► Akinesis

Akinetic Mutism

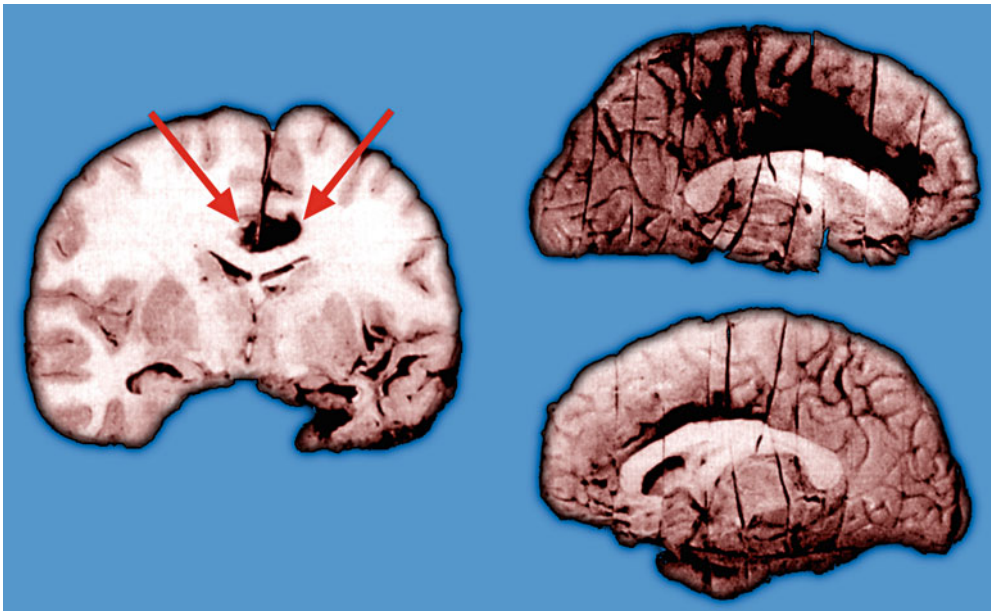
Michael S. Mega
Brain Institute Providence Health System
Portland, OR, USA

Synonyms

A spectrum of motivational impairment has abulia at one end and akinetic mutism at the other. Coma vigil is not akinetic mutism; it arises when a comatose patient regains the sleep-wake cycle, eyes open during the day and closed during sleep at night, usually after 2 weeks of a brain lesion that produces irreversible coma. Coma vigil is also referred to as a persistent vegatative state. When brain lesions disconnect all descending motor output but preserve conscious awareness the patient is said to be *locked in*. In akinetic mutism, patients still respond to their internal and external environment – and thus are not in coma, and they are not locked in since they can accomplish motor output, given sufficient motivation.

Short Description or Definition

The fully formed akinetic mute state usually results from bilateral anterior cingulate lesions (Fig. 1). Patients are



Akinetic Mutism. Figure 1 *Arrows* show the left greater than right anterior cingulate lesions due to bilateral anterior cerebral artery (ACA) ischemic stroke. Bilateral ACA lesions usually result in death due to loss of all limbic motivational input to prefrontal cortex

profoundly apathetic, incontinent, and akinetic. They do not initiate eating or drinking and if speech occurs, it is restricted to terse responses. They seem awake, visually tracking objects, but displaying no emotions – even during painful circumstances, they remain indifferent. The akinetic mute state also results from bilateral subcortical paramedian diencephalic and midbrain lesions possibly affecting the ascending reticular core, medial forebrain bundles, and isolated bilateral globus pallidus lesions.

Categorization

When anterior cingulate lesions are bilateral, limbic, cognitive, and motor activation is disrupted producing profound akinetic mutism. Loss of ascending input from the reticular core, due to bilateral lesions of the medial forebrain bundle, may also produce akinetic mutism. Rarely are complete bilateral lesions seen in humans, more frequently partial circuit disruption results in a graded loss in motivation depending upon which circuit is damaged.

Five frontal-subcortical circuits have been named according to their function or cortical site of origin: the motor circuit, originating in the supplementary motor area, and the oculomotor circuit, originating in the frontal eye fields, are dedicated to motor function. The dorsolateral prefrontal, lateral orbitofrontal, and anterior cingulate circuits support executive cognitive functions, personality, and motivation, respectively (Mega & Cummings, 1994). Each of the five circuits has the same member structures: the frontal lobe, striatum, globus pallidus, substantia nigra, and thalamus. There is a progressive spatial compaction of the circuits as they travel through the basal ganglia. A lesion anywhere along the path of a circuit will produce the same clinical result but only in the globus pallidus interna are all the frontal-subcortical circuits in such a compact spatial volume that a relatively small lesion can have profound effects.

Epidemiology

Akinetic mutism is exceedingly rare when permanent, since a bilateral lesion is necessary and usually results in death. Unilateral anterior cerebral artery (ACA) strokes are the usual cause of transient akinetic mutism, but ACA strokes only make up 1% of all cerebral vascular lesions.

Natural History, Prognostic Factors, and Outcomes

The natural history of akinetic mutism, when it arises from a unilateral lesion, is usually a 2-week period of gradual improvement from the fully formed syndrome to near-complete recovery presumably enabled by contralateral limbic activation gaining access to deafferented networks. The outcome from bilateral lesions is usually death, given no ability for cross-hemispheric motivation. Thus, prognosis will rely upon neuroimaging documenting the extent of the lesion.

Neuropsychology and Psychology

Extracingulate connections support a segregation of the cingulate into functional subregions (for a complete discussion of these circuits, ► *Cingulate Gyrus*). Paralleling the general distinction between posterior granular sensory cortices and anterior agranular executive cortices, the anterior cingulate can be considered an executive region for affective motivation and cognition, while the posterior cingulate, with its prominent granular layer IV receiving sensory input, is engaged in visuospatial and memory processing. The interconnections between the anterior and posterior cingulate allow for regulatory control by the anterior executive effector regions over posterior sensory processing and reciprocal modulation of that regulatory input by the posterior cingulate.

Three anterior effector regions include a *visceral effector region* inferior to the genu of the corpus callosum encompassing area 25, the anterior subcallosal portions of 24a–b, and 32; a *cognitive effector region* that includes most of the supracallosal area 24, and areas 24a′–b′ and 32′; and a *skeletomotor effector region* within the depths of the cingulate sulcus, that includes areas 24c′/23c on the ventral bank, with 24c′g and 6c on the dorsal bank. These three cingulate effector regions integrate ascending input concerning the internal milieu of the organism with visceral motor systems, cognitive-attentional networks, and skeletomotor centers to produce the affective motivation necessary for the organism's engagement in the environment.

Circumscribed lesions in humans are rarely confined to one region of the cingulate. With an anterior lesion, the cognitive, skeletomotor, and visceral effector regions are often affected. Bilateral lesions result in an akinetic mute state. The loss of spontaneous motor activity results when the lesion involves the supplementary motor area and the skeletomotor effector region. When these two motor regions are spared, motor activity will be normal but the patient will demonstrate profound indifference, docility, and the loss of motivation to engage in a task. They can be led by the examiner to engage in a task but will fail to self-generate sustained directed attention. They lack cognitive motivation.

The role of the anterior cingulate as a cognitive effector is appreciated within the realm of language. Language, a cognitive function, is distinguished from the motor function of speech. Transcortical motor aphasia (TCMA) is the usual result of left anterior medial or anterior dorsolateral prefrontal lesions. The classic syndrome of TCMA is initial mutism that resolves in days to weeks, yielding a syndrome featuring delayed initiation of brief utterances without impaired articulation, excellent repetition, inappropriate word selection, agrammatism, and poor comprehension of complex syntax. Activation of dorsolateral prefrontal cortices enabling language and speech arises from two sources: the anterior cingulate and the supplementary motor area (with the cingulate skeletomotor region). When the executive prefrontal cortex (areas 9, 10, and 46) is disrupted, cognitive language deficits are prominent (TCMA, type I); when motor neurons in area 4, devoted to the speech apparatus, are disconnected from their activation, speech hesitancy and impoverished output ensues (TCMA, type II). These two functional realms are separable and can be disconnected anywhere along two pathways. Direct damage to the supplementary motor area or its outflow to the motor cortex traveling in the anterior superior paraventricular white matter will produce TCMA type II. Direct damage to the anterior cingulate, its outflow to areas 9, 10, and 46, or to the caudate – via the subcallosal fasciculus, just inferior to the frontal horn of the lateral ventricle – will disrupt frontal-subcortical circuits involved in motivation and executive cognitive function. The initial muteness has been described by a patient after recovery from an anterior cingulate/supplementary motor infarction as a loss of the "will" to reply to her examiners, because she had "nothing to say," her "mind was empty," and "nothing mattered" (Damasio & Van Hoesen, 1983).

The loss of will to initiate a motor function results from supplementary motor or cingulate skeletomotor region damage, while poor initiation of a cognitive process results from lesions in supracallosal cingulate areas. Loss of emotional vigilance ranging from flattened affect to neglect can be produced by surgery in this region. Anterior cingulate lesions in monkeys – difficult subjects

in which to evaluate subtle behavioral changes – produce either no observable change or result in a transient stupor with ensuing lethargy, tameness, disturbed intraspecies social behavior, and decreased pain sensitivity (Pribram & Fulton, 1954). Removal of the anterior cingulate (areas 24 and 32) in humans (cingulectomy) has been employed as a treatment for epilepsy, psychiatric, and pain disorders.

The cingulum bundle has also been the site of surgical lesions (cingulumotomy when only the bundle is transected, or cingulotomy when cingulate cortex is also removed) to treat psychiatric and pain disorders. The cingulum contains the efferents and afferents of the cingulate to the hippocampus, basal forebrain, amygdala, and all cortical areas, as well as fibers of passage between hippocampus and prefrontal cortex, and from the median raphe to the dorsal hippocampus. Surgical ablation of the anterior portion (sparing fibers relevant to memory function) is most successful when treating aggression, extreme anxiety, obsessive–compulsive behaviors, and severe pain. Psychotic symptoms show only a temporary response. The only prospective long-term follow-up of patients undergoing supracallosal anterior cingulotomy for the treatment of medically refractory obsessive–compulsive disorder revealed a clear response in 28% and a partial response in 17% (Baer, Rauch, Ballantine, Martuza, Cosgrove, Cassem, et al., 1995). Including the subcallosal anterior cingulate/medial orbital cortex may provide the best result in treating the refractory obsessive–compulsive patient (Hay, Sachdev, Cumming, Smith, Lee, Kitchener, et al., 1993) due to the elimination of the visceromotor aspects of the disorder. Postsurgical personality changes are subtle after the acute attentional disorder resolves. Although formal cognitive testing is unaltered, affect is flattened. Motivation for previous enjoyments, such as reading, hobbies, and even spectator sports, is lost (Tow & Whitty, 1953); subtle changes that reflect the loss of higher *cognitive* motivation. The three anterior cingulate regions, by virtue of the distinct functional systems they coordinate, are the conduits through which limbic motivation can activate feeling, thought, and movement – partial lesions produce partial aspects of the akinetic mute state depending upon their location.

Subcortical lesions can also produce the fully formed syndrome. Carbon monoxide poisoning with resultant apathy and placidity was described in a patient with a ventral pallidal lesion who also had hypoperfusion on single photon emission computed tomography (SPECT) predominately in the cingulate bilaterally (Mori, Yamashita, Takauchi, & Kondo, 1996). Hypometabolism on ^{18}F-fluorodeoxyglucose positron emission tomography (FDG-PET) in frontal cortex has also resulted from pallidal lesions (Laplane, Levasseur, Pillon, Dubois, Baulac, Mazoyer, et al., 1989) disconnecting their cortical targets. Yet, when pallidal lesions result from carbon monoxide poisoning, microscopic cortical lesions may contribute to the functional imaging abnormalities. Ventral extension of a pallidal lesion appears to disconnect the anterior cingulate circuit, in nonhuman primates and humans (Mega & Cohenour, 1997), from limbic drive. Bilateral paramedian or anterior thalamic lesions (Nagaratnam, Nagaratnam, Ng, & Diu, 2004), caudate (Grunsfeld & Login, 2006), or putamen (Ure, Faccio, Videla, Caccuri, Giudice, Ollari, et al., 1998) lesions will also disrupt the anterior cingulate frontal-subcortical circuit.

Evaluation

Evaluation of the patient suspected of suffering from akinetic mutism is to first rule out other causes of possible unresponsiveness. Documenting the response to first verbal stimuli, and then sensory stimuli, will provide evidence for or against coma. Patients in coma will not respond to internal (e.g., hunger) or external (e.g., pain) stimuli. All patients who survive the myriad of insults producing coma will regain the sleep-wake cycle and will eventually open their eyes spontaneously. They are then described as being in a persistent vegetative state. The locked-in patient will blink to command and can be taught to use blinking as a form of communication. The patient with akinetic mutism will respond to stimuli but will not initiate an unprovoked response. When any patient with limited response is encountered, a brain imaging study is required in their evaluation.

Treatment

Time is the best treatment for unilateral lesions producing akinetic mutism since after the acute phase of the lesion (4–6 weeks) the patients usually recover limbic activation from unaffected regions. When subcortical lesions destroy ascending dopaminergic fibers in the medial forebrain bundle, patients may respond to dopaminergic agonist (Psarros, Zouros, & Coimbra, 2003), or paradoxically antagonists of the D2 receptor (Brefel-Courbon et al., 2007) and GABA activation (Spiegel, Casella, Callender, & Dhadwal, 2008), perhaps due to blocking feedback-loop inhibition.

Cross References

- ▶ Abulia
- ▶ Amotivation
- ▶ Apathy
- ▶ Cingulate Gyrus

References and Readings

Baer, L., Rauch, S. L., Ballantine, H. T., Martuza, R., Cosgrove, R., Cassem, E., et al. (1995). Cingulotomy for intractable obsessive-compulsive disorder: prospective long-term follow-up of 18 patients. *Archives of General Psychiatry, 52*, 384–392.

Brefel-Courbon, C., Payoux, P., Ory, F., Sommet, A., Slaoui, T., Raboyeau, G., et al. (2007). Clinical and imaging evidence of zolpidem effect in hypoxic encephalopathy. *Annals of Neurology, 62*(1), 102–105.

Damasio, A. R., & Van Hoesen, G. W. (1983). Focal lesions of the limbic frontal lobe. In K. M. Heilman & P. Satz (Eds.), *Neuropsychology of human emotion* (pp. 85–110). New York: Guilford.

Grunsfeld, A. A., & Login, I. S. (2006). Abulia following penetrating brain injury during endoscopic sinus surgery with disruption of the anterior cingulate circuit: case report. *BMC Neurology, 6*, 4.

Hay, P., Sachdev, P., Cumming, S., Smith, J. S., Lee, T., Kitchener, P., et al. (1993). Treatment of obsessive-compulsive disorder by psychosurgery. *Acta Psychiatrica Scandinavica, 87*, 197–207.

Laplane, D., Levasseur, M., Pillon, B., Dubois, B., Baulac, M., Mazoyer, B., et al. (1989). Obsessive-compulsive and other behavioural changes with bilateral basal ganglia lesions. *Brain: A Journal of Neurology, 112*, 699–725.

Mega, M. S., & Cohenour, R. C. (1997). Akinetic mutism: a disconnection of frontal-subcortical circuits. *Neurology, Neuropsychology, and Behavioral Neurology, 10*, 254–259.

Mega, M. S., & Cummings, J. L. (1994). Frontal subcortical circuits and neuropsychiatric disorders. *Journal of Neuropsychiatry and Clinical Neurosciences, 6*, 358–370.

Mori, E., Yamashita, H., Takauchi, S., & Kondo, K. (1996). Isolated athymhormia following hypoxic bilateral pallidal lesions. *Behavioral Neurology, 9*, 17–23.

Nagaratnam, N., Nagaratnam, K., Ng, K., & Diu, P. (2004). Akinetic mutism following stroke. *Journal of Clinical Neuroscience: Official Journal of the Neurosurgical Society of Australasia, 11*(1), 25–30.

Pribram, K. H., & Fulton, J. F. (1954). An experimental critique of the effects of anterior cingulate ablations in monkey. *Brain: A Journal of Neurology, 77*, 34–44.

Psarros, T., Zouros, A., & Coimbra, C. (2003). Bromocriptine-responsive akinetic mutism following endoscopy for ventricular neurocysticercosis. Case report and review of the literature. *Journal of Neurosurgery, 99*(2), 397–401.

Spiegel, D. R., Casella, D. P., Callender, D. M., & Dhadwal, N. (2008). Treatment of akinetic mutism with intramuscular olanzapine: a case series. *Journal of Neuropsychiatry and Clinical Neurosciences, 20*(1), 93–95.

Tow, P. M., & Whitty, C. W. M. (1953). Personality changes after operations of the cingulate gyrus in man. *Journal of Neurology, Neurosurgery, and Psychiatry, 16*, 186–193.

Ure, J., Faccio, E., Videla, H., Caccuri, R., Giudice, F., Ollari, J., et al. (1998). Akinetic mutism: a report of three cases. *Acta Neurologica Scandinavica, 98*(6), 439–444.

Alcohol Abuse

Nate Ewigman
University of Florida
Gainesville, FL, USA

Synonyms

Alcoholism; Binge drinking; Excessive alcohol use

Short Description or Definition

Alcohol abuse refers to a "maladaptive pattern of alcohol [use] leading to clinically significant impairment or distress." The DSM-IV Criteria for alcohol abuse are

DSM-IV-TR Criteria for Alcohol Abuse

1. A maladaptive pattern of alcohol abuse leading to clinically significant impairment or distress, as manifested by one or more of the following, occurring within a 12-month period:
   - Recurrent alcohol use resulting in failure to fulfill major role obligations at work, school, or home (e.g., repeated absences or poor work performance related to substance use; substance-related absences, suspensions, or expulsions from school; or neglect of children or household).
   - Recurrent alcohol use in situations in which it is physically hazardous (e.g., driving an automobile or operating a machine).
   - Recurrent alcohol-related legal problems (e.g., arrests for alcohol-related disorderly conduct).
   - Continued alcohol use despite persistent or recurrent social or interpersonal problems caused or exacerbated by the effects of the alcohol (e.g., arguments with spouse about consequences of intoxication or physical fights).
2. These symptoms must never have met the criteria for alcohol dependence.

Although alcohol abuse is diagnosed primarily by observed or reported impairment and distress related to alcohol use, the *Dietary Guidelines for Americans* recommends no more than one drink per day for women and two drinks per day for men (USDA, 2005).

Categorization

In the DSM-IV-TR, alcohol abuse is differentiated from alcohol dependence in that the former consists of drinking that impairs functioning without withdrawal symptoms and is thus diagnosed only when dependence is not present (Hasin, Van Rossem, McCloud, & Endicott, 1997). An alcohol abuser may continue to drink despite awareness of the potential negative physical, social, and legal consequences.

Epidemiology

Alcohol abuse is associated with diseases of the liver, hypertension, neurological damage, and cardiac diseases such as heart failure. In 2000, alcohol abuse was responsible for 85,000 deaths in the U.S. National data suggest that the prevalence of DSM-IV-TR alcohol abuse (not including alcohol dependence) was 4.65% in 2001–2002. At that time, alcohol abuse was more common among men, younger respondents, and Whites. From 1991–1992 to 2001–2002, the prevalence of alcohol abuse increased, especially among young African American and Hispanics and in both men and women (Grant et al., 2004). It appears that alcohol abuse is generally more severe with earlier onset in age of alcohol use (Grant, Stinson, & Harford, 2001). Results from a national survey suggest that close to one fifth of adolescents and adults engaged in binge drinking one or more times within the last 30 days (US DHHS, 2002).

Natural History, Prognostic Factors, Outcomes

In *The Natural History of Alcoholism Revisited*, George Vaillant (1995) described alcohol dependence as a condition of gradual onset over 5–15 years of continuous alcohol abuse. He found that the average age of onset was 29 years among a cohort of delinquent youth and 41 among a higher educated group. In the cohorts that Vaillant (1995) studied, the prevalence of alcoholism increased until age 40 and then declined at a rate of 2–3% per year thereafter.

Potential risk factors for alcohol abuse in adolescence and early adulthood include being in areas of high availability and accessibility, sensation seeking and low harm-avoidance in youth, family history of alcohol abuse, liberal family attitude toward alcohol use, lack of family closeness, and early behavioral problems (Hawkins, Catalano, & Miller, 1992). Another risk factor appears to be comorbid mental disorders. Epidemiological data suggest that 37% of people who have an alcohol disorder also have another mental disorder (Regier et al., 1990), emphasizing the importance of mental and behavior health screening. In terms of prognostic factors, Vaillant (1995) suggests that those who achieve "long-term sobriety usually [are characterized by] (1) a less harmful, substitute dependency; (2) new relationships; (3) sources of inspiration and hope; and (4) experiencing negative consequences of drinking."

In Vaillant (1995) delinquent youth cohort, by age 70, 54% had already died, 32% were abstinent, 12% were still abusing alcohol, and 1% were controlled drinkers (i.e., drinking but not abusing).

Neuropsychology and Psychology of Alcohol Abuse

In a review of the literature of neuropsychological deficits in chronic alcohol abusers, Chelune and Parker (1981) found patterns of neurological damage such as cerebral atrophy, ventricular enlargement, and decreased cerebral blood flow. Approximately 10% of chronic alcohol abusers have neurocognitive deficits commensurate with diagnoses of alcohol-related amnesia or dementia. A large portion of those without diagnosable neurocognitive deficits still evince disturbed neuropsychological performance (Rourke & Grant, 2009). Alcoholics generally function in the average to above average range on IQ tests with consistently lower performance IQ (PIQ) scores relative to verbal IQ (VIQ). Their PIQ scores are similar to those of persons with brain damage, whereas VIQ scores are comparable with those of normal controls (Chelune & Parker, 1981; Rourke & Grant, 2009). However, this discrepancy is not diagnostic of alcoholism. Within the Wechsler subtests, Block Design appears to be the most frequently impaired relative to normal controls in all studies reviewed. Block Design impairment has been cited as an effective discriminator between alcoholics and non-alcoholics. Object Assembly and Digit Symbol were also impaired relative to normal controls in more than 3/4 of the studies. Other tests that have revealed impairment in alcoholics include the Category Test, Wisconsin Card Sorting Test, Raven's Progressive, Shipley–Hartford Abstract Age, and other tests of abstract thinking. Alcoholics also generally perform poorly on Part B of the Trail Making Test relative to matched control groups (Chelune & Parker, 1981).

Overall, the most consistently impaired neuropsychological domains include verbal and nonverbal learning and perceptual-motor skills. More broadly, most reviews conclude that abstraction-executive abilities are impaired among alcohol abusers (Rourke & Grant, 2009). Despite the consistency of these neuropsychological findings, many of the samples from these studies are recently detoxified adults. Grant and Adams (2009) point out that neuropsychological recovery typically occurs following the first year – and perhaps more – of detoxification.

Although the exact mechanisms of these neuropsychological deficits are not known, some of the major hypotheses attempting to explain these deficits have been (Chelune & Parker, 1981):

1. Chronic alcohol abuse results in premature aging of the brain.
2. Chronic alcohol abuse leads to global generalized CNS dysfunction.
3. Chronic alcohol abuse differentially disrupts the right hemisphere of the brain.
4. Chronic alcohol abuse exerts its detrimental effect *on the* anterior-basal regions of the brain.
5. Chronic alcohol abuse produces a generalized CNS impairment that is particularly disruptive of the fronto-parietal association areas of the brain.

More recent neural hypotheses of the mechanisms of neuropsychological deficits include reduced regional blood flow to the frontal lobes, reduction in metabolites (e.g., NAA) that indicate lack of neuronal integrity, frontal-striatal and cerebellar dysfunction manifesting as loss of dendritic arbor (Rourke & Grant, 2009). Grant and Adams (2009) note that molecular mechanisms of the influence of chronic alcohol abuse on neuropsychological functioning are largely unknown.

Evaluation

A common screening tool for alcohol abuse is the CAGE questionnaire (Ewing, 1984; see An even briefer CAGE Questionnaire, Table B).The CAGE is highly effective at identifying problem drinkers among adults (Bernadt, 1982). Two "yes" responses on the CAGE indicate that the respondent should be investigated further. The questionnaire asks the following questions:

- Have you ever felt you needed to *C*ut down on your drinking?
- Have people *A*nnoyed you by criticizing your drinking?
- Have you ever felt *G*uilty about drinking?
- Have you ever felt you needed a drink first thing in the morning (*E*ye-opener) to steady your nerves or to get rid of a hangover?

Other brief assessments for alcohol abuse include the POSIT and CRAFFT for adolescents (Knight, Sherritt, Harris, Gates, & Chang, 2003), the Michigan Alcoholism Screen Test (MAST) for adults (Magruder-Habib, Stevens, & Alling, 1993), and the AUDIT-C for both adults and adolescents (Bush et al., 1998). According to Fiellin, Reid, and O'Connor (2000), the CAGE and the AUDIT are the superior screening instruments in primary care settings compared with other alcohol abuse screeners and other clinical methods. The CAGE is superior at detecting diagnosable abuse and dependence and the AUDIT is superior at detecting at risk and harmful drinking (Fiellin et al., 2000).

Treatment

Treatment ranges from support groups to rehabilitation centers. Treatments of alcohol abuse appear to be largely psychosocial. In a systematic review, brief psychosocial interventions among primary care patients were found to be effective at reducing alcohol consumption (Kaner et al., 2007). Although well-known support groups such as Alcoholic Anonymous (AA) have been helpful to many people and likely constitute the most accessible form of treatment, evidence has not supported AA's effectiveness at reducing alcohol problems (Ferri, Amato, & Davoli, 2006). Medical treatments of alcohol abuse focus on reducing craving. Naltrexone (Chick et al., 2000) and Acomprosate (Garbutt, West, Carey, Lohr, & Crews, 1999) have been found to be effective at reducing craving. However, most medications are aimed at dependence, not abuse symptoms.

Cross References

- ▶ Alcohol Brain Syndrome
- ▶ Alcohol Dependence
- ▶ Blood Alcohol Level
- ▶ Fetal Alcohol Syndrome
- ▶ Michigan Alcoholism Screen Test
- ▶ Substance Abuse
- ▶ Wernicke-Korsakoff's Syndrome

References and Readings

Bernadt, M. W. (1982). Comparison of questionnaire and laboratory tests in the detection of excessive drinking and alcoholism. *Lancet, 6*, 325–328.

Chelune, G. J., & Parker, J. B. (1981). Neuropsychological deficits associated with chronic alcohol abuse. *Clinical Psychology Review, 1*, 181–195.

Chick, J., Anton, R., Checinski, K., Croop, R., Drummond, D. C., Farmer, R. et al. (2000). A multicentre, randomized, double-blind, placebo-controlled trial of naltrexone in the treatment of alcohol dependence or abuse. *Alcohol, 35*, 587–593.

Ewing, J. A. (1984). Detecting alcoholism: The CAGE questionnaire. *JAMA, 252*, 1905–1907.

Ferri, M. M. F., Amato L., & Davoli M. (2006). Alcoholics anonymous and other 12-step programmes for alcohol dependence. *Cochrane Database of Systematic Reviews*, Issue 3, Art. No.: CD005032. doi: 10.1002/14651858.CD005032.pub2

Fiellin, D. A., Reid, M. C., & O'Connor, P. G. (2000). Screening for alcohol problems in primary care: A systematic review. *Archives of Internal Medicine, 160*(13), 1977–1989.

Garbutt, J. C., West, S. L., Carey, T. S., Lohr, K. N., & Crews, F. T. (1999). Pharmacological treatment of alcohol dependence: A review of the evidence. *JAMA, 281*, 1318–1325.

Grant, B. F., Dawson, D. A., Stinson, F. S., Chou, S. P., Dufour, M. C., & Pickering, R. P. (2004). The 12-month prevalence and trends in DSM-IV alcohol abuse and dependence: United States, 1991–1992 and 2001–2002. *Drug and Alcohol Dependence, 74*, 223−234.

Grant, I., Adams K. M. (Eds.) (2009). Neuropsychological assessment of neuropsychiatric disorders (3rd ed., pp. 127–158.). New York: Oxford University Press.

Grant, B. F., Stinson, F. S., & Harford, T. C. (2001). Age at onset of alcohol use and DSM-IV alcohol abuse and dependence: A 12-year follow-up. *Journal of Substance Abuse, 13*, 493–504.

Hasin, D. S., Van Rossem, R., McCloud, S., & Endicott, J. (1997). Alcohol dependence and abuse diagnoses: Validity in a community sample of heavy drinkers. *Alcoholism, Clinical and Experimental Research, 21*, 213–219.

Hawkins, J. D., Catalano, R. F., & Miller, J. Y. (1992). Risk and protective factors for alcohol and other drug problems in adolescence and early adulthood: Implications for substance abuse prevention. *Psychological Bulletin, 112*, 64–105.

Knight, J. R., Sherritt, L., Harris, S. K., Gates, E. C., & Chang, G. (2003). Validity of brief alcohol screening tests among adolescents: A comparison of the AUDIT, POSIT, CAGE, and CRAFFT. *Alcoholism, Clinical and Experimental Research, 27*, 67–73.

Magruder-Habib, K., Stevens, H. A., & Alling, W. C. (1993). Relative performance of the MAST, VAST, and CAGE versus DSM-III-R criteria for alcohol dependence. *Journal of Clinical Epidemiology, 46*, 435–441.

Regier, D. A., Farmer, M. E., Rae, D. S., Locke, B. Z., Keith, S. J., Judd, L. L., et al. (1990). Comorbidity of mental disorders with alcohol and other drug abuse. Results from the epidemiologic catchment area (ECA) study. *JAMA, 264*, 2511–2518.

Rourke, S. B., & Grant, I. (2009). The neurobehavioral correlates of alcoholism. In I. Grant & K. M. Adams (Eds.), *Neuropsychological assessment of neuropsychiatric and neuromedical disorders* (3rd ed., pp. 398–454). New York: Oxford University Press.

U.S. Department of Health and Human Services. Substance Abuse and Mental Health Services Administration(US DHHS). (2002). *Results from the 2001 national household survey on drug abuse: Volume I. Summary of national findings (Office of Applied Studies, NHSDA Series H-17 ed.) (BKD461, SMA 02–3758)*. Washington, DC: U.S. Government Printing Office. Retrieved March 14, 2009, from the World Wide Web: http://www.oas.samhsa.gov/nhsda/2k1nhsda/vol1/Chapter3.htm

United States Department of Agriculture and United States Department of Health and Human Services (USDA). (2005). *Dietary guidelines for Americans: Chap. 9 – Alcoholic beverages* (pp. 43–46). Washington, DC: US Government Printing Office.

Vaillant, G. E. (1995). *The natural history of alcoholism revisited.* Cambridge, MA: Harvard University Press.

Alcohol Addiction

► Alcoholism

Alcohol Amnesic Disorder

► Korsakoff's Syndrome

Alcohol Dependence

Glenn S. Ashkanazi
University of Florida-College of Public Health and Health Professions
Gainesville, FL, USA

Synonyms

Alcoholism

Definition

As described in DSM-IV, alcohol dependence is a set of symptoms encompassing dysfunction in cognitive, behavioral, and physiological domains caused by continued alcohol use. A pattern of repeated alcohol ingestion exists, resulting in increasing amounts consumed in order to obtain the desired effect (i.e., tolerance) and characteristic symptoms if use is suddenly suspended (i.e., withdrawal). There is a perceived loss of control over drinking, exhibited by repeated failed attempts to decrease or quit drinking. Individuals may spend increasing amounts of time

in drinking-related behaviors without being able to stop, despite being aware that drinking is causing, or exacerbating, psychological or medical problems. Cognitive consequences can include memory loss, difficulty performing familiar tasks, poor or impaired judgment, and problems with language.

Cross References

- ▶ Alcohol Abuse
- ▶ Alcohol Dementia
- ▶ Alcoholic Brain Syndrome
- ▶ Substance Abuse
- ▶ Substance Abuse Disorders
- ▶ Wernicke–Korsakoff Syndrome

References and Readings

American Psychiatric Association (1994). *Diagnostic and statistical manual of mental disorders* (4th ed.). Washington, DC: American Psychiatric Association.

Alcoholic Amnestic Disorder

▶ Wernicke-Korsakoff Syndrome

Alcoholic Brain Syndrome

Glenn S. Ashkanazi
University of Florida-College of Public Health and Health Professions
Gainesville, FL, USA

Synonyms

Alcoholic dementia; Alcoholic hallucinosis; Delirium tremens; Korsakoff's syndrome; Wernicke–Korsakoff syndrome

Short Description or Definition

"Alcoholic brain syndrome" is a collection of several syndromes associated with the acute or chronic use of alcohol, resulting in significant impairment on normal brain functioning (APA Dictionary of Psychology, 2007).

Categorization

As mentioned in the definition, alcoholic brain syndrome encompasses several syndromes.

1. *Alcohol withdrawal delirium*: A reversible condition that develops after cessation of chronic, extreme alcohol intake. Symptoms include disturbed consciousness (e.g., disruption in attention/concentration), disruption in memory, orientation, and language beyond what would be expected from typical alcohol withdrawal.
2. *Alcohol-induced persisting dementia*: A chronic condition that includes multiple cognitive deficits as a result of prolonged alcohol abuse. Cognitive areas generally impaired include memory, speech, motor/sensory functions and executive functions. Global impairment in intellectual functioning evolves gradually over time.
3. *Alcohol-induced persisting amnestic disorder*: A persistent disturbance in memory functioning caused by chronic alcohol abuse. Memory impairment is severe enough to cause significant disturbance in occupational or social functioning.
4. *Wernicke's encephalopathy (WE)*: A syndrome resulting from chronic alcoholism leading to nutritional deficiency (i.e., Vitamin B1 [Thiamine] and characterized by acute confusion, ataxia, sluggish pupillary reflexes, and nystagmus and memory deficits). The syndrome can result in coma or death. Lesions are centered in the midbrain, cerebellum, and diencephalon.
5. *Korsakoff's syndrome*: This condition often follows episodes of WE. Thiamine deficiency, as a result of chronic, severe alcohol abuse, leads to a dense anterograde and retrograde amnesia. Patients with Korsakoff's syndrome can store information for only a few seconds before they forget it. The resulting amnesia is thought to be due to damage in the mammillary bodies, anterior or dorsomedial nuclei (or both) of the thalamus.

Another common feature is confabulation, in which the patient recounts detailed and convincing memories for events that have never happened.

6. *Alcohol-induced psychotic disorder*: A condition involving the presence of delusions and/or hallucinations due to the physiological effects of alcohol.

Epidemiology

Up to 2 million alcoholics have developed permanent and debilitating conditions that require lifetime custodial care. A number of factors influence how and to what extent alcohol affects the brain. These include the age at which the person started drinking, duration of drinking, amount of alcohol consumed, drinking style/pattern, patient's age, education, genetic background, family history of alcoholism, neuropsychiatric risk factors (e.g., prenatal alcohol exposure), and general health status. Studies comparing men and women's sensitivity to alcohol-induced brain damage have not been conclusive.

Poor nutrition has been a major contributor to the development of alcohol-induced brain damage. Up to 80% of alcoholics have a deficiency in thiamine (i.e., Vitamin B1). This vitamin is an essential nutrient required by all tissues including the brain. Some of these people will progress to WE. Approximately 80–90% of alcoholics with Wernicke's develop Korsakoff's psychosis, which is more prevalent in men aged 45–65. Women who develop this condition tend to do so at a younger age (i.e., 35–55).

Natural History, Prognostic Factors, and Outcomes

WE is a medical emergency and requires immediate treatment, as it can lead to death in approximately 20% of untreated cases. Symptoms can develop within hours and can be easily missed as many mimic intoxication. If treatment is given in time, usually through the administration of thiamine, progression of symptoms can be slowed or stopped. Ocular abnormalities usually recover within a few days to a few weeks, but ataxia takes 1–2 months longer to resolve. The acute confusion/delirium usually improves within 1–2 days after the treatment but may take 1–3 months to completely clear.

If treatment is not provided, then irreversible brain damage, or even death, is possible. Of those who survive, approximately 85% develop Korsakoff's syndrome. However, not every person who develops Korsakoff's syndrome has a previous episode of Wernicke's. Some will develop Korsakoff's gradually with either no known history or brief episodes of Wernicke's. Some patients are initially comatose or semiconscious and only when the acute disorder has resolved is the underlying Korsakoff's syndrome manifest. These patients are still susceptible to developing Wernicke's, especially if drinking were to continue.

Loss of some cognitive functions including memory in Korsakoff's syndrome may be permanent. Once the patient has developed Korsakoff's, the treatment strategies are not clear. However, it is important for patients to remain abstinent from alcohol. Depending on the degree of memory and executive function impairment, and availability of family support, patients with Korsakoff's may require long-term custodial care.

Neuropsychology and Psychology of Alcoholic Brain Syndrome

The classic symptom in Korsakoff's syndrome is the inability to form new memories (i.e., anterograde amnesia). However, patients also demonstrate significant deficits in their ability to recall incidents or events from their own past as well (i.e., episodic memory). Memory for facts, concepts, and language (i.e., semantic memory) is variable while perceptual-motor memory is thought to be preserved.

The inability to recall previously learned information (i.e., retrograde amnesia) can often extend back 20–30 years in a person's life with Korsakoff's patients. Generally, a temporal gradient exists such that memories from the more distant past are recalled better than the more recent ones. The basis of this extensive retrograde amnesia is still a matter of great controversy.

These patients are typically younger than most patients presenting to dementia services and because they often present as initially confused, with concomitant frontal lobe pathology, they are more likely to demonstrate aggressive, agitated behaviors and anxiety. Those with irreversible brain damage are unlikely to be able to live alone but also typically lack available social services. These patients often have a difficult time maintaining social and familial relationships and live isolated lives.

Evaluation

For patients who meet the DSM-IV criteria for WE or Korsakoff's syndrome, neuropsychological assessment is useful for documenting functions that are impaired, the severity of impairment, and the prognostic factors involved in determining the patient's ability to manage daily life either independently or with assistance. However, it is preferable for the neuropsychological assessment to occur when the patient has been abstinent from alcohol for a long enough period of time to insure that the acute symptoms of alcohol withdrawal have subsided.

Treatment

The primary treatment option for patients experiencing alcoholic brain syndrome is to stop drinking and remain abstinent. Without additional alcohol exposure, the recovery from the delirium caused by alcohol is usually good. This is obviously the first treatment to be utilized. As mentioned above, thiamine deficiency is an important contributor to alcohol-related brain damage; therefore, Vitamin B1 supplementation is necessary. Initially, the vitamins can be given intravenously or intramuscularly followed by oral administration. WE responds well to high-dose vitamins, and such treatment can prevent the occurrence of severe, chronic Korsakoff's syndrome. Secondarily, nutritional counseling to promote a vitamin-rich and balanced diet is also part of this initial treatment protocol, especially for longer-term recovery and prevention.

Cross References

- ▶ Alcoholism
- ▶ Amnesia
- ▶ Anterograde Amnesia
- ▶ Dementia
- ▶ Encephalopathy
- ▶ Episodic Memory
- ▶ Korsakoff's Syndrome
- ▶ Organic Brain Syndrome
- ▶ Retrograde Amnesia
- ▶ Semantic Memory
- ▶ Substance Abuse

References and Readings

Kopelman, M., Thomson, A., Guerrini, I., & Marshall, E. (2009). The Korsakoff Syndrome: Clinical aspects, psychology and treatment. *Alcohol & Alcoholism, 44*(2), 148–154.

Martin, P., Singleton, C., & Hiller-Sturmhofel, S. (2003). The role of thiamine deficiency in alcoholic brain disease. *Alcohol Research & Health, 27*(2), 134–142.

Oscar-Berman, M., & Marinkovic, K. (2003). Alcoholism and the brain: An overview. *Alcohol Research & Health, 27*(2), 125–133.

Parsons, O. (1996). Alcohol abuse and alcoholism. In R. Adams, O. Parsons, J. Culbertson, & S. Nixon (Eds.), *Neuropsychology for clinical practice: Etiology, assessment, and treatment of common neurological disorders.* Washington, DC: American Psychological Association.

Rourke, S., & Grant, I. (2009). The neurobehavioral correlates of alcoholism. In I. Grant & K. M. Adams (Eds.), *Neuropsychological assessment of neuropsychiatric and neuromedical disorders* (3rd ed.). New York, NY: Oxford University Press.

White, A. (2003). What happened? Alcohol, memory blackouts, and the brain. *Alcohol Research & Health, 27*(2), 186–196.

Alcoholic Dementia

▶ Alcoholic Brain Syndrome

Alcoholic Hallucinosis

▶ Alcoholic Brain Syndrome

Alcoholic Polyneuropathy

▶ Korsakoff's Syndrome

Alcoholic Psychosis

▶ Korsakoff's Syndrome

Alcoholism

Glenn S. Ashkanazi
University of Florida-College of Public Health and Health Professions
Gainesville, FL, USA

Synonyms

Alcohol abuse; Alcohol addiction; Alcohol dependence; Problem drinking; Substance abuse

Definition

The term "alcoholism" has a variety of definitions. For some, it is a disease that makes a person dependent on alcohol, causes an obsession with alcohol and inability to control how much they drink even though their drinking causes serious problems in their relationships, health, work, and finances. Others do not define it as a "disease" per se but rather a "condition," behavioral in nature, which results in continued consumption of alcohol despite health problems and negative social consequences. For some, the definition *must* include the concepts of

addiction and physiological withdrawal mechanisms, while for others, these are consequences of drinking.

It is common for laypeople to equate any kind of excessive drinking with alcoholism. Those in the mental health fields see that disorders related to alcohol use lie along a continuum of severity that *may* include physical dependency/withdrawal (i.e., alcohol dependence) or may involve impaired drinking habits that lead to health or social problems/consequences but without dependency/withdrawal (i.e., alcohol abuse). According to the *APA Dictionary of Psychology*, alcoholism is the popular term for "alcohol dependence."

Historical Background

The term "alcoholism" was first used in 1849 by a physician, Magus Haas, to describe the systematic adverse effects of alcohol overconsumption. In the USA, it became a popular term in the 1930s as a result of the growth of Alcoholics Anonymous (AA). Previously, society viewed those who drank to excess as immoral, weak of character, and irresponsible. Society's response was punishment and removal of overconsumers from sober society to protect the community. With the rise of AA, and their publication (i.e., the "Big Book"), the view of alcoholism changed from character flaw to medical disease. AA viewed alcoholism as a physical allergy to alcohol accompanied by an obsession with drinking. This organization began to dispel the previously held beliefs that alcoholics were unemployable, destitute, and isolated individuals by demonstrating that some highly respected people who had been alcohol dependent had eventually overcome their disorder and went on to lead productive lives.

Epidemiology

The epidemiology of alcoholism can be confusing and contradictory, depending on the definition being utilized and the measurement tool. The generally accepted overall rate of occurrence of alcoholism in the USA is 10%. The U.S. National Longitudinal Alcohol Epidemiologic Study concluded that alcoholism is prevalent in 20% of adult hospital inpatients and in 17% of community-based primary care practices. A 1985 U.S. National Hospital Survey found that 528,000 patients were discharged from hospitals with a primary diagnosis of substance abuse, and for 81% (428,000), alcohol was the abused substance.

According to a 2001 survey conducted by the National Institute on Alcohol Abuse and Alcoholism (NIAAA) in the USA, approximately 48% of adults (aged 12 or older) reported being current drinkers of alcohol (approximately 109 million). That number drops to 44% when the age is 18 or older. Approximately 20% of persons aged 12 or older participated in binge drinking at least once in 30 days prior to the 2001 survey. "Heavy drinking" was reported by 5.7% of the 12 or older population (12.9 million). The highest prevalence for both binge and heavy drinking was for those in the 18–25 age groups with the peak rate occurring at age 21. Studies have found those who begin drinking at an earlier age are at higher risk to develop dependency. Those Americans who wait till age 21 are 4 times less likely to become dependent than those who begin drinking before the age of 15 (i.e., 40% who start before age 15 develop dependency on alcohol at some point in their lives). The risk for developing dependency declines with age, as the prevalence rate for alcoholism in those persons greater than 65 years old is 3%.

There are other nonage risk factors as well. Those with lower education and lower socioeconomic status are also at higher risk. There are also gender differences as men are at minimum 2.5 times more likely to be defined as "alcoholic" as women; however, the proportion of female alcoholics is increasing. White, non-Hispanic, individuals are more likely to develop alcoholism than African-Americans. The risk for Hispanics is generally the same as Whites.

Alcoholism is estimated to be the third leading cause of preventable death in the USA (after smoking and obesity). In the USA, 85,000 deaths are attributable to alcohol each year at a cost of $185 billion. The NIAAA estimates that intoxication is present in 30–60% of homicides, 22% of suicides, 33–50% of automobile accidents, 67% of drownings, and 70–80% of fire-related deaths. More than 50% of American adults have a close family member who has or has had alcoholism. Approximately one in four children younger than 18 in the USA is exposed to alcohol abuse or alcohol dependence in their family.

Internationally, the World Health Organization estimates that there are 140 million people worldwide that are alcohol dependent and they account for 3.5% of the total cases of disease worldwide, which is a higher rate than tobacco or illicit drugs.

Current Knowledge

Causes

There is no identifiable single cause of alcoholism. Scientists believe that a myriad of factors play a role in the development of alcoholism.

1. *Genetics*: Previous twin and adoption studies have demonstrated that genes play an important role in the development of alcoholism. Researchers found that identical twins (i.e., identical genes) have a higher concordance rate for drinking behavior than fraternal twins. Other studies have cast some doubt on these twin studies by suggesting the environment of identical twins is more alike than fraternal twins, thus suggesting a weakening of the argument in favor of genes.

In the adoption studies, researchers found that whether reared by biologic or adoptive parents, the sons of males with alcohol problems are 4 times more likely to have alcohol problems than sons of persons who are not. In either case, epidemiologic studies indicate that alcoholism tends to run in families. Alcoholics are 6 times more likely than nonalcoholics to have blood relatives who are alcohol dependent. In summary, a person's genetic makeup can predispose them to alcoholism or not.

2. *Peer influence*: Social networks that include heavy drinkers and alcohol abusers increase an individual's risk for alcoholism.
3. *Cultural influence*: Cultures that include well-established taboos against drunkenness and rules regarding drinking have lower alcoholism rates than those who do not.
4. *Psychiatric conditions*: Certain psychiatric diagnoses increase the risk of alcoholism. These include ADHD, panic disorder, schizophrenia, and antisocial personality disorder.

Screening

There are a variety of measures for alcoholism including the following:

1. CAGE: The CAGE is named for the four questions asked of a patient before any questions regarding quantities drank are asked.
   a Have you ever felt the need to **C**ut down on your drinking?
   b Have people **A**nnoyed you by criticizing your drinking?
   c Have you ever felt **G**uilty about drinking?
   d Have you ever felt you needed a drink in the morning to steady your nerves or get rid of a hangover? (**E**ye-opener)

The CAGE has been extensively validated. Those who answer "YES" to two or more questions are 7 times more likely to be alcohol dependent. It is not an adequate measure by itself but can alert a health-care provider to probe further. Another weakness is that it tends to be less reliable with populations with lower alcoholism rates (e.g., elderly) and does not identify "hazardous drinking."

2. Alcohol Use Disorders Identification Test (AUDIT): The AUDIT can detect both hazardous drinking and alcohol abuse. It does not need to be administered face to face like the CAGE. It was developed by the World Health Organization and yields scores for consumption, dependency, and alcohol-related problems.
3. Alcohol Dependence Data Questionnaire: More sensitive than the CAGE and can distinguish abuse versus dependence.

Diagnosis

Health-care providers most often use the *Diagnostic Statistical Manual of the Mental Disorders, Fourth Edition, Text Revision* (DSM-IV-TR) criterion for alcohol dependence. The diagnosis requires three of the following criteria:

1. Maladaptive pattern of the use leading to impairment/distress as manifested by three or more of the below occurring in the same 12-month period.
   - Tolerance
   - Withdrawal
   - Drink more frequently or in larger amounts than intended
   - Persistent desire to drink or unsuccessful efforts to cut down or control use
   - Great deal of time spent in acquiring/using alcohol or recovering from its effects
   - Important social, occupational, or recreational activities given up or reduced because of alcohol
   - Drinking continues despite knowledge of persistent or recurrent physiological, or psychological problems caused or exacerbated by drinking

Treatment

There are several well-accepted avenues of treatment.

1. *Psychosocial*: Studies have shown that simple, brief interventions can be effective in those not severely alcohol dependent. One of those getting an extensive trial has been "Motivation Interviewing" based on

Prochaska's Five Stages of Change Model. A summary of the treatment approach is as follows:

- *Precontemplation* – Patient expresses no interest or need for change. The health-care professional's options are limited. They can point to discrepancies between the patient's goals and behavior and recommend 2 weeks of abstinence.
- *Contemplation* – Patient expresses ambivalence or skepticism about change. The provider should work to influence them in direction of change, provide information about the dangers of alcohol abuse, and recommend an abstinence trial.
- *Preparation* – Patient accepts need for change and makes plans to accomplish changed drinking goal.
- *Action* – Patient recognizes problem in drinking behavior and takes observable steps to decrease alcohol use. Professional reinforces decision for change and may introduce self-help groups and/or medications.
- *Maintenance* – Patient and professional work together to maintain change and prevent relapse.

2. *Medications*: The most common medications in the treatment of alcoholism are:
   - *Disulfiram* (*Antabuse*) – Prevents the elimination of acetaldehyde, which is a by-product of alcohol metabolism. Results in unpleasant side effects in persons still drinking including nausea, dizziness, headache, flushing, vomiting, heart palpitations, and sudden drop in blood pressure. Disulfiram needs to be taken daily to be effective. However, in at least one large clinical trial it did not increase abstinence.
   - *Naltrexone* (*ReVia*) – May work by blocking the positive effects felt from drinking by blocking opiate receptors in the brain thereby decreasing craving for alcohol. Clinical studies have found a modest decrease in relapse (12–20%). This drug has an unknown cause of action.
   - *Acamprosate* (*Campral*) – Used to maintain abstinence once alcoholics have stopped drinking. Thought to work by stabilizing the chemical balance in the brain. In clinical trials, the one year abstinence rates have been 18% and 12% at two years.

3. *Self-help groups*: Perhaps the best-known organization involving alcoholism is AA. Until the mid-1930s in the USA, alcohol-dependent persons who could not afford a private hospital or private psychiatrist could only find help in state hospitals, jails, or churches. AA was the first self-directed approach toward treatment. The AA treatment model includes self-help groups, utilizing psychological principles organized in small local community groups. The "12 steps" of AA encourage confrontation of denial, admission of powerlessness over alcohol, and strives for people to atone for harm caused by their behavior while drinking. It encourages its members to live ethically with a reliance on a "higher power." It is this sense of AA as a "religion" that has led to nonreligious self-help groups including rational recovery, LifeRing, and SOS.

Future Directions

The following are areas needing continued study:

1. *Genetic research* – current and future studies are looking at individuals with a family history of alcoholism to pinpoint the location of genes that influence vulnerability to alcoholism. This line of study will assist in the early identification of individuals at risk and of new, gene-based treatment approaches.
2. *Treatment approaches* – The NIAAA has been funding a study called "Project MATCH" whose goal is to identify variables important in predicting outcome based on patient characteristics and treatment design.
3. *Medications* – Naltrexone was the first drug approved by the FDA in 45 years to help alcoholics stay sober following detoxification. More research is needed.

Cross References

- ▶ Alcoholic Brain Syndrome
- ▶ Fetal Alcohol Syndrome
- ▶ Korsakoff's Syndrome
- ▶ Michigan Alcoholism Screening Test
- ▶ Motivational Interviewing
- ▶ Substance Abuse Disorders
- ▶ Twin Studies
- ▶ Wernicke–Korsakoff's Syndrome

References and Readings

National Institute on Alcohol Abuse and Alcoholism. *Etiology and natural history of alcoholism.* URL Accessed on June 1, 2009 (http://pubs.

niaaa.nih.gov/publications/social/module2etiology&naturalhistory/module2.html).
National Institute on Alcohol Abuse and Alcoholism. *Helping patients who drink too much: A clinician's guide.* URL Accessed on June 1, 2009 (http://www.niaaa.nih.gov/Publications/EducationTrainingMaterials/guide.htm).
Schuckit, M. (2000). *Drug and alcohol abuse: A clinical guide to diagnosis and treatment.* New York, NY: Kluwer Academic/Plenum Publishers.
U.S. Department of Health and Human Services and SAMHSAs National Clearinghouse for Alcohol and Drug Information. Accessed URL on June 1, 2009 (http://ncadistore.samhsa.gov/catalog/facts.aspx?topic=3).

Alertness

Chris Loftis
STG International
Alexandria, VA, USA

Synonyms

Awareness; Consciousness; Watchfulness

Definition

A state of being mentally perceptive and responsive to external stimuli. A "readiness to respond" that can be detected by Electroencephalography (EEG). Alertness is susceptible to fatigue; maintaining a constant level of alertness is difficult, particularly for monotonous tasks demanding continuous attention. Stimulants such as nicotine, caffeine, and amphetamines can temporally boost alertness. Diminished alertness is often associated with the physiological response of yawning, which may boost the alertness of the brain. Impaired alertness is a common symptom of a number of conditions, including narcolepsy, attention deficit disorder, traumatic brain injury, chronic fatigue syndrome, depression, Addison's disease, and sleep deprivation.

Cross References

► Alertness
► Electroencephalography

Alexia

Steven Z. Rapcsak, Pélagie M. Beeson
The University of Arizona
Tucson, AZ, USA

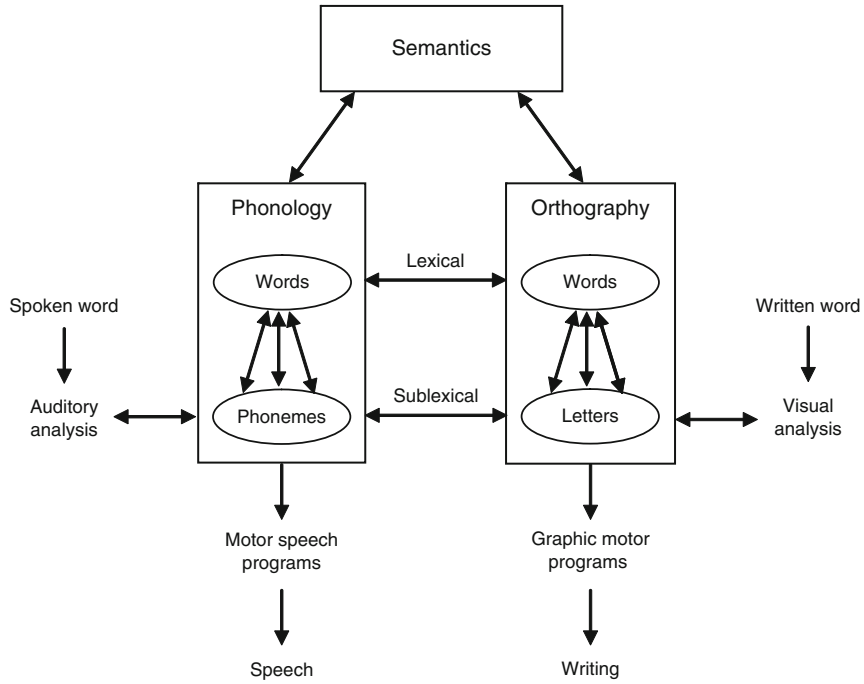
Short Description or Definition

The term alexia is applied to acquired disorders of reading produced by neurological injury in individuals with normal premorbid literacy skills. Clinically, patients with alexia have difficulty in recognizing, pronouncing, or comprehending written words. Although alexia can occur in relative isolation, it is more frequently encountered in the context of spoken language dysfunction or aphasia. Most individuals with alexia have concommitant spelling impairment or agraphia, suggesting that reading and spelling rely on shared cognitive representations and neural substrates. Acquired alexia needs to be distinguished from developmental dyslexia reflecting a failure to attain normal reading skills.

Categorization

Alexia is not a single clinical entity. Instead, there are several distinct forms of alexia characterized by specific combinations of impaired and preserved reading abilities and associated with unique lesion profiles. The three most commonly encountered alexia syndromes include pure alexia/letter-by-letter reading, phonological/deep alexia, and surface alexia. In order to understand the neuropsychological mechanisms underlying different subtypes of alexia, it is important to briefly review the cognitive processes involved in normal reading.

Reading is a complex cognitive skill that requires rapid visual discrimination of letters and words, as well as the ability to link information about visual word forms (orthography) with knowledge about word sounds (phonology) and word meanings (semantics). According to an influential dual-route model of reading (Coltheart, Rastle, Perry, Langdon, & Ziegler, 2001), perceptual processing of written words begins with visual feature analysis and letter shape detection (Fig. 1). Following the letter identification stage, the model postulates two distinct procedures or processing routes for deriving phonology from print. The lexical route requires the activation of memory representations of written word forms stored in the orthographic lexicon, followed by



Alexia. Figure 1 A cognitive model indicating the component processes involved in reading

the retrieval of the corresponding spoken word forms from the phonological lexicon. The lexical route is normally used to read familiar words and can support the processing of both regular words that have predictable spelling–sound relationships (e.g., spring) and irregular words that contain atypical letter–sound or grapheme–phoneme mappings (e.g., choir). By contrast, the sublexical route operates on units smaller than the whole word and is thought to rely on the serial conversion of individual graphemes to the corresponding phonemes. The sublexical route is essential for accurate reading of unfamiliar words or nonwords (e.g., nace) because these novel items, by definition, do not have preexisting representations in the orthographic or phonological lexicon. The sublexical route can also be used to generate plausible pronunciations for regular words that strictly obey spelling–sound conversion rules. However, processing irregular words by the sublexical procedure results in regularization errors (e.g., *have* read to rhyme with *save*). Thus, according to dual-route theory, only the lexical reading route can deliver a correct response to irregular words. Note that the model depicted in Fig. 1 also includes an indirect route from orthography to phonology via the semantic system. The activation of word meanings by this semantic reading route is critical for written word comprehension. However, whether semantic mediation is also normally required for accurate oral reading of familiar words is a topic of controversy (Coltheart et al., 2001; Plaut, McClelland, Seidenberg, & Patterson, 1996; Woollams, Lambon Ralph, Plaut, & Patterson, 2007). In summary, skilled reading depends on interactions between visual/orthographic processing, phonology, and semantics. Damage to these functional domains or the disruption of the transfer of information between the cognitive/brain systems that support these operations results in alexia.

Epidemiology

Alexia is commonly observed in right-handed individuals following damage to the language-dominant left hemisphere. Although it is most frequently caused by stroke, alexia can follow any kind of focal injury (e.g., trauma, tumor) to the brain regions critical for implementing the various cognitive operations necessary for normal reading. Alexia is also often seen in the setting of neurodegenerative disorders, especially in patients with primary progressive aphasia/semantic dementia or Alzheimer's disease. In general, the specific alexia profile is determined

not so much by the etiology of the brain damage than by the location of the responsible lesions.

Natural History, Prognostic Factors, Outcomes

The prognosis for recovery from alexia depends both on the etiology of the lesion and the extent of the underlying brain damage. Alexia following stroke tends to show some spontaneous recovery over time, but patients with extensive brain damage may never regain useful reading function and typically stop reading for pleasure. In individuals with neurodegenerative disorders, progressive worsening of the reading impairment is observed along with the gradual deterioration of other language and cognitive functions.

Neuropsychology and Psychology of Alexia

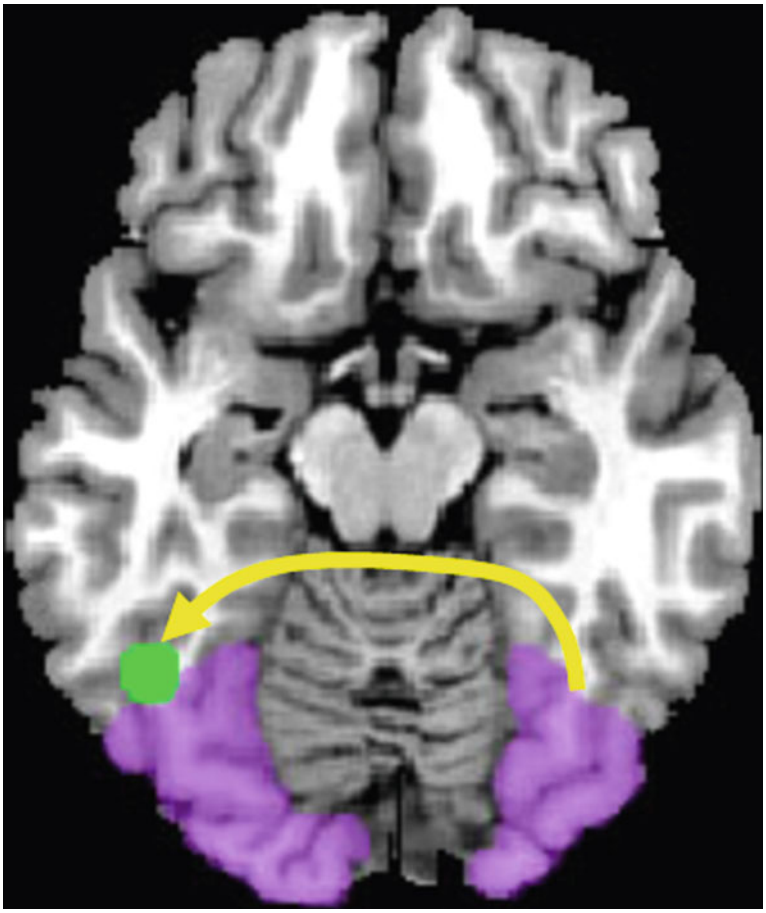
Pure Alexia/Letter-By-Letter Reading

In pure alexia, the rapid visual identification of familiar words that characterizes normal skilled reading is disrupted. Reading is slow and laborious, often relying on a serial letter-naming strategy known as "letter-by-letter" reading. Typically, there is a monotonic increase in reading latencies as a function of the number of letters in the word, giving rise to an abnormal *word length effect* that is considered the hallmark feature of the syndrome. Varying degrees of letter identification difficulty are present and visual reading errors are common (e.g., chain – charm). Collectively, these behavioral observations suggest that visual processing impairment plays a critical role in the pathogenesis of pure alexia (Behrmann, Plaut, & Nelson, 1998). Although the reading disorder may be unaccompanied by significant aphasia or agraphia, many patients with pure alexia demonstrate concommitant anomia and spelling impairment (Rapcsak & Beeson, 2004). Furthermore, patients often perform poorly on nonreading tasks that require fine-grained visual discrimination, suggesting that the reading impairment is part of a more general visual processing deficit (Behrmann et al., 1998). Within the framework of the cognitive model depicted in Fig. 1, pure alexia is attributable to dysfunction at the visual feature analysis and/or letter identification stages of reading, or it may be produced by damage to the orthographic lexicon. Damage to any of these visual processing components would be expected to interfere with the rapid perceptual identification of familiar orthographic word forms and result in an abnormal word length effect in oral reading.

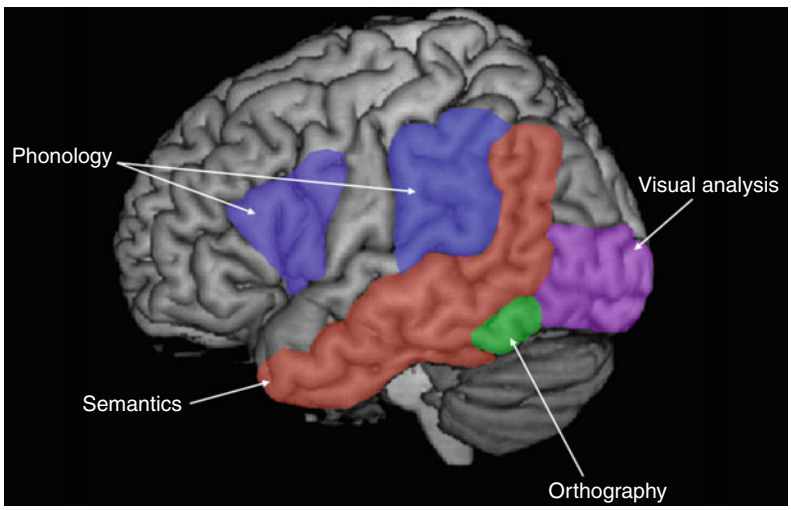
Pure alexia/letter-by-letter reading is most commonly seen following left inferior occipito-temporal damage caused by posterior cerebral artery strokes. It has been proposed that the critical lesions degrade or disrupt visual input to the visual word-form area (VWFA) or directly damage the VWFA itself (Cohen et al., 2003; Epelbaum et al., 2008). The VWFA is consistently activated in functional imaging studies of reading in normal individuals and has been localized to the mid-lateral portions of the left fusiform gyrus (BA37) (Cohen et al., 2002; Jobard, Crivello, & Tzourio-Mazoyer, 2003) (Fig. 2). The VWFA receives converging input from bilateral posterior occipital areas (BA17,18/19) involved in visual feature analysis and letter shape detection and it integrates this information into larger perceptual units corresponding to whole words (Fig. 2). Activation of the VWFA is sensitive to the orthographic familiarity of the letter string, consistent with the notion that this cortical region may constitute the neural substrate of the orthographic lexicon. The orthographic codes computed by the VWFA are subsequently transmitted to cortical systems involved in the phonological and semantic components of reading (Fig. 3). Importantly, it has been shown that spelling familiar words also activates the VWFA (Beeson et al., 2003). These observations confirm the central role for the VWFA in orthographic processing and support the view that the same orthographic lexical representations mediate reading and spelling. Consistent with this hypothesis, patients with damage to the VWFA are likely to show evidence of reading and spelling impairment attributable to the loss of word-specific orthographic representations (Rapcsak & Beeson, 2004).

Phonological/Deep Alexia

Phonological alexia is characterized by a disproportionate difficulty in processing nonwords compared with familiar words, giving rise to an exaggerated *lexicality effect* in reading (Crisp & Lambon Ralph, 2006; Patterson & Lambon Ralph, 1999; Rapcsak et al., 2009). Attempts to read nonwords often result in real word responses known as lexicalization errors (e.g., nace – name). Although in phonological alexia reading of familiar words (both regular and irregular) is relatively preserved, performance is typically influenced by lexical-semantic variables including word frequency (high>low), imageability (concrete>abstract), and grammatical class (nouns>verbs > functors). Deep alexia includes all the



Alexia. Figure 2 Location of the visual word form area (VWFA) (indicated by *green circle*) as determined by functional neuroimaging studies of reading. This region receives input from bilateral posterior occipital visual areas (shown in purple). Arrow indicates callosal transfer of information initially processed by right visual cortex



Alexia. Figure 3 Cortical regions involved in reading

characteristic features of phonological alexia, but it is distinguished from the latter by the production of prominent semantic reading errors (e.g., boy – son) (Coltheart, Patterson, & Marshall, 1980). Although phonological and deep alexia were originally considered separate entities, there is now much evidence to suggest that the difference between these syndromes is quantitative rather than qualitative. Thus, phonological and deep alexia are more appropriately considered as points along a continuum, with the latter representing a more severe version of the former (Crisp & Lambon Ralph, 2006; Rapcsak et al., 2009).

Phonological alexia is typically encountered in patients with aphasia syndromes characterized by phonological impairment (i.e., Broca's, conduction, Wernicke's). Furthermore, it has been shown that most patients with phonological alexia demonstrate prominent deficits and increased lexicality effects in spoken language tasks that require the manipulation and maintenance of sublexical phonological information (e.g., repetition, rhyme judgments, phoneme segmentation and blending), and also that such non-orthographic measures of phonological ability correlate with and are predictive of reading performance (Crisp & Lambon Ralph, 2006; Rapcsak et al., 2009). These observations suggest that the written and spoken language impairments in phonological alexia have a common origin and are merely different manifestations of a central or modality-independent phonological deficit (Crisp & Lambon Ralph, 2006; Patterson & Lambon Ralph, 1999; Rapcsak et al., 2009). Consistent with this view, the reading disorder in phonological alexia is usually accompanied by a qualitatively similar spelling impairment (phonological agraphia) (Rapcsak et al., 2009). According to dual-route models (Fig. 1), poor nonword reading in phonological alexia is attributable to damage to the sublexical route, while the relatively preserved real word reading performance of these patients reflects the residual functional capacity of the lexical and semantic routes. The general phonological impairment observed in the vast majority of patients suggests that the most common site of damage may be at the level of the phoneme units (with additional damage to the phonological lexicon in more severe cases), as these phonological processing components are shared between written and spoken language tasks.

Phonological alexia is most often associated with damage to a network of *perisylvian* cortical regions involved in speech production/perception and phonological processing in general. Components of this distributed phonological system include posterior-inferior frontal gyrus/Broca's area (BA44/45), precentral gyrus (BA4/6), insula, superior temporal gyrus/Wernicke's area (BA22), and supramarginal gyrus (BA40) (Rapcsak et al., 2009). Consistent with the phonological deficit hypothesis, there is an excellent neuroanatomical correspondence between the location of the lesions that produce phonological alexia and the location of the perisylvian cortical areas that show activation in normal individuals during a variety of written and spoken language tasks requiring phonological processing (Jobard et al., 2003; Rapcsak et al., 2009; Vigneau et al., 2006). As predicted by the continuum model, there is considerable overlap between the perisylvian lesion profiles of patients with phonological and deep alexia, although the damage in deep alexia tends to be more extensive. In fact, the massive destruction of left-hemisphere language areas in deep alexia has lead to the hypothesis that reading performance in these patients may be mediated by the intact right hemisphere (Coltheart et al., 1980).

Surface Alexia

In surface alexia the main difficulty involves reading irregular words, especially when these items are of low frequency. Regular words of comparable frequency are processed more efficiently, and the discrepancy in performance between words with predictable versus atypical spelling–sound relationships is reflected by an increased *regularity effect* in reading. Nonword reading is typically preserved. According to dual-route theory, surface alexia is attributable to dysfunction of the lexical reading route (Fig. 1). Specifically, it has been suggested that the reading disorder in some cases may result from damage to the orthographic lexicon (Coltheart et al., 2001; Patterson, Marshall, & Coltheart, 1985). Due to the loss of word-specific orthographic knowledge, patients with this type of deficit will be forced to rely on a sublexical grapheme–phoneme conversion strategy that produces phonologically plausible regularization errors on irregular words. Low-frequency irregular words are especially vulnerable because the activation of representations in the orthographic lexicon is normally modulated by word frequency and the relative refractoriness of low-frequency items may be further exaggerated by the brain damage. Consistent with the notion that reading and spelling rely on shared orthographic representations, patients with surface alexia following damage to the orthographic lexicon show similar difficulty in spelling irregular words (surface agraphia) (Patterson et al., 1985; Rapcsak & Beeson, 2004). Alternatively, surface alexia may result from damage to central semantic representations (Woollams et al.,

2007). Specifically, it has been proposed that accurate oral reading of low-frequency irregular words normally requires additional support from the semantic reading route and cannot be mediated efficiently by pathways that rely on direct transcoding between orthographic and phonological representations (Plaut et al., 1996). With the degradation of semantic knowledge, the relative inadequacy of non-semantic reading routes is revealed and manifests itself as surface alexia. Consistent with the semantic deficit hypothesis, many patients with surface alexia perform poorly on verbal and nonverbal cognitive tasks requiring semantic processing (e.g., picture naming, verbal fluency, spoken word and picture comprehension). Furthermore, the severity of the semantic impairment on these nonreading tasks has been shown to correlate with reading accuracy for low-frequency irregular words (Woollams et al., 2007). The proposed central semantic deficit may also explain the frequent co-occurrence of surface alexia and surface agraphia (Graham, Patterson, & Hodges, 2000).

In contrast to the strong association between perisylvian damage and phonological alexia, surface alexia is typically encountered in the setting of *extrasylvian* brain pathology. Although uncommon in patients with stroke, surface alexia has been described in individuals with left temporo-parietal lesions centered on posterior middle/inferior temporal gyrus and angular gyrus (BA20/21,37/39), and also following inferior occipito-temporal lesions that involved the VWFA (Rapcsak & Beeson, 2004; Vanier & Caplan, 1985). As expected, patients with surface alexia following VWFA damage also showed evidence of visual processing impairment and features of pure alexia/letter-by-letter reading (Rapcsak & Beeson, 2004). A particularly dramatic and pure form of surface alexia is consistently observed in patients with semantic dementia (SD) (Woollams et al., 2007). SD is a subtype of primary progressive aphasia/frontotemporal dementia in which the neurodegenerative process has a predilection for left anterior and inferolateral temporal cortex, including the temporal pole, middle/inferior temporal gyri, and anterior fusiform gyrus (BA38,20/21) (Galton et al., 2001; Mummery et al., 2000). Surface alexia has also been described in patients with Alzheimer's disease (Patterson, Graham, & Hodges, 1994) and is likely to reflect the frequent involvement of left temporo-parietal cortex by the disease process. Although distributed over a large anatomical area, the disparate extrasylvian lesion sites in surface alexia seem to have in common the potential for disrupting either lexical orthographic or semantic processing. Specifically, in patients with VWFA involvement the reading disorder may reflect damage to the orthographic lexicon resulting in the loss of word-specific orthographic knowledge. By contrast, in patients with anterior temporal lobe lesions, and possibly also in patients with posterior temporo-parietal damage, surface alexia may be attributable to the degradation of central semantic representations. The latter hypothesis is supported by functional imaging studies of semantic processing in normal individuals that have shown activation of a large-scale left-hemisphere extrasylvian cortical network that included both anterior temporal lobe and posterior temporo-parietal sites (Vigneau et al., 2006; Binder, Desai, Graves, & Conant, 2009) (Fig. 3).

Evaluation

In evaluating patients with alexia it is important to assess the status of all the relevant component processes involved in reading (Fig. 1). A comprehensive battery should include tests of letter and word recognition, as well as measures of oral reading and reading comprehension. The evaluation should allow the clinician to identify the nature of the functional impairment and to locate the level of breakdown with reference to a cognitive model of normal reading. It is equally important to document relatively spared reading abilities and the use of compensatory strategies by the patient, as this information may be helpful in planning treatment. The assessment of alexia is best accomplished by the use of commercially available reading batteries (e.g., Kay, Lesser, & Coltheart, 1992).

Treatment

A variety of behavioral treatment approaches have shown positive outcomes in the rehabilitation of alexia. In general, treatment is directed toward strengthening the impaired reading procedure/route or it encourages the use of compensatory strategies to bypass the functional deficit (for a review, see Beeson & Rapcsak, 2006).

Cross References

- ▶ Agraphia
- ▶ Aphasia
- ▶ Dyslexia
- ▶ Phonological/Deep Agraphia
- ▶ Surface Agraphia

References and Readings

Beeson, P. M., & Rapcsak, S. Z. (2006). Treatment of alexia and agraphia. In J. H. Noseworthy (Ed.), *Neurological therapeutics: Principles and practice* (2nd ed., pp. 3045–3060), London: Martin Dunitz.

Beeson, P. M., Rapcsak, S. Z., Plante, E., Chargualaf, J., Chung, A., Johnson, S. C., et al. (2003). The neural substrates of writing: A functional magnetic resonance imaging study. *Aphasiology, 17*, 647–665.

Behrmann, M., Plaut, D. C., & Nelson, J. (1998). A literature review and new data supporting an interactive account of letter-by-letter reading. *Cognitive Neuropsychology, 15*, 7–51.

Binder, J. R., Desai, R. H., Graves, W. W., & Conant, L. L. (2009). Where is the semantic system? A critical review and meta-analysis of 120 functional neuroimaging studies. *Cerebral Cortex, 19*, 2767–2796.

Cohen, L., Lehéricy, S., Chochon, F., Lemer, C., Rivaud, S., & Dehaene, S. (2002). Language-specific tuning of visual cortex? Functional properties of the visual word form area. *Brain, 125*, 1054–1069.

Cohen, L., Martinaud, O., Lemer, C., Lehéricy, S., Samson, Y., Obadia, M., et al. (2003). Visual word recognition in the left and right hemispheres: Anatomical and functional correlates of peripheral alexias. *Cerebral Cortex, 13*, 1313–1333.

Coltheart, M., Patterson, K., & Marshall, J. C. (1980). *Deep dyslexia.* London: Routledge & Kegan Paul.

Coltheart, M., Rastle, K., Perry, C., Langdon, R., & Ziegler, J. (2001). DRC: A dual route cascaded model of visual word recognition and reading aloud. *Psychological Review, 108*, 204–256.

Crisp, J., & Lambon Ralph, M. A. (2006). Unlocking the nature of the phonological-deep dyslexia continuum: The keys to reading aloud are in phonology ad semantics. *Journal of Cognitive Neuroscience, 18*, 348–362.

Epelbaum, S., Pinel, P., Gaillard, R., Delmaire, C., Perrin, M., Dupont, S., et al. (2008). Pure alexia as a disconnection syndrome: New diffusion imaging evidence for an old concept. *Cortex, 44*, 962–974.

Galton, C. J., Patterson, K., Graham, K., Lambon Ralph, M. A., Williams, G., Antoun, N., et al. (2001). Differing patterns of temporal atrophy in Alzheimer's disease and semantic dementia. *Neurology, 57*, 216–225.

Graham, N. L., Patterson, K., & Hodges, J. R. (2000). The impact of semantic memory impairment on spelling: Evidence from semantic dementia. *Neuropsychologia, 38*, 143–163.

Jobard, G., Crivello, F., & Tzourio-Mazoyer, N. (2003). Evaluation of the dual route theory of reading: A metaanalysis of 35 neuroimaging studies. *NeuroImage, 20*, 693–712.

Kay, J., Lesser, R., & Coltheart, M. (1992). *Psycholinguistic assessments of language processing in aphasia* (*PALPA*). East Sussex, England: Lawrence Erlbaum Associates.

Mummery, C. J., Patterson, K., Price, C. J., Ashburner, J., Frackowiak, R. S. J., & Hodges, J. R. (2000). A voxel-based morphometry study of semantic dementia: Relationship between temporal lobe atrophy and semantic memory. *Annals of Neurology, 47*, 36–45.

Patterson, K., Graham, N., & Hodges, J. R. (1994). Reading in dementia of the Alzheimer type: A preserved ability? *Neuropsychology, 8*, 835–407.

Patterson, K., & Lambon Ralph, M. A. (1999). Selective disorders of reading? *Current Opinion in Neurobiology, 9*, 235–239.

Patterson, K. E., Marshall, J. C., & Coltheart, M. (1985). *Surface dyslexia: Neuropsychological and cognitive studies of phonological reading.* London: Lawrence Erlbaum.

Plaut, D. C., McClelland, J. L., Seidenberg, M. S., & Patterson, K. (1996). Understanding normal and impaired word reading: Computational principles in quasi-regular domains. *Psychological Review, 103*, 56–115.

Rapcsak, S. Z., & Beeson, P. M. (2004). The role of left posterior inferior temporal cortex in spelling. *Neurology, 62*, 2221–2229.

Rapcsak, S. Z., Beeson, P. M., Henry, M. L., Leyden, A., Kim, E. S., Rising, K., et al. (2009). Phonological dyslexia and dysgraphia: Cognitive mechanisms and neural substrates. *Cortex, 45*(5), 575–591.

Vanier, M., & Caplan, D. (1985). CT correlates of surface dyslexia. In K. E. Patterson, J. C. Marshall, & M. Coltheart (Eds.), *Surface dyslexia: Neuropsychological and cognitive studies of phonological reading* (pp. 511–525). London: Lawrence Erlbaum.

Vigneau, M., Beaucousin, V., Hervé, P. Y., Duffau, H., Crivello, F., Houdé, O., et al. (2006). Meta-analyzing left hemisphere language areas: Phonology, semantics, and sentence processing. *NeuroImage, 30*, 1414–1432.

Woollams, A., Lambon Ralph, M. A., Plaut, D. C., & Patterson, K. (2007). SD-squared: On the association between semantic dementia and surface dyslexia. *Psychological Review, 114*, 316–339.

Alexia Without Agraphia

► Alexia

Alexithymia

Joel W. Hughes
Kent State University
Kent, OH, USA

Definition

A deficit in apprehending, experiencing, and describing emotions, including difficulty in perceiving and understanding the feelings of others. In particular, difficulty in distinguishing between emotions and bodily sensations that indicate emotional arousal.

Current Knowledge

The term "alexithymia" was coined by the late psychiatrist Peter Sifneos to describe patients who could not find the appropriate words to describe their emotional states. Literally meaning "without words for emotions" in Sifneos' native Greek, Alexithymia is a trait that overlaps

with a number of medical and psychiatric disorders. Alexithymia is associated with somatic complaints such as headaches, lower back pain, irritable bowel syndrome, and fibromyalgia. It is also associated with psychiatric conditions such as anorexia nervosa, autism spectrum disorders including Asperger's, major depressive disorder, panic disorder, posttraumatic stress disorder, and substance abuse.

Cross References

► Emotional Intelligence

References and Readings

Sifneos, Peter E. Alexithymia: Past and present. *The American Journal of Psychiatry*, 153, 137–142.

Taylor, Graeme J; Bagby, R. Michael and Parker, James DA (1997). Disorders of Affect Regulation: Alexithymia in Medical and Psychiatric Illness. Cambridge: Cambridge University Press. ISBN 052145610X.

Taylor GJ, & Taylor HS (1997). Alexithymia. In M. McCallum & W.E. Piper (Eds.) Psychological mindedness: A contemporary understanding. Munich: Lawrence Erlbaum Associates.

"Alice in Wonderland" Syndrome

► Metamorphopsia

Alien Hand Syndrome

Gary Goldberg, Matthew E. Goodwin
Virginia Commonwealth University School of Medicine/ Medical College of Virginia
Richmond, VA, USA

Synonyms

Anarchic hand; Callosal apraxia; Diagnostic dyspraxia; Dr. Strangelove syndrome; Intermanual conflict; Magnetic apraxia; Wayward hand

Short Description or Definition

Alien hand syndrome (AHS) is a relatively rare manifestation of damage to specific brain regions involved in voluntary movement. The core observation is the patient report that one of his/her hands is displaying purposeful, coordinated, and goal-directed behavior over which the patient feels he/she has no voluntary control. The patient fails to recognize the action of one of his hands as his own. The hand, effectively, appears to manifest a "will of its own." This unique involuntary movement disorder is characterized by coordinated, well-organized, and clearly goal-directed limb movements that would otherwise be indistinguishable from normal voluntary movement. This definition excludes disordered, non-purposeful, and dyskinetic movements associated with other involuntary movement disorders such as chorea, athetosis, hemiballism, and myoclonus.

The alien hand can be engaged in performing a specific goal-directed task or the purposeful use of an external object. Distinguishing this condition from asomatognosia, there is typically normal awareness and recognition of the limb reported by the patient. However, the patient perceives a lack of self-agency ("I am not doing that. . .") with regard to the observed behavior of the limb, but displays intact "ownership" (". . .even though I know this is my hand").

Categorization

Three variants of AHS have been described, each with unique behavioral manifestations and neuroanatomical correlations. These variants include the frontal, callosal, and posterior forms.

Frontal Form

Neuroanatomy

The most common variant is the "frontal" form. It is associated with damage to the medial surface of the cerebral hemisphere in the frontal region. This variant has been described in cerebral infarction in the territory of the anterior cerebral artery, with tumors involving the medial surface of the cerebral hemisphere, and in other conditions affecting the function of the medial frontal lobe region. When the region of injury extends posteriorly to involve the medial aspect of the prefrontal gyrus associated with the primary motor cortex (PMC), the patient may present with crural hemiparesis, with greater weakness in the leg as compared to the arm. This

presentation corresponds to the topographical organization of the PMC with control of lower limb movement located more medially than the areas that control the upper limb. The frontal variant is seen with involvement of the medial aspect of the premotor cortex anterior to PMC including the supplementary motor area (SMA) and anterior cingulate cortex (ACC). In functional activation studies, the medial frontal cortex has also been found to activate spontaneously with complex purposeful movements and with internal imaging of voluntary movement, suggesting that it may serve as a higher level system that modulates the activation of PMC in accordance with volitional aspects of the performance. The readiness potential that precedes an overt voluntary movement by over 1,000 ms arises through activation of the anteromedial frontal cortex, suggesting that excitation of this region precedes the appearance of the overt movement and activation of the PMC. Activation of the ACC is involved in intentional suppression of prepotent responses as tested with the Stroop test. These areas may serve as a higher-level system modulating the activation of PMC in accordance with the volitional aspects of the performance.

Clinical Presentation

Behaviors seen frequently with the frontal variant include involuntary, visually driven reaching and grasping onto objects, an inability to voluntarily release these objects, and utilization behavior in which the presence of a frequently encountered object such as a comb or a toothbrush elicits behavior in which the object may be put to use independent of the social context. A grasp reflex to tactile stimulation is often present in the affected hand. The patient may wake themselves up from sleep by grasping and pulling their own body parts. Patients may show a prepotent tendency to be drawn toward external objects. They also may demonstrate alien-associated sexual self-stimulation or involuntary fondling of another's body, a great source of public embarrassment (Ong Hai and Odderson, 2000). Interestingly, while the patient clearly manifests purposeful involuntary coordinated behaviors in the affected limb, when they attempt to willfully move the limb, this is effortful and difficult. Voluntary movement in the affected limb is often hypokinetic and hypometric with greater activation of the axial and proximal limb muscles compared to the distal muscles controlling the wrist and fingers, even though these muscles are readily activated in the alien movements. Generally, these alien behaviors appear in the hand contralateral to the damaged hemisphere regardless of hemispheric dominance. When the dominant hemisphere is damaged, in addition to alien hand behavior in the nondominant hand, they may experience difficulty with the initiation of spontaneous speech while being able to follow verbal commands and repeat phrases without difficulty. These findings are consistent with a transcortical motor aphasia that affects spontaneous verbalization and production of propositional language more than repetition and responsive language. Alternatively, this could be understood as an inability to initiate spontaneous verbal output. The patient may thus be viewed as partially mute due to the relative akinesia seen with medial frontal cortex injury.

Callosal Form

Neuroanatomy

The "callosal" variant is seen with an isolated lesion of the corpus callosum. The voluntary motor systems of the two hemispheres are isolated from each other due to lost interhemispheric communication. This variant has been described most frequently as a transient condition following callosotomy. It may also be seen following infarction or tumors selectively involving this structure.

Clinical Presentation

In the "callosal" variant of AHS, the appearance of "intermanual conflict" or "self-oppositional" behaviors is the predominant feature. Grasping behaviors and externally driven reaching movements seen in the frontal variant are notably less prominent. When there is a major disconnection between the two hemispheres resulting from callosal injury, the language-linked dominant hemisphere agent that maintains its primary control over the contralateral dominant limb effectively loses its direct and linked control over the separate "agent" based in the nondominant hemisphere (and, thus, the nondominant limb), which had been previously responsive and "obedient" to the dominant agent. The possibility of purposeful action in the nondominant limb occurring outside of the realm of influence of the dominant agent thus can occur. In the callosal variant, the problematic alien hand is consistently the nondominant hand, while the dominant hand is the identified "good" controlled hand. The patient may express frustration and bewilderment at the conflicting and disruptive behavior of the alien hand whose motivations remain inaccessible to consciousness. There may be an attentional component that modulates the appearance of these episodes of self-oppositional behavior since intermanual conflict is observed more frequently when the patient is fatigued, stressed, or is engaged in effortful multitasking activity. Occasionally,

rather than acting in a contradictory manner, the two hands are observed to be engaged in two different and entirely unrelated activities as if being guided by completely separate and independent intentions.

In a dramatic example of this behavior, one patient was observed to initiate smoking a cigarette by pulling the cigarette out of the package and placing it in her mouth with the controlled dominant hand followed by the alien nondominant hand, rather than beginning to light the cigarette, suddenly reaching up, pulling it out of the her mouth, and throwing it across the room. Astonished, the patient reasoned that perhaps the alien hand was not in favor of her smoking!

The callosal and frontal variants are often seen in combination with a corresponding overlap of observed behaviors. For example, following cerebral infarction in the territory of the anterior cerebral artery, there may be ischemic injury to both the medial frontal lobe and the corpus callosum. In this circumstance, there may be both visually directed reaching and grasping alien behaviors in the limb contralateral to the area of injury as well as episodes of intermanual conflict. However, a clear differentiation between apparent intermanual conflict due to attempts to restrain alien behaviors associated with the frontal variant (e.g., as in the case of "self-grasping" described below), and true intermanual conflict, in which the two hands are directed toward independently contradictory purposes, may be difficult to differentiate.

Posterior or "Sensory" Form

Neuroanatomy

The third identified variant of AHS is the "posterior" or "sensory" form, which appears most often with a parietal or parieto-occipital focus of circumscribed damage. As in the frontal variant, the alien behavior appears in the hand contralateral to the damaged hemisphere.

Clinical Presentation

In the patient with the posterior variant, the movement of the affected alien limb is typically less organized and often has an ataxic instability particularly with visually guided reaching. The limb also may show proprioceptive sensory impairment with hypesthesia, so that kinesthetic impairment limits the monitoring of limb position. Visual field deficits as well as hemi-inattention may be seen on the same side as the alien hand. In this variant, the limb may be observed to lift up off of support surfaces involuntarily and "levitate" in the air seemingly to avoid contact with support surfaces. It may also be seen to withdraw from objects approaching the hand in distinct contrast to the reaching and grasping behaviors that are seen in the frontal variant. The alien hand may assume a characteristic posture of fully extended digits with the palmar surface retreating from environmental objects, an observation that has been labeled an "instinctive avoidance reaction" by Denny-Brown and has also been referred to as the "parietal hand." At times, grasping behaviors can also be observed with the posterior variant.

Alien hand behavior has also been reported in association with subcortical thalamic infarction. In addition to having been observed in the context of stroke, tumors and surgical sectioning of the corpus callosum, alien hand behavior has been described in association with a number of progressive neurodegenerative disorders including corticobasal degeneration, multiple sclerosis, spongiform encephalopathy, and Alzheimer's disease. When AHS appears with these progressive encephalopathies, it is usually accompanied by various forms of motor apraxia, along with multiple additional cognitive disturbances characteristic of the particular condition.

Epidemiology

While there are no epidemiologic studies of the occurrence of AHS variants in association with acquired brain damage, it can be assumed that this is a relatively rare but striking manifestation of neurologic pathology.

Pathophysiology and Prognosis

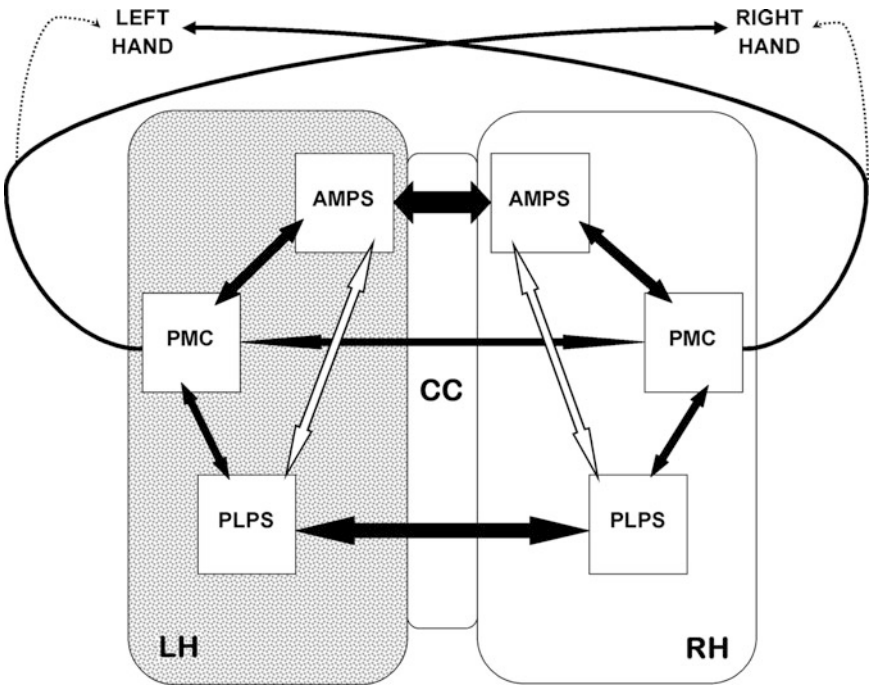
Adapting the concept developed by Derek Denny-Brown regarding positive and negative cortical tropisms based in the parietal lobe and frontal lobes (Denny-Brown, 1956, 1966), respectively, a heuristic model has been proposed. In this model, there are two separable but interactive components of an intrahemispheric premotor intentional system that modulate the output of the PMC of the hemisphere and its direct influence over the spinal motor nuclei innervating the muscles of the contralateral distal upper limb (Goldberg and Bloom, 1990).

The first component is a posterolateral premotor system (PLPS) based in the posterior parietal region that is involved in generating movements of the contralateral arm and hand that are directed toward external objects and are responsive to externally sensed contingencies. The second component is an anteromedial premotor system (AMPS) based in the medial frontal region that is involved in generating movements in the contralateral

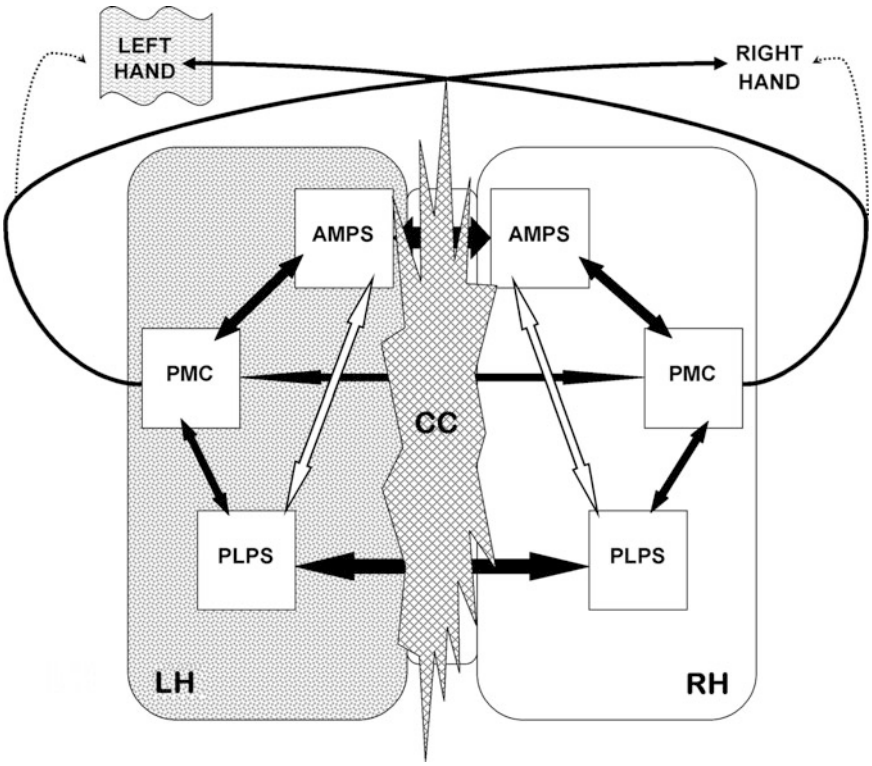
upper limb that are directed by an internal action plan and driven by an anticipatory model of future contingencies. It presumably is also involved in activating withdrawal movements that pull the limb back and away from external stimuli. It also functions to withhold action directly responsive to surrounding objects through inhibitory influence over the PLPS. These two systems are proposed to be in a metastable balance through mutually inhibitory influence. Together, these two hemispheric agency systems form an integrated intrahemispheric agency system. Furthermore, each intrahemispheric agency system has the capability of acting autonomously in its control over the contralateral limb, although overall unitary control by a conscious agent is maintained through interhemispheric communication between these systems via the corpus callosum at the cortical level and other interhemispheric commissures linking the two cerebral hemispheres at the subcortical level. Thus, conscious human agency can be thought of as emerging through the linked and coordinated action of at least four major premotor systems, two in each hemisphere. The overall general configuration of this heuristic model is shown in Fig. 1.

It is proposed that AHS, in its different variants described above, appears due to damage either to the corpus callosum in the callosal variant (Fig. 2), the AMPS of either hemisphere in the frontal variant (Figs. 3 and 4), or to the PLPS of either hemisphere in the posterior variant (Figs. 5 and 6).

The common factor in these anomalous conditions is the relative sparing of the PMC region controlling the contralesional alien hand, while the premotor regions involved in the intentional selection of action and the



Alien Hand Syndrome. Figure 1. Heuristic model for understanding alien hand syndrome (AHS).
Abbreviations: RH, Right Hemisphere; LH, Left Hemisphere; CC, Corpus Callosum; PMC, Primary Motor Cortex; AMPS, Anteromedial Premotor System; PLPS, Posterolateral Premotor System.
This view is shown looking down from above the vertex with the face located at the top of the drawing and the back of the head noted at the bottom of the drawing, the left side to the left and the right side to the right of the diagram. The open bidirectional arrow between the AMPS and the PLPS indicates an interaction characterized by mutually interactive inhibition creating a complementary metastable control of the contralateral hand. Solid arrows indicate facilitatory connections or connections that maintain synchrony and coherence between the connected structures. Output from PMC is directed primarily to the contralateral limb with some less potent ipsilateral projections illustrated by a dotted line. See text for further detail. Note that the left hemisphere is stippled in the diagram designating this as the dominant hemisphere for most individuals in correspondence with a dominant right hand



Alien Hand Syndrome. Figure 2. The callosal variant of AHS. Theoretical explanatory model for the alien behaviors observed in callosal damage. In this instance, there are findings consistent with callosal apraxia in addition to intermanual conflict associated with the complete separation of the two intrahemispheric premotor intentional control systems. The limbs appear to be operated by two relatively autonomous control systems. The intentional premotor system in the dominant hemisphere is linked to the language system while that of the nondominant hemisphere is separated from it. The dominant hand is understood as connected to self while the nondominant hand is not. The alien hand in this variant is the nondominant hand. This is indicated by the stippled overlay on the left nondominant hand

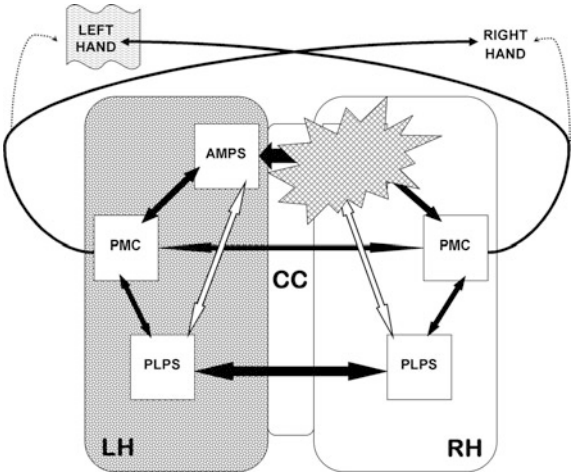
inhibition of automatic behaviors in response to external factors are impaired.

A recent fMRI study of cortical activation patterns associated with alien and non-alien movement has demonstrated that alien movement is in fact characterized by isolated activation of PMC without concomitant activation of intrahemispheric premotor regions, while voluntary behavior includes the activation of PMC in concert with activation of intrahemispheric premotor regions (Assal, Schwartz, & Vuilleumier, 2007).

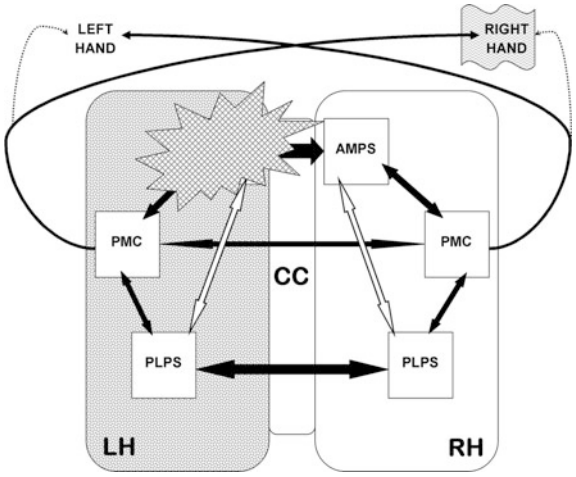
Neuropsychology and Psychology of AHS

The presence of AHS can cause the patient significant psychological distress as the hand seems to possess the capability for acting autonomously, independent of their conscious voluntary control. The patient may become fearful that they will be held accountable for consequences of an action of the alien hand over which they do not feel control. The patient may display "auto-criticism" complaining that the alien hand is not doing what it has been "told to do" and is therefore characterized as disobedient, wayward, or "evil." They may even physically strike the alien hand with the controlled hand as a "punishment" intended to discourage its wayward behavior, or constrain the movement of the alien hand by grasping tightly onto it with the controlled hand ("self-grasping"). They may verbally address and instruct the hand as if it were an unruly child acting autonomously and in need of correction. Conversely, they may respond to these contrary actions with amusement.

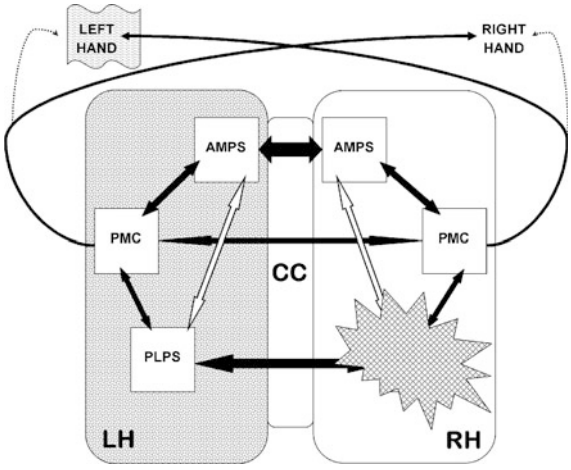
Given the predicament created, the patient may develop depersonalization and dissociate themselves from the unintended actions of the hand. They often choose to



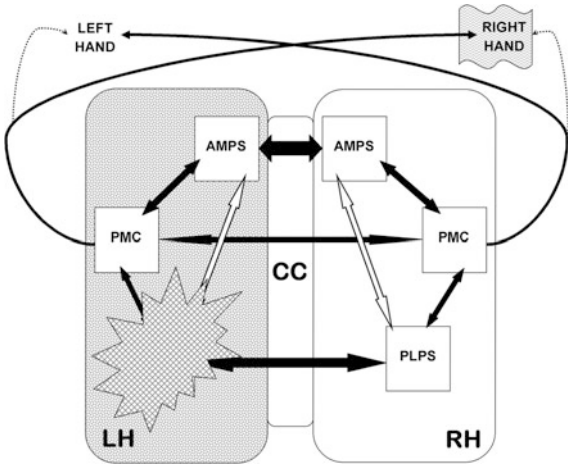
Alien Hand Syndrome. Figure 3. The nondominant frontal variant of AHS. Theoretical explanatory model for the alien behaviors observed in the frontal variant associated with damage to the AMPS of the nondominant hemisphere. In this case, the contralesional nondominant hand develops alien hand findings due to the release by disinhibition of the reaching and grasping behaviors driven from the dominant PLPS



Alien Hand Syndrome. Figure 4. The dominant frontal variant of AHS. Theoretical explanatory model for the alien behaviors observed in the frontal variant associated with damage to the AMPS of the dominant hemisphere. In this case, the contralesional dominant hand develops alien hand findings due to the release by disinhibition of the reaching and grasping behaviors driven from the dominant PLPS. In addition, spontaneous expressive language initiation is impaired due to the role of the AMPS of the dominant hemisphere in the initiation of verbal output



Alien Hand Syndrome. Figure 5. The nondominant posterior variant of AHS. Theoretical explanatory model for the alien behaviors observed in the posterior variant associated with damage to the PLPS of the nondominant hemisphere. In this case, the contralesional nondominant hand develops alien hand findings due to the release by disinhibition of behaviors driven from the nondominant AMPS



Alien Hand Syndrome. Figure 6. The dominant posterior variant of AHS. Theoretical explanatory model for the alien behaviors observed in the posterior variant associated with damage to the PLPS of the dominant hemisphere. In this case, the contralesional dominant hand develops alien hand findings due to the release by disinhibition of behaviors driven from the dominant AMPS

identify an external "alien" source for the voluntary control of the hand, or assign a distinct personality to the hand as a way of seeking a satisfactory narrative to explain this perplexing situation.

From a psychological perspective, it is helpful to counsel the patient regarding the organic basis of their problem and provide assurance that there is a rational explanation for their concerns and that there is evidence that these problems can be treated and may gradually improve over time.

In AHS, different regions of the brain are able to command purposeful limb movements, without generating the conscious feeling of self-control over these movements. There is thus a dissociation between the actual execution of the physical movements of the limb and the process that produces an internal sense of voluntary control over the movements. This latter process, impaired in AHS, normally produces the conscious sensation that movement is being internally initiated and produced by an active self. Presumably, this process differentiates between "re-afference" (i.e., the return of kinesthetic sensation from the self-generated "active" limb movement) and "ex-afference" (i.e., kinesthetic sensation generated from an externally produced "passive" limb movement). It may do this by giving rise to a parallel output signal from motor regions, a so-called "efference copy." The efference copy is then translated into a corollary discharge, which conveys the expected re-afferent sensory response from the commanded movement. The corollary discharge can then be used in somatosensory cortex to distinguish re-afference from ex-afference and thus differentiate a self-produced active movement from a movement resulting from external forces. AHS may thus involve impaired production and transmission of either an efference copy or a corollary discharge signal.

Evaluation

Evaluation of the patient with AHS involves careful observation of limb movement in various naturalistic contexts, along with reports from the patient regarding their sense of control over these movements. The relative dependence of movement on external context should be evaluated through assessment for utilization behaviors elicited by the presentation of external objects commonly encountered in daily activities. A phenomenologic approach to assessing and documenting the motor behavior and linking it to introspective report from the patient is essential. Not only should the verbal reports of the patient be noted, but also the associated affect. The limb should be evaluated for evidence of a grasp reflex with both tactile and visual stimulation. The ability to release objects that have been grasped should also be assessed. Evaluation for callosal apraxia and impairment of interhemispheric transfer of information should be included. When the posterior variant of AHS is suspected, a visual field assessment and somatosensory examination of the affected limb should be completed as well as assessment for hemi-inattention. Evidence of a tendency to withdraw the limb from tactile and visual stimulation should also be elicited and noted.

Treatment

There is no definitive specific treatment for AHS but a number of different rehabilitative approaches have been described. Furthermore, in the presence of unilateral damage within a single cerebral hemisphere, there is often a gradual reduction in the frequency of alien behaviors observed over time and a gradual restoration of voluntary control over the affected hand. This suggests that neuroplasticity in the bihemispheric and subcortical brain systems involved in voluntary movement production can serve to reestablish functional connection between the executive production process and the internal self-generation and volitional registration process. Exactly how this may occur is not well understood but could involve a reorganization within residual elements of the intrahemispheric premotor systems both at the cortical and subcortical levels. In addition, some degree of expanded participation of the intact ipsilateral hemisphere may be involved in the recovery process by extending ipsilateral motor projections.

Different strategies can be used to reduce the interference of the alien hand behavior in the ongoing coherent controlled actions being performed by the patient. In the frontal variant, an object such as a cane can be placed in the grip of the alien hand so that it does not reach out to grasp onto other objects, thus impeding the patient's forward progress during walking. In another approach, voluntary control of the limb is developed by training the patient to perform a specific task with the alien limb, such as moving the alien hand to contact a specific object or a highly salient environmental target. Through training to enhance volitional control, the patient can effectively override the alien behavior when it occurs. Recognizing that alien behaviors in the frontal variant are often sustained by tactile input, another approach involves simultaneously "muffling" the actions of the alien hand and limiting sensory feedback by placing it in a restrictive "cloak" such as a specialized soft foam hand orthosis or,

alternatively, an everyday oven mitt. Of course, this then limits the degree to which the hand can engage in functional goals. It may also be possible to develop improved participation of ipsilateral hemispheric premotor mechanisms by engaging the patient in coordinated bimanual activities that necessitate cooperative coordination mechanisms within residual intact components of the motor control system in both hemispheres.

Cross References

- ▶ Anterior Cingulate
- ▶ Apraxia
- ▶ Corpus Callosum
- ▶ Environmental Dependency
- ▶ Movement Disorder
- ▶ Utilization Behavior

References and Readings

Assal, F., Schwartz, S., & Vuilleumier, P. (2007). Moving with or without will: Functional neural correlates of alien hand syndrome. *Annals of Neurology, 62*, 301–306.

Biran, I., & Chatterjee, A. (2004). Alien hand syndrome. *Archives of Neurology, 61*, 292–294.

Denny-Brown, D. (1956). Positive and negative aspects of cerebral cortical functions. *North Carolina Medical Journal, 17*, 295–303.

Denny-Brown, D. (1966). *The cerebral control of movement.* Liverpool: Liverpool University Press.

Frith, C. D., Blakemore, S.-J., & Wolpert, D. M. (2000). Abnormalities in the awareness and control of action. *Philosophical Transactions of the Royal Society of London, 355*, 1771–1788.

Giovanetti, T., Buxbaum, L. J., Biran, I., & Chatterjee, A. (2005). Reduced endogenous control in alien hand syndrome: Evidence from naturalistic action. *Neuropsychologia, 43*, 75–88.

Goldberg, G., & Bloom, K. K. (1990). The alien hand sign. Localization, lateralization, and recovery. *American Journal of Physical Medicine and Rehabilitation, 69*, 228–238.

Goldberg, G. (1992). Premotor systems, attention to action and behavioural choice. In J. Kien, C. McCrohan, & W. Winlow (Eds.), *Neurobiology of motor programme selection. New approaches to mechanisms of behavioural choice* (pp. 225–249). Oxford: Pergamon.

Ong Hai, B. G., & Odderson, I. R. (2000). Involuntary masturbation as a manifestation of stroke-related alien hand syndrome. *Archives of Physical Medicine and Rehabilitation, 79*, 395–398.

Pack, B. C., Stewart, K. J., Diamond, P. T., & Gate, S. D. (2002). Posterior-variant alien hand syndrome: Clinical features and response to rehabilitation. *Disability and Rehabilitation, 24*, 817–818.

Scepkowski, L. A., & Cronin-Golomb, A. (2003). The alien hand: Cases, categorizations, and anatomical correlates. *Behavioral and Cognitive Neuroscience Reviews, 2*, 261–277.

Sumner, P., & Husain, M. (2008). At the edge of consciousness: Automatic motor activation and voluntary control. *Neuroscientist, 14*, 474–486.

ALL

- ▶ Acute Lymphoblastic Leukemia

Allele

John DeLuca
Kessler Foundation Research Center
West Orange, NJ, USA

Definition

Allele is an alternate form of a gene, which is the basic unit of inheritance. A gene is located at a particular site on the chromosome, and can have several alleles for that locus. For example, A, B, and O are different alleles for the ABO blood-type marker locus of a gene. Alleles greatly influence the expression of physical and behavioral phenotypes or traits such as eye color. For instance, the apolipoprotein E (APoE) gene is a well-known risk factor for developing Alzheimer's disease. The APoE gene has three common alleles: epsilon 2, epsilon 3, and epsilon 4. There is some evidence that carriers of the APoE epsilon 4 allele are at a greater risk for the development of Alzheimer's disease. In contrast, the APoE epsilon 3 allele has been suggested as a "protective" factor in the development of Alzheimer's disease (Plomin, Defries, Craig, & McGuffin, 2003).

Cross References

- ▶ Alzheimer's Disease
- ▶ Apolipoprotein E (ApoE)
- ▶ Chromosome
- ▶ Deoxyribonucleic Acid (DNA)
- ▶ Gene
- ▶ Phenotype

References and Readings

Plomin, R., Defries, J. C., Craig, W., & McGuffin, P. (2003). *Behavioral genetics in the postgenomic era.* Washington, DC: American Psychological Association.

Allesthesia

John E. Mendoza
Tulane University Medical Center
New Orleans, LA, USA

Definition

Misperception of the location of a stimulus. Although it can occur in other modalities, it is most commonly elicited by tactile stimulation and is often seen in the presence of other symptoms of unilateral asomatognosia. If a tactual stimulus is applied to the side of the body contralateral to a hemispheric lesion, the allesthetic patient may perceive the nature of the stimulus correctly but identify it as being applied to the comparable area on the opposite (unaffected) side of the body. In some instances the stimulus may be perceived as being on the same side of the body to which it was applied, but displaced significantly from the point of the actual stimulation (usually toward the midline). When present, this phenomenon likely results from post-rolandic (parietal) lesions of the right rather than the left hemisphere. More rarely it has been associated with brainstem lesions.

Cross References

► Asomatognosia

Allokinesia

Douglas I. Katz
Boston University School of Medicine
Boston, MA, USA

Definition

This phenomenon refers to a motor response in the wrong limb, contralateral to the requested side, sometimes opposite to the direction requested.

Current Knowledge

Allokinesia is often associated with neglect syndromes, usually involving damage to the right hemisphere. It is the motor counterpart of alloesthesia. Typically, a patient moves the right limb in response to a request to move the left limb or moves towards the right, away from the neglected side, when asked to move toward the neglected side. In animal models, the phenomena has been associated with frontal, arcuate gyrus lesions (Heilman, Valenstein, Day, & Watson, 1995) and disconnections of frontal and posterior parietal cortices (Burcham, Corwin, Stoll, & Reep, 1997).

Cross References

► Allesthesia
► Neglect Syndrome

References and Readings

Burcham, K. J., Corwin, J. V., Stoll, M. L., & Reep, R. L. (1997). Disconnection of medial agranular and posterior parietal cortex produces multimodal neglect in rats. *Behavioural Brain Research, 86*(1), 41–47.

Heilman, K. M., Valenstein, E., Day, A., & Watson, R. (1995). Frontal lobe neglect in monkeys. *Neurology, 45*(6), 1205–1210.

Alpha Rhythm

Cindy B. Ivanhoe, Natasha K. Eaddy
Baylor College of Medicine
Houston, TX, USA

Synonyms

Alpha waves; Berger's waves

Definition

Electromagnetic oscillations in the frequency range of 8–12 Hz arising from synchronous and coherent electrical

activity of the thalamic pacemaker cells in the human brain. Also called Berger's wave.

Current Knowledge

Alpha waves are believed to arise from the white matter of the occipital lobes. They increase during periods of relaxation with eyes closed. Alpha waves are thought to represent activity in the visual cortex and are associated with feelings of calmness and relaxation. Alpha waves increase when eyes are closed and during meditation and are associated with creativity and mental coordination.

References and Readings

Bragatti, J. A., De Moura Cordova, N., Rossato, R., & Bianchin, M. M. (2007). Alpha coma and locked-in syndrome. *Journal of Clinical Neurophysiology, 24*(3), 308.

Min, B. K., Busch, N. A., Debener, S., Kranczioch, C., Hansimayr, S., Engel, A. K., et al. (2007). The best of both worlds: Phase reset of human EEG alpha activity and additive power contribute to ERP generation. *International Journal of Psychophysiology, 65*(1), 58–68.

Alpha Waves

► Alpha Rhythm

Alphabetic Principle

► Phonics

Alpha-Synuclein Inclusions

► Lewy Bodies

Alprazolam

John C. Courtney
Children's Hospital of New Orleans
New Orleans, LA, USA

Generic Name

Alprazolam

Brand Name

Xanax, Xanax XR

Class

Benzodiazepine

Proposed Mechanism(s) of Action

Binds to benzodiazepine receptors at the GABA-A ligand-gated channel, thus allowing for neuronal hyperpolarization. Benzodiazepines enhance the inhibitory action of GABA via boosted chloride conductance.

Indication

Generalized Anxiety and Panic Disorders

Off Label Use

Other anxiety disorders, irritable bowel syndrome, insomnia, adjunctive treatment in mania and psychosis, premenstrual dysphoric disorder.

Side Effects

Serious

Respiratory depression, hepatic dysfunction (rare), renal dysfunction and blood dyscrasias, grand mal seizures

Common

Sedation, fatigue, depression, dizziness, memory problems, disinhibition, confusion, ataxia, slurred speech

References and Readings

Physicians' Desk Reference (62nd ed.). (2007). Montvale, NJ: Thomson PDR.
Stahl, S. M. (2007). *Essential psychopharmacology: The prescriber's guide* (2nd ed.). New York, NY: Cambridge University Press.

Additional Information

Drug Interaction Effects: http://www.drugs.com/drug_interactions.html
Drug Molecule Images: http://www.worldofmolecules.com/drugs/
Free Drug Online and PDA Software: www.epocrates.com
Gene-Based Estimate of Drug interactions: http://mhc.daytondcs.com:8080/cgi bin/ddiD4?ver=4&task=getDrugList
Pill Identification: http://www.drugs.com/pill_identification.html

ALS

► Anterolateral System

ALSFRS

► Amyotrophic Lateral Sclerosis Functional Rating Scale

ALSFRS-R

► Amyotrophic Lateral Sclerosis Functional Rating Scale

Alterations

► Polymorphism

Altered

► Transgenic

Altered Testing Procedures

► Modified Testing

Alternate Forms

► Polymorphism

Alternate Test Forms

Kyle E. Ferguson[1], Grant L. Iverson[2]
[1]University of British Columbia
Vancouver, BC, Canada
[2]University of British Columbia & British Columbia Mental Health & Addiction Services
Vancouver, BC, Canada

Synonyms

Equivalent forms; Parallel forms

Definition

Alternate test forms are designed to avoid or reduce *content-* or *item-specific* practice effects that are associated with repeated administrations of the same neuropsychological test(s) (Benedict & Zgaljardic, 1998). Examination of the manuals for many intellectual and neuropsychological tests illustrate that practice effects are common, especially over brief retest intervals (e.g., days or weeks). Regarding test construction, alternate test forms should include the same number of items, and the items should be of equivalent difficulty. Moreover, the test instructions, time limits, examples, and format should be identical to the original instrument developed during standardization, to reduce measurement error (Jackson, 2009). Of course, measurement error can never be eliminated. For example, content-sampling error and time-sampling error – inherent in all test–retest paradigms – are always concerns in developing alternate test forms (Strauss, Sherman, & Spreen, 2006). Additionally, alternate test forms cannot control other factors such as positive carry-over effect (i.e., developing better test-taking strategies), familiarity with the testing context (i.e., novelty

effects), performance anxiety, and regression to the mean, among others (Benedict & Zgaljardic, 1998; Busch, Chelune, & Suchy, 2006; Salinsky, Storzbach, Dodrill, & Binder, 2001). This might, to some extent, explain why some studies show that alternate test forms reduce or eliminate practice effects, whereas other studies do not.

Current Knowledge

Alternate test forms are developed by administering an equivalent test – comprising items of similar difficulty – to the same group of examinees or normative sample, shortly before or after being administered the original test form. Scores from the two forms are then correlated (This is called alternate form reliability, or equivalent or parallel form reliability), which yields a reliability coefficient – otherwise known as the coefficient of equivalence. If the original and alternate test forms are truly equivalent, then there would be (theoretically) a one-to-one correspondence between the two sets of scores (Petersen, 2008). Moreover, their means and variances would also be very similar. Therefore, the coefficient of equivalence should be high (i.e., >0.80; Sattler, 2001). Of course, though they appear similar, the two forms are often not of equivalent difficulty, or otherwise parallel. Thus, in the absence of employing special empirical procedures like test equating, which "fine-tune the test construction process" (Petersen, 2008, p. 99), the two forms cannot be used interchangeably.

Test equating refers to a class of statistical concepts and procedures that adjust for differences in difficulty level on alternate test forms (Please note that these procedures adjust for differences in test difficulty, not differences in content (see Kolen & Brennan, 2004)), so that the forms can be used interchangeably (see Kolen & Brennan, 2004, pp. 2–3, for a discussion of this procedure; White & Stern, 2003). Test equating establishes, empirically, "a relationship between raw scores on two test forms that can then be used to express the scores on one form in terms of the scores on the other form" (Petersen, Kolen, & Hoover, 1989, p. 242; see also Dorans & Holland, 2000; Petersen, 2008). Common types of test equating are Item Response Theory (IRT), linear, and equipercentile (Ormea, Reeb, & Riouxc, 2001).

The Neuropsychological Assessment Battery (Stern & White, 2003), Hopkins Verbal Learning Test-Revised (Brandt & Benedict, 2001), Brief Visuospatial Memory Test-Revised (Benedict, 2001), and Wide Range Achievement Test-Fourth Edition (Wilkinson & Robertson, 2006) are several examples of tests (or test batteries) that provide alternate test forms. With the above caveats in mind, alternate test forms can be useful in serial neuropsychological evaluations.

Cross References

- ▶ Item Response Theory
- ▶ Reliable Change Index
- ▶ Test Construction
- ▶ Test Reliability and Validity

References and Readings

Benedict, R. H., & Zgaljardic, D. J. (1998). Practice effects during repeated administrations of memory tests with and without alternate forms. *Journal of Clinical and Experimental Neuropsychology, 20*(3), 339–352.

Benedict, R. H. B. (2001). *Brief visuospatial memory test - revised.* Odessa, FL: Psychological Assessment Resources.

Brandt, J., & Benedict, R. H. B. (2001). *Hopkins verbal learning test-revised.* Odessa, FL: Psychological Assessment Resources.

Busch, R. M., Chelune, G. J., & Suchy, Y. (2006). Using norms in neuropsychological assessment. In D. K. Attix & K. A. Welsh-Bohmer (Eds.), *Geriatric neuropsychology: Assessment and intervention* (pp. 133–157). New York: Guilford.

Dorans, N. J., & Holland, P. W. (2000). Population invariance and equitability of tests: Basic theory and the linear case. *Journal of Educational Measurement, 37*, 281–306.

Jackson, S. L. (2009). *Research methods and statistics: A critical thinking approach* (3rd ed.). Belmont, CA: Wadsworth Cengage Learning.

Kolen, M. J., & Brennan, R. L. (2004). *Test equating, scaling, and linking: Methods and practices* (2nd ed.). New York: Springer.

Ormea, D., Reeb, M. J., & Riouxc, P. (2001). Premorbid IQ estimates from a multiple aptitude test battery: Regression vs. equating. *Archives of Clinical Neuropsychology, 16*, 679–688.

Petersen, N. S. (2008). A discussion of population invariance of equating. *Applied Psychological Measurement, 32*, 98–101.

Petersen, N. S., Kolen, M. J., & Hoover, H. D. (1989). Scaling, norming, and equating. In R. L. Linn (Ed.), *Educational measurement* (3rd ed., pp. 221–262). New York: Macmillan.

Salinsky, M. C., Storzbach, D., Dodrill, C. B., & Binder, L. M. (2001). Test-retest bias, reliability, and regression equations for neuropsychological measures repeated over a 12–16-week period. *Journal of the International Neuropsychological Society, 7*(5), 597–605.

Sattler, J. M. (2001). *Assessment of children: Cognitive applications* (4th ed.). San Diego: Jerome M. Sattler.

Stern, R. A., & White, T. (2003). *Neuropsychological assessment battery.* Lutz, FL: Psychological Assessment Resources.

Strauss, E., Sherman, E. M. S., & Spreen, O. (2006). *A compendium of neuropsychological tests: Administration, norms, and commentary* (3rd ed.). New York: Oxford University Press.

White, T., & Stern, R. A. (2003). *Neuropsychological assessment battery: Psychometric and technical manual.* Lutz, FL: Psychological Assessment Resources.

Wilkinson, G. S., & Robertson, G. J. (2006). *Wide range achievement test* (4th ed.). Lutz, FL: Psychological Assessment Resources.

Alzheimer, Alois (1864–1915)

Katherine S. McClellan[1], Anna Bacon Moore[2]
[1]Atlanta Veterans Affairs Medical Center
Decatur, GA, USA
[2]Emory University School of Medicine
Atlanta, GA, USA

Major Appointments

- Intern – Mental Asylum at Frankfurt am Main, 1888–1895
- Senior Physician – Mental Asylum at Frankfurt am Main, 1895–1903
- Researcher – Royal Psychiatric Clinic and District Mental Asylum, Munich, 1903–1912
- Assistant Professor – Ludwig-Maximilian University, Munich, 1904–1912
- Chief Physician – Royal Psychiatric Clinic and District Mental Asylum, Munich, 1906–1909
- Professor of Psychiatry – Psychiatry Clinic of Silesian Friedrich-Wilhelm University, Breslau, 1912–1915

Major Honors and Awards

- Extraordinary Professor, Ludwig-Maximilian University (1909)
- *Geheimer Ministerialrat* (Cabinet Councillor) (1915)

Landmark Clinical, Scientific, and Professional Contributions

- Alois Alzheimer was both an excellent clinician and a notable researcher. He is best remembered for being the first to definitively describe the symptoms and cerebral lesions of the disease now known as Alzheimer's Disease. Nonetheless, his contributions to science and medicine did not begin, nor do they end, there. He was one of the leaders of the movement to implement the nonrestraint principle (explained more fully below) in asylums. His neurohistological work advanced the idea that psychiatric diseases were biological in origin. And, through his roles as both doctor and scientist, he contributed to our understanding of a variety of conditions such as cerebral atherosclerosis, alcoholism, and general paresis.

Short Biography

In the German municipality Marktbreit, Alois Alzheimer was born on June 14, 1864 to Eduard and Theresia Alzheimer. Eduard, a Royal Notary, provided his family with a comfortable upbringing. Although Alois had only an older brother when he was born, six more siblings followed him. Alois spent the first four years of his education at Catholic school in Marktbreit, until his family left the area to find a new home with superior educational opportunities for the children. The family's chosen residence was in Aschaffenburg, and in 1874, Alois moved there in order to study at the Royal Humanistic Gymnasium. Alois completed his high-school degree in 1883 with excellent grades. He then decided to study medicine because of his aptitude and fondness for the natural sciences, as well as a sense of duty to mankind.

He enrolled at the Royal Friedrich Wilhelm University in Berlin for the 1883–1884 winter semester. In his psychiatry lecture there, he learned of John Conolly's nonrestraint principle. Also called open treatment, the nonrestraint principle proposed the novel view that the mentally ill should be treated with a minimal amount of physical constraint. Although Berlin was the medical capital of Germany, Alois disliked Berlin and its distance from his family. Therefore, he was transferred to the University of Würzburg (Lower Franconia, Germany), where his older brother was studying. As an aside, due to the influence of his older brother, Alois joined and later held several officer positions in the Franconian Corps. His histology professor, Alfred von Kölliker, gave him his first experience with microscopes and staining techniques, which lead to his passion for forensic psychiatry. In the fall of the following year, Alois left to spend his winter semester at the Eberhard Karls University of Tübingen. He returned in 1887 to the Würzburg Anatomical Institute's department of microscopy to write his doctoral thesis, "On the Earwax Glands." The intricate figures he presented in the paper, as in all his papers, were proof of how scrupulously he conducted his research and clinical work. With the completion of his thesis, Alois Alzheimer received his doctor of medicine degree. He passed the state medical examination and was awarded a license to practice medicine in 1888.

Shortly thereafter, he became a personal physician to a mentally ill woman and traveled with her for five months. Emil Sioli, the director of the Municipal Asylum for the Insane and Epileptic in Frankfurt am Main had advertized for an intern, specifically hoping for a competent doctor

who was also adept with a microscope. Upon his return, the 24-year old Dr. Alzheimer was hired immediately. Dr. Franz Nissl also was hired as senior physician for the asylum. Nissl not only became one of Alzheimer's closest friends, but also taught him a powerful staining technique for highlighting neuronal cell bodies (the Nissl stain), that helped Alzheimer achieve success in his histological studies. Sioli's main goal for the asylum was to fully employ the nonrestraint principle. Alzheimer was particularly skilled at gaining the trust of patients through conversation, and he often documented these conversations. The dialogues often were central to diagnosing a patient, and even more so to research. His talent in clinical interviewing was such that clinicians who later read his notes had sufficient information to evaluate his opinions and to make their own diagnoses. Alzheimer drew on his microscopy and forensic psychiatry training, to do histological investigations into the physical origins of psychiatric disorder. In Frankfurt, his topics of study included epilepsy, senile dementia, criminal minds, and a variety of psychoses. He established himself as a well-rounded physician by publishing papers on a wide variety of topics. Aside from his duties as a physician and researcher, he also appeared as an expert before courts and presented at many scientific meetings. While at Frankfurt, Alzheimer became an expert on general paresis, which later became the subject of his postdoctoral thesis.

In Algeria, a personal physician who had been traveling with a man suffering from general paresis sent a telegram to Alzheimer in 1892 to request that he treat the worsening patient. Alzheimer obliged and went to North Africa. He intended to bring the patient back to his hospital in Germany, but the patient died before reaching Germany, leaving his wife, Cecilie, a widow. Alzheimer and Cecilie became close friends, and eventually the widow asked him to marry her. They were married in April 1894 in the registry office of Frankfurt. Because Cecilie was Jewish, she had to convert to Catholicism before the two could be married by the church in February 1895. On March 10, 1895, their first child, Gertrud, was born, and Dr. Nissl was chosen to be her godfather. But Nissl soon moved to work with Emil Kraepelin in Heidelberg. Nissl's departure created room for Alzheimer to be promoted to senior physician within Sioli's asylum. Also that year, to lessen the overcrowding of the main hospital, a new branch asylum opened. With this addition, Sioli and Alzheimer furthered their goal of fully implementing the nonrestraint principle by instituting duration baths rather than isolation. The asylum became known as a revolutionary clinic, and it elevated the reputations of all its doctors. But above all, in 1901, Alzheimer met the patient who would immortalize his name: Auguste D. Auguste had been admitted to the asylum because of delusional and excessively forgetful behavior. Although at admission she was disoriented, anxious, and suspicious, over time she became unruly and disruptive. Alzheimer was particularly intrigued by her case for the duration of her stay in the hospital.

Alzheimer's second child, Hans, was born in 1896, and his third, Maria, was born in 1900. However, the lavish lifestyle he had lived with Cecilie ended when she died in February 1901. Alzheimer's sister, Elisabeth, took over his household. Though she was strict, she became an integral part of the family. Without Cecilie, Alzheimer no longer had a reason to stay in Frankfurt. After his application to be director of a regional asylum was rejected, he joined Nissl in Heidelberg in 1903 and went to work for Emil Kraepelin. The group he joined there was an international team of researchers. Later that same year, Kraepelin was named director of the Royal Psychiatric Clinic and the District Mental Asylum in Munich. Alzheimer followed him, but was not paid in Munich due to the lack of a position for him, and also his desire to manage his own time. Despite his absence from Frankfurt, Alzheimer still received updates on Auguste D.

By this point, Alzheimer's thesis on general paresis was finished, but because he moved twice in such a short time, he had not yet turned it in. Alzheimer submitted his postdoctoral thesis to the Ludwig-Maximilian University in Munich with the hopes of gaining associate professorship. In it, he published not only his clinical dialogues, but also his postmortem histological findings. With this paper, he asserted that histological examinations could definitively show the presence of general paresis. Until then, few doctors suspected that syphilis was a cause of general paresis, but shortly thereafter the link between the two was found. His work was surpassed by the discovery of a way to diagnose syphilis, without resorting to autopsies. In August 1904, he joined the university's medical faculty.

Because of his experience at remodeling the Frankfurt clinic, Alzheimer was fundamental in finishing the plans for the new Munich clinic. He furnished his anatomic laboratory with the best equipment and the brightest students – many of whom went on to make great contributions to science, including Ugo Cerletti – electrical shocks to generate convulsions, Hans Gerhard Creutzfeldt and Alfons Jakob – Creutzfeldt-Jakob disease, Frederic Lewy – Lewy bodies, and others. Alzheimer was made

chief physician in 1906, a paid position, but also one that took away much of his time in the laboratory.

Two topics that consumed Alzheimer in Munich were psychiatric symptoms resulting from pathological anatomy and classification of mental illnesses by etiology. The latter faced much opposition from the scientific community. Yet, the most opposition he ever faced was his presentation of the Auguste D. case. Auguste D. had always fascinated Alzheimer. He had paid special attention to her, taking copious notes about their conversations. When he moved away, he still received updates about her condition, which worsened progressively until her death. When Auguste D. died in 1906, her files, brain, and spinal cord were sent to Munich. Alzheimer, along with his student Gaetano Perusini, immediately began examining the case. In Tübingen, Alzheimer presented her case in a lecture entitled "On a Peculiar Severe Disease Process of the Cerebral Cortex," in which he described the lesions (now known to be neurofibullary tangles) that he believed caused Auguste's symptoms. Based on records from the time, his peers did not bother to ask questions, nor were there any comments about the lecture in the minutes. He later published the entire lecture, but still it received little attention. He then tasked Perusini to find more patients, similar to Auguste D. in the clinic. Perusini found four cases and published an article entitled "On Clinically and Histologically Peculiar Mental Illnesses in Advanced Age." Another student of Alzheimer's, Francesco Bonfiglio found another case of presenile dementia, and also published on the disease. Spurred by Bonfiglio's paper, Kraepelin included a section on "Alzheimer's Disease," in the 1910 edition of his text book *Clinical Psychiatry*. This publication is acknowledged as the origin of the term. Alzheimer himself never referred to it as "Alzheimer's Disease," though he had later publications on the disease. Alzheimer decided to resign his post as chief physician in order to devote more time to research, specifically traveling to study epilepsy. Although he was no longer employed by Kraepelin, Alzheimer undertook the responsibilities of coeditor of Kraepelin's *Journal of Complete Neurology and Psychiatry*.

Recognition for Alzheimer and the disease carrying his name began to spread. In 1912, the Silesian Friedrich-Wilhelm University in Breslau asked him to join their faculty as a full professor of psychiatry. During the move to Breslau, Alzheimer fell ill, but nevertheless assumed his duties with vivacity. His patients and coworkers, including Georg Stertz, Ottfried Förster, and Ludwig Mann, took notice of his kind, yet authoritative presence. In 1913, his health forced him to visit a private clinic. Though he returned to work, his health had not improved. This did not impede his ability to make significant contributions to science: in 1913 he found the syphilis pathogen in the central nervous system of a patient with general paresis.

After a long illness, Alois Alzheimer died on December 19, 1915 from a heart condition and kidney failure. Though no one immediately took over his pursuit of an understanding of Alzheimer's disease, people recommenced research on Alzheimer's disease cases in the 1950s. Studies of the disease began in earnest after Martin Roth's assertion in the 1960s that Alzheimer's disease was the most common cause of senile dementia. In the 1970s, Robert Katzman further propelled the surge of interest in Alzheimer's disease by stating that it was one of the most widespread diseases. Since then, the amount of research on Alzheimer's disease has increased exponentially, resulting in multiple foundations and centers devoted solely to the disease that Alois Alzheimer's colleagues considered trivial.

Cross References

- ▶ Alzheimer's Dementia
- ▶ Alzheimer's Disease
- ▶ Paresis

References and Readings

Engstrom, E. (2007). Researching dementia in imperial Germany: Alois Alzheimer and the economies of psychiatric practice. *Culture, Medicine, and Psychiatry, 31*, 405–413.

Graeber, M., Kösel, S., Egensperger, R., Banati, R., Müller, U., Bise, K., et al. (1997). Rediscovery of the case described by Alois Alzheimer in 1911: Historical and molecular genetic analysis. *Neurogenetics, 1*, 73, 80.

Lage, J. (2006). 100 years of Alzheimer's disease (1906–2006). *Journal of Alzheimer's Disease, 9*, 15–26.

Maurer, K., & Maurer, U. (1998). *Alzheimer: The life of a physician and the career of a disease.* New York: Columbia University Press.

Morris, R., & Salmon, D. (2007). The centennial of Alzheimer's disease and the publication of "Über eine eigenartige Erkankung der Hirnrinde" by Alöis Alzheimer. *Cortex, 43*, 821–825.

Small, D., & Cappai, R. (2006). Alois Alzheimer and Alzheimer's disease: A centennial perspective. *Journal of Neurochemistry, 99*, 708–710.

Snyder, P., & Pearn, A. (2007). Historical note on Darwin's consideration of early-onset dementia in older persons, thirty-six years before Alzheimer's initial case report. *Alzheimer's and Dementia, 3*, 137–142.

Zilka, N., & Novak, M. (2006). The tangled story of Alois Alzheimer. *Bratisl Lek Listy, 107*, 343–345.

Alzheimer's Dementia

JoAnn T. Tschanz, Aaron Andersen
Utah State University
Logan, UT, USA

Synonyms

Alzheimer's disease; Early-onset Alzheimer's disease; Familial Alzheimer's disease; Senile dementia of the Alzheimer's type

Short Description or Definition

One of the leading causes of dementia in late-life, Alzheimer's disease (AD), is a progressive neurodegenerative disorder characterized by a gradual onset and progressive course, affecting memory and other cognitive domains. For a diagnosis, the cognitive impairments of AD must not occur exclusively in the context of a delirium, and must be of sufficient severity to cause impairment in social or occupational functioning. Diagnoses of AD (Possible or Probable AD) are based on the history and presentation of clinical symptoms, evidence of cognitive impairment, and the exclusion of other causes of dementia such as stroke, metabolic disorders, or other conditions that may account for the cognitive impairment. A diagnosis of Definite AD is based upon postmortem neuropathological analysis and is made when there are sufficient numbers of senile plaques and neurofibrillary tangles in specific brain regions.

Categorization

AD may be categorized according to age of onset, family history, or presenting clinical features. Age categories distinguish between senile and pre-senile onset (onset before age 65). Classifications based on family history (familial AD vs. sporadic AD) distinguish AD forms that show high heritability. Familial AD is rare, generally of pre-senile onset, and has been associated with mutations in the APP gene on chromosome 21, Presenilin 1 gene on chromosome 14, and Presenilin 2 gene on chromosome 1 (Hardy, 2003). Its transmission resembles an autosomal dominant pattern (Morris & Nagy, 2004).

AD has also been classified according to the clinical presentation of symptoms. Its most common presentation involves early and significant memory impairment. Variants to this presentation have been reported in the literature, and they include a visual (posterior) form with significant impairment in higher-level processing of visual stimuli, an aphasic form with significant language involvement, and a frontal form with prominent impairment of executive functions. At autopsy, these variants usually exhibit AD neuropathology in brain regions typically involved in the specific neuropsychological domain (Grabowski & Damasio, 2004).

Epidemiology

Prevalence and Incidence. AD is the most common cause of dementia in late-life, accounting for 50–70% of all cases (Malaspina Corcoran, Schobel, & Hamilton, 2008). Current estimates suggest that 4.5 million individuals suffer from AD in the US, and projections based on population trends suggest an increase to 13.2 million by 2050 (U.S. Department of Health and Human Services, 2006). The overall prevalence of AD is about 5–6% in individuals aged 65 years or older in North America, and doubles approximately every 5 years after the age of 60. Estimates suggest a prevalence of 1% at age 60, 16% between ages 80 to 85, and 26 to 45% for those above age 85. Incidence rates also exhibit an age-related increase. Studies report differing patterns of AD prevalence and incidence at the upper end of the lifespan, with some reporting a plateau at very old ages (age 90 or 100; Mendez & Cummings, 2003).

Risk Factors. Increasing age is among the strongest risk factor for AD. Other risk factors include the ε4 allele of the Apolipoprotein E (APOE) gene, positive family history (also in sporadic AD), low education (possibly due to less neural reserve), female gender (even after accounting for differential survival), and history of head trauma and vascular factors such as high cholesterol and high blood pressure. Some risk factors occurring earlier in the lifespan affect AD risk. Studies suggest that high blood pressure or high serum cholesterol in *midlife* increases the risk of AD later in life. Although inconsistent, some studies report that treatment with antihypertensive medications or cholesterol lowing agents reduces the risk for AD (Soininen, Kivipelto, Laakso, & Hiltunen, 2003). Recent studies have also examined the role of insulin resistance and diabetes in AD risk. Among potential "protective" factors, data from epidemiological studies suggest a *lower*

risk of AD among women receiving hormone replacement therapy. However, a large randomized clinical trial of estrogen and estrogen + progesterone in elderly women suggested an *increase* in all-cause dementia in those receiving the combination hormone treatment. Thus, hormone therapy is not recommended for cognitive health (Malaspina et al., 2008). Other factors under active investigation are diet, nutrients and nutrient supplements such as antioxidant vitamins, omega 3 fatty acid, medications such as non-steroidal anti-inflammatory agents, and lifestyle practices such as physical activity and cognitive and social engagement.

Natural History, Prognostic Factors, Outcomes

The clinical course of AD is usually one of a gradual onset of symptoms with progressive decline. Many scientists believe the disease process starts in the brain decades before overt symptoms emerge. A preclinical phase, characterized primarily by episodic memory deficits, heralds the onset of symptoms. This stage, also referred to as mild cognitive impairment (MCI), lasts approximately 1–3 years. Progression to dementia is characterized by increasing severity of cognitive impairment with severe memory deficits, visuospatial impairment, and other perceptual disturbances. Language impairment begins with mild naming difficulties and circumlocutory speech, but progresses to include comprehension deficits. Apraxia (difficulty performing learned motor tasks in the absence of impairment in primary motor or sensory functions) and impaired executive functions and computational ability are also apparent. Behavioral changes are common with indifference, irritability, and sadness, progressing to delusions and, in some individuals, more severe psychiatric disturbances such as hallucinations and agitation. In end stages, there is severe deterioration of all cognitive functions, speech is generally unintelligible, and motor rigidity and urinary and fecal incontinence are present. Death may occur as the result of other causes such as pneumonia or infections (Mendez & Cummings, 2003). On postmortem exam, the brain is characterized by generalized atrophy and sulcal and ventricular enlargement. Figure 1a displays gross atrophy of an AD brain compared with a brain from a cognitively normal elderly individual. Figure 2 displays a coronal section of an AD brain at the level of the hippocampus.

The duration of the entire disease course from MCI to death is highly variable. Survival estimates from symptom onset range from 2 to 20 years. The mean survival has been reported as approximately 10 years, but some studies have reported considerably shorter duration of 3 years. More rapid rate of disease progression has been associated with early, prominent language impairment, frontal features, and extrapyramidal signs (Mendez & Cummings, 2003).

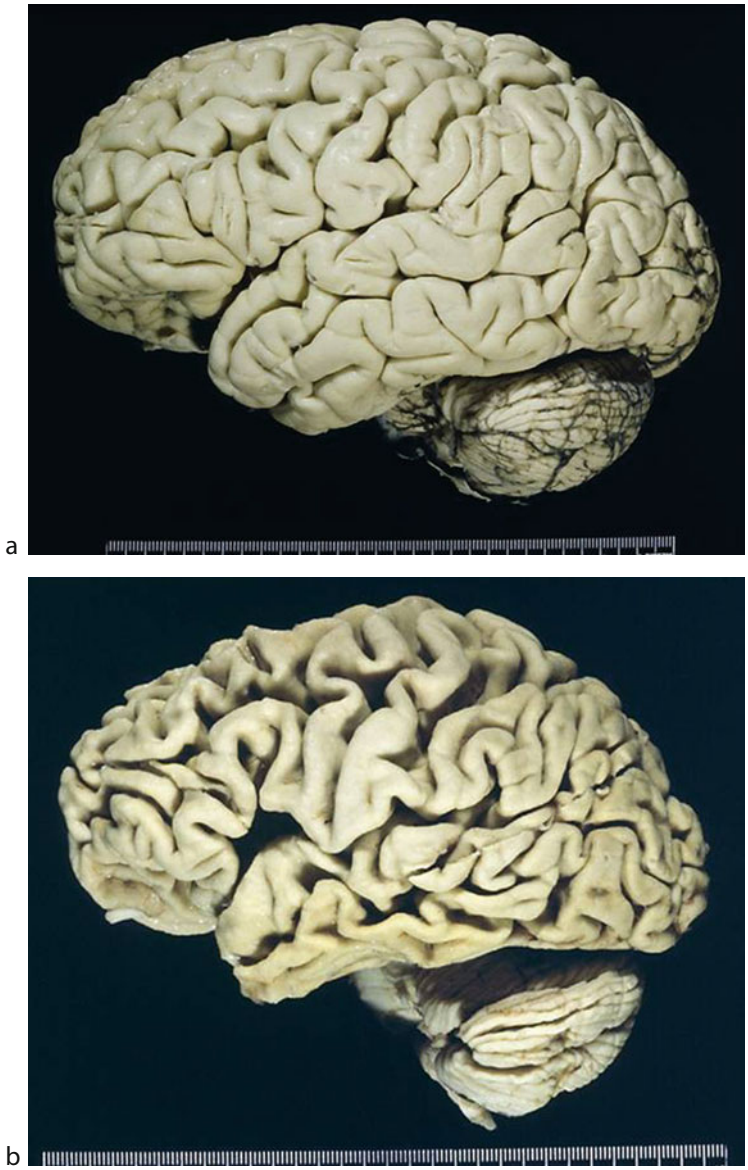
Neuropsychology and Psychology of Alzheimer's Dementia

Neuropsychological Deficits

The neuropsychology of AD follows the clinical progression. In early stages, memory is almost always involved, with specific deficits in learning new information. Remote memory such as memory for autobiographical or other knowledge-based systems (semantic memory) is relatively unaffected. In early stages, standardized testing with word lists may reveal relative preservation of immediate or working memory, but impairment in delayed recall. There is usually some benefit from cuing or recognition procedures. With progression, cuing is no longer helpful, and remote recall is affected. Implicit memory may be relatively spared as patients show evidence of learning on priming and procedural motor tasks. Orientation to time and place is also affected in AD (Knopman & Selnes, 2003).

Language impairments progress from mild anomia and word finding difficulties in early stages, to include impairment in comprehension and writing. Errors in speech (paraphasias) become more common, and word substitutions become progressively less related to the target words. Repetition of speech may be relatively unaffected until late in the disease course (Knopman & Selnes, 2003; Mendez & Cummings, 2003). Tests of verbal fluency and confrontation naming are especially sensitive to early changes in language. Visuospatial disturbances may be subtle or nonexistent in the earliest stages of AD. In moderate and severe stages, impairment may be evident on figure copying tasks or judgment of line orientation (Knopman & Selnes, 2003). Figure 3 displays characteristic examples of visuoconstructional impairment in four representative patients with AD.

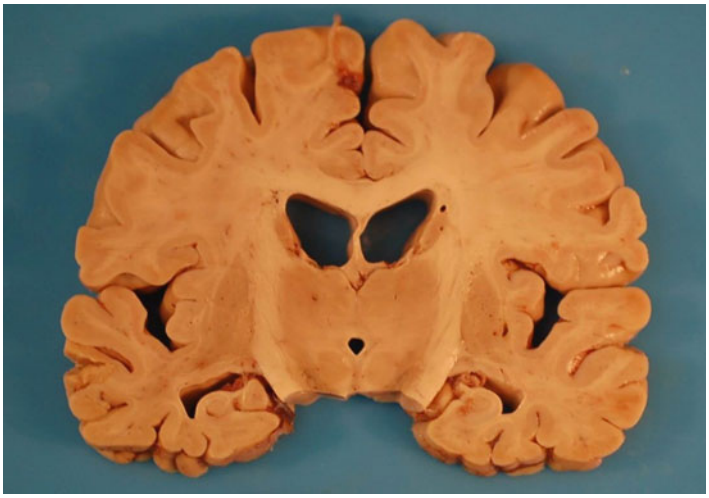
Impaired abstract reasoning, sustained attention, planning, judgment, and problem solving may characterize impairment in executive functions. Deficits in executive functions may be demonstrated on tests of verbal fluency, trailmaking, and set shifting. Tests such as the Rey Complex



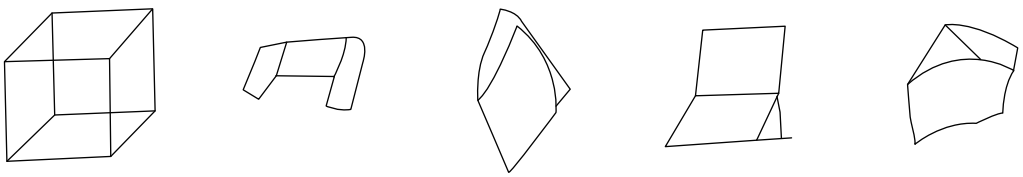
Alzheimer's Dementia. Figure 1 (**a**) and (**b**) display the brains from a cognitively normal elderly individual and an individual who suffered from advanced AD, respectively. Note the severe atrophy apparent in the AD brain (Photo courtesy of Christine Hulette, M.D., Bryan Alzheimer Disease Research Center, Duke University. Reproduced with permission from Elsevier Limited)

figure and clock drawing may also elicit impairment in executive functions with poor planning and execution of the tasks. Deficits in working memory may be evident on tasks requiring mental manipulation or divided attention (Knopman & Selnes, 2003).

Other neurocognitive aspects of AD include apraxia and anosognosia. In mild AD, deficits in praxis are not common but emerge later in the disease course. Assessment of apraxia may involve pantomiming the execution of a task. Anosognosia or an unawareness of disability is quite common (Knopman & Selnes, 2003). Standardized assessment approaches are few. Some approaches rely on clinical observation, noting a discrepancy between self-report of cognitive impairment and test performance, or a discrepancy between caregiver and patient report of impairment.



Alzheimer's Dementia. Figure 2 Display of the atrophy in AD in this coronal section including the hippocampi. Note the dilated lateral ventricles and loss of inferior temporal mass (Photo courtesy of Steven S. Chin, M.D., Ph.D., University of Utah Health Sciences Center)



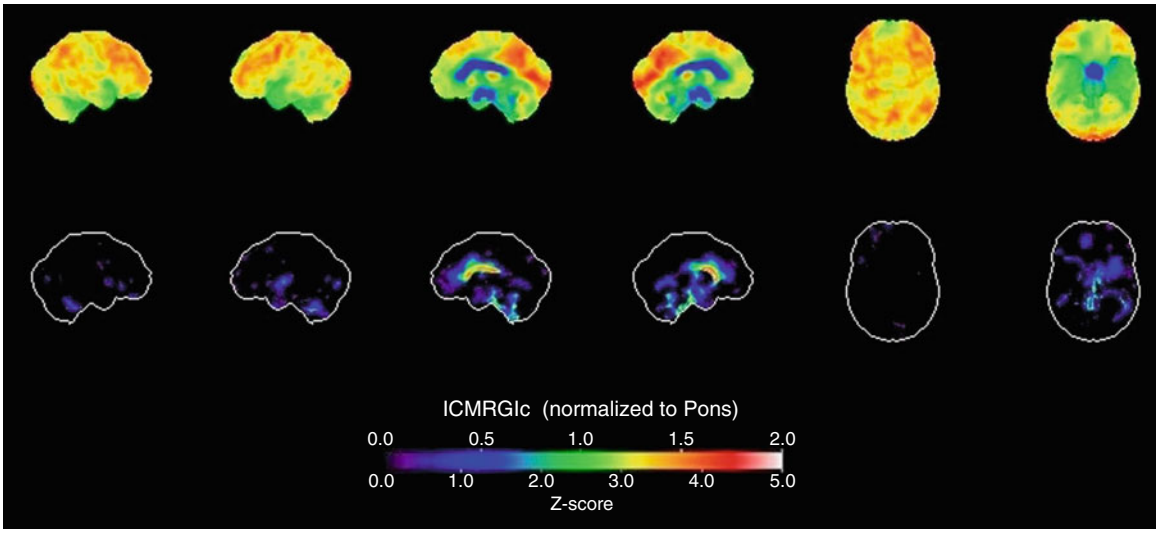
Alzheimer's Dementia. Figure 3 Display of the visuoconstructional impairments in the drawings of four individuals with Possible or Probable AD. The stimulus is the left-most figure

Behavioral Symptoms

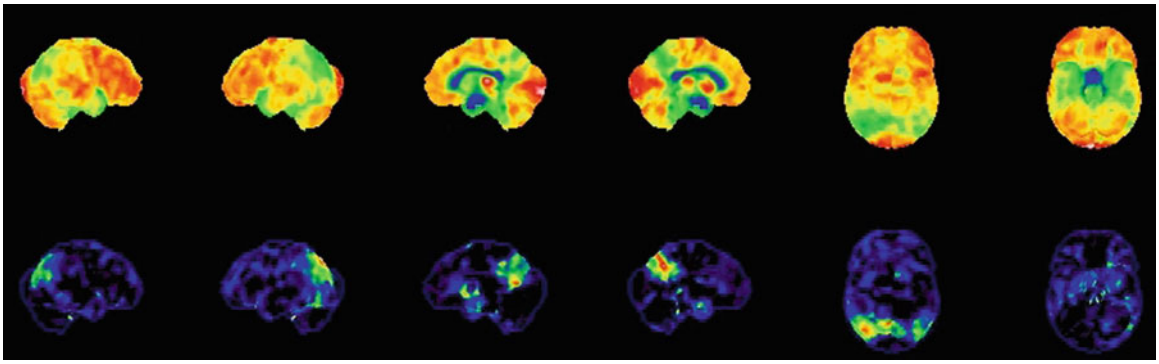
Behavioral changes are extremely common in AD, with nearly all individuals exhibiting at least one symptom at some point over the disease course. Among the most common of these changes is apathy, characterized by a lack of interest and indifference. Anxiety, irritability, and depression are also common, as are delusions. Some patients may exhibit hallucinations, and particularly challenging for caregivers and family are disruptive behaviors such as agitation and aggression. The course of behavioral symptoms is variable, with severe episodes alternating with milder ones, raising questions about environmental triggers. Noting the co-occurrence of one or more behavioral disturbances, some scientists believe these symptoms are better conceptualized as behavioral s*yndromes*, with implications for underlying brain pathology. Several questionnaires are available for assessing behavioral symptoms, ranging from a single symptom questionnaire to larger inventories of multiple symptoms. Assessment of behavioral symptoms is particularly important in an AD evaluation as their presence may suggest other causes of dementia.

Evaluation

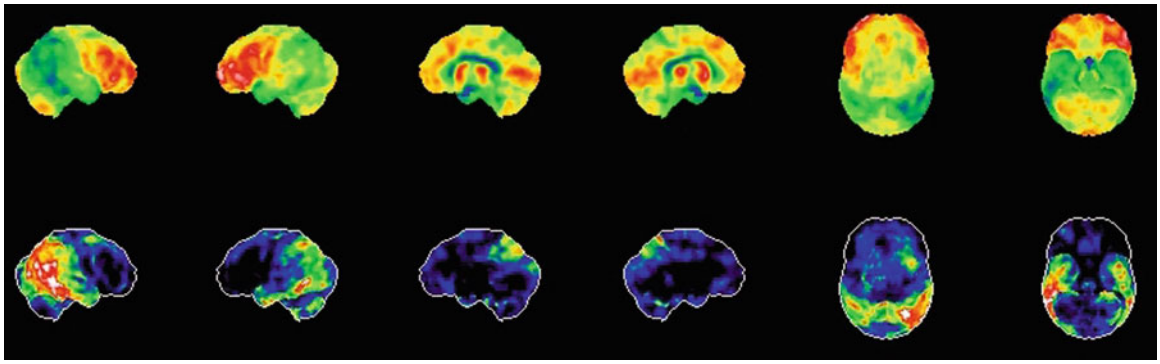
A through clinical work-up is important for diagnosing AD or determining the etiology of dementia. Critical elements of an evaluation include a detailed clinical history and mental status and physical exams. Due to inaccurate reporting by patients, interview with a reliable informant is necessary. Laboratory, neuroimaging, and neuropsychological testing are important to exclude other causes of dementia. Laboratory testing may include a blood count, routine chemistries, thyroid function, and B12 levels. Neuroimaging with MRI or CT may reveal generalized cerebral atrophy with associated sulcal widening and ventricular enlargement. In early stages of the disorder, the brain may appear normal on MRI/CT. PET



Alzheimer's Dementia. Figure. 4. Seventy-four year old control subject with normal cognition. The top row shows normal brain metabolic activity and the bottom row shows very few regions of hypometabolism. The areas of significant hypometabolism indicated in the medial views are due to this individual having enlarged lateral ventricles relative to normative subjects. Figures 4–6 These images are processed FDG-PET images obtained from elderly subjects. The images have been processed using Neurostat sterotactic surface projections to illustrate the changes of the brain in Alzheimer's disease. Subject scans are shown in two rows in each figure, depicting projections onto six surfaces: R-lateral, L-lateral, R-medial, L-medial, Superior and Inferior. The top row in each figure displays regional glucose metabolism with ''cooler'' colors (purple, blue) reflecting areas of hypometabolism. The bottom row in each figure displays relative glucose metabolism for each participant as compared with a normative sample of 27 cognitively normal elderly individuals. In this bottom series, the images display the statistical significance, expressed as Z-scores, of the hypometabolism when compared to those of the normative sample. The brighter colors (red, white) represent areas of significant hypometabolism and the cooler colors of blues and purples represent relatively normal brain metabolism (All photographs courtesy of Norman L. Foster, M.D. and Angela Y. Wang, Ph.D., Center for Alzheimer's Care, Imaging and Research, University of Utah)



Alzheimer's Dementia. Figure. 5. Sixty year old subject clinically diagnosed with MCI. The top row shows symmetric decreases in metabolic activity in both hemispheres of the brain. Abnormalities are primarily in the parietal lobe (shown in the R-lateral and L-lateral views) and the posterior cingulate cortex (shown in the R-medial and L-medial views), as seen in the green regions. The bottom row confirms that these regions (green, yellow and red areas) are indeed significantly (Z-scores $\geq$ 2.5) hypometabolic. This pattern is a distinguishing feature of AD seen in FDG-PET studies (All photographs courtesy of Norman L. Foster, M.D. and Angela Y. Wang, Ph.D., Center for Alzheimer's Care, Imaging and Research, University of Utah)



Alzheimer's Dementia. Figure. 6. Seventy-two year old subject clinically diagnosed with AD. This subject shows an even greater and more widely distributed decrease in glucose metabolism. Parietal and temporal lobes and posterior cingulate cortex (green and blue region in the top row) are affected. The statistically significant changes in metabolic pattern (red and white regions in the lower row) are much greater than the MCI case (All photographs courtesy of Norman L. Foster, M.D. and Angela Y. Wang, Ph. D., Center for Alzheimer's Care, Imaging and Research, University of Utah)

imaging is a more sensitive technique for detecting changes in brain function in early stages. Reduced glucose metabolism, usually in the temporo–parietal and posterior cingulate regions, is a consistent pattern in early AD. Figures 4 through 6 display the pattern of glucose hypometabolism in MCI and AD compared with a cognitively normal elderly individual. Neuropsychological testing is important to establish the degree of cognitive impairment and to identify patterns that may be suggestive of specific dementing illnesses. Additional tests such as sampling cerebrospinal fluid for tau and amyloid-B42 assays may be helpful as supplemental procedures in complex cases (Mendez & Cummings, 2003).

Treatment

Treatment for AD is palliative, with medications and therapies providing symptom management. Medications most commonly used are cholinesterase inhibitors that functionally address the cholinergic deficit of AD by blocking the activity of the acetylcholine degrading enzyme, acetylcholinesterase. These medications are modestly effective, and patients and families may observe an improvement in some cognitive and behavioral symptoms. However, the medications do not modify the trajectory of disease progression. In general, cholinesterase inhibitors are well-tolerated. The use of the first FDA-approved drug of this class, tacrine, however, is rarely administered now because of risk of liver toxicity. Other medications include donepezil, rivastigmine, and galantamine. Side effects include gastrointestinal symptoms such as diarrhea, nausea, and vomiting (Orgogozo, 2003). Memantine, an NMDA glutamate receptor blocker, has been approved for use in moderate and severe AD. This drug is believed to be effective by reducing neuronal excitotoxicity. Other treatments include the use of psychotropic medications (such as antidepressant and antipsychotic medications) to address the behavioral or neuropsychiatric symptoms. Cognitive rehabilitation may be attempted early in the disease course while patients are still able to participate. Psychoeducation, behavioral techniques, music therapy, and caregiver support and interventions are also important elements of clinical care.

Cross References

- ▶ Alois Alzheimer
- ▶ Aricept (Donepezil)
- ▶ Cholinesterase Inhibitors
- ▶ Dementia
- ▶ Neurofibrillary Tangles
- ▶ Senile Dementia
- ▶ Senile Plaques

References and Readings

Grabowski, T. J., & Damasio, A. R. (2004). Definition, clinical features and neuroanatomical basis of dementia. In M. M. Esiri, V. M.-Y. Lee, & J. Q. Trojanowski (Eds.), *The neuropathology of dementia* (2nd ed., pp. 1–33). Cambridge, UK: Cambridge University Press.

Hardy, J. (2003). The genetics of Alzheimer's disease. In K. Iqbal & B. Winblad (Eds.), *Alzheimer's disease and related disorders: research*

advances (pp. 151–153). Bucharest, Romania: Ana Asian International Academy of Aging.
Knopman, D., & Selnes, O. (2003). Neuropsychology of dementia. In K. M. Heilman & E. Valenstein's (Eds.), *Clinical neuropsychology* (4th ed., pp. 574–616). New York: Oxford University Press.
Malaspina, D., Corcoran, C., Schobel, S., & Hamilton, S. P. (2008). Epidemiological and genetic aspects of neuropsychiatric disorders. In S. C. Yudofsky & R. E. Hales' (Eds.), *Neuropsychiatry and behavioral neurosciences* (5th ed., pp. 301–362). Washington, DC: American Psychiatric Association Press.
Mendez, M. F., & Cummings, J. L. (2003). *Dementia a clinical approach* (3rd ed.). Philadelphia: Butterworth.
Morris, J. H., & Nagy, Z. (2004). Alzheimer's disease. In M. M. Esiri, V. M.-Y. Lee, & J. Q. Trojanowski (Eds.), *The neuropathology of dementia* (2nd ed., pp. 161–206). Cambridge, UK: Cambridge University Press.
Orgogozo, J.-M. (2003). Treatment of Alzheimer's disease with cholinesterase inhibitors. An update on currently used drugs. In K. Iqbal & B. Winblad (Eds.), *Alzheimer's disease and related disorders: Research advances* (pp. 663–675). Bucharest, Romania: Ana Asian International Academy of Aging.
Soininen, H., Kivipelto, M., Laakso, M., & Hiltunen, M. (2003). Genetics, molecular epidemiology and cardiovascular risk factors of Alzheimer's disease. In K. Iqbal & B. Winblad (Eds.), *Alzheimer's disease and related disorders: Research advances* (pp. 53–62). Bucharest, Romania: Ana Asian International Academy of Aging.
U.S. Department of Health and Human Services. (2006). *Journey to discovery. 2005–2006 Progress report on Alzheimer's disease.* Washington, DC: U.S. Department of Health and Human Services.

Alzheimer's Disease

Russell H. Swerdlow, Heather Anderson
Jeffrey M. Burns
University of Kansas School of Medicine
Kansas City, KS, USA

Definition

A neurodegenerative disease of the brain characterized clinically by insidious, chronic, and progressive cognitive decline, and histologically by cerebral accumulations of the proteins beta amyloid (plaques) and tau (tangles).

Historical Background

In 1902, a woman called Auguste D. came under the care of Dr. Alois Alzheimer, then at the University of Frankfurt. The patient manifested changes in behavior and cognition. Her clinical course was characterized by progressive paranoia, delusional thinking, disorientation, and poor memory. She was institutionalized for the last 3 years of her life. Upon her death, Alzheimer analyzed her brain using a silver stain, and described both extracellular and intracellular protein accumulations. The extracellular protein accumulations were termed plaques and the intraneuronal protein accumulations were called tangles. Alzheimer presented the results of this autopsy in 1906. Several other similar cases of relatively "presenile" (i.e., arbitrarily defined as an onset prior to age 55–65) clinical dementia associated with plaques and tangles were noted by Alzheimer and others over the next 4 years. In 1910, Alzheimer's departmental chair, Emil Kraepelin, published a textbook covering the fields of neurology and psychiatry, and referred to patients with presenile dementia, plaques, and tangles as having "Alzheimer's disease."

Concurrently, other investigators, such as Oscar Fischer, also reported plaque presence in elderly demented individuals. These individuals were older than those with "presenile" dementia (i.e., generally older than age 55–65). As the commonality of progressive dementia in the elderly was well recognized, the presence of plaques in elderly demented individuals was felt to represent a normal phenomenon. Such individuals were not diagnosed with Alzheimer's disease. Instead, cognitive decline in elderly adults was attributed to normal aging or other poorly described conditions, such as "hardening of the arteries." As a result, Alzheimer's disease remained relatively uncommon for a number of subsequent decades.

In the 1960s, investigators began comparing elderly demented subjects to those diagnosed with "presenile" Alzheimer's disease. Notable similarities were observed regarding the clinical course (chronic and progressive), the clinical features (cognitive decline that featured evolution of an amnestic state, followed by behavioral changes), and histopathology (plaques and tangles). By the 1970s, the number of demented elderly was growing fast as demographic shifts in the aging population combined with increased recognition of the syndrome. At this point, the original definition of Alzheimer's disease (as described by Alzheimer and named by Kraepelin) was expanded to account for all dementing individuals with plaques and tangles, although some separation of these groups was envisioned. Those meeting the original criteria of plaque and tangle dementia in presenile adults were designated as having dementia of the Alzheimer type (DAT), while the previously unconsidered elderly cases were designated as having senile dementia of the Alzheimer type (SDAT). With increasing recognition of the problem, Alzheimer's disease very quickly became

incredibly common, as well as a Western civilization health priority.

In the USA, the 1980s saw the establishment of federally funded Alzheimer's disease research centers, which began to systematically study the clinical course of this progressive dementia, mostly in the common SDAT form. Academic research began to unravel the chemical makeup of plaques and tangles. Investigations into patterns and causes of neurodegeneration were performed. This advancing knowledge enhanced the ability of clinicians to diagnose Alzheimer's disease at increasingly subtle stages, as well as the ability to pharmacologically intervene to achieve partial, temporary symptomatic benefit in at least some individuals.

Current Knowledge

Scientific Perspective

The plaques seen in persons with Alzheimer's disease contain several aggregated proteins. The major constituent is a protein called amyloid beta (Aβ). "Beta" is a chemical term that specifies a certain pattern of protein folding. "Amyloid" is a general term that refers to proteins that give a particular appearance when exposed to a particular type of stain, Congo red. The beta amyloid, or Aβ, found in the brains of Alzheimer's disease patients derives from a particular protein called the amyloid precursor protein (APP).

In the human brain, the APP is 695 amino acids long. It is a transmembrane protein. One end (the carboxy end) is found inside neurons, in the cytoplasm. The other end (the amino end) extends outside the cell. In between the cytoplasmic and extracellular portions is a stretch that runs through the membrane. The normal function of APP is not well known. APP is digested by different enzymes, which cut the protein at different points. An enzyme complex called the beta secretase (BACE) cuts APP in its extracellular portion. An enzyme or group of enzymes referred to as the alpha secretase cuts APP in its intramembrane segment. The gamma secretase cuts APP twice, both times in its intramembrane segment. Both of the gamma secretase cuts occur closer to the carboxy end of the APP than the alpha secretase cut.

Different cutting combinations generate various APP by-products. Cutting of an APP by beta and gamma secretases generates a 38–43 amino acid stretch, and this stretch tends to assume a beta folding conformation and has the features of an amyloid protein (i.e., birefringence under the microscope when stained with Congo red). The 40 and 42 amino acid-long variants of Aβ predominate in plaques, and are often designated Aβ40 and Aβ42. Aβ42 seems to be particularly important to the formation of the amyloid plaques of Alzheimer's disease, probably because this version of the protein is quite insoluble. When Aβ accumulations begin to form in brain, they are not associated with disrupted cell elements and are called "diffuse plaques." Another type of more evolved plaque can also be found in Alzheimer's disease patients, in which Aβ becomes condensed at the center of the plaque, and the vicinity of the plaque is associated with disrupted cell elements such as degenerating axons and dendrites. As axons and dendrites are collectively called "neurites," this type of plaque is called a "neuritic plaque."

The tangles of Alzheimer's disease are found primarily in neurons. Under the microscope tangles have a fibrous quality to them, and hence tangles in Alzheimer's disease are referred to as "neurofibrillary tangles." Neurofibrillary tangles consist of a protein called tau. Normally, tau is found in association with microtubules, which act as a skeleton, or "cytoskeleton" supporting the cellular structure. The function of tau appears to be the stabilization of these microtubules. Like many proteins, after its production tau is modified by the addition and subtraction of phosphate groups on certain amino acids, especially serine and threonine. During embryonic development, tau is heavily phosphorylated, but during youth and early adulthood this heavily phosphorylated pattern is rare if at all seen. In Alzheimer's disease, though, tau again takes on a heavily phosphorylated pattern, which is felt to reflect an abnormal physiologic event and is referred to as tau "hyperphosphorylation." Hyperphosphorylated tau molecules begin to pair off, a process called "dimerization." Hyperphosphorylated tau dimers, also called "paired helical filaments," are quite insoluble and begin to aggregate with each other. This aggregation, typically visible extending from cell bodies into axons, comprises the neurofibrillary tangle.

As impressive as this advancing understanding of plaque and tangle composition is, recognizing what constitutes these aggregations does not address why they form. In this regard, genetic studies of DAT subjects who inherit the disorder in an autosomal dominant fashion have had a large impact. Several hundred such families have been documented. In these families the disease affects about 50% of each generation, with typical onset occurring in the 3rd, 4th, 5th, or 6th decades. A small number of these families have demonstrable mutations in the gene that encodes the APP. This gene is located on chromosome 21, the same chromosome that is present in excess in Down's syndrome. Down's syndrome patients

invariably accumulate Aβ plaques in their 5th decade. A somewhat larger number of these families have mutations in the gene that encodes a protein called presenilin 1. This gene is found in chromosome 14. Presenilin 1 protein constitutes part of the gamma secretase complex. A smaller number of families have mutation of a related gene on chromosome 1, which encodes a related protein, presenilin 2. Presenilin 2 can also participate in formation of the gamma secretase. Mutations in the genes that encode APP, presenilin 1, and presenilin 2 all enhance the production of Aβ42. This has lent support to the "amyloid cascade hypothesis," which posits as Aβ42 is generated it begins to interfere with neuronal function, kill neurons, and generate the other histologic features seen in Alzheimer's disease. While the logic underlying this hypothesis is obvious, it is important to keep in mind it assumes the very small subset of early-onset, autosomal dominant Alzheimer's disease (which accounts for far less than 1% of those affected) have a similar if not identical etiology to the common sporadic, late-onset cases that constitute the vast majority. In those subjects, what initiates Aβ42 production remains an open area of debate. Conceivably, population diversity in genes that contribute to APP production or processing could cause Aβ42 to appear. Environmental factors could lead to Aβ42 formation. Also, a variety of age-related factors promote Aβ42 formation.

Other factors are recognized to play a role in Alzheimer's disease, and where these factors fit into or what they tell us about the etiologic hierarchy of the disease is unclear. One factor relates to the *APOE* gene on chromosome 19. The *APOE* gene shows population variability due to the presence of two polymorphic positions. The common *APOE* variants are the ε2, ε3, and ε4 forms. The *APOE* ε4 form is over represented in those with Alzheimer's disease, where it seems to move up the age of presentation in those destined to develop the disorder. Mitochondrial function is also altered in Alzheimer's disease, and these alterations are not limited to the brain.

Diagnostic Perspective

Dementia is defined as cognitive decline that has advanced to that point it interferes with activities of daily living. While dementia has many different etiologies, Alzheimer's disease is the most common cause of dementia, accounting for 50–60% of dementia verified by neuropathological examination of the brain at autopsy. The clinical diagnosis (i.e., diagnosis in life) of Alzheimer's disease is made in patients who have progressive dementia with no other systemic or brain diseases that could account for the progressive cognitive decline. A diagnosis of "definite Alzheimer's disease" can only be diagnosed at autopsy by the presence of plaques and tangles (although in some schemas tangles are not requisite) in an individual with a clinical history suggestive of dementia. The presence of plaques and tangles in typical brain regions (mesial temporal, parietal, and inferior frontal structures) is quite common in elderly persons with the clinical syndrome of Alzheimer's disease. As a result of the high prevalence of Alzheimer's disease with advancing age (at least one commonly quoted study estimates approximately half of those over the age of 85 have it), the specificity of the clinical diagnosis is high. Recognition of how common Alzheimer's disease is in later life has also served to enhance clinician awareness, thus improving sensitivity of the diagnosis. In the hands of an experienced physician, clinical diagnostic accuracy is excellent.

Criteria originally designed to facilitate identification of subjects for clinical trials have helped to standardize clinical diagnostic approaches. These criteria, such as those proposed by the National Institute of Neurologic, Communicative Disorders, and Stroke (NINCDS) and the Alzheimer's Disease and Related Disorders Association (ADRDA) in the 1980s emphasize the importance of establishing that a progressive dementia exists in a patient. Two basic approaches are commonly used toward this end. One is to demonstrate a pattern of cognitive domain strengths and weaknesses that reliably suggest decline from a previous level of cognitive function has emerged. For example, defective memory retention in the presence of another defective cognitive domain (language, executive function, visuospatial function, and praxis) in an elderly patient with cognitive complaints and an otherwise unremarkable physical exam is strongly suggestive of Alzheimer's disease. The other approach focuses more on defining the degree and nature of emerging declines in daily living activities. This latter technique focuses extensively on collateral history obtained from family members or friends of the patient.

The diagnosis is made primarily through clinical impression, although that impression is influenced by a small set of recommended laboratory and imaging tests. These tests are serologic (vitamin B12 level, thyroid function tests, electrolytes with renal and hepatic indices, and a blood cell count) and structural (brain imaging by either computed tomography or magnetic resonance imaging) in nature. As currently used, they mostly serve to rule out the presence of concomitant pathologies that can interfere with cognition. Although this has contributed to the view that the Alzheimer's disease diagnosis is one of exclusion,

it should be noted that certain patterns of cognitive decline elicited by clinical history or demonstrable by neuropsychological testing are so typical of Alzheimer's disease they can be used to support a diagnosis of inclusion. It is important to note, though, that at the time of this writing PET and *APOE* genotyping are not commonly used in the diagnosis of Alzheimer's disease and cannot by themselves establish a diagnosis of Alzheimer's disease.

Treatment Perspective

Although Alzheimer's disease is currently neither reversible nor curable, it is possible to treat its symptoms. The first approved treatment for Alzheimer's disease was tacrine, a cholinesterase inhibitor. This drug increased levels of brain acetylcholine by antagonizing its synaptic degradation. Increasing brain cholinergic tone was identified as a pharmacologic target because Alzheimer's disease patients show a profound loss of acetylcholine due to degeneration of cholinergic neurons in the basal forebrain. Safer cholinesterase inhibitors (donepezil, rivastigmine, and galantamine) have since superseded tacrine. In addition to inhibiting acetylcholinesterase, rivastigmine also inhibits buytrylcholinesterases that also hydrolyze acetylcholine, and galantamine is an allosteric modulator of acetylcholine nicotinic receptors. Each agent shows a similar overall degree of efficacy, although the individual with Alzheimer's disease may respond to or tolerate one drug better than the other. Treatment cohorts followed for 12 weeks to 3 years indicate that as a group, those started on cholinesterase inhibitors tend to perform and appear slightly improved compared to their immediate pretreatment baseline. This improvement appears detectable for 6–12 months. By 12 months, though, treatment groups return to their pretreatment performance as ascertained by cognitive testing, clinical impression, and caregiver impression. Beyond 12 months, patients continuously decline below their pretreatment baseline, although for at least the next several years patients appear to perform better on cognitive testing than would otherwise be expected. The clinical meaningfulness of this sustained benefit has fueled considerable debate. Benefits have been observed on measures of cognitive ability, functional ability, behavior, and caregiver stress.

At the time of this writing, memantine is the only non-cholinesterase inhibitor specifically approved for the treatment of Alzheimer's disease. Under in vitro conditions, memantine blocks a cation channel associated with the NMDA type of glutamate-activated ionotropic receptors. Whether or not this is its primary mechanism of action in Alzheimer's disease has been questioned. In any case, cohorts of patients with moderate or severe Alzheimer's disease, when randomized to memantine, perform better on measures of cognitive and functional performance than do concurrent placebo treatment groups. In severe Alzheimer's disease, the magnitude of observed benefit is similar to that obtained with donepezil. Memantine and donepezil have been studied in combination with each other. Subjects with mini-mental state exam scores of 5–14, who were already on donepezil, did better as a group when memantine was added to their treatment regimen than when placebo was added. Demonstrable benefits in mild Alzheimer's disease are lacking and thus the role of memantine in the mild stages of Alzheimer's disease is not clear.

A single study concluded high-dose vitamin E (2000 iu each day) might slightly slow decline in Alzheimer's disease patients. More recent general evidence, though, suggests taking more than 400 iu of vitamin E on a daily basis increases overall mortality. The marginality of any vitamin E benefit, in conjunction with safety concerns, has reduced enthusiasm for the use of vitamin E in Alzheimer's disease. Although a variety of other prescription medications (estrogens, statins), nonprescription medications (nonsteroidal anti-inflammatories), and nutraceuticals (gingko biloba) have been considered for the treatment of Alzheimer's disease, published data to date on all other treatment options has been at worst negative and at best insufficient to earn regulatory approval.

Other drug categories are commonly used to treat targeted symptoms associated with Alzheimer's disease. For instance, antipsychotic medications are often used to treat agitated behavior. Some studies do show efficacy in this regard, although other studies have argued the limited behavioral benefits antipsychotics may confer is canceled out by increased morbidity.

Future Directions

Scientific Perspective

In the short term, considerable effort will be directed at additional studies of Aβ dynamics and homeostasis. Research will focus on the toxicities of different degrees of Aβ aggregation (especially oligomers, defined as short, soluble polymers of amyloid), cellular mechanisms of Aβ disposal, and tissue-level mechanisms of Aβ disposal.

Research over the longer term will need to address the fact that the predominant etiologic hypothesis, the amyloid cascade hypothesis, cannot yet explain why Aβ

homeostasis changes in most of those affected or how Aβ might give rise to other aspects of Alzheimer's disease pathology. It is possible the amyloid cascade hypothesis will prove valid in those with early onset, autosomal dominant Alzheimer's disease caused by mutations of the genes encoding APP, presenilin 1, and presenilin 2 proteins, but not the late-onset cases (the vast majority). Disproving the amyloid cascade hypothesis in the late-onset cases will likely require two events. First, interventions that attempt to treat Alzheimer's disease by targeting Aβ will need to show absent or limited efficacy. Second, other hypotheses better able to explain the overall Alzheimer's clinical and pathological big picture will need to demonstrate viability and durability.

Diagnostic Perspective

Because it will likely prove easier in the future to prevent neurodegeneration rather than reverse it, the ability to render an early, accurate diagnosis is crucial. Also, the ability to treat the disease (either symptomatically or disease modifying) increases the importance of early diagnosis. A confluence of neuropsychologic/clinical longitudinal studies performed in conjunction with careful histopathologic correlation has already allowed a syndrome called mild cognitive impairment (MCI) to be defined. MCI is known to represent a precursor of the Alzheimer syndrome in the majority of those diagnosed with it, and in more than half the MCI syndrome simply represents early Alzheimer's disease. There is an emerging consensus that the line between "normal" age related cognitive decline and clinically excessive cognitive decline, at least on an etiologic level, is a blurry one. Accordingly, by the time MCI is diagnosable in many individuals, substantial irreversible brain change has occurred. Techniques and technologies for pushing the limits of the diagnosis to stages that precede MCI are therefore needed.

Most development toward this end focuses on the study of potential "biomarkers." Biomarkers can be entities detectable in extractable tissues, such as blood or cerebrospinal fluid (CSF). For example, CSF tau levels increase in Alzheimer's disease, while CSF Aβ levels decline. When used in conjunction with fluorodeoxyglucose PET, which shows the brain's ability to consume glucose, investigators have been able to develop algorithms that predict future cognitive decline in elderly adults with MCI, and even in individuals before they manifest cognitive complaints.

Biomarkers can also be demonstrated in vivo. For instance, ligands that bind amyloid plaques or both amyloid plaques and neurofibrillary tangles can be administered intravenously, and the degree of brain ligand retention measured using PET. This approach can provide an estimate of an individual patient's plaque burden. Development of techniques such as this will increasingly render the diagnosis of Alzheimer's disease one of inclusion. Even so, this technology may, like others, turn out to serve best as an adjunct to the clinical diagnosis as opposed to the principal determinant of the diagnosis. The reason for this is that a substantial percentage of nondemented individuals have relatively high plaque burdens. The significance of increased plaque burden in nondemented individuals will need to be determined with prospective long-term studies.

Treatment Perspective

None of the treatments approved for use in Alzheimer's disease are approved for use in MCI, although available data argue cholinesterase inhibition (at least with donepezil) may provide a marginal benefit. Such a benefit would not be surprising, especially if MCI represents very early Alzheimer's disease in most people.

Over a decade of experience with symptomatic treatment has made it abundantly clear that disease-modifying treatments are required. Most current approaches toward disease modification are targeted to Aβ homeostasis. Inhibition of its production (gamma secretase inhibitors and modifiers), its targeted removal (active and passive immunization approaches), prevention of its aggregation, and enhancement of enzymatic degradation are all under active pursuit. To date, a phase II Aβ vaccination trial (AN1792) was halted when several of the subjects developed encephalitis. Other data obtained through this trial suggest the approach was successful in reducing cerebral amyloid plaques. However, the most extensive published clinical data from AN1792 indicate that one year after vaccination, the rate of cognitive decline was similar to (unchanged from or only very slightly reduced from) the rate of decline shown by the placebo group of that trial. A phase III trial of tramiprosate, which retards Aβ aggregation, was negative. A phase III trial of a gamma secretase modifying agent (R-flurbiprofen) is underway. Phase III trials of agents intended to humorally remove Aβ are scheduled.

If attacking Aβ fails to meaningfully benefit Alzheimer's disease patients, the validity of the amyloid cascade hypothesis in late-onset, sporadic Alzheimer's disease will be called into question. If this happens, new models for drug design will be needed. Currently, mice expressing a

mutant APP transgene, sometimes in conjunction with other mutant human transgenes, serve as the gold standard for preclinical testing of potential Alzheimer's disease treatments.

Cross References

- ▶ Alzheimer's Dementia
- ▶ Memory Impairment
- ▶ Mental Status Examination
- ▶ Mini Mental State Exam
- ▶ Neurobehavioral Cognitive Status Examination
- ▶ Senile Dementia

References and Readings

Amaducci, L. A., Rocca, W. A., & Schoenberg, B. S. (1986). Origin of the distinction between Alzheimer's disease and senile dementia: how history can clarify nosology. *Neurology, 36*, 1497–1499.

Blacker, D., & Tanzi, R. E. (1998). The genetics of Alzheimer disease: current status and future prospects. *Archives of Neurology, 55*, 294–296.

Blessed, G., Tomlinson, B., & Roth, M. (1968). The association between quantitative measures of dementia and of senile change in the cerebral grey matter of elderly subjects. *The British Journal of Psychiatry, 114*, 797–811.

Campion, D., Dumanchin, C., Hannequin, D., Dubois, B., Belliard, S., Puel, M., et al. (1999). Early-onset autosomal dominant Alzheimer disease: prevalence, genetic heterogeneity, and mutation spectrum. *The American Journal of Human Genetics, 65*, 664–670.

Corder, E. H., Saunders, A. M., Strittmatter, W. J., Schmechel, D. E., Gaskell, P. C., Small, G. W., et al. (1993). Gene dose of apolipoprotein E type 4 allele and the risk of Alzheimer's disease in late onset families. *Science, 261*, 921–923.

De Leon, M. J., & Klunk, W. (2005). Biomarkers for the early diagnosis of Alzheimer's disease. *Lancet Neurology, 5*, 198–199.

Evans, D. A., Funkenstein, H. H., Albert, M. S., Scherr, P. A., Cook, N. R., Chown, M. J., et al. (1989). Prevalence of Alzheimer's disease in a community population of older persons. Higher than previously reported. *JAMA, 262*, 2551–2556.

Gearing, M., Mirra, S. S., Hedreen, J. C., Sumi, S. M., Hansen, L. A., & Heyman, A. (1995). The Consortium to establish a registry for Alzheimer's disease (CERAD). Part X. Neuropathology confirmation of the clinical diagnosis of Alzheimer's disease. *Neurology, 45*, 461–466.

Gilman, S., Koller, M., Black, R. S., Jenkins, L., Griffith, S. G., Fox, N. C., et al. (2005). Clinical effects of Abeta immunization (AN1792) in patients with AD in an interrupted trial. *Neurology, 64*, 1553–1562.

Hardy, J., & Allsop, D. (1991). Amyloid deposition as the central event in the aetiology of Alzheimer's disease. *Trends in Pharmacological Sciences, 12*, 383–388.

Hardy, J. A., & Higgins, G. A.(1992). Alzheimer's disease: the amyloid cascade hypothesis. *Science, 256*, 184–185.

Katzman, R. (1976). The prevalence and malignancy of Alzheimer's disease: a major killer. *Archives of Neurology, 33*, 217–218.

Khachaturian, Z. S. (1985). Diagnosis of Alzheimer's disease. *Archives of Neurology, 42*, 1097–1106.

Klunk, W. E., Engler, H., Nordberg, A., Wang, Y., Blomqvist, G., Holt, D. P., et al. (2004). Imaging brain amyloid in Alzheimer's disease with Pittsburgh Compound-B. *Annals of Neurology, 55*, 306–319.

Mayeux, R., Saunders, A. M., Shea, S., Mirra, S., Evans, D., Roses, A. D., et al. (1998). Utility of the apolipoprotein E genotype in the diagnosis of Alzheimer's disease. Alzheimer's Disease Centers Consortium on Apolipoprotein E and Alzheimer's Disease. *The New England Journal of Medicine, 338*, 506–511.

McKhann, G., Drachman, D., Folstein, M., Katzman, R., Price, D., & Stadlan, E. M. (1984). Clinical diagnosis of Alzheimer's disease: report of the NINCDS-ADRDA Work Group under the auspices of Department of Health and Human Services Task Force on Alzheimer's Disease. *Neurology, 34*, 939–944.

Morris, J. C. (2006). Mild cognitive impairment is early-stage Alzheimer disease: time to revise diagnostic criteria. *Archives of Neurology, 63*, 15–16.

Mosconi, L., De Santi, S., Li, J., Tsui, W. H., Li, Y., Boppana, M., et al. (2007). Hippocampal hypometabolism predicts cognitive decline from normal aging. *Neurobiol Aging*. doi:10.1016/j.neurobiolaging.2006.12.008.

National Institute on Aging, and Reagan Institute Working Group on Diagnostic Criteria for the Neuropathological Assessment of Alzheimer's Disease. (1997). Consensus recommendations for the postmortem diagnosis of Alzheimer's disease. *Neurobiology of Aging, 18*(4 Suppl.), S1–2.

Petersen, R. C., Smith, G. E., Waring, S. C., Ivnik, R. J., Tangalos, E. G., & Kokmen, E. (1999). Mild cognitive impairment: clinical characterization and outcome. *Archives of Neurology, 56*, 303–308.

Petersen, R. C., Thomas, R. G., Grundman, M, Bennett, D., Doody, R., Ferris, S., et al. (2005) Vitamin E and donepezil for the treatment of mild cognitive impairment. *The New England Journal of Medicine, 352*, 2379–2388.

Ronald and Nancy Reagan Research Institute of the Alzheimer's Association and the National Institute on AgingWork Group. (1998). Consensus report of the work group on: molecular and biochemical markers of Alzheimer's disease. *Neurobiology of Aging, 19*, 109–116.

Sano, M., Ernesto, C., Thomas, R. G., Klauber, M. R., Schafer, K., Grundman, M., et al. (1997). A controlled trial of selegiline, alpha-tocopherol, or both as treatment for Alzheimer's disease. The Alzheimer's Disease Cooperative Study. *The New England Journal of Medicine, 336*, 1216–1222.

Scheuner, D., Eckman, C., Jensen, M., Song, X., Citron, M., Suzuki, N., et al. (1996). Secreted amyloid beta-protein similar to that in the senile plaques of Alzheimer's disease is increased in vivo by the presenilin 1 and 2 and APP mutations linked to familial Alzheimer's disease. *Nature Medicine, 2*, 864–870.

Schneider, L. S., Tariot, P. N., Dagerman, K. S., Davis, S. M., Hsiao, J. K., et al. (2006). Effectiveness of atypical antipsychotic drugs in patients with Alzheimer's disease. *The New England Journal of Medicine, 355*, 1525–1538.

Snowdon, D. A., Kemper, S. J., Mortimer, J. A., Greiner, L. H., Wekstein, D. R., & Markesbery, W. R. (1996). Linguistic ability in early life and cognitive function and Alzheimer's disease in late life. Findings from the Nun Study. *JAMA, 275*, 528–532.

Swerdlow, R. H. (2007). Is aging part of Alzheimer's disease, or is Alzheimer's disease part of aging? *Neurobiology of Aging, 28*, 1465–1480.

Alzheimer's Disease Cooperative Study ADL Scale

Jessica Fish
Medical Research Council Cognition & Brain Sciences Unit
Cambridge, UK

Synonyms

Alzheimer's disease co-operative study ADL scale for mild cognitive impairment (ADCS-ADL-MCI); Alzheimer's disease co-operative study ADL scale for severe impairment (ADCS-ADL-sev).

Description

The ADCS-ADL assesses the competence of patients with Alzheimer's Disease (AD) in basic and instrumental activities of daily living (ADLs). It can be completed by a caregiver in questionnaire format, or administered by a clinician/researcher as a structured interview with a caregiver. All responses should relate to the 4 weeks prior to the time of rating. The six basic ADL items each take an ADL (e.g., eating) and provide descriptions of level of competence, with the rater selecting the most appropriate option (e.g., ate without physical help and used a knife; used a fork or spoon but not a knife; used fingers to eat; was usually fed by someone else). The 16 instrumental ADL items follow the format "In the past 4 weeks, did s/he *use the telephone*," with the response options of yes/no/don't know. If the response is "yes," a rating is then made regarding his/her competence according to a set of descriptions tailored to that activity (e.g., for the telephone item, whether the person looked up phone numbers and made calls, made calls only to well-known numbers without referring to a directory, made calls only to well-known numbers using a telephone directory, answered the phone but did not make calls, or only spoke when put on the line). Adapted versions of the scale suitable for people with MCI (ADCS-MCI-ADL) and moderate-severe AD (ADCS-ADL-sev) have also been developed. Scores on the 24-item ADCS-ADL range from 0 to 78, those on the 18-item ADCS-MCI-ADL range from 0 to 57, and on the 19-item ADCS-ADL-sev from 0 to 54, where higher scores reflect greater competence (see section "Psychometric Data" for further details). The entire instrument takes 15–30 min to administer.

Historical Background

The ADCS is a United States-based initiative that aims to conduct research informing the prevention and treatment of AD, as well as developing measures for use in people with AD, particularly in clinical trials. The ADCS-ADL was the first ADL scale to be developed for use specifically in clinical trials with people with AD across the range of severity. The 23 items in the standard version were selected from a pool of 45 items based upon a stringent set of psychometric criteria (see Section "Psychometric Data"). Using the same criteria, Galasko et al. (2005) developed a version of the ADCS-ADL for more severely impaired participants, which is known as the ADCS-ADL-sev, and a version for people with MCI has also been developed (ADCS-MCI-ADL, Perneczky et al., 2006). The ADCS-ADL has been used in a variety of clinical trials.

Psychometric Data

Galasko et al. (1997) selected the items for the ADCS-ADL from a pool of 45 items thought to be relevant to the target population on the basis of existing scales and clinical experience. To determine which ADLs were most suitable for inclusion, the 45-item version was administered at baseline, 6 months and 12 months later to 64 elderly controls and 242 people with AD, stratified by MMSE score at baseline assessment. Half of participants were additionally assessed at 1 and 2 months post-baseline. An item was included in the final measure if it fit the criteria that it: was performed either premorbidly or at baseline by >90% of participants (showing it was applicable to the target group), had a kappa agreement statistic at 1–2 months of >0.4 (indicating good test-retest reliability), had a significant correlation with MMSE score (indicating appropriate scaling and validity), and showed decline over 12 months in at least 20% of participants (indicating validity and sensitivity to change).

Galasko et al. (2005) used the same criteria in the development of the ADCS-ADL-sev, based on longitudinal data of 145 patients with Mini-Mental State Examination (MMSE) scores between 0 and 15. Galasko et al. reported good test-retest reliability (baseline-1 month $r = 0.94$, baseline-2 months $r = 0.89$,

month1–month2 $r = 0.94$), and there was evidence of convergent validity based upon the strong correlation between ADCS-ADL-sev and other global impairment measures (ADCS-ADL-sev – MMSE $r = 0.64$; ADCS-ADL-sev – Severe Impairment Battery $r = 0.71$). The mean score on first test was 25.4 (SD 12.7, maximum obtainable 54), with a mean decline of 5.6 points (SD 7.5) over 6 months and 10.3 points (SD 10.3) over 12 months.

Perneczky et al. (2006) have found that the ADCS-MCI-ADL scale can discriminate people with MCI from control participants (a cut-off score of 52 gives sensitivity of 0.89 and specificity of 0.97).

Clinical Uses

The ADCS-ADL and its variants are the only ADL scales designed with AD specifically in mind, and can provide a fairly detailed assessment of competence in a variety of ADLs. Galasko et al. (2005) state that the measure takes too long to administer for it to be widely adopted in clinical practice, but it would be useful in intervention studies, and the ADL-sev in particular where the severity of the disorder may render measures such as the MMSE unsuitable due to floor effects. The careful selection of items for the ADCS-ADL suggests that they are eminently suitable for use in clinical trials. Perneczky et al. (2006) found that even patients with a diagnosis of Mild Cognitive Impairment exhibit deficits in instrumental ADLs on the ADCS-ADL-MCI, and that scores can successfully discriminate patients with MCI from healthy controls; as such, results from this scale may be useful in forming an MCI diagnosis.

Cross References

- ▶ Bristol Activities of Daily Living Scale
- ▶ Disability Assessment for Dementia
- ▶ Lawton–Brody iADL Scale
- ▶ The Activities of Daily Living Questionnaire

References and Readings

Galasko, D., Bennett, D., Sano, M., Ernesto, C., Thomas, R., Grundman, M., et al. (1997). An inventory to assess activities of daily living for clinical trials in Alzheimer's disease. The Alzheimer's disease Cooperative Study. *Alzheimer's Disease and Associated Disorders, 11*(S2), S33–S39.

Galasko, D., Schmitt, F., Thomas, R., Jin, S., Bennett, D., & Ferris, S. (2005). Detailed assessment of activities of daily living in moderate to severe Alzheimer's disease. *Journal of the International Neuropsychological Society, 11*, 446–453.

Perneczky, R., Pohl, C., Sorg, C., Hartmann, J., Komossa, K., Alexopoulos, P., et al. (2006). Complex activities of daily living in mild cognitive impairment: Conceptual and diagnostic issues. *Age and Ageing, 35*, 240–245.

Alzheimer's Disease Co-operative Study ADL Scale for Mild Cognitive Impairment (ADCS-ADL-MCI)

▶ Alzheimer's Disease Cooperative Study ADL Scale

Alzheimer's Disease Co-operative Study ADL Scale for Severe Impairment (ADCS-ADL-sev)

▶ Alzheimer's Disease Cooperative Study ADL Scale

Amantadine

▶ Symmetril (Amantadine)

Ambidexterity

John E. Mendoza
Tulane University Medical Center
New Orleans, LA, USA

Definition

Ambidexterity is the tendency for one to be more or less equally proficient in carrying out complex or skilled motor tasks with either the right or the left hand. While complete ambidexterity is relatively rare, mixed

proficiencies or preferences are not uncommon, with men more frequently demonstrating such mixed preferences than women. Tan (1988) found that approximately 66% of the population was noted to express a strong right-handed preference, while a little more than 3% were predominately left handed. The remaining 30% evidenced mixed hand preferences. As noted elsewhere in this volume, handedness is a common, but not the only measure of what is referred to as "cerebral dominance." Another of the more frequent indices of dominance is language, which is typically organized primarily in the left hemisphere. While in the majority of non-brain-injured individuals, the control of both complex motor skills and language functions rest within the left hemisphere, this may not always be the case, particularly for those who are either left handed or ambidextrous. It has been shown that while right hemisphere dominance for language is quite rare in right-handers, it could approach 30% in strong left-handers. Individuals who are ambidextrous or whose parents are left handed tend to fall somewhere in between these two groups with regard to the hemispheric localization of language. Furthermore, the localization of language may not be an all-or-none phenomena. While one hemisphere may be more predominant, language functions may be mediated to some extent by both hemispheres. Individuals with mixed or anomalous dominance, including those who were ambidextrous, tend to have a greater incidence of at least some degree of bilateral representation of language. In the event of unilateral strokes, such individuals may evidence less severe residual aphasic deficits when compared to patients with strongly lateralized language when that hemisphere is affected.

Cross References

► Anomalous Dominance
► Dominance (Cerebral)

References and Readings

Benson, D. F., & Geschwind, N. (1985). Aphasia and related disorders: A clinical approach. In M. Mesulam (Ed.), *Principles of behavioral neurology* (pp. 193–238). Philadelphia: F.A. Davis Co.

Knecht, S., Drager, B., Deppe, M., Bode, L., Lohmann, H., Floel, A., et al. (2000). Handedness and hemispheric language dominance in healthy humans. *Brain, 123*, 2512–2518.

Pieniadz, J. M., Naeser, M. A., Koff, E., & Levine, H. L. (1983). CT scan hemispheric asymmetry measurements in stroke cases with global aphasia: Atypical asymmetries associated with improved recovery. *Cortex, 19*, 371–391.

Pujol, J., Deus, J., Losilla, J. M., & Capdevila, A. (1999). Cerebral lateralization of language in normal left-handed people studied by functional MRI. *Neurology, 52*, 1038–1043.

Tan, Ü. (1988). The distribution of hand preference in normal men and women. *International Journal of Neuroscience, 41*, 35–55.

Ambiguous Personality Assessment

► Projective Technique

American Academy of Clinical Neuropsychology (AACN)

Rebecca McCartney
Emory University/Rehabilitation Medicine
Atlanta, GA, USA

Membership

American Academy of Clinical Neuropsychology (AACN) is an organization for psychologists who have achieved board certification in the specialty of Clinical Neuropsychology, under the American Board of Clinical Neuropsychology (ABCN). Membership in the Academy consists of three classes: Active, Senior, and Affiliate. Active members are elected from among psychologists who have been certified in clinical neuropsychology by the ABCN in affiliation with the American Board of Professional Psychology (ABPP). Senior members are elected from among Active members who have been Academy members, for a period of no less than the five preceding years, are age 65 or older or disabled, and are fully retired from the active practice of clinical neuropsychology. They continue to be listed in the membership directory of the academy, and they continue to receive any newsletters distributed to Academy members. Senior members have no financial obligations to the Academy and are allowed to continue to subscribe to any journal available through the Academy. At the time of this publication, there were 367 active senior members in the United States and 20 members in Canada. Affiliate members are elected from among all others who are intellectually interested in the purposes of the Academy and wish to participate in its non-voting activities. All members are provided with a subscription to *The Clinical Neuropsychologist*, access to the AACN Clinical Discussion Email List, and discounted fees to meetings and workshops.

Presidents of the Academy include Byron P. Rourke, (1995–1996), Wilfred van Gorp (1996–2002), Catherine A. Mateer (2002–2004), Robert L. Mapou (2004–2006), Jerry J. Sweet (2006–2008).

Major Areas or Mission Statement

AACN's stated mission is to maintain the standards of Clinical Neuropsychology through support of the board certification process of ABCN. The Academy holds the following objectives: (1) Support for the principles, policies, and practices that seek the attainment of the best in clinical neuropsychological patient care. (2) The pursuit of excellence in psychological education, especially as it concerns the clinical neuropsychological sciences. (3) The pursuit of high standards in the practice of clinical neuropsychology and support of the credentialing activities of the ABCN. (4) Support for the quest of scientific knowledge by support for research in neuropsychology and related fields. (5) The communication of scientific and scholarly information through continuing education (CE), scientific meetings, and publications. (6) Provision for communication with other groups and representation for clinical neuropsychological opinion to best achieve and preserve the purposes of the Academy.

Landmark Contributions

AACN was founded in 1996. The first appointed president was Byron Rouke, Ph.D. and the first elected president was Wilfred Van Gorp, Ph.D. AACN cosponsored the Houston Conference on Specialty Education and Training in Clinical Neuropsychology in 1997. This conference was a national consensus conference of neuropsychological organizations held with the purpose of establishing training guidelines for clinical neuropsychology. The Houston Conference guidelines have since become the model for most programs offering formal training in clinical neuropsychology. AACN held its first annual conference in 2003. During that same year, *The Clinical Neuropsychologist* became AACN's official journal. In 2007, AACN began on-line Continuing Education (CE) programs.

Major Activities

AACN hosts one conference each year. This conference is open to both members and nonmembers. The official journal published by AACN is *The Clinical Neuropsychologist.*

Cross References

- ▶ American Board of Clinical Neuropsychology (ABCN)
- ▶ International Neuropsychological Society
- ▶ National Academy of Neuropsychology

References and Readings

Boake, C. (2008). Clinical neuropsychology. *Professional Psychology: Research and Practice, 39*(2), 234–239.

Boake, C., & Bieliauskas, L. A. (2007). Development of clinical neuropsychology as a psychological specialty: A timeline of major events. *The ABPP Specialist, 26*, 42–43.

Yeates, K. O., & Bieliauskas, L. A. (2004). The American Board of Clinical Neuropsychology and American Academy of Clinical Neuropsychology: Milestones past and present. *The Clinical Neuropsychologist, 18*, 489–493.

American Academy of Neurology (AAN)

Catherine M. Rydell
American Academy of Neurology
Saint Paul, MN, USA

Address (and URL)

American Academy of Neurology
1080 Montreal Avenue
Saint Paul, Minnesota 55116
www.aan.com
(800) 879-1960 (US)
(651) 695-2717 (international)
(651) 361-4800 (fax)

Membership

The American Academy of Neurology (AAN), established in 1948, is an international professional association of more than 21,000 neurologists and neuroscience professionals dedicated to providing the best possible care for patients with neurological disorders. The AAN is strongly committed to its mission of ensuring the maintenance of the principles and standards set forth in the AAN mission statement.

Approximately 22,000 members reside in the USA and 4,000 are international members. Membership includes clinicians, academicians, researchers, business administrators, residents, fellows, and medical students.

Major Areas or Mission Statement

The vision of the AAN is to be indispensable to its members. The mission of the AAN is to promote the highest-quality neurologic care and enhance member career satisfaction. To accomplish these purposes, the AAN has established the following organizations to support its membership:

- The American Academy of Neurology Foundation (AAN Foundation), established in 1993, raises funds to support clinical research in neurologic disorders.
- AAN Enterprises, Inc. (AEI), a for-profit subsidiary of the AAN, was formed in 1999 by the AAN to develop new sources of revenue to pay for state-of-the-art products and services for its membership.
- The American Academy of Neurology Professional Association (AANPA) was established in 2007 and includes all AAN members. The AANPA created a political action committee, BrainPAC, to represent the interests of USA neurologists in Washington, DC.

Landmark Contributions

The AAN was founded in 1948 by A. B. Baker, MD, chair of the neurology department of the University of Minnesota, in response to the difficulties of one of his residents, Joseph Resch, in finding a society that he could join to continue his education and network with fellow neurologists. Baker was aided by Adolph L. Sahs, MD, of the University of Iowa; Francis M. Forster, of Jefferson Medical Hospital in Philadelphia; and Russell DeJong, MD, of the University of Michigan. Baker served as the first Academy president, and Forster and Sahs later had terms as president. DeJong was the founding editor-in-chief of the journal *Neurology*®, which began publication in 1951.

The AAN had 52 founding members. The establishment of the Academy, coupled with the increased need for neurologists due to World War II, helped elevate the status of neurology as a practice distinct from psychiatry. In 1947, there were between 300 and 325 physicians in the USA who designated themselves as primary neurologists, and there were 32 residency positions available nationwide. By 1970, there were 2,727 primary neurologists and some 700 residents in training. By the end of 2007, there were more than 16,000 neurologists in the USA. Currently, nearly 2,200 residents have memberships with the AAN.

Major Activities

Physician Education and Lifelong Learning

The AAN's Annual Meeting is one of the largest gatherings of neurology professionals in the world. Held each spring, the event attracts nearly 13,000 clinicians, academicians, researchers, exhibitors, and media representatives to share the latest in neurology science and education. The AAN also offers members three-day regional conferences in the fall of each year, and occasional workshops. Education activities and programs are structured to support the ongoing development of neurology professionals from medical students to accomplished clinicians and scientists.

Science and Research

The Annual Meeting is a leading forum for sharing the latest developments in science and research, as is the weekly peer-reviewed journal *Neurology*®. AAN scientific awards, presented at the Annual Meeting, honor outstanding achievements in neurology, from aspiring medical students to veteran researchers. Through the AAN foundation, the AAN provides support to young researchers through more than a dozen clinical research training fellowships, enabling them to pursue research initiatives and helping them to secure academic appointments and future fundings.

Clinical Practice

The AAN develops clinical practice guidelines to assist its members in clinical decision making related to the prevention, diagnosis, treatment, and prognosis of neurologic disorders. Each guideline makes specific practice recommendations based upon a rigorous and comprehensive evaluation of all available scientific data. The AAN also develops position statements on a variety of ethical issues to help guide neurologists and others in decision making. Members also rely on the AAN for the latest information on coding, reimbursement, quality initiatives, patient safety, and practice management issues.

Advocacy

To help foster changes in health care that will benefit patients and enhance the practice of neurology, the AAN presents advocacy training opportunities for members

through the Donald M. Palatucci Advocacy Leadership Forum, and the Kenneth M. Viste, Jr., MD, Neurology Public Policy Fellowship. Members also participate in the annual Neurology on the Hill visits to the USA Capitol in Washington, DC. The AANPA's BrainPAC political action committee also is instrumental in representing neurology's interests on the federal level and supporting federal legislators who support the profession and patients with neurologic disorders.

Publishing

AAN Enterprises, Inc., has four highly successful publications published by Lippincott Williams and Wilkins. The weekly journal *Neurology*® is the most widely read peer-reviewed neurology journal in North America. *Neurology Today*®, published biweekly, leads all other neurology tabloids in readership. *Neurology Now*®, a bimonthly patient-oriented magazine available in AAN member offices, currently has about 256,000 subscribers. *Continuum: Lifelong Learning in Neurology*®, the AAN's bimonthly continuing education monograph, is recognized by the American Board of Psychiatry and Neurology as a key tool for maintenance of certification. AEI also publishes the monthly member magazine *AANnews*, which focuses on AAN activities, events, and services; a book series for patient and their families on treating and living with neurologic disorders; and textbooks geared toward professionals.

Cross References

► Neuropsychiatry

References and Readings

Visit the AAN online at *www.aan.com*.

American Academy of Pediatrics

Debbie Linchesky
American Academy of Pediatrics
Elk Grove Village, IL, USA

Membership

The American Academy of Pediatrics (AAP) has approximately 60,000 members in the USA, Canada, Mexico, and many other countries. Members include pediatricians, pediatric medical subspecialists, and pediatric surgical specialists. More than 34,000 members are board-certified and called Fellows of the American Academy of Pediatrics (FAAP).

Major Areas or Mission Statement

The AAP is committed to the attainment of optimal physical, mental, and social health and well-being for all infants, children, adolescents, and young adults.

Landmark Contributions

The AAP was founded in June 1930 by 35 pediatricians who met in Detroit in response to the need for an independent pediatric forum to address children's needs. When the AAP was established, the idea that children have special developmental and health needs was a new one. Preventive health practices now associated with child care – such as immunizations and regular health exams – were only just beginning to change the custom of treating children as "miniature adults."

Major Activities

One of the AAP's major activities is to further the professional education of its members. Continuing education courses, annual scientific meetings, seminars, publications and statements from committees, councils, and sections form the basis of a continuing postgraduate educational program.

More than 30 committees develop many of the AAP's positions and programs. Committees have interests as varied as injury and poison prevention, disabled children, sports medicine, nutrition, and child health financing.

The AAP currently has six councils and 48 sections consisting of more than 41,500 members with interest in specialized areas of pediatrics. This includes a section for resident physicians with more than 9,000 members. Sections and councils present educational programs for both their members and the general membership of the AAP in order to highlight current research and practical knowledge in their respective subspecialties.

The AAP publishes *Pediatrics*, its monthly scientific journal; *Pediatrics in Review*, its continuing education journal; and its membership news magazine, *AAP News*.

It also publishes manuals on such topics as infectious diseases and school health. In its public education efforts, the AAP produces patient education brochures and a series of child care books written by AAP members.

The AAP executes original research in social, economic, and behavioral areas and promotes funding of research. It maintains a Washington, DC office to ensure that children's health needs are taken into consideration as legislation and public policy are developed. The AAP's state advocacy staff provides assistance to chapters, promoting issues such as child safety legislation and Medicaid policies that increase access to care for low-income children.

American Board of Clinical Neuropsychology (ABCN)

Michael Westerveld[1], Keith O. Yeates[2]
[1]Florida Hospital
Orlando, FL, USA
[2]Nationwide Children's Hospital
Columbus, OH, USA

Address (and URL)

The American Board of Clinical Neuropsychology (ABCN) is an organization that awards board certification to practicing clinical neuropsychologists. It is a member of the American Board of Professional Psychology (ABPP). Information about ABCN can be obtained from the ABCN web site (www.theabcn.org) and also at the ABPP web site (www.abpp.org).

Mail correspondence for ABCN can be directed to:

Department of Psychiatry (F6248, MCHC-6)
University of Michigan Health System
1500 East Medical Center Drive, SPC 5295
Ann Arbor, MI 48109-5295

Membership

As of May, 2010 ABCN had awarded 748 diplomas. Diplomates from throughout the USA, District of Columbia, and Canada are represented among the ranks of ABCN. Awarding of the ABCN diplomate is based primarily on clinical knowledge and skill, as demonstrated throughout the examination process which includes a written examination, practice sample review, and oral examination. Because the diploma is based on peer review of clinical competency, the majority of ABCN diplomates are active clinicians. However, many also engage in clinical and basic science research, teaching, and a wide range of other professional activities.

The ABCN Board of Directors consists of 15 members elected by diplomates in good standing. The term of office is 5 years. Officers of the Board (President, Vice President, Secretary, Treasurer) are elected by the Board from among active elected directors. Elected Board members may serve no more than two consecutive terms. In addition to elected Board members, there is an examination chairperson, selected by the Board for a term of 5 years.

Major Areas or Mission Statement

According to the ABCN bylaws, the organization exists to develop and maintain procedures to examine the qualifications of candidates for board certification in Clinical Neuropsychology, to conduct the examinations and award certificates to qualified candidates, to maintain a registry of certificate holders, and to serve the public welfare by identifying practitioners who have obtained advanced education and training in clinical neuropsychology and demonstrated the ability to apply such skills in a competent manner.

Landmark Contributions

ABCN was incorporated in 1981. After the findings of the joint Division 40-INS task force on Education, Accreditation, and Credentialing in 1981 (published in 1984[5] and republished in the first issue of *The Clinical Neuropsychologist* in 1987[7]) established requisite education and training experiences, the need for a means of identifying well-trained and competent practitioners was recognized. A planning group (Linas Bieliauskas, Louis Costa, Edith Kaplan, Muriel Lezak, Charles Matthews, Steven Mattis, Manfred Meier, and Paul Satz) incorporated ABCN in Minneapolis in 1981. The organization was formed with the intention of affiliating with the ABPP, a unifying governing body for independently incorporated specialty examining boards akin to the ABMS for medical specialties. After the first examinations were completed in 1983, ABCN formally affiliated with ABPP (also in 1983) and the first ABPP–ABCN diplomas were awarded in 1984. The first President of ABCN was Manfred Meier, who served from 1983 until 1991.

ABCN was initially established as an organization solely charged with awarding diplomas to applicants successfully demonstrating competency through the examination process. In 1988, it became a membership organization and began charging dues so that resources for further development of the organization could be built. This included creation and maintenance of a written examination in consultation with Professional Examination Services (PES). After years of development and pilot testing to assure validity and reliability of the written examination, in 1993, ABCN began to require that new candidates pass the written examination prior to submitting practice samples. The written examination is regularly reviewed for content updates to remove outdated items and assure that advances in clinical practice and knowledge in the field are reflected in the examination.

The American Academy of Clinical Neuropsychology (AACN), an organization originally comprised of ABCN diplomates, was formed in 1996. ABPP had received legal advice that there was potential for conflict of interest in the roles of credentialing bodies that also engaged in advocacy. As a result, the academy was formed to fulfill the advocacy and professional development role. AACN has grown significantly and now includes an affiliate member category for neuropsychologists who have not yet received their ABCN diploma, and for affiliated professionals who are not neuropsychologists. Although ABPP has recently received a different legal opinion that allowed member boards to once again merge with their academies, ABCN and AACN have grown and function well in their complementary roles and at this time have no plans to merge.

In 1997, a landmark conference regarding education and training for clinical neuropsychologists was held in Houston (the "Houston Conference on Specialty Education and Training in Clinical Neuorpsychology"). Attending the conference were representatives from each of the professional neuropsychology organizations, and the proceedings were published in 1998. In 2002, the ABCN Board of Directors voted to adopt the Houston Conference training guidelines as requisite training to be eligible for the ABCN diplomate. Candidates who received their degrees after January 1, 2005 are expected to have had training and experience consistent with the guidelines laid out in the Houston Conference proceedings.

In 2007, ABCN began to consider subspecialization within the field, and address examination and recognition of special competencies, such as pediatric neuropsychology. At that time, ABPP did not have a model for subspecialization, and worked with ABCN to develop a framework to address issues such as overlap with other boards and recognition of special competencies of existing board members. As a result, the Pediatric Special Interest group was formed, and held the first meeting in 2009 during the AACN Conference.

Table 1 presents a timeline summary of major landmarks for ABCN.

Major Activities

ABCN's primary activities are developing, maintaining, and conducting the examination. The examination process consists of four distinct steps. First, the education and training experiences of the applicant are reviewed, initially at the ABPP central office, where the application is examined for graduate training, internship, and licensure status. Applications are then forwarded to ABCN for review of advanced specialty training. Any practicing clinical neuropsychologist with a doctoral-level degree who possesses a valid license to practice psychology is eligible to

American Board of Clinical Neuropsychology (ABCN). Table 1 Timeline for major ABCN milestones

1981 ABCN incorporated in Minnesota
1983 First set of examinations completed
1983 Formal affiliation between ABCN and ABPP established
1984 First ABCN/ABPP diplomates awarded
1988 ABCN bylaws revised to create membership organization
1989 ABCN designated Specialty Council in Clinical Neuropsychology by ABPP
1993 Written examination formally instituted
2002 AACN establishes mentoring program to promote board certification through ABCN
2002 ABCN votes to adopt Houston Conference guidelines for eligibility for board certification, beginning in 2005
2002 Written examination updated to reflect Houston Conference guidelines
2004 500th ABCN diploma awarded
2004 BRAIN Website and Listserv group formed
2005 Houston Conference education and training requirements implemented
2007 Committee to study subspecialization formed
2009 700th diploma awarded
2009 Pediatric Neuropsychology special interest group formed

apply. Beginning in 2005, applicants for the ABCN diploma are expected to complete training consistent with the Houston Conference on Specialty Education and Training in Clinical Neuropsychology. This includes coursework in the areas outlined in the Houston Conference, and completion of a formal 2-year postdoctoral residency program in Clinical Neuropsychology. However, recognizing that the field has evolved, applications from candidates who obtained their graduate training prior to implementation of the Houston Conference standards are evaluated according to the standards in place at the time their degree was granted, provided they can demonstrate that the pertinent requirements were met during their training (see www.theabcn.org for detailed requirement listings). Candidates who are respecializing in neuropsychology, or who recently completed respecialization programs, are expected to have education and training experiences consistent with the requirements in place at the time of their respecialization, not the date of their original degree.

Once an applicant's credentials have been reviewed and accepted, the next step in the examination process is a written examination. The written examination consists of 100 multiple-choice questions that cover a range of topics in neuropsychology. It is intended to evaluate the candidate's breadth of knowledge and to assure that they have the foundational knowledge necessary for competent practice in clinical neuropsychology. It is administered at major conferences, including the AACN conference, National Academy of Neuropsychology (NAN) annual meeting, International Neuropsychology Society (INS) North American Meeting, and the American Psychological Association (APA) meeting. It was developed and is maintained in association with PES.

Once a candidate has passed the written examination, the next step is submission of a practice sample consisting of two typical cases in the candidate's practice. The practice samples are reviewed by at least three independent, board certified neuropsychologists.

Following acceptance of the practice sample, the candidate is invited to sit for the oral examination that consists of three parts – practice sample, fact-finding, and ethics/professional development. The practice sample section of the orals provides the candidate an opportunity to discuss their practice as applied to the specific cases they submitted. The cases also serve as a starting point leading to more in-depth discussion of differential diagnosis, and general information about the nature of the disorder in the case and related conditions. The fact-finding section of the oral examination is an opportunity for the candidate to demonstrate clinical skills. The candidate is presented with a brief description of a case, and is asked to inquire about background history, test data, and related medical information to arrive at a clinical diagnosis and conclusion. Along the way, the candidate may be asked about their rationale for test selection, their differential diagnostic considerations, and how test results may support or otherwise aid in diagnosis and treatment planning. The professional and ethical portion of the examination is an opportunity for the candidate to demonstrate knowledge of important ethical considerations in the practice of neuropsychology, as well as discuss important issues for the field.

A comprehensive overview of the examination process was published in 2008 (Armstrong, et al., 2008).

Currently, ABCN conducts written examinations at four major conferences each year:

International Neuropsychology Society (INS North American Meeting)
American Academy of Clinical Neuropsychology (AACN)
American Psychological Association (APA)
National Academy of Neuropsychology (NAN)

Oral examinations are conducted twice annually in Chicago, Illinois, hosted by Rush University Medical Center. One examination is conducted each autumn (usually late October, or early November) and the other in the spring (usually early May).

The AACN holds an annual conference for continuing education, professional development, and furthering the growth of the profession through advocacy. The meeting is held annually in June.

Cross References

- ▶ American Academy of Clinical Neuropsychology (AACN)
- ▶ American Board of Professional Psychology (ABPP)
- ▶ American Psychological Association (APA)
- ▶ International Neuropsychology Association (INS)
- ▶ Meier, Manfred John (1929–2006)
- ▶ National Academy of Neuropsychology (NAN)

References and Readings

Armstrong, K., Beebe, D. W., Hilsabeck, R. C., & Kirkwood, M. W. (2008). Board certification in clinical neuropsychology: A guide to becoming ABPP/ABCN certified without sacrificing your sanity. Oxford Press.

Bieliauskas, L. A., & Matthews, C. G. (1987). American Board of Clinical Neuropsychology: Policies and procedures. *The Clinical Neuropsychologist, 1*, 21–28.

Bieliauskas, L. A., & Matthews, C. G. (1990). American Board of Clinical Neuropsychology Update, 1990. *The Clinical Neuropsychologist, 4*, 337–343.

Bieliauskas, L. A., & Matthews, C. G. (1997). The American Board of Clinical Neuropsychology, 1996 update: Facts, data, and information for potential candidates. *The Clinical Neuropsychologist, 11*, 222–225.

Hannay, H. J., Bieliauskas, L., Crosson, B. A., Hammeke, T. A., Hamsher, K. deS., & Koffler, S. (Eds.). (1998). Proceedings of the Houston Conference on specialty education and training in clinical neuorpsychology. *Archives of Clinical Neuropsychology, 13,* 157–250.

Ivnik, R. J., Haaland, K. Y., & Bieliauskas, L. A. (2000). American Board of Clinical Neuropsychology special presentation. *The Clinical Neuropsychologist, 14*, 261–268.

Report of the Division 40/INS Joint Task Force on Education, Accreditation, and Credentialing (1984). Division 40 Newsletter, Vol. 2, no. 2, pp. 3–8.

Reports of the ins - division 40 task force on education, accreditation, and credentialing (1987). *The Clinical Neuropsychologist, 1*(1), 29–34.

Yeates, K. O., & Bieliauskas, L. A. (2004). The American Board of Clinical Neuropsychology and American Academy of Clinical Neuropsychology: Milestones past and present. *The Clinical Neuropsychologist, 18*, 489–493.

American Board of Pediatric Neuropsychology

Peter Dodzik
American School of Professional Psychology-Schaumburg
Schaumburg, IL, USA

Membership

The American Board of Pediatric Neuropsychology (ABPdN) was developed in 1996 by a coalition of clinical practitioners, representing institutions hiring pediatric neuropsychologists. The original group conceived the board to advance their belief that a unique interplay exists between neurodevelopmental issues and neuropsychological assessment that requires special sets of expertise not readily assessed by the then existing boarding entities. Following discussion with colleagues who were members of medical practice and psychology boards, the coalition elected to establish an independent certifying authority. The examination process evolved into a comprehensive and multilevel process that includes a written application including clinical case vignettes used to determine decision-making strategies of the applicant, scope of practice and a thorough assessment of organized training in pediatric neuropsychology (from graduate school to continuing education), written examination, a practice sample submission, and an oral examination. The ABPdN does not have a "grand fathering" policy, and thus, all existing board members were required to complete all new phases of the examination process to ensure equality of standards among boarded members.

As of early 2010, 111 neuropsychologists have submitted applications to ABPdN and 75 members have passed the ABPdN examination process. At present, there are 57 active and five emeritus members of the board from 21 states, Canada, and Puerto Rico.

Major Areas or Mission Statement

Board certification in pediatric neuropsychology serves to assist consumers by offering supportive evidence of the competence of the pediatric neuropsychologists. The ABPdN is the only board certification organization with the sole purpose of examining and certifying competence in pediatric neuropsychology.

Landmark Contributions

Members of ABPdN practice in a variety of settings including universities, teaching hospitals, general hospitals, hospital trauma centers, private practices, rehabilitation facilities, stroke centers, memory disorder centers, group practices, and child development centers. Current members hold academic affiliations at over 40 colleges and universities. Several members have developed tests commonly used in the practice of pediatric and general neuropsychology. Member accomplishments include past president of APA Division 40, current and past presidents of four State Psychology Boards, past president of National Academy of Neuropsychology, past and present editor of *Archives of Clinical Neuropsychology*, past editor of *Journal of School Psychology*, and the owner/moderator of PEDS-NPSY, a pediatric list-serve with over 1,600 members.

Major Activities

The ABPdN is the board-certifying arm of the American Academy of Pediatric Neuropsychology (AAPN), which is devoted to training and promotion of the field of pediatric neuropsychology. The AAPN, in affiliation with the American College of Professional Neuropsychology, holds an annual conference each spring with topics related to the field of pediatric neuropsychology.

The primary activity of ABPdN is conducting the board certification process. Board examination through the ABPdN involves several stages. The format of the ABPdN's examination processes has been constant since the examinations held in 2004, but the procedures continue to be reviewed and amended. The purpose of the ABPdN examination process is to ensure that the examinee has demonstrated competency to practice pediatric neuropsychology. The specific stages are discussed below and more detail can be obtained from the ABPdN web site (Beljan, Bos, Courtney, & Dodzik, 2006). The overall pass rate for each stage of the examination process is between 73% and 81%.

Credential Review

Minimum training and education standards include completion of a doctoral degree from a regionally accredited program in applied psychology that was, at the time the degree was granted, accredited by the APA, CPA, or was listed in the publication *Doctoral Psychology Programs Meeting Designation Criteria* (ASPPB National Register designation committee, 2008). Membership in the National Register of Health Service Providers in Psychology, the Canadian Register of Health Service Providers, or those holding the Certificate of Professional Qualification qualify as meeting the doctoral requirements for membership. Licensure or certification at the independent practice level as a psychologist in the state, province, or territory in which the psychologist actively practices is also required. The applicant must be practicing as a pediatric neuropsychologist and must have completed an Association of Psychology Postdoctoral and Internship Center (APPIC) or APA accredited internship that included a documented rotation or concentration in neuropsychology, and 2 years of postdoctoral supervised experience in neuropsychology, at least 50% of that being pediatric-oriented. In addition, each applicant reviewed by the Board must provide the following:

1. Education
   a) Undergraduate degree transcript
   b) Graduate degree transcript
   c) Internship verification contact information
   d) Postdoctoral residency verification contact information
   e) Postdoctoral fellowship verification contact information (if applicable)
   f) Detailed description of training in pediatric neuropsychology (narrative)
2. Continuing education
   a) Verification of CEUs in pediatric neuropsychology for the past 3 years
3. Clinical work
   a) Clinical appointment verification contact information
   b) Breakdown of clinical practice by age, disorders, and ethnic background
   c) Completion of clinical vignettes
4. Educational appointment (if applicable)
   a) Academic institution verification contact information

The application is first reviewed by the Examination Chair for completion and accuracy of documents and licensure status. The application is then reviewed by a panel of three reviewers. A passing score by two of the three reviewers is required to move to the next stage of the examination. Each reviewer evaluates the application for consistent and thorough training in pediatric neuropsychology at multiple levels of training.

Practice Sample

The purpose of the practice sample is to determine the applicant's clinical knowledge. While the written examination was designed to assess content-specific knowledge with regard to pediatric neuropsychology, the practice sample allows the board to evaluate the day-to-day skills of the applicant. To that end, the sample should reflect a typical patient seen in the applicant's clinical practice. Practice samples may include assessment or intervention techniques. After an application is reviewed and the candidate is determined to be board-eligible, they will then be invited to provide a practice sample that reflects their typical work in pediatric neuropsychology. Prior to taking the objective and oral examination, the candidate must prepare and tender a written sample of an original pediatric neuropsychological examination performed solely by the candidate. Appropriate samples may also include case analysis/interventions and supervision sessions.

Written Examination

The third step is the written exam, a 100 question, multiple-choice instrument designed and constructed by other pediatric neuropsychologists whose purpose is to assess the candidate's breadth of knowledge in pediatric neuropsychology. The questions were first assessed for face validity, clustered for content area, rank-ordered, deleted or refined,

reanalyzed, debated, approved, and then compiled into a larger item pool for random selection by domain each year. A passing score of 70% is required. Each exam includes the following basic core areas:

- Psychometrics
- Pediatric Neurosciences
- Psychological and Neurological Development
- Neuropsychological and Neurological Diagnostics
- Ethics and Legal Issues
- Research Design Review for Clinical Application
- Intervention Techniques
- Consultation and Supervisory Practices

Oral Examination

This part of the examination process is comprised of a review of the candidate's practice sample, the nature and application of neuropsychological knowledge to their current practice, appreciation for ethical issues and obligations, and a review of the candidate's views and philosophy on pediatric neuropsychology. The oral examination also includes a mock case review, in which the candidate is given information about a fictional case, and they develop and articulate their working hypothesis. The oral examination is intended to be a collegial opportunity for the reviewers to validate the candidate's ability to "think on their feet" and discern their preparation and readiness for board certification.

The first portion of the oral examination permits the examination team to consider the scope of the candidate's body of training and how they practice pediatric neuropsychology (e.g., acute care, rehabilitation, outpatient, assessment, and/or treatment) so that the fact-finding and practice sample review can be conducted in the most relevant fashion. This section is broken into two parts: Part I: The examinee will explain their background.

- The examinee will provide a history of their educational and professional background. Special consideration should be given to their pediatric neuropsychological training and background.
- The examinee will explain their current role as a pediatric neuropsychologist and the issues their typical clientele present.

Part II: The examinee will demonstrate pertinent knowledge of practical pediatric neuropsychology.

The next segment of the oral examination allows the candidate to present the material in their practice sample and to provide an overview of the history, evaluation process, and outcome of the case. The examiners evaluate their ability to articulate the major findings and their rationale. Candidates discuss their rationale in such areas as:

(1) Test selection (if applicable): psychometric properties, test validity/reliability, limitations for use, and exclusion of all competing diagnoses.
(2) Test interpretation (if applicable): alternate interpretations of findings, conflict resolution within the data, discussion of strengths and weaknesses, and environmental and cultural factors.
(3) Diagnostic conclusions: alternate diagnosis, ultimate understanding of neuropathology, prognosis, progression, lateralizing/localizing effects, pathognomic signs, causality, environmental conditions, and effects on neural development.
(4) Recommendations and treatment planning: best practices for treatment, availability, prognosis, funding, delivery options, cost/benefit analysis, iatrogenic outcomes, parental compliance/agreement, and ethical issues.
(5) Consultation and supervision (if applicable): best practices for communication of data, delivery options, supervisee needs/relationships, and rapport/therapeutic relationship.

This process is intended to be collegial and the examiners endeavor to be sensitive to the different and yet equally viable approaches within pediatric neuropsychology. The purpose is to ascertain the Candidate's logic and thought processes and to allow them to demonstrate these skills.

During the ethics segment, there is discussion of one or two standardized vignettes, and the candidate is expected to present relevant comments on the ethical dilemmas, thoughtfully weighing them in the light of the APA ethics principles, professional practice standards, and relevant statutes.

Cross References

► American Psychological Association (APA), Division 40
► National Academy of Neuropsychology (NAN)

References and Readings

ASPPB National Register designation committee (2008). Retrieved October 1, 2009 from http://www.nationalregister.org/designate_stsearch.html

Beljan, P., Bos, J., Courtney, J., & Dodzik, P. (2006). Preparation guide for examination and certification by the American Board of Pediatric Neuropsychology. Retrieved from http://abpdn.org/docs/study-guide.pdf

For additional information please see the web site at www.abpdn.org.

American Board of Professional Psychology (ABPP)

Christine Maguth Nezu
Drexel University – Hahnemann Campus
Philadelphia, PA, USA

Membership

The American Board of Professional Psychology (ABPP) has 3,074 currently active board-certified specialists in membership. As a national-in-scope credentialing organization in professional psychology, its membership is comprised doctoral-level psychologists who provide professional services and consultation and are licensed to practice psychology in the jurisdiction in which they practice. Completion of a doctoral degree, completion of a qualified internship, relevant postdoctoral experience, and relevant jurisdictional licensure as a psychologist are the minimum prerequisites for approval to take an ABPP board certification exam.

Major Areas or Mission Statement

The American Board of Professional Psychology (ABPP) is a national-in-scope credentialing organization that has been awarding board certification in professional psychology specialties for over 60 years (Bent, Packard & Goldberg, 1999; Finch, Simon & Nezu, 2006; Packard & Reyes, 2003). ABPP describes the value of its credential as one that "provides peer and public recognition of demonstrated competence in an approved specialty area in professional psychology" (American Board of Professional Psychology, 2008). Moreover, ABPP board certification is increasingly associated with greater opportunities for career growth, including employment opportunities, practice mobility between jurisdictions, and financial compensation (American Board of Professional Psychology; Sweet, Nelson & Moberg, 2006).

ABPP is currently a unique and unitary umbrella organization with multiple specialty boards that include cognitive-behavioral, clinical, clinical child and adolescent, clinical health, clinical neuropsychology, counseling, couples and family, forensic, group, school, rehabilitation, organizational, business, and consulting, and psychoanalysis. Many professional psychologists seek dual certifications that reflect the full scope of their specialties. Examples of these might include clinical and cognitive-behavioral, clinical neuropsychology and rehabilitation, or counseling and group.

For a licensed psychologist to be "board eligible," each of the 13 boards require that he or she meets both generic and specialty eligibility criteria concerning education, professional training, and licensure in the jurisdiction where professional services are provided. Once an individual's credentials are reviewed and approved, the individual seeking board certification moves to the next phase of their candidacy process. In clinical neuropsychology and forensic specialties, this necessitates passing a written examination. In all other specialties, the candidates are not required to take a written exam, and may move directly to the final phases in the process. For all specialties, this includes first submitting a professional practice sample. After the practice sample is approved, the oral examination (final phase) is typically scheduled. Specialty boards may also provide a "senior option" regarding practice samples submitted by candidates with at least 15 years of experience post licensure who may submit samples of their professional work such as publications, treatment manuals, program manuals, or a comprehensive summary of their professional practice, to satisfy the requirements of a professional practice sample.

With regard to both practice samples and oral exams, the candidate's competency is assessed across various domains. These competency domains may be *functional* in nature, and include the day-to-day activities of specialty practice, such as assessment, intervention, and/or consultation that are informed by a scientific literature base. They also include foundational competencies, such as ethics, individual and cultural diversity, and interpersonal competence, which cut across all of a specialist's other activities. The competency model upon which ABPP board certification is based, draws from several important sources such as the APA-sponsored Competencies Conference in 2002 and resulting Task Force on Assessment of Competence in Professional Psychology (Kaslow et al., 2007), and a review of competency assessment models developed both within (e.g., Assessment of Competence Workgroup from Competencies Conference – Roberts, Borden, Christiansen, & Lopez, 2005; Leigh et al, 2007) and outside (e.g., American Council for Graduate Medical Education and American Board of Medical Specialties, 2000) of the profession of psychology.

There is a strong consensus among many professional psychologists that the American Board of Professional Psychology represents a high degree of integrity regarding

specialty board certification and serves as a gold standard for demonstration of specialty competency in professional psychology.

Landmark Contributions

The origins of ABPP can be traced back to its establishment in 1947 as the American Board of Professional Examiners in Psychology (Bent et al., 1999). The intention of the original board was to ensure that individuals were qualified to perform the professional service activities associated with clinical and counseling psychology. However, as professional psychology expanded its scope and depth, the organization changed its name to the American Board of Professional Psychology to reflect the expansion of specialization activities that were emerging for professional psychologists. As a result, the number of its affiliated specialty boards and associated academies has grown from 3 to 13, reflecting this professional expansion and the breadth of specialties that have emerged over that past 5 decades (Finch et al., 2006; Packard & Reyes, 2003).

Major Activities

Each of the psychology specialty boards under the ABPP umbrella has an elected trustee who participates as a member of the ABPP Board of Trustees as the overall governance group of the ABPP. Each specialty board assumes the responsibility for developing and carrying out the ABPP specialty examinations. The ABPP central office, under the management of a full-time Executive Officer, executes important day-to-day functions for all of the 13 specialty boards. These include generic candidacy verification of applicants, budget maintenance and accounting responsibilities, record keeping, development and maintenance of an ABPP Directory, development and editing responsibility for the ABPP website, monitoring the organization relative to ethical/legal issues, planning of conference and governance activities, and general administrative support. The primary publication of the organization, *The Specialist*, is published twice annually and available to all members in both electronic and printed format. The organization website (www.ABPP.org) contains important information regarding the mission, governance, and organizational documents. For the public, the website contains listings of board-certified specialists across specialties and practice jurisdictions. For interested applicants, it contains application instructions as well as other helpful information. The organization will publish its first book, *Becoming Board Certified by the American Board of Professional Psychology (ABPP)* in 2009.

Cross References

- ▶ American Academy of Clinical Neuropsychology (AACN)
- ▶ American Board of Clinical Neuropsychology (ABCN)
- ▶ American Board of Rehabilitation Psychology (ABRP)

References and Readings

American Council for Graduate Medical Education and American Board of Medical Specialties (2000). *Toolbox of assessment methods.* Chicago, IL: American Council for Graduate Medical Education and American Board of Medical Specialties.

American Board of Professional Psychology (2008). Retrieved June 25, 2008, from http://www.abpp.org

Bent, R. J., Packard, R. E., & Goldberg, R. W. (1999). The American board of professional psychology. *Professional Psychology: Research and Practice, 30*, 65–73.

Datillio, F. M. (2002). Board certification in psychology: Is it really necessary? *Professional Psychology: Research and Practice, 33*, 54–57.

Finch, A. J., Simon, N. P., & Nezu, C. M. (2006). The future of clinical psychology: Board certification. *Clinical Psychology: Science and Practice, 13*, 254–257.

Kaslow, N. J., Rubin, N. J., Bebeau, M. J., Leigh, I. W., Lichtenberg, J. W., Nelson, P. D., Portnoy, S. M., & Smith, I. L. (2007). Guiding principles and recommendations for the assessment of competence. *Professional Psychology: Research and Practice, 38*, 441–451.

Leigh, I. W., Smith, I. L., Bebeau, M. J., Lichtenberg, J. W., Nelson, P. D., Portnoy, S., Rubin, N. J., & Kaslow, N. J. (2007). Competency assessment models. *Professional Psychology: Research & Practice, 38*, 463–473.

Nezu, C. M., Finch, A. J., & Simon, N. P. (Eds.) (2009, in press), *Becoming board certified by the American board of professional psychology (ABPP)*. New York: Oxford University Press.

Packard, T., & Reyes, C. J. (2003). Specialty certification in professional psychology. In M. J. Prinstein & M. D. Patterson (Eds.), *The portable mentor: Expert guide to a successful career in psychology* (pp. 191–208). New York: Plenum.

Roberts, M. C., Borden, K. A., Christiansen, M. D., & Lopez, S. J. (2005). Fostering a culture shift: Assessment of competence in the education and careers of professional psychologists. *Professional Psychology: Research and Practice, 36*, 355–361.

Sweet, J. J., Nelson, N. W., & Moberg, P. J. (2006). The TCN/AACN 2005 "Salary Survey": Professional practices, beliefs, and incomes of U.S. Neurophysiologists. *The Clinical Neuropsychologist, 20*, 325–364.

American Board of Professional Neuropsychology (ABN)

John E. Meyers
Private Practice, Neuropsychology
Mililani, Hawaii, USA

Membership

The American Board of Professional Neuropsychology (ABN) comprises 350 (as of 2010) neuropsychologists who have doctoral degrees, and they are licensed as psychologists and have completed the ABN diplomate examination process.

ABN was established in 1982 by a group of clinical neuropsychologists, all of whom were diplomates of the American Board of Professional Psychology (ABPP), to provide peer regulation of the practice of professional neuropsychology. The process of obtaining the ABN diplomate is a dynamic one which has changed over the years and is expected to evolve as the field of neuropsychology evolves. Initially, in addition to obtaining a doctoral degree, licensure as a psychologist, and completing a number of years of postdoctoral experience in neuropsychology, early applicants were required to show evidence of specialized training in neuropsychology and to provide supervisory evaluations of their competency in professional neuropsychology.

Between 1982 and 1985, following a review of credentials and supervisory evaluations, work samples were required. These were graded by multiple examiners on a pass/fail basis. Individuals who passed this final step were awarded a diplomate. Individuals who did not pass evaluation were allowed to apply for a "Certificate in Professional Neuropsychology," indicating that they had some training in neuropsychology but not sufficient to be awarded diplomate status. This was initially intended as an interim credential as part of the process of obtaining a diplomate. After 1985, this process was abandoned as increasing numbers of neuropsychology training programs became available.

In February of 1989, the ABN was reorganized and the bylaws were modified. An annual dues structure was instituted and ABN became a membership organization whose only credential is a diplomate. This newly established organization mandated continuing education for active membership. It was required that all those who had a "Certificate in Professional Neuropsychology" complete the diplomate process to maintain membership. At this time, an oral examination and essay examination were added to the case study reviews, and all previous members were allowed the opportunity to undergo the expanded examination process. Those who successfully completed the process, including the new oral examination, were given full diplomate status in ABN.

After 1991, those who did not successfully complete the additional oral examination were no longer listed as diplomates through ABN. The oral examination included three 1 h sessions dealing with ethics, the work sample, and general knowledge. ABN no longer required letters of competency from supervisors but instead required letters of recommendation from other neuropsychologists.

In 2004, the diplomate evaluation process was again reevaluated and work began on substituting a multiple-choice general knowledge examination for the oral examination on the same subject. This process took several years to complete, and as of January 1, 2009, all applicants were required to complete the multiple-choice written examination; the essay examination was dropped in favor of the multiple-choice exam. In 2008, the original acronym for ABN was changed from ABPN to ABN to avoid confusion with the American Board of Psychiatry and Neurology.

The current examination procedure includes:

1. Review of credentials and letters of recommendation
2. A 100-question multiple-choice examination
3. A case study-work samples review
4. A 1-h ethics oral examination and
5. A 1-h work style oral examination

The multiple-choice written examination covers areas of general knowledge based on the recommended guidelines of the Houston Conference. The ethics examination addresses ethical situations and current ethical dilemmas, and the work style examination covers clinical vignettes and clinical decision-making.

Major Areas or Mission Statement

ABN recognizes and encourages the pursuit of excellence in the practice of clinical neuropsychology. ABN's primary objective is the establishment of professional standards of expertise for the practice of clinical neuropsychology. Through its credentialing and examination processes and its continuing education requirement, the ABN offers to the medical community, the public, and to individuals

who have a need for applied neuropsychological services, a process whereby competent professional neuropsychologists can be identified.

To achieve the standards set forth by the ABN for competent professional practice of neuropsychology, the following outcome objectives have been developed:

- Validate the skills of clinical practitioners
- Identify competent practitioners
- Provide public information about professional neuropsychology
- Document the maintenance of competence of professional neuropsychology practitioners with continuing education requirements
- Provide individuals, organizations, and agencies who use neuropsychology services with a referral directory of ABN diplomates

Recognition by ABN signifies to the public and to other health professionals a high level of competency in applied neuropsychology. The ABN does not ascribe to any specific theoretical framework. While recognizing the importance and contribution of a graduate education in neuropsychology and subsequent specialty training, the ABN believes that the critical element in the practice of professional neuropsychology is the application of that training to client issues and needs.

Landmark Contributions

"Applied Neuropsychology," a peer reviewed edited journal, is the official journal of the ABN.

Major Activities

ABN holds annual board of directors' meetings in the spring and at the National Academy of Neuropsychology (NAN) conference. Associated with ABN is the American College of Professional Neuropsychology (ACPN) whose purpose is to provide continuing education programs in neuropsychology.

The ACPN is approved by the American Psychological Association to provide continuing education programs. Every year, ACPN offers continuing education at an annual conference and at general membership meetings held in conjunction with other neuropsychological or psychological organizations. Twice a year, the board of directors and committee chairs meet to organize ABN's professional activities. ABN candidate examinations and examiner training workshops are held a minimum of twice a year at locations throughout the country. A workshop on the ABN examination process is held at least once a year. Individual candidate mentoring is offered throughout the year.

References and Readings

http://www.neuropsychologyboard.org/

Bennett, T. L., Horton, A. M., Jr. & Elliott, R. W. (1999). American Board of Professional Neuropsychology (ABPN). *Bulletin of the National Academy of Neuropsychology, 14*, 7–9.

Elliott, R. W., & Horton, A. M., Jr. (1994). Philosophy of the American Board of Professional Neuropsychology. *Bulletin of the National Academy of Neuropsychology, 11*, 14–15.

Elliott, R. W., & Horton, A. M., Jr. (1995). History and current status of the American Board of Professional Neuropsychology. *The Independent Practitioner, 15*, 175–177.

Goldstein, G. (2001). Board certification in clinical neuropsychology: Some history, facts and opinions. *Journal of Forensic Neuropsychology, 2*, 57–65.

Horton, A. M. Jr., Crown, B. M., & Reynolds, C. R. (2001). American Board of Professional Neuropsychology: An Update-2001. *Journal of Forensic Neuropsychology, 2*, 67–78.

American Board of Rehabilitation Psychology

Daniel E. Rohe
Mayo Clinic
Rochester, Minnesota

Membership

The American Board of Rehabilitation Psychology (ABRP) is one of 13-member boards of the American Board of Professional Psychology (ABPP). The ABRP consists of 135 (as of 2010) doctoral-level psychologists who are primarily engaged in provision of clinical services to individuals and their families affected by a wide range of disabilities and chronic health conditions including brain injury, spinal cord injury, amputations, chronic pain, multiple sclerosis, cancer, and sensory impairment such as blindness and deafness. In addition to clinical services, the majority of the members also engage in research, teaching, and administration of rehabilitation programs. Rehabilitation psychologists are also involved in interdisciplinary teamwork with other medical and rehabilitation providers. Rehabilitation psychologists who are boarded in the specialty reside in 30 states and Canada.

Major Areas or Mission Statement

The mission of the ABRP is to protect the public and enhance the quality of health care by certifying rehabilitation psychologists who demonstrate the knowledge, skills, and attitudes essential to maximize quality of life for individuals with disabilities and chronic illness. The vision of the ABRP is that all psychologists practicing in rehabilitation will be boarded in the specialty. Psychologists who obtain the diplomate in rehabilitation psychology must meet the generic requirements for specialty certification by the ABPP that include a doctoral degree in psychology from an accredited degree program and licensure as a psychologist for independent practice in the USA or Canada. The ABRP-specific eligibility requirements include: completion of a recognized internship program and 2 years of supervised practice in rehabilitation psychology. In addition, the candidate must have completed at least 3 years of experience in rehabilitation psychology. Given the diverse training experiences of rehabilitation psychologists, the credential review includes significant reliance on the ratings of supervisors (two required) and the endorsement of colleagues and peers (two required). The candidate then submits a two-part practice sample (typically two case reports) that is evaluated by three ABRP examiners. Finally, the candidate completes an oral examination on: two clinical vignettes, their practice sample, and an ethics examination. The entire examination process is designed to ensure that each candidate demonstrates the foundational and the functional competencies required of the diplomate in rehabilitation psychology. The foundational competencies fall in four domains: interpersonal interactions, individual and cultural diversity, ethical and legal foundations, and professional identification. The functional competencies encompass science base and application, assessment, intervention, consultation, and consumer protection.

Landmark Contributions

The primary contribution of ABRP is providing the opportunity for psychologists who are dedicated to the health and welfare of individuals with disabilities and chronic illness to be certified as rehabilitation psychologists. The ABRP began as a Credentials Committee within the Division of Rehabilitation Psychology in 1993. This committee met throughout 1993 and 1994 and incorporated as the American Board of Rehabilitation Psychology in 1995. On December 4, 1994 they established bylaws and elected officers: Richard Cox (president, 1994–2000), Bernard Brucker (vice-president), Mitchell Rosenthal (secretary), Daniel Rohe (treasurer). The members at large were: Bruce Caplan, David Cox, Harry Parker, Anthony Ricci, James Whelan, and Mary Willmuth. Subsequent board presidents have been Mitchell Rosenthal (2000–2004), Bernard Brucker (2004–2008), and Daniel Rohe (current president).

The second major contribution is the crafting of an organization that reflected the values of the professionals who created it. The ABRP devised an innovative examination process that is user-friendly, collegial, competency-based, and affirming of the candidate. The ABRP was the first board to devise a proactive mentoring program that has a credentialed colleague personally guide the applicant through each step of the process.

The third major contribution is cosponsorship of the annual Rehabilitation Psychology meeting with the Division of Rehabilitation Psychology that began in 1999. The annual meeting has become an institutionalized opportunity for leaders in the field to meet, present research, and promote the specialty to new students.

Major Activities

The major activity of ABRP is cosponsorship of the Annual Conference of Rehabilitation Psychology with Division 22 of the American Psychological Association. This conference occurs the last weekend of February and provides the opportunity to earn continuing education credits. The conference provides ABRP sponsored educational sessions that explain the process of attaining the diplomate in rehabilitation psychology to interested candidates. The conference features nationally recognized leaders in the field of rehabilitation psychology. The ABRP board works in tandem with the American Academy of Rehabilitation Psychology (AARP). The AARP is a separate organization with overlapping board membership with the ABRP board. The AARP contributes the operational support required for organizing the Annual Conference of Rehabilitation Psychology.

Cross References

- ▶ American Board of Professional Psychology (ABPP)
- ▶ American Psychological Association (APA), Division 22
- ▶ Rehabilitation Psychology

References and Readings

Frank, R., Rosenthal, M., & Caplan, B. (Eds.). (2009). *Handbook of rehabilitation psychology* (2nd ed.). Washington, DC: American Psychological Association.

Nezu, C., Finch, A., Jr., & Simon, N. (Eds.). (2009). *Becoming board certified by the American board of professional psychology.* New York, NY: Oxford University Press, Inc.

American College of Professional Neuropsychology (ACPN)

John E. Meyers
Private Practice, Neuropsychology
Mililani, Hawaii, USA

Address (and URL)

The American College Of Professional Neuropsychology (ACPN)
c/o Michael Raymond, Ph.D., ABN
Executive Director for ABN
John Heinz Institute of Rehabilitation Medicine, Neuropsychology Services
150 Mundy Street
Wilkes-Barre. PA 18702
Tel.: (570)826-3771
http://www.neuropsychologyboard.org/

Membership

The American College of Professional Neuropsychology (ACPN) is a membership organization formed on September 1, 1995 that is composed of 350 (2009) Neuropsychologists who have doctoral degrees, are licensed as psychologists, and have completed the Diplomate examination process.

Major Areas or Mission Statement

The academic arm of the American Board of Professional Neuropsychology (ABN) is the ACPN. The mission of the ACPN is to promote and provide the highest levels of services related to professional neuropsychology, for the benefit of the public and the profession.

Landmark Contributions

In addition to the continuing education benefit, ACPN also has an official quarterly journal, Applied Neuropsychology, which is dedicated to the presentation of practitioner-based scholarly research.

Diplomates of the ABN who are in good standing are automatically Fellows of ACPN and may use the acronym FACPN on their signature line. Members of other neuropsychological organizations may also join the ACPN as Affiliate members and receive a subscription to Applied Neuropsychology, and participate in ACPN continuing education programs.

Major Activities

ACPN is accredited by the American Psychological Association to sponsor continuing education for psychologists. ACPN has two general meetings a year. One meeting, National Academy of Neuropsychology (NAN) annual conference, a continuing education breakfast, is typically held at the fall. The second yearly meeting is a multiday conference, usually held in the spring. This is a much larger conference with multiple speakers, presentations, and a poster session highlighting recent clinically relevant studies and papers.

Cross References

▶ American Board of Professional Neuropsychology (ABN)

American Congress of Rehabilitation Medicine

Marcel P. J. M. Dijkers
Mount Sinai School of Medicine
New York, NY, USA

Membership

Membership is about 800, consisting of clinicians and nonclinicians with an interest in medical rehabilitation research, and training in medicine, psychology, occupational and physical therapy, nursing, speech and language pathology, political science, etc. Medical rehabilitation concerns restoration of function for individuals who as a

result of stroke, traumatic brain injury, spinal cord injury, amputation, and other disorders have impairments and activity limitations that are primarily physical in nature, but often also include cognitive and behavioral deficits; it is to be distinguished from psychiatric rehabilitation, addictions rehabilitation, etc., although there is overlap in methods and sometimes clientele. Members share an interest in rehabilitation research, and the translation of research-based knowledge into formats that are of use to medical rehabilitation clinicians. About 70 members are located outside the USA, especially in Canada.

Mission Statement

"The mission of the American Congress of Rehabilitation Medicine is to enhance the lives of persons living with disabilities through a multidisciplinary approach to rehabilitation, and to promote rehabilitation research and its application in clinical practice" (About ACRM, 2008).

"The American Congress of Rehabilitation Medicine serves people with disabling conditions by promoting rehabilitation research and facilitating information dissemination and the transfer of technology. We value rehabilitation research that promotes health, independence, productivity, and quality of life for people with disabling conditions. We are committed to research that is relevant to consumers, educates providers to deliver best practices, and supports advocacy efforts that ensure adequate public funding for our research endeavors" (About ACRM, 2008).

"To develop and implement our vision, ACRM will seek the involvement of rehabilitation professionals, including clinicians, senior level service managers, administrators, educators, and researchers. We will call upon the leaders in rehabilitation to identify current best practices and best providers at all levels of care. We will disseminate this information to the field at our regional and national meetings, through directed position papers, and in our journal, *Archives of Physical Medicine and Rehabilitation*" (About ACRM, 2008).

Landmark Contributions

The American Congress of Rehabilitation Medicine was established in 1923 as the American College of Radiology and Physiotherapy, a professional organization of physicians who had a clinical interest in diagnostic and therapeutic radiology, as well as the therapeutic application of electricity and other physical therapies (About ACRM, 2008). Reflecting the ongoing differentiation between radiologists and what (much later) would be called physiatrists, the name was changed to American Congress of Physical Therapy in 1925. To emphasize its link to medicine rather than allied health, the organization renamed itself American Congress of Physical Medicine in 1944.

While World War I had given rise to the development of rehabilitation, the involvement of physicians had been limited – rehabilitation was centered on the vocational rehabilitation of discharged servicemen. During and after World War II, however, a number of physicians became specialists in rehabilitation and started to apply methods they had used with servicemen to the treatment of civilians with amputations, spinal cord injury, stroke, and developmental disabilities such as cerebral palsy. To avoid the creation of a separate organization involving physicians with very similar interests and therapeutic regimens, a "shotgun marriage" between physiatrists and rehabilitation physicians was acknowledged in 1952 with expansion of the name of the organization to American Congress of Physical Medicine and Rehabilitation (Zeiter, 1954).

In the 1960s, the Congress opened its membership to nonphysician rehabilitation professionals, first only those holding a doctoral degree (1965), then also to nurses and therapists with an (earned) master's degree (Anonymous, 1998). To acknowledge the diminishing emphasis on physical medicine, the Congress changed its name again, to American Congress of Rehabilitation Medicine, in 1966. ACRM accepted rehabilitation professionals with a bachelor's degree as members starting in 1986. The first nonphysician to become president of the organization took office in 1977; neuropsychologists who have served as president include Leonard Diller, Mitchell Rosenthal, and Wayne Gordon.

In recent years, ACRM has redefined itself as an organization focusing on rehabilitation science, with strong interest in both generating knowledge through research and knowledge translation to bring research results to the clinic in a format that practitioners can use (Hart, 1997; Heinemann, 2006; Wilkerson, 2004). It now is primarily a group of creators, transmitters, and consumers of research-based rehabilitation knowledge, both those with clinical training (physicians, occupational and physical therapists, psychologists, etc.) and those without (engineers, political scientists, etc.), bound by the conviction that collaboration of disciplines is the best way to solve the problems inherent in disablement and the rehabilitation of persons with impairment, activity limitations, and participation restrictions. The insignia of the organization still reflects ACRM's roots in physical

medicine, including the traditional symbols for the four elements: water, earth, fire, and air.

Major Activities

ACRM communicates with its members through its scientific journal (the *Archives of Physical Medicine and Rehabilitation* – APM&R), a newsletter (*Rehabilitation Outlook*) and weekly *E-news*, an electronic digest of time-sensitive news. An annual scientific meeting of 3–4 days, often held jointly with other scientific and professional organizations, brings together members and nonmembers to discuss research findings, research methods, and issues relevant to the funding, implementation, and dissemination of rehabilitation research.

A number of standing committees offer members an opportunity to work on issues of special interest. Current committees include the International Committee (focusing on the communications between US and foreign rehabilitation research specialists), the Clinical Practice Committee (dealing with issues of evidence-based practice and related matters), and the Involving Consumers in Rehabilitation Research Committee. The Early Career Committee aims to assist individuals new to rehabilitation research in mastering the scientific, administrative, and personal aspects of a career in rehabilitation research.

Over the years, a number of interdisciplinary special interest groups (ISIGs) have existed under the aegis of ACRM; current groups include ISIGs focused on spinal cord injury, stroke, the measurement of participation, and traumatic brain injury.

The Brain Injury ISIG (BI-ISIG) grew out of the ACRM Head Injury Task Force, first called together in 1979. The BI-ISIG, which attracts large numbers of psychologists and especially neuropsychologists, has played a crucial role in the development of services for individuals with traumatic brain injury (TBI) in the United States. A definition of mild TBI often used in the literature emerged from the work of this group (American-Congress-of-Rehabilitation-Medicine.-Head-Injury-Interdisciplinary-Special-Interest-Group, 1993). The *Journal of Head Trauma Rehabilitation* (*JHTR*) was founded by a physician (Sheldon Berrol) and a psychologist (Mitchell Rosenthal) who were active in the BI-ISIG, as well as involved with the fledgling National Head Trauma Foundation, now the Brain Injury Association of America. There is significant overlap between the BI-ISIG membership and both the Editorial Board of *JHTR* and the leadership of the TBI Model Systems of Care (demonstration and research grant programs supported by the National Institute on Disability and Rehabilitation Research since 1987). There also is considerable overlap between the membership of the BI-ISIG and Divisions 22 (Rehabilitation Psychology) and 40 (Clinical Neuropsychology) of the American Psychological Association. The BI-ISIG publishes a newsletter, *Moving Ahead*. Intense collaboration in research and clinical care occurs among the BI-ISIG members, who have their own task forces and come together in an additional annual meeting.

APM&R began in 1920 as the *Journal of Radiology*, the private property of a Dr. Albert A. Tyler (Cole, 1999). The journal changed its name to the *Archives of Physical Therapy, X-ray, Radium*, in 1926; in 1930, Dr. Tyler gave the journal to ACRM (then still named the American Congress of Physical Therapy) as a "debt-free, unencumbered gift." The later changes in the name of the journal parallel the changes in the name of its owner. It became the *Archives of Physical Therapy* in 1938, the *Archives of Physical Medicine* in 1945; in 1953, the journal became the *Archives of Physical Medicine and Rehabilitation*, the name it still has (Nelson, 1969). However, the content has shifted gradually from emphasis on physical medicine, with a fairly low research basis, to an accent on rehabilitation as carried out by all disciplines that play a role in medical rehabilitation. It now is almost exclusively a research journal, with non-US contributions constituting over half the contents (Dijkers, 2009).

The journal probably gives the best indication of the role of neuropsychology in rehabilitation settings, and of neuropsychologists in ACRM. The first paper with neuropsycholog* in its title or abstract was published in 1975. Almost 200 have been published since, but they did not become an annual presence until 1984. The number now averages ten a year. In scanning the contributions of neuropsychologists to APM&R, a number of characteristics of neuropsychology in rehabilitation stand out:

- Many of these papers are coauthored with representatives of other disciplines, especially physicians.
- Several straddle neuropsychology and rehabilitation psychology, reflecting the fact that in many rehabilitation programs psychologists need to wear multiple hats.
- The focus, especially in recent years, is as much on treatment as on diagnosis, with cognitive rehabilitation for TBI and other diagnostic groups most prominent.
- A great variety of diagnostic groups have been studied, including those with peripheral vascular disease amputations, post-polio fatigue, multiple sclerosis,

sickle-cell disease, progressive supranuclear palsy, myotonic muscular dystrophy, and spinal cord injury. However, over the years and especially recently, stroke and TBI have been the etiologies of disability that rehabilitation neuropsychologists have most often been concerned with.

While the American Congress of Rehabilitation Medicine is not an organization of psychologists, let alone neuropsychologists, it is safe to say that it has played a key role in the development of neuropsychology for medical rehabilitation patients in the United States. In the foreseeable future, it probably will continue to be the forum in which these specialists, especially those who are interested in research, interact with nurses, speech/language pathologists, neuroscientists, and other specialties that contribute to rehabilitation.

References and Readings

About ACRM. (2008). Retrieved August 25, 2008, from http://www.acrm.org/about/index.cfm

American-Congress-of-Rehabilitation-Medicine.-Head-Injury-Interdisciplinary-Special-Interest-Group. (1993). Definition of mild traumatic brain injury. *Journal of Head Trauma Rehabilitation, 8*(3), 86–87.

Anonymous. (1998). Development of the American Congress of Rehabilitation Medicine into a multidisciplinary professional society: Final report of the Professional Development Committee, 1969–1972. *Archives of Physical Medicine and Rehabilitation, 79*(12 Suppl. 2), 4–12.

Cole, T. M. (1999). ACRM presidential address. In the clothing of challenge. American Congress of Rehabilitation Medicine. *Archives of Physical Medicine and Rehabilitation, 80*(2), 127–129.

Dijkers, M. P. (2009). International Collaboration and Communication in Rehabilitation Research. *Archives of Physical Medicine and Rehabilitation, 90*(5), 711–716.

Hart, K. A. (1997). Rehabilitation research: The new focus of the American Congress of Rehabilitation Medicine. *Archives of Physical Medicine and Rehabilitation, 78*(12), 1287–1289.

Heinemann, A. W. (2006). ACRM's evolving mission: Opportunities to promote rehabilitation research. *Archives of Physical Medicine and Rehabilitation, 87*(2), 157–159.

Kottke, F. J., & Knapp, M. E. (1988). The development of physiatry before 1950. *Archives of Physical Medicine and Rehabilitation, 69 Spec No*, 4–14.

Krusen, F. H. (1969). Historical development in physical medicine and rehabilitation during the last forty years. Walter J. Zeiter Lecture. *Archives of Physical Medicine and Rehabilitation, 50*(1), 1–5.

Nelson, P. A. (1969). History of the Archives – A journal of ideas and ideals. *Archives of Physical Medicine and Rehabilitation, 50*(7), 367–405.

Rusk, H. A. (1969). The growth and development of rehabilitation medicine. *Archives of Physical Medicine and Rehabilitation, 50*(8), 463–466.

Wilkerson, D. L. (2004). Individual, science, and society: ACRM's mission and the body politic. *Archives of Physical Medicine and Rehabilitation, 85*(4), 527–530.

Zeiter, W. J. (1954). The history of the American Congress of Physical Medicine and Rehabilitation. *Archives of Physical Medicine and Rehabilitation, 35*(11), 683–688.

American National Adult Reading Test (ANART)

► Weschler's Adult Reading test

American Psychological Association (APA)

Wade Pickren
Ryerson University
Toronto, ON, Canada

Address and URL

750 First Street NE, Washington, DC 20002-4242 (www.apa.org)

Membership

150,000 as of 2010

Major Areas or Mission Statement

The mission of the APA is to advance the creation, communication, and application of psychological knowledge to benefit society and improve people's lives.

Landmark Contributions

The American Psychological Association (APA) was founded in 1892 by a small group of men interested in what was called "the new psychology." Its founding at this particular time can best be understood as part of the large number of changes occurring in the USA at that time. The emergence of a number of what are now standard academic disciplines, psychology, economics, political

science, biochemistry, physiology, in the last 2 decades of the nineteenth century was part of a reorganization of American knowledge production, reflecting a division of intellectual labor similar to the division of manufactory labor. Like its fellow disciplines, the new psychology grew and prospered as it responded to the needs of American society.

Within the modern university system that emerged after the U.S. Civil War, the new disciplines quickly developed advanced degrees that provided credentials, which served to validate the discipline's members as experts in their special field. This occurred in parallel with the progressive movement in politics, which called for a more efficient, less corrupt, social order. The synergism of these two developments, specialized expertise and rationalized government, helped create the demand for trained personnel to fill the new professional niches created by the demands for a more efficient society. Psychology was one of the most successful of the new disciplines to make itself useful for the social management of an increasingly complex and diversified society.

In July 1892, G. Stanley Hall (1844–1924) met with a small group of men to discuss the possibility of organizing a psychological association. Although the details of the meeting are not known, the group elected 31 individuals, including themselves, to membership, with Hall as the first President. The first meeting of the new American Psychological Association (APA) was held in December 1892 at the University of Pennsylvania. The basic governance of the APA at this time was consisted of a small council with an executive committee. This plan remained in effect until the reorganization of APA during World War II.

Membership growth of the APA was modest over the first 50 years of its existence. From 31 members in 1892, there were 125 members in 1899, 308 in 1916, 530 in 1930, and 664 in 1940. In 1926, a new class of nonvoting membership was formed, associate, and most of the growth occurred in that class after 1926, so that there were 2,079 associate members in 1940. Many of these associates were individuals doing practical or applied work in psychology and who also belonged to one of the applied associations that emerged in this time. Realizing that the growth of applied psychology represented a potential threat to its preeminence, the leaders of APA sought to reorganize the association during World War II. Under this reorganization plan, the APA merged with other psychological organizations and created divisions to represent special fields of interest. There were initially 17 divisions (19 were proposed). The result was an association that was much more broadly based than before the War and that was organized around an increasingly diffuse conceptualization of psychology. Now, the association's scope included professional practice and the promotion of human welfare, as well as the practice of the science of psychology. This flexibility in scope has remained to the present time, as new challenges and demands have arisen.

Psychology boomed after the end of World War II, with the greatest increase in membership coming between 1945 and 1970. This was due to intense interest in the field, especially in the domains of clinical and applied psychology, among returning serviceman, many of whom saw the great need for better psychological services firsthand during the war. Institutional or structural factors that facilitated this growth included the GI Bill, the new Veterans Administration Clinical Psychology training program, and the creation of the National Institute of Mental Health. For the first time, psychology was a field, both science and practice, that was richly funded for training and research. This was, as one scholar termed it, The Golden Age of Psychology. The rapid and incredible growth in APA's membership reflected this trends, as membership grew 630% from 1945 to 1970, from 4,183 members (1945) to 30,839 (1970). By comparison, from 1970 to 2000, APA membership grew to 88,500, with another 70,500 affiliates.

Part of what facilitated this growth was the new divisional structure of the APA that grew out of the reorganization plan during World War II. Now, members could join a special interest group within APA and find other like-minded members. Of course, this also facilitated the fractionation of psychology and pushed the field away from any sense of unity that it may have held prior to the war. Nineteen divisions were approved in 1944, with the two most numerous being clinical and personnel (now counseling). This reflected the sectional structure of the American Association of Applied Psychology (AAAP, f. 1937), which had emerged in 1937 as the chief rival to the APA and had been the chief reason for the reorganization. Because the Psychometric Society (Division 4) decided not to join and after Division 11, Abnormal Psychology and Psychotherapy, merged with Division 12, Clinical Psychology, the number of active divisions was reduced to 17. Growth in the number of divisions was slow until the 1960s, only three more were added, in part because many of the older members, then in leadership positions, were quite resistant to increasing the number of divisions. The growth in the number of divisions since the 1960s has been consistent, with 54 divisions now part of the APA structure. Many of the newer divisions reflect the growth

of particular practice areas, for example, Division 50, Addictions. However, there has also been growth in special interest areas that belie any simple science/practice dichotomy, for example, Society for the Psychology of Women, Society for the History of Psychology, International Psychology, Media Psychology, or the Study of Men and Masculinity.

Major Activities

The effect on APA governance of the divisional structure and the growth of state and provincial psychological organizations has been marked. As mentioned, prior to World War II, APA's governance structure was a small council with an executive committee. After the reorganization and the end of the war, the Council of Representatives has grown in number to accommodate representation from each division and from state and provincial psychological associations, thus making governance somewhat unwieldy. Various plans have been tried over the years to ensure a voice for each of the areas and interests groups in psychology on the council and it remains a dynamic situation. One result of the growth of professional psychology, especially clinical and counseling psychology, on governance has been the increase in the representation of professional interests, for example, licensing, specializations, etc., in the deliberations of the council. At times, this has led to tension between the representatives of psychological science and those whose main commitment is to advancing professional practice. In historical retrospect, it seems clear that this tension was inherent in the reorganization of APA, as the association reflected developments in the field.

As a membership organization, APA has often been perceived as inadequately representing one or more its constituencies. It has been the case, more often than not, that the resulting tension was resolved and the unhappy parties remained within the association. However, there have also been more serious disagreements that have resulted in new organizations being formed. In the late 1950s, a group of experimental psychologists grew unhappy with what they perceived as APA's drift from scientific psychology. By the end of 1959, this group formed the Psychonomic Society in order, they asserted, to foster psychology as a science without a need to attend to professional issues. The Psychonomic Society remains a very viable and valuable organization of scientists to the present moment; many of its members remained APA members, as well. A more serious division occurred in the mid- to late 1980s, as tensions between those who wanted APA to remain a primarily scientific organization and those who sought a greater emphasis by the association on professional practice rose to a boil. A proposed reorganization plan was defeated by a vote of the membership and almost immediately a large group of dissident psychological scientists, including former APA Presidents, left the APA to form what is now the Association for Psychological Science (APS). Still, after a period of struggle, both organizations are strong, stable representatives of psychology, with many psychologists belonging to both associations.

One result of the split that led to the formation of APS is that professional interests have grown stronger within APA. As the number of psychologists devoted to professional practice grew and gained greater influence in the APA governance structure, a new unit was established in the APA Central Office. The Office of Professional Practice was created in the mid-1980s with a mandate to focus on applied practice activities, especially the promotion of health-care practice. To finance the expansion of activities, a special assessment was levied on psychologists licensed for health-care practice. With this money, the office was able to engage in consultation, technical assistance, and legal and legislative assistance for professionals. The office also began to work closely with state associations to enhance practice issues and support efforts relevant to legislation in state legislatures. Within a few years, the range of activities led to the need to create the Practice Directorate within APA. Since that time, the Practice Directorate has played the important roles of handling all practice-related programs and has been responsible for the coordination of practice efforts in legal and legislative arenas. The special assessment and the Practice Directorate represented a special moment in APA's history in that they enhanced the power of clinical and professional practice both within and without APA.

Even so, APA has maintained a commitment to the promotion of psychological science. It publishes more than 40 peer-reviewed scientific journals. Internally, in the APA Central Office, this is represented by the Science Directorate. Since the late 1980s, the Central Office has been reorganized to better represent the diverse constituencies of the membership. Beginning with the formation of the Practice Directorate in the late 1980s, other Directorates were formed in the hope that the interests of all the membership would be better represented. As of 2009, there were the Practice, Education, Science, and Public Interest Directorates. From a historical perspective, it is too soon to determine whether this approach represents

an advance for the association or a further balkanization of the field.

APA remains the world's largest membership organization of psychologists. It has a fascinating past, marked by growth, conflict, and increasing diversification.

Cross References

► Advocacy; Entries 77–86 (excluding 84); Entries 376, 377
► American Psychological Association Division 22
► American Psychological Association Division 40

References and Readings

Dewsbury, D. A. (1997). On the evolution of divisions. *American Psychologist, 52*, 733–741.

Evans, R. B., Sexton, V. S., & Cadwallader, T. C. (Eds.). (1992). *The American Psychological Association: A historical perspective.* Washington, DC: American Psychological Association.

Fernberger, S. W. (1932). The American Psychological Association: A historical summary, 1892–1930. *Psychological Bulletin, 29*, 1–89.

Guthrie, R. V. (1998). *Even the rat was white: A historical view of psychology.* Boston: Allyn and Bacon.

Pickren, W. E., & Schneider, S. F. (Eds.). (2005). *Psychology and the National Institute of Mental Health: A historical analysis of science, practice, and policy.* Washington, DC: APA Books.

American Psychological Association (APA), Division 22

William Stiers
Johns Hopkins University School of Medicine
Baltimore, MD, USA

Membership

The American Psychological Association (APA) Division 22 – Rehabilitation Psychology is composed of over 1,111 (2009) psychologists who provide clinical services (91%), teach (65%), conduct research (41%), manage rehabilitation programs (37%), and perform other activities too. They work in hospitals and clinics (40%), in university, college, medical school (27%), and other settings, and are also in independent practice (28%).

Major Areas or Mission Statement

The Division of Rehabilitation Psychology works to unite psychologists and others interested in the prevention and rehabilitation of disability and chronic illness. Rehabilitation Psychology Practice is a specialty within the domain of professional healthcare psychology, which applies psychological knowledge and skills on behalf of individuals with disabilities and chronic health conditions in order to maximize their health and welfare, independence and choice, functional abilities, and role participation. Such disabilities include spinal cord injury, brain injury, stroke, amputations, burns, work-related injuries, multiple traumatic injuries, chronic pain, cancer, heart disease, multiple sclerosis, neuromuscular disorders, AIDS, developmental disorders, psychiatric impairment, substance abuse, impairments in sensory functioning, and other physical, mental and/or emotional impairments. The broad field of Rehabilitation Psychology also includes rehabilitation program development and administration, research, teaching, public education and development of policies for injury prevention and health promotion, and advocacy for persons with disabilities and chronic health conditions.

Landmark Contributions

1. Rehabilitation psychologists have worked in medical settings as part of teams of healthcare professionals for more than half a century, long before psychologists were regularly involved in other healthcare settings.
2. Division 22 was established in 1958, one of the earlier divisions in APA.
3. Division 22 members conducted the initial research on individual, interpersonal, and social changes related to changes in appearance and physical capacity, as well as the social psychology of stereotyping and prejudice faced by persons with disability.
4. Division 22 members were among the pioneers helping psychology understand the world of work, how the same can be affected by impairment and disability, and issues about vocational rehabilitation.
5. Rehabilitation psychologists have developed the principles of cognitive rehabilitation, and have served as leaders in the federal model systems programs for traumatic brain injury, spinal cord injury, and burns.
6. Board Certification in Rehabilitation Psychology was established in 1997.

Major Activities

The journal *Rehabilitation Psychology* is published quarterly by the APA.

Division 22, in conjunction with the American Board of Rehabilitation Psychology, holds an annual conference in the spring.

Cross References

- ► American Psychological Association (APA)
- ► Rehabilitation Psychology

References and Readings

American Psychological Association. (2008). A closer look at Division 22: A growing field meets the challenges of war. *Monitor on Psychology, 38*(8), 54–55.

Frank, R., Rosenthal, M., & Caplan, B. (Eds.). (2009). *Handbook of rehabilitation psychology* (2nd ed.). Washington, DC: American Psychological Association.

Larson, P., & Sachs, P. (2000). A history of Division 22. In D. A. Dewsbury (Ed.), *Unification through division: Histories of the divisions of the American Psychological Association* (Vol. 5, pp. 33–58). Washington, DC: American Psychological Association.

American Psychological Association (APA), Division 40

William B. Barr
New York University School of Medicine
New York, USA

Membership

The Division of Clinical Neuropsychology (Division 40) is one of 56 specialty divisions recognized by the American Psychological Association (APA). Since its inception, it has become one of APA's largest and most active divisions. In its nearly 30 years, membership has grown from 433 psychologists to its current numbership of 5,315, which currently makes it the second largest of all APA divisions behind only the Independent Practice Division (Division 42). The division's representation to the APA council has grown over the years from its initial one representative to the current allotment of four seats. This trend coincides with Division 40's increasing influence within APA and increasing recognition of neuropsychology as a clinical specialty.

Eligibility for membership is based on the criteria required for Associate, Member, or Fellow status in the APA. Additional requirements include demonstrated interest in the field of neuropsychology and its scientific development, public dissemination, and/or clinical applications. All members of the division have rights and privileges to hold office and serve on division committees, vote in regular elections, attend various meetings of the division, and receive publications of the division. Information for joining Division 40 can be obtained on the division's website at http://www.div40.org/membership.html.

APA statistics indicate that the majority of Division 40 members are women (55%). Ethnic minority members constitute 8% of the membership, consistent with larger APA trends. Approximately, 80% of the division memberships have Ph.D. in clinical psychology or a related field. Nearly half (42%) of the members work in independent settings. Most other members work in medical schools, hospitals, and university settings. Many combine their work in institutional and private-practice settings. Membership surveys have indicated that psychologists in Division 40 spend a substantially larger amount of time (>40%) in assessment activities than other APA members (<15%). Approximately, one third of the members are actively involved in research activities. Approximately, 40% are involved in clinical training.

Major Areas or Mission Statement

Division 40 was formed in 1980 with the mission of enhancing the understanding of brain-behavior relationships and the application of such knowledge to human problems. Activities of the division encompass the areas of science (e.g., presentations at the annual meeting of APA, awards for outstanding scientific contributions), practice (e.g., Current Procedural Terminology "CPT" billing codes, educational brochures for patients), education and training (e.g., neuropsychology graduate student organization), and specialty public interest groups (e.g., women, minorities, geriatrics, rural, etc.).

The division upholds APA bylaws and enacted its own divisional bylaws in 1980, which were subsequently revised to their current form in 1997. Over the years, Division 40 has provided published guidelines on many aspects of neuropsychological practice and training while also

fostering continued development of the science of neuropsychology through activity of its committees. The division advances scientific knowledge in the field of neuropsychology through its support of publication and presentation of scientific papers at professional conferences, including the APA's annual convention.

Landmark Contributions

Psychologists interested in the developing field of neuropsychology began participating on a regular basis at APA meetings during the 1960s. The origins of Division 40 can be traced back to the development of the International Neuropsychological Society (INS), which is known as the field of neuropsychology's first formal organization. Informal meetings of psychologists interested in neuropsychological issues were held at the annual APA meeting dating back to 1965. The INS was formally organized in 1967 as an outgrowth of these meetings with the goal of serving as a scientific and educational organization. The need for formal representation in APA became increasingly apparent as professional issues regarding practice, education, and training in neuropsychology began to emerge. Leaders in the field, including Arthur Benton, Louis Costa and Manfred Meier, saw the need for the development of an organization to promote the growing specialty of clinical neuropsychology that was independent of INS and APA's Division of Clinical Psychology (Division 12). The application to establish a Division of Clinical Neuropsychology was submitted to APA and approved by its Council of Representatives in September 1979. The formation of Division 40 was made effective in January 1980, consistent with APA procedures. The division's first President was Dr. Harold Goodglass with Dr. Gerald Goldstein serving as both the Secretary and Treasurer. The presidents of the division include many of the most prominent names in the field of neuropsychology (Table 1).

One of the division's earliest activities included working with the INS Task Force on Education, Accreditation, and Credentialing (TFEAC) in establishing guidelines for doctoral, internship, and postdoctoral training in clinical neuropsychology. Recommendations provided by that group, calling for a combination of training experiences in psychology and the neurosciences, continues as the field's dominant model of training. The INS task force was eventually discontinued as it became increasingly evident that professional issues were becoming the domain of Division 40. A listing of publications of other professional guidelines and statements developed by Division 40 committees and task forces are provided in Table 2. The purpose of these guidelines was to facilitate an adherence to standards for professionals in the field of clinical neuropsychology with the ultimate goal of ensuring the quality of services provided to consumers.

During the 1990s, a task force from Division 40 led by Manfred Meier successfully submitted a petition for clinical neuropsychology to become the first psychological specialty recognized by the APA's Commission on Recognition of Specialties and Proficiencies in Professional Psychology (CRSPP). Recognition of clinical neuropsychology as a specialty became official in 1997. This was followed by a set of activities, working in conjunction with the National Academy of Neuropsychology (NAN), American Board of Clinical Neuropsychology (ABCN), American Academy of Clinical Neuropsychology (AACN), and the Association of Postdoctoral Programs in Clinical Neuropsychology

American Psychological Association (APA), Division 40. Table 1 Presidents of division 40 (clinical neuropsychology)

1980s	1990s	2000s
1979–1980 Harold Goodglass	1989–1990 Charles G. Matthews	1999–2000 Gordon J. Chelune
1980–1981 Harold Goodglass	1990–1991 Raymond S. Dean	2000–2001 Jason Brandt
1981–1982 Louis Costa	1991–1992 Steven Mattis	2001–2002 Allan F. Mirsky
1982–1983 Nelson M. Butters	1992–1993 Oscar Parsons	2002–2003 Antonio Puente
1983–1984 Thomas J. Boll	1993–1994 Robert K. Heaton	2003–2004 Kathleen J. Haaland
1984–1985 Lawrence C. Hartledge	1994–1995 Carl Dodrill	2004–2005 Robert J. Ivnik
1985–1986 Manfred J. Meier	1995–1996 Kenneth M. Adams	2005–2006 Russell M. Bauer
1986–1987 Edith F. Kaplan	1996–1997 Eileen B. Fennell	2006–2007 Keith O. Yeates
1987–1988 Byron P. Rourke	1997–1998 Linas A. Bieliauskas	2007–2008 Thomas A. Hammeke
1988–1989 Gerald Goldstein	1998–1999 Cecil R. Reynolds	2008–2009 Glenn E. Smith

American Psychological Association (APA), Division 40. Table 2 Published guidelines from division 40 committees and task forces

Year	Activity
1987	Guidelines for Doctoral Training Programs in Clinical Neuropsychology
1987	Task Force Report on Computer-Assisted Neuropsychological Evaluation
1988	Guidelines of Continuing Education in Clinical Neuropsychology
1989	Definition of a Clinical Neuropsychologist
1989	Guidelines Regarding the Use of Nondoctoral Personnel in Clinical Neuropsychological Assessment
1991	Recommendations for Education and Training of Nondoctoral Personnel in Clinical Neuropsychology
1991	Guidelines for Computer-Assisted Neuropsychological Rehabilitation and Cognitive Remediation

(APPCN) in developing an integrated model for specialty training in clinical neuropsychology. Representatives from these organizations and various training programs across the USA met in 1997 for what was termed The Houston Conference on Specialty Training in Clinical Neuropsychology. The conference led to the development and publication of a document describing an integrated model of education and training. Interactions between Division 40 and these other groups continue through an organization called the Clinical Neuropsychology Synarchy (CNS).

Major Activities

Officers of Division 40 include President, President-Elect, Past President, Secretary, and Treasurer. These positions are elected by the general membership with the term of President lasting 1-year and the roles of Secretary and Treasurer lasting 3-years. The officers serve on an Executive Committee (EC) joined by various Division Committee Chairs, Divisional Representatives to APA Council, and three Members-at-Large. Meetings of the EC are held twice yearly, with one of the meetings held at the North American meeting of the INS in mid-winter and the other coinciding with the APA convention in the summer. Presidents of the division preside at meetings and serve as the Chairperson of the EC. Terms of office begin and end at the completion of the annual business meeting held during the summer.

The division has four standing committees including Membership, Fellowship, Elections, and Program Committees and four continuing committees consisting of the Science Advisory, Education Advisory, Practice Advisory, and Public Interest Advisory Committees. Special Committees, including Task Force Committees, can also be established by vote of the Executive Committee, when the need arises. The Committee on APA Relations and the Publications and Communications Committee are examples of these. The President, in consultation with the EC, appoints chairs of all divisional committees and task forces. Summaries of divisional activities, minutes of executive committee meetings, and committee reports are published biannually in *Newsletter 40*, the official division newsletter.

Continued commitments to training have been demonstrated by the formation of the Division 40 Association for Neuropsychology Students in Training (ANST) and the establishment of an Early Career Psychologists committee. Committees and mentoring programs have been established for women entering the field and for ethnic minority members. Brochures describing an introduction to clinical neuropsychology are available through the division's Public Interest Advisory Committee (PIAC). The Practice Advisory Committee (PAC) provides monitoring of legislative activities and both local and national activities affecting the practice of clinical neuropsychology. This committee is also responsible for interactions with government agencies such as the Centers for Medicare and Medicaid Services (CMS). The PAC worked with other organization in establishing a new set of CPT testing codes aimed at optimizing reimbursement for neuropsychological services. These codes were officially implemented in 2006.

The division has maintained its goal of integrating science and practice. The Science Advisory Committee (SAC) continues in its role of producing scientific programs for the APA's annual convention. Studies on neurologic syndromes, assessment, and developmental issues are among the topics most commonly presented in the Division 40 program at the annual APA meeting. The SAC also provides a number of awards for students and early career psychologists establishing careers in neuropsychological research. More recent SAC activities include integration of neuropsychology's scientific activities with APA and government agencies such as the National Institutes of Health (NIH).

Division 40 does not publish or provide an official journal. However, over the years, the division has maintained a close relationship with *The Clinical Neuropsychologist (TCN)*, a journal focusing on clinical issues relevant to neuropsychologists. The journal has published a number of statements and guidelines prepared by Division 40

task forces relevant to the practice of neuropsychology and abstracts from Division 40's scientific program at APA. In 1989, *TCN* also began to publish regular listings of training programs in neuropsychology. In 2006, a user-interactive revision of the list was developed by the Education Advisory Committee (EAC) and transferred to the Division 40 web site. The listing currently includes 31 doctoral training programs, 42 internships, and 78 sites offering postdoctoral residencies for specialty training in clinical neuropsychology. The web site also includes descriptions of other divisional activities and links to the division's archival material.

Cross References

► American Academy of Clinical Neuropsychology (AACN)
► American Psychological Association (APA)
► International Neuropsychological Society
► National Academy of Neuropsychology

References and Readings

Adams, K. M., & Rourke, B. P. (Eds.) (1992). *The TCN guide to professional practice in clinical neuropsychology.* Berwyn, PA: Swets & Zeitlinger.

Costa, L. (1998). Professionalization in neuropsychology: The early years. *The Clinical Neuropsychologist, 12*, 1–7.

Meier, M. J. (1992). Modern clinical neuropsychology in historical perspective. *American Psychologist, 47*, 550–558.

Meier, M. J. (2002). In search of knowledge and competence. In A. Y. Stringer, E. L. Cooley, & A-L. Christensen (Eds.), *Pathways to prominence in neuropsychology: Reflections of twentieth century pioneers.* New York: Psychology Press.

Puente, A. E., & Marcotte, A. C. (2000). A history of Division 40 (clinical neuropsychology). In D. A. Dewsbury (Ed.), *Unification through division: Histories of the divisions of the American Psychological Association, Volume V.* Washington, DC: American Psychological Association Press.

American Speech-Language-Hearing Association (ASHA)

Lemmietta McNeilly
American Speech-Language-Hearing Association
Rockville, MD, USA

Membership

The American Speech-Language-Hearing Association is the professional, scientific, and credentialing association for 140,000 members and affiliates who are speech-language pathologists, audiologists, and speech, language, and hearing scientists in the USA and at the international level.

Major Areas or Mission Statement

Vision: Making effective communication a human right, accessible, and achievable for all.

Mission

Empowering and supporting speech-language pathologists, audiologists, and speech, language, and hearing scientists by:

- Advocating on behalf of persons with communication and related disorders
- Advancing communication science
- Promoting effective human communication

Landmark Contributions

ASHA has had several names during its 83-year history. The first was the American Academy of Speech Correction (1925). The current name, The American Speech-Language-Hearing Association (ASHA), was adopted in 1978. ASHA is the nation's leading professional, credentialing, and scientific organization for speech-language pathologists, audiologists, and speech/language/hearing scientists. ASHA has been the guardian of these professions for over 75 years, initiating the development of national standards for each discipline and certifying professionals for 55 years.

ASHA began in 1925 at an informal meeting of the National Association of Teachers of Speech (NATS) in Iowa City, IA, an organization of people working in the areas of rhetoric, debate, and theater. Robert W. West was the first president of the association from 1925 to 1928. Its members were becoming increasingly interested in speech correction and wanted to establish an organization to promote "scientific, organized work in the field of speech correction." Accordingly, in December of that year, the American Academy of Speech Correction – ASHA's original predecessor – was born.

ASHA has grown exponentially since its inception – from 25 members in 1925 to 140,000 in 2010. ASHA opened its first national office on January 1, 1958 in Washington, DC. The association subsequently moved four times, most recently settling in its current location in Rockville, MD in 2008. ASHA's new national office is

a LEED certified green building – the first nonprofit company's building of that distinction in Maryland.

Major Activities

Publications: The ASHA Leader; American Journal of Audiology; American Journal of Speech-Language Pathology; Journal of Speech, Language, and Hearing Research; Language, Speech, and Hearing Services in Schools; and Perspectives.
Conferences: Annual convention and three niche conferences: Healthcare, Schools, and State Policy Workshop as well as several web events annually.

References and Readings

Interdisciplinary approaches to Brain Damage written by the joint committee http://www.asha.org/docs/html/PS1990–00093.html
Selected practice documents related to Adult Neurogenics are featured in ASHA's Online Practice Policy documents. http://www.asha.org/academic/curriculum/slp-aneuro/deskref
Structure and Function of an Interdisciplinary Team for Persons with Acquired Brain Injury http://www.asha.org/docs/html/GL2007–00288.html
Memory Assessment on an Interdisciplinary Rehabilitation Team: A Theoretically Based Framework. http://ajslp.asha.org/cgi/content/full/16/4/316?maxtoshow=&HITS=10&hits=10&RESULTFORMAT=&fulltext=memory+assessment&searchid=1&FIRSTINDEX=0&sortspec=relevance&resourcetype=HWCIT

American Speech-Language-Hearing Association Functional Assessment of Communication Skills for Adults

Carole Roth
Naval Medical Center
San Diego, CA, USA

Synonyms

ASHA-FACS

Description

The ASHA-FACS was designed as a quick and easily administered measure of functional communication behaviors at the level of disability, based on direct observations by speech-language pathologists or significant others who are familiar with the client's typical communication performance across the following domains: Social Communication; Communication of Basic Needs; Reading, Writing, and Number Concepts; and Daily Planning. Within each domain, specific functional behaviors are rated on a 7-point scale of independence, ranging from "does" the activity fully independently, through five levels of "does with" varying degrees of assistance to "does not" perform the activity. For example, Social Communication concerns the ability to use names of familiar people, exchange information on the telephone, answer yes/no question and follow directions, understand facial expressions and tone of voice, comprehend nonliteral meaning, and understand TV and radio programs. Communication of Basic Needs assesses ability to recognize familiar faces and voices, express feelings and make known needs and wants, and respond in an emergency. Reading, Writing, and Number Concepts examine the ability to understand simple signs, use reference materials, understand printed material and follow written directions, complete forms, write messages, and make money transactions. Finally, Daily Planning evaluates the ability to tell time, sequence numbers for using a telephone, maintain a schedule of appointments and use a calendar, and read a map. Each domain is rated globally on the basis of a Scale of Qualitative Dimensions (i.e., adequacy, appropriateness, promptness, and communication sharing). The measure yields domain and dimension mean scores, overall scores, and profiles of both Communication Independence and Qualitative Dimensions.

The ASHA-FACS includes:

- A 117-page manual
- A CD version to allow automatic tabulation of the measures for recording incremental client assessments in MS Excel used in PC or Apple/Macintosh
- A paper-and-pencil version with score summary and profile forms that purchasers can copy
- A rating key on a 5" x 7" card
- An electronic index of ICD-9-CM codes

Historical Background

ASHA-FACS evolved from the wave of healthcare accountability and the widespread need for an effective instrument to measure the functional communication of adults who have speech, language, or cognitive impairments for purposes of justifying payment, defining service

eligibility, and judging the value of care. Developed in 1995 by ASHA, it reflects the collaborative effort of more than 70 individuals, both ASHA members and related professionals. The first version of the measure, the ASHA Functional Communication Measures (Frattali, C.M.1998), was developed for use with both children and adults. The FCMs consisted of 12 rating scales, each representing a separate communication process and rated on an 8-point scale of independence. Development of the FCMs was funded by the National Institute on Child Health and Human Development, National Institutes of Health. The FCMs were determined to be unsuitable for use with children, and as a result of other limitations, a second group of experts specifically in adult communication disorders edited the FCMs, proposed a multidimensional scoring system, and renamed the instrument.

Further revisions in 1992 included a reconceptualization of the framework to measure at the level of disability, consistent with the World Health Organization's International Classification Scheme, resulting in the final title, the ASHA Functional Assessment of Communication Skills for Adults (ASHA-FACS). The design of the ASHA-FACS was based on a definition of functional communication formulated in 1990 by an ASHA advisory group: "the ability to receive or to convey a message, regardless of the mode, to communicate effectively and independently in natural environments" (cited in Frattali, C.M.1995).

Psychometric Data

The usability, sensitivity, reliability, and validity of the ASHA-FACS were demonstrated through two separate pilot tests and one field test. The first version was piloted in 1993 to determine the measure's usability, resulting in the development of a 7-point observational rating scale. A second pilot test confirmed the usability of the revised version, and acceptable levels of reliability and validity were found. A more sensitive scoring system for capturing qualitative information about the nature of a client's functional communication led to the addition of a second scoring feature, the 5-point Scale of Qualitative Dimensions.

To establish interrater reliability, the ASHA-FACS was completed independently for 51 subjects by two examiners within a 48-h period. Interrater reliability correlations on the seven assessment domain scores ranged from 0.72 to 0.92. Overall communication independence scores had high interrater agreement (mean correlation = 0.95) as did overall scores (mean correlation = 0.90). Intrarater reliability for communication independence mean scores by assessment domain ranged from 0.95 to 0.99 and intrarater reliability of overall communication independence scores was 0.99. Intrarater reliability of qualitative dimension mean scores ranged from 0.94 to 0.99 and 0.99 for the overall qualitative dimension scores.

The ASHA-FACS was moderately correlated with other measures of language and cognitive function as demonstrated by external criterion measures used with subjects with aphasia and cognitive-communication impairments from traumatic brain injury. A significant correlation of 0.76 ($\alpha = 0.05$ level) was obtained between Western Aphasia Battery (WAB) (Kertesz, 1982), Aphasia Quotients (AQs), and ASHA-FACS overall scores. Statistically significant correlations were obtained between ASHA-FACS domain scores and WAB subtest scores, with the exception of correlations between WAB fluency scores and reading and writing domain scores from the ASHA-FACS. Correlations between the ASHA-FACS domain score and overall score and each of the Functional Independence Measure (FIM) scales (FIM 4.0; SUNY at Buffalo Research Foundation, 1993) were statistically significant (ranging from 0.42 to 0.82), with the exception of the social interaction scale of the FIM. External validation data for the subjects with cognitive-communication impairments ranged from 0.76 to 0.85 between the Scales of Cognitive Ability for Traumatic Brain Injury (SCATBI) (Adamovich & Henderson, 1992) severity scores and the ASHA-FACS scores, and a 0.84 correlation between the ASHA-FACS overall scores with the SCATBI severity scores. These correlations were all statistically significant at the $\alpha = 0.05$ level. Statistically significant correlations were found between ASHA-FACS domain and overall scores with the Rancho Los Amigos Levels of Cognitive Functioning (Hagen, Malkmus, & Durham, 1979) (correlations ranged from 0.64 to 0.83) and FIM scores (correlations ranged from 0.50 to 0.80). Nonsignificant correlations were obtained from SCATBI subtest scores and ASHA-FACS domain scores obtained from the mild to moderately impaired TBI group.

High internal consistency and social validity were reported. Internal consistency indicated that most item scores covered the full 7-point rating scale, showed high inter-item correlations between items within assessment domains, were internally consistent with respect to assessment domain, and that all items were measuring the

same underlying construct. The data indicated that all domain scores correlated with overall ASHA-FACS scores. Evaluation of social validity was accomplished by correlating overall ASHA-FACS scores with measures scored by family members or friends of subjects. These measures included the Communicative Effectiveness Index (CETI; Lomas et al., 1989) and a Rating of Overall Communication Effectiveness, a single overall index of each subjects' communication effectiveness rated on a scale from 1 (lowest) to 7 (highest). These data indicated high positive correlations between ASHA-FACS overall scores and Ratings of Overall Communication Effectiveness by clinicians (i.e., r = 0.81). ASHA-FACS overall scores did not correlate well with family members' or friends' Ratings of Overall Communication Effectiveness or CETI scores. CETI ratings were consistently higher than those measured using the ASHA-FACS.

Clinical Uses

ASHA-FACS was designed for clinicians to rate functional communication behaviors of adults with speech, language, and cognitive-communication disorders resulting from left hemisphere stroke and from traumatic brain injury.

In a review of the evidence leading to recommended best practices for assessment of individuals with cognitive-communication disorders after TBI, the ASHA-FACS was one of a few standardized, norm-referenced tests that met most established criteria for validity and reliability for use with this clinical population (Turkstra, Coelho, & Ylvisaker, 2005). It was one of only four of the 31 tests reviewed that evaluated performance outside clinical settings. It was unique in that it was based on research about daily communication needs in the target population and incorporated consumer feedback about ecological validity into the design. The research is rich in the many clinical benefits of the ASHA-FACS. For example, this instrument has been used to measure communication disability relative to quality of life in chronically aphasic adults (Ross & Wertz, 2002; Davidson, Worrall, & Hickson, 2003), to evaluate the effectiveness of functionally based communication therapy (Worrall & Yiu, 2000), and to evaluate real-life outcomes of aphasia interventions (Kagan et al., 2008). Using Rasch analysis of the ASHA-FACS Social Communication Subtest (SCS), Donovan, Rosenbek, Ketterson, & Velozo (2006) demonstrated that caregivers were reliable respondents who could use the SCS to rate therapy progress and functional outcomes.

References and Readings

Adamovich, B., & Henderson, J. (1992). *Scales of cognitive ability for traumatic brain injury.* Chicago: Riverside.

Davidson, B., & Worrall, L. (2002). The assessment of activity limitation in functional communication: Challenges and choices. In A. E. Hillis (Ed.), *The handbook of adult language disorders: Integrating cognitive neuropsychology, neurology, and rehabilitation* (pp. 19–34). New York: Psychology Press.

Davidson, B., Worrall, L., & Hickson, L. (2003). Identifying the communication activities of older people with aphasia: Evidence from naturalistic observation. *Aphasiology, 17*(3), 243–264.

Donovan, N. J., Rosenbek, J. C., Ketterson, T. U., & Velozo, C. A. (2006). Adding meaning to measurement: Initial Rasch analysis of the ASHA FACS Social Communication Subtest. *Aphasiology, 20*(2–4), 362–373.

Frattali, C. M. (Ed.) (1998). Measuring modality-specific behaviors, functional abilities, and quality of life. In *Measuring outcomes in speech-language pathology.* (P. 203). New York: Thieme.

Frattali, C. M., Thompson, C. K., Holland, A. L., Wohl, C. B., & Ferketic, M. M. (1995). *The American Speech-Language-Hearing Association Functional Assessment of Communication Skills for Adults (ASHA FACS).* Rockville, MD: ASHA.

Frattali, C. M., Thompson, C. M., Holland, A. L., Wohl, C. B., & Ferketic, M. M. (1995). The FACS of life ASHA FACS—a functional outcome measure for adults. *ASHA, 37*(4), 40–46.

Hagen, C., Malkmus, D., & Durham, P. (1979). Levels of cognitive functioning. In *Rehabilitation of the head-injured adult: Comprehensive physical management* (Appendix C., pp. 87–89). Downey, CA: Professional Staff Association of Rancho Los Amigos Hospital.

Kagan, A., Simmons-Mackie, N., Rowland, A., Huijbregts, M., Shumway, E., McEwen, S., Threats, T., & Sharp, S. (2008). Counting what counts: A framework for capturing real-life outcomes of aphasia intervention. *Aphasiology, 22*(3), 258–280.

Kertesz, A. (1982). *Western Aphasia Battery.* New York: Grune & Stratton.

Lomas, J., Pickard, L., Bester, S., Elbard, H., Finlayson, A., & Zoghaib, C. (1989). The Communicative Effectiveness Index: Development and psychometric evaluation of a functional communication measure for adults. *Journal of Speech and Hearing Disorders, 54,* 113–124.

Ross, K. B., & Wertz, R. T. (2002). Relationships between language-based disability and quality of life in chronically aphasic adults. *Aphasiology, 16*(8), 791–800.

State University of New York at Buffalo Research Foundation. (1993). *Guide for use of the Uniform Data Set for Medical Rehabilitation: Functional independence measure.* Buffalo, NY: Author.

Turkstra, L. S., Coelho, C., & Ylvisaker, M. (2005). The use of standardized tests for individuals with cognitive-communication disorders. *Seminars in Speech and Language, 26*(4), 215–222.

Worrall, L., & Yiu, E. (2000). Effectiveness of functional communication therapy by volunteers for people with aphasia following stroke. *Aphasiology, 14*(9), 911–924.

Worrall, L., McCooey, R., Davidson, B., Larkins, B., & Hickson, L. (2002). The validity of functional assessments of communication and the activity/participation components of the ICIDH-2: Do they reflect what really happens in real-life? *Journal of Communication Disorders, 35*(2), 107–137.

Americans with Disabilities Act of 1990

Robert L. Heilbronner
Chicago Neuropsychology Group
Chicago, IL, USA

Historical Background

The Americans with Disabilities Act (ADA) was signed by President George Bush in 1990 and went into effect in 1992. It is regarded by many as the most sweeping civil rights legislation since the Civil Rights Act of 1964, with its intent to assist people with disabilities to obtain jobs and achieve the goal of full functioning in the workplace. The ADA contains provisions that outlaw discrimination against people with disabilities (including those with learning disabilities and mental disorders) in hiring, training, compensation, and benefits (Bell, 1997) and mandates that employers provide "reasonable accommodations" for disabled workers who could qualify for jobs if such assistance is provided. It also protects individuals against retaliation for filing charges or otherwise being involved in an Equal Employment Opportunity Commission (EEOC)-related action. The act requires that people with disabilities be treated like nondisabled persons, unless it is determined that a certain individual's disability produces significant hindrances to one's involvement in a particular endeavor. It was established due to Congress's recognition of a large number of Americans with one or more disabilities and the discrimination experienced by such individuals with respect to employment and access to services.

Current Knowledge

The ADA includes several sections that cover different types of activities, most notably, employment (Title I), public services (Title II), public accommodations and services operated by private entities (Title III), access to telecommunications (Title IV), and miscellaneous provisions (Title V). Psychologists often conduct evaluations of disabled individuals to determine "reasonable accommodations" in accordance with the ADA. The most common referral involves Title 1, employment issues. The ADA requires that an evaluator assesses four distinct areas: (a) disability, (b) qualifications to perform an essential function of the job, (c) reasonable accommodations, and (d) threats to others. The "reasonable accommodations" are typically broken down by short-term accommodations as well as long-term accommodations.

References and Readings

Americans with Disabilities Act of 1990, 42 U.S.C. 12101–12213 et seq.

Bell, C. (1997). The Americans with disabilities act, mental disability and work. In R. Bonnie, & J. Monahan (Eds.), *Mental disorder, mental disability and the law.* Chicago: University of Chicago Press.

Foote, W. M. (2003). Forensic evaluation in Americans with disabilities act cases. In A. Goldstein (Ed.), *Handbook of psychology (Vol. 11). Forensic psychology.* New Jersey: Wiley.

Melton, G. B., Petrila, J., Poythress, N. G., & Slobogin, C. (1997). *Psychological evaluations for the courts: A handbook for mental health professionals and lawyers.* New York: Guilford.

More detailed information regarding the Americans with Disabilities Act of 1990 can be found at www.ada.gov

Amitriptyline

John C. Courtney
Children's Hospital of New Orleans
New Orleans, LA, USA

Generic Name

Amitriptyline

Brand Name

Elavil

Class

Tricyclic Antidepressant

Proposed Mechanism(s) of Action

Increases available norepinephrine and serotonin, blocks serotonin reuptake and may desensitize both serotonins 1A and beta adrenergic receptors.

Indication

Depression

Off Label Use

Neuropathic pain, fibromyalgia, headache, and insomnia

Side Effects

Serious

Paralytic ileus, hyperthermia, lowered seizure threshold, sudden death, cardiac arrhythmias, tachycardia, QTc prolongation, hepatic failure, mania, potential for activation of suicidal ideation

Common

Blurred vision, constipation, urinary retention, increased appetite, dry mouth, diarrhea, heartburn, weight gain, fatigue, weakness, dizziness, anxiety, sexual dysfunction, sweating, rash, and itching

References and Readings

Physicians' Desk Reference (62nd ed.). (2007). Montvale, NJ: Thomson PDR.

Stahl, S. M. (2007). *Essential psychopharmacology: The prescriber's guide* (2nd ed.). New York, NY: Cambridge University Press.

Additional Information

Drug Interaction Effects: http://www.drugs.com/drug_interactions.html
Drug Molecule Images: http://www.worldofmolecules.com/drugs/
Free Drug Online and PDA Software: www.epocrates.com
Gene-Based Estimate of Drug interactions: http://mhc.daytondcs.com:8080/cgi bin/ddiD4?ver=4&task=getDrugList
Pill Identification: http://www.drugs.com/pill_identification.html

AML

► Acute Myelogenous Leukemia

Amnesia

Ginette Lafleche
Memory Disorders Research Center, Boston University School of Medicine and VA Boston Healthcare System
Boston, MA, USA

Definition

Amnesia refers to the loss of ability to recall facts, events, or concepts encountered prior to the onset of illness (retrograde amnesia) or to the loss of ability to form new memories (anterograde amnesia), or both. Although anterograde and retrograde amnesia can occur in isolation, they most often appear together following a single cause. That cause is most frequently a neurologic insult or illness, but can also be psychogenic. In most cases, the memory loss is permanent, but it can be temporary, as for example, in transient global amnesia.

Cross References

► Anterograde Amnesia
► Memory Impairment
► Retrograde Amnesia
► Transient Global Amnesia

References and Readings

Baddeley, A. D., Kopelman, M. D., & Wilson, A. W. (2002). *The handbook of memory disorders.* Chichester, UK: Wiley.

Amnestic Disorder

Beth Springate
University of Connecticut
Storrs, CT, USA

Synonyms

Global amnesia

Short Description or Definition

Amnestic disorders are defined by a global loss in explicit memory that is persistent and stable. The hallmark feature of this disorder is extreme anterograde amnesia (impairment in the ability to form new explicit memories) in the absence of any other extensive cognitive losses. Individuals with amnestic disorders may display an impairment in memory which is not lasting (e.g., transient global amnesia), progressive (e.g., Alzheimer's disease), or occurs in combination with declines in other cognitive domains.

Categorization

Amnestic disorders can result from a variety of causes, including hypoxic/anoxic events, infections (e.g., herpes simplex encephalitis), and lesions such as those that occur following stroke or surgical ablation, and are associated with damage to several brain regions. Two subtypes of amnestic disorders have received the most attention: bitemporal amnesia and diencephalic amnesia (e.g., Korsakoff's syndrome and patients with discrete thalamic or mammillary body lesions). A third subtype, basal forebrain amnesia, is viewed as clinically distinctive and has been studied to a lesser degree (Bauer, Grande, and Valenstein, 2003).

Epidemiology

Amnestic disorders can be observed in several classes of patients including following viral infections (e.g., herpes encephalitis), anoxic/hypoxic events (e.g., after heart attack or near-drowning), Korsakoff's syndrome, bilateral temporal lobectomies, and cerebrovascular events. However, global amnestic syndromes themselves are relatively rare. For example, herpes simplex encephalitis carries a 70% mortality rate without treatment. The cognitive impairments in survivors are ranging, and in one study of long-term survivors 19 of 22 participants experienced some form of memory impairment although only five subjects had memory difficulties that were categorized as severe (Utley et al., 1997). In a review of studies of cerebral anoxia, Caine and Watson (2000) conclude that while 54% of case studies describe memory impairments, only 19% report memory deficits in isolation.

Natural History, Prognostic Factors, and Outcomes

The amnestic disorder is exemplified by the case study of H.M. H.M. had intractable epilepsy that was treated with a radical, experimental surgery in which his medial temporal lobes were removed bilaterally. His resection included the hippocampal formation and adjacent structures including most of the amygdala and parahippocampal gyrus, including the entorhinal cortex. Following surgery, H.M. developed severe anterograde amnesia which manifested as deficient episodic and semantic memory. In addition, he developed partial retrograde amnesia for events within 19 months before his surgery. However, earlier memories were unaffected, and his working memory and procedural memory (skill learning) also remained intact (Corkin, 2002; Scoville & Milner, 1957).

Course: Onset is often acute due to the nature of the pathological processes that cause amnestic disorders (e.g., cerebrovascular events, anoxic/hypoxic events, surgical ablation, and infections such as herpes encephalitis). As amnestic disorders are caused by the destruction of brain structures, deficits are persisting and stable without expectation of improvement or further decline barring any additional injury.

General neuropsychological profile: Patients exhibit deficits in explicit memory marked by significant anterograde amnesia. They may also exhibit retrograde amnesia (disruption in the ability to recall previously learned information), although this is typically less severe and exhibits a temporal gradient with older memories less likely to be disturbed. Attention, working memory, procedural memory, implicit learning, and general cognition remain largely intact.

Amnestic disorders resulting from bitemporal or diencephalic insults are the most frequently studied and similar in their neuropsychological profiles. Although early studies suggested that individuals with bitemporal amnesias have a more rapid forgetting rate, McKee and Squire (1992) found equivalent forgetting curves for pictures when severity of amnesia was controlled. Both subtypes of amnesia display a degree of retrograde amnesia (Kopelman, Stanhope, & Kingsley, 1999). Bauer, Grande, and Valenstein (2003) argue that despite these similarities, some deficits are unique to patients with diencephalic amnestic disorders; although some studies suggest patients with Korsakoff's syndrome display a unique deficit in memory for temporal order (e.g., Squire, 1982; Kopelman et al., 1999), others fail to support this finding (Downes et al., 2002).

Basal forebrain amnesia typically results from vascular lesions or aneurysm surgery in the region of the anterior communicating artery. After basal forebrain damage, patients may demonstrate extensive anterograde amnesia (Bottger et al., 1998; Tidswell et al., 1995). Confabulation is common and may relate to the extent of orbitofrontal involvement (Hashimoto, Tanaka, & Nakano, 2000), but it often subsides following the acute phase while the amnestic state remains. There is evidence that patients with basal forebrain amnesia benefit from the presentation of cues to enhance recall (Osimani et al., 2006).

Evaluation

As amnestic disorders are defined by deficits in new learning, memory is the cognitive domain that should be emphasized within a neuropsychological evaluation that also includes assessment of other areas of cognitive function such as orientation, attention, language, executive functions, visuospatial skills, and psychological functioning. Patients fitting the classic amnestic disorder profile will exhibit deficits in memory with generally intact cognition within other domains.

It is important to establish the specific nature of patients' memory impairments. Immediate memory span (typically assessed through tests such as Digit and Spatial Span from the Wechsler Memory Scales) should be within the normal range. Anterograde learning may be assessed with measures such as list learning, story learning, or figure memory. While patients will be able to retain items and repeat them back as long as they can keep them in memory, learning curves are typically flat, and an intervening distractor task will cause items to be lost completely. The use of cues or yes/no recognition format, which typically facilitates memory in most individuals, will not aid recall in these patients. Explicit anterograde learning will be equally impaired regardless of the type of memory test (free recall, cued recall, and recognition), stimulus material (e.g., words, pictures, and sounds), and sensory modality through which information is acquired (e.g., visual, auditory, and somatosensory).

In addition, retrograde amnesia and memory for remote events can be examined in a qualitative manner by inquiring about autobiographical events as well as memories that one can assume to be present in most people from a given society such as pictures of famous individuals. The aspects of memory that remain intact in classic amnestic disorder patients (such as semantic memory and motor skill learning) should also be assessed.

The main differential diagnoses to consider include delirium and dementia. Delirium is defined by a disturbance in attention and consciousness, both of which are intact in amnestic disorders. Although dementias present similarly to amnestic disorders in that patients often present with memory impairments, cognitive decline (rather than stability) occurs and impairments in other cognitive domains such as language or executive functions are present.

Treatment

Treatment of amnestic disorders is nonspecific and focused primarily on management of symptoms. Cognitive rehabilitation and memory training programs, which emphasize the teaching of mnemonic strategies or the use of external memory aids such as note-taking or audiotaping in order to enhance patients' functioning in daily life, have been used to improve memory in individuals with dementia and other disorders. Theoretically, these programs would be useful for individuals with amnestic disorders. However, without the ability for patients to consciously recall they have learned these strategies and remember to implement them, these programs are likely of little value for patients with amnestic disorders.

The use of pharmacologic agents to treat amnestic disorders is not well studied, and large randomized controlled trials are lacking. In an open-label pilot study, Benke et al. (2005) administered donepezil, a cholinesterase inhibitor, to patients with a chronic amnestic syndrome from a ruptured and repaired aneurysm of the anterior communicating artery, anterior cerebral, or pericallosal artery. Some measures of performance on a list-learning task improved significantly during the 12-week medication administration period, suggesting future double-blinded controlled studies would be useful to more thoroughly examine the potential utility of cholinergic medications.

In addition, due to their memory impairment, patients are likely to experience impairments in their social and vocational activities and may also require supervised living situations and a guardian for legal and medical concerns.

Cross References

- ► Amnesia
- ► Amnestic Syndrome
- ► Dissociative Amnesia
- ► Korsakoff's Syndrome
- ► Temporal Lobectomy

References and Readings

Bauer, R. M., Grande, L., & Valenstein, E. (2003). Amnesic disorders. In K. M. Heilman, & E. Valenstein (Eds.), *Clinical neuropsychology* (pp. 495–573). New York: Oxford University Press.

Benke, T., Köylü, B., Delazer, M., Trinka, E., & Kemmler, G., (2005). Cholinergic treatment of amnesia following basal forebrain lesion due to aneurysm rupture – an open-label pilot study. *European Journal of Neurology, 12*, 791–796.

Bottger, S., Prosiegel, M., Steiger, H., & Yassouridis, A. (1998). Neurobehavioral disturbances, rehabilitation outcome, and lesion site in patients after rupture and repair of anterior communicating artery aneurysm. *Journal of Neurology, Neurosurgery, and Psychiatry, 65*, 93–102.

Caine, D., & Watson, J. D. G. (2000). Neuropsychological and neuropathological sequelae of cerebral anoxia: a critical review. *Journal of the International Neuropsychological Society, 6*, 86–99.

Corkin, S. (2002). What's new with the amnesic patient H.M.? *Nature Reviews: Neuroscience, 3*, 153–160.

Downes, J. J., Mayes, A. R., MacDonald, C., & Hunkin, N. M. (2002). Temporal order memory in patients with Korsakoff's syndrome and medial temporal amnesia. *Neuropsychologia, 40*, 853–861.

Hashimoto, R., Tanaka, Y., & Nakano, I. (2000). Amnesic confabulatory syndrome after focal basal forebrain damage. *Neurology, 54*, 978–980.

Kopelman, M. D., Stanhope, N., & Kingsley, D. (1999). Retrograde amnesia in patients with diencephalic, temporal lobe or frontal lesions. *Neuropsychologia, 37*, 939–958.

McKee, R. D., & Squire, L. R. (1992). Both hippocampal and diencephalic amnesia result in normal forgetting for complex visual material. *Journal of Clinical and Experimental Neuropsychology, 14*, 103.

Osimani, A., Vakil, E., Blinder, G., Sobel, R., & Abarbanel, J. M. (2006). Basal forebrain amnesia: a case study. *Cognitive and Behavioral Neurology, 19*, 65–70.

Scoville, W. B., & Milner, B. (1957). Loss of recent memory after bilateral hippocampal lesions. *Journal of Neurology, Neurosurgery, and Psychiatry, 20*, 11–21.

Squire, L. R. (1982). Comparisons between forms of amnesia: some deficits are unique to Korsakoff's syndrome. *Journal of Experimental Psychology: Learning, Memory, and Cogntion, 8*, 560–571.

Tidswell, P., Dias, P. S., Sagar, H. J., Mayes, A. R., & Battersby, R. D. E. (1995). Cognitive outcome after aneurysm rupture: relationship to aneurysm site and perioperative complications. *Neurology, 45*, 875–882.

Utley, T. F. M., Ogden, J. A., Gibb, A., McGrath, N., & Anderson, N. E. (1997). The long-term neuropsychological outcome of herpes simplex encephalitis in a series of unselected survivors. *Neuropsychiatry, Neuropsychology, and Behavioral Neurology, 10*, 180–189.

Amnestic Syndromes

Ginette Lafleche, Mieke Verfaellie
VA Boston Healthcare System and Boston University School of Medicine
Boston, MA, USA

Short Description or Definition

The amnesic syndromes are a collection of neurological disorders characterized by a dense global amnesia that includes both anterograde and retrograde components (► Anterograde Amnesia and Retrograde Amnesia).

Categorization

The amnesic syndromes can be classified according to cause or site of damage. Etiologically, they are caused by cerebrovascular disease, herpes simplex encephalitis, Wernicke–Korsakoff syndrome, anoxia, anterior communicating artery aneurysm (ACoA), and tumors. Neuropathologically, amnesia can arise from damage to the medial temporal lobes, the midline diencephalic nuclei, the basal forebrain, or from disruption of some of their interconnections such as the fornix. Most amnesic syndromes are chronic, and are due to structural damage to critical brain structures, but amnesia can also be transient, due to functional disruption of these brain structures (see Transient Global Amnesia).

Neuropsychology of the Amnesic Syndromes

Herpes Simplex Encephalitis (HSE)

HSE is a viral infection of the brain that begins as a flu-like illness with headaches and fever, followed by lethargy, confusion, and disorientation. If left untreated, amnesia, agnosia, and aphasia can develop. Patients who do not undergo a complete recovery can suffer a broad range of cognitive deficits that persist, but some are left with only an isolated amnesic syndrome. Their Presentation is similar to that of HM who became unable to form new memories after undergoing a neurosurgical operation in which a large portion of the medical temporal region of his brain was removed bilaterally.

Neuropathologically, the virus preferentially infects limbic regions in the temporal lobe including the

hippocampus and adjacent entorhinal, perirhinal and parahippocampal cortices, as well as the amygdala and polar limbic cortices. Damage often extends to the lateral aspect of the temporal lobe, damaging the anterolateral aspect, the inferior aspect, or both. Anterior extension of damage into ventromedial areas such as the insular cortex and the basal forebrain has also been documented. The severity of memory impairment following HSE shows substantial variation that is directly proportional to the extent of medial temporal lobe damage (Stefanacci, Buffalo, Schmolck, & Squire, 2000). Lesions are often asymmetrical, and this will define the clinical presentation. If damage to the left temporal region is greater, verbal memory problems dominate, whereas if right temporal damage is greater, nonverbal aspects of memory are predominantly impaired, such as memory for faces and designs. Patients whose lesions extend into lateral temporal regions may also suffer from a severe retrograde amnesia that is thought to be due to damage to convergence zones in anterior temporal areas. Damage primarily to right anterior temporal regions is more likely to result in a loss of personal episodic memories (O'Connor, Butters, Miliotis, Eslinger, & Cermak, 1992), and that to the left temporal cortex is associated with loss of semantic knowledge (DeRenzi, Liotti, & Nichelli, 1987). Cases with unusual category-specific semantic impairments have also been described, such as differential loss of knowledge of concrete versus abstract concepts or animate versus inanimate concepts.

Anoxia

Anoxic brain injury can result from any of a number of diverse etiologies including cardiac arrest, respiratory distress, carbon monoxide poisoning, or drug overdose. These clinical conditions all diminish or cut off the supply of oxygen to the brain, either through reduced blood flow or reduced blood oxygen saturation. The physiological consequences of such anoxic events are complex. Brain areas particularly vulnerable to anoxic injury include the hippocampus, basal ganglia, and watershed areas of the cerebral cortex. The clinical manifestations of anoxia are highly variable, but memory impairment is a common manifestation. A review of 58 studies of cerebral anoxia showed that while damage to hippocampal structures was common, damage restricted to the hippocampus was seen in only 18% of patients (Caine & Watson, 2000). Accordingly, in a majority of patients, memory impairment occurs in the context of generalized cognitive impairment. Significant changes in executive abilities and motor functioning are particularly common (Lim et al., 2004). In a minority of patients, anoxic injury leads to isolated amnesia.

Relatively selective developmental amnesia has been documented in children and adolescents who experienced an anoxic event shortly after birth. Gadian et al. (2000) reported on five cases, all of whom had selective bilateral hippocampal atrophy. Neuropsychological results revealed that all of the children performed poorly on tasks of episodic memory, but attention, reasoning abilities, and visuospatial skills were intact. Strikingly, these children were able to acquire a considerable amount of new semantic knowledge, as indicated by the fact that they were successfully able to attend mainstream schools. The relative preservation of semantic learning in these children has been ascribed to the integrity of subhippocampal cortical areas, including entorhinal and perirhinal cortices.

Wernicke–Korsakoff Syndrome

► Wernicke–Korsakoff Syndrome.

Cerebrovascular Accidents

Bilateral posterior cerebral artery (PCA) infarction is a well-recognized cause of amnesia. Because the left and right PCA arise from the bifurcation of a common source, strokes that occur upstream from the bifurcation can affect the medial temporal lobes bilaterally, causing a dense global amnesia. Neuroanatomical studies of patients with PCA infarction have revealed that lesions in the posterior parahippocampus or the collateral isthmus (a pathway connecting the posterior parahippocampus to association cortex) are critical for the memory impairment (Von Cramon, Hebel, & Schuri, 1988). When damage extends posteriorly to include occipitotemporal cortices, deficits beyond amnesia are often seen.

Early in their clinical course, patients with PCA infarction exhibit a global confusion that eventually resolves into an isolated amnestic syndrome or may be associated with additional neuropsychological deficits, such as visual field defects, alexia, color agnosia, or anomia. The memory disturbance is characterized by a classic profile of consolidation deficits in the context of normal working memory and normal intelligence. There may or may not be associated retrograde amnesia. Memory problems have also been described with unilateral, usually left, PCA infarction. In such cases, the memory impairment can be transient or permanent, and is typically limited to verbal material. Memory deficits in patients with right

PCA have been less well studied, but such examination is complicated by the perceptual problems that frequently accompany right PCA infarction.

Thalamic strokes can also lead to significant memory loss. Because the relevant thalamic centers are small and adjacent to one another, it is difficult to establish associations between site of damage and clinical deficits. A recent review (Van der Werf et al., 2000) suggests that damage to the mammillo-thalamic tract (MTT) invariably causes anterograde amnesia, and that no amnesia occurs in the absence of damage to the MTT. Medial dorsal lesions cause a memory disturbance that is mild in comparison to the severe amnesia that arises when the lesion extends to the MTT. Patients with thalamic amnesia exhibit executive dysfunction, increased sensitivity to interference, and variability in the persistence and extent of retrograde amnesia.

ACoA Aneurysm

Rupture of ACoA can result in a memory disorder that ranges from mild to severe. The ACoA provides blood supply to the basal forebrain, the anterior cingulate, the anterior hypothalamus, the anterior columns of the fornix, the anterior commissure, and the genu of the corpus callosum. The pathological consequences of a ruptured aneurysm may be a result of infarction directly, or secondary to subarachnoid hemorrhage, vasospasm, and hematoma formation. Because of the various neuropathological consequences, the clinical profiles associated with ACoA aneurysm are more variable than those seen with diencephalic or medial temporal lobe injuries, and the impairments are often more global in nature (DeLuca & Diamond, 1995).

The acute phase of recovery following rupture and repair of ACoA aneurysm is characterized by a severe confusional state and a marked attentional disorder. As the confusion resolves, memory problems become more apparent. These can vary from mild impairments to severe amnesia. A temporally graded retrograde amnesia is also frequently present. Other symptoms, including executive dysfunction, confabulation, and poor insight, are likely to be part of the resulting clinical syndrome if the lesion extends to the medial frontal lobes. The clinical outcome of patients with more extensive lesions is typically worse than that of patients with lesions limited to the basal forebrain.

The amnesia associated with ACoA aneurysm has a marked frontal dysexecutive component. Performance on recognition tests is often better preserved than on recall tests, particularly following a delay. This reflects a disruption of strategic retrieval processes that allow access to information stored in memory. Deficient strategic memory processes also contribute to poor encoding, and the use of organizational strategies at encoding can enhance patients' performance. A failure to adequately monitor the outcome of memory search can also occur, and this manifests as a tendency toward high level of false alarms in recognition tests. In extreme cases, this can lead to impairment in recognition memory that exceeds that seen in recall. Other features linked to frontal dysfunction include impaired source memory and temporal tagging.

Evaluation

Although a primary focus of the assessment in amnesia is on memory function, it is important to assess other cognitive domains as well, including general intelligence, attention, executive functions, language, semantic knowledge, and visuospatial skills. Such a comprehensive approach is required to distinguish whether a patient presents with a pure amnesic syndrome or with memory impairment in the context of more pervasive cognitive difficulty. New learning abilities should be assessed by measures of free recall, cued recall, and recognition, and should examine both immediate and delayed retention. Information derived from specific aspects of performance, such as the shape of the learning curve, comparison of recall and recognition performance, and effects of delay, all provide important pointers to the nature of the memory breakdown (e.g. inefficiencies in encoding, retrieval, or consolidation) and may inform remediation.

A variety of standardized tests are available to assess memory function, and the reader is referred to Lezak, Howieson, & Loring, 2004, for specific examples. The most commonly used standardized memory test is the Wechsler Memory Scale-III or IV, which consists of a series of subtests that probe various aspects of verbal and nonverbal memory in different formats. Assessment of remote memory should cover knowledge of public events and people, personal facts, and autobiographical events. Such assessment can be challenging, because there are few standardized measures available, and corroboration from a caregiver may be needed to establish the accuracy of reported personal memories. With respect to general fund of knowledge, areas of assessment include knowledge of famous names and faces, public news events, and new vocabulary that has recently entered the language. Several structured interviews have been developed to examine recollection of personal events and facts.

Treatment

There is no pharmacological or cognitive treatment that can restore memory in amnesia. However, cognitive rehabilitation approaches have been developed that aim at fostering routines and habits that will increase independence, productivity, and quality of life. The choice of rehabilitation approach should be informed by both cognitive and psychosocial/emotional factors. Cognitive factors include premorbid skills and abilities and current neuropsychological functioning. A clear delineation of impaired and preserved aspects of memory is critical to guide rehabilitation efforts, as is identification of other areas of cognitive impairment that might hamper therapeutic efforts. Of the psychosocial/emotional factors, insight and motivation are perhaps the two most influential predictors of rehabilitation success. Patients need to have some awareness of their deficits and have some degree of internal drive to understand the value of, and engage in, the rehabilitation process.

Several treatment approaches take advantage of preserved nondeclarative memory abilities to teach patients new information or skills. One approach that capitalizes on preserved implicit perceptual memory is the vanishing cues technique. Patients are guided to provide the correct information in response to perceptual cues, through the use of implicit memory. Once successful, cues are gradually reduced, eventually leading to the spontaneous generation of the to-be-learned information. This technique has proven successful for learning new vocabulary and concepts. Important caveats, however, are that such learning is a slow and laborious process, and the information learned is typically inflexible and only accessible in the exact form it was learned. An important consideration in the use of implicit memory techniques is the avoidance of errors, as patients have no recollection of their mistakes and consequently, errors, just like correct responses, can be primed. Other methods capitalize on preserved procedural learning and use repetition to teach skills and habits that support activities of daily living. Examples of external compensatory aids that rely on procedural memory are the use of notebooks, diaries, and alarm clocks. Electronic devices such as computers, smartphones, and paging systems have great flexibility as compensatory aids, but training in the use of such technology requires very lengthy practice sessions, and transfer of learning outside the training sessions can be difficult. It is therefore most appropriate for individuals who have premorbid experience with such devices and are highly motivated to use them.

For individuals with milder memory impairments, it may also be possible to directly focus on enhancing impaired forms of memory through the use of internal strategies. The choice of strategy will be dependent on the nature of the memory process that appears defective. Examples of such techniques include enhanced organization of the to-be-learned information through chunking or categorizing, and elaboration of the material, whether through verbal associations or the creation of visual images. Such strategies fall under the category of internal memory aids.

There are no specific methods of treatment available to restore memories from the past. Information and pictures of emotionally neutral facts about one's life can be reintroduced and incorporated in the selected treatment approach. However, emotionally laden facts, such as the death of a family member, can trigger repeated emotional responses that can interfere with adjustment and are best avoided in the early stage of treatment. By nature, relearned personal experiences about one's life will be recalled without the emotional texture of the original event; however, they can play an important role in helping patients fill in the narrative of their own life.

Cross References

- ▶ Anterograde Amnesia
- ▶ Retrograde Amnesia
- ▶ Transient Global Amnesia

References and Readings

Baddeley, A. D., Kopelman, M. D., & Wilson, A. W. (2002). *The handbook of memory disorders.* Chichester, UK: Wiley.

Caine, D., & Watson, J. D. G. (2000). Neurospsychological and neuropathological sequelae of cerebral anoxia: A critical review. *Journal of the International Neuropsychological Society, 6*, 86–99.

DeLuca, J., & Diamond, B. J. (1995). Aneurysm of the anterior communicating artery: A review of neuroanatomical and neuropsychological sequelae. *Journal of Clinical and Experimental Neuropsychology, 17*, 100–121.

DeRenzi, E., Liotti, M., & Nichelli, P. (1987). Semantic amnesia with preservation of autobiographical memory: A case report. *Cortex, 23*, 578–597.

Gadian, D. G., Aiardi J., Watkins, K. E., Porter, D. A., Mishkin, M., & Vargha-Khadem, F. (2000). Developmental amnesia associated with early hypoxic-ischaemic injury. *Brain, 123*, 499–507.

Lezak, M. D., Howieson, D. B., & Loring, D. W. (2004). *Neuropsychological assessment.* New York: Oxford University Press.

O'Connor, M. G., Butters, N., Miliotis, P., Eslinger, P., & Cermak, L. S. (1992). The dissociation of anterograde and retrograde amnesia in a patient with herpes simplex encephalitis. *Journal of Clinical and Experimental Neuropsychology, 14*, 159–178.

Stefanacci, L., Buffalo, E. A., Schmolck, H., & Squire, L. R. (2000). Profound amnesia after damage to the medial temporal lobe: A

neuroanatomical and neuropsychological profile of patient E. P. *The Journal of Neuroscience, 20*, 7024–7036.
Van der Werf, Y. D., Witter, M. P., Uylings, H. B., & Jolles, J. (2000). Neuropsychology of infarctions in the thalamus: A review. *Neuropsychologia, 38*, 613–627.
Von Cramon, D., Hebel, N., & Schuri, U. (1988). Verbal memory and learning in unilateral posterior cerebral infarction, *Brain, 111*, 1061–1077.

Amnion Rupture

► Anencephaly

Amorphognosis

John E. Mendoza
Tulane University Medical Center
New Orleans, LA, USA

Definition

Amorphognosis is that aspect of tactile agnosia which refers specifically to deficits in the ability to appreciate (identify) the external form of an object such as its shape, size, or other contour features by tactual manipulation alone. In the absence of more elementary somatosensory disturbances resulting from either peripheral nerve or the dorsal column system, such deficits suggest lesions in the contralateral postcentral gyrus of the parietal lobe or in its adjacent association cortices.

Cross References

► Ahylognosia
► Astereognosis
► Tactile Agnosia

References and Readings

Bauer, R. M., & Demery, J. A. (2003). Agnosia. In K. Heilman & E. Valenstein (Eds.), *Clinical neuropsychology* (4th ed., pp. 236–295). New York: Oxford University Press.
Hecaen, H., & Albert, M. L. (1978). Chapter 6. Disorders of somesthesis and somatognosis. In *Human neuropsychology*. New York: Wiley.

Amorphosynthesis

► Hemiinattention
► Neglect
► Neglect Syndrome
► Visual Neglect

Amotivational

► Apathy

Amoxapine

John C. Courtney
Children's Hospital of New Orleans
New Orleans, LA, USA

Generic Name

Amoxapine

Brand Name

Ascendin

Class

Tetracyclic antidepressant

Proposed Mechanism(s) of Action

Amoxapine inhibits reuptake of norepinephrine and noradrenaline. It is also known to antagonize Serotonin 2A receptors, thus increasing presynaptic release of amines. Mild Dopamine 2 blockade.

Indication

Reactive depressive disorder, psychotic depression, and depression accompanied by anxiety or agitation.

Off Label Use

Depressive phase of a bipolar disorder, anxiety, insomnia, neuropathic pain, and treatment resistant depression.

Side Effects

Serious

Paralytic ileus, hyperthermia, lowered seizure threshold, sudden death, cardiac arrhythmias, tachycardia, QTc prolongation, hepatic failure, intraocular pressure, mania, and potential for activation of suicidal ideation.

Common

Blurred vision, constipation, urinary retention, increased appetite, dry mouth, diarrhea, heartburn, weight gain, fatigue, weakness, dizziness, anxiety, sexual dysfunction, sweating, rash, and itching. Can cause extrapyramidal symptoms such as akathisia and potentially tardive dyskinesia.

References and Readings

Physicians' Desk Reference (62nd ed.). (2007). Montvale, NJ: Thomson PDR.

Stahl, S. M. (2007). *Essential psychopharmacology: The prescriber's guide* (2nd ed.). New York, NY: Cambridge University Press.

Additional Information

Drug Interaction Effects: http://www.drugs.com/drug_interactions.html
Drug Molecule Images: http://www.worldofmolecules.com/drugs/
Free Drug Online and PDA Software: www.epocrates.com
Gene-Based Estimate of Drug interactions: http://mhc.daytondcs.com:8080/cgi bin/ddiD4?ver=4&task=getDrugList
Pill Identification: http://www.drugs.com/pill_identification.html

Amphetamine

JoAnn T. Tschanz[1], Katherine Treiber[1,2]
[1]Utah State University
Logan, UT, USA
[2]University of Massachusetts Medical School
Worcester, MA, USA

Synonyms

D-Amphetamine; Dextroamphetamine; Dexedrine

Definition

Amphetamine refers to a group of synthetic chemicals with psychoactive stimulant effects. There are two forms, dextro-amphetamine (D-amphetamine) and levo-amphetamine (L-amphetamine), of which D-amphetamine is the more biologically active. Chemical modifications to the basic structure have produced derivatives with even more potent psychoactive properties. For example, addition of a second methyl group to the chemical structure creates methamphetamine, a highly addictive drug. Modification of the benzene ring of the amphetamine structure creates methylenedioxy-methamphetamine (MDMA) or Ecstasy, another drug with high addiction and abuse potential (Iversen, Iversen, Bloom, & Roth, 2009).

The behavioral effects of amphetamine include increased alertness, confidence, and euphoria. The drug also reduces fatigue and enhances performance on cognitive tasks, possibly by increasing attention and working memory. However, cognitive enhancement is not a universal effect. Reportedly, working memory is enhanced only among those with poor ability and may be detrimental to those with high ability (Iversen et al., 2009). In animals, there is a dose-dependent effect of increasing activity such as locomotion and at higher doses, stereotyped motor behaviors. The reinforcing properties of amphetamine have been demonstrated in operant conditioning studies. The drug also increases systolic and diastolic blood pressure, respiration, and heart rate, among its other autonomic nervous system effects (Feldman, Meyer, & Quenzer, 1997). Amphetamine or its derivatives have been used for clinical purposes (see History). However, its clinical use has been limited due to its abuse potential and dangerous autonomic effects (Iversen et al., 2009).

The biological mechanism underlying the psychoactive effects of amphetamine is believed to occur by

enhancing the release and blocking the reuptake of the monoamine neurotransmitters dopamine, norepinephrine, and serotonin (Feldman et al., 1997; Iversen et al., 2009). At high doses, the drug also inhibits the metabolism of catecholamines by the enzyme monoamine oxidase. Chronic use of amphetamine has been associated with damage to selective dopamine and serotonin neurons and receptors (Feldman et al., 1997; Gouzoulis-Mayfrank & Daumann, 2009). Methamphetamine is also a potent neurotoxin, although its toxic effects predominantly involve the serotonergic system (Feldman et al., 1997; Gouzoulis-Mayfrank & Daumann, 2009). The reinforcing properties of amphetamine are hypothesized to reflect increased dopamine neurotransmission in the subcortical structure, the nucleus accumbens.

Historical Background and Clinical Relevance

First introduced and marketed as a nasal or bronchial decongestant in the 1930s, amphetamine was sought for its psychoactive effects and as an appetite suppressant. It was used in the military to enhance attention and counteract the effects of sleep deprivation (Iversen et al., 2009; Meyer & Quenzer, 2005). Amphetamine and its derivatives have also been used for the treatment of narcolepsy, attentional problems, and as a stimulant in the general population (Meyer & Quenzer, 2005).

Over time, the addictive properties of amphetamine were realized, particularly of its potent derivatives. The acute effects of amphetamine-based drugs are enhanced by use of a rapid route of administration such as intravenous injection. Following a short-term "rush" however, a period of restless agitation, depression, irritability, and other negative symptoms ensues. Repeated, continuous administrations are followed by a let down, with a prolonged period of sleep. This alternating cycle, when repeated, results in a substantial physical toll on the body. As with other drugs of abuse, dependence and tolerance can develop with chronic use, leading to the administration of increasing doses to achieve the desired effects. With sustained chronic use, negative effects may emerge. These include repetitive, stereotyped behaviors as well as a psychotic syndrome consisting of hallucinations and paranoid delusions. This syndrome, known as "amphetamine psychosis" is notably similar to the symptoms of paranoid schizophrenia and has provided some support for the dopamine hypothesis of schizophrenia. However, qualitative differences between the two conditions also exist (e.g., greater tendency for visual hallucinations to occur in amphetamine psychosis vs. schizophrenia; Iversen et al., 2009). As reported above, other negative effects of chronic amphetamine abuse include neurotoxic damage to neurotransmitter systems. Impairments in attention and memory have also been reported which may persist even after a period of prolonged abstinence (Gouzoulis-Mayfrank & Daumann, 2009; Iversen et al., 2009).

Future Directions

Research into the psychoactive and behavioral effects of amphetamine has helped advance knowledge of the psychological role of several monoamine neurotransmitters and their relevance to clinical conditions such as addiction and schizophrenia and the neurochemistry underlying some cognitive processes such as attention and working memory. Future research will undoubtedly utilize advances in technology to elucidate the neural structures and pathways associated with reward circuits involved in addictions, examine the neuroplasticity of the nervous system after chronic abuse, and clarify the moderating role of genetics in the behavioral response to amphetamine and other compounds (Iversen et al., 2009).

Cross References

► D-Amphetamine
► Dopamine

References and Readings

Feldman, R. S., Meyer, J. S., & Quenzer, L. F. (1997). Stimulants: Amphetamine and cocaine. In *Principles of neuropsychopharmacology* (pp. 549–568). Sunderland, MA: Sinauer Associates.

Gouzoulis-Mayfrank, E., & Daumann, J. (2009). Neurotoxicity of drugs of abuse-the case of methylenedioxyamphetamines (MDMA, ecstasy), and amphetamines. *Dialogues in clinical Neuroscience, 11*, 305–317.

Iversen, L. L., Iversen, S. D., Bloom, F. E., & Roth, R. H. (2009). Psychostimulants. In *Introduction to neuropsychopharmacology* (pp. 447–472). New York: Oxford University Press.

Meyer, J. S., & Quenzer, L. F. (2005). Psychomotor stimulants: Cocaine and the amphetamines. In *Psychopharmacology: Drugs, the brain and behavior* (pp. 292–300). Sunderland, MA: Sinauer Associates.

AMPS

► Assessment of Motor Process Skills

Amusia

John E. Mendoza
Tulane University Medical Center
New Orleans, LA, USA

Current Knowledge

"Music" involves both complex qualities such as familiar melodies, rhythm, or tempo, and more elementary aspects such as discrimination of timbre, pitch, or tone. While lesions of the temporal lobes are fairly consistently implicated, the hemispheric localization of lesions responsible for specific deficits has been more controversial. Music, like language, is composed of individual, temporally sequenced stimuli (musical notes, melodies, tunes), each capable of being analyzed with regard to particular features such as pitch and timbre, functions that would appear to be more in keeping with the suspected operations of the left hemisphere. By contrast, melodies may also be perceived as a gestalt, which is more characteristic of right hemisphere functions. There is evidence that well-trained musicians come to rely more heavily on the left hemisphere for processing certain aspects of music when compared with non-musicians. However, the right hemisphere evidences superiority for both the perception and expression of music in studies of non-musicians. Thus, the strategies by which various musical elements are approached, as well as the leading hemisphere in appreciating those elements, are most likely determined in part by one's prior musical experience or training. In summary, while both the right and left hemispheres are apparently involved in the expression and perception or appreciation of music, the specific contributions of each are still somewhat of a mystery.

Amygdala

Rory McQuiston
Virginia Commonwealth University
Richmond, VA, USA

Synonyms

Amygdaloid body; Amygdaloid nucleus

Historical Background

The amygdala was originally described by Burdach in the late nineteenth century as an almond-shaped structure situated deep in the anterior temporal lobe of the central nervous system. The amygdala was subsequently shown to be important for the appropriate processing of emotional information in nonhuman primates by Kluver and Bucy in the 1930s. This permitted McLean to include the amygdala in the group of brain structures that make up the limbic system thought to be involved in processing of emotional information. Since then progress has continued toward understanding the role that the amygdala plays in processing and encoding emotional information in the mammalian central nervous system.

Current Knowledge

The amygdala is an almond-shaped structure located in the medial temporal lobe of mammals. However, the first description of this almond-shaped structure only referred to a portion of the amygdala called the basal nucleus. Currently, the amygdala is described as a collection of different subnuclei or subareas, one of which is the basal nucleus. The nuclei have been grouped together based on their phylogenetic similarities or similarities in their neuronal elements. Older phylogenetic nuclei include the olfactory areas (i.e., cortical nucleus and nucleus of the olfactory tract) and the central and medial nuclei. More recent phylogenetic structures include areas similar to the neocortex such as the lateral, basal, and accessory basal nuclei, which are collectively referred to as the basolateral region or complex. Based on similarities in their neuronal components, various nuclei of the amygdala have been defined as neocortical-like nuclei (such as the basolateral complex) that consist of glutamatergic pyramidal-like neurons or striatal-like nuclei (such as the central and medial nuclei) that consist of GABAergic medium spiny neurons.

In humans, the amygdala is located under the uncus of the limbic lobe at the anterior end of the hippocampus. It also merges with the periamygdaloid cortex and abuts the putamen and tail of caudate nucleus. As a whole, the amygdala receives diverse inputs from throughout the central nervous system. The basolateral complex receives inputs encoding somatosensory, visual, auditory, gustatory, olfactory, and visceral information from the dorsal thalamus, prefrontal cortex, cingulate, parahippocampal gyrus, insular cortex, and sensory associational areas. The central and medial nuclei receive inputs from olfactory centers, hypothalamus (ventromedial and lateral),

dorsomedial and medial nuclei of the thalamus, and visceral inputs from the parabrachial nuclei, solitary nucleus and periaqueductal gray of the brainstem. Outputs from the amygdala are equally diverse. They leave via two predominant pathways. The central nucleus contributes to the stria terminalis where its efferents make connections with the hypothalamus (preoptic nuclei, ventromedial nucleus, anterior nucleus, and lateral hypothalamic areas), nucleus accumbens, septal nuclei, and rostral portions of the caudate and putamen. However, the primary output of the amygdala is the ventral amygdalofugal pathway. Through this pathway, the basolateral complex sends inputs to the hypothalamus, septal nuclei, sustantia innominata, prefrontal, cingulate, insular, and inferior temporal cortices. Through the same pathway, the central nucleus projects diffusely in the brainstem innervating the dorsal vagus, raphe, locus coeruleus, parabrachial nuclei, and the periaqueductal gray. It is the interplay between the diverse afferents projecting to the amygdala, processing within the amygdala, and the effect of the amygdala on its targets that contribute to the emotional assessment of incoming sensory information and coordinated behavioral responses.

Most of what is known about human amygdala function comes from studies of patients with damage to the amygdala. However, most damage in humans is not restricted to the amygdala alone and patients with damage to larger areas of the medial temporal lobe have more profound deficits. Nonetheless, patients with temporal lobe damage including the amygdala display a number of emotional and inappropriate behavioral deficits. These include impaired fear responses, hypersexuality, hyperorality, and hyperattention. These behaviors were originally described by Kluver and Bucy in nonhuman primates.

Much of what is known about functional circuitry within the amygdala and how it relates to encoding of emotion has been gleaned from studies in rodents. The amygdala can be divided into many subareas based on functional circuitry. Lateral to the amygdala is the piriform cortex, which encodes olfactory information. Olfactory information from the piriform cortex, and other olfactory structures, projects to the most ventral and lateral portion of the amygdala, the cortical nuclei. The cortical nuclei in turn project medially to the ventrally located medial nuclei, which is a major output for olfactory information from the amygdala. However, less is known about the ventrally located olfactory associated amygdala nuclei compared to the more dorsal multisensory nuclei. The more dorsal nuclei receive information from all sensory modalities. The major inputs to the amygdala innervate the lateral nuclei. The lateral nuclei are the most dorsally located within the amygdala, medial to the piriform cortex, and underneath the striatum. The lateral nuclei receive associational inputs encoding a single sensation (somatosensory, visual, auditory, gustatory, olfactory, or visceral). This is the first stage where sensory input is assigned emotional value and also where some emotional memories may be stored (however, the amygdala as a site for storing emotional memories remains a contentious issue). Although the lateral nuclei projects to multiple areas within and outside the amygdala, a major output is the basal nuclei (located ventral to the lateral nuclei) where the initial sensory processing of the lateral nuclei is integrated with inputs from highly processed areas including polymodal sensory areas and areas involved in memory formation like the hippocampus. The lateral and basal nuclei project medially to the central nucleus either directly or indirectly through intercalated cells (intercalated cells separate the basolateral complex from the central and medial nuclei). The central nuclei send much of the processed emotional content from the amygdala to the rest of the brain. Thus, the central nucleus is seen as the output region of the amygdala. The central nucleus produces emotional responses through its effects on its various targets throughout the central nervous system. For example, the central nucleus produces arousal through its innervation of modulatory systems in the brain stem that release norepinephrine, dopamine, serotonin, and acetylcholine. Its input to the periaqueductal gray produces freezing, startle, analgesia, and cardiovascular changes associated with fear. It also innervates the parabrachial nucleus where it affects pain processing. Its inputs to the dorsal motor vagal nucleus controls parasympathetic nervous system function and it also affects vagal nerve function through its projection to the solitary nucleus. Finally, the central nuclei projects to the hypothalamus where it controls the release of hormones and activates the sympathetic nervous system.

In summary, the amygdala is a complex group of nuclei that receive diverse inputs from various regions of the central nervous system to assess emotional value. Similarly, after extensive processing, its outputs innervate a diverse group of regions in the central nervous system to exert its effect. The result is that the amygdala is involved in encoding fear, reward, aggression, sexual, maternal, and ingestive behaviors. This results in effects on cognition, attention, perception, and memory formation. Therefore, it is not surprising that amygdala dysfunction has been associated with anxiety disorders such as posttraumatic stress disorder, phobias and panic attacks, depression, and schizophrenia.

Future Directions

Most of what is known about emotional information processing performed by the amygdala has been gleaned from studies of fear conditioning. However, the amygdala also likely plays a role in the encoding of positive emotions associated with rewarding stimuli. Currently, efforts are being made toward understanding the different types of emotional values encoded in the amygdala. Also, it remains somewhat contentious whether emotional memory is actually stored by the amygdala. It is of great interest to determine where emotional memories are stored in the amygdala (possibly the lateral nuclei) and precisely what types of memories are being stored by the amygdala, that is, whether these memories are of conscious declarative forms or more procedural reflexive forms. Understanding how the amygdala contributes to the formation of different forms of emotional memory will likely provide insights for the treatment of several psychiatric illnesses such as posttraumatic stress disorder, phobias, anxiety, and depression.

Cross References

- ▶ Efferent
- ▶ Insular Lobe
- ▶ Limbic System
- ▶ Locus Ceruleus
- ▶ Midbrain Raphe
- ▶ Neocortex
- ▶ Striatum
- ▶ Temporal Lobes

References and Readings

Ledoux, J. (2007). The amygdala. *Current Biology, 17*, 868–874.

Ledoux, J. E. (2000). Emotion circuits in the brain. *Annual Review of Neuroscience, 23*, 155–184.

Phelps, E. A., & Ledoux, J. E. (2005). Contributions of the amygdala to emotion processing: from animal models to human behavior. *Neuron, 48*, 175–187.

Sah, P., Faber, E. S., Lopez De Armentia, M., & Power, J. (2003). The Amygdaloid complex: anatomy and physiology. *Physiological Reviews, 83*, 803–834.

Amygdaloid Body

- ▶ Amygdala

Amygdaloid Nucleus

- ▶ Amygdala

Amyloid Plaques

JoAnn T. Tschanz
Utah State University
Logan, UT, USA

Synonyms

Diffuse plaques; Neuritic plaques; Senile plaques

Definition

Amyloid plaques refer to an aggregation of beta amyloid protein found in the extracellular space between neurons in the brain. Amyloid plaques may be of diffuse, pre-amyloid type, or neuritic, mature senile type. The latter is recognized as one of the neuropathological hallmarks of Alzheimer's disease (AD). Mature amyloid plaques are spherical in shape and consist of a central beta-amyloid core, fibrillary outward extensions, and surrounding dystrophic neurites (elements of degenerating neurons). Unlike the mature and senile plaques, diffuse plaques have an amorphous, irregular shape, and lack the surrounding neurites.

Current Knowledge

It is unknown if the diffuse plaques later form into senile plaques. Both plaque types contain the amyloid β protein (Aβ), a portion of a larger neuronal transmembrane protein of unknown function. Other differences between senile and diffuse plaques include their regional distribution in the brain. Diffuse plaques are common in the basal ganglia structures of the caudate nucleus and putamen as well as the cerebellum, where neuritic plaques are rare. In AD, neuritic plaques are more commonly found in the neocortex (Morris & Nagy, 2004).

References and Readings

Morris, J. H., & Nagy, Z. (2004). Alzheimer's disease. In M. M. Esiri, V. M.-Y. Lee, & J. Q. Trojanowski (Eds.), *The neuropathology of dementia* (2nd ed., pp. 161–206). Cambridge, UK: Cambridge University Press.

Amyotrophic Lateral Sclerosis

Alexander I. Tröster
University of North Carolina School of Medicine
Chapel Hill, NC, USA

Synonyms

Lou Gehrig's disease

Short Description or Definition

The features of amyotrophic lateral sclerosis (ALS) were first described by Charcot in the nineteenth century. ALS is a progressive, fatal neurodegenerative disease affecting upper and lower motor neurons, although increasingly ALS is recognized as a multisystem disorder whose manifestations may also include cognitive and behavioral changes. Most patients present with motor neuron symptoms at disease onset, and as the disease progresses, persons with ALS demonstrate impairments in speech, swallowing, breathing, and use of upper and lower limbs, with eventual paralysis. The cognitive changes, the prevalence of which is not well studied but estimates range from about 20 to 50%, most often involve executive dysfunction. Deficits in visuospatial, language, and memory functions are more inconsistently observed. When dementia is seen, it resembles a frontotemporal lobar degeneration or frontotemporal dementia characterized by personality change, irritability, diminution of insight, poverty of planning, abstraction and initiation, and obsessiveness.

Categorization

Categorizations can be based on genetics, neurological levels inferred from symptoms, and diagnostic probability. At least eight familial variants of ALS (ALS 1–8) have been identified, though the vast number of cases (about 90%) is sporadic. Of these eight, six forms are inherited in autosomal dominant manner, and two in autosomal recessive manner.

Three neurological levels are most often identified in the expression of ALS symptoms: bulbar, cervical, and lumbar. A fourth (thoracic) level is rarely encountered clinically. Persons with bulbar onset demonstrate problems with speech (dysarthria) and/or swallowing (dysphagia), and may have disease that affects lower or upper motor neurons (or both), showing features of bulbar palsy (facial weakness, limited palatal movement and lingual atrophy, weakness, and fasciculation) and/or pseudobulbar palsy (emotional lability, dysarthria, and brisk jaw jerk). Persons with cervical onset can also show upper and or lower motor neuron involvement and have upper limb signs. Such signs may include proximal weakness (shoulder abduction as required in toothbrushing or combing) or distal weakness (carrying out pincer grip movements). Lumbar onset patients have involvement of lower motor neurons and proximal weakness (e.g., difficulty in climbing stairs) or foot drop (resulting in tripping).

The most widely accepted clinical diagnostic criteria (the El Escorial criteria) define definite ALS by the presence of both upper and lower motor neuron signs in three regions, probable ALS by signs in two regions, possible ALS by signs in one region, and suspected ALS by *only* lower *or* upper motor neuron signs in one or more regions. The *suspected ALS* category may be the most controversial, and some consider the presence of only upper motor neuron signs to represent primary lateral sclerosis, while the presence of only lower motor neuron signs represents spinal muscular atrophy.

Also controversial is the notion that FTD and ALS are part of the same spectrum of disorders. This idea is supported by observations that persons with ALS may develop FTD and persons with FTD or primary progressive aphasia (PPA) may develop ALS as well as by pathologic (ubiquitin-positive, tau-negative, and synuclein-negative neuronal inclusions in some forms of ALS and FTD) and genetic findings. Nonetheless, some propose a categorization of ALS dependent upon the presence or absence of cognitive and behavioral features, namely ALS, ALS with cognitive impairment, ALS with behavioral impairment, and ALS with FTD. This categorization apparently fails to consider that about 25% of patients may have both cognitive and behavioral abnormalities.

Epidemiology

The incidence of ALS is about 1.5–2.5 per 100,000 per year and a prevalence of about 6 per 100,000. Prevalence and incidence of cognitive impairment is not well studied, but it has been estimated that cognitive impairment occurs in 20–50% of patients. Although one study in a specialty clinic indicated a prevalence of FTD features in about 40% of patients with ALS, this might represent an overestimate, given sampling bias, and the figure may be as low as 5%.

Natural History, Prognostic Factors, Outcomes

Incidence of ALS peaks in the 60s and drops rapidly thereafter. A broad estimate of mortality is that 50% of patients do not survive beyond 3 years from symptom onset, but that some may survive 10 years or more. Three epidemiologic studies provide fairly consistent survival data using time of diagnosis as the reference point (though diagnostic confirmation may lag onset by 13–18 months): 78% at 1 year, 56% at 2 years, and 32% at 4 years. Several factors are associated with poorer prognosis: low-forced vital capacity, bulbar onset (often less tolerant of forced ventilation), older age at onset, and shorter interval between first symptom and presentation. Patients attending tertiary and specialized ALS clinics tend to show longer survival and treatment with *riluzole*, on average, extends life by 3 months. Longer survival is seen in persons with only upper or lower motor neuron disease, though as noted, it is controversial whether variants such as primary lateral sclerosis are ALS.

Neuropsychology and Psychology of Amyotrophic Lateral Sclerosis

Most common among cognitive declines in ALS is executive dysfunction. Card sorting tasks demanding of conceptualization and cognitive flexibility are less sensitive to executive deficits in ALS than are verbal fluency tasks demanding initiation and deployment of efficient word retrieval strategies. Retrieval of verbs, putatively more dependent upon frontal lobe integrity than upon phonemic or semantic fluency tasks (requiring word retrieval by initial sound or membership in semantic categories, respectively) may be the most susceptible to ALS. Verbal fluency decrements are observed even if one controls for motor and speech impairments. Another task sensitive to deficits in ALS, and particularly to pseudobulbar ALS, are Tower tasks that place a premium on spatial working memory and planning. Similarly, another test of working memory (digit span backward, requiring examinees to repeat increasingly long series of digits in reverse order of presentation) has also been shown to be sensitive to ALS.

Language (unlike motor speech) is less likely disrupted by ALS, although language task impairments are observed in patients with ALS and dementia. Despite performing well on nonverbal semantic knowledge and grammar tasks, patients with ALS and dementia perform poorly on verbal tasks, making semantic paraphasic errors on naming tests. Some studies have observed tendencies toward echolalia, stereotypy of expression, and perseveration in ALS.

When deficits in memory are observed in ALS, they are more likely to be evident on immediate than delayed recall tasks. Some take this to implicate poorer executive control over encoding processes, whereas others might invoke slowed information processing as an explanation. The finding that patients can benefit disproportionately from the provision of recognition cues relative to free recall formats suggests that retrieval deficits might also be implicated, or that shallow levels of encoding are sufficient to support recognition but not recall.

Concerning behavioral changes, rating scales have revealed that as many as two thirds of persons with ALS show one or more of irritability, disinhibition, inflexibility, restlessness, and apathy. Apathy and questionable or poor social judgment are more likely to be observed in patients with bulbar onset ALS. Surprisingly, although reactive depressive reactions may occur after diagnosis, major depression is quite rare among ALS patients (about 10%). Symptoms of depression are common, occurring in about half of patients. Persons with ALS may in particular experience hopelessness and end-of-life concerns. Pathological laughing or crying, as seen in pseudobulbar syndromes, should not be confused with depression.

Evaluation

Although consensus guidelines for assessment of cognition in ALS are expected in the future; currently only older suggestions are available. Experimental modifications of tests to eliminate timing and minimize motor requirements, while facilitating patient performance, have unknown sensitivity. Persons with hypophonic speech might be provided an amplifier. Computers as augmentative communication devices, while not practical in traditional neuropsychological assessment, can be helpful in interviewing the patient. Yes–no or forced-choice recognition paradigms might allow patients to demonstrate knowledge of memoranda.

Verbal fluency tests are likely to be helpful in determining which patients might require fuller evaluations because traditional screening instruments, such as the Mini Mental State Exam, are not sensitive to cognitive impairment in ALS. In addition to measures of executive function, naming, and memory, it is important to include in assessments self- or informant rating scales capturing behavioral changes such as apathy, irritability, depression, disinhibition, etc. Such measures are helpful in identifying those persons with behavioral changes or the behavioral variant of FTD.

Treatment

There are no curative treatments for ALS. The only drug approved for ALS is *riluzole*, a glutamate release inhibitor that shows moderate benefit and extends life on an average of 3 months. Palliative care (symptomatic control and quality of life optimization in the absence of a cure) is recommended from the outset, and numerous ameliorative therapies, often multidisciplinary, are available. Cramps and spasticity can be treated with a variety of medications including, for example, *carbamazepine*, *quinine*, *baclofen*, and *tizanidine*. Drooling can be treated with anticholinergics such as *scopolamine*, although there is a risk of confusion and memory problems in older patients, and *amitriptyline*, which may also alleviate depression and pathological laughing and crying, may be preferable. Speech therapy is helpful both for swallowing problems and dysarthria, although ultimately, severe swallowing problems necessitate change in diet and choking may necessitate percutaneous endoscopic gastrostomy (PEG) placement. When communication becomes too difficult due to speech problems or difficulty breathing, computers can be used to facilitate communication, in some cases even when paralysis is present. Because breathing difficulty and shortness of breath can be distressing to the patient, a benzodiazepine or *morphine* use is recommended. Respiratory insufficiency can be alleviated with noninvasive ventilation and later invasive ventilation. Mood disturbances and family bereavement issues can be dealt with by counseling and social work intervention. Physical and occupational therapy may also be helpful to facilitate mobility and, perhaps to lesser extent, strength and range of motion.

Cross References

- ▶ Assistive Technology
- ▶ Cortical Motor Pathways
- ▶ Frontal Lobes
- ▶ Frontal Temporal Dementia
- ▶ Frontotemporal Lobar Degeneration
- ▶ Speech

References and Readings

Averill, A. J., Kasarskis, E. J., & Segerstrom, S. C. (2007). Psychological health in patients with amyotrophic lateral sclerosis. *Amyotrophic Lateral Sclerosis, 8*, 243–254.

Boeve, B. F. (2007). Links between frontotemporal lobar degeneration, corticobasal degeneration, progressive supranuclear palsy, and amyotrophic lateral sclerosis. *Alzheimer Disease and Associated Disorders, 21*, S31–S38.

Brownlee, A., & Palovcak, M. (2007). The role of augmentative communication devices in the medical management of ALS. *Neurorehabilitation, 22*, 445–450.

Lewis, M., & Rushanan, S. (2007). The role of physical therapy and occupational therapy in the treatment of amyotrophic lateral sclerosis. *Neurorehabilitation, 22*, 451–461.

Logroscino, G., Traynor, B. J., Hardiman, O., Chio, A., Couratier, P., Mitchell, J. D., et al. (2008). Descriptive epidemiology of amyotrophic lateral sclerosis: New evidence and unsolved issues. *Journal of Neurology, Neurosurgery and Psychiatry, 79*, 6–11.

Lomen-Hoerth, C. (2008). Amyotrophic lateral sclerosis: From bench to bedside. *Seminars in Neurology, 28*, 205–211.

McCluskey, L. (2007). Palliative rehabilitation and amyotrophic lateral sclerosis: A perfect match. *Neurorehabilitation, 22*, 407–408.

Mitchell, J. D., & Borasio, G. D. (2007). Amyotrophic lateral sclerosis. *Lancet, 369*, 2031–2041.

Mitsumoto, H., & Rabkin, J. G. (2007). Palliative care for patients with amyotrophic lateral sclerosis: "Prepare for the worst and hope for the best". *Journal of the American Medical Association, 298*, 207–216.

Phukan, J., Pender, N. P., & Hardiman, O. (2007). Cognitive impairment in amyotrophic lateral sclerosis. *Lancet Neurology, 6*, 994–1003.

Radunovic, A., Mitsumoto, H., & Leigh, P. N. (2007). Clinical care of patients with amyotrophic lateral sclerosis. *Lancet Neurology, 6*, 913–925.

Strong, M. J., Grace, G. M., Orange, J. B., & Leeper, H. A. (1996). Cognition, language, and speech in amyotrophic lateral sclerosis: A review. *Journal of Clinical and Experimental Neuropsychology, 18*, 291–303.

Amyotrophic Lateral Sclerosis Functional Rating Scale

Michelle Marie Tipton-Burton
Santa Clara Valley Medical Center
San Jose, CA, USA

Synonyms

ALSFRS; ALSFRS-R

Description

The Amyotrophic Lateral Sclerosis Functional Rating Scale is a validated instrument designed to assess the functional status and the disease progression in patients with amyotrophic lateral sclerosis (ALS). It is a tool that can be used to monitor functional change in a patient over time. The ALSFRS is a 10-item functional inventory which was devised for use in therapeutic trials in ALS. Each item is rated on a 0–4 scale, (with 0 being severely

impaired and 4 being normal) by the patient and/or caregiver, yielding a maximum score of 40 points. The ALSFRS assesses the patients' levels of self-sufficiency in areas of self-feeding, grooming, ambulation and communication, and swallowing.

Historical Background

The ALSFRS was developed because then current used clinimetric scales being utilized at the time were contaminated with impairment measurements did not measure the broad range of disabilities that result from ALS, and did not lend themselves to sub-score analysis that was based entirely on disability components (Feinstein, 1987; Louwerse et al., 1990; Streiner & Norman, 1989).

The ALSFRS is a validated rating instrument for monitoring the progression of disability in patients with ALS. One weakness of the ALSFRS, as it was originally designed, was that it granted disproportionate weighting to limb and bulbar, as compared to respiratory dysfunction. The ALS Functional Rating Scale Revised version that is also validated incorporates additional assessments of dyspnea, orthopnea, and the need for ventilator support. The Revised ALSFRS (ALSFRS-R) retains the properties of the original scale and shows strong internal consistency and construct validity.

Psychometric Data

The ALSFRS was developed as an internally consistent, reliable, and valid measure of disability in ALS patients as part of the Amyotrophic Lateral Sclerosis Ciliary Neurotrophic Factor (ALS CNTF) Treatment Study (ACTS Phase 1–11 Study Group, 1996). The ability of the ALSFRS to be responsive to change in the clinical status of ALS patients was evaluated cross-sectionally and prospectively over time in phase 1 and phase 2 studies of CNTF in ALS.

The ALSFRS has been validated both cross-sectionally and longitudinally against muscle strength, the Schwab and England ADL rating scale, the Clinical Global Impression of Change (CGIC) scale, and independent assessments of patient's functional status (Cedarbaum & Stambler, 1997).

Clinical Uses

The ALSFRS is a straightforward instrument that can be utilized across disciplines to assess the functional status of an individual diagnosed with ALS. The tool has also been utilized to evaluate the disease progression, predict hospital length of stay and survival time in ALS patients treated with tracheostomy-intermittent positive-pressure ventilation. Through observation and interview the evaluator assesses the following measures: speech, salivation, swallowing, handwriting, cutting food/handling utensils, turning in bed and adjusting bed clothes, walking, climbing stairs, and breathing.

Cross References

► Amyotrophic Lateral Sclerosis

References and Readings

ALS CNTF Treatment Study (ACTS) Phase 1–11 Study Group. (1996). The Amyotrophic Lateral Sclerosis Functional Rating Scale. Assessment of activities of daily living in patients with Amyotrophic Lateral Sclerosis. *Archives of Neurology, 53*, 141–147.

Cedarbaum, J. M., & Stambler, N. (1997). Performance of the Amyotrophic Lateral Sclerosis Functional Rating Scale (ALSFRS) in multicenter clinical trials. *Journal of the Neurological Sciences, 152*(Suppl 1), S1–S9.

Herndon, R. M. (2006). *Handbook of neurologic rating scales* (p. 96). New York: Demos Medical Publishing.

Lo Coco, D., Marchese, S., La Bella, V., Piccoli, T., & Lo Coco, A. (2007). The amyotrophic lateral sclerosis functional rating scale predicts survival time in amyotrophic lateral sclerosis patients on invasive mechanical ventilation. *Chest, 132*(1), 64–69.

Analysis of Covariance

► ANCOVA/MANCOVA

Analysis of Variance

Michael D. Franzen
Allegheny General Hospital
Pittsburgh, PA, USA

Synonyms

ANOVA

Definition

Analysis of variance (ANOVA) is a method of examining and evaluating possible statistical relations among

variables. ANOVA involves a general model of independent and dependent variables as well as a mathematical model of calculating statistical relations among the variables. The independent variables are categorical in nature and the dependent variables are continuous in nature. Although ANOVA is frequently used to evaluate potential causality in an experiment, a significant finding in an ANOVA does not automatically indicate a casual relation. The determination of causality requires experimental manipulation of the independent variables with subsequent changes in the dependent variables. A finding of statistical significance in ANOVA indicates the likelihood of a systematic relation between variables.

Cross References

► Analysis of Covariance (ANCOVA)
► Multivariate Analysis of Variance

References and Readings

Iverson, G. R., & Norpoth, H. (1987). *Analysis of variance*. Newbury Park, CA: Sage Publications.
Watson, P. (2009). Review of analysis of variance and covariance: How to choose and construct models for the life sciences. *Psychological Medicine, 39*, 695–696.

ANAM

► Automated Neuropsychological Assessment Metrics

Anarchic Hand

► Alien Hand Syndrome

Anarthria

Carole Roth
Naval Medical Center
San Diego, CA, USA

Synonyms

Speechlessness

Definition

Anarthria is speechlessness due to a severe loss of neuromuscular control over the speech musculature (Duffy, 2005). The term typically refers to the most severe form of dysarthria. Language and cognition of the anarthric patient may be intact but their disordered neuromuscular system prevents speech. Anarthric patients have an intact drive or motivation to speak but are unable. Writing remains intact (Marcie & Hecaen, 1979). A lesion in the outflow pathway from Broca's area leads to anarthria (Caplan & Chertkow, 1989, p. 295).

Cross References

► Dysarthria

References and Readings

Caplan, D., & Chertkow, H. (1989). In D. P. Kuehn, M. L. Lemme, & J. M. Baumgartner (Eds.), *Neural bases of speech, hearing, and language. Chapter 10 Neurolinguistics* (pp. 292–302). Boston: College-Hill, Little, Brown.
Duffy, J. R. (2005). *Motor speech disorders: Substrates, differential diagnosis, and management*. St. Louis, MO: Elsevier Mosby.
Marcie, P., & Hecaen, H. (1979). Agraphia: writing disorders associated with unilateral cortical lesions. In K. M. Heilman & E. Valenstein (Eds.), *Clinical Neuropsychology* (Chapter 4, p. 96). Oxford: Oxford University Press.

ANCOVA/MANCOVA

Michael Franzen
Allegheny Neuropsychiatric Institute
Pittsburgh, PA, USA

Synonyms

Analysis of covariance

Definition

ANCOVA or analysis of covariance is a variant of the ANOVA model in which the statistical effect of a

nuisance variable is removed mathematically from the analysis in order to clarify the relations between the independent and the dependent variables. The optimal situation would be if the independent variable levels or groups were not related to the nuisance variable. However, if the nuisance variable is related to the dependent variable and if the nuisance variable is systematically represented among the independent variables, ANCOVA may be used to partial out the statistical effect of the nuisance variable or covariate. This is not a substitute for removing the effect through experimental design. For example, level of education may be statistically related to performance on a memory test. If two groups of depressed and nondepressed individuals differ systematically on the basis of their level of education, any difference found with regard to performance on a memory test might be due to the different level of education. By employing ANCOVA and using education level as the covariate, the researcher may have a clearer understanding of the relation between the presence of depression and performance on the memory test.

Although there are different mathematical methods for conducting an ANCOVA including the use of multiple regression (which see), ANCOVA under the general linear model provides a useful conceptualization of the underlying idea. We can think of calculating the regression between the covariate and the dependent variable and then residualizing the influence of the covariate. Then an ANOVA can be conducted on the residual values. In order to use ANCOVA, the data must satisfy a few basic assumptions. There must be a linear relation between the covariate and the dependent variable. The slope of the regression for each group or level of the independent variable must be the same. The error term should be normally distributed with a mean of zero. The covariate should not be affected by the independent variable.

Cross References

► Analysis of Variance (ANOVA)

References and Readings

Belin, T. R., & Normand, S.-L. T. (2009). The role of ANCOVA in analyzing experimental data. *Psychiatric Annals, 39*, 753–759.

Watson, P. (2009). Review of Analysis of variance and covariance: How to choose and construct models for the life sciences. *Psychological Medicine, 39*, 695–696.

Wildt, A. R. & Ahtola, O. T. (1978). *Analysis of covariance.* Beverly Hills: Sage.

Anencephaly

Erin D. Bigler, Jo Ann Petrie
Brigham Young University
Provo, Utah, USA

Synonyms

Amnion rupture; Congenital defects; Exencephaly; Lack of neural tube closure; MRI; Neural tube defects

Short Description or Definition

Using "*an*" in front of an anatomical descriptor signifies *absence*. *Cephalic* is Greek for *head* with *encephalon* specifically referring to the brain. Therefore, the term *anencephaly* is used to denote a congenital defect in the development of the head, including the meninges, the cranium, and the scalp and, in particular, abnormal brain growth, with an almost completely diminished *prosencephalon* (*telencephalon* + *diencephalon*) or forebrain and only rudimentary development of the brain stem.

Categorization

Anencephaly results from the failure of closure of the headend of the neural tube in early fetal development (first 3–4 weeks) with subsequent neural tube defects (NTD) including lack of formation of the brain, skull and scalp. Loss of the forebrain includes loss of the two cerebral hemispheres, the connecting corpus callosum, neocortex, thalamus, hypothalamus and other structures of the limbic system – the amygdala, hippocampus, caudate nucleus, ventricles, etc., and all of their connections (Kolb & Whishaw, 2008). These structures comprise the majority of human brain tissue and are required for almost all sensation perception and basic physiological functions including body temperature control, eating,

sleeping, and motor function, and cognition, language, memory, emotion, thought processing, inhibition, decision making, and/or reasoning.

Epidemiology

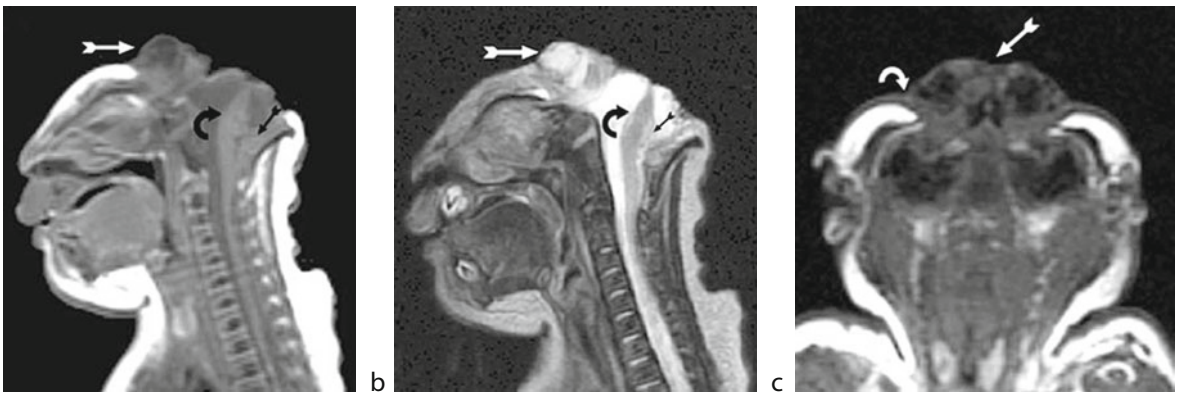
Anencephaly results from NTD (Cohen, 2002; Detrait et al., 2005; Dias & Partington, 2004; Mitchell, 2005) with approximately 1 in 1,000 births born with NTD; these may be associated with genetics, nutrition, environment, or a combination of all three. There is a known higher prevalence of females born with anencephaly NTD as compared to males (James, 1980). Over the past 3 decades, worldwide research has found an association between prenatal folic acid deficits leading to folate deficiencies (National Institutes of Health: Office of Dietary Supplements, 2009) and NTD (see also Calvo & Biglieri, 2008; Kondo, Kamihira, & Ozawa, 2009; Wolff, Witkop, Miller, & Syed, 2009). While all the causes of open NTD are not known, research indicates that daily consumption of 4 mg/day of folic acid by women before and during pregnancy brings about a 70% reduction in NTD (Centers for Disease Control and Prevention, 1991, 2008; Cornel & Erickson, 1997; McLone, 2003; MRC Vitamin Study Research Group, 1991).

Natural History, Prognostic Factors, and Outcomes

With the major portion of an infant's brain being undeveloped, particularly the cerebrum, and coupled with the brain often being exposed *in utero*, the anencephalic infant is frequently stillborn. An infant born alive with anencephaly is, as a rule, blind, deaf, unconscious, and may only reflexively respond. With only a basic brain stem and a nonfunctioning cerebrum, prognosis is poor; anencephalic infants will never gain consciousness and will only have minimal reflex actions such as breathing. There may be intermittent sound or touch responses; however, no further progress can be expected (see National Institute of Neurological Disorders and Stroke, 2010).

Neuropsychology and Psychology of Anencephaly

There is essentially no assessment that neuropsychological testing can offer given the absence of cortical development in the anencephalic infant who does survive. Such children have reflexive function only (i.e., breathing and some responses to sound or touch can manifest) and will rarely survive longer than a few hours or days.



Anencephaly. Figure 1 Magnetic resonance imaging (MRI) findings of the head and neck 8 h after birth. (**a**) Sagittal T1-weighted, (**b**) sagittal T2-weighted, and (**c**) coronal T1-weighted images show cranial schisis. The normal skin stops at the skull base and encircles abnormally developed cerebral structures, the so-called area cerebrovasculosa (white arrows). Along the border of the skull defect the skin seems to be in continuity with the superficial layer of the area cerebrovasculosa, probably the pia mater (curved white arrow). The posterior fossa is funnel-shaped. A rudimentary brain stem (curved black arrows) and primordium of cerebellum (small black arrows) are present. The cervical spine is normal (From Calzolari et al., 2004, With permission)

Neuropsychologists should have an empathetic awareness of this condition; they may be asked to consult with parents and families about the nature of the infants' deficits and the poor prognosis (Ashwal, 2005).

Evaluation

Although the pathogenesis of anencephaly is still not fully understood, several studies suggest that *exencephaly* or the lack of skull growth or separation following NTD allows the cerebral tissue to be exposed in utero causing damage from the amniotic fluid (Calzolari, Gambi, Garani, & Tamisari, 2004). As can be seen in Fig. 1, even though there are other anomalies of physical development associated with the presence of anencephaly, the most dramatic is a failure of brain development.

Treatment

Ultimately, mortality rate is 100% with anencephaly. Some anencephalic children do survive from hours to days but rarely longer and in a persistent vegetative state (Payne & Taylor, 1997); thus, treatment is purely supportive. The presence of a surviving infant with anencephaly raises numerous ethical questions about care, treatment, and maintenance (Batavia, 2002; Cook, Erdman, Hevia, & Dickens, 2008; Obeidi, Russell, Higgins, & O'Donoghue, 2010), including the importance of continued research for better ways to prevent and treat neurological birth defects.

Cross References

- ► Ethics in the Practice of Neuropsychology
- ► Forebrain
- ► National Institute of Neurological Disorders and Stroke
- ► National Institutes of Health (NIH)

References and Readings

Ashwal, S. (2005). Recovery of consciousness and life expectancy of children in a vegetative state. *Neuropsychological Rehabilitation, 15*, 190–197.

Batavia, A. I. (2002). Disability versus futility in rationing health care services: Defining medical futility based on permanent unconsciousness – pvs, coma, and anencephaly. *Behavioral Sciences & The Law, 20*, 219–233.

Calvo, E. B., & Biglieri, A. (2008). [impact of folic acid fortification on women's nutritional status and on the prevalence of neural tube defects]. *Archives of Argentina Pediatrics, 106*, 492–498.

Calzolari, F., Gambi, B., Garani, G., & Tamisari, L. (2004). Anencephaly: MRI findings and pathogenetic theories. *Pediatric Radiology, 34*, 1012–1016.

Centers for Disease Control and Prevention (1991). Use of folic acid for prevention of spina bifida and other neural tube defects – 1983–1991. *MMWR Morbidity and Mortality Weekly Report, 40*, 513–516.

Centers for Disease Control and Prevention (2008). Prevalence of neural tube defects and folic acid knowledge and consumption – puerto rico, 1996–2006. *MMWR Morbidity and Mortality Weekly Report, 57*, 10–13.

Cohen, M. M., Jr. (2002). Malformations of the craniofacial region: Evolutionary, embryonic, genetic, and clinical perspectives. *American Journal of Medical Genetics, 115*, 245–268.

Cook, R. J., Erdman, J. N., Hevia, M., & Dickens, B. M. (2008). Prenatal management of anencephaly. *International Journal of Gynecology & Obstetrics, 102*, 304–308.

Cornel, M. C., & Erickson, J. D. (1997). Comparison of national policies on periconceptional use of folic acid to prevent spina bifida and anencephaly (SBA). *Teratology, 55*, 134–137.

Detrait, E. R., George, T. M., Etchevers, H. C., et al. (2005). Human neural tube defects: Developmental biology, epidemiology, and genetics. *Neurotoxicology and Teratology, 27*, 515–524.

Dias, M. S., & Partington, M. (2004). Embryology of myelomeningocele and anencephaly. *Neurosurgical Focus, 16*, E1.

James, W. H. (1980). The sex ratios of anencephalics born to anencephalic-prone women. *Developmental Medicine and Child Neurology, 22*, 618–622.

Kolb, B., & Whishaw, I. Q. (2008). *Fundamentals of human neuropsychology.* New York: Worth Publishers.

Kondo, A., Kamihira, O., & Ozawa, H. (2009). Neural tube defects: Prevalence, etiology and prevention. *International Journal of Urology, 16*, 49–57.

McLone, D. G. (2003). The etiology of neural tube defects: The role of folic acid. *Child's Nervous System, 19*, 537–539.

Mitchell, L. E. (2005). Epidemiology of neural tube defects. *American Journal of Medical Genetics. Part C. Seminars in Medical Genetics, 135C*, 88–94.

MRC Vitamin Study Research Group (1991). Prevention of neural tube defects: Results of the medical research council vitamin study. *Lancet, 338*, 131–137.

National Institute of Neurological Disorders and Stroke. (2010, January 14, 2010). NINDS anencephaly information page. National Institutes of Health: Reducing the burden of neurological disease Retrieved March 16, 2010, from http://www.ninds.nih.gov/disorders/anencephaly/anencephaly.htm

National Institutes of Health: Office of Dietary Supplements. (2009, 4/15/2009). Dietary supplement fact sheet: Folate. Dietary Supplement Fact sheets Retrieved March 16, 2010, from http://dietary-supplements.info.nih.gov/factsheets/folate.asp

Obeidi, N., Russell, N., Higgins, J. R., & O'Donoghue, K. (2010). The natural history of anencephaly. *Prenatal Diagnosis.* doi:10.1002/pd.2490.

Payne, S. K., & Taylor, R. M. (1997). The persistent vegetative state and anencephaly: Problematic paradigms for discussing futility and rationing. *Seminars in Neurology, 17*, 257–263.

Wolff, T., Witkop, C. T., Miller, T., & Syed, S. B. (2009). Folic acid supplementation for the prevention of neural tube defects: An update of the evidence for the U.S. Preventive services task force. *Annals of Internal Medicine, 150*, 632–639.

Aneurysm

Bruce J. Diamond
William Paterson University
Wayne, NJ, USA

Synonyms

Blood-filled dilatation

Short Description or Definition

An aneurysm is an abnormal blood-filled dilatation of a blood vessel that can occur in vascular innervated areas (Webster's New Explorer Medical Dictionary, 2006). Aneurysms generally develop due to trauma, infections, congenital defects, or degenerative diseases (Parkin & Leng, 1993).

Categorization

Intracranial aneurysms are commonly classified as saccular, mycotic, traumatic, arteriosclerotic, dissecting, or neoplasmic. Giant aneurysms greater than 2.5 cm in diameter are believed to be congenital anomalies and mostly are located on the anterior and middle cerebral, and carotid and basilar arteries (Ropper, Brown, Adams, & Victor, 2005).

Epidemiological Factors

Ruptured aneurysms, specifically the saccular type, are the most common cause of subarachnoid hemorrhage (SAH) after 20 years of age. This type of aneurysm accounts for about 80% of nontraumatic aneurysms.

Natural History, Prognostic Factors, and Outcomes

Unruptured aneurysms may be symptomatic and manifested as cranial nerve palsies. Ruptured cerebral aneurysms can be associated with states of consciousness ranging from lethargy to coma. Outcome depends on location and severity of bleeding. A sudden loss of consciousness is a presenting feature in about 20% of cases. Commonly observed systemic complications and sequelae are vasospasms, rebleeding, hydrocephalus, herniation, seizures, cardiodysrhythmias, and respiratory depression (Bonner & Bonner, 1991).

Neuropsychological and Medical Outcomes

Symptoms and signs can include retinal hemorrhage, papilledema, and meningeal signs with seizure activity commonly observed. Focal signs are prominent within the first 24 h (e.g., parenchymal dissection, hyperfusion distal to the aneurysm site, cerebral edema). Vasospasm may be the cause of focal signs within the 48–72 h window. Cognitive, psychiatric, and behavioral impairments following aneurysm rupture will depend on the site and extent of damage, secondary sequelae, complications, and pre-morbid health (see Table 1).

Assessment and Treatment

The Hunt-Hess grading scale is used for prognosis and for timing of surgical interventions. Diagnostic evaluations commonly include CT scans, angiography, and MR angiography. Surgical treatment consists of clipping and endovascular embolization of the aneurysm, and pharmacologic interventions may include calcium channel blockers (e.g., nimodipine) in order to reduce the severity of vasospasm (Bonner & Bonner, 1991).

Aneurysm. Table 1 Symptoms that may be associated with ruptured and unruptured cerebral aneurysms (From Bonner & Bonner, 1991)

Ruptured aneurysms	Unruptured aneurysms
Parenchymal dissection	Headache, nuchal rigidity
Hyperfusion	Neurologic deficit
Cerebral edema	Drowsiness, confusion, focal neurologic deficit
Cognitive impairments	Decerebrate rigidity/vegetative disturbance possible
Disturbances in personality	Deep coma

Cross References

- ▶ Anterior Cerebral Artery
- ▶ Anterior Communicating Artery
- ▶ Herniation Syndromes
- ▶ Hydrocephalus

References and Readings

Bonner, J. S., & Bonner, J. J. (1991). *The little black book of neurology: A manual for neurologic house officers* (2nd ed.). St Louis, MO: Mosby-Year Book.

Parkin, A., & Leng, R. C. (1993). *Neuropsychology of the amnestic syndrome.* Hove, UK: Lawrence Erlbaum.

Ropper, A. H., Brown, R. H., Adams, R. D., & Victor, M. (2005). *Adams & Victor's principles of neurology.* New York: McGraw-Hill.

Webster's new explorer medical dictionary (new ed.). (2006). Springfield, MA: Merriam-Webster.

Aneurysmal Subarachnoid Hemorrhage

- ▶ Subarachnoid Hemorrhage

Angelman Syndrome

Kristin D. Phillips[1], Bonita P. Klein-Tasman[2]
[1]Medical College of Wisconsin
Milwaukee, WI, USA
[2]University of Wisconsin-Milwaukee
Milwaukee, WI, USA

Short Description or Definition

Angelman syndrome is a neurodevelopmental disorder caused by one of several genetic mechanisms involving maternal chromosome 15, specifically the region 15q11–13. Characteristic physical features include a large chin, deep-set eyes, a wide mouth, and microcephaly. Additionally, seizure disorder, ataxia, hypotonia, developmental delays, and a lack of expressive language are commonly observed. Behaviorally, individuals with Angelman syndrome are known for a happy temperament, frequent laughter, inattention/hyperactivity, and stereotyped behaviors (Clayton-Smith & Laan, 2003).

Categorization

Deletion or mutation of genetic material on chromosome 15q11–13 can result in one of two distinct neurodevelopmental disorders, depending upon whether the genetic material is from the maternal or paternal chromosome. This parent of origin effect is known as "imprinting." Note that the 15q11–13 region is differently imprinted in maternal and paternal chromosomes, and both imprintings are needed for normal development. If a maternal deletion occurs, the result is Angelman syndrome; but if paternal, then the result is Prader–Willi syndrome. Therefore, Angelman and Prader–Willi have been termed "sister syndromes" or "sister disorders."

There are four main classes of Angelman syndrome, based upon four primary genetic mechanisms by which it occurs (Clayton-Smith & Laan, 2003). Each of these classes involves expression of the maternal chromosome region 15q11–13, which includes the UBE3A gene. In the general population, UBE3A is expressed only from the maternal chromosome in particular regions of the brain, and the UBE3A gene on the paternal chromosome is inactive. In Angelman syndrome, as a result of the deletion, only about 10% of UBE3A is expressed (Williams, 2005).

Epidemiology

Exact prevalence rates of Angelman syndrome are unknown but have been estimated between 1/10,000 and 1/40,000 (Clayton-Smith & Laan, 2003). See Table 1 for estimates by subtype.

Natural History, Prognostic Factors, and Outcomes

Angelman syndrome was first described by Dr. Harry Angelman in 1965. He observed several pediatric patients whom he referred to as "puppet children," in light of their happy expressions and "jerky" movements. This term was later abandoned, and the disorder came to be known as Angelman syndrome. Diagnostic clinical criteria were developed by Williams and colleagues in 1995 and revised in 2006 (Williams et al., 2006).

The prenatal and perinatal history of children with Angelman syndrome is typically unremarkable, and developmental delays first become evident around 6–12 months of age (Cassidy et al., 2000). In addition to microcephaly, a flat occiput (microbrachycephaly) is commonly observed. Puberty typically occurs on time. There

Angelman Syndrome. Table 1

Genetic mechanism	Incidence	Definition
De novo deletion	70%	Deletion on maternal chromosome region 15q11–13
Uniparental disomy	2–3%	Both copies of chromosome 15 are inherited from the father, rather than one from each parent
Imprinting defect	2–5%	Genes become inactivated as a result of a disruption in genes controlling the imprinting process itself, or the imprinting center
UBE3A mutation	10–15%	
Unknown	10–15%	

(Cassidy, Dykens, & Williams, 2000; Clayton-Smith & Laan, 2003; Williams, 2005)

Angelman Syndrome. Figure 1

is generally no evidence of reduced lifespan, although the severity of associated medical conditions (e.g., seizures) certainly impacts health and the overall quality of life. Additionally, the longstanding motor difficulties in this population often translate into mobility issues later in life (Clayton-Smith & Laan, 2003).

Although epilepsy is common in Angelman syndrome, it is not universal, with estimates of about 80% in this population (Clayton-Smith & Laan, 2003). A variety of seizure types has been reported, including atypical absence, myoclonic, atonic, and tonic–clonic. Seizures usually appear in early childhood, with some indication of improvement during late childhood/adolescence, although the majority of adults continue to have seizures. EEGs are typically abnormal, and characteristic EEG patterns have been described.

Variability is evident in the phenotypic expression of Angelman syndrome depending upon the specific genetic mechanism by which it occurs. Those with Angelman syndrome due to a de novo deletion appear most severely affected, including more severe medical and physical problems, as well as greater motor and language deficits (e.g., Clayton-Smith & Laan, 2003; Levitas, Dykens, Finucane, & Kates, 2007). In contrast, those with uniparental disomy have less-severe ataxia and seizures, better nonverbal communication skills, and fewer dysmorphic facial features. Individuals with Angelman syndrome due to an imprinting center defect also appear to have milder clinical presentations. Those with UBE3A mutations have been found to have the more-severe medical and physical problems seen in individuals with de novo deletions, but

Angelman Syndrome. Figure 2

fewer difficulties with motor and language skills than these individuals (Clayton-Smith & Laan, 2003).

Neuropsychology and Psychology of Angelman Syndrome

Neuroanatomical findings have demonstrated anomalous Sylvian fissures in individuals with Angelman syndrome (Leonard et al., 1993), in addition to marked cerebellar atrophy (Jay, Becker, Chan, & Perry, 1991). Cognitive functioning typically falls in the severe-to-profound range of intellectual disability (Peters, Goddard-Finegold, Beaudet, Madduri, Turcich, & Bacino, 2004). Similarly, adaptive functioning is delayed, with a relative strength in socialization and a relative weakness in motor skills (Peters et al., 2004). A primary feature of Angelman syndrome is limited expressive language, typically ranging from no language to very few single words. There are relative strengths in nonverbal communication and receptive language. Marked deficits occur in fine motor skills.

A happy temperament has been reported among individuals with Angelman syndrome, characterized by frequent smiling and laughter, which persists across the lifespan and is most evident in social interactions (e.g., Clayton-Smith, 2001; Clayton-Smith & Laan, 2003). Parents have rated their children with Angelman syndrome lower on irritability and lethargy, in comparison to individuals with other developmental disabilities (Summers & Feldman, 1999). A variety of behavioral difficulties have been reported, the most common including inattention and hyperactivity (Clarke & Marston, 2000; Summers, Allison, Lynch, & Sandler, 1995). However, there is some indication that these behavioral difficulties improve with age (Clayton-Smith, 2001). Stereotyped behaviors, such as hand flapping, have been observed. In addition, individuals with Angelman syndrome often have an attraction to water and shiny objects. These latter findings have led to the conclusion that the incidence of autism spectrum disorders is high in this population; however, this may be overdiagnosed in Angelman syndrome given the severe-to-profound intellectual disability. Sleep problems are common, including issues like falling asleep, staying asleep, and being easily roused from sleep. Feeding problems have also been reported.

Evaluation

Angelman syndrome is confirmed through genetic testing. Fluorescence in-situ hybridization (FISH) testing is typically employed to identify genetic deletions, whereas DNA-methylation testing can be used to detect uniparental disomy or imprinting defects.

Treatment

There is no "cure" for Angelman syndrome itself. Given the high incidence of seizure disorder, management and follow-up by a neurologist is usually necessary. Anticonvulsant medications have been utilized to manage seizures. Clonazepam, valproic acid, and phenobarbital appear to be most effective in addressing seizures in Angelman syndrome. Sleep difficulties have successfully been addressed through behavioral and pharmacological intervention.

Involvement in interventions such as occupational, physical, and speech/language therapy is typically recommended to address language and motor deficits. In addition to speech/language therapy, alternative communication methods typically need to be explored. Special education programming is also indicated in light of cognitive deficits. Very few behavioral intervention studies have been conducted for individuals with Angelman syndrome. Behavioral training has been used to increase communication and daily living skills.

Cross References

- ▶ Ataxia
- ▶ Developmental Delay
- ▶ Epilepsy
- ▶ Intellectual Disabilities
- ▶ Microcephaly
- ▶ Prader–Willi Syndrome
- ▶ Seizure
- ▶ Syndrome

References and Readings

Angelman Syndrome Foundation, Inc. (2009). Retrieved November 6, 2008, from http://www.angelman.org/

Cassidy, S. B., Dykens, E., & Williams, C. A. (2000). Prader-Willi and Angelman syndromes: Sister imprinted disorders. *American Journal of Medical Genetics, 97*, 136–146.

Clarke, D. J., & Marston, G. (2000). Problem behaviors associated with 15q- Angelman syndrome. *American Journal on Mental Retardation, 105*, 25–31.

Clayton-Smith, J. (2001). Angelman syndrome: Evolution of the phenotype in adolescents and adults. *Developmental Medicine and Child Neurology, 43*, 467–480.

Clayton-Smith, J., & Laan, L. (2003). Angelman syndrome: A review of the clinical and genetic aspects. *Journal of Medical Genetics, 40*, 87–95.

Jay, V., Becker, L. E., Chan, F. W., & Perry, T. L. Sr. (1991). Puppet-like syndrome of Angelman: a pathologic and neurochemical study. *Neurology, 41*, 416–422.

Leonard, C. M., Williams, C. A., Nicholls, R. D., Agee, O. F., Voeller, K. K., Honeyman, J. C., et al. (1993). Angelman and Prader-Willi syndrome: A magnetic resonance imaging study of differences in cerebral structure. *American Journal of Medical Genetics, 46*, 26–33.

Levitas, A., Dykens, E., Finucane, B., & Kates, W. (2007). Behavioral phenotype of genetic disorders. In R. Fletcher, E. Loschen, C. Stavrakaki, & M. First (Eds.), *Diagnostic manual – intellectual disability: A textbook of diagnoses of mental disorders in persons with intellectual disability.* Kingston, NY: NADD Press.

Peters, S. U., Goddard-Finegold, J., Beaudet, A. L., Madduri, N., Turcich, M., & Bacino, C. A. (2004). Cognitive and adaptive behavior profiles of children with Angelman syndrome. *American Journal of Medical Genetics, 128*, 110–113.

Summers, J. A., Allison, D. B., Lynch, P. S., & Sandler, L. (1995). Behaviour problems in Angelman syndrome. *Journal of Intellectual Disability Research, 39*, 97–106.

Summers, J. A., & Feldman, M. A. (1999). Distinctive pattern of behavioral functioning in Angelman syndrome. *American Journal on Mental Retardation, 104*, 376–384.

Williams, C. A. (2005). Neurological aspects of the Angelman syndrome. *Brain & Development, 27*, 88–94.

Williams, C. A., Beaudet, A. L., Clayton-Smith, J., Knoll, J. H., Kyllerman, M., Laan, L. A., et al. (2006). Angelman syndrome 2005: Updated consensus for diagnostic criteria. *American Journal of Medical Genetics, 140*, 413–418.

Angiitis

► Vasculitis

Angio

► Carotid Angiography

Angiography, Cerebral

John Whyte
Moss Rehabilitation Research Institute
Albert Einstein Healthcare Network
Elkins Park, PA, USA

Synonyms

(Cerebral) arteriography

Definition

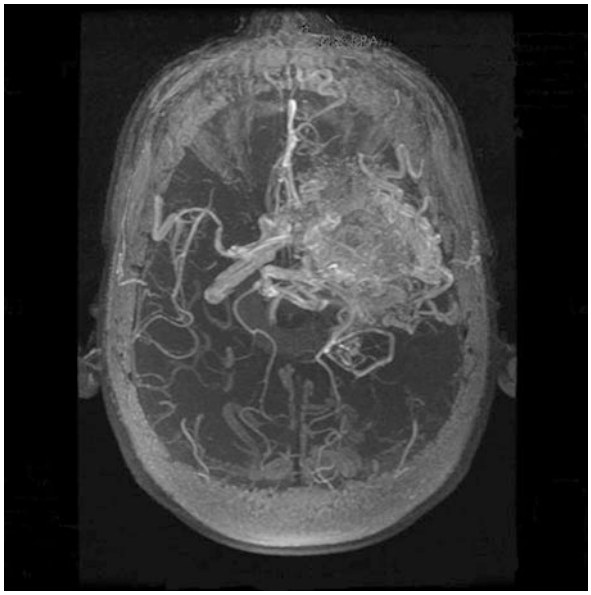
Angiography refers to a set of procedures designed to image the arterial circulation. As such, cerebral angiography refers specifically to the imaging of the cerebral arterial tree.

Current Knowledge

Historical background: Angiography was initially introduced into medical practice in the late 1940s. Traditional catheter angiography involves introduction of a catheter through a large peripheral artery (typically the femoral artery), threading it to its desired location, and injection of radio-opaque contrast medium while obtaining radiographic images. The introduction of computerized tomographic angiography (CT angiography) in the 1970s allowed the administration of contrast material intravenously rather than intra-arterially, since the reconstructed tissue slices allow visualization of the contrast in the arteries or organs of interest. Magnetic resonance (MR) angiography was added to the diagnostic armamentarium in the early 1990s. MR digital subtraction angiography can visualize the arterial circulation via detection of moving water molecules in blood, without the attendant risks of toxicity from the contrast medium or radiation exposure (Fig. 1). It has the additional advantage of revealing abnormalities in the vessel wall, not merely luminal filling defects. However, contrast agents designed for visibility in MR scanning, and administered intravenously, can further enhance visualization.

Psychometric data: The sensitivity, specificity, and positive predictive value of the various forms of angiography are dependent on the disorder under study and its prevalence in the sample being investigated. Overall, however, less invasive forms of angiography have increasingly supplanted the catheter-based methods, because of comparable accuracy. In one recent porcine model, for example, estimated degree of arterial narrowing did not differ significantly between catheter and digital subtraction imaging methods, and the correlation between methods was highly significant.

Clinical uses: Angiography can be performed to visualize occult vascular pathology such as unruptured aneurisms, arteriovenous malformations, or the abnormal vascular supply of tumors. It can also be performed to localize the source of clinically significant bleeding, as in the case of ruptured aneurisms, or to locate the sites of narrowing or occlusion by atherosclerotic plaque, thrombus, arterial dissection, or external compression.



Angiography, Cerebral. Figure 1 Figure CA1 shows a large arteriovenous malformation in the left frontal lobe as revealed by an unenhanced MR angiogram

Cross References

- ▶ Computed Tomography
- ▶ Digital Subtraction Angiography
- ▶ Magnetic Resonance Imaging

References and Readings

Anzalone, N., Scotti, R., & Iadanza, A. (2006). MR angiography of the carotid arteries and intracranial circulation: Advantage of a high relaxivity contrast agent. *Neuroradiology, 48*(Suppl. 1), 9–17.

Bracard, S., Anxionnat, R., & Picard, L. (2006). Current diagnostic modalities for intracranial aneurysms. *Neuroimaging Clinics of North America, 16*(3), 397–411.

Paciaroni, M., Caso, V., & Agnelli, G. (2005). Magnetic resonance imaging, magnetic resonance and catheter angiography for diagnosis of cervical artery dissection. *Frontiers of Neurology and Neuroscience, 20*, 102–118.

Rhee, T. K., Park, J. K., Cashen, T. A., Shin, W., Schirf, B. E., Gehl, J. A. et al. (2006). Comparison of intraarterial MR angiography at 3.0 T with x-ray digital subtraction angiography for detection of renal artery stenosis in swine. *Journal of Vascular and Interventional Radiology, 17*(7), 1131–1137.

Angioma

- ▶ Hemangioma

Angioma, Cavernous Angioma

Jennifer Tinker
Drexel University
Philadelphia, PA, USA

Synonyms

Cavernous hemangioma; Cavernoma; Cerebral cavernous malformation (CCM); Cavernous venous malformation

Definition

Cavernous angiomas are benign vascular malformations found within the CNS. They are typically found supratentorially (approximately 80%), predominantly in the frontal and temporal lobes. Infratentorially, cavernous angiomas are most commonly found in the pons and cerebellar hemispheres (Sage & Blumbergs, 2001). Originally thought to be relatively rare and most commonly detected during autopsy, the advent of MRI has led to an increased detection, with incidence rates now estimated between 0.02% and 0.8% of the general population. The size of the well-circumscribed, "mulberry-like" mass can range from less than 1 cm to greater than 4 cm. Prevalence rates are relatively equivalent among men and women. While it can remain asymptomatic lifelong, symptomatic presentation is most commonly seen in the third and fourth decades of life. However, newly symptomatic cases have been well-reported throughout the life span. Clinical manifestations, when present, vary significantly and generally correlate to location of the lesion. Most commonly reported symptoms include headache (6–65%), seizure (23–52%), focal neurological deficit (20–45%), and intracranial hemorrhage (13–25%) (Conway & Rigamonti, 2006). Despite the regional affinity for frontal and temporal regions, no studies have specifically examined for selective neuropsychological deficits. Treatment can include observation, surgical resection, or stereotactic radiosurgery.

References and Readings

Conway, J. E., & Rigamonti, D. (2006). Cavernous malformations: A review and current controversies. *Neurosurgery Quarterly, 16*(1), 15–23.

Sage, M. R., & Blumbergs, P. C. (2001). Cavernous haemangiomas (angiomas) of the brain. *Pathological-Radiological Correlation, 45*, 247–256.

Angioplasty

Elliot J. Roth
Northwestern University
Chicago, IL, USA

Synonyms

Coronary angioplasty; Percutaneous transluminal coronary angioplasty (PTCA)

Definition

Angioplasty is a minimally invasive clinical procedure to dilate blood vessels narrowed or blocked by atherosclerosis.

Current Knowledge

Angioplasty is most commonly performed on the coronary arteries that supply blood to the heart muscle, but it is also performed on carotid arteries, peripheral blood vessels in the limbs, and elsewhere. Angioplasty may be used to treat coronary artery disease, which often presents with persistent angina (chest pain) or a myocardial infarction (heart attack), as well as cerebrovascular disease causing stroke or transient ischemic attacks, renal artery stenosis causing kidney dysfunction, and peripheral artery disease, usually in the blood vessel of the leg.

In this procedure, a small incision is made over the skin of a peripheral artery (usually the femoral artery in the thigh), and the artery is punctured to gain access into the blood vessel. A thin catheter is then inserted into the blood vessel, and both blood vessels and catheter are visualized by radiographic fluoroscopy. The catheter is then pushed further into the vessel (guided by fluoroscopic images). When the tip of the catheter reaches the target blood vessel, a previously folded balloon at the end of the catheter is inflated to flatten the plaque in the vessel wall, thereby reducing the blockage and expanding the diameter of the artery. Usually, a stent, a metal mesh tube of small diameter that was also at the end of the catheter, is then placed inside the vessel and expanded by manipulating the catheter tip. The result is a dilated artery and improved blood flow through the vessel.

This procedure is done to prevent the vessel from becoming blocked again. It is a relatively safe procedure, and complications are rare, but they include allergy, bleeding, clotting, stroke, kidney failure, and reblockage of the newly opened artery. After the procedure, patients usually remain on bedrest for a short time and are instructed to use antiplatelet medications. It is estimated that more than one million people with heart disease undergo angioplasty every year in the USA.

Cross References

- ▶ Angiography
- ▶ Atherosclerosis
- ▶ Cerebrovascular Disease
- ▶ Coronary Disease
- ▶ Myocardial Infarction
- ▶ Peripheral Vascular Disease
- ▶ Stent

References and Readings

American College of Cardiology, American Heart Association, Society for Cardiovascular Angiography and Interventions: ACC/AHA/SCAI 2005 Guideline Update for Percutaneous Coronary Intervention: A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (ACC/AHA/SCAI Writing Committee to Update the 2001 Guidelines for Percutaneous Coronary Intervention) (2006). *Circulation, 113*, e166–e286.

Angular Acceleration

- ▶ Rotational Acceleration

Angular Gyrus Syndrome

- ▶ Gerstmann's Syndrome

Anhedonia

- ▶ Apathy

A

Anomalous Dominance

John E. Mendoza
Tulane University Medical Center
New Orleans, LA, USA

Synonyms

Mixed dominance

Definition

Anomalous dominance describes any pattern of cerebral organization of function in which the left hemisphere is *not* primarily responsible for initiating propositional speech and processing written or spoken language.

Current Knowledge

Since the left hemisphere primacy for language is typical of most right-handers (who represent the vast majority of the population), it is considered to be the "dominant" pattern of brain organization. Hence, any pattern that differs from this is considered to be *anomalous*. Most deviations occur in left-handers, approximately 30% of whom exhibit some form of anomalous dominance for language where these functions are organized either primarily in the right hemisphere ("reversed dominance") or are more bilaterally represented. Although anomalous dominance can occur in right-handers, this is rare and, when present, is often a consequence of some early developmental defect or brain trauma. Other associations that have been reported to be related to anomalous patterns of hemispheric organization of language are female gender, mixed hand preference (ambidexterity), and family history of sinistrality. In these situations, there is an increased tendency for language functions to be organized in both hemispheres. Support for this hypothesis comes in part from radiographic studies which show a tendency for males when compared with females to have greater anatomical asymmetry in the region of the frontal operculum (Broca's area) and in the temporal operculum (planum temporale), both key language areas. This apparent tendency for greater bilateral representation of language has been suggested as a possible explanation for (1) the earlier development (on average) of language in females than in males, and (2) the superior recovery of language functions following strokes seen in some left-handers.

Cross References

▶ Dominance (Cerebral)

References and Readings

Geschwind, N., & Galaburda, A. M. (1987). *Cerebral lateralization: Biological mechanisms, associations, and pathology.* Cambridge, MA: MIT Press.

Geschwind, N., & Galaburda, A. (1985). Cerebral lateralization. *Archives of Neurology, 42*, 428–459; 521–552; 634–654.

Herron, J. (Ed) (1980). *Neuropsychology of left-handedness.* New York: Academic.

Anomia

Anastasia Raymer
Old Dominion University
Norfolk, VA, USA

Synonyms

Naming impairments; Word finding difficulties

Definition

Anomia generally refers to instances of word finding difficulty that occur during the course of conversational discourse. It is often documented clinically in confrontation picture naming tasks.

Current Knowledge

Anomia can occur in healthy individuals who occasionally experience difficulty in thinking of an intended word during conversation, also known as the tip-of-the-tongue state (Biedermann, Ruh, Nickels, & Coltheart, 2008). It is a frequent occurrence in individuals with left hemisphere brain damage and aphasia (Raymer, 2005). Typically associated with difficulties for nouns, anomia also can affect the ability to retrieve other classes of words, such as verbs and adjectives. Word finding requires several steps, including semantic processes in which the speaker has an idea or meaning to convey and phonological processes in which the speaker selects an appropriate

word to express that meaning (Raymer & Rothi, 2008). These different steps in word finding engage different parts of the brain distributed throughout the left cerebral hemisphere. Therefore, when brain damage occurs, anomia will accompany different types of aphasia, and different types of anomic errors can arise. It is important to note that anomia and anomic aphasia are not synonymous. Anomia is the primary symptom of anomic aphasia and also can be observed in virtually all other forms of aphasia (e.g., Broca's aphasia, Wernicke's aphasia), both as initial and residual signs when other signs and symptoms of aphasia have resolved.

When anomia occurs, a number of errors can be seen (Goodglass, Kaplan, & Barresi, 2001). At times, the moment of anomia leads to complete inability to retrieve a word. Other times, an inappropriate word is retrieved, also known as a paraphasia. Sometimes, the error word is somehow related to the intended word in meaning (semantic paraphasia, e.g., saying 'dog' for cat) or sound characteristics (phonologic paraphasia, e.g., saying 'crat' for cat). Sometimes, the moment of word finding difficulty is filled with a description of the intended word or circumlocution (e.g., 'That thing that meows and has whiskers. I can't think of the name.'). In severe forms of anomia, neologisms may occur in which the uttered word may not be recognizable at all (e.g., saying 'bilan' for cat).

Cross References

- ▶ Circumlocution
- ▶ Confrontation Naming
- ▶ Paraphasia
- ▶ Phonemic Paraphasia
- ▶ Semantic Paraphasia
- ▶ Word Finding

References and Readings

Biedermann, B., Ruh, N., Nickels, L., & Coltheart, M. (2008). Information retrieval in tip of the tongue states: New data and methodological advances. *Journal of Psycholinguistic Research, 37*, 171–198.

Goodglass, H., Kaplan, E., & Barresi, B. (2001). *The assessment of aphasia and related disorders* (3rd ed.). Philadelphia: Lippincott, Williams, & Wilkins.

Goodglass, H., & Wingfield, A. (Eds.) (1997). *Anomia: Neuroanatomical and cognitive correlates.* San Diego: Academic Press.

Laine, M., & Martin, N. (2006). *Anomia: Theoretical and clinical aspects.* New York: Psychology Press.

Raymer, A. M. (2005). Naming and word retrieval problems. In L.L. LaPointe (Ed.), *Aphasia and related neurogenic language disorders* (3rd ed., pp. 72–86). New York: Thieme.

Raymer, A. M., & Rothi, L. J. G. (2008). Cognitive neuropsychological approaches to assessment and treatment: Impairments of lexical comprehension and production. In R. Chapey (Ed.), *Language intervention strategies in adult aphasia* (5th ed., pp. 607–631). Baltimore: Lippincott, Williams & Wilkins.

Anomic Aphasia

Anastasia Raymer
Old Dominion University
Norfolk, VA, USA

Definition

Anomic aphasia is the language impairment that involves only word finding difficulties or pure anomia in contrast to other forms of aphasia (Goodglass et al., 2001). Other language modalities typically are intact, including auditory comprehension of language, repetition of words and sentences, and spontaneous generation of sentences.

Current Knowledge

Anomic aphasia is a form of language disorder associated with acquired brain damage typically affecting the left cerebral hemisphere (Raymer, 2005). Anomic aphasia can be manifest as a difficulty in retrieving specific intended words, often nouns, but sometimes verbs, during the course of sentence generation. The grammatical characteristics of the sentence remain intact. The moments of word retrieval difficulty lead to long pauses, insertion of filler words, or selection of wrong words (paraphasias) during conversation or other word retrieval activities, most commonly in tasks requiring individuals to name pictures. Also common in anomic aphasia is circumlocution, in which the speaker cannot think of the intended word and instead describes or provides associated information about the word.

When anomic aphasia occurs as a result of an acute neurologic event (e.g., stroke), it can be accompanied by pure alexia and difficulties with color identification (Goodglass et al., 2001). Acutely, anomic aphasia has been described following left temporal/occipital lesions (e.g., area 37) and left thalamic lesions (Raymer, Moberg, Crosson, Nadeau, & Rothi, 1997; Raymer, Foundas et al., 1997). Anomic aphasia also can be seen chronically as individuals recover from other forms of aphasia. In that case, the accompanying symptoms and neural correlates of anomic aphasia vary.

Cross References

- ▶ Anomia
- ▶ Circumlocution
- ▶ Confrontation Naming
- ▶ Paraphasia
- ▶ Phonemic Paraphasia
- ▶ Semantic Paraphasia
- ▶ Word Finding

References and Readings

Goodglass, H., Kaplan, E., & Barresi, B. (2001). *The assessment of aphasia and related disorders* (3rd ed.). Philadelphia: Lippincott, Williams, & Wilkins.

Goodglass, H. & Wingfield, A. (Eds.) (1997). *Anomia: Neuroanatomical and cognitive correlates.* San Diego: Academic Press.

Laine, M. & Martin, N. (2006). *Anomia: Theoretical and clinical aspects.* New York: Psychology Press.

Raymer, A. M. (2005). Naming and word retrieval problems. In L. L. LaPointe (Ed.), *Aphasia and related neurogenic language disorders* (3rd ed., pp. 72–86). New York: Thieme.

Raymer, A. M., Foundas, A., Maher, L., Greenwald, M., Morris, M., Rothi, L. J. G. et al. (1997). Cognitive neuropsychological analysis and neuroanatomic correlates in a case of acute anomia. *Brain and Language, 58*, 137–156.

Raymer, A. M., Moberg, P., Crosson, B., Nadeau, S., & Rothi, L. J. G. (1997). Lexical-semantic deficits in two patients with dominant thalamic infarction. *Neuropsychologia, 35*, 211–219.

Anosmia

Holly James Westervelt, Nicole C. R. McLaughlin
Alpert Medical School of Brown University
Providence, RI, USA

Synonyms

Anosphrasia

Short Description or Definition

Anosmia is defined as a lack of the sense of smell or an inability to detect odors of any kind. In the strictest sense, "anosmia" refers to a total lack of olfactory ability, though the term is often used more loosely to refer also to partial or diminished sense of smell. There are multiple additional terms describing olfactory abilities. *Normosmia* is the intact ability to perceive odors. *Hyposmia* is a more precise term to describe decreased ability to perceive smells, whereas *hyperosmia* is the increased ability to perceive odors. *Dysosmia* (a.k.a. *parosmia)* refers to distortions in the sense of smell, including *cacosmia* (distortion of a smell as particularly unpleasant) and *phantosmia* (an olfactory hallucination, or the sensation of a smell in the absence of a stimulus).

Epidemiology

Olfactory dysfunction is present in at least 1% of individuals under the age of 65, with some estimates suggesting total anosmia in as much as 5% of the population. Rates of impairment increase dramatically with age, with approximately 25% of older adults showing deficits in olfaction (Murphy et al., 2002). In patients presenting to chemosensory clinics, olfactory deficits are reported to be related to disability and quality of life, though most individuals with olfactory deficits are unaware of them. It is well established that throughout the lifespan, women show more acute olfactory abilities than men.

Causes

The causes of olfactory impairments are typically categorized as: (1) conductive/transport impairments, (2) sensory/sensorineural deficits, or (3) central olfactory neural impairment, though these categories are not mutually exclusive. The understanding of the potential causes of olfactory deficits will be enhanced by a brief review of the olfactory system, though it is noted that the olfactory pathways within the central nervous system (CNS) are not entirely agreed upon.

Anatomy of the Olfactory System

The sensation of smell is the brain's perception of odor in response to odorants activating olfactory receptors. Odors enter the nose, where they come in contact with the olfactory epithelium, made up of olfactory receptors. Olfactory receptor cells (first order neurons) send signals along the olfactory nerve (first cranial nerve) to the mitral cells of the olfactory bulb, where olfactory axons synapse with second-order neurons in the olfactory bulb. Each olfactory receptor type sends a signal to a particular region of the olfactory bulb. Mitral cell axons project through the olfactory tract and lateral olfactory stria to

the primary olfactory cortex, which is primarily made up of the piriform cortex. Other structures receiving direct input include the anterior olfactory nucleus, olfactory tubercle, amygdala, and rostral entorhinal cortex (Gotfried & Zald, 2005). Projections from these primary areas extend to secondary olfactory regions in the hippocampus, hypothalamus, thalamus, amygdala, and agranular insula, enabling encoding of odors into memory as well as emotional processing of specific odors (Gotfried & Zald, 2005). There are also projections to the orbitofrontal cortex (OFC), and it is believed that the OFC mediates conscious perception of odors; lesions to this area often lead to impaired olfactory abilities (Gotfried & Zald, 2005). In addition to the activation of the first cranial nerve, certain smells may also activate the trigeminal nerve (CNV), which mediates sensations associated with certain odorants, including burning, cooling, irritation, or tickling sensations. Activation of the trigeminal nerve may allow the "detection" of some odors, even in the presence of primary olfactory impairments. Cranial nerve zero (nervus terminalis) may also play some role in olfaction, though its function is poorly understood in humans.

Conductive/Transport Impairment

Olfactory impairment within this category arises from obstruction of nasal passages. Typical causes of obstruction include nasal inflammation, such as from allergies or upper respiratory infection (URI), or other structural interference, such as nasal polyps. URI is the most common cause of smell loss, and is often transient. Permanent smell loss due to URI can occur, presumably reflecting direct insult to the neuroepithelium, and becomes more likely in older age.

Sensorineural/Central Olfactory Neural Impairment

Olfactory deficits within these categories arise from damage to the neuroepithelium and/or impairment or impingement of central olfactory structures from CNS disease. There are numerous congenital, endocrine, neurological/neurodegenerative, nutritional/metabolic, and psychiatric disorders that have been shown to be associated with olfactory deficits (for a review of these causes, see Murphy, Doty, & Duncan, 2003). In addition, injury, medications (for review see Doty & Bromley, 2004), environmental toxins (for review see Upadhyay & Holbrook, 2004), structural lesions, and medical/surgical interventions (for review see Murphy et al., 2003) can affect neural functioning. The Table 1 provides a small sampling of disorders that can be associated with olfactory loss. Given the vast number of disorders that have shown olfactory deficits, theories have been postulated that olfactory impairment may be a nonspecific marker of CNS dysfunction. This is likely not the case, given that the degree of deficit can differ widely among disorders, there exists significant range of deficits among patients within disorders, and the deficits can be unrelated to disease stage or magnitude of disease symptoms in some diseases but not others. Rather, it is probable that the presence and degree of olfactory involvement is related to the relative degree of structural or biochemical damage to the specific regions of the brain involved in olfactory transduction.

Anosmia. Table 1 Sampling of disorders associated with olfactory deficits

Alcoholism/Korsakoff's syndrome	Multiple sclerosis
Alzheimer's disease	Multiple system atrophy
Amyotrophic lateral sclerosis	Parkinson dementia complex of Guam
Corticobasal degeneration	Parkinson's disease
Dementia with Lewy bodies	Progressive supranuclear palsy
Diabetes mellitus	REM sleep behavior disorder
Down's syndrome	Restless leg syndrome
Frontotemporal dementia	Schizophrenia
Head injury	Sjögren's syndrome
Human immunodeficiency virus	Syphilis
Huntington's disease	Temporal lobe epilepsy
Mild cognitive impairment	Vascular dementia

Neurodegenerative Diseases

Interest in olfaction in neurodegenerative disorders began most intensely in the 1980s, with a focus on Alzheimer's disease (AD) and Parkinson's disease (PD). It was initially thought that these two disorders, which were often thought of as the prototypical examples of cortical and subcortical diseases, would share an early and notable deficit. Olfactory deficits were then identified in a variety of neurodegenerative disorders, making olfactory loss a nonspecific finding, though the degree of impairment may be useful in distinguishing some disorders. The cause of olfactory deficits in neurodegenerative diseases is unknown (for a review of potential causes, see Smutzer, Doty, Arnold, & Trojanowski, 2003). The deficits may be due at least in part to neurotransmitter system

alterations, especially dopamine and acetylcholine. Damage to central processing areas is also a likely explanation, particularly involvement of the olfactory bulb and tracts, as relevant neuropathologic changes (e.g., neurofibrillary tangles, amyloid plaques, dystrophic neurites, Lewy bodies, and disproportionate neuronal loss) are often seen in these areas. Other relevant central processing areas (e.g., entorhinal cortex), however, also show neuropathologic changes, as may peripheral structures (e.g., olfactory epithelium).

Parkinson's Disease Olfactory impairment is a prominent, common, and early feature of Parkinson's disease (PD; see Doty, 2003a, b, for a review). The deficits tend to be bilateral, and are more common than some of the hallmark symptoms of PD, such as tremor. Olfactory deficits may be present before the motor symptoms become evident, and are apparent with both threshold and identification tasks. The size of the effect is astounding (ranging from 1.17 to 12.15 in a meta-analysis; Mesholam, Moberg, Mahr, & Doty, 1998), though the majority of patients are not completely anosmic. Deficits do not appear to correlate with the extent of cognitive or motor involvement, do not respond to treatment, and do not appear to be progressive over time.

Other Parkinsonian Spectrum Disorders Other Parkinsonian disorders, such as corticobasal degeneration (CBD), multiple system atrophy, and progressive supranuclear palsy, are also associated with olfactory deficits, though the impairments tend to be more mild than is seen in PD (Doty, 2003a, b). These findings suggest that olfactory functioning may be useful in distinguishing PD from other parkinsonian disorders, though a more recent study of olfaction in CBD raises some question of potentially more notable deficit in this disorder than was previously described (Pardini, Huey, Cavanagh, & Grafman, 2009).

Alzheimer's Disease and Mild Cognitive Impairment There has been fairly good consistency in the literature for most of the studies examining olfaction in Alzheimer's disease (AD; see Doty, 2003a, b, for a review). The size of the effect is extremely large, ranging from 0.98 to 8.55 in a meta-analysis (Mesholam et al., 1998), though, as in PD, patients are typically not completely anosmic. Odor identification deficits are always found; odor detection deficits are more inconsistently demonstrated and may be a later symptom. The odor identification deficit does not seem to be primarily due to a general cognitive deficit and deficits worsen with disease progression. Although group studies have shown consistent deficits in odor identification, it should be noted that the presence of deficits is not a universal finding among patients with AD, making odor identification tests imperfect screening instruments for the disorder.

Odor identification has also been studied recently in patients with mild cognitive impairment (MCI) and cognitively intact older adults with and without genetic risk for future cognitive decline. Several longitudinal studies have demonstrated that odor identification has a strong relationship with memory performance, even in healthy older adults performing within normal limits on cognitive measures (Devanand et al., 2000; Wilson et al., 2007). These studies also show that odor identification is a unique and significant predictor of future cognitive decline above and beyond baseline memory performance, as well as a good predictor of conversion to dementia in patients with MCI. In cross-sectional studies of MCI subtypes, patients with both amnestic and non-amnestic subtypes perform modestly worse than healthy older adults but better than patients with dementia (Devanand et al., in press; Westervelt, Bruce, Coon, & Tremont, 2008). In using olfactory performance to distinguish MCI subtypes, results are mixed, though when significant differences have been found between subtypes, the magnitude of the difference is of questionable clinical significance. Together, these studies suggest that when a notable olfactory deficit is observed in patients with MCI, there is substantial risk of future decline. However, odor identification measures may not be particularly clinically useful in early detection or early differential diagnosis for the modal patient.

Dementia with Lewy Bodies Olfaction in dementia with Lewy bodies (DLB) was first described in a study that crudely measured anosmia with a brief detection task (McShane et al., 2001). Forty percent of patients with DLB were found to be anosmic, in contrast with 16% of patients with AD, and 6% of the healthy controls. The presence of smell loss was not found to be associated with concurrent AD and DLB pathology on autopsy. Subsequent studies confirmed anosmia to be more common in DLB than in AD, with anosmia present in 56–65% of patients with DLB (and some degree of smell loss in nearly 90%), but in only 11–23% of AD patients (Olichney et al., 2005; Westervelt, Stern, & Tremont, 2003). Assessment of anosmia has been shown to improve the sensitivity of diagnostic criteria for DLB, with minimal loss of specificity (Olichney et al., 2005). Combined, these few studies raise the possibility that olfactory measures may be useful in distinguishing AD from DLB.

Other Dementias Olfactory deficits have also been described in other dementias, including recent, consistent findings of smell deficits in frontotemporal dementia that are generally of the magnitude of deficits seen in AD (Luzzi et al., 2007; McLaughlin & Westervelt, 2008; Pardini et al., 2009), and, in vascular dementia to a similar or lesser extent to that seen in AD (Gray, Staples, Murren, Dhariwal, & Bentham, 2001; Knupfer & Spiegel, 1986).

Head Injury

Olfactory loss is fairly common following head injury (for review, see Costanza, DiNardo, & Reiter, 2003), with the incidence of anosmia ranging from approximately 5 to 60%. These latter estimates represent the incidence among patients with severe head injury, though total anosmia can occur even after very mild injury. Partial or unilateral loss may be less likely to be detected than total anosmia. Deficits may be caused by a variety of mechanisms, including sinus/nasal injury, shearing of the olfactory nerve, or contusion/hemorrhage in central processing regions. In regard to shear injuries, the axons of the olfactory receptor cells are particularly susceptible to injury as they pass through the body ridges of the cribiform plate. Coup and contra-coup forces are likely to result in anosmia, with occipital blows most frequently causing smell loss.

Schizophrenia

Olfactory deficits have been well-studied in schizophrenia (for review, see Doty, 2003a, b). Deficits have been shown to be of lesser magnitude than typically seen in AD and PD, progress with disease duration, and are most associated with negative symptoms of the disease. In patients showing olfactory deficits, the impairments appear early in the disease, perhaps in prodromal stages. There does not appear to be any notable relationship with antipsychotic medication use or cigarette smoking. Odor identification deficits correlate most strongly with measures of executive functioning in this population, rather than those of medial temporal lobe functioning. All aspects of olfaction appear to be impaired (i.e., identification, threshold, discrimination, and memory).

Evaluation

Clinical History

Obtaining a detailed clinical history is critical in assessing olfactory deficits. Symptoms should be clearly defined, and the clinician should attempt to determine the extent and duration of the perceived loss, as well as the occurrence of any event associated with the deficit (e.g., head injury, illness). Fluctuations in symptoms may be most suggestive of obstructive causes, but need to be distinguished from paroxysmal events. Medical history should be carefully assessed, as multiple medical conditions and medications may be associated with olfactory alterations. Referral for an ENT evaluation may be warranted. Olfactory hallucinations, in particular, require careful work-up as they may be indicative of seizure or tumor, and are less likely of primary psychiatric origin.

Classes of Assessment

There are three classes of olfactory assessment methods: psychophysical, electrophysiological, and psychophysiological, with psychophysical assessment being the most common and most clinically relevant.

Psychophysiological

Psychophysiological assessment of olfactory abilities relies on the measurement of changes in the autonomic nervous system after presentation of an odorous stimuli, through such methods as heart rate and blood pressure. These methods are rarely used.

Electrophysiological

Electrophysiological assessments examine electrical activity generated in response to an odorant and are primarily research tools. Electro-olfactograms (EOG) use electrodes placed on the human olfactory epithelium to directly assess olfactory abilities. Olfactory event-related potentials (ERP) are recorded from the scalp surface, measuring electroencephalographic activity after presentation of brief, precisely defined odorous stimuli. For example, chemosensory ERP's can be obtained after stimulation of olfactory nerve (olfactory ERPs) or the trigeminal nerve (somatosensory ERPs). Absence of olfactory ERPs in presence of somatosensory ERPs suggests olfactory deficits. These measures are sensitive to age and gender effects. Chemosensory evoked potentials are unable to discern where the impairment is within the olfactory pathway, but are considered among the only objective ways of establishing smell loss.

Psychophysical

Psychophysical methods are the most commonly used assessment practices in both clinical and research settings. In these techniques, stimuli are presented, and the patient or participant reports their perception (detection, discrimination, identification); this category can be further sub-divided into threshold and suprathreshold tasks.

Threshold Testing

Threshold testing is used to determine at what concentration a patient or participant can accurately detect the presence of an odor. Two methods have been developed to determine this threshold: the method of limits procedure and the single staircase procedure. In the method of limits procedure, a low concentration of a specific odor is presented, and the concentration is increased until it can be detected. In the single staircase procedure, the concentration is increased following trials in which the participant cannot detect the odor, and decreased following correct detection. There are commercially available smell threshold tests, for example, using felt-tipped pens and squeeze bottles. Olfactometers can be used to present precise amounts of odorants through constant airflow. However, many of these techniques can be cumbersome for clinical use.

Suprathreshold Tasks

Suprathreshold tasks include rating scales/magnitude estimation scales, odor identification tasks, and odor memory/recognition tasks. When using rating scales, the participant rates the amount of the attribute perceived (e.g., pleasantness); these may include category scales (which category describes sensation) and line scales (placement of mark on line with descriptors). When using a magnitude estimation scales, a participant will assign a number to stimuli in relation to relative intensity.

Odor Identification Tasks *Odor identification tasks* also suprathreshold tasks, require participants to identify odors, often by presenting scratch-and-sniff items, tinctures in jars, or odorant-soaked tampons. These tasks almost invariably include multiple choice options, as odor identification is otherwise extremely challenging even for individuals with intact olfactory abilities. These tasks are easy to administer and the most frequent type of task used in clinical settings, but can be somewhat costly depending on the task. The most widely used odor identification task is the University of Pennsylvania Smell Identification Task (UPSIT), which consists 40 micro-encapsulated odorants presented in a 4-option, multiple choice format. Other, briefer measures include 12-item versions (e.g., Cross-Cultural Smell Identification Test/Brief Smell Identification Test (BSIT), the BSIT-A designed especially for AD, the BSIT-B designed especially for PD) and a 3-item screen (Pocket Smell Test). The UPSIT and BSIT both have associated norms. Sniffin' Sticks includes both a threshold task and an odor identification task, and is extensively normed in European samples (Hummell, Kobal, Gudziol, & Mackay-Sim, 2007).

Odor Memory Test *Odor memory test* involve having the individual smell an odor (or group of odors), and after a specified period of time, recognize the odor from a set of distracters. Often, novel, non-descript odors are utilized to minimize the ability to label, and interference tasks are introduced during delays to minimize rehearsal of the odor labels/qualifiers.

Other Olfactory Assessment Tools

The Sniff Magnitude Test

The sniff magnitude test is a recently developed clinical measure of olfaction based on the reflex-like reduction in sniffing that occurs in response to detection of odors (especially unpleasant odors), but does not occur when sniffing non-odorized air (Frank, Dulay, & Gestland, 2003). This response is observed in people with normal sense of smell, but is absent in those with anosmia. The task involves having the patient sniff a canister that releases either a blank or an odor, while wearing a nasal cannula connected to a device to measure the negative pressure created by the sniff. The test is quick to administer (about 5 min) and has minimal, if any, reliance on cognition, linguistic ability, and familiarity of odors.

Neuroimaging

Imaging, particularly MRI, is clearly important for identification of structural lesions that may be impinging on the olfactory system, or in assisting in diagnosis of other neurologic disorders that may account for smell loss. CT is frequently used in identifying sinonasal disease. MRI can also be useful in evaluating changes in olfactory bulb volume due to viral, traumatic, or idiopathic olfactory dysfunction, with good relationship demonstrated between objective olfactometry (with chemosensory evoked potentials) and bulb volume. Functional scans, in particular fMRI and PET, are also often used as research tools in studying the functional organization of olfaction. These studies have shown involvement in the amygdala, piriform cortex, OFC, insula, anterior cingulate, thalamus, caudate, subiculum, upper pons, and cerebellar vermis, with different activation patterns depending on the nature of the task (e.g., sniffing, smelling single odors, discrimination, identification, etc.).

Treatment

Treatment is most promising in patients with smell loss associated with conduction problems. For example,

antibiotic treatment, steroids, and allergy management may be helpful in reducing deficits associated with inflammatory disease. Surgical removal of other obstructions, such as nasal polyps, can also be effective in restoring olfactory ability. In contrast, treatment of sensorineural/central neural problems is often less effective. Exceptions may include resection of tumors impinging on the olfactory system and, in some cases, resection of epileptogenic foci associated with olfactory seizures. Iatrogenic effects of medications are typically reversible with discontinuation of the medication and eventual improvement in smell is expected after cessation of smoking. Recent work also suggests that olfactory training may improve olfaction in some patients (Hummel et al., 2009). Zinc or vitamin therapies are at times prescribed to treat olfactory loss, but there is little evidence of benefit in the absence of associated deficiencies. Typically, the more severe and long-standing the smell loss, the less likely recovery is in sensorineural/central neural disorders. Especially for individuals who do not respond to treatment, education about the safety implications of smell loss is important, given concerns of the patient's failure to detect hazardous odors (e.g., smoke) or spoiled food. Nutritional status may also be compromised in patients with olfactory deficits, and use of flavor enhancements in foods can be helpful in improving food intake (Schiffman, 2000).

Cross References

- ► Cranial Nerves
- ► Olfaction
- ► Olfactory Bulb
- ► Olfactory Tract

References and Readings

Costanza, R. M., DiNardo, L. J., & Reiter, E. R. (2003). Head injury and olfaction. In R. L. Doty (Ed.), *Handbook of olfaction and gustation* (2nd ed.). New York: Marcel Dekker.

Devanand, D. P., Michaels-Marston, K. S., Liu, X., Pelton, G. H., Padilla, M., Marder, K., et al. (2000). Olfactory deficits in patients with mild cognitive impairment predict Alzheimer's disease at follow-up. *American Journal of Psychiatry, 157*, 1344–1405.

Devanand, D. P., Tabert, M. H., Cuasay, K., Manly, J. J., Schupf, N., Brickman, A. M., et al. (in press). Olfactory identification deficits and MCI in a multi-ethnic elderly community sample. *Neurobiology of Aging*.

Doty, R. L. (2003a). Odor perception in neurodegenerative diseases. In R. L. Doty (Ed.), *Handbook of olfaction and gustation* (2nd ed.). New York: Marcel Dekker.

Doty, R. L. (Ed.). (2003b). *Handbook of olfaction and gustation* (2nd ed.). New York: Marcel Dekker.

Doty, R. L., & Bromley, S. M. (2004). Effects of drugs on olfaction and taste. *Otolaryngologic Clinics of North America, 37*, 1229–1254.

Frank, R. A., Dulay, M. F., & Gestland, R. C. (2003). Assessment of the Sniff Magnitude Test as a clinical test of olfactory function. *Physiology & Behavior, 78*, 195–204.

Gotfried, J. A., & Zald, D. H. (2005). On the scent of human olfactory orbitofrontal cortex: Meta-analysis and comparison to non-human primates. *Brain Research Brain Research Review, 50*, 287–304.

Gray, A. J., Staples, V., Murren, K., Dhariwal, A., & Bentham, P. (2001). Olfactory identification is impaired in clinic-based patients with vascular dementia and senile dementia of the Alzheimer type. *International Journal of Geriatric Psychiatry, 16*, 513–517.

Hummell, T., Kobal, G., Gudziol, H., & Mackay-Sim, A. (2007). Normative data for the "sniffin'sticks" including tests of odor identification, odor discrimination, and olfactory thresholds: an upgrade based on a group of more than 3000 subjects. *European Archives of Otorhinolaryngology, 264*, 237–243.

Hummel, T., Rissom, K., Reden, J., Hähner, A., Weidenbecher, M., & Hüttenbrink, K. B. (2009). Effects of olfactory training in patients with olfactory loss. *Laryngoscope, 119*, 496–499.

Knupfer, L., & Spiegel, R. (1986). Differences in olfactory test performance between normal aged, Alzheimer and vascular type dementia individuals. *International Journal of Geriatric Psychiatry, 1*, 3–14.

Luzzi, S., Snowden, J. S., Neary, D., Coccia, M., Provinciali, L., & Lambon Ralph, M. A. (2007). Distinct patterns of olfactory impairment in Alzheimer's disease, semantic dementia, frontotemporal dementia, and corticobasal degeneration. *Neuropsychologia, 45*, 1823–1831.

McLaughlin, N., & Westervelt, H. J. (2008). Odor identification deficits in frontotemporal dementia: A preliminary study. *Archives of Clinical Neuropsychology, 23*, 119–123.

McShane, R. H., Nagy, Z., Esiri, M. M., King, E., Joachim, C., Sullivan, N., et al. (2001). Anosmia in dementia is associated with Lewy bodies rather than Alzheimer's pathology. *Journal of Neurology, Neurosurgery, and Psychiatry, 70*, 739–743.

Mesholam, R. I., Moberg, P. H., Mahr, R. N., & Doty, R. L. (1998). Olfaction in neurodegenerative disease. A meta-analysis of olfactory functioning in Alzheimer's and Parkinson's diseases. *Archives of Neurology, 55*, 84–90.

Murphy, C., Doty, R. L., & Duncan, H. J. (2003). Clinical disorders of olfaction. In R. L. Doty (Ed.), *Handbook of olfaction and gustation* (2nd ed.). New York: Marcel Dekker.

Murphy, C., Schubert, C. R., Cruickshanks, K. J., Klein, B. E., Klein, R., & Nondahl, D. M. (2002). Prevalence of olfactory impairment in older adults. *Journal of the American Medical Association, 288*, 2307–2312.

Olichney, J. M., Murphy, C., Hofstetter, C. R., Foster, K., Hansen, L. A., Thal, L. J., et al. (2005). Anosmia is very common in the Lewy body variant of Alzheimer's disease. *Journal of Neurology, Neurosurgery, and Psychiatry, 76*, 1342–1347.

Pardini, M., Huey, E. D., Cavanagh, A. L., & Grafman, J. (2009). Olfactory function in corticobasal syndrome and frontotemporal dementia. *Archives of Neurology, 66*, 92–96.

Schiffman, S. S. (2000). Intensification of sensory properties of food for the elderly. *Journal of Nutrition, 130*, 9275–9305.

Smutzer, G. S., Doty, R. L., Arnold, S. E., & Trojanowski, J. Q. (2003). Olfactory system neuropathology in Alzheimer's disease Parkinson's disease, and schizophrenia. In R. L. Doty (Ed.), *Handbook of olfaction and gustation* (2nd ed.). New York: Marcel Dekker.

Upadhyay, U. D., & Holbrook, E. H. (2004). Olfactory loss as a result of toxic exposure. *Otolaryngologic Clinics of North America, 37*, 1185–1207.
Westervelt, H. J., Bruce, J. M., Coon, W. G., & Tremont, G. (2008). Odor identification in mild cognitive impairment subtypes. *Journal of Clinical and Experimental Neuropsychology, 30*, 151–156.
Westervelt, H. J., Stern, R. A., & Tremont, G. (2003). Odor identification deficits in diffuse Lewy body disease. *Cognitive and Behavioral Neurology, 16*, 93–99.
Wilson, R. S., Schneider, J. A., Arnold, S. E., Tang, Y., Boyle, P. A., & Bennett, D. A. (2007). Olfactory identification and incidence of mild cognitive impairment in older age. *Archives of General Psychiatry, 64*, 802–808.

Anosodiaphoria

John E. Mendoza
Tulane University Medical Center
New Orleans, LA, USA

Definition

Anosodiaphoria is defined as the failure to fully appreciate the significance of a neurological deficit as a result of a brain lesion.

Current Knowledge

Following certain injuries to the brain, most commonly strokes in the right hemisphere, a patient may fail to recognize (deny) the resulting neurological deficit(s), such as paralysis. This latter condition is known as anosognosia. With time, patients typically show increased awareness of the deficit. For example, if asked, they might acknowledge that a stroke has occurred and that their ability to use their arm or leg has been affected. However, the patient might fail to fully appreciate the extent or functional implications of the deficit, attribute it to another more benign factor (such as being right-handed), or otherwise appear relatively unconcerned about it. This latter condition has been termed anosodiaphoria (Adair, Schwartz, & Barrett, 2003; Critchley, 1969). Thus, while acknowledging that his arm and/or leg are/is "weak," a patient may talk about his plans to return to work in the near future, although that may be totally unrealistic, given the severity of his condition and the nature of his work. There does not appear to be any clear consensus as to the etiology of this condition, the level of denial of which might be seen to vary from one day to the next. The more common hypotheses are that the anosodiaphoria likely reflects the same type of neglect or inattention that results in the original anosognosia, only less severe, is a result of a general emotional flattening or indifference that can follow right hemispheric lesions, or a combination of the two. (Heilman, Blonder, Bowers, & Valenstein, 2003).

Cross References

► Anosognosia
► Denial (of Illness)

References and Readings

Adair, J. C., Schwartz, R. L., & Barrett, A. M. (2003). Anosognosia. In K. Heilman & E. Valenstein (Eds.), *Clinical neuropsychology* (4th ed., pp. 185–214). New York: Oxford University Press.
Critchley, M. (1969). *The parietal lobes.* New York: Hafner.
Heilman, K. M., Blonder, L. X., Bowers, D., & Valenstein, E. (2003). Emotional disorders associated with neurological diseases. In K. M. Heilman & E. Valenstein (Eds.), *Clinical neuropsychology* (4th ed., pp. 447–478). New York: Oxford University Press.
Prigatano, G. P., & Schacter, D. L. (Eds.), (1991). *Awareness of deficit after brain injury.* New York: Oxford.

Anosognosia

Kenneth M. Heilman
University of Florida College of Medicine and the Malcom Randall Veteran's Affairs Medical Center
Gainesville, FL, USA

Synonyms

Self-awareness

Definition

Anosognosia is a disorder characterized by denial of illness or lack of awareness of disability.

Historical Background

In the clinic, it is very common to see patients who suffer with a neurological disease, such as stroke, but who

appear to deny illness or be unaware of their disabilities. Seneca, the Stoic philosopher noted this about 2,000 years ago, but the first modern description of a patient with unawareness-denial was by von Monakow (1885). Although there were other investigators who wrote about this striking disorder, it was Babinski (1914), who coined the term *anosognosia*. This word comes from three roots: a = without, noso = disease, gnosis = knowledge. In addition to describing patients who were unaware of their illness or disability, Babinski described other patients who appeared to be aware but remained unconcerned. He called this disorder, *anosodiaphoria*.

There are many forms of anosognosia and these forms are related to the nature of a patient's disability. When Babinski first used this term, the patients he described denied or were unaware of their hemiparesis. Anton (1898) described patients who were unable to see because they had destroyed their primary visual cortex, but were unaware or denied their blindness. Patients with Korsakoff's amnesic disorder are unaware of their memory loss and aphasic patients such as those with Wernicke's aphasia appear to be unaware of their jargon speech.

Current Knowledge

Although of great academic interest, the presence of anosognosia or anosodiaphoria has important medical implications. For example, there are now treatments for stroke that must be given within hours of the onset of symptoms. The patients who are unaware of their disabilities or undervalue their importance might not seek immediate medial attention. In addition, people who have disabilities but are not aware of these disabilities might inadvertently injure themselves and/or others. Rehabilitation works best, when patients are strongly motivated to get well. When a person is either unconcerned or unaware of their disabilities, they are not motivated and unmotivated patients are less likely to benefit from these treatments. They might even refuse to undergo rehabilitation and they might not take their medications that can reduce their disability or possibly prevent further possible brain damage.

Possible Mechanisms of Anosognosia for Hemiplegia

Patients with hemispheric strokes often develop an inability to use the arm-hand on the contralesional side of their body (hemiparesis). Many of these patients will be unaware of their weakness and when asked about the presence of weakness, they will deny this disability. Several, not mutually exclusive, mechanisms have been used to explain this phenomenon.

Psychological denial. Weinstein and Kahn (1955) who brought modern attention to this syndrome, posited that for many people having a stroke with weakness was a psychologically traumatic event, and the means by which some people deal with this trauma is to use psychological denial. To test this hypothesis, Weinstein and Kahn studied patients who had anosognosia and found that even before their stroke these patients frequently used this denial defense mechanism.

Some investigators have noted that anosognosia for hemiplegia is more often associated with a left than right hemiparesis. The psychological denial theory of anosognosia cannot explain this asymmetry. Many patients with left hemisphere injury, however, are aphasic and have problems with both the comprehension of questions (What is wrong with you? Are you weak?) as well as speaking–answering questions. Thus, Weinstein and Kahn thought what appeared to be a hemispheric asymmetry was induced by a sampling bias.

Using selective hemispheric anesthesia (the Wada study) and questioning the patient after they recover from anesthesia revealed that unawareness of the hemiplegia (anosognosia) was more common with the right than left hemisphere anesthesia (Gilmore et al., 1992). After the selective hemispheric anesthesia has worn off there is no aphasia or a need for psychological denial. The right–left hemisphere asymmetries found were within subjects, and thus premorbid personality can also not account for this asymmetry. Although this study suggests that denial cannot entirely explain anosognosia for hemiplegia, denial might be used by many people to help deal with diseases and disabilities.

Failure of feedback. To know something is impaired, a person requires feedback. Many investigators have suggested that it is a failure of feedback, induced by either sensory loss (e.g., proprioception and hemianopia) or inattention neglect, spatial or personal, that accounts for anosognosia of hemiplegia. That inattention neglect is more commonly associated with right hemisphere injury might also account for the asymmetries of anosognosia.

Studies from our laboratory have revealed when undergoing selective right hemisphere anesthesia, during the time these patients demonstrate shoulder weakness their shoulder proprioception is intact. To learn if this disorder could be related to neglect, spatial or personal, we brought their hemiplegic left forelimb over to the right

side of their body and to their right visual field. To make certain subjects see their hand, we wrote a number on their hand and subjects were able to read these numbers. Despite these strategies many, but not all, patients still denied weakness of that hand. Thus, a failure of feedback can only explain anosognosia in some patients. In support of this postulate, several investigators have reported dissociations between the presence of spatial neglect and anosognosia.

Asomatognosia hypothesis. While patients with personal neglect might be unaware of the parts of their body, patients with asomatognosia do not feel or claim that certain body parts belong to them. It has been posited that asomatognosia is caused by the alteration of the brain's representation of the body, a body schema. Like spatial and personal neglect, asomatognosia is more commonly associated with right than left hemisphere lesions. If patients with right hemisphere injury do not believe their left arm-hand belongs to them, they will not recognize their own weakness. During right hemispheric anesthesia, the patients with left hemiplegia were shown their left hand or someone else's left hand in a restricted view box that projected to their right visual field. The patients were asked if the hand they were viewing was their own or another person's hand. We found that there were some patients who had anosognosia who also had asomatognosia, but only a small proportion. Thus, asomatognosia can also not fully account for this disorder.

Disconnection hypothesis. When a patient with a complete callosal disconnection receives a stimulus to the left visual field or on the left side of the body and is asked to tell the examiner the nature of the stimulus, the left language–speech hemisphere often confabulates a response. Geschwind (1965) noted that large right hemisphere lesions can both injure the right hemisphere's cortex and intrahemispheric networks, as well as induce a interhemispheric disconnection. Thus, when asked about weakness, the left hemisphere which is disconnected from the right will confabulate a response – "I am not weak." The observation mentioned above, where during the right hemisphere anesthesia the patient's left hand is brought over to the right visual field and thus has access to the left language–speech dominant hemisphere, also tests this disconnection hypothesis. As mentioned, in few patients when their arm could be visualized in the right visual field left hemisphere, they did recognize their weakness. In these cases, we cannot be sure if their anosognosia was induced by a failure in feedback or a disconnection. Future research will have to learn if these mechanisms can be dissociated. However, as mentioned above this procedure only helps a small minority of patients.

Phantom movements. Limb amputation is often associated with a perception that the limb is still present and this perception is thought to be related to the continued presence of a brain representation of that missing phantom limb. When patients with a hemiparesis are asked to move a limb, many often perceive that the paretic limb is moving, and this phantom movement in combination with impaired feedback might account for anosognosia. During selective hemispheric anesthesia (Wada test), we had blindfolded subjects with left hemiplegia attempt to raise their paretic left arm and we then asked them to raise their right (non-paretic) arm to the same level as they perceived left arm. Some of the patients we tested did raise their right arm, suggesting that they had phantom movements, but we found no significant relationship between phantom movements and anosognosia.

Intentional motor disorder. Patients with right hemisphere lesions often demonstrate contralesional limb akinesia also called motor neglect. Many of these patients do not attempt to spontaneously move their akinetic arm and while less common some do not even attempt to move this arm to command. Limb akinesia can occur both with and without a hemiplegia. Patients with limb akinesia might not discover that they are weak because they do not attempt to move this left arm. If they do not attempt to move this arm, they will not experience a dissociation between their expectations and performance, and it is this dissociation that alerts people that there is a problem. Providing external motivation such as suggestions or commands might entice patients to attempt a movement and with these commands some patients do discover their weakness. Electromyographic studies have also provided evidence in support of this akinesia hypothesis.

Summary. Based on the above discussion it appears that several mechanisms might contribute to the presence of anosognosia for hemiplegia.

Possible Mechanisms of Anosognosia for Amnesia and Cortical Blindness

Damage to three interconnected brain networks can produce amnesia, an impairment in the episodic memory system: (1) the medial temporal lobe – Papez circuit (e.g., hippocampus, entorhinal and perirhinal cortex, fornix, the mammillary bodies, the mammillothalamic tract, the anterior thalamus, and the retrosplenial cortex); (2) the dorsomedial thalamus; and (3) the basal forebrain (medial septal nucleus and the diagonal band of Broca), which provide acetylcholine to the hippocampus. Amnesic patients with medial temporal lesions are often aware

of their disability and patients with damage to the basal forebrain and to the medial thalamus are often unaware of their memory deficit.

The reason for this dichotomy is not fully known, but the dorsomedial thalamic nucleus is heavily connected with the frontal lobes and damage to this dorsomedial nucleus induces frontal dysfunction. Damage to the basal forebrain is also often associated with frontal dysfunction. Frontal lobe dysfunction is often associated with impaired recall but not recognition, suggesting that the problem is not with the consolidation of memories, but rather retrieval. The patients with amnesia from a thalamic or basal forebrain injury, more often confabulate memories than do those with medial temporal lobe damage. Since these patients retrieve memories and have no means of testing these memories' veracity, they might be unaware that their recall is incorrect and therefore they might be unaware of their memory disorder.

Blindness. Patients with Anton's syndrome have blindness from damage to their primary visual cortex, usually from stroke. These patients often deny their blindness, confabulate responses, and are unaware they are blind, anosognosic. The reason why these patients are not aware of their blindness is not known. We examined a patient with Anton's syndrome who had intact visual imagery. Perhaps since these patients have intact visual imagery and cannot receive visual input, this imagery is mistaken for online input.

Possible Mechanisms for Unawareness of Aphasia

Patients with Wernicke's aphasia speak in jargon, cannot comprehend, name, or repeat. Many are not aware that they are aphasic and that they are speaking in jargon. For example, we saw a patient, who when speaking jargon, became angry when he was not understood. It has been posited that Wernicke's aphasia is induced by injury to the phonological lexicon – a store of learned word sounds. To be aware that an error has been made, a person needs to have a normal representation of the targeted behavior. Since patients with Wernicke's aphasia have destroyed their representations of word sounds when they speak jargon, they have no representations with which to compare their speech and are thus unaware of their errors.

We have also reported patients who appear to have an intact input lexicon (e.g., can understand speech) but who make phonological errors and are not aware that they made these errors. If these patients' speech is recorded and played back to them, they do detect their errors, suggesting that their unawareness might have been related to not being able to closely attend to their output. These aphasic patients might have focused their attention on what they were attempting to say rather than how they said it.

Future Directions

Anosognosia, the failure to recognize a disease or a disability, might delay treatment, interfere with rehabilitation, and put people in danger. Patients might be anosognosic for a variety of neurological disorders such as weakness, sensory loss, personal and spatial neglect, memory loss, and aphasia. There appears to be a variety of mechanism that might account for anosognosia including psychological denial, impaired and false feedback, alterations of the body schema, failures to test systems, and to initiate behaviors. Future research is needed. In addition to continuing to define and test possible mechanisms, effective treatments for these disorders are needed.

Cross References

- ▶ Attention
- ▶ Awareness
- ▶ Consciousness
- ▶ Impaired Self-Awareness

References and Readings

Anton, G. (1898). Blindheit nach beiderseitiger Gehirnerkrankung mit Verlust der Orienterung in Raume. *Mitt. Ver. Arzte Steirmark, 33*, 41–46.

Babinski, J. (1914). Contribution à l'etude des troubles mentaux dans l'hémiplégie organique cérébrale (anosognosie). *Revue Neurologique, 27*, 845–847.

Clare, L., & Halligan, P. (Eds.). (2006). *Pathologies of awareness: Bridging the gap between theory and practice.* New York: Psychology Press.

Geschwind, N. (1965). Disconnexion syndromes in animals and man. *Brain, 88*, 237–294, 585–644.

Gilmore, R. L., Heilman, K. M., Schmidt, R. P., Fennell, E. M., & Quisling, R. (1992). Anosognosia during Wada testing. *Neurology, 42*, 925–927.

Prigatano, G. P., & Schacter, D. L. (1991). *Awareness of deficit after brain injury: Clinical and theoretical issues.* New York: Oxford University Press.

von Monakow, C. (1885). Experimentelle und pathologisch-anatomische Untersuchungen über die Beziehungen der sogenannten Sehphäre zu

den infrakorticalen Opticuscentren und zum N. opticus. *Archiv fur Psychiatrie und Nervenkrankheiten, 16*, 151–199.
Weinstein, E. A., & Kahn, R. L. (1955). *Denial of illness: Symbolic and physiological aspects.* Springfield, IL: Charles C. Thomas.

Anosphrasia

► Anosmia

ANOVA

► Analysis of Variance

Anoxia

Bruce J. Diamond
William Paterson University
Wayne, NJ, USA

Synonyms

Oxygen deficiency; Severe hypoxia

Definition

Anoxia refers to a hypoxia (i.e., deficiency in the oxygenation of the arterial blood) of sufficient severity to result in permanent neurologic damage (Webster's New Explorer Medical Dictionary, 2006). The brain has little to no reserve of oxygen or glucose, consequently an anoxic episode of 4–6 min can result in neuronal cell death or necrosis because of impairment in cellular metabolism. In contrast to anoxia, hypoxia refers to a reduction in oxygenation, rather than a complete loss of oxygenation (Zillmer & Spiers, 2001).

Etiology

Anoxia can result from a number of conditions including cardiac arrest, carbon monoxide poisoning, stroke, brain injury, and complications due to anesthesia. It is thought that cells exposed to anoxia release glutamate. The CA1 cells of the hippocampus contain high concentrations of glutamate and they are particularly vulnerable to subnormal oxygenation levels. Therefore, it appears that the action of glutamate on these cells is the putative mechanism mediating cell death in this region of the hippocampus and helps explain many of the signs and symptoms associated with anoxia (Bonner & Bonner, 1991).

Signs and Symptoms

Anoxia often results in impairments in memory, executive, and motor function. This is likely due to the fact that anoxia is associated with damage to limbic and subcortical regions, in addition to the frontal lobes and the cerebellum (Golden, Zillmer, & Spiers, 1992).

Neuropsychological and Psychological Outcomes

Anoxia can result in impairments in anterograde memory (which in its most severe form may manifest as an amnestic disorder). Presenting symptoms may also include impairments in awareness and affect as well as confabulatory behavior. Anoxia associated with cardiac arrest may include amnesia, in addition to bibrachial paresis, cortical blindness, and visual agnosia. Carbon monoxide poisoning may be associated with affective disturbances as well as cortical and anoxia induced dysfunction (Aminoff, Simon, & Greenberg, 2005).

Cross References

► Carbon Monoxide Poisoning
► Glutamate
► Hippocampus

References and Readings

Aminoff, M. J., Simon, R. P., & Greenberg, D. A. (2005). *Clinical neurology.* New York: McGraw-Hill.
Bonner, J. S., & Bonner, J. J. (1991). *The little black book of neurology: A manual for neurologic house officers.* (2nd ed.). St Louis: Mosby-Year Book.
Golden, C. J., Zillmer, E. A., & Spiers, M. V. (1992). *Neuropsychological assessment and intervention.* Springfield, IL: Charles C.Thomas.
Webster's new explorer medical dictionary (New Edition). (2006). Springfield, MA: Merriam-Webster.
Zillmer, E. A., & Spiers, M. V. (2001). *Principles of neuropsychology.* Belmont, CA: Wadsworth/Thomson Learning.

Anoxic Encepathopathy

► Anoxia

Antagonist

► Receptor Spectrum

Anterior Aphasia

► Broca's Aphasia

Anterior Cerebral Artery

Bruce J. Diamond
William Paterson University
Wayne, NJ, USA

Synonyms

ACA; Cerebral artery

Definition

The anterior cerebral artery (ACA) arises as the medial branch of the bifurcation of the internal carotid artery (ICA) (Sawada & Kazui, 1995) and supplies the anterior three-quarters of the medial surface of the frontal and parietal lobes, the anterior 80% of the corpus callosum, the frontal basal cerebral cortex, the anterior diencephalon, and deep structures. Innervated areas also include the medial-orbital surface of the frontal lobe, frontal pole, and a small strip of the lateral surface of the cerebral hemisphere along the superior border (Ropper, Brown, Adams, & Victor, 2005). The largest branch (Heubner's artery) supplies the head of the caudate, the anterior globus pallidus, and the anterior limb of the internal capsule.

Categories

The ACA can be divided into five segments A1–A5, although it should be noted that some of the literature is describing the A1 segment when referring to the ACA (Sawada & Kazui, 1995).

Medical, Neuropsychological, and Psychological Symptoms

Infarctions in the territory of this artery are associated with a variety of clinical signs and symptoms involving gait, limb sensation, abulia, lack of spontaneous activity, urinary incontinence, frontal and memory impairments, in addition to emotional dysregulation (apathy) (Brust, 1995).

Cross References

► Anterior Communicating Artery

References and Readings

Brust, J. C. M. (1995). Agitation and delirium. In J. Bogousslavsky, & L. Caplan (Eds.), *Stroke syndromes* (pp. 134–139). Cambridge: Cambridge University Press.

Ropper, A. H., Brown, R. H., Adams, R. D., & Victor, M. (2005). *Adams & Victor's principles of neurology.* New York: McGraw-Hill.

Sawada, T., & Kazui, S. (1995). Anterior cerebral artery. In J. Bogousslavsky, & L. Caplan (Eds.), *Stroke syndromes* (pp. 235–246). Cambridge: Cambridge University Press.

Anterior Cingulate Cortex

Ronald A. Cohen, Anna MacKay-Brandt
Brown University
Providence, RI, USA

Synonyms

ACC

Structure

The anterior cingulate cortex (ACC) is a mesocortical paralimbic area located anterior to the corpus callosum

and posterior to the prefrontal cortex. The ACC was once viewed as a single limbic structure, forming an important part of the "Papez" circuit, though in reality analysis of its cytoarchitecture indicates that it consists of regions with different cell types. Its cell characteristics are agranular, and therefore are distinct from the cortex.

The ACC encompasses several Broadmann areas, including areas 24, 25, 32, and 33. The ACC wraps around the corpus callosum, having the appearance of a collar or belt. In fact, the term cingulum means belt in Latin. A large volume of the ventral ACC consists of Area 24, which merges with the posterior cingulate cortex (Area 23) along the posterior half of the corpus callosum. The division between the ACC and posterior cingulate is undifferentiated to a large extent, though these areas can be separated based on the cortical layer IV in the posterior cingulate. Anterior to Area 24 is the subgenual cortex (Area 25), which may be considered to be distinct from other ACC areas. Anterior to this region is the dorsal ACC, including areas 32 and 33. The midanterior section of the ACC is often termed midcingulate (mACC), while the more posterior section is termed perigenual cingulate (pACC). These areas have distinct cell characteristics, and there is strong evidence of functional differences across subareas of the ACC.

Primary afferent input to the ACC is received via axons from the midline and intralaminar thalamic nuclei, with the anterior nucleus receiving input from mamillary neurons, which in turn has projections from the subiculum. The ACC is associated with a large white-matter bundle, the cingulum, through which signals are transmitted to other limbic areas. As a paralimbic area, the ACC is a transition area between subcortical and limbic structures, such as the amygdala and cortical areas, most notably in the frontal lobes. The posterior ACC has heavy input from the amygdala, whereas the mid-ACC receives greater input from parietal areas. Connections between the ACC and the mesial, ventral, and orbital frontal areas appear to be particularly important for emotional and behavioral regulation.

Function

Current knowledge regarding the functions of the ACC has its origins in the psychosurgical efforts of the mid-twentieth century. At that time, the role of the frontal lobes in emotion and behavioral control were recognized, and frontal lobotomy was experimented with as a means of treating a variety of psychiatric conditions, including severe depression and schizophrenia. While frontal lobotomy resulted in a reduction in agitation and other severe psychiatric symptoms, surgical removal of the frontal lobe caused severe cognitive dysfunction. Given that the orbital frontal region was considered to be particularly important for the control of impulses and emotional regulation, subsequent psychosurgical approaches typically restricted ablation to these areas, often through leukotomy. Unfortunately, patients undergoing this procedure often exhibited marked personality change, with flattening of affect, apathy, and other undesirable effects. A third generation of psychosurgical procedures ensued with efforts to target brain areas more selectively. The ACC was a point of focus because of its association with both limbic areas as well as the frontal cortex. Beginning in the late 1950s, cingulotomy was developed as an alternative to frontal ablation. Early studies suggested that it had few adverse cognitive effects, and that it seemed helpful for certain patients, particularly those with intractable obsessive–compulsive symptoms, chronic pain, and opiate dependence. There was also some evidence that it was helpful for patients with severe chronic depression, though the basis for these effects may relate to reductions in emotional tension, obsessive thought processes, and other depression-associated problems.

Literature on the psychosurgical effects of cingulotomy provided compelling evidence that the ACC plays a role in human emotional experience and regulation. Furthermore, there is also evidence that the ACC influences autonomic nervous system response, including heart rate, blood pressure, and galvanic skin response, with these responses showing alterations in the rate of habituation following cingulotomy (Cohen et al., 1995). Yet, most early studies of the effects of cingulotomy suggested that the ACC had little impact on intellectual ability or most neuropsychological functions. Postsurgery patients tended not to experience significant memory, language, or visual change. Subsequent controlled studies indicated that while these functions are largely spared following cingulotomy, there are alterations in some attention-related functions, most notably attentional focus, intention, and response selection and control (Cohen et al., 2001). These changes correspond with reductions in emotional tension and distress, and also a tendency for reduced self-initiation of behavior (Cohen et al., 2001).

Recent experimental evidence suggests a functional dissociation between the posterior and middle ACC. The mid-ACC plays a role in response selection and control, including intention and planning to act or to engage in cognitive operations. It has also been implicated in

processing new motor programs, working memory, and mismatch detection. In contrast, the posterior ACC appears to play a more direct role in emotional processing, though these areas are likely highly interconnected, enabling the integration of emotional and attentional processes (Bush, Luu, & Posner, 2000).

Interest in the functional significance of ACC increased dramatically with the advent of functional neuroimaging methods. Activation of the ACC is evident across a wide range of tasks. In fact, it is among the most responsive areas of the brain on fMRI. This probably reflects the fact that it plays an increased role when tasks require motivation and drive to complete and where there is demand for attentional effort and focus.

The ACC plays a significant role in response to the conflict during cognitive tasks associated with decision making and the need to resolve competing or discrepant information (Botvinick et al., 1999). Some cognitive neuroscientists argue that conflict monitoring is the primary function of the ACC, though it seems likely that this capacity is closely associated with the broader functions of regulation of drive, emotion, attention, and response intention; and selection, initiation, and persistence relative to situational demands.

Illness

Focal brain diseases affecting only the ACC are rare. However, the ACC is vulnerable to the effects of tumor, stroke, and other neurological conditions involving anterior cortical infarction or mass action. Unilateral ablation of the ACC in laboratory studies of primates, and also secondary to stroke, has been shown to produce hemineglect syndrome, providing further evidence that the ACC plays an important role in attention. There is evidence of ACC dysfunction secondary to atrophy associated with neurodegenerative conditions, such as Alzheimer's disease, which may contribute to symptoms of apathy and behavioral inertia in certain patients. However, these changes are usually part of a much more global pattern of brain abnormality.

The ACC plays a more obvious role in psychiatric illness and also the range of normal behavior. Activation of the ACC occurs in association with increased levels of distress and emotional tension and anxiety. It also tends to be associated with obsessive rumination and preoccupation with internal states and signals, such as pain and impulses to seek reward. Accordingly, the ACC has been implicated in substance abuse, including opiate addiction and nicotine dependence. Citalopram binds to the serotonin transporter at very high levels in the posterior ACC, which may account for the effects of this type of drug on reducing mood, anxiety, and pain symptoms. There is also evidence that functional response of the ACC varies as a function of risk-reward dynamics, appetitive state, and motivation. Neuroimaging studies have begun to point to its role in a variety of behavior problems, such as obesity and inactivity.

Cross References

- ▶ Apathy
- ▶ Executive Function
- ▶ Intention
- ▶ Psychosurgery

References and Readings

Ballentine, H. T. Jr., Levey, B. A., Dagi, T. F., & Diriunas, I. B. (1977). Neurosurgical treatment in psychiatry, pain, and epilepsy. In W. H. Sweet, S. Obrador, & J. G. Martin-Rodriques (Eds.), *Cingulotomy for psychiatric illness: Report of 13 years experience* (pp. 333–353). Baltimore, MD: University Park Press.

Bush, G., Luu, P., & Posner, M. I. (2000). Cognitive and emotional influences in anterior cingulate cortex. *Trends in Cognitive Sciences, 4*(6), 215–222.

Botvinick, M., Nystrom, L. E., Fissell, K., Carter, C. S., & Cohen, J. D. (1999). Conflict monitoring versus selection-for-action in anterior cingulate cortex. *Nature, 402*(6758), 179–181.

Cohen, R. A., Kaplan, R. F., Meadows, M. E., & Wilkinson, H. (1994). Habituation and sensitization of the orienting response following bilateral anterior cingulotomy. *Neuropsychologia, 32*(5), 609–617.

Cohen, R. A., Kaplan, R. F., Zuffante, P., Moser, D. J., Jenkins, M. A., Salloway, S., et al. (1999). Alteration of intention and self-initiated action associated with bilateral anterior cingulotomy. *Journal of Neuropsychiatry and Clinical Neurosciences, 11*(4), 444–453.

Cohen, R. A., Paul, R., Zawacki, T. M., Moser, D. J., Sweet, L., & Wilkinson, H. (2001). Emotional and personality changes following cingulotomy. *Emotion, 1*(1), 38–50.

Devinsky, O., Morrell, M. J., & Vogt, B. A. (1995). Contributions of anterior cingulate cortex to behaviour. *Brain, 118*(Pt. 1), 279–306.

Anterior Cingulate System

- ▶ Mesial Frontal System

A

Anterior Commissure

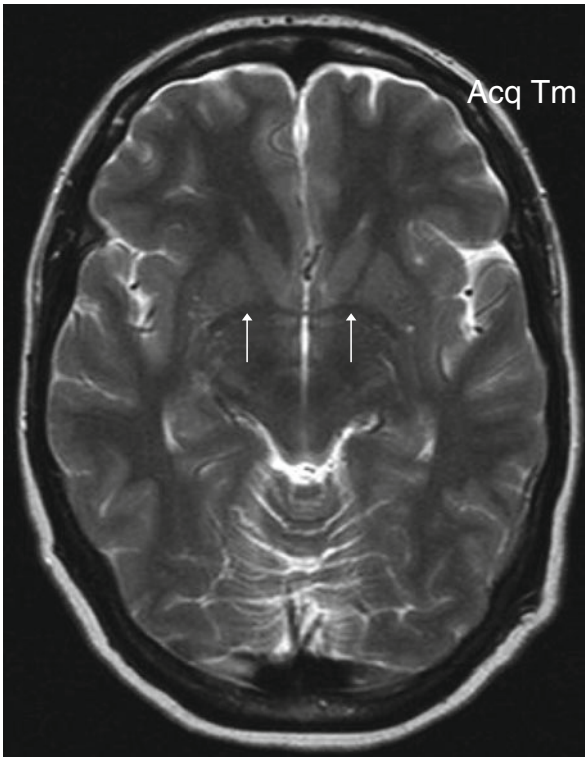
John E. Mendoza
Tulane University Medical Center
New Orleans, LA, USA

Synonyms

Interhemispheric commissure

Definition

A relatively small commissure in the basal forebrain lying above the optic chiasm and anterior to the main columns of the fornix that connects homologous areas of the middle and inferior temporal gyri, including parts of the olfactory cortices (Fig. 1).



Anterior Commissure. Figure 1

Anterior Communicating Artery

Bruce J. Diamond
William Paterson University
Wayne, NJ, USA

Synonyms

Communicating artery; ACoA

Description

The anterior communicating artery (ACoA) interconnects the two anterior cerebral arteries just rostral to the optic chiasm and resides at the anterior portion of the Circle of Willis.

Ruptured ACoA aneurysms may impact a variety of neurologic, neuropsychological, and psychological functions. This may, in part, be due to the fact that the perforating branches of the ACoA supply the anterior hypothalamus, mesial anterior commissure, lamina termininalis, and areas implicated in executive function, memory, and affect (e.g., fornix and basal forebrain, septal nuclei, nucleus accumbens, diagonal band, and the medial substantia innominata) (DeLuca & Diamond, 1995; Sawada & Kazui, 1995). The profound memory disorders that may be associated with ACoA aneurysm rupture do not appear to directly involve neuroanatomic areas traditionally implicated in amnesia, which makes the ACoA artery of both clinical and theoretical interest.

Etiology

ACoA aneurysms may develop as a result of trauma, infections, degenerative diseases, or a congenital defect (Parkin & Leng, 1993). Aneurysms often become symptomatic as a result of subarachnoid hemorrhage (SAH) following rupture (Riina, Lemole, & Spetzler, 2002). SAH has an overall incidence of 10 to 16 per 100,000 and is a major cause of mortality and morbidity (Clinchot, Kaplan, Murray, & Pease, 1994).

Mechanisms

Ruptured ACoA aneurysms alter the hemodynamic circulation of the anterior portion of the Circle of Willis, often

resulting in cerebral infarction and impairments in cognition, personality, and functional activities (DeLuca & Diamond, 1995; McCormick, 1984). Damage to the basal forebrain region may help account for many of the cognitive impairments that are observed in ACoA aneurysm due to the fact that the basal forebrain region contains cholinergic neurons that project to the hippocampus and amygdala, via the medial forebrain bundle to the entire cerebral cortex. Damage to this area would, therefore, particularly interfere with cholinergic activation of structures and circuits implicated in memory within the medial temporal lobe (Schnider & Landis, 1995). Moreover, vascular compromise of the perforating branches of the ACoA are believed to impact functional areas (e.g., executive function, memory, and affect) that are innervated by these vascular branches. There is general agreement in the literature suggesting that personality changes following ACoA aneurysm are a result of frontal lobe dysfunction, particularly in the medio-basal zones along the distribution of the anterior cerebral artery. The subcallosal perforating artery has, in fact, been implicated in and may mediate personality changes and memory impairments.

Epidemiological Factors

Rupture of cerebral aneurysms strikes at a mean age of 50 years and accounts for 5–10% of all strokes (Dombovy, Drew-Cates, & Serdans, 1998), and approximately 85–95% of all aneurysms develop at the anterior portion of the cerebral arterial supply, primarily at the Circle of Willis (Adams & Biller, 1992; Ropper, Brown, Adams, & Victor, 2005). The ACoA is one of the most common sites of cerebral aneurysm and is the most frequent site of cerebral infarct following aneurysm rupture (DeLuca & Diamond, 1995; McCormick, 1984). About 30–40% of cerebral aneurysms affect the ACoA artery, and 90% of cases are asymptomatic (Beeckmans, Vancoillie, & Michiels, 1998; Manconi, Paolino, Casetta, & Granieri, 2001) with various reports suggesting that the incidence of rupture is highest between 40 and 70 years of age (McCormick, 1984; Sethi, Moore, Dervin, Clifton, & MacSweeney, 2000) and that rupture occurs more frequently in females (i.e., 60% of cases) (Adams & Biller, 1992).

Natural History, Prognostic Factors, and Outcomes

With respect to impairment and chronicity, acute ACoA patients are more impaired than chronic ones with differences most notable on tests of executive and memory function. Relationships between recovery of executive function and temporal gradients in retrograde amnesia have been reported, with improvements in executive function accompanied by parallel improvements in the severity of retrograde amnesia. Improvement in the recall of complex visual-spatial information and an enhanced ability to benefit from an executive learning strategy have also been reported with little improvement on traditional measures of memory or executive function (Diamond, DeLuca, & Kelley, 1997a). Recovery from neuropsychological disturbances is generally poorer in patients with ventral frontal lesion compared to those with basal forebrain and striate lesions.

Surgical outcome and prognosis following aneurysms depend on multiple factors (e.g., initial clinical status, localization of aneurysm, age, and the morphological characteristics of the aneurysm). Comparisons of clipping versus endovascular embolization procedures have shown that, in a number of studies, clipped patients have more severe cognitive impairments than embolization patients and that 33% of clipped patients had impairments in memory and executive functioning (Chan, Ho, & Poon, 2002).

Generally, the severity of cognitive impairment has predictive value for functional status particularly with respect to levels of required supervision at discharge (Saciri & Kos, 2002).

Some work suggests that recovery of executive function and not short- and long-term memory may, in fact, be the best predictor of the ability to return to work (DeLuca & Diamond, 1995).

Neuropsychological and Psychological Outcomes

Neuropsychological

It is generally concluded that verbal intellectual skills, language functions, visuo-spatial skills, and attention/concentration are within normal limits or only mildly impaired, although complex concentration appears to be reduced. An increased sensitivity to interference may be a defining feature among ACoA amnesics and between ACoA amnesics and diencephalic-mesial and temporal amnesics. More severe impairments are seen in delayed versus immediate memory and in executive function (DeLuca & Diamond, 1995). Impairments in spatio-temporal discrimination appear similar to other populations with frontal lobe dysfunction (Schacter, 1987).

Implicit memory involving data- and concept-driven retrieval processes and behavioral and physiological indices (Diamond, Mayes, & Meudell, 1996) appears to be relatively intact, although the evidence is sparse. Procedural memory on serial reaction time and mirror-reading tasks also appears to be preserved.

Spatial working memory in ACoA patients has been reported to be impaired, and the impairment profile is similar to patients with temporal lobe excisions. ACoA patients have displayed impairments in semantic memory, and difficulties to both the acquisition and recall of verbal information showing little initial learning, a passive learning style, a flat learning slope, and impaired recognition discrimination, in addition to emitting a high number of intrusions and false positives (Diamond, DeLuca, & Kelley, 1997b). ACoAs have shown impairments in information processing and autobiographical memory (especially for events associated with context). ACoA amnesics (i.e., with putative basal forebrain damage) have exhibited impairments in delay eyeblink classical conditioning (Myers et al., 2001), event-related potentials (ERPs), and in prospective remembering.

Psychological

ACoAs have displayed increased risk-taking on tasks in which choices were associated with different magnitudes of reward and punishment. Confabulation is observed in a subset of ACoA aneurysm patients and is manifested by statements or actions that involve distortions that are unintentional (Moscovitch & Melo, 1997) with two distinct types of confabulation generally recognized in the literature, spontaneous and provoked (Kopelman, 1987). The key difference between provoked and spontaneous confabulation is that in spontaneous confabulation the confabulation guides actions. Recovery from confabulation appears to parallel improvement in temporal context confusion, and recovery can occur in the absence of significant improvement on traditional tests of memory and executive function.

With respect to psychosocial outcomes, a significant percentage of SAH survivors are left with cognitive, emotional, and behavioral changes that can profoundly impact their daily lives. Compared with controls, SAH patients display an increased incidence of mood disturbance, cognitive impairment, and lower levels of independence, and participation on measures that reflect social functioning. Levels of productive employment are generally reduced and many patients show clinically significant posttraumatic stress symptomatology (see Table 1 for a list of neuropsychological and psychological impairments).

Assessment and Treatment

Given the wide range of impairments associated with ACoA aneurysm, it may be advisable for clinicians to use assessments that focus on those impairments that

Anterior Communicating Artery. Table 1 Neuropsychological and psychological impairments associated with ACoA aneurysm

Awareness, self-monitoring, and personality	Memory	Cognitive/executive/mood
Disorders of awareness:	Semantic Memory	Attention
Confabulation	Prospective Memory	Cognitive Estimation
Anosognosia	Visuo-Spatial	Decision-making
Executive dysfunction	Working Memory	Dual Task Performance
Intrusions	Recall/Recognition	Learning
		Proactive Interference
		Mood
		Delay eyeblink conditioning
Motor/sensory	**Language**	**Autonomic and event-related potentials (ERP)**
Paraparesis syndrome	Dichotic listening	Electrocardiogram (ECG)
Visuomotor skill learning	Phonemic fluency	Delayed ERP (P300): Auditory
Alien hand syndrome	Verbal fluency	Delayed ERP (P300): Visual
Visual-sensory function (unruptured aneurysms)		Prolonged QTc intervals

are most salient and have the greatest impact on activities of daily living (ADLs). Impairments in memory, executive function, and attention/concentration as well as mood figure prominently following ACoA aneurysm rupture and should be part of routine assessment. For example, assessments should examine set-shifting (e.g., Wisconsin Card Sort Test (WCST) and Trails B), verbal and visual fluency (e.g., CFT/FAS and Design Fluency Test), verbal recall and recognition (e.g., California Verbal Learning Test (CVLT)), visual recall (e.g., Rey–Osterreith Complex Figure Test (ROCFT)), sustained attention (e.g., Cancellation Test), information processing speed (e.g., *n*-back tasks), and impaired abstraction (e.g., Cognitive Estimation Test (CET)).

In some cases, modification of existing assessment tools can be an effective way to enhance the assessment process. For example, the Rey–Osterrieth Organizational and Extended Memory (ROEM) test, which is a modification of the ROCFT, was reported to help identify mechanisms underlying the nature of the impaired memory in ACoA amnesics by using measures of recall and recognition (e.g., subunit recognition, spatial arrangement, and whole figure recognition). Moreover, encoding and recall were improved by using an executive organizational strategy, in addition to identifying patients who were more likely to benefit from such an intervention (Diamond, DeLuca, & Kelly, 1997a; Prignatano & DeLuca, 1999).

Some work suggests that cognitive rehabilitation can help increase compensatory strategies for attention and memory dysfunction and that rehabilitation can help improve professional activities as well as ADLs with positive rehabilitation outcomes primarily associated with changes in memory and attention. In a mixed sample of SAH patients, a majority of survivors who receive inpatient rehabilitation attain physical independence but impairments in cognition and ADLs persist in upwards of 40% of the patients (Dombovy, Drew-Cates, & Serdans, 1998). Patients have generally shown impairments 1–5 years poststroke, in visual short-term memory, reaction-time, verbal long-term memory, concentration, and language and information processing. Evaluation several years after SAH associated with ACoA aneurysm rupture has shown that cognitive problems negatively correlate with the level of community integration and that impairments in visual memory, verbal memory, and executive function are most frequently observed. Therefore, while being characterized as having a good outcome, many ACoA patients continue to exhibit persistent cognitive impairments that negatively impact psychosocial functioning (Ravnik et al., 2006).

Cross References

- ▶ Activities of Daily Living (ADL's)
- ▶ Amnesia
- ▶ Aneurysm
- ▶ Anterior Cerebral Artery
- ▶ Confabulation
- ▶ Executive Functioning
- ▶ Rey Complex Figure Test

References and Readings

Adams, H. P., & Biller, J. (1992). Hemorrhagic intracranial vascular disease. In A. B. Baker & R. J. Joynt (Eds.), *Clinical neurology* (vol. 2). Philadelphia: J. B. Lippincott.

Beeckmans, K., Vancoillie, P., & Michiels, K. (1998). Neuropsychological deficits in patients with an anterior communicating artery syndrome: A multiple case study. *Acta Neurologica Belgica, 98*(3), 266–278.

Chan, A., Ho, S., & Poon, W. S. (2002). Neuropsychological sequelae of patients treated with microsurgical clipping or endovascular embolization for anterior communicating artery aneurysm. *European Neurology, 47*, 37–44.

Clinchot, D. M., Kaplan, P., Murray, D. M., & Pease, W. S. (1994). Cerebral aneurysms and arteriovenous malformations: Implications for rehabilitation. *Archives of Physical Medicine and Rehabilitation, 75*(12), 1342–1351.

Cummings, J. L., & Trimble, M. R. (1995). *A concise guide to neuropsychiatry and behavioral neurology.* Washington, DC: American Psychiatric Press.

DeLuca, J., & Diamond, B. J. (1995). Aneurysm of the anterior communicating artery: A review of neuroanatomical and neuropsychological sequelae. *Journal of Clinical and Experimental Neuropsychology, 17*(1), 100–121.

Diamond, B. J., Mayes, A. R., & Meudell, P. (1996). Autonomic and recognition indices of aware and unaware memory in amnesics and healthy subjects. *Cortex, 32*, 439–459.

Diamond, B. J., DeLuca, J., & Kelley, S. M. (1997a). Executive and memory impairment in patients with anterior communicating artery aneurysm. *Brain and Cognition, 35*, 340–341.

Diamond, B. J., DeLuca, J., & Kelley, S. M. (1997b). Verbal learning in anterior communicating artery aneurysm and multiple sclerosis patients: Performance on the California verbal learning test. *Applied Neuropsychology. 4*, 89–98.

Dombovy, M. L., Drew-Cates, J., & Serdans, R. (1998). Recovery and rehabilitation following subarachnoid haemorrhage: Part II. Long-term follow-up. *Brain Injury, 12*(10), 887–894.

Kopelman, M. D. (1987). Two types of confabulation. *Journal of Neurology, Neurosurgery and Psychiatry, 50*(11), 1482–1487.

Manconi, M., Paolino, E., Casetta, I., & Granieri, E. (2001). Anosmia in a giant anterior communicating artery aneurysm. *Archives of Neurology, 58*(9), 1474–1475.

McCormick, W. F. (1984). Pathology and pathogenesis of intracranial saccular aneurysms. *Seminars in Neurology, 4*(3), 291–303.

Moscovitch, M., & Melo, B. (1997). Strategic retrieval and the frontal lobes: Evidence from confabulation and amnesia. *Neuropsychologia, 35*(7), 1017–1034.

Myers, C. E., DeLuca, J., Schultheis, M. T., Schnirman, G. M., Ermita, B. R., Diamond, B. J., Warren, S. G., & Gluck, M. (2001). Impaired delay eyeblink classical conditioning in individuals with anterograde amnesia resulting from anterior communicating artery aneurysm. *Behavioral Neuroscience, 115*(3), 560–570.

Parkin, A., & Leng R. C. (1993). *Neuropsychology of the amnestic syndrome:* Hove, U.K.: Lawrence Erlbaum.

Prignatano, G., & DeLuca, J. (1999). Methodological issues in research on neuropsychological and intellectual assessment. In P. C. Kendall, J. Butcher, & G. Holmbeck (Eds.), *Handbook of research methods in clinical psychology* (pp. 241–250). New York: Wiley.

Ravnik, J., Starovasnik, B., Šešok, S., Pirtošek3, Z., Švigelj, V., Bunc, G., et al. (2006). Long-term cognitive deficits in patients with good outcomes after aneurysmal subarachnoid hemorrhage from anterior communicating artery. *Croat Medical Journal, 47*, 253–263.

Riina, H. A., Lemole, G. M., Jr., & Spetzler, R. F. (2002). Anterior communicating artery aneurysms. *Neurosurgery, 51*(4), 993–996.

Ropper, A. H., Brown, R. H., Adams, R. D., & Victor, M. (2005). *Adams & Victor's principles of neurology.* New York: McGraw-Hill.

Saciri, B. M., & Kos, N. (2002). Aneurysmal subarachnoid haemorrhage: Outcomes of early rehabilitation after surgical repair of ruptured intracranial aneurysms. *Journal of Neurology Neurosurgery and Psychiatry, 72*(3), 334–337.

Sawada, T., & Kazui, S. (1995). Anterior cerebral artery. In J. Bogousslavsky & L. Caplan (Eds.), *Stroke Syndromes* (pp. 235–246). Cambridge: Cambridge University Press.

Schnider, A., & Landis, T. (1995). Memory loss. In J. Bogousslavsky & L. Caplan (Eds.), *Stroke syndromes* (pp. 145–150). Cambridge, MA: Cambridge University Press.

Schacter, D. L. (1987). Implicit memory: History and current status. *Journal of Experimental Psychology: Learning, Memory and Cognition, 13*, 501–518.

Sethi, H., Moore, A., Dervin, J., Clifton, A., & MacSweeney, J. E. (2000). Hydrocephalus: Comparison of clipping and embolization in aneurysm treatment. *Journal of Neurosurgery. 92*(6), 991–994.

Anterograde Amnesia

Ginette Lafleche, Mieke Verfaellie
VA Boston Healthcare System and Boston University School of Medicine
Boston, MA, USA

Short Description or Definition

Anterograde amnesia is an inability to recall or recognize events, facts, or concepts to which one was exposed following the onset of illness.

Brief Historical Background

Current scientific understanding of anterograde amnesia began largely with the study of patient HM. In 1953, at age 27, HM underwent bilateral resection of the medial temporal lobes for alleviation of refractory seizures, which had become progressively more severe following a head injury he had suffered at age 9. The resection was successful in reducing his seizures but, unexpectedly, following the treatment he was unable to remember his normal daily activities. For example, he could not recall eating his meal within minutes of having finished it, and he could not remember having had a conversation minutes after it ended. He was unable to remember his regular caregivers, even though he could converse and interact normally with them when they were present. These findings established that intact medial temporal lobes are critical for normal memory function. HM's medial temporal lobe resection had left him with a dense anterograde amnesia, despite his having intact intelligence, attention, language function, and social skills. With respect to his memory for the events that preceded his surgery, it was initially thought that his retrograde amnesia (▶ Retrograde Amnesia) was limited to approximately 2 years prior to the operation, but more recent findings indicate that he had a more extensive retrograde amnesia that extended to 11 years before the surgery. Subsequent neuropsychological studies of HM and other amnesic individuals have further informed our current understanding of both impaired and preserved memory function in amnesia (Corkin, 1984).

Neuropsychology of Anterograde Amnesia

Patients suffering from anterograde amnesia have great difficulty in bringing to mind information to which they were exposed following the onset of their illness. These patients have preserved immediate memory, in that they can hold in mind a current topic of conversation and can repeat a string of digits with no delay, but, following any distraction or delay, memory for the information is lost. Episodic memory or memory for personal events is severely impaired and, as a result, patients no longer form a record of their lives. The nature of this loss is global, in that it includes both verbal and nonverbal information in all sensory modalities. It encompasses both personally experienced events (episodic memory) and impersonal facts or concepts (semantic memory). Together these two forms of memory comprise declarative (or explicit) memory, and are what the plain term "memory" refers to in common usage. An important insight to arise from the study of patients with anterograde amnesia is that not all forms of long-term memory are impaired. Forms of

memory that do not require deliberate reference to a prior experience, often referred to as nondeclarative (or implicit) memory, remain intact.

Failure of declarative memory in amnesia can arise from a number of different etiologies. These include anoxia, herpes simplex encephalitis (HSE), anterior communicating artery aneurysm (ACoA), Wernicke-Korsakoff syndrome (WKS), and stroke. The amnesia is a direct consequence of damage to the medial temporal lobes (i.e., HSE; anoxia), the midline diencephalon (i.e., WKS; stroke), basal forebrain structures (i.e., ACoA), or some of the fiber tracts that link these regions. These amnesias are usually permanent. In contrast, in transient global amnesia (TGA) there is temporary dysfunction of memory-related brain structures including the hippocampal formation and thalamus. Episodes of TGA typically last no more than 24 h, after which the patient's new-learning returns to normal, but a permanent amnesic gap remains for the period of the attack (► Transient Global Amnesia).

The ability to remember newly encountered information depends on a number of stages, including the processing and representation of immediate experience (encoding), the transfer of that encoded information to long-term storage (consolidation), and its re-manifestation in consciousness upon deliberate recall (retrieval) at a later time. Disruption of any one of these stages could lead to anterograde amnesia. In patients with medial temporal or diencephalic lesions, encoding and retrieval are thought to be relatively intact. Such patients perform normally on intelligence tests, and on short-term memory tests, suggesting adequate encoding (Baddeley, 1995). Furthermore, impaired retrieval is unlikely to be the cause of their failed explicit memory, because memories from many years ago can still be retrieved. Therefore, it is assumed that their impairments reflect deficient consolidation. The medial temporal lobes, through interactions with neocortical regions, are thought to be critical for consolidation. They bind together into a coherent representation the different aspects of an event that are neocortically represented (Eichenbaum, 2006).

Generally, the size of the causative brain lesion is directly proportional to the density of the amnesia, but the specific location of the lesion will also impact on the nature of the memory impairment. For example, if the damage is limited to the hippocampal formation, performance on recall tasks is impaired, but performance on recognition tasks can remain intact (Mayes, Holdstock, Isaac, Hunkin & Roberts, 2002). To account for these findings, it has been suggested that two distinct processes contribute to explicit memory; the first is "recollection," the intentional, effortful process by which aspects of a past episode are recovered. The second is "familiarity," a subjective feeling that arises when information is processed fluently and comes to mind easily. Whereas performance on recall tasks depends on the ability to recollect contextually appropriate information, performance on recognition tasks can be supported by either recollection or familiarity. Thus, the pattern of performance of patients with limited hippocampal lesions is thought to reflect impaired recollection, but preserved familiarity. Such a pattern is consistent with findings from neuroimaging and neurophysiological studies that suggest that the hippocampus proper is critical for recollection, whereas familiarity is supported by the perirhinal cortex. If the damage is more extensive and extends beyond the hippocampus to include other medial temporal lobe structures such as the perirhinal cortex, then both recollection and familiarity are affected, leading to striking impairments on tests of recognition as well as recall.

The degree of impairment in new semantic learning is also a function of the extent of the medial temporal lobe lesion. Patients with injury limited to the hippocampus are able to acquire some new facts and concepts postmorbidly, although inefficiently, but patients with more extensive medial lobe damage show minimal ability to do so (Verfaellie, 2000).

In patients who suffered anoxia or a rupture of an aneurysm of the anterior communicating artery, frontal lobe impairments may be superimposed on the core amnesia (► Amnestic Syndromes). In such cases the anterograde amnesia will be exacerbated by additional impairments in encoding and retrieval. Executive functions such as planning, organizing, monitoring, and control of attention, all depend on the integrity of the frontal lobes. Executive impairments will interfere with the ability to mentally manipulate and organize information during deliberate encoding, and will also disrupt initiation and evaluation of memory search during effortful retrieval. The latter can lead to unusually high levels of intrusions in recall, or false alarms in recognition, a phenomenon known as enhanced susceptibility to false memory.

Despite such pervasive impairments in declarative memory, patients with anterograde amnesia show intact performance in a variety of forms of nondeclarative memory. These include procedural learning (the acquisition of new skills or habits), eyeblink conditioning (learning to blink the eyes in response to a tone because of the repeated association of the tone with an air puff to the eye), and repetition priming (improved accuracy or speed of

performance for stimuli to which an individual was recently exposed) (Verfaellie & Keane, 2002). These forms of nondeclarative memory depend on neural circuits in the basal ganglia, cerebellum, or neocortex that remain spared in amnesia (Squire, 1994).

Evaluation

Anterograde amnesia refers to a severe and permanent inability to learn new information in the presence of otherwise normal intelligence, attention span, perception, reasoning, and language ability. The evaluation of anterograde amnesia must therefore, as a first step, include a comprehensive neuropsychological work-up to determine whether other areas of cognitive functioning are intact and, if not, whether any deficits found contribute to the memory disorder. With regard to assessment of memory functioning itself, there are a variety of standardized tests available, and Lezak, Howieson, and Loring (2004) provide a comprehensive review of the most commonly used ones. Assessing performance on recall and recognition tests is an essential component of the evaluation, because their comparison can reveal the nature of the memory processes that are affected. Both verbal and nonverbal memory should be examined, and memory should be tested both shortly after learning and following a longer delay, to assess the rate of forgetting. Other factors of diagnostic importance are a patient's sensitivity to interference and his or her ability to use organizational strategies at encoding and retrieval. While a comprehensive assessment of anterograde memory typically includes a variety of different tests, each developed for a specific purpose, the use of a single standardized memory battery that evaluates all major aspects of new learning can provide a good overview of memory functioning. The Wechsler Memory Scale-III (Wechsler, 1997) is probably the most widely-used instrument for this purpose. In addition to indices of Immediate Memory and General (Delayed) Memory, it provides an index of Working Memory, and, in patients with anterograde amnesia, a split on the order of 20 points is to be expected between Working Memory and Immediate/General Memory.

Treatment

Rehabilitation interventions in amnesia aim at increasing day-to-day functional adaptation and independence. A wide array of intervention techniques is available, and the choice among them should be informed by cognitive factors such as premorbid abilities and skills as well as post-morbid neuropsychological strengths and weaknesses, including the severity of amnesia. Contributing non-cognitive factors include premorbid lifestyle and habits, and educational background. Contributing emotional factors include insight and motivation, which are essential for any treatment choice, because the absence of either will undermine rehabilitation efforts.

Remediation of patients with severe amnesia relies largely on those aspects of memory that are preserved, such as procedural learning and priming. Techniques that capitalize on procedural learning use repetition to drill skills and habits, ranging from essential activities of daily living to simple assembly tasks and cognitive skills. Such skill learning is frequently involved when teaching a patient to use an external memory aid, such as a memory notebook, calendar, diary, appointment book, or written reminders. The memory notebook is a preferred compensatory instrument for amnesics because it is divided into sections that are personally tailored to a patient's life (i.e., daily tasks, future plans, notes section, and so on). More sophisticated technology, in the form of computerized paging systems, electronic assistants, alarms, and timers, is most useful for individuals who had some proficiency in the use of such devices premorbidly. Learning to use such devices de novo may pose high demands on working memory or episodic memory, which is problematic for memory disordered patients. In such instances, it is important to break the task down into small steps that can be practiced independently. Once the steps become automatized, they can then be gradually integrated.

Other methods rely on preserved priming abilities (Verfaellie, 2000). One technique is the vanishing cues technique, which has been used to teach amnesics computer-related vocabulary, business-related terms, and novel concepts, through gradual reduction of cues that elicit correct answers. Another technique is errorless learning. Error elimination requires explicit recollection of the learning episode, and thus densely amnesic patients have great difficulty eliminating errors. Their performance relies primarily on implicit memory, which typically leads to production of the strongest response. If that response is incorrect, the error is likely to be further strengthened across subsequent learning trials, thus interfering with learning the correct response.

For patients with milder memory impairments, strategies aimed at strengthening the impaired form of memory are more appropriate. Such patients may

benefit from rehearsal and re-learning of the material. Spaced repetitions, across different time intervals and different spatial locations, are especially beneficial as they enhance the likelihood that information will be richly encoded, thus enhancing the chances that a free-standing memory will be integrated with preexisting memories. For patients whose memory impairment reflects impairment in effortful encoding and retrieval, techniques that promote enhanced organization (e.g., chunking, thematic organization) and elaboration (e.g., verbal mnemonics, visual imagery) at the time of learning may be useful. In a sense, elaboration provides the learner with alternative retrieval routes that may enhance recall.

Cross References

► Amnesia
► Retrograde Amnesia

References and Readings

Baddeley, A. D. (1995). The psychology of memory. In A. D. Baddeley, B. A. Wilson, & F. N. Watts (Eds.), *Handbook of memory disorders* (pp. 3–25). New York: John Wiley & Sons.

Corkin, S. (1984). Lasting consequences of bilateral medial temporal lobectomy: Clinical course and experimental findings in H. M. *Seminars in Neurology, 4*, 249–259.

Eichenbaum, H. (2006). Memory binding in hippocampal relational networks. In H. D. Zimmer, A. Mecklinger, & U. Linderberger (Eds.), *Handbook of binding and memory: Perspectives from cognitive neuroscience* (pp. 25–51). New York: Oxford University Press.

Lezak, M. D., Howieson, D. B., & Loring, D. W. (2004). *Neuropsychological assessment* (4th ed.). New York: Oxford University Press.

Mayes, A. R., Holdstock, J. S., Isaac, C. L., Hunkin, N. M., & Roberts, N. (2002). Relative sparing of item recognition memory in a patient with adult-onset damage limited to the hippocampus. *Hippocampus, 12*, 325–340.

Squire, L. S. (1994). Declarative and nondeclarative memory: Multiple brain systems supporting learning and memory. In D. L. Schacter, & E. Tulving (Eds.), *Memory systems 1994* (pp. 203–232). Cambridge, MA: MIT Press.

Verfaellie, M. (2000). Semantic learning in amnesia. In L. S. Cermak (Ed.), *Handbook of neuropsychology* (2nd ed., pp. 335–354). Amsterdam: Elsevier Science.

Verfaellie, M., & Keane, M. M. (2002). Impaired and preserved memory processes in amnesia. In L. R. Squire, & D. L. Schacter (Eds.), *Neuropsychology of memory* (3rd ed., pp. 35–46). New York: Guilford Press.

Wechsler, D. (1997). *WMS-III manual*. New York: Psychological Corporation.

Anterolateral System

John E. Mendoza
Tulane University Medical Center
New Orleans, LA, USA

Synonyms

ALS; Spinothalamic tract

Definition

One of two ascending pathways in the spinal cord that carry conscious sensory information from the upper and lower extremities, trunk, and posterior portion of the head to the brain (the other being the lemniscal system).

Current Knowledge

Of the two ascending somatosensory pathways (the other being the posterior columns or lemniscal system) the anterolateral system (ALS) is the more primitive and polysynaptic and is primarily responsible for the sensations of pain, temperature, and crude ("less well defined") or simple touch. Input into the ALS is derived from both specialized cutaneous receptors and free nerve endings in the skin. These sensory impulses then travel centrally (toward the cord) in the peripheral nerves. Just outside the cord, the peripheral nerves bifurcate into the dorsal and ventral nerve roots. The dorsal roots, which carry sensory information, then synapse in the gray matter of the cord (dorsal horns) on the same side in which they enter. Secondary fibers then cross the midline of the cord in the ventral white commissure and ascend in the ventral–lateral portion of the spinal cord as the ventral and lateral spinothalamic tracts. While these two tracts were once described as carrying different and distinct types of sensory information, the current thinking is that they have extensive functional overlap and hence should be considered as a single anterolateral system. These second-order fibers of the ALS ascend in the ventral lateral portion of the cord and then in the lateral and later in the dorsolateral portions of the brainstem. These ascending pathways continue to ventral posterior lateral nucleus of the thalamus. From the thalamus, third-order neurons project to the somatosensory cortices in the parietal lobes of the

brain. Because the nerve fibers making up the ALS cross the midline within a few vertebral segments of where they enter the cord, lesions affecting the ALS will result in contralateral deficits.

Cross References

► Medial Lemniscus (Posterior Columns)

References and Readings

Mendoza, J. E., & Foundas, A. L. (2008). The somatosensory systems. In J. E. Mendoza & A. L. Foundas (Eds.), *Clinical neuroanatomy – A neurobehavioral approach* (pp. 23–47). New York: Springer.

Anti-Anxiety Drugs

► Anxiolytics

Anti-Anxiety Medications

► Anxiolytics

Anticholinergic

Mary Pat Murphy
MSN, CRRN
Paoli, PA, USA

Synonyms

Anticholinergic medications

Definition

Anticholinergic agents alter the balance of neurotransmitters in the central and peripheral nervous system inhibiting parasympathetic nerve impulses. Specifically, the agents diminish acetylcholine and allow for the increase of dopamine. Anticholinergic medications are divided into three categories based on their specific receptor targets in the nervous system and in other sites in the body: antimuscarinic, ganglionic blockers, and neuromuscular blockers. The receptor subtypes affect the brain, salivary glands, smooth muscle, and ciliary muscles of the eye. Categories of medications are clinically used for the antimuscarinic effects and include medications for urinary spasmodics and overactive bladder, anticholinergic antiparkinson's agents, antivertigo medications, gastrointestinal antispasmodics, mydriatic medications, and medications for bronchospasm. Another group of medications not primarily targeting the cholinergic receptors include sedating antihistamines, tricyclic antidepressants, muscle relaxants, some antipsychotics, antiarrythmics, and antiemetics. Neuropsychologists should be aware of the medications their patients are taking and the potential impact on neuropsychological test results. It is necessary to differentiate between medication side-effects and true consequences or neurologic disorder.

Anticholinergic. Table 1 Anticholinergic medications clinically used for the antimuscarinic effects

Medications for neurogenic bladder including urge incontinence, for overactive bladder	Oxybutynin (Ditropan), tolterodine (Detrol), trospium (Sanctura), solifenacin (Vesicare), darifenacin (Enablex)
Anticholinergic antiparkinson's medication	Benztropine (Cogentin), trihexyphenidyl (Artane)
Antivertigo medication	Meclizine (Antivert), scopolamine (Transderm Scop)
Gastrointestinal antispasmodics medications	Diphenoxylate/atropine (Lomotil), belladonna (Donnatal)
Medications for bronchospasm	Tiotropium (Spiriva), ipratropium (Atrovent)

Anticholinergic. Table 2 Anticholinergic medications not primarily targeting the cholinergic receptors

Sedating antihistamines	Diphenhydramine (Benadryl), hydroxyzine (Vistaril), cyproheptadine (Periactin)
Tricyclic antidepressants	Amoxaprine (Asendin), amytriptyline (Elavil), desipramine (Norpramin), imipramine (Tofranil), nortriptyline (Pamelor)
Certain antipsychotics	Clozapine (Clozeril), olanzapine (Zyprexia), risperidone (Risperdal)
Muscle relaxants	Dantrolene (Dantrium), cyclobenzaprine (Flexeril)

Current Knowledge

Anticholinergic medications are used in treating a variety of medical conditions. Anticholinergic drugs are used in treating a variety of conditions including Parkinson's disease and other Parkinsonian-like disorders; gastrointestinal disorders such as diverticulitis; respiratory disorders such as asthma; and genitourinary disorders such as prostatitis.

Side Effects

Anticholinergic side effects can be caused by a wide range of medications. Anticholinergic medications have peripheral and central side effects including dry mouth, blurred vision, urinary retention or difficulty initiating voiding, constipation or bowel obstruction, decreased sweating, increased heart rate, ataxia, increased body temperature, agitation, confusion, delirium, memory impairment, decreased attention, dizziness, and drowsiness.

Certain populations are at greater risk for adverse events related to anticholinergic medications. They include older adults who already experience a decrease in acetylcholine production; men with benign prostatic hypertrophy, patients with glaucoma, and individuals with dementia who are already taking cholinesterase inhibitors.

The elderly and patients with brain injury are often prescribed medications with anticholinergic properties to address medical issues for bladder management, increased muscle tone, and behavior (atypical antipsychotics). There may be a cumulative effect of taking multiple medications which act on the cholinergic system. Anticholinergic side effects in older adults include an increase in delirium, diminished ADLs, and decrease in cognition (Fick et al., 2003; Han et al., 2001).

Cross References

► Acetylcholine
► Dopamine
► Neurotransmitters

References and Readings

Fick, D. M., Cooper, J. W., Wade, W. E., Waller, J. L., Maclean, J. R., & Beers, M. H. (2003). Updating the Beers criteria for potentially inappropriate medication use in older adults: results of a US consensus panel of experts. *Archives of Internal Medicine, 163*(22), 2716–2724.

Han, L., McCusker, J., Cole, M., Abrahamowicz, M., Primeau, F., & Élie, M. (2001). Use of medications with anticholinergic effect predicts clinical severity of delirium symptoms in older medical inpatients. *Archives of Internal Medicine, 161*(8), 1099–1105.

Lieberman, J. A. (2004). Managing anticholinergic side effects. *Journal of Clinical Psychiatry, 6*(Suppl. 2), 20–23.

Anticholinergic Medications

► Anticholinergic

Anticholinesterase Inhibitors

JoAnn T. Tschanz[1], Katherine Treiber[1,2]
[1]Utah State University
Logan, UT, USA
[2]University of Massachusetts Medical School
Worcester, MA, USA

Synonyms

Acetylcholinesterase inhibitors; ACHE inhibitors; AchEIs; Cholinesterase inhibitors

Definition

Anticholinesterase inhibitors are a class of substances that affect the cholinergic neurotransmitter system and are often used for clinical purposes in the treatment of memory disorders such as Alzheimer's disease (AD). Nonclinical uses include agricultural applications such as pesticides and military applications such as the development of neurotoxins. Acetylcholine is normally released by the presynpatic neuron and activates receptors on the postsynaptic cell. Acetylcholinesterase is the primary enzyme that breaks down acetylcholine in the synaptic cleft. Cholinesterase inhibitors block the activity of this enzyme, allowing the neurotransmitter substance to remain in the synaptic cleft longer to stimulate postsynaptic receptors.

Current Knowledge

Clinical Indications

Cholinesterase inhibitors are often used in the treatment of memory and other cognitive disorders. In AD, degeneration of brain cholinergic neurons has been associated with progressive cognitive deterioration. Because cholinesterase inhibitors do not reverse or stop the progressive

degeneration of cholinergic neurons, their effectiveness is greatest early in the course of the disease, while existing neurons are able to continue to produce and release acetylcholine (Orgogozo, 2003). Other compounds such as memantine (which acts on the glutamatergic system) have been approved for use in moderate to severe dementia.

Formulation and Side Effects

Several cholinesterase inhibitors are available, such as donepezil, galantamine, and rivastigmine. The primary mode of intake is oral, although a cutaneous route through a dermal patch has been developed. Common side effects of cholinesterase inhibitors include nausea, vomiting, diarrhea, and anorexia. Less common are insomnia and cardiovascular symptoms such as bradycardia. Drug tolerability may be enhanced by varying dosing and titration rates to achieve therapeutic levels (Orgogozo, 2003).

Other Applications

In addition to its distribution in the brain, acetylcholine is also present at the neuromuscular junction and plays an important role in the body's motor functions. Cholinesterase inhibitors developed for agricultural or military applications may affect the motor system by causing an accumulation of acetylcholine at the neuromuscular junction leading to excessive excitation of muscles and a cessation of muscle contraction (due to overexcitation). Autonomic functions may also be affected due to cholinergic innervation of cardiac and smooth muscles. Thus, cholinesterase inhibitors are potent neurotoxins that are used as insecticides or in warfare (Iversen, Iversen, Bloom, & Roth, 2009).

Cross References

► Acetylcholine
► Alzheimer's Disease

References and Readings

Iversen, L. L., Iversen, S. D., Bloom, F. E., & Roth, R. H. (2009). *Acetylcholine. Introduction to neuropsychopharmacology* (pp. 128–149). New York: Oxford University Press.

Orgogozo, J.-M. (2003). Treatment of Alzheimer's disease with cholinesterase inhibitors. An update on currently used drugs. In K. Iqbal, & B. Winblad (Eds.), *Alzheimer's disease and related disorders: Research advances* (pp. 663–675). Bucharest: Ana Asian International Academy of Aging.

Anticoagulation

Elliot J. Roth
Northwestern University
Chicago, IL, USA

Synonyms

Antithrombotic therapy

Definition

Anticoagulation refers to the prevention of blood from clotting.

Current Knowledge

An anticoagulant is a chemical that prevents coagulation. The body contains a number of naturally occurring physiological anticoagulants, but other anticoagulants are used as pharmacological agents to prevent and treat thrombotic disorders such as coronary artery disease causing ischemic heart disease, cerebrovascular disease causing stroke, peripheral arterial disease causing limb ischemia, and venous thromboembolic disease.

Commonly used anticoagulation medications include warfarin (Coumadin®), heparin, and low molecular weight heparin compounds such as enoxaparin (Lovenox®), tinzaparin (Innohep®), and dalteparin (Fragmin®).

New anticoagulants are under development. Dosages of these medications can be adjusted using blood tests that measure the levels of certain clotting functions, which can be used to monitor the effectiveness of the medication regimen. Optimum ranges for the results of these tests are available for specific conditions and clinical situations.

Predictably, adverse effects of these medications are largely hemorrhagic in nature. Prolonged bleeding from simple superficial lacerations, internal hemorrhage into gastrointestinal system, brain, or muscles in the pelvis or leg occurs with greater frequency, depending on the level of anticoagulation. Rarely, a paradoxical thrombotic disorder might occur as a *result* of using one of these medications. On balance, the benefits of using certain anticoagulants in selected situations outweigh the risks of the medications, but primarily in controlled

circumstances when clinical and laboratory monitoring is feasible and when the patient does not have risk of falls, injuries, or other contraindications.

Cross References

- ▶ Atherosclerosis
- ▶ Central Venous Thrombosis
- ▶ Cerebral Embolism
- ▶ Heparin
- ▶ Thrombosis
- ▶ Venous Thrombosis
- ▶ Warfarin

References and Readings

Dentali, F., Douketis, J. D., Gianni, M., Lim, W., Crowther, M. A. (2007) Meta-analysis: Anticoagulant prophylaxis to prevent symptomatic venous thromboembolism in hospitalized medical patients. *Annals of Internal Medicine, 146*, 278–288.

Hirsh, J., Guyatt, G., Albers, G. W., Harrington, R., Schünemann, H. J. (2008). Executive summary: antithromotic and thrombolytic therapy, 8th Edition: American College of Chest Physicians evidence-based clinical practice guidelines. *Chest, 133*, 71S–105S.

Anticonvulsants

Mary Pat Murphy
MSN, CRRN
Paoli, PA, USA

Synonyms

Antiepileptic drugs (AED)

Definition

A group of medications used in the management of epilepsy.

Current Knowledge

The selection of an AED depends on the type of seizure, age of patient, and gender. According to the literature, monotherapy is the goal for the treatment of epilepsy, choosing medications targeting seizure control with fewest side effects. Monotherapy also makes it easier to monitor side effects. Usually, if one drug fails, another medication is trialed. If the initial AED fails, the physician typically will wean this medication and try another first-line drug. If monotherapy fails, polytherapy may be tried. The physician will maximize the first-line dose and then add a second-line medication. General monitoring for AEDs includes the frequency and severity of seizures, adverse events and side effects, and monitoring of plasma. The chart below identifies FDA indications for commonly used AEDs.

Mechanism of Action for AEDs

Phenytoin, carbamazepine, lamotrigine, gabapentin, topiramate, and valproate block sodium channel and impede generation of high-frequency action potentials. Some of the drugs may also reduce high-threshold calcium currents, resulting in a decrease in excitatory transmitter release. In therapeutic ranges, barbiturates and diazepam derivatives enhance GABA responses. Topiramate may enhance GABAergic inhibition. Gabapetin may promote nonsynaptic GABA release. Phenobarbital is a long-acting barbiturate with sedative, hypnotic, and anticonvulsant properties. It acts on the GABA receptors, increasing synaptic inhibition. This has the effect of

Anticonvulsants. Table 1 Commonly used AED

	Partial seizures	Tonic–clonic	Absence
First-line drugs	Carbamazepine	Valproate	Ethosuximide
	Phenytoin	Phenytoin	Valproate
	Valproate	Carbamazepine	
	Topiramate	Topiramate	
Second-line drugs (alternative therapy)			
	Primidone	Lamotrigine	
	Gabapentin	Gabapentin	
	Phenobarbital	Primidone	Clonazepam
	Primidone	Phenobarbital	Primidone
	Valproate	Topiramate	
	Felbamate (use when other alternative medications have failed)	Felbamate (use when other alternative medications have failed)	

elevating the seizure threshold and reducing the spread of seizure activity in the brain. Phenobarbital may also inhibit calcium channels.

First-Line Medications

Valproate (Depakote)

Indication

Labeled indications include control of epilepsy (seizures disorders). As an AED, it can be used as monotherapy and adjunctive treatment of tonic–clonic, partial complex seizures, and simple and complex absence seizures. It can be used as an adjunctive treatment in patients who have multiple types of seizures.

Contraindications

The medication should be prescribed cautiously for individuals with liver disease and urea cycle disorders and for pregnant women.

Adverse events/side effects

Weight gain, thrombocytopenia, and elevated liver enzymes may be dose related. When initially starting the medication, patients may complain of nausea and diarrhea. Hyperammonemia has been reported and may be present despite normal liver function testing. In the elderly, there is a possible increase in somnolence.

Drug interactions

Medications that **may increase valproate levels** include felbamate, rifampin, and chlorpromazine; medications that valproate may affect include carbamazepine, amitriptyline, nortriptyline, clonazepam, ethosuximide, lamotrigine, phenobarbital, phenytoin, tolbutamide, and lorazepam.

Phenytoin (Dilantin)

Indication

Phenytoin is the oldest and one of the most effective medications in the treatment of a wide range of seizure types. The labeled use is for tonic–clonic and partial complex seizures. It is often used as a first-line drug choice for monotherapy. The usual dose is 300 to 400 mg/day. An extended-release capsule allows for onetime a day dosing. The therapeutic range is 10–20.

Adverse events/side effects

Phenytoin can be administered intravenously. As a result, **specific adverse events/side effects** can include hypontension, bradycardia, dysrhythmias, and cardiac changes, as well as venous irritation and thrombophlebitis.

Other **adverse events/side effects** include gingival hyperplasia, hirstism, rash, hepatitis, megaloblastic anemia, thrombocytopenia, Stevens–Johnson syndrome, systemic lupus Erythematosus, and folic acid deficiency.

Drug interactions

Drug interactions are many and include (but are not limited to) chloramphenicol, dexamethasone, doxycycline, furosemide, haloperidol, meperidine, methadone, oral contraceptives, theophylline, and warfarin. Non-AEDs that effect phenytoin levels include alcohol, antacids, folic acid, rifampin, tube feedings, alcohol, cimetidine, fluoxetine, imipramine, INH, omeprazole, propoxyphene, sulfonamides, and trazadone.

Carbamazepine (Tegretol)

Indication

Carbamazepine is indicated as a first-line drug for use as an anticonvulsant for partial seizures, generalized tonic–clonic, and mixed seizures, but not absence seizures. It is generally nonsedating within therapeutic range. It is also indicated in the treatment of trigeminal neuralgia.

Adverse events/side effects

Adverse events associated with carbamazepine include aplastic anemia and agranulocytosis. Pretreatment hematology testing should be completed to obtain a baseline. The patient should be monitored and treatment should be discontinued with hematology changes. Stevens–Johnson syndrome (an exfoliating dermatitis) has been reported. Carbamazepine has mild anticholinergic properties, so patients with intraocular eye pressure should be monitored. Carbamazepine should not be used in pregnant women. Patients should be cautioned against drinking alcohol.

In the beginning of treatment, patients report side effects including dizziness, drowsiness, nausea, and vomiting.

Medications that affect carbamazepine plasma levels

Drugs that increase plasma levels include cimetidine, danazol, macrolides, erythromycin, troleandomycin, fluoxitine, nefazoned, loratadine, terfenadine, INH, propoxyphene, verapamil, grapedfruit juice, protease inhibitors, and valproate. Medications that **decrease** carbamazepine plasma levels include cisplatin, felbamate,

rifampin, phenobarbital, phenytoin, primidone, methsuximide, and theophylline.

Topamax (Topiramate)

Topiramate is considered effective as a monotherapy for individuals with partial complex or generalized tonic–clonic seizures. It is also effective as an adjunctive treatment for partial complex and generalized tonic–clonic seizures.

Adverse events/side effects

Metabolic acidosis is an **adverse event** associated with topiramate. Conditions that predispose individuals include renal disease, severe respiratory disorders, status epilepticus, and diarrhea. Measurement of baseline and periodic sodium bicarbonate is recommended. Other side effects/adverse events include kidney stones, paresthesia of the extremities, acute myopia and glaucoma, decreased sweating and hyperthermia, cognitive-related dysfunction, psychiatric/behavioral disturbances, and somnolence or fatigue.

Drug interactions

Concomitant administration of topiramate and valproate has been associated with hyperammonia. Topiramate concentrations affect phenytoin and valproate. Topiramate concentrations are affected by phenytoin, carbamazepine, valproate, and lamotrigine.

Ethosuximide (**Zarontin**) has been approved for absence (petit mal) seizures. Adverse events/side effects include blood dyscrasias; decreased cognition including drowsiness, dizziness, irritability, hyperactivity, and fatigue; and ataxia. There have been reports of increased tonic–clonic seizures.

Second-Line Medications

Gabapentin (Neurontin)

Gabapentin is effective as an adjunctive therapy in the treatment of partial seizures with and without generalization.

Adverse events/side effects

Include dizziness, ataxia, weight gain, gi upset, somnolence, and other symptoms of CNS depression.

Drug interactions

Antacids decrease their bioavailability.

Lamotrigine (Lamictal)

Lamotrigine is effective as monotherapy for individuals with partial complex seizures; it is also considered effective as an adjunctive therapy for partial complex seizures and generalized tonic–clonic seizures. It is thought to inhibit voltage-sensitive sodium channel mechanisms. It is well tolerated and does not seem to have cognitive altering side effects. A therapeutic plasma concentration has not been established for lamotrigine.

Side effects/adverse events

Include rash, fatigue, dizziness, diplopia, and ataxia. Angioedema, nystagmus, and hematuria also may occur.

Drug interactions

Medications that **decrease** lamotrigine's effectiveness include carbamazepine, valproate, phenobarbital, primidone, and acetaminophen.

Febamate (**Felbatol**) has been approved for adjunctive therapy or monotherapy for individuals with partial complex or tonic–clonic seizures. This medication is recommended when other therapies have been tried and have failed.

Adverse events/side effects

This medication potentially causes aplastic anemia or hepatotoxicity and should be used with extreme care by a knowledgeable physician when other therapies have been tried. Other side effects/adverse events include anorexia, vomiting, and insomnia.

Drug interactions

Felbatol affects phenytoin, valproate, and carbamazepine concentrations.

Barbiturates (Second Line)

Phenobarbital

Indication

Labeled indications include control of epilepsy (seizures disorders) and as a sedative/hypnotic medication for short-term treatment of insomnia. As an AED, it can be used as monotherapy in the treatment of generalized (tonic–clonic), simple, or partial complex seizures; for myoclonic epilepsy; and for neonatal and febrile seizures in children. It has also been prescribed for eclamptic seizures during pregnancy.

Contraindications

The medication should be prescribed cautiously for individuals with liver disease, CHF, and hypovolemic shock and for pregnant women. The medication does cause both physical and psychological drug dependence; for this reason, it is not a first-line medication of choice for individuals with drug dependence. If prescribed for sleep, it should not be used longer than 2 weeks and prescribed for the elderly because of its long half-life. Patients should avoid alcohol and other CNS depressants while taking phenobarbital. Other contraindications include preexisting CNS depression, severe uncontrolled pain (may mask symptoms) porphyria, and severe respiratory disease with obstruction or dyspnea. Abrupt discontinuation may cause seizures.

Adverse events/side effects

Adverse affects include sedation, ataxia, cognitive impairment, may cause a paradoxical effect including hyperactivity and problems with sleep, megablastic anemia (responds to folic acid) and rash, exfoliative dermatitis and Stevens-Johnson Syndrome.

Non-AEDs affected by phenobarbital

Phenobarbital may interfere with the effectiveness of *acetaminophen* and increase liver damage. The effectiveness of beta-blockers except Atenolol, Levobunolol, Metipranolol, and Nadolol, oral contraceptives, chloramphenicol, chlorpromazine, cimetidine, corticosteroids, cyclosporine, desipramine, doxycycline, folic acid, griseofulvin, haloperidol, meperidine, methadone, nortriptyline, quinidine, theophylline, and warfarin may be compromised when taking phenobarbital.

Non-AEDs affecting phenobarbital levels

Chloramphenicol, propoxyphene, and quinine may increase phenobarbital levels. Chlorpromazine, folic acid, and prochlorperazine may decrease phenobarbital levels. There may be increased toxicity with benzodiazapines, CNS depressants, and methylphenidate.

Primidone (Mysoline) is related in structure to barbiturates. It is used in the management of tonic–clonic, partial complex, and focal seizures. The adverse events/side affects and drug interactions are similar to phenobarbital.

Benzodiazepines

This class of medication is not typically used as first-line medications. As a class, they can produce CNS depression and behavioral changes. Other adverse reactions include tachycardia, chest pain, headache, constipation, nausea, and ataxia.

Medications include the following:

Clonazepam (Klonopin) is effective as an adjunctive medication for individuals with absence, tonic–clonic, and myoclonic seizures. Diazepam (Valium) and Lorazepam (Ativan) can be used to treat status epilepticus.

Cross References

- ▶ Epilepsy
- ▶ GABA
- ▶ Seizure

References and Readings

Lanctôt, K., Herrmann, N., Mazzotta, P., Khan, L., & Ingber, N. (2004). GABAergic function in Alzheimer's disease: Evidence for dysfunction and potential as a therapeutic target for the treatment of behavioural and psychological symptoms of Dementia. *Canadian Journal of Psychiatry, 49*(7), 439–453.

MacQueen, G., & Young, T. (2003). Cognitive effects of atypical antipsychotics: focus on bipolar spectrum disorders. *Bipolar Disorders, 5*, 53–61.

Yasseen, B., Colantonio, A., & Ratcliff, G. (2008). Prescription medication use in persons many years following traumatic brain injury. *Brain Injury, 22*(10), 752–757.

Antidepressant Responsive Disorders

- ▶ Unexplained Illness

Antidepressants

JoAnn T. Tschanz[1], Katherine Treiber[1,2]
[1]Utah State University
Logan, UT, USA
[2]University of Massachusetts Medical School
Worcester, MA, USA

Definition

Antidepressants are a class of medications that are used primarily in the treatment of clinically severe

mood or anxiety disorders. The majority of effective antidepressants currently in use enhance neurotransmission of serotonin and/or norepinephrine. Generally, this is achieved by blocking the reuptake of the neurotransmitter substance(s), inhibiting the enzymes responsible for its metabolism, or directly stimulating the postsynaptic receptors (Iversen, Iversen, Bloom, & Roth, 2009). Several antidepressants are also used in treating generalized anxiety disorder, panic disorder, and obsessive–compulsive disorder (Bourin & Lambert, 2002). Other conditions for which antidepressants have demonstrated efficacy include eating disorders (Powers & Bruty, 2009), neuropathic pain (O'Connor & Dworkin, 2009), stress incontinence, nocturnal eneuresis, ejaculatory disorders (Michel, Ruhe, de Groot, Castro, & Oelke, 2006), migraine headaches, fibromyalgia (Stone, Viera, & Parman, 2003), attention-deficit/hyperactivity disorder (Chung, Suzuki, & McGough, 2002), smoking, insomnia, and possibly pathological gambling (Grant & Grosz, 2004).

There are several classes of antidepressant medications. Tricyclic antidepressants (TCAs) block the reuptake of monoaminergic neurotransmitters and monoamine oxidase inhibitors (MAOIs) inhibit their metabolism. Other compounds are more selective in blocking the reuptake of specific neurotransmitters (selective serotonin reuptake inhibitors or SSRIs and noradrenergic reuptake inhibitors or NRIs). Compounds with dual serotonergic and noradrenergic actions have also been developed (Iversen et al., 2009).

Regardless of the type of antidepressant, the compounds are similar in their effectiveness and the time course of their effects. The lag between the initiation of antidepressant treatment and the alleviation of symptoms generally takes 2–6 weeks for the maximal response. The delay in treatment response suggests that the therapeutic effects may result from "downstream" events that reflect the brain's adaptation to treatment (Iversen et al., 2009). Alternative treatments with a shorter treatment lag are under active investigation (see Future Directions).

Antidepressant medications differ in their profile of side effects. First-generation MAOIs, which inhibit the activity of both MAO-A and MAO-B, were known for potentially serious side effects if patients also consumed foods containing tyramine (fermented products such as wine or cheese). Potential effects included headache, hypertension, cerebral hemorrhage, and death. Newer-generation MAOIs that act more selectively on MAO-A do not require the dietary restriction from tyramine-containing foods. Common side effects associated with TCAs include dry mouth, urinary retention, sedation, orthostatic hypotension, and weight gain. A concern with this medication is the narrow therapeutic index, which raises the risk of death with overdose. SSRIs do not carry the same health concerns as MAOIs or TCAs. Common side effects of SSRIs include nausea and sexual dysfunction. A topic of much controversy is a possible increase in risk of suicidal ideation and behavior (see Current Knowledge). Side effects reported with mixed SSRI–NRIs (e.g., velaxafine), include headache, dry mouth, sedation, hypertension, and constipation (Iversen et al., 2009).

Current Knowledge

Approximately 60–70% of persons treated with antidepressants show a positive response. The lack of response in 30–40% of depressed individuals (at least to SSRIs) may be due in part to the effects of genes. Variations in the serotonin transporter gene (often referred to as 5-HTTLPR) modify the response of depressed persons to SSRIs. Compared to those with a long (L) allele of this gene, persons with a short allele exhibit poorer response to SSRI treatment. Variations in 5-HTTLPR may also influence the experience of side effects (Horstmann & Binder, 2009).

The response rate to placebo in clinical trials of antidepressants is relatively high, ranging from 30 to 50%. The placebo response is greater among individuals with mild depressive symptoms, and recent meta-analyses of clinical trials of second-generation antidepressants indicate significant treatment effects only among those with severe symptoms (Fournier et al., 2010; Kirsch et al., 2008).

Significant concerns of an increased risk of suicidal ideation and behavior (suicidality) have arisen over the use of new-generation antidepressants. The US Food and Drug Administration (FDA) has released several advisories that antidepressant use may increase the risk of suicidality among children, adolescents, and young adults (http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/2007/ucm108905.htm). A meta-analysis of clinical trial data with SSRIs has confirmed a moderate increase in risk of suicidality among pediatric patients (Hammad, Laughren, & Racoosin, 2006). These observations are in contrast to epidemiological data that indicate reduced rates of *completed* suicides. Some have hypothesized that the higher risk of suicidality with antidepressant treatment likely occurs in a subset of high-risk patients with agitated major depression or unrecognized bipolar disorder (Rihmer & Akiskal, 2006).

Future Directions

More research is needed to examine the safety of antidepressant treatment in pediatric and young adult populations. Thorough characterization of patients may help clarify whether certain subgroups are more vulnerable to develop suicidal behaviors while receiving antidepressants. Additionally, antidepressants are not effective for 30–40% of depressed patients. Current work is exploring alternative treatments, for example, testing antagonists of NMDA glutamate receptors for an antidepressant effect. This approach stems from observations in animal models that exposure to an inescapable stressor (shock) produces learned helplessness and also disrupts long-term potentiation in the hippocampus, an NMDA-dependent process. It is hypothesized that NMDA receptors may also play a role in the development of learned helplessness, and similar to the effects of antidepressants, antagonism of these receptors may block its development. Initial clinical studies with ketamine, an NMDA antagonist, show a significant antidepressant effect within 2 h. In addition to a more rapid treatment effect, it is hoped that glutamate-based therapies will alleviate depressive symptoms among those unresponsive to current treatments (Skolnick, Popik, & Trullas, 2009).

Cross References

► Depression
► Selective Serotonin Reuptake Inhibitors (SSRIs)
► Serotonin

References and Readings

Bourin, M., & Lambert, O. (2002). Pharmacotherapy of anxious disorders. *Human Psychopharmacology: Clinical Experimental, 17*, 383–400.

Chung, B., Suzuki, A. R., & McGough, J. J. (2002). New drugs for treatment of attention-deficit/hyperactivity disorder. *Expert Opinion Emerging Drugs, 7*, 269–276.

FDA Press Release. Extracted from http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/2007/ucm108905.htm on 1/21/2010

Fournier, J. C., DeRubeis, R. J., Hollon, S. D., Dimidjian, S., Amsterdam, J. D., Shelton, R. C., et al. (2010). Antidepressant drug effects and depression severity: A patient-level meta-analysis. *JAMA, 303*, 47–53.

Grant, J. E., & Grosz, R. (2004). Pharmacotherapy outcome in older pathological gamblers: A preliminary investigation. *Journal of Geriatric Psychiatry and Neurology, 17*, 9–12.

Hammad, T. A., Laughren, T., & Racoosin, J. (2006). Suicidality in pediatric patients treated with antidepressant drugs. *Archives of General Psychiatry, 63*, 332–339.

Horstmann, S., & Binder, E. B. (2009). Pharmacogenomics of antidepressant drugs. *Pharmacology and Therapeutics, 124*, 57–73.

Iversen, L. L., Iversen, S. D., Bloom, F. E., & Roth, R. H. (2009). Antidepressants and Anxiolytics. *Introduction to Neuropsychopharmacology* (pp. 306–335). New York: Oxford University Press.

Kirsch, I., Deacon, B. J., Huedo-Medina, T. B., Scoboria, A., Moore, T. J., Johnson, B. T. (2008). Initial severity and antidepressant benefits: A meta-analysis of data submitted to the food and Drug Administration. *PlOS Medicine, 5*, e45.

Michel, M. C., Ruhe, H. G., de Groot, A. A., Castro, R., & Oelke, M. (2006). Tolerability of amine uptake inhibitors in urologic diseases. *Current Drug Safety, 1*, 73–85.

O'Connor, A. B., & Dworkin, R. H. (2009). Treatment of neuropathic pain: An overview of recent guidelines. *American Journal of Medicine, 122*(Suppl. 10), S22–32.

Powers, P. S., & Bruty, H. (2009). Pharmacotherapy for eating disorders and obesity. *Child Adolescent Psychiatric Clinics of North America, 18*, 175–187.

Rihmer, Z., & Akiskal, H. (2006). Do antidepressants t(h)reat(en) depressives? Toward a clinical judicious formulation of the antidepressant-suicidality FDA advisory in light of declining national suicide statistics from many countries. *Journal of Affective Disorders, 94*, 3–13.

Skolnick, P., Popik, P., & Trullas, R. (2009). Glutamate-based antidepressants: 20 years on. *Trends in Pharmacological Sciences, 30*, 563–569.

Stone, K. J., Viera, A. J., & Parman, C. L. (2003). Off-label applications for SSRIs. *American Family Physician, 68*, 498–504.

Antiepileptic Drugs (AED)

► Anticonvulsants

Antihistamines

Stephanie A. Kolakowsky-Hayner
Santa Clara Valley Medical Center,
Rehabilitation Research Center
San Jose, CA, USA

Synonyms

Histamine antagonist; Inverse histamine agonists

Definition

Antihistamines are commonly used to treat allergies; H_1 receptor inverse agonists typically reduce swelling and vasodilation within the nasal area. H_1 receptor antagonists include cetirizine, diphenhydramine also known as

benadryl, desloratadine, doxylamine, ebastine, fexofenadine, loratadine, pheniramine, and promethazine. H_2 inverse agonists reduce gastric acid and are used to treat ulcers and reflux. H_2 receptor antagonists include cimetidine, famotidine, lafutidine, nizatidine, ranitidine, and roxatidine. H_3 and H_4 receptor antagonists are experimental in nature and are being investigated for their cognitive enhancing and immunomodulation abilities. Additionally, antihistamines may be used to treat off-label issues such as motion sickness, anxiety, and insomnia.

Neuropsychologists must be aware of the potential effects of antihistamines on the physical, emotional, and cognitive functioning of their patients. Side effects of antihistamine use may include dry nose and mouth, drowsiness, dizziness, headache, upset stomach, loss of appetite, irritability, motor slowness, diminished processing speed, and impaired visual skills. Antihistamine effects are exacerbated by the use of alcohol and other substances, which in turn will be of further detriment to neuropsychological testing.

Cross References

- ► Pharmacodynamics
- ► Pharmacokinetics
- ► Psychopharmacology

References and Readings

Hindmarch, I., & Shamsi, Z. (1999). Antihistamines: Models to assess sedative properties, assessment of sedation, safety and other side-effects. *Clinical & Experimental Allergy, 29*, 133–142.

Parsons, M., & Ganellin, C. (2006). Histamine and its receptors. *British Journal of Pharmacology, 147*, S127–S135.

Theunissen, E., Vermeeren, A., van Oers, A., van Maris, I., & Ramaekers, J. (2004). A dose-ranging study of the effects of mequitazine on actual driving, memory and psychomotor performance as compared to dexchlorpheniramine, cetirizine and placebo. *Clinical & Experimental Allergy, 34*(2), 250–258.

van Ruitenbeek, P., Vermeeren, A., Smulders, F., Sambeth, A., & Riedel, W. (2009). Histamine H_1 receptor blockade predominantly impairs sensory processes in human sensorimotor performance. *British Journal of Pharmacology, 157*(1), 76–85.

Vuurman, E., Rikken, G., Muntjewerff, N., de Halleux, F., & Ramaekers, J. (2004). Effects of desloratadine, diphenhydramine, and placebo on driving performance and psychomotor performance measurements. *European Journal of Clinical Pharmacology, 60*(5), 307–313.

Zlomuzica, A., Ruocco, L., Sadile, A., Huston, J., & Dere, E. (2009). Histamine H_1 receptor knockout mice exhibit impaired spatial memory in the eight-arm radial maze. *British Journal of Pharmacology, 157*(1), 86–91.

Antihypertensives

Mary Pat Murphy
MSN, CRRN
Paoli, PA, USA

Definition

Antihypertensives are pharmacologic agents used to lower blood pressure to normal levels or near normal levels. The initiation and intensity of drug treatment depends on blood pressure level, the individual's risk factors (smoking, dyslipidemia, diabetes mellitus, older than 60, male, postmenopausal women, and family history of cardiovascular disease for women under 65 and men under 55 years of age), and target organ damage (e.g., ► stroke or ► TIA, nephropathy, ► peripheral artery disease, ► retinopathy) or cardiovascular disease. Cardiovascular risks decrease when the blood pressure is below 139/89. Typical agents for treating hypertension include diuretics, beta-blockers, ACE (angiotensin converting enzyme) inhibitors, calcium channel blockers, peripheral alpha selective blockers, central alpha2 agonists, direct vasodilators, and adrenergic antagonists.

Current Knowledge

Hypertension is a risk factor for stroke, myocardial infarction, renal failure, congestive heart failure, progressive atherosclerosis, and dementia. Treatment reduces the risks of heart disease as well as cardiovascular morbidity. For Stage I hypertension, the blood pressure ranges from 140/90 to 159/99; Stage II and Stage III blood pressure, the systolic number is greater than 160 and diastolic is greater than 100.

Monotherapy is preferred initially. The first line of treatment is beta-blockers and diuretics for uncomplicated hypertension individuals who do not have preexisting coronary disease, diabetes, or proteinuria. In patients with diabetes mellitus, renal disease or CHF, ACE inhibitors and angiotensin receptor antagonists are the appropriate initial therapy. Typically, the patient is started on a low dose of long-acting, once daily drug, and the dose is titrated until the blood pressure is lowered. If blood pressure is not controlled with the dose of a single drug, a second agent from a different class is recommended. Combination therapy provides more

rapid control of hypertension and is recommended for patients with stages II and III hypertension. Triple-drug therapy may be required if the blood pressure control is not achieved. Some patients have resistant hypertension. A fourth line of medications may be required.

Classes of Antihypertensives

Diuretics

Diuretics decrease blood pressure by causing diuresis, which results in decreased blood volume, cardiac output, and stroke volume. They fall into three categories: thiazides, loop diuretics, and potassium-sparing diuretics. **Thiazide**'s onset of action occurs within 2–3 h. Their half-life is 8–12 h allowing for once daily dosing. Trade names include Hygroton, Hydrodiuril, Lozol, and Zaroxolyn.

Loop diuretics act in the loop of Henle in the kidney and are less effective in the long term. Their duration is 6 h. These agents are indicated with CHF or nephrotic syndrome. Bumex, Edecrin, Lasix, and Demadex are trade names.

Potassium-sparing agents cause minimal diuresis and are relatively ineffective in lowering the blood pressure. The medications correct thiazide-induced potassium and magnesium losses. Medication trade names include Midamor, Aldactone, and Dyrenium.

Adverse Events

Most complications occur related to dose and duration of use. Hypokalemia is a side effect, but can be managed with potassium chloride or use of potassium-sparing agents.

Acute gouty arthritis, muscle cramps, development of diabetes, nocturia or incontinence, and sun sensitivity have been noted as clinical side effects.

Beta-Blocking Agents

Beta1-receptors are located in the heart and kidneys and regulate heart rate and cardiac contractility. Beta2-receptors regulate bronchodilation and vasodilation. Beta-blockers decrease blood pressure by blocking the beta-receptors. Some beta-blockers are cardioselective – that is, they do not block the beta2-receptors, therefore do not cause bronchoconstriction. These medications include Lopressor, Kerlone, Tenormin, Sectral and Zebeta, Corgard, Inderal, and Cartrol.

Side Effects

The most common side effects of beta-blockers are fatigue, dizziness, bronchospasm, nausea, and vomiting. Beta-blockers should not be discontinued abruptly but should be tapered over 14 days to prevent withdrawal which includes unstable angina, myocardial infarction, and death.

ACE Inhibitors

This class of antihypertensives inhibits ACE which converts angiotensin I to II – a potent vasoconstrictor. This is a first-line therapy for patients with diabetes and proteinuria. Mediations include Lotensin, Capoten, Vasotec, Monopril, Zestril, Univasc, Accupril, Altace, and Mavik.

Side effects include cough, hypotension, hyperkalemia, rash, loss of taste, leukopenia, and neutropenia. They are contraindicated in pregnancy and for patients with bilateral real artery stenosis.

Calcium Channel Blockers

Calcium channel blockers relax the cardiac and smooth muscle by blocking calcium channels that allow calcium into the cells. The result is vasodilation. They also decrease the heart rate and slow cardiac conduction. Medications include Calan, Cardizem, Norvasc, Plendil, Procardia Cardene, Sular, and DynaCirc.

Side Effects

Side effects include GI upset, edema, and hypotension. Rare side effects include bradycardia, CHF, and AV block. Other adverse effects include dizziness, headache, shortness of breath, gingival hyperplasia, and edema.

Contraindications

Calcium channel blockers should not be prescribed for individuals with second- and third-degree heart block or left ventricular dysfunction.

Other Classes of Antihypertensives

Peripheral alpha1- receptors (Cardura, Minipress, and Hytrin), central alpha2 (Clonidine, Aldomet, Tenex, and Wytension), direct vasodilators (Apresoline and Loniten), and adrenergic antagonists (Serpasil, Ismelin and Hylorel) are the remaining categories of antihypertensives. They are mainly used as second- and third-line medications.

Cross References

- ▶ Psychopharmacology
- ▶ Stroke
- ▶ Transient Ischemic Attack (TIA)

References and Readings

August, P. (2003). Initial treatment of hypertension. *New England Journal of Medicine, 348*, 610–617.
Cranwell-Bruce, L. (2008). Antihypertensives. *MEDSURG Nursing, 17*(5), 337–341.
Ernst, M., & Moser M. (2009). Use of diuretics in patients with hypertension. *New England Journal of Medicine, 361*, 2153–2164.
Houston, M. C., Pulliam Meador, B., & Moore Schipani, L. (2000). *Handbook of antihypertensive therapy* (10th ed.). Philadelphia: Hanley & Belfus.
Staessen, J., & Birkenhager, W. (2005). Evidence that new antihypertensives are superior to older drugs. *Lancet, 366*(9489), 869–871.

Antiplatelet Therapy

Elliot J. Roth
Northwestern University
Chicago, IL, USA

Definition

Antiplatelet therapy uses specific pharmacological agents (antiplatelet agents) to inhibit the ability of platelets to clump together to form blood clots, or thromboses, primarily in arteries. It is commonly used in people with atherosclerosis (narrowing of the arteries).

Current Knowledge

Platelets are naturally occurring cells (actually, portions of cells) that circulate in the blood. They clump, or aggregate, under certain conditions to initiate the formation of blood clots. These platelet clumps are then further bound together by the protein, fibrin. Together, the fibrin and the platelet clump comprise the thrombus or blood clot. Thrombi are useful in that they stop bleeding in normal circumstances. When there is a break in an artery, allowing blood to leave the vessel, platelets become activated by attaching to the wall of the blood vessel at the site of the bleeding, and by attracting fibrin and other coagulation factors to the area to stop the bleeding. However, if the blood clot forms *inside* the artery, it can block the flow of blood to the tissue that is supplied by the artery, which can result in tissue damage. A clot forming in the coronary artery causes ischemic heart disease (which may present as angina or myocardial infarction), and when the blood clot forms in the carotid or cerebral arteries, it may cause a stroke.

Many studies have demonstrated the effectiveness of aspirin and other antiplatelet agents in preventing heart attack and stroke in certain situations, for primary and secondary prevention. This favorable effect is based on the ability of these agents to inhibit the chemicals that cause platelets to clump together initiating blood clot formation.

Aspirin is the prototypical antiplatelet agent. Other currently available antiplatelet agents include ticlopidine (Ticlid®), clopidogrel (Plavix®), and dipyridamole (Persantine®).

Cross References

▶ Atherosclerosis
▶ Cerebrovascular Disease
▶ Coronary Disease
▶ Ischemic Stroke
▶ Myocardial Infarction
▶ Peripheral Vascular Disease
▶ Stent
▶ Thrombosis

References and Readings

Tran, H., & Anand, S. S. (2004). Oral antiplatelet therapy in cerebrovascular disease, coronary artery disease, and peripheral arterial disease. *JAMA, 292*, 1867–1874.

Antipsychotic

▶ Neuroleptics

Antipsychotic Medications

▶ Antipsychotics

Antipsychotics

Helen M. Carmine
ReMed
Paoli, PA, USA

Synonyms

Antipsychotic medications; Atypicals (antipsychotics); Conventional antipsychotics; High-potency/low-potency

groups of antipsychotics; Neuroleptics; Standard antipsychotics

Definition

Agents used for the treatment of psychotic disorders, severe mental illnesses, and mood/behavior disorders not responsive to other medication/behavioral interventions. Broader application/often "off-label" use of these medications to address thought/behavior disorders in various populations including adults with dementia, traumatic brain injury, developmental disorders with behavioral symptoms unresponsive to other treatments, and individuals with depression who are not responsive to antidepressant therapy alone. Specifically in TBI populations, according to B.C. McDonald et al. (2002), individuals with TBI whose cognition and behaviors are disorganized, and agitated, there may be a role for neuroleptics agents. Another study by Ahmed and Fuiji (1998) identified that individuals who have a brain injury experience a two- to fivefold greater risk of developing psychosis than the general population, and may require treatment with atypical antipsychotics to help restore behavioral and cognitive stability.

Historical Background

Antipsychotic medications according to Preston, Neal, and Talaga (2006) have "truly revolutionized" the treatment of psychotic disorders. Conventional/Typical Antipsychotics act primarily through blockade of dopamine D2 receptors. Chlorpromazine(Thorazine)/a phenothiazine was first used in 1952 as a postoperative agent, but quickly became a standard treatment for sedation and reducing psychotic symptoms of psychiatric patients, and soon many other "phenothiazines" were developed (Preston, Neal, and Talaga, 2006). The role of dopamine 2 postsynaptic receptor blockade led to the development of future dopamine blockers that are chemically targeted to reduce and selectively block/weakly block dopamine to minimize side effects. Since that time, off-label use of these agents has benefited other populations. These agents were called "neuroleptics" because as a result of their dopamine blockade, they also lead to other neurological side effects/undesired effects. The newer antipsychotics, known as "atypicals," are strong serotonin blockers (5-HT2A and 5-HT2C) and produce varying degrees of dopamine blockade, weakly blocking D2 receptors and D1 receptors and also act on the serotonin, dopamine, and GABA neurotransmitter systems. This multiple pathway approach may help with the individualization and selection of the best agent based on the individual's response.

Current Knowledge

Standard antipsychotics have been used since the 1950s for their sedating effects on individuals with psychosis/psychotic symptoms. As phenothiazines were known to produce these effects as postoperative sedation agents, the sedating effect led to the development of additional standard antipsychotic agents produced and utilized through the 1980s, including, but not limited to agents such as Thorazine, Mellaril, Stelazine, Prolixin, Navane, and Trilafon. These standard antipsychotic agents were divided into high- and low-potency groups based on their profiles indicating desirable/undesirable effects including sedation, anticholinergic/parasympathetic side effects including urinary and bowel retention, dry mouth and cardiovascular effects, and extrapyramidal symptoms as a result of their dopamine blockade, their effects on sympathetic blockade/alpha adrenergic blockade leading to hypotension and dizzinesss and the effects of neurotramsission leading to involuntary movements (tardive dyskinesias) and extrapyramidal symptoms. Other adverse effects noted with typical antipsychotics include lowering seizure threshold, thermal dysregulation, hormonal dysregulation including hyperprolactinemia, and a fatal but rare side effect known as neuroleptic malignant syndrome characterized by fever, rigidity, and confusion. Obviously, all medication agents require close monitoring and may also require other agents to address undesired effects, or lowering of the antipsychotic agent or change in administration time to minimize untoward effects.

Newer "atypical" or "novel" agents with Clozaril (Clozapine) as the first agent in this category have been noted to be effective in significantly reducing the symptoms of psychosis, particularly when other agents are unsuccessful by targeting specific dopamine receptors, or block/ inhibit reuptake of serotonin. The most significant difference is in the reduction of the negative symptoms and the lower risk of developing tardive dyskinesias. However, Clozaril effects on the bone marrow may lead to a severe blood disorder/agranulocytosis. Clozaril requires adherence to an FDA protocol for Complete Blood Count/ANC monitoring based on threshold values. Newer atypical agents were developed to improve the reduction of negative symptoms, improve

cognition, decrease risk of tardive dyskinesias, and other neurological changes resulting from these agents.

Newer "atypical/novel" antipsychotic agents have included Risperidone, Zyprexa, Seroquel, Geodon, Abilify, and, most recently, Saphris. However, with these newer "atypical antipsychotics," other concerning side effects have been exposed including metabolic changes leading to alterations in carbohydrate and lipid metabolism, possible diabetes, and excessive weight gain. All of these newer agents require routine monitoring of weight, blood sugar, and lipid profile studies to control the potential adverse effects while achieving improvement in both positive/negative symptoms of psychosis. Treatment duration with these agents is individually maximized based on response to reduction in positive symptoms of chronic thought disorders/psychosis. Shorter treatment durations may be possible in acute onset of delirium, acute psychoses, or brief reactive psychosis.

Future Directions

The use of the newer atypical agents has been shown to produce a reduction in hostility and aggression in schizophrenic patients, elderly patients with dementia, and empirically with individuals experiencing aggression and agitation in TBI. The next generation of agents will be directed at further reducing overall side effects while maximizing treatment response and symptom reduction while returning to optimal daily functioning and cognitive, mood, and behavioral stability.

Cross References

► Neuroleptics
► Psychopharmacology
► Psychotic Disorder

References and Readings

Ahmed, I. I., & Fuiji, D. (1998). Posttraumatic Psychosis. *Seminars in Clinical Neuropsychology, 3*(1), 23–33.

McDonald, B. C., Flashman, L. A., & Saykin, A. J. (2002). Executive dysfunction following traumatic brain injury: neural substrates and treatment strategies. *NeuroRehabilitation, 17*(4), 333–344.

Meredith, C., Jaffe, C., Ang-Lee, K., & Saxon, A. (2005). Implications of chronic methamphetamine use: A literature review. *Harvard Review of Psychiatry, 13*(3), 141–154.

Preston, J., O'Neal, J. H., & Talaga, M. C. (2006). *Child and adolescent clinical psychopharmacology made simple.* Oakland, CA, US: New Harbinger Publications.

Savitz, J., van der Merwe, L., Stein, D., Solms, M., & Ramesar, R. (2008). Neuropsychological task performance in bipolar spectrum illness: genetics, alcohol abuse, medication and childhood trauma. *Bipolar Disorders, 10*(4), 479–494.

Voruganti, L., & Awad, A. (2004). Neuroleptic dysphoria: Towards a new synthesis neuroleptic dysphoria. *Psychopharmacology, 171*(2), 121–132.

Wozniak, J., Block, E., White, T., Jensen, J., & Schulz, S. (2008). Clinical and neurocognitive course in early-onset psychosis: a longitudinal study of adolescents with schizophrenia-spectrum disorders. *Early Intervention in Psychiatry, 2*(3), 169–177.

Antithrombotic Therapy

► Anticoagulation

Anxiety

Joel W. Hughes
Kent State University
Kent, OH, USA

Synonyms

Fear

Definition

Anxiety is an unpleasant state characterized by affective, cognitive, and physiological elements such as fear, worry, apprehension, and tension.

Anxiety is similar to the emotion of fear, although the function of chronic anxiety is often to avoid or mask true fear through mechanisms of anxiety such as worry and anticipation of negative future outcomes. The physiological manifestations of anxiety include increased blood pressure, increased breathing rate (often shallow), increased heart rate, other cardiac symptoms (e.g., pain, "skipped" beats), gastrointestinal distress including nausea, stomach aches, increased motility of the gut, and diarrhea, generalized bodily distress such as fatigue and pain. Cognitively, anxiety is frequently characterized by an overestimation of the probability of a negative future outcome and an exaggeration of the consequences of the negative outcome. For example, an anxious person may

believe that it is likely that they will fail a test with catastrophic consequences.

Anxiety often occurs in response to external stressors. It can be a normal reaction to stress, in which case anxiety can help coping behavior by focusing attention, mobilizing energy, and increasing goal-directed behavior. However, anxiety can also be a reaction to internal (physiological) cues or a generalized and pervasive mood without identifiable precipitants. When anxiety is an excessive reaction, or present in the absence of any true challenges or dangers, it is considered pathological. Individuals with pathological levels of anxiety are typically high in "trait" anxiety, which is a stable and enduring tendency to respond with anxiety to a wide variety of situations. Individuals high in trait anxiety are often also high in neuroticism.

Historical Background

Anxiety is basic to human experience and has been documented and treated since the beginning of recorded history. The relation between anxiety and health complaints has been recognized since the seventeenth century, although psychiatric nosology did not become well developed until the last century. A number of anxiety disorders have been delineated in contemporary psychiatric writings and are described in the most recent edition of the Diagnostic and Statistical Manual of Mental Disorders published by the American Psychiatric Association.

Current Knowledge

Although anxiety can be learned, it is thought to have a biological basis in the amygdala and hippocampus. When individuals are exposed to potentially dangerous or harmful stimuli, brain imaging often shows increased activity in the amygdala accompanied by participant reports of increased anxiety. Excessive anxiety can also compromise performance on neuropsychological tests, especially by interfering with attention and cognitive efficiency.

When suspected, the level of anxiety should be assessed. Anxiety is often measured using the Beck Anxiety Inventory or Hamilton Anxiety Scale. They do not diagnose anxiety disorders, but give a dimensional measure of anxiety.

Effective treatment of anxiety almost always involves exposure to the feared stimulus. Treatments are based on the principles of classical conditioning, and the goal is to extinguish the fear response through exposure and habituation. Exposure can be in vivo or imaginal, and therapy frequently uses cognitive techniques to modify anxiety-generating cognitions. Anxiolytic medication is also often prescribed.

Cross References

- ▶ Anxiolytics
- ▶ Beck Anxiety Inventory

References and Readings

Allen, L. B., McHugh, R. K., & Barlow, D. H. (2008). Emotional disorders: A unified protocol. In D. H. Barlow (Ed.), *Clinical handbook of psychological disorders: A step-by-step treatment manual* (4th ed., pp. 216–249). New York, NY: Guilford Press.

American Psychiatric Association (2000). *Diagnostic and statistical manual of mental disorders* (4th ed.), Text Revision. Washington, DC: American Psychiatric Association.

Anxiolytics

Stephanie A. Kolakowsky-Hayner
Santa Clara Valley Medical Center,
Rehabilitation Research Center
San Jose, CA, USA

Synonyms

Anti-anxiety drugs; Anti-anxiety medications

Definition

Anxiolytics are prescription drugs used to reduce the severity and extent of symptoms due to anxiety-related disorders. Often known as benzodiazepines, these drugs are used to treat generalized anxiety disorder, panic attacks, phobias, and other ongoing issues of excessive fear and dread. Medical illness often associated with high levels of anxiety also includes brain injury, heart disease, and COPD. There are six approved anxiolytics in the USA today including the popular Diazepam (Valium), Lorazepam (Ativan), and Alprazolam (Xanax). Anxiolytics are designed to impact neurotransmitters in the amygdala by increasing gamma-aminobutyric acid (GABA), an inhibitory neurotransmitter that diminishes the fear response.

Neuropsychologists must be aware of the potential effects of anxiolytics on the physical, emotional, and cognitive functioning of their patients. Anxiolytics are highly addictive and are often abused when used as a recreational drug. Patients may also become dependant on their medication if on increased doses for long periods of time. Side effects of anxiolytics may include excessive drowsiness to the point of sedation; suicidal thoughts; unexplained excitement, rage, anger, or hostility; confusion and cognitive slowing; balance and dizziness issues; diminished motor and visual skills; and breathing issues. Negative side effects may impact neuropsychological testing and treatment and these effects should be considered in treatment planning and recommendations.

Cross References

- ► Benzodiazepines
- ► Diazepam
- ► GABA
- ► Psychopharmacology

References and Readings

Cosci, F., Schruers, K., Faravelli, C., & Griez, E. (2004). The influence of alcohol oral intake on the effects of 35% CO_2 challenge: A study in healthy volunteers. *Acta Neuropsychiatrica, 16*(2), 107–109.

Deacon, R., Bannerman, D., & Rawlins, J. (2002). Anxiolytic effects of cytotoxic hippocampal lesions in rats. *Behavioral Neuroscience, 116* (3), 494–497.

Karl, T., Duffy, L., Scimone, A., Harvey, R., & Schofield, P. (2007). Altered motor activity, exploration and anxiety in heterozygous neuregulin 1 mutant mice: Implications for understanding schizophrenia. *Genes, Brain & Behavior, 6*(7), 677–687.

Lanctôt, K., Herrmann, N., Mazzotta, P., Khan, L., & Ingber, N. (2004). GABAergic function in Alzheimer's disease: Evidence for dysfunction and potential as a therapeutic target for the treatment of behavioural and psychological symptoms of dementia. *Canadian Journal of Psychiatry, 49*(7), 439–453.

McHugh, S., Deacon, R., Rawlins, J., & Bannerman, D. (2004). Amygdala and ventral hippocampus contribute differentially to mechanisms of fear and anxiety. *Behavioral Neuroscience, 118*(1), 63–78.

Treit, D., & Menard, J. (1997). Dissociations among the anxiolytic effects of septal, hippocampal, and amygdaloid lesions. *Behavioral Neuroscience, 111*(3), 653–658.

Apallesthesia

- ► Pallanesthesia

Apallic Syndrome

- ► Persistent Vegetative State

Apathy

Laura L. Frakey
Memorial Hospital of Rhode Island and Alpert Medical School of Brown University
Pawtucket, RI, USA

Synonyms

Abulia; Amotivational; Anhedonia; Negative symptom

Short Description or Definition

In the vernacular, the word apathy generally refers to indifference or a lack of feeling or concern. In clinical settings, "apathy" is often conceptualized as a lack of drive or motivation, a lack of responsiveness (behavioral or emotional) to stimuli, or a lack of initiation, or a reduction in self-generated, purposeful behavior.

Epidemiology

Apathy has been described in a variety of psychiatric, neurological, and medical conditions, including depression, schizophrenia, Alzheimer's disease, frontotemporal dementia, mild cognitive impairment (MCI), Parkinson's disease, progressive supranuclear palsy, Huntington's disease, cortical basal degeneration, dementia with Lewy bodies, stroke, vascular dementia, cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy (CADASIL), traumatic brain injury (TBI), anoxic encephalopathy, Wernicke–Korsakoff syndrome, hydrocephalus, human immunodeficiency virus (HIV), multiple sclerosis, apathetic hyperthyroidism, chronic fatigue syndrome, vitamin B12 deficiency, Lyme disease, and drug intoxication and withdrawal.

Following an extensive review of the literature, van Reekum et al. (2005) summarized the prevalence rates of apathy in many of the above-named conditions derived from studies that employed a variety of assessment

measures (see below). Combining data from multiple studies, these authors report point prevalence rates of 60.3% in Alzheimer's disease, 46.7% in TBI, 60.3% in persons with focal frontal lesions, 33.8% in vascular dementia, 34.7% poststroke, 22.2% in dementia with Lewy bodies, 29.8% in HIV, 20.5% in multiple sclerosis, and 53.3% in patients with major depression. Studies examining apathy in other neurological conditions have found prevalence rates of 41% in CADASIL (Reyes et al., 2009), 90% in frontotemporal dementia, 91% in progressive supranuclear palsy, 59% in Huntington's disease, and 33% in Parkinson's disease (Levy et al., 1998). Apathy is also one of the most commonly observed neuropsychiatric symptoms in MCI (Apostolova and Cummings, 2008).

While the above-described findings related to clinic-based samples, apathy has also been reported in a community-based sample of older adults with prevalence rates of 1.4% in cognitively normal elderly, 3.1% in mild cognitive syndrome, and 17.3% in dementia (Onyike et al., 2007). Apathy also appears to be quite common in nursing home settings, with one study reporting a prevalence rate of 84.1% (Wood et al., 2000). Apathy may also appear as an adverse effect of some prescription drugs, including selective serotonin reuptake inhibitors (SSRIs) (Hoehn-Saric et al., 1990).

Natural History, Prognostic Factors, Outcomes

The word apathy comes from the Greek word "apatheia", meaning, an "absence of feeling." The Stoic philosophers used this term to connote the total freedom from emotions and passions which were thought to compromise rationality and the desired state of mental tranquility. However, over the centuries, the term apathy came to refer to a lack of reactivity and became viewed as pathological rather than desirable.

While apathy can be observed as a symptom associated with a variety of psychiatric, neurological, and medical conditions, some authors have argued that apathy, in some circumstances, may represent a neuropsychiatric syndrome as well. Marin (1991) defined an apathy syndrome as a loss of motivation which could not be attributed to emotional distress, intellectual impairment, or a diminished level of consciousness. In contrast, apathy, as a symptom, was defined as a loss of motivation due to a disturbance of intellect, emotion, or level of consciousness (Marin, 1991). Apathy is not considered an independent syndrome in the current DSM-IV, though it does appear as a nonspecific symptom for several other disorders. The merits of including apathy as a stand-alone disorder in the upcoming DSM-V revision are currently being debated.

Prognostically, there is evidence to suggest that apathy may be associated with more severe impairment and negative outcomes. For example, a longitudinal study examining apathy in persons with Alzheimer's disease found that apathy at the baseline was associated with faster cognitive and functional decline at follow-up (Starkstein et al., 2006) There is also some evidence that apathy may precede the development of Alzheimer's disease. One longitudinal study of patients with MCI found that those patients who converted to Alzheimer's disease had higher rates of apathetic symptomatology (91.7%) than those patients who did not convert (26.9%) (Robert et al., 2006). Apathy has also been found to be significantly associated with lower cognitive functioning and more severe motor symptoms in persons with Parkinson's disease (Pedersen et al., 2009). Apathetic symptomatology has also been found to be negatively associated with functional improvement in rehabilitation settings after strokes (Hama et al., 2007) and increased risk for mortality in nursing home residents with dementia (van Dijk et al., 1994).

Studies have also found that apathy is associated with decreased performance of activities of daily living (ADLs) in persons with stroke (Mayo et al., 2009; Starkstein et al., 1993), vascular dementia (Zawacki et al., 2002), frontotemporal dementia (Kipps et al., 2009), dementia with Lewy bodies (Ricci et al., 2009), and major depression (Steffens et al., 1999). Alzheimer's disease patients with apathy are more likely to be impaired on basic activities of daily living (dressing, bathing, toileting, transferring, walking, and eating) than nonapathetic Alzheimer's disease patients, even when matched on degree of cognitive impairment (Albert et al., 1996; Stout et al., 2003). In addition, apathy has been found to account for 27% of the variance in instrumental activities of daily living scores (medication management, shopping, finances) in patients with Alzheimer's disease (Boyle et al., 2003).

Finally, apathy does not only impact the patient. Due to impairments in motivation, individuals with apathy can require more support and management, which can, in turn, result in increased caregiver burden and stress. The caregivers of patients with Alzheimer's disease-related apathy have been shown to report significantly elevated levels of distress and perceived burden compared to those who are caring for less apathetic patients with a similar level of cognitive impairment (Kaufer et al., 1998). Caregiver distress secondary to neuropsychiatric symptoms,

including apathy, has been implicated in the eventual institutionalization of many patients with Alzheimer's disease (Scott et al., 1997; Steele et al., 1990).

Neuropsychology and Psychology of Apathy

In clinical practice and research, apathy is often mistaken for depression, though it is a distinct syndrome that can be distinguished from depression (Levy et al., 1998; Marin, 1991; Starkstein et al., 2001). The syndromes of depression and apathy share some symptoms (Table 1) and may co-occur in that same individual, making diagnosis a challenging exercise. (Damsio and Van Hosen, 1983). For example, an apathetic demented patient who presents with fatigue, sleep disturbance, poor appetite and weight loss, poor concentration, and anhedonia, may be diagnosed with a major depressive disorder even in the absence of dysphoria (Ishii et al., 2009). A number of studies have found apathy to be correlated with high scores on various depression measures (Rabkin et al., 2000; Ready et al., 2003; Starkstein et al., 2006). However, this correlation may be due to the fact that many clinical measures of depression include questions assessing the symptoms of both apathy and depression, which may lead to misdiagnosis.

Apathy may be distinguished from depression by the absence of dysphoric mood symptoms such as sadness, guilt, hopelessness, and helplessness. The difference in mood states, dysphoric versus emotionally indifferent, is the most useful characteristic in making a differential diagnosis between apathy and depression. Apathy can be thought of as a syndrome of primary motivational loss and diminished emotional reactivity, while depression reflects a syndrome of mood disturbance.

Apathy. Table 1 Symptoms of apathy and depression

Symptoms of apathy	Overlapping symptoms	Symptoms of depression
Loss of motivation and initiation	Lack of interest in events or activities	Dysphoria
Lack of persistence	Lack of energy	Hopelessness
Diminished emotional reactivity	Psychomotor slowing	Guilt
Reduced social engagement	Fatigue	Pessimism
	Poor insight	Suicidal ideation
		Loss of appetite
		Sleep problems

The mechanisms of apathy are not fully understood, though most theories suggest it involves disruption of the frontal-subcortical neural circuit. This circuit begins with the anterior cingulate cortex, and continues to the ventral striatum, the globus pallidus, and the thalamus, before looping back to the anterior cingulate cortex. It has been hypothesized that neuropathological changes and alterations in regional chemistry, especially acetylcholine, dopamine, and serotonin, in this circuit, are responsible for the clinical manifestation of apathy (David et al., 2008; Franceschi et al., 2005; Landes et al., 2001; Mega & Cummings, 1994). Apathy with impaired motivation and indifference has most strongly been associated with damage to anterior cingulate cortex (ACC) (Damsio & Van Hosen, 1983). In the most extreme cases, damage to the ACC results in akinetic mutism, and a complete loss of initiation and motivation. Single photon emission computed tomography (SPECT) studies of patients with Alzheimer's disease found that apathy was strongly and inversely correlated with right anterior cingulate activity (Benoit et al., 1999) or with a bilateral reduction in cingulate activity (Migneco et al., 2001).

Frontal regions have also been implicated in the manifestation of apathy. Neuroimaging studies have found apathy in AD patients to be correlated with hypoperfusion in frontotemporal regions (Benoit et al., 1999; Craig et al., 1996). In one study, apathetic stroke patients showed reduced regional cerebral blood flow in the right dorsolateral prefrontal cortex and the left frontotemporal regions (Okada et al., 1997). Subcortical regions may also be implicated in the presence of apathy. In one study, apathy was seen in 80 stroke patients with lesions to posterior limb of the internal capsule (Starkstein et al., 1993). Apathy has also been observed with lesions to the right hemisphere subcortical structures following TBI (Finset & Andersson, 2000).

Evidence from neuropsychological studies suggests that apathy may be associated with cognitive impairment, in particular, executive dysfunction. Apathetic patients with Alzheimer's disease have been shown to have greater executive functioning deficits, abilities thought to be mediated by the frontal lobes, than depressed patients with Alzheimer's disease (Kuzis et al., 1999). Another study found that apathetic patients with Alzheimer's disease showed significantly greater deficits on measures of

executive functioning, but performed similarly on other neuropsychological measures not dependent on executive function (McPherson et al., 2002). Apathy has also been associated with executive dysfunction in other clinical populations, including TBI (Andersson & Bergedalen, 2002), Parkinson's disease (Starkstein et al., 1992), progressive supranuclear palsy (Litvan et al., 1998), and HIV (Castellon et al., 2000).

Evaluation

Formal assessment measures for apathy focus on those symptoms of apathy that are distinct from depression. The most commonly employed assessment instruments for apathy in clinical and research settings include the Apathy Evaluation Scale (AES), the Neuropsychiatric Inventory (NPI), and the Frontal Systems Behavior Scale (FrSBe). Less commonly used but validated measures include the Dementia Apathy Interview and Rating, the Lille Apathy Rating Scale, the Apathy Inventory, the Behavior Rating Scale for Dementia, and the Scale for the Assessment of Negative Symptoms in Alzheimer's disease. Of note, while several of these measures include self-report versions, these may fail to identify apathy in patients with reduced insight, and, therefore, informant measures may be more helpful in assessing for apathy.

The AES comes in a clinician-administered version, an informant version, and a self-report version, all of which have been shown to have satisfactory reliability (Marin et al., 1991). The clinician-administered version (AES-C) of this measure is a semi-structured interview which includes 18 items and is focused on behavior that has been present during the past month. Each item falls into one of four categories (cognitive, behavior, emotional, or other) and is rated on a 4-point Likert scale, with higher scores representing a greater degree of apathy. A recent study examined the AES-C and found it to be valid and reliable for identifying and quantifying apathy, and found that using a cut-off score of 40.5 resulted in good sensitivity and moderate specificity (Clarke et al., 2007a; Clarke et al., 2007b).

The FrSBe (Grace & Malloy, 2001) was specifically designed to assess for behavioral changes associated with frontal lobe dysfunction and comes in a self-report and informant version. This questionnaire consists of 46 items and asks the respondent to rate the patient's behavior on each item using a five-point Likert scale. Respondents are asked to rate the patient's behavior both before and after the onset of illness or injury. Subscales assess apathy, disinhibition, and executive dysfunction. This allows for an estimation of the extent to which current problem behaviors represent a change from premorbid functioning. T-scores greater than 65 are clinically significant. The FrSBe has been shown to be reliable, valid, and sensitive to behavior change due to frontal lobe damage (Grace et al., 1999), Alzheimer's disease (Stout et al., 2003), TBI (Lane-Brown & Tate, 2009), and a variety of other neurological conditions.

The NPI is a structured interview conducted with an informant designed to assess for the presence of 12 neuropsychiatric symptoms, including apathy (Cummings, 1997). A positive response to a screening question indicates the presence of the symptom and leads to further questions about the behavior and eventual ratings of the symptom severity (mild, moderate, or severe) and the amount of caregiver distress it causes. The Neuropsychiatric Inventory Questionnaire (NPI-Q) (Kaufer et al., 2000) is a self-administered questionnaire completed by a caregiver or informant that assesses for the presence of the same 12 symptoms and asks for ratings of severity and caregiver distress using the same rating scale as the NPI interview. Importantly, both of these versions of the NPI include separate questions for depression and apathy. The NPI asks caregivers to consider whether the behavior has been present for the past month. The NPI has been shown to have good reliability and validity; however, unlike the other measures discussed, there is no recommended cut-off score for clinical significance. Of note, while the AES and FrSBe provide more nuanced assessments of apathy, the NPI is the most widely reported measure of apathy reported in the literature. This is likely due to the fact that the NPI assesses for a wide array of neuropsychiatric symptomatology, and is often used in intervention studies for a variety of conditions of which apathy may be one symptom, but not a cardinal feature of a disorder.

Treatment

Nonpharmacologic interventions for apathy tend to focus on introducing new sources of interest and stimulation. Pet therapy, art therapy, and physical therapies may be useful in decreasing apathy, though the efficacies of these interventions have not been examined in a systematic fashion with apathetic patients. Increasing opportunities for socialization and encouraging participation in social activities may also be helpful. Patients should be encouraged to be as functionally autonomous as possible. Sensory deficits and pain should be managed so that these do not interfere with activities. Implementing exercise

programs and scheduled activities may also be beneficial in enhancing initiation and motivation. While there have been few studies on behavioral interventions specifically for apathy, there is some evidence that behavioral therapy may be helpful in reducing apathetic symptomatology. One randomized controlled study comparing "reminiscence therapy" (a treatment modality designed to facilitate recall of experiences from the past to promote intrapersonal and interpersonal functioning) to a time and attention control group (one-on-one time with an activity therapist) found that apathy was reduced for both groups of patients with dementia (Politis et al., 2004). Another study showed that individualized functional and occupational training reduced apathy in patients with mild to moderate-stage dementia (Lam et al., 2010). Behavioral activation therapy (BA) is an intervention which focuses on alleviating depression by increasing the individual's exposure to rewarding and reinforcing stimuli by increasing activation and decreasing avoidance behaviors (Dimidjian & Davis, 2009). This behavioral approach includes goal setting, activity scheduling, problem solving, and self-monitoring, to get patients to become more active and, thus, increase exposure to reward, and positive reinforcement to combat depressive symptomatology. It has been shown to be comparable to cognitive behavior therapy and pharmacotherapy (paroxetine) in reducing depressive symptomatology in placebo-controlled studies (Dimidjian et al., 2006; Sturmey, 2009). While this intervention has not been examined in the treatment of apathy, its focus on increased activity and exposure to pleasant, rewarding experiences would appear to be particularly well-suited to address the lack of interest, motivation, and anhedonia that characterize apathy. Future research may show this to be a promising intervention for both depression and apathy.

Psychoeducation for families and caregivers can also be beneficial. Oftentimes, apathy is mischaracterized as a "willful behavior" (e.g., stubbornness or laziness) by caregivers who do not recognize that these behaviors are related to neurological, psychiatric, and medical comorbidities. Educating families on the underlying causes for a patient's low initiation and motivation may help lessen perceived caregiver burden and stress.

Currently, there is no FDA-approved pharmacological intervention for apathy, however, many different medications, including acetylcholinesterase inhibitors, psychostimulants, dopaminergic drugs, and atypical antipsychotics, have been used "off-label" to treat apathetic symptomatology. Methylphenidate and dextroamphetamine are psychostimulant medications that are commonly used to treat attention deficit/hyperactivity disorder (AD/HD) and narcolepsy. These medications have also been used to treat apathy in Alzheimer's disease, normal pressure hydrocephalus, Parkinson's disease, cerebrovascular accidents, and depression (Chatterjee & Fahn, 2002; Jansen et al., 2001; Keenan et al., 2005; Padala et al., 2007b; Spiegel et al., 2009). However, most of the evidence for the efficacy of these medications on apathy comes from case reports or case series. These medications can also have negative side effects, including insomnia, loss of appetite, anxiety, and higher blood pressure, which may deter their use with vulnerable populations (Ishii et al., 2009). Other "stimulating" medications such as modafinil (Padala et al., 2007a) and selegiline (Newburn & Newburn, 2005) have been reported to reduce apathy in case studies, however, further study is needed.

Reductions in apathy with the use of dopaminergic agents such as bromocriptine (Powell et al., 1996) and amantadine (Swanberg, 2007; van Reekum et al., 1995) have been reported in a few case studies, but no randomized clinical trials have been conducted to date. Apathetic-type symptoms and behavior may be seen in schizophrenic patients with negative symptoms. Atypical antipsychotic medications such as risperidone, olanzapine, and clozapine have been shown to be helpful in reducing negative symptoms in schizophrenia (van Reekum et al., 2005). However, none of the studies to date has specifically examined apathy, and these medications can be associated with serious negative side effects such as tardive dyskinesia, akathisia, extra pyramidal symptoms, and orthostatic hypotension.

As previously noted, apathy is the most common neuropsychiatric symptom associated with Alzheimer's disease, and modest improvements in apathy have been seen in patients with Alzheimer's disease who are treated with acetylcholinesterase inhibitor medications (Cummings, 2000; Mega et al., 1999). Currently, there are three acetylcholine inhibitor medications approved for use in the United States: donepezil, galantamine, and rivastigmine. A recent meta-analysis identified 14 randomized, placebo-controlled trials of monotherapy with these medications in patients with Alzheimer's disease that reported a behavioral outcome (Rodda et al., 2009). Of these, only four were specifically designed to assess behavioral outcomes, and the rest used behavioral outcomes as secondary measures. Overall, three of the 14 studies reviewed reported a statistically significant improvement in the overall score on the Neuropsychiatric Inventory, and only one found a significant reduction in apathy, specifically (Gauthier et al., 2002).

Cross References

- ▶ Akinetic Mutism
- ▶ Avolition
- ▶ Cingulate Gyrus
- ▶ Lethargy
- ▶ Major Depression
- ▶ Motivation

References and Readings

Albert, S. M., Del Castillo-Castaneda, C., Sano, M., Jacobs, D. M., Marder, K., Bell, K., et al. (1996). Quality of life in patients with alzheimer's disease as reported by patient proxies. *Journal of American Geriatric Society, 44*(11), 1342–1347.

Andersson, S., & Bergedalen, A. M. (2002). Cognitive correlates of apathy in traumatic brain injury. *Neuropsychiatry Neuropsychology and Behavioral Neurology, 15*(3), 184–191.

Apostolova, L. G., & Cummings, J. L. (2008). Neuropsychiatric manifestations in mild cognitive impairment: A systematic review of the literature. *Dementia and Geriatric Cognitive Disorders, 25*(2), 115–126.

Benoit, M., Dygai, I., Migneco, O., Robert, P. H., Bertogliati, C., Darcourt, J., et al. (1999). Behavioral and psychological symptoms in alzheimer's disease. Relation between apathy and regional cerebral perfusion. *Dementia and Geriatric Cognitive Disorders, 10*(6), 511–517.

Boyle, P. A., Malloy, P. F., Salloway, S., Cahn-Weiner, D. A., Cohen, R., & Cummings, J. L. (2003). Executive dysfunction and apathy predict functional impairment in alzheimer disease. *American Journal of Geriatric Psychiatry, 11*(2), 214–221.

Castellon, S. A., Hinkin, C. H., & Myers, H. F. (2000). Neuropsychiatric disturbance is associated with executive dysfunction in hiv-1 infection. *Journal of International Neuropsychological Society, 6*(3), 336–347.

Chatterjee, A., & Fahn, S. (2002). Methylphenidate treats apathy in Parkinson's disease. *Journal of Neuropsychiatry and Clinical Neurosciences, 14*(4), 461–462.

Clarke, D. E., Reekum, R., Simard, M., Streiner, D. L., Freedman, M., & Conn, D. (2007a). Apathy in dementia: An examination of the psychometric properties of the apathy evaluation scale. *Journal of Neuropsychiatry and Clinical Neurosciences, 19*(1), 57–64.

Clarke, D. E., Van Reekum, R., Patel, J., Simard, M., Gomez, E., & Streiner, D. L. (2007b). An appraisal of the psychometric properties of the clinician version of the apathy evaluation scale (aes-c). *International Journal of Methods in Psychiatric Research, 16*(2), 97–110.

Craig, A. H., Cummings, J. L., Fairbanks, L., Itti, L., Miller, B. L., Li, J., et al. (1996). Cerebral blood flow correlates of apathy in alzheimer disease. *Archives of Neurology, 53*(11), 1116–1120.

Cummings, J. L. (1997). The neuropsychiatric inventory: Assessing psychopathology in dementia patients. *Neurology, 48*(5 Suppl 6), S10–16.

Cummings, J. L. (2000). The role of cholinergic agents in the management of behavioural disturbances in alzheimer's disease. *International Journal of Neuropsychopharmacology, 3*(7), 21–29.

Damsio, A. R., & Van Hosen, G. W. (1983). Emotional disturbances associated with focal lesions of the frontal lobe. In K. M. Heilman, & P. Satz, (Eds.), *Neuropsychology of Human Emotion,* New York: Guilford.

David, R., Koulibaly, M., Benoit, M., Garcia, R., Caci, H., Darcourt, J., et al. (2008). Striatal dopamine transporter levels correlate with apathy in neurodegenerative diseases a spect study with partial volume effect correction. *Clinical Neurology and Neurosurgery, 110*(1), 19–24.

Dimidjian, S., & Davis, K. J. (2009). Newer variations of cognitive-behavioral therapy: Behavioral activation and mindfulness-based cognitive therapy. *Current Psychiatry Reports, 11*(6), 453–458.

Dimidjian, S., Hollon, S. D., Dobson, K. S., Schmaling, K. B., Kohlenberg, R. J., Addis, M. E., et al. (2006). Randomized trial of behavioral activation, cognitive therapy, and antidepressant medication in the acute treatment of adults with major depression. *Journal of Consulting and Clinical Psychology, 74*(4), 658–670.

Finset, A., & Andersson, S. (2000). Coping strategies in patients with acquired brain injury: Relationships between coping, apathy, depression and lesion location. *Brain Injury, 14*(10), 887–905.

Franceschi, M., Anchisi, D., Pelati, O., Zuffi, M., Matarrese, M., Moresco, R. M., et al. (2005). Glucose metabolism and serotonin receptors in the frontotemporal lobe degeneration. *Annals of Neurology, 57*(2), 216–225.

Gauthier, S., Feldman, H., Hecker, J., Vellas, B., Ames, D., Subbiah, P., et al. (2002). Efficacy of donepezil on behavioral symptoms in patients with moderate to severe alzheimer's disease. *International Psychogeriatrics, 14*(4), 389–404.

Grace, J., & Malloy, P. F. (2001). *Frontal Systems Behavior Scale. Professional Manual.* Lutz, FL: Psychological Assessment Resources.

Grace, J., Stout, J. C., & Malloy, P. F. (1999). Assessing frontal lobe behavioral syndromes with the frontal lobe personality scale. *Assessment, 6*(3), 269–284.

Hama, S., Yamashita, H., Shigenobu, M., Watanabe, A., Hiramoto, K., Kurisu, K., et al. (2007). Depression or apathy and functional recovery after stroke. *International Journal of Geriatric Psychiatry, 22*(10), 1046–1051.

Hoehn-Saric, R., Lipsey, J. R., & McLeod, D. R. (1990). Apathy and indifference in patients on fluvoxamine and fluoxetine. *Journal of Clinical Psychopharmacology, 10*(5), 343–345.

Ishii, S., Weintraub, N., & Mervis, J. R. (2009). Apathy: A common psychiatric syndrome in the elderly. *Journal of the American Medical Directors Association, 10*(6), 381–393.

Jansen, I. H., Olde Rikkert, M. G., Hulsbos, H. A., & Hoefnagels, W. H. (2001). Toward individualized evidence-based medicine: Five "n of 1" trials of methylphenidate in geriatric patients. *Journal of American Geriatrics Society, 49*(4), 474–476.

Kaufer, D. I., Cummings, J. L., Christine, D., Bray, T., Castellon, S., Masterman, D., et al. (1998). Assessing the impact of neuropsychiatric symptoms in alzheimer's disease: The neuropsychiatric inventory caregiver distress scale. *Journal of American Geriatrics Society, 46*(2), 210–215.

Kaufer, D. I., Cummings, J. L., Ketchel, P., Smith, V., MacMillan, A., Shelley, T., et al. (2000). Validation of the npi-q, a brief clinical form of the neuropsychiatric inventory. *Journal of Neuropsychiatry and Clinical Neurosciences, 12*(2), 233–239.

Keenan, S., Mavaddat, N., Iddon, J., Pickard, J. D., & Sahakian, B. J. (2005). Effects of methylphenidate on cognition and apathy in normal pressure hydrocephalus: A case study and review. *British Journal of Neurosurgery, 19*(1), 46–50.

Kipps, C. M., Mioshi, E., & Hodges, J. R. (2009). Emotion, social functioning and activities of daily living in frontotemporal dementia. *Neurocase,* 1–8.

Kuzis, G., Sabe, L., Tiberti, C., Dorrego, F., & Starkstein, S. E. (1999). Neuropsychological correlates of apathy and depression in patients with dementia. *Neurology, 52*(7), 1403–1407.

Lam, L. C., Lui, V. W., Luk, D. N., Chau, R., So, C., Poon, V., et al. (2010). Effectiveness of an individualized functional training program on affective disturbances and functional skills in mild and moderate dementia-a randomized control trial. *International Journal of Geriatric Psychiatry, 25*(2), 133–141.

Landes, A. M., Sperry, S. D., Strauss, M. E., & Geldmacher, D. S. (2001). Apathy in alzheimer's disease. *Journal of American Geriatrics Society, 49*(12), 1700–1707.

Lane-Brown, A. T., & Tate, R. L. (2009). Measuring apathy after traumatic brain injury: Psychometric properties of the apathy evaluation scale and the frontal systems behavior scale. *Brain Injury, 23*(13–14), 999–1007.

Levy, M. L., Cummings, J. L., Fairbanks, L. A., Masterman, D., Miller, B. L., Craig, A. H., et al. (1998). Apathy is not depression. *Journal of Neuropsychiatry and Clinical Neurosciences, 10*(3), 314–319.

Litvan, I., Cummings, J. L., & Mega, M. (1998). Neuropsychiatric features of corticobasal degeneration. *Journal of Neurology, Neurosurgery & Psychiatry, 65*(5), 717–721.

Marin, R. S. (1991). Apathy: A neuropsychiatric syndrome. *Journal of Neuropsychiatry and Clinical Neurosciences, 3*(3), 243–254.

Marin, R. S., Biedrzycki, R. C., & Firinciogullari, S. (1991). Reliability and validity of the apathy evaluation scale. *Journal of Psychiatry Research, 38*(2), 143–162.

Mayo, N. E., Fellows, L. K., Scott, S. C., Cameron, J., & Wood-Dauphinee, S. (2009). A longitudinal view of apathy and its impact after stroke. *Stroke, 40*(10), 3299–3307.

McPherson, S., Fairbanks, L., Tiken, S., Cummings, J. L., & Back-Madruga, C. (2002). Apathy and executive function in alzheimer's disease. *Journal of International Neuropsychological Society, 8*(3), 373–381.

Mega, M. S., & Cummings, J. L. (1994). Frontal-subcortical circuits and neuropsychiatric disorders. *Journal of Neuropsychiatry and Clinical Neurosciences, 6*(4), 358–370.

Mega, M. S., Masterman, D. M., O'Connor, S. M., Barclay, T. R., & Cummings, J. L. (1999). The spectrum of behavioral responses to cholinesterase inhibitor therapy in alzheimer disease. *Archives of Neurology, 56*(11), 1388–1393.

Migneco, O., Benoit, M., Koulibaly, P. M., Dygai, I., Bertogliati, C., Desvignes, P., et al. (2001). Perfusion brain spect and statistical parametric mapping analysis indicate that apathy is a cingulate syndrome: A study in alzheimer's disease and nondemented patients. *Neuroimage, 13*(5), 896–902.

Newburn, G., & Newburn, D. (2005). Selegiline in the management of apathy following traumatic brain injury. *Brain Injury, 19*(2), 149–154.

Okada, K., Kobayashi, S., Yamagata, S., Takahashi, K., & Yamaguchi, S. (1997). Poststroke apathy and regional cerebral blood flow. *Stroke, 28*(12), 2437–2441.

Onyike, C. U., Sheppard, J. M., Tschanz, J. T., Norton, M. C., Green, R. C., Steinberg, M., et al. (2007). Epidemiology of apathy in older adults: The cache county study. *American Journal of Geriatric Psychiatry, 15*(5), 365–375.

Padala, P. R., Burke, W. J., & Bhatia, S. C. (2007a). Modafinil therapy for apathy in an elderly patient. *Annals of Pharmacotherapy, 41*(2), 346–349.

Padala, P. R., Burke, W. J., Bhatia, S. C., & Petty, F. (2007b). Treatment of apathy with methylphenidate. *Journal of Neuropsychiatry and Clinical Neurosciences, 19*(1), 81–83.

Pedersen, K. F., Larsen, J. P., Alves, G., & Aarsland, D. (2009). Prevalence and clinical correlates of apathy in Parkinson's disease: A community-based study. *Parkinsonism & Related Disorders, 15*(4), 295–299.

Politis, A. M., Vozzella, S., Mayer, L. S., Onyike, C. U., Baker, A. S., & Lyketsos, C. G. (2004). A randomized, controlled, clinical trial of activity therapy for apathy in patients with dementia residing in long-term care. *International Journal of Geriatric Psychiatry, 19*(11), 1087–1094.

Powell, J. H., al-Adawi, S., Morgan, J., & Greenwood, R. J. (1996). Motivational deficits after brain injury: Effects of bromocriptine in 11 patients. *Journal of Neurology, Neurosurgery & Psychiatry, 60*(4), 416–421.

Rabkin, J. G., Ferrando, S. J., van Gorp, W., Rieppi, R., McElhiney, M., & Sewell, M. (2000). Relationships among apathy, depression, and cognitive impairment in hiv/aids. *Journal of Neuropsychiatry and Clinical Neurosciences, 12*(4), 451–457.

Ready, R. E., Ott, B. R., Grace, J., & Cahn-Weiner, D. A. (2003). Apathy and executive dysfunction in mild cognitive impairment and alzheimer disease. *American Journal of Geriatric Psychiatry, 11*(2), 222–228.

Reyes, S., Viswanathan, A., Godin, O., Dufouil, C., Benisty, S., Hernandez, K., et al. (2009). Apathy: A major symptom in cadasil. *Neurology, 72*(10), 905–910.

Ricci, M., Guidoni, S. V., Sepe-Monti, M., Bomboi, G., Antonini, G., Blundo, C., et al. (2009). Clinical findings, functional abilities and caregiver distress in the early stage of dementia with lewy bodies (dlb) and alzheimer's disease (ad). *Archives of Gerontology and Geriatrics, 49*(2), e101–e104.

Robert, P. H., Berr, C., Volteau, M., Bertogliati, C., Benoit, M., Sarazin, M., et al. (2006). Apathy in patients with mild cognitive impairment and the risk of developing dementia of alzheimer's disease: A one-year follow-up study. *Clinical Neurology and Neurosurgery, 108*(8), 733–736.

Rodda, J., Morgan, S., & Walker, Z. (2009). Are cholinesterase inhibitors effective in the management of the behavioral and psychological symptoms of dementia in alzheimer's disease? A systematic review of randomized, placebo-controlled trials of donepezil, rivastigmine and galantamine. *International Psychogeriatrics, 21*(5), 813–824.

Scott, W. K., Edwards, K. B., Davis, D. R., Cornman, C. B., & Macera, C. A. (1997). Risk of institutionalization among community long-term care clients with dementia. *Gerontologist, 37*(1), 46–51.

Spiegel, D. R., Kim, J., Greene, K., Conner, C., & Zamfir, D. (2009). Apathy due to cerebrovascular accidents successfully treated with methylphenidate: A case series. *Journal of Neuropsychiatry and Clinical Neurosciences, 21*(2), 216–219.

Starkstein, S. E., Fedoroff, J. P., Price, T. R., Leiguarda, R., & Robinson, R. G. (1993). Apathy following cerebrovascular lesions. *Stroke, 24*(11), 1625–1630.

Starkstein, S. E., Jorge, R., Mizrahi, R., & Robinson, R. G. (2006). A prospective longitudinal study of apathy in alzheimer's disease. *Journal of Neurology, Neurosurgery & Psychiatry, 77*(1), 8–11.

Starkstein, S. E., Mayberg, H. S., Preziosi, T. J., Andrezejewski, P., Leiguarda, R., & Robinson, R. G. (1992). Reliability, validity, and clinical correlates of apathy in Parkinson's disease. *Journal of Neuropsychiatry and Clinical Neurosciences, 4*(2), 134–139.

Starkstein, S. E., Petracca, G., Chemerinski, E., & Kremer, J. (2001). Syndromic validity of apathy in alzheimer's disease. *American Journal of Psychiatry, 158*(6), 872–877.

Steele, C., Rovner, B., Chase, G. A., & Folstein, M. (1990). Psychiatric symptoms and nursing home placement of patients with alzheimer's disease. *American Journal of Psychiatry, 147*(8), 1049–1051.

Steffens, D. C., Hays, J. C., & Krishnan, K. R. (1999). Disability in geriatric depression. *American Journal of Geriatric Psychiatry, 7*(1), 34–40.

Stout, J. C., Wyman, M. F., Johnson, S. A., Peavy, G. M., & Salmon, D. P. (2003). Frontal behavioral syndromes and functional status in probable alzheimer disease. *American Journal of Geriatric Psychiatry, 11*(6), 683–686.

Sturmey, P. (2009). Behavioral activation is an evidence-based treatment for depression. *Behavior Modification, 33*(6), 818–829.

Swanberg, M. M. (2007). Memantine for behavioral disturbances in frontotemporal dementia: A case series. *Alzheimer Disease and Associated Disorders, 21*(2), 164–166.

van Dijk, P. T., Dippel, D. W., & Habbema, J. D. (1994). A behavioral rating scale as a predictor for survival of demented nursing home patients. *Archives of Gerontology and Geriatrics, 18*(2), 101–113.

van Reekum, R., Bayley, M., Garner, S., Burke, I. M., Fawcett, S., Hart, A., et al. (1995). N of 1 study: Amantadine for the amotivational syndrome in a patient with traumatic brain injury. *Brain Injury, 9*(1), 49–53.

van Reekum, R., Stuss, D. T., & Ostrander, L. (2005). Apathy: Why care? *Journal of Neuropsychiatry and Clinical Neurosciences, 17*(1), 7–19.

Wood, S., Cummings, J. L., Hsu, M. A., Barclay, T., Wheatley, M. V., Yarema, K. T., et al. (2000). The use of the neuropsychiatric inventory in nursing home residents. Characterization and measurement. *American Journal of Geriatric Psychiatry, 8*(1), 75–83.

Zawacki, T. M., Grace, J., Paul, R., Moser, D. J., Ott, B. R., Gordon, N., et al. (2002). Behavioral problems as predictors of functional abilities of vascular dementia patients. *Journal of Neuropsychiatry and Clinical Neurosciences, 14*(3), 296–302.

Aphasia

Janet Patterson
East Bay
Hayward, CA, USA

Short Description or Definition

"Aphasia is an acquired communication disorder caused by brain damage, characterized by impairments of language modalities; speaking, listening, reading and writing; it is not the result of a sensory or motor deficit, a general intellectual deficit, confusion or a psychiatric disorder" (Hallowell & Chapey, 2008, p. 3). Aphasia is typically acquired suddenly as a result of a stroke and can also appear following traumatic brain injury or other neurological events such as tumor or disease. When aphasia develops slowly over time and is the only behavioral symptom present, the diagnosis is typically primary progressive aphasia (PPA). Aphasia is often classified according to the appearance of a constellation of behavioral symptoms such as impairment in auditory comprehension, reading comprehension, naming, production of grammatically correct sentences, repetition, writing, and presence of paraphasic (substitution) sound or word errors (e.g., saying *table* for *chair* or *p*ork for *f*ork).

Categorization

Many systems have been proposed to classify aphasia types (Kertesz, 1979). Each system represents a theoretical perspective of aphasia and identifies aphasia types according to the constellation of behavioral characteristics. Classification systems can be dichotomous (e.g., fluent vs. nonfluent or comprehension deficit vs. production deficit), anatomically and behaviorally based (e.g., Boston classification system of aphasia types, such as ▶ Broca's aphasia), behaviorally based (e.g., Schuell's system of multimodality, unidimensional impairment, such as aphasia with visual involvement), based on severity (e.g., mild, moderate, or severe), or follow a processing model (e.g., cognitive neuropsychological model of naming; Kay, Lesser, & Coltheart, 1996). Classification systems are useful for a general understanding of an individual's communication ability; however, controversy exists regarding their clinical utility. Some individuals with aphasia show symptoms that match more than one type of aphasia and others show symptoms that do not fit into any of the classification categories. Studies examining classification report 35–70% success in classifying participants as one aphasia type. Table 1 shows three classification systems, with general characteristics of each aphasia type.

Epidemiology

Aphasia resulting from stroke occurs in approximately 80,000 people each year, affecting about 30% of individuals who have a first-ever ischemic or hemorrhagic stroke. Approximately, one million people in the United States are living with aphasia following stroke. Aphasia resulting from traumatic brain injury and other causes is difficult to estimate.

Natural History, Prognostic Factors, Outcomes

Reports of language disorder following brain injury have existed for hundreds of years, initially primarily as case

Aphasia. Table 1 Three examples of aphasia classification systems showing aphasia types and general characteristics of each type

Dichotomous classification	
Type	**Characteristics**
Nonfluent aphasia	Limited speech output
	Effortful speech output
	Content words retained; function words omitted
	May or may not have articulation difficulties
	Melodic contour altered
Fluent aphasia	Approximates normal rate and sentence length
	Content words omitted in severe fluent aphasia
	Circumlocution present in mild fluent aphasia
	Melodic contour preserved
Anatomical and behavioral classification	
Type	Characteristics
Broca's aphasia	Nonfluent aphasia; expressive aphasia
	Effortful output
	Reduced phrase length and syntactic complexity; content words usually preserved
	Auditory comprehension may or may not be impaired
	Impairments in reading, writing, naming, and repetition
	Right hemiplegia often present
Wernicke's aphasia	Fluent aphasia; receptive aphasia
	Auditory comprehension usually impaired
	Impairments of reading, writing, naming, and repetition
	Paraphasic errors
	Melodic contour retained
Conduction aphasia	Fluent aphasia
	Auditory comprehension preserved
	Impairment in repetition
	Naming may be impaired
	Error recognition typically preserved
Global aphasia	Nonfluent aphasia
	Impairments in auditory comprehension, reading writing, naming, and repetition
	Limited functional communication often preserved
Anomic aphasia	Fluent aphasia
	Auditory and reading comprehension and repetition preserved
	Word retrieval deficit
Transcortical motor aphasia	Nonfluent aphasia
	Auditory comprehension and naming may be impaired
	Repetition preserved
	Paraphasic errors and perseveration present

Aphasia. Table 1 (Continued)

Type	Characteristics
Transcortical sensory aphasia	Fluent aphasia
	Auditory comprehension impaired
	Paraphasic errors
	Repetition preserved
	Naming may be impaired
Behavioral classification	
Type	Characteristics
Simple aphasia	Mild impairment
	Multimodality impairment (comprehension of spoken language; speech; reading; writing)
	No specific perceptual, sensorimotor, or dysarthric components
Aphasia with visual involvement	Mild aphasia
	Central impairment of visual modality
Aphasia with persisting dysfluency	Mild aphasia
	Verbal dysfluency
Aphasia with scattered findings	Moderate aphasia
	Impairments in one or more modalities
	Functional communication preserved
Aphasia with sensorimotor involvement	Severe aphasia
	Impaired output
Aphasia with intermittent auditory imperception	Severe aphasia
	Impaired auditory comprehension
Irreversible Aphasia syndrome	Severe aphasia
	Impairments in all modalities (comprehension of spoken language; speech; reading; writing)

reports. Paul Broca and Carl Wernicke in the late 1800s presented clinical data relating behavioral and anatomical information, localizing language ability to the left hemisphere, and ultimately having their names adopted to identify anatomical areas in the brain related to patterns of language behavior. Current studies of persons with aphasia use neuroimaging techniques to further elucidate the behavioral and anatomical relationship.

Aphasia in the first few months after a stroke is the acute stage and is often characterized by spontaneous recovery of language and communication deficits. In the chronic stage, an individual learns to live with aphasia and return to life activities. Prognosis for recovery is variable and dependent upon both internal patient factors (e.g., severity of aphasia, type and extent of lesion, or concomitant medical problems) and external factors (e.g., family support or communication interaction opportunities). Personal variables such as age, education, and gender do not systematically influence prognosis (Pedersen, Jorgensen, Nakayama, Raaschou, & Olsen, 2004).

Aphasia recovery occurs most rapidly immediately following the brain injury, as the brain begins to heal itself. Studies have shown that recovery also continues for years post stroke and treatment (Moss & Nicholas, 2006). Outcome measures documenting change are impairment-based (e.g., change in naming ability) or activity/participation-based (e.g., increased participation in social activities), following the World Health Organization's International Classification of Functioning, Disability and Health (ICF; WHO, 2001). Some persons with aphasia recover to near normal premorbid language and communication performance while others remain severely aphasic. Almost every person has the potential for some level of functional communication, from being an independent communicator in a variety of communication interactions to being dependent upon an alternative or

augmentative communication system or a conversational partner.

Neuropsychology and Psychology of Aphasia

Cognitive neuropsychology has brought to aphasia evaluation and treatment a set of models of human cognitive mechanisms and processes thought to underlie language performance. An individual's performance on several linguistic tasks is examined for patterns of impaired and spared cognitive processes to infer the cognitive architecture that underlies the performance. For example, in a model of lexical processing, the linguistic tasks might be lexical recognition (word/nonword identification), auditory comprehension (pointing to a named word), and naming a picture (confrontation naming). An individual who scores high on auditory comprehension and reading words tasks but low on confrontation naming may be inferred to show a deficit in phonological output lexicon but have an intact semantic system and ability to use phonic skills to read a word. That is, the individual may have intact semantic knowledge and be aware of the phonological form of a word and be able to read it, but lack the phonological skills to generate the verbal label. The performance pattern serves to direct treatment to the impaired processes, using the spared processes as strengths. Cognitive neuropsychological models of language processing frequently used in aphasia assessment and treatment, however, are not without criticism as being descriptive and not prescriptive, and requiring time-consuming assessment.

In contrast to the deficit-specific models of cognitive neuropsychology, the psychology of aphasia in assessment and treatment recognizes the importance of an individual's psychosocial state, quality of life, functional communication abilities, and communication network. Tanner (2003) proposed an eclectic approach to examine the psychology of aphasia from three perspectives: effects of brain injury, psychological defenses and coping styles, and responses to loss. This view speaks to the importance of an individual's premorbid personal characteristics, their ability to adjust to change, and their external support network as they and their family learn to live with aphasia. Several models and tools exist to guide assessment and treatment in these areas. For example, quality-of-life scales ask questions about topics such as family support and general outlook on life (e.g., Communication-Related Quality of Life Scale; Cruice et al., 2003). Social network diagrams illustrate the breadth and depth of an individual's support and communication networks (e.g., Blackstone & Berg, 2003). Several scales have been developed to screen for depression. Some have a linguistic bias or rely on caregiver report while others have been adapted to be "aphasia friendly" and not depend exclusively on complex written sentences. Three examples of instruments to examine depression are the Stroke Aphasia Depression Questionnaire (SADQ) (Lincoln, Sutcliffe, & Unsworth, 2000), the Aphasia Depression Questionnaire (Benaim, Cailly, Perennou, & Pelissier, 2004) and the Visual Analog Mood Scale (Stern, Arruda, Hooper Wolfner & Morey, 1997). The SADQ while designed for persons with aphasia has a linguistic bias and is intended to rely on caregiver report. The ADQ is a nine item tool used to assess post-stroke depression in persons who are hospitalized after a stroke. The VAMS is an example of a non-linguistic mood scale used for self-report of depressive symptoms.

Evaluation

Approaches to evaluation of aphasia vary with the conceptualization of aphasia.

Some approaches take an impairment-based approach, viewing aphasia as a disorder of selected abilities while others, such as the Life Participation Approach to Aphasia (Chapey et al., 2008) take an activity/participation approach, viewing aphasia as a disruption to communication and placing the person with aphasia and his or her family at the center of clinical decision-making activities. (Schuell, Jenkins & Jimenez-Pabon, 1964) proposed a Stimulation-Facilitation model based on auditory comprehension stimuli that are individually adapted to persons with aphasia. Chapey et al. support a Cognitive Stimulation model, which views communication as a problem-solving and decision-making task. Following the World Health Organization ICF (2001), models of assessment and treatment typically incorporate information at levels of impairment and activity/participation. Group treatment has gained popularity in recent years, recognizing the value of social connectedness (Avent, 1977; Kearns & Elman, 2008). Lubinski (2008) discussed an environmental model, suggesting that clinicians consider physical and social environments of a person with aphasia to enhance treatment effects. Finally, psychosocial models of intervention focus on integrating an individual into a communicating society and promoting their participation in personally relevant activities (Simmons-Mackie, 2008). Regardless of the approach, in order to understand the linguistic and

communicative abilities and needs of an individual, it is important to conduct an evaluation within a culturally sensitive framework.

Three types of aphasia tests are commonly used to assess language and communication abilities in persons who have aphasia: screening tests (short assessments that may be administered at bedside), comprehensive aphasia tests (batteries containing several subtests such as naming, reading, and writing), and tests of specific linguistic or communicative function (e.g., syntactic function or naming) (Patterson, 2008). In addition, assessment of aphasia and its impact on a person's life includes testing cognitive abilities (e.g., memory), testing executive functioning (e.g., divided attention), observing a person in activities of daily communication, and interviewing the person with aphasia and family members about the impact of aphasia on life participation and functional communication.

In aphasia assessment it is as important to determine the presence or absence of aphasia, and presence of concomitant disorders, as well as to classify aphasia type or describing aphasia symptoms. Examples of disorders that may accompany aphasia but that are not aphasia are apraxia of speech, dysarthria, dementia, memory impairment, or psychiatric problems. These concomitant disorders will affect treatment planning and task selection. Medical conditions, such as diabetes, cardiovascular disease, and any medications the patient takes may affect performance and should also be noted in the assessment report.

The goals of evaluation will vary depending upon factors such as severity of aphasia, age, and time post-onset. For example, an individual with mild aphasia who anticipates returning to work should have an assessment that includes detailed information on linguistic processing and a job task analysis to determine the linguistic requirements of the position. This information may be used to determine the individual's ability to return to a job, to identify communication requirements of the job, and to guide employment-related treatment. In contrast, evaluation for an individual with severe aphasia and concomitant severe apraxia of speech may require an evaluation focused on functional communication strategies to use with familiar communication partners within a contained environment.

Treatment

The acute stage of aphasia is the first few months after a stroke as the brain recovers from injury, and is often characterized by spontaneous recovery of language and communication deficits, while in the chronic stage of aphasia an individual learns to live with aphasia and return to life activities. There are many well-validated, effective techniques for aphasia rehabilitation, particularly for chronic aphasia. These range from general stimulation approaches to treatments aimed at specific signs of aphasia, and are chosen according to the patient's individual needs, goals, aphasia characteristics, and etiology. For aphasia due to acute-onset causes (e.g., vascular etiologies or trauma), therapy has been demonstrated to be effective both early after onset as well in the chronic stage. For aphasia due to progressive etiologies, therapy has been shown to be effective in maintaining functional communication and maximizing quality of communication life to the extent possible given the medical diagnosis.

Pharmacological intervention for aphasia may be undertaken for direct treatment of the language deficit or administered to address a concomitant disorder, such as depression. Although research in this area is encouraging, to date no pharmacologic treatment has emerged as consistently improving linguistic function without adverse side effects (Greener, Enderby, & Whurr, 2001; Murray & Clark, 2006; Troisi et al., 2002).

Treatment for aphasia historically focused primarily on restitution of function using impairment-based treatment techniques, with treatment targets such as word or sentence production, or writing. Examples of these treatment techniques are Melodic Intonation Therapy, a semantic or phonologic cueing hierarchy, and confrontation naming. More recently, treatment goals have expanded to include activity/participation based treatments such as functional communication and group therapy. Examples of activity/participation treatment methods are book groups for persons with aphasia (with the linguistic level of the book modified to be aphasia friendly), reciprocal scaffolding (e.g., Avent, Patterson, Lu, & Small, 2009), and supported conversation (e.g., Kagan, Black, Duchan, Simmons-Mackie, & Square, 2001).

The four principles of evidence-based practice, current best practices, clinical expertise, client/patient values, and context of treatment, guide treatment planning. Clinical practice research and clinical trials support the efficacy and effectiveness of aphasia therapy. Systematic reviews, such as the one for constraint-induced language therapy (Cherney, Patterson, Raymer, Frymark, & Schooling, 2008), and meta-analyses (e.g., Robey, 1998) report the evidence from group studies and single-subject research studies for a specific treatment or aphasia

therapy in general. Cherney and Robey (2008) and the Academy of Neurological Communication Disorders and Sciences (ANCDS, 2008) present analyses of treatment effect sizes of aphasia treatment for specific treatment areas such as syntax and language comprehension.

Cross References

- ▶ Agnosia
- ▶ Agrammatism
- ▶ Agraphia
- ▶ American Speech-Language-Hearing Association (ASHA)
- ▶ Anarthria
- ▶ Anomic Aphasia
- ▶ Aphasia Tests
- ▶ Apraxia of Speech
- ▶ Augmentative or Alternative Communication (AAC)
- ▶ Boston Diagnostic Aphasia Examination
- ▶ Boston Naming Test
- ▶ Broca's Aphasia
- ▶ Carl, Wernicke
- ▶ Conduction Aphasia
- ▶ Crossed Aphasia
- ▶ Cue
- ▶ Dysarthria
- ▶ Dysgraphia
- ▶ Edith Kaplan
- ▶ Evidence-Based Practice
- ▶ Fluent Aphasia
- ▶ Global Aphasia
- ▶ Harold Goodglass
- ▶ Melodic Intonation Therapy
- ▶ Multilingual Aphasia Examination
- ▶ Neurosensory Center Comprehensive Examination for Aphasia
- ▶ Paragrammatism
- ▶ Paraphasia
- ▶ Paul Broca
- ▶ Pragmatic Communication
- ▶ Progressive Aphasia
- ▶ Semantic Paraphasia
- ▶ Speech–Language Therapy
- ▶ Subcortical Aphasia
- ▶ Telegraphic Speech
- ▶ Transcortical Motor Aphasia
- ▶ Transcortical Sensory Aphasia
- ▶ Wernicke's Aphasia
- ▶ Wernicke-Lichtheim Model of Aphasia
- ▶ Western Aphasia Battery

References and Readings

Academy of Neurological Communication Disorders and Sciences. (2008). Practice guidelines of the ANCDS: Evidence based practice guidelines for the management of communication disorders in neurologically impaired individuals. http://www.ancds.org/index.php?option=com_content&view=article&id=9&Itemid=9. Accessed 3/29/10.

Avent, J. R. (1997). *Manual of Cooperative Group Treatment for Aphasia.* New York: Elsevier.

Avent, J., Patterson, J., Lu, A., & Small, K. (2009). Reciprocal scaffolding treatment: A person with aphasia as clinical teacher. *Aphasiology, 23*, 110–119.

Benaim, C., Cailly, B., Perennou, D., & Pellissier, J. (2004). Validation of the Aphasic Depression Rating Scale. *Stroke, 35*, 1692–1969.

Blackstone, S., & Hunt Berg, S. (2003). *Social networks: A communication inventory for individuals with complex communication needs and their communication partners.* Monterey, CA: Augmentative Communication Inc.

Chapey, R., Duchan, J. F., Elman, R. J., Garcia, L. J., Kagan, A., Lyon, J., et al. (2008). Life participation approach to aphasia: A statement of values for the future. In R. Chapey (Ed.), *Language intervention strategies in aphasia and related neurogenic communication disorders* (5th ed., pp. 279–289). Philadelphia: Wolters Kluwer.

Cherney, L. R., Patterson, J. P., Raymer, S. M., Frymark, T., & Schooling, T. (2008). Evidence-based systematic review: Effects of intensity of treatment and constraint-induced language therapy for individuals with stroke-induced aphasia. *Journal of Speech-Language-Hearing Research, 51*, 1282–1299.

Cherney, L. R., & Robey, R. R. (2008). Aphasia treatment: recovery, prognosis and clinical effectiveness. In R. Chapey (Ed.), *Language intervention strategies in aphasia and related neurogenic communication disorders* (5th ed., pp. 186–202). Philadelphia: Wolters Kluwer.

Cruice, M., Worral, L., Hickson, L., & Murison, R. (2003). Finding focus for quality of life with aphasia: Social and emotional health, and psychological well-being. *Aphasiology, 17*, 333–353.

Davis, G. A. (2006). *Aphasiology: Disorders and clinical practice.* Englewood Cliffs, NJ: Prentice Hall.

Greener, J., Enderby, P., & Whurr, R. (2001). Pharmacological treatment for aphasia following stroke. *Cochrane Database of Systematic Reviews.* Issue 4. Art. No.: CD000424. doi: 10.1002/14651858.CD000424.

Hallowell, B., & Chapey, R. (2008). Introduction to language intervention strategies in aphasia. In R. Chapey (Ed.), *Language intervention strategies in aphasia and related neurogenic communication disorders* (5th ed., pp. 3–19). Philadelphia: Wolters Kluwer.

Kagan, A., Black, S. E., Duchan, J. F., Simmons-Mackie, N., & Square, P. (2001). Training volunteers as conversational partners using "Supported Conversation for Adults with aphasia" (SCA): A controlled trial. *Journal of Speech-Language-Hearing Research, 44*, 624–638.

Kay, J., Lesser, R., & Coltheart, M. (1996). Psycholinguistic assessments of language processing in aphasia (PALPA): An introduction. *Aphasiology, 10*, 159–215.

Kearns, K., & Elman, R. (2008). Group therapy for aphasia: Theoretical and practical considerations. In R. Chapey (Ed.), *Language intervention strategies in aphasia and related neurogenic communication disorders* (5th ed., pp. 376–398). Philadelphia: Wolters Kluwer.

Kertesz, A. (1979). *Aphasia and associated disorders: Taxonomy localization and recovery.* New York: Grune & Stratton.

Lincoln, N. B., Sutcliffe, L. M., & Unsworth, G. (2000). Validation of the Stroke Aphasic Depression Questionnaire (SADQ) for use with patients in hospital. *Clinical Neuropsychological Assessment, 1*, 88–96.

Lubinski, R. (2008). Environmental approach to adult aphasia. In R. Chapey (Ed.), *Language intervention strategies in aphasia and related neurogenic communication disorders* (5th ed., pp. 319–349). Philadelphia: Wolters Kluwer.

Moss, A., & Nicholas, M. (2006). Language rehabilitation in chronic aphasia and time postonset: A review of single-subject data. *Stroke, 37*, 3043–3051.

Murray, L. L., & Clark, H. M. (2006). *Neurogenic disorders of language: Theory driven clinical practice* (Chap. 10). Clifton Park, NY: Thompson Delmar Learning.

Patterson, J. P. (2008). Assessment of language disorders in adults. In R. Chapey (Ed.), *Language intervention strategies in aphasia and related neurogenic communication disorders* (pp. 64–160). Baltimore: Wolters Kluwer.

Pedersen, P. M., Jorgensen, H. S., Nakayama, H., Raaschou, H. O., & Olsen, T. S. (2004). Aphasia in acute stroke: Incidence, determinants, and recovery. *Annals of Neurology, 38*, 659–666.

Robey, R. R. (1998). A meta-analysis of outcomes in the treatment of aphasia. *Journal of Speech-Language-Hearing Research, 41*, 172–187.

Schuell, H., Jenkins, J., & Jimenez-Pabon, E. (1964). *Aphasia in adults.* New York: Harper medical Division.

Simmons-Mackie, N. (2008). Social approaches to aphasia intervention. In R. Chapey (Ed.), *Language intervention strategies in aphasia and related neurogenic communication disorders* (5th ed., pp. 290–318). Philadelphia: Wolters Kluwer.

Stern, R. A., Arruda, J. E., Hooper, C. R., Wolfner, G. D., & Morey, C. E. (1997). Visual analog mood scales to measure internal mood state in neurologically impaired patients: Description and initial validity evidence. *Aphasiology, 11*, 59–71.

Tanner, D. C. (2003). Eclectic perspectives on the psychology of aphasia. *Journal of Allied Health, 32*, 256–260.

Troisi, E., Paolucci, E., Silvestrini, M., Matteis, M., Vernieri, F., Grasso, M. G., et al. (2002). Prognostic factors in stroke rehabilitation: The possible role of pharmacological treatment. *Acta Neurologica Scandinavica, 105*, 100–106.

World Health Organization. (2001). International Classification of Functioning, Disability and Health. Geneva: Author. http://www.who.int/classifications/icfbrowser/. Accessed 30 March, 2010.

Aphasia Assessment

► Aphasia Tests

Aphasia Diagnosis

► Aphasia Tests

Aphasia Diagnostic Profiles

Janet Patterson
California State University
East Bay, Hayward, CA, USA

Description

The Aphasia Diagnostic Profiles (ADP; Helm-Estabrooks, 1992) is an impairment-based measure (World Health Organization, 2001) designed to assess language and communication skills in persons with aphasia, primarily following stroke. The ADP consists of nine subtests, each of which yields a standard score and percentiles. The subtests assess speech, language, and communication in all modalities (verbal and written) and the test emphasizes conversational interaction; verbal instructions to the patient are written in an informal style in the manner of conversation (e.g. "Well now, that's out of the way, I'm going to turn on the tape recorder").

Responses are typically scored on a five-point scale: immediately correct; mostly correct; some correct; fully incorrect; no response. Scores from the subtests are combined to produce five profiles describing the level of impairment of aphasia. The profiles are the Aphasia Classification Profile, the Aphasia Severity Profile, the Alternative Communication Profile, the Error Profiles, and the Behavioral Profile. Other scores of interest are the ADP Phrase length (average length of longest three phrases); Correct Information Units (new pieces of information), and Index of Wordiness (Correct Information Units relative to total number of words). Table 1 shows the titles and a brief description of the nine subtests and five profiles.

The ADP is used to classify an individual's aphasia type as nonfluent, borderline fluent, or fluent. Using the lexical retrieval score, ADP phrase length, auditory comprehension score, and repetition score, the ADP further classifies the aphasia type as global, mixed nonfluent, Broca's, transcortical motor, Wernicke's, transcortical sensory, conduction, or anomic aphasia, following the conventions of the Boston aphasia classification system.

The ADP was created in part to address the need for a comprehensive aphasia battery that could be administered in a relatively brief time (40–50 min) in a medical setting. The manual is clearly written with explicit administration and scoring instructions. The record form is easy to use and facilitates the completion of the profile scores.

Aphasia Diagnostic Profiles. Table 1 Aphasia diagnostic profiles: Nine subtests and five profiles

ADP Subtests	
Subtest	**Description**
Personal information	Verbal response to questions
Writing	Complete Patient Information Sheet
Reading	Read items on Patient Information Sheet
Fluency	Produce connected speech in three contexts
Naming	Name familiar pictured items
Auditory language comprehension	Answer questions – word, sentence, and story levels
Repetition	Repeat words and phrases
Elicited gestures	Pretend to complete action
Singing	Sing 3 familiar songs
ADP Profiles	
Profile	**Description**
Aphasia Classification Profile	Identifies aphasia type (based on the Boston classification system)
Aphasia Severity Profile	Indicates specific strengths and weaknesses
Alternative Communication Profile	Identifies patient's strongest response modalities and guides therapy
Error Profiles	Identify the communicative value of a patient's responses
Behavioral Profile	Indexes the patient's overall emotional state during testing

Historical Background

The ADP was first published in 1992 and since then has been frequently used in clinical and research activities. Numerous studies of aphasia treatment use the ADP as a measure of behavior change following intervention.

Psychometric Data

The ADP manual reported that it was standardized on 290 adults with neurological impairments (222 potentially aphasic adults) and 40 nonaphasic adults. The median age of these individuals was 70 years. The manual further reported reliability coefficients (inter-item consistency) for subtest raw scores that ranged from 0.73 (Behavioral Score) to 0.96 (Repetition), with most of the coefficients in the 0.90s. Test–retest coefficients ranged from 0.64 (Elicited Gestures) to 0.91 (Information Units). The ADP has a strong theoretical and psychometric foundation but has not been subjected to additional psychometric evaluation.

Clinical Uses

Three characteristics make the ADP a valuable clinical assessment tool: the theoretical foundation and close relationship to the Boston aphasia classification system, the structure of the test and clarity of the administration manual, and the amount of administration and scoring time required. It is also notable that both verbal and nonverbal modalities of communication are included in the assessment. One limitation of the ADP is that it does not examine any linguistic, psycholinguistic, or neuropsychological behavior in detail; additional tests in specific areas would be required to obtain in-depth information as part of an extensive diagnostic evaluation.

Cross References

- ▶ Anomia
- ▶ Anomic Aphasia
- ▶ Aphasia
- ▶ Aphasia Tests

A

- ▶ Boston Diagnostic Aphasia Examination
- ▶ Broca's Aphasia
- ▶ Carl, Wernicke
- ▶ Conduction Aphasia
- ▶ Edith Kaplan
- ▶ Global Aphasia
- ▶ Harold Goodglass
- ▶ Repetition
- ▶ Speech/Communication Disabilities
- ▶ Speech-Language Therapy
- ▶ Transcortical Motor Aphasia
- ▶ Transcortical Sensory Aphasia
- ▶ Wernicke's Aphasia

References and Readings

Helm-Estabrooks, N. (1992). *Aphasia diagnostic profiles.* Austin, TX: Pro Ed Inc.

World Health Organization. (2001). *International classification of functioning, disability and health.* http://www.who.int/classifications/icfbrowser/

Aphasia Evaluation

- ▶ Aphasia Tests

Aphasia Tests

Janet Patterson
California State University
Hayward, CA, USA

Synonyms

Aphasia assessment; Aphasia diagnosis; Aphasia evaluation

Description

Tests of aphasia are used to diagnose the type and severity of aphasia and related disorders and to plan intervention for the speech, language, and communication deficits demonstrated by persons who have aphasia following brain injury (PWA). Three types of aphasia tests are commonly used to assess language and communication abilities in PWA: screening tests, comprehensive aphasia tests, and tests of specific linguistic or communicative function (Patterson, 2008). In addition, assessment of aphasia and its impact on a person's life includes testing cognitive abilities and related disorders (e.g., memory), testing executive functioning (e.g., attention and planning), observing a person in activities of daily communication (e.g., social functional communication or work-related communication), interviewing the person with aphasia and family members, and determining an individual's candidacy for use of alternative and augmentative communicative systems (e.g., an alphabet board to spell words, drawing, or a commercially available device).

Historical Background

Aphasia has been assessed more or less systematically for many years. Clinical observation was the earliest method of assessment, and the first standardized test was published in 1926 by Henry Head. In the ensuing years, several comprehensive aphasia tests and specific linguistic tests appeared. Each comprehensive test is based upon a theoretical model of aphasia, and although the tests contain common subtests (e.g., sentence repetition), the test results and aphasia diagnoses vary. For example, the *Minnesota Test for Differential Diagnosis of Aphasia* (Schuell, 1965) assesses language performance across several modalities and rests upon Schuell's theory of aphasia as a unitary reduction in language across modalities with or without accompanying perceptual or motor deficits. In contrast, the *Boston Diagnostic Aphasia Examination* (Goodglass, Kaplan, & Baressi, 2001) relates speech and language behavioral deficits to neurological lesions. With yet a different perspective, Luria (1966) proposed a comprehensive examination for aphasia through nonstandardized observation of language performance in several modalities, but without specific subtests.

In recent years, several tests have emerged to assess specific language or communication functions in PWA. For example, the *ASHA-FACS* (Frattali et al., 1995) assesses functional communication skills such as participating in conversation, while the *Reading Comprehension Battery for Aphasia* (LaPointe & Horner, 1998) evaluates reading performance in several contexts, such as single words and paragraphs.

Psychometric Data

The availability of psychometric data for aphasia tests ranges from prolific and well documented for some tests

to minimal or nonexistent for others, and the data appear in scholarly journals as well as in the test manuals. Spreen and Risser (2003) and Strauss, Sherman, and Spreen (2006) provide overviews of psychometric data for many general aphasia tests and supplemental language tests. Few studies, and none recently, compared psychometric data across tests. In evaluating a general or supplemental test for aphasia, several factors should be considered, including size and definition of the standardization sample; reports of item, concurrent and predictive validity; test-retest, interrater and intrarater reliability; report of raw score means, standard deviations, and ranges; information about test development, examiner qualifications, administration instructions, scoring, and interpretation; and normative data.

Although it is difficult to judge which of the many aphasia tests best meets all the factors mentioned above, there are four tests that are frequently used in clinical settings and have the most psychometric data published about them: *Boston Diagnostic Aphasia Examination, Boston Naming Test, Token Test* (and *Revised Token Test*), and *Western Aphasia Battery.*

Clinical Uses

Screening Tests for Aphasia

Screening tests for aphasia are brief and may be administered at bedside. Their purpose is to rapidly determine the presence of aphasia or the need for further assessment. A screening test may be independent (e.g., *Quick Assessment for Aphasia*; Tanner & Culbertson, 1999) or a shortened form of a comprehensive aphasia battery, such as the *Western Aphasia Battery* (WAB; Kertesz, 2006).

Comprehensive Aphasia Batteries

A comprehensive aphasia battery is based on a theoretical model of aphasia and contains several subtests. For example, the *Boston Diagnostic Aphasia Examination* (Goodglass et al., 2001) has 34 subtests and the performance pattern is used to classify an individual with an aphasia type (e.g., ▶ Broca's aphasia). Although some subtests of comprehensive aphasia batteries may appear similar, the data obtained from each of the subtests and the resulting aphasia diagnosis will vary according to the theoretical model of aphasia which underlies the test. Other comprehensive aphasia batteries are the *Western Aphaisa Battery* (Kertesz, 2006), *the Multilingual Aphasia Examination* (Benton, Hamsher, Rey, & Sivan, 1994), and *the Neurosensory Center Comprehensive Examination for Aphasia* (Spreen & Benton, 1977).

Tests of Specific Linguistic or Communication Function

Tests of specific functions provide detailed information about a person's abilities in one area of linguistic or communication ability and are particularly useful for persons who have severe or minimal aphasia and for whom comprehensive aphasia batteries would understate communication strengths and weaknesses. Three examples are the *Revised Token Test* (McNeil & Prescott, 1978) for auditory comprehension, the *Boston Naming Test* (Goodglass, Kaplan & Weintraub, 2001) for oral naming, and the *Psycholinguistic Assessments of Language Processing in Aphasia* (Kay, Lesser, & Coltheart, 1992).

Tests of Cognitive-Communication Abilities and Related Functions

Tests of cognitive-communicative abilities related to language functions have been included as part of comprehensive aphasia batteries (e.g., the ▶ Raven's Progressive Matrices [Raven, Raven, & Court, 1995] as part of the Cortical Quotient in the WAB) or administered independently (e.g., ▶ Wechsler Memory Scale; Wechsler, 2009).

Tests of Functional Communication

Functional communication abilities in PWA are assessed through observation or the use of specific tests. Functional communication includes verbal and nonverbal methods of conveying information in activities of daily living, such as reading signs, greeting individuals and participating in conversation. Functional communication assessed through observation can be contextually bound, such as assessing conversation with familiar or unfamiliar partners. Tests of functional communication are intended to simulate activities of daily living but typically are acontextual. Two examples of tests of functional communication are the *Communicative Activities of Daily Living* – 2 (Holland, A. L., Frattali, C. M. & Fromm, D. 1999) and the *Assessment of Language-Related Functional Activities* (Baines, Heeringa, & Martin, 1999).

Cross References

- ▶ Activities of Daily Living
- ▶ Aphasia
- ▶ Augmentative or Alternative Communication
- ▶ Boston Diagnostic Aphasia Examination
- ▶ Boston Naming Test
- ▶ Luria, Alexander Romanivich (1902–1977)
- ▶ Multilingual Aphasia Examination
- ▶ Neurosensory Center Comprehensive Examination for Aphasia
- ▶ Wechsler Memory Scales
- ▶ Western Aphasia Battery

References and Readings

Baines, K. A., Martin, K. W., & Heeringa, H. M. (1999). *ALFA: Assessment of Language Related Functional Acclivities.* Austin TX: Pro-Ed.

Benton, A. L., Hamsher, K. deS., Rey, G. J., & Sivan, A. B. (1994). *Multilingual Aphasia Examination* (MAE-3). Lutz FL: Psychological Assessment Resources Inc (PAR).

Davis, G. A. (2007). *Aphasiology: Disorders and clinical practice* (2nd ed.). Boston: Pearson Allyn & Bacon.

Frattali, C. M., Thompson, C. K., Holland, A. L., Wohl, C. B., & Ferketic, M. M. (1995). *The American Speech-Language-Hearing Association Functional Assessment of Communication Skills in Adults.* Rockville, MD: The American Speech-Language-Hearing Association.

Goodglass, H., Kaplan, E., & Weintraub, S. (2001). *Boston Naming Test* (2nd ed.). Austin TX: Pro-Ed.

Goodglass, H., Kaplan, E., & Baressi, B. (2001). *Boston Diagnostic Aphasia Examination* (3rd ed.). San Antonio, TX: Psychological Corporation.

Head, H. (1926). *Aphasia and kindred disorders of speech.* New York: MacMillan.

Holland, A. L., Frattali, C. M., & Fromm, D. (1999). *Communicative Activities of Daily Living - 2nd Edition.* San Antonion: Psychological Corporation.

Kay, J., Lesser, R., & Coltheart, M. (1992) *Psycholinguistic Assessment of Language Processes in Aphasia.* London: Taylor & Francis Group.

Kertesz, A. (2006). *Western Aphasia Battery.* New York: Grune & Stratton.

LaPointe, L. L., & Horner, J. (1998). *Reading Comprehension Battery for Aphasia* (RCBA-2). San Antonio TX: Pearson.

Luria, A. R. (1966). *Higher cortical functions in man.* New York: Basic Books.

McNeil, M. R., & Prescott, T. E. (1978). *Revised Token Test.* Austin, TX: Pro-Ed.

Patterson, J. P. (2008). Assessment of language disorders in adults. In R. Chapey (Ed). *Language intervention strategies in aphasia and related neurogenic communication disorders* (5th ed., pp. 64–160). Baltimore: Wolters Kluwer.

Raven, J., Court, & Raven, J. C. (1995). *Raven's Progressive Matrices.* San Antonio: The Psychological Corporation.

Schuell, H. (1965). *Minnesota Test for Differential Diagnosis of Aphasia.* Minneapolis: University of Minnesota Press.

Spreen, O., & Benton, A. L. (1977). *Neurosensory Center Comprehensive Examination for Aphasia.* Victoria BC: University of Victoria Neuropsychology Laboratory.

Spreen, O., & Risser, A. H. (2003). *Assessment of aphasia.* Oxford: Oxford University Press.

Strauss, E., Sherman, E. M. S., & Spreen, O. (2006). *A compendium of neuropsychological tests: Administration, norms and commentary* (3rd ed.). Oxford: Oxford University Press.

Wechsler, D. M. (2009) *Wechsler Memory Scale - 4th Edition.* San Antonio TX: Psychological Corporation.

Aphonia

Lyn Turkstra
University of Wisconsin-Madison
Madison, WI, USA

Synonyms

Mutism

Definition

Mutism is the complete absence of voice, i.e., adduction and vibration of the vocal folds is insufficient for vocal production. Aphonia may be associated with vocal fold paralysis; trauma; severe cases of inflammation, edema, or scarring of the vocal folds; benign or malignant diseases of the vocal folds that interfere with vocal fold closure; neurologically based movement disorders (e.g., spasmodic dysphonia); overuse of the voice; or somatoform disorders (e.g., in forms of elective mutism). Aphonia may be intermittent or episodic. For example, individuals with spasmodic dysphonia may have periodic, abnormal abduction or adduction of the vocal folds that may be perceived as voice breaks. Individuals who stutter also may have periodic voice breaks, in this case associated with tight adduction of the vocal folds.

When voice loss is incomplete, or when vocal quality is affected without complete loss of voice (e.g., if the voice is hoarse), it is referred to as dysphonia. Aphonia and dysphonia refer specifically to abnormal sound output from the phonatory sound source (i.e., the larynx), and should be distinguished from anarthria or dysarthria, which are disorders of articulation, i.e., related to the movements of the tongue, lips, jaw, and soft palate. Accordingly, dysphonia or aphonia can occur independently from anarthria or dysarthria.

Cross References

► Dysphonia

References and Readings

Merati, A., & Bielamowicz, S. (Eds.). (2007). *Textbook of voice disorders.* San Diego: Plural Publishing.

Stemple, J. C., Glaze, L. E., & Klaben, B. G. (2000). *Clinical voice pathology, theory & management* (3rd ed.). Thompson Learning (now Florence, KY: Cengage Learning).

APM

► Advanced Progressive Matrices

APOE

► Apolipoprotein E

Apolipoprotein E

John DeLuca
Kessler Foundation Research Center
West Orange, NJ, USA

Definition

Apolipoprotein E (ApoE) is a polymorphic plasma glycoprotein that transports cholesterol and other lipids, and has been shown to be involved in the growth and repair of neurons. There is also some evidence to suggest that ApoE is involved in lipid redistribution after demyelination. The ApoE protein is mapped to chromosome 19 and is polymorphic with three major isoforms, each of which translates into three alleles of the gene: ApoE-2, ApoE-3, and ApoE-4. ApoE-2 is associated with the genetic disorder type III hyperlipoproteinemia. There is also some evidence that this allele may serve as a protective role in the development of Alzheimer's disease (AD). ApoE-3 is found in approximately 64% of the population, and is considered as the "neutral" ApoE genotype. ApoE-4 has been implicated in atherosclerosis and AD, and impaired cognitive functioning. More specifically, ApoE-4 has been shown to be a major risk factor for development of AD and has been associated with subtle neuropsychological deficits in preclinical AD. Brain changes associated with ApoE-4 in AD include: increased counts of amyloid plaques and neurofibrillary tangles; smaller medial temporal lobe structures; reduced glucose metabolism; and depletion of cholinergic markers in the hippocampus, frontal, and temporal cortices. ApoE-4 has also been associated with adverse recovery after traumatic brain injury (TBI). Person with TBI with the ApoE-4 allele are ten times more likely to develop AD than those without the ApoE-4 allele. In multiple sclerosis, ApoE-4 has been found to be associated with rapid disease progression and increased cognitive impairment, although the findings for cognitive impairment have been inconsistent.

Cross References

► Alzheimer's Disease

References and Readings

Plomin, R., Defries, J. C., Craig, I. W., & McGuffin, P. (2003). *Behavioral genetics in the postgenomic era.* Washington DC: American Psychological Association.

Apoptosis

Kathleen L. Fuchs
University of Virginia Health System
Charlottesville, VA, USA

Synonyms

Programmed cell death

Definition

Apoptosis is both a normal developmental process to rid the body of overproduced cells as well as a sign of pathology in mature neural systems. Apoptosis involves activation of caspases – proteins that cleave other proteins in order to inactivate or modulate them to trigger

"pro-death" molecular pathways. The resulting cellular debris is then removed by microglia in the central nervous system. Abnormal protein cleavage and cell death has been implicated in neurodegenerative disorders such as Alzheimer's disease as well as autoimmune disorders such as multiple sclerosis.

Cross References

- ▶ Alzheimer's Disease
- ▶ Multiple Sclerosis

References and Readings

Hengartner, M. O. (2000). The biochemistry of apoptosis. *Nature, 407*, 770–776.
Yuan, J., & Yankner, B. A. (2000). Apoptosis in the nervous system. *Nature, 407*, 802–809.

Appalic Syndrome

Dona Ec Locke
Mayo Clinic
Scottsdale, AZ, USA

Synonyms

Persistent vegetative state

Definition

Appalic syndrome is an older term that has been replaced by **persistent vegetative state**. The vegetative state is a clinical condition of complete unawareness of the self and the environment, accompanied by sleep–wake cycles with either complete or partial preservation of hypothalamic and brain-stem autonomic functions. A thorough clinical evaluation may be required to distinguish between persistent vegetative state and other conditions, including coma, brain death, and locked-in syndrome.

Cross References

- ▶ Brain Death
- ▶ Coma
- ▶ Locked-in Syndrome
- ▶ Minimally Conscious State
- ▶ Minimally Responsive State

References and Readings

(May 26, 1994). Medical Aspects of the Persistent Vegetative State—First of Two Parts. *NEJM, 330*, 1499–1508.
Multi-society Task Force on PVS. Medical Aspects of the Persistent Vegetative State-Second of Two Parts. NEJM, 330,1572–1579.

Apperceptive Visual Agnosia

John E. Mendoza
Tulane University Medical Center
New Orleans, LA, USA

Definition

Inability or marked difficulty in visually identifying an object or picture of an object as a result of impaired perceptual abilities. In apperceptive agnosia, in addition to problems in the visual identification of an object, patients show impairment in reproducing (e.g., by drawing) the object or image and even matching the item to a similar one within a visual array. This contrasts with associative visual agnosia in which identification may also be impaired but the patient can usually render a reasonable representation (e.g., a drawing or graphomotor copy) of the object that cannot be visually identified and can visually match it to a sample. Apperceptive visual agnosia likely results from a defect in the secondary association areas of the visual cortex and is usually found in patients who complain of general loss or reduction in visual acuity.

Cross References

- ▶ Associative Visual Agnosia

References and Readings

Bauer, R. M., & Demery, J. A. (2003). Agnosia. In K. Heilman & E. Valenstein (Eds.), *Clinical neuropsychology* (4th ed., pp. 236–295). New York: Oxford University Press.

DeRenzi, E., & Spinnler, H. (1966). Visual recognition in patients with unilateral cerebral disease. *Journal of Nervous and Mental Disease, 142*, 513–525.

DeRenzi, E., Scotti, G., & Spinnler, H. (1969). Perceptual and associative disorders of visual recognition. Relationship to the side of the cerebral lesion. *Neurology, 19*, 634–642.

Applied Behavior Analysis

Anthony Cuvo
Southern Illinois University
Carbondale, IL, USA

Definition

Applied behavior analysis (ABA) is "the science in which tactics derived from the principles of behavior are applied to improve socially significant behavior and experimentation is used to identify the variables responsible for the improvement in behavior" (Cooper, Heron, & Heward, 2007, p. 690).

Historical Background

The most notable figure in ABA is B. F. Skinner whose book, *The Behavior of Organisms* (1938), described his animal research on operant conditioning. Skinner explained how behavior operates on the environment and is a function of its environmental consequences. Subsequently, Skinner explained the application of behavioral principles and processes discovered in the animal laboratory to a utopian society (1948), human behavior (1953), verbal behavior (1957), teaching (1968), and other issues related to ABA.

Research on the application of basic behavioral principles and processes to important societal concerns began to emerge in the middle of the twentieth century. The *Journal of Applied Behavior Analysis,* the flagship journal of the discipline, began publication in 1968 as an outlet for the emerging ABA research. In the initial issue of that journal, the defining characteristics of ABA were identified as being applied, behavioral, analytical, technological, conceptually systematic, effective, and capable of producing generalizable outcomes (Baer, Wolf, & Risley, 1968). Since then, ABA research has found a welcome home in numerous professional journals in various disciplines. The Association for Behavior Analysis-International was established in 1974 and is ABA's principal professional organization.

Rationale or Underlying Theory

From a behavioral systems perspective, behavioral development is a function of the reciprocal interaction of a person's: (a) genetic-constitutional makeup, (b) history of interactions, (c) current physiological conditions, (d) current environmental conditions, and (e) behavioral dynamics or behavior change over time (Novak & Peláez, 2004). Treatment providers should consider all these factors when developing behavioral programs for individuals with neuropsychological disorders. A major conceptual focus of ABA is to understand, explain, and control the operant behavior of humans in their environment.

The most basic form of operant conditioning is the probabilistic strengthening of a response by its reinforcing consequences and the weakening of a response by its punishing consequences. For example, access to extra computer time might reinforce the timely completion of academic work by students with attention deficit disorder, and loss of free play might punish their noncompliance. In addition to control of behavior by its consequences, behavior can be evoked by stimuli that precede it. For example, a written or pictorial prompt might evoke a medication taking response by a person with acquired head injury. The beneficial treatment effects and avoidance of adverse effects by not taking the medication might increase the probability that the person will take it.

The probability that a response actually will occur at a given time can be influenced by contextual variables. For example, severe symptoms of allergies on a particular day might increase the aversiveness of otherwise tolerable academic task demands on a student with attention deficit disorder and increase the probability that the student will engage in task escape behavior that day.

During the past decade, there has been a growing body of research on relational responding and relational frame theory (e.g., Hayes, Barnes-Holmes, & Roche, 2001; Sidman, 1994) that has provided the conceptualization and supporting empirical data to account for a broader range of phenomena relevant to ABA. For example, the theory explains how individuals who experience painful medical procedures can develop a wide range of fears to various persons, settings, and objects (Friman, 2007).

Goals and Objectives

ABA treatment goals, regardless of neuropsychological population, can be broadly classified as efforts to promote the acquisition, maintenance, fluency (i.e., rate), and generalization of adaptive behavior, as well as the

reduction of challenging behavior. An individual's treatment goals and objectives should be determined by an analysis of the person's behavioral excesses and deficits based on their expectations in the environmental context (i.e., goals should be socially valid).

The social validity of treatment goals can be determined more formally either by social comparison or subjective evaluation techniques (Kazdin, 1977). The former relies on considering an individual's behavior with respect to that of an appropriate comparison group. For example, the classroom out-of-seat behavior of a child with hyperactivity could be compared with that of his classmates who serve as the social validation criterion. Does the child's out-of-seat behavior fall unacceptably outside the range of his or her peers? Subjective evaluation relies on the opinion of key persons in the environment as a social validation criterion. For example, the teacher might rate the child's out-of-seat behavior daily with respect to its acceptability. Is the child's out-of-seat behavior unacceptable in the opinion of the teacher? Treatment participants also could assist in setting their own goals as part of a self-management program.

The specific behavioral topographies that are the goals of change might differ across individuals (e.g., by population, type and severity of disability, setting). Treatment goals also can have commonality across different clinical populations (e.g., rate of performing academic behavior by children with attention deficit/hyperactivity disorder and cerebral palsy; reduction of physically aggressive behavior by individuals with acquired head injury and encephalitis). Thus, practitioners should focus on understanding the person–context relationship when formulating treatment goals, and not solely on a person's diagnosis.

Individuals with various neuropsychological disorders have had treatment goals related to specific target behaviors, such as: (a) acquired brain injury (aggression, vocational behavior); (b) attention deficit/hyperactivity disorder (off-task, academic behavior); (c) autism (communication, social skills); (d) cerebral palsy (conversation, walking); (e) dementia, including Alzheimer's disease (incontinence, wandering); (f) encephalitis (sexual and violent behavior); (g) epilepsy (diet compliance, seizure awareness); and (h) Tourette's syndrome (vocal and motor tics).

Treatment Participants

ABA has had wide application of its treatment procedures to various clinical and nonclinical populations, including those with neuropsychological disorders, as well as key people in their environment (e.g., staff, parents). Treatment participants have been of diverse ages, diagnoses, and severity of disability. Intervention has occurred in both laboratory and natural settings for numerous adaptive and challenging behaviors to meet goals and objectives, such as those previously stated. The largest body of research and application can be found for persons with developmental disabilities, especially intellectual disability, and more recently autism spectrum disorders. For approximately 50 years, research and application for individuals with intellectual disability has occurred across the lifespan, severity of the disability, behavioral topographies, and in institutional and community settings. ABA research and applications to autism have been more limited, but noteworthy, with children being the most frequent recipient of treatment. There is a much smaller, but nevertheless important, body of ABA treatment demonstrations for individuals with other neuropsychological disorders, including acquired head injury, Alzheimer's disease, attention deficit/hyperactivity disorder, cerebral palsy, dementia, epilepsy, learning disabilities, schizophrenia, and Tourette's syndrome. ABA based treatments have much to offer these under-studied populations, their families, and the staff who serve them. The breadth of applicability of ABA-based treatments across clinical and nonclinical populations can be attributed to the generality of the underlying principles and processes of the science of behavior.

Treatment Procedures

As previously stated, ABA is the science of behavior and not a treatment per se. Treatments typically include a number of components that are applications of the science of behavior; however, claims about the efficacy of individual components cannot be made independently of the whole treatment package. A common component of ABA treatment packages is differential reinforcement (i.e., reinforcing the desired response and withholding reinforcement or using a behavior reduction tactic for undesired responses). For example, the pathological tongue thrust during mealtime of a 10-year old boy with mental retardation and spastic cerebral palsy was treated by presenting food when his tongue was in and pushing the tongue back into his mouth with a spoon when he thrust out his tongue and expelled food (Thompson, Iwata, & Poynter, 1979). Amount of attention was differentially provided to control breath-holding for a 7-year old girl with mental retardation and Cornelia-de-Lange syndrome (Kern, Mauk, Marder, & Mace, 1995) and the

bizarre vocalizations of an adult with schizophrenia (Wilder, Masuda, O'Conner, & Baham, 2001). Noncontingent attention (i.e., increasing attention overall without respect to a specific target behavior) has been used effectively for reducing disruptive vocalizations by elderly dementia patients (Buchanan & Fisher, 2002); noncontingent escape (i.e., allowing escape from an activity regardless of behavior) has been used for treating aggression during bathroom routines for the same population (Baker, Hanley, & Mathews, 2006).

To increase the likelihood that response consequences serve a reinforcing function, stimulus preference assessments are formally conducted. For example, the relative preference of 33 food items was assessed to help a 15-year old girl with uncontrolled epilepsy maintain compliance to a ketogenic diet (Amari, Grace, & Fisher, 1995). Highly preferred foods were used to reinforce compliance to the diet. Allowing individuals to make choices among activities to be performed is another tactic to promote desired behavior (e.g., on-task by individuals with traumatic brain injury) and reduce challenging behavior.

Several behavioral components are important when teaching new behavior. Often, shaping by successive approximations is required to teach behavior. For example, a 5-year old child with mental retardation and spina bifida was taught the use of crutches by breaking the task down into a 10-step sequence (Horner, 1971). Prompts or cues usually are required to evoke an unlearned response. Examples include physical prompts (e.g., physically guiding a child to use crutches), modeling (e.g., video demonstrating a typically developing child undergoing a medical exam), visual prompts (e.g., picture or written memory aides for adults with Alzheimer's disease or acquired brain injury), and verbal instructions (i.e., telling people what to do). ABA research has also demonstrated procedures to transfer control of responding from the prompt to natural cues (e.g., from the memory aide that prompts going to the next activity to the time on the clock).

Environmental arrangements are also helpful in controlling behavior. A visual cloth barrier on an unsafe restricted area reduced entry to that area by dementia patients who wandered (Feliciano, Vore, LeBlanc, & Baker, 2004). Furniture was rearranged to be more conducive to conversation, and mealtime routines were rearranged to improve behavior in dementia patients (Melin & Gotestam, 1981). Classroom environmental arrangements of various types are standard practice to control the behavior of children with autism.

There is a considerable literature base on ABA approaches to reduce the challenging behavior of persons with neuropsychological disorders. Best practice today involves performing a functional behavioral assessment to form a hypothesis regarding the cause of challenging behavior. For example, treatment for a person's self-injurious behavior should be developed based on an understanding of why that person's problem behavior occurs in a given context. The specific self-injurious behavior might be reinforced by receiving social attention or tangible items from others, escape or avoidance from aversive stimuli (e.g., task demands, irritation from eczema), automatic reinforcement (e.g., sensory self-stimulation), or a combination of these consequences. Functional behavioral assessment procedures include various descriptive, indirect (e.g., interview, rating scales), and experimental methods. Treatment procedures are then derived from the hypothesized function of the problem behavior indicated by the functional behavioral assessment. For example, the inappropriate sexual behavior of a 9-year old boy with acquired brain injury was determined to be reinforced by social attention (Fyffe, Kahng, Fittro, & Russell, 2004). Treatment derived from that hypothesis consisted of functional communication training and withholding attention for the inappropriate behavior.

An example of a comprehensive treatment package with multiple components is a study that evaluated the efficacy of training children with autism to pass the state mandated vision screening when they started school (Simer & Cuvo, 2009). The package included components to teach the visual discriminations required (i.e., preference assessment, choice making, match-to-sample discrimination discrete trial training, transfer of stimulus control, differential reinforcement), and additional components to reduce escape/avoidance behavior (i.e., desensitization, extinction, reinforcement of alternative behavior).

Behavioral principles and processes can explain the behavior of social units at all levels (e.g., individual, family, staff, organizations), and ABA interventions can be applied to each of these social levels. Treatment programs are individualized with respect to frequency and duration, with a general goal to assist the social unit achieve as much independence as feasible. The distinguishing feature of ABA treatments is that they are based on an analysis of the function of behavior in its environmental context, derived from the science of behavior (i.e., primarily operant conditioning), and assessed for efficacy at the level of individuals and not groups as a whole.

Efficacy Information

The efficacy of ABA derived treatments most typically has been established by small *n* single subject experimental

designs that control for threats to internal validity. External validity is established by multiple systematic replications that expand the generality of the findings. The body of ABA treatment efficacy research has increased significantly over the decades since the 1960s. There are substantial treatment efficacy and effectiveness data for basic behavioral processes and their application to persons with neuropsychological disorders. Thousands of studies have demonstrated the efficacy of interventions that teach or strengthen behavior. Efficacy has been demonstrated for procedures that involve basic reinforcement processes, token reinforcement, self-management, shaping, chaining, prompting, transfer of stimulus control, and other behavioral processes and techniques. Likewise, numerous studies have provided evidence for the efficacy of behavior reduction procedures based on processes such as extinction, punishment, response cost, timeout, and differential reinforcement of various types. During the past 25 years, the efficacy of deriving treatment hypotheses for challenging behavior from a functional behavioral assessment has been clearly demonstrated by a large number of systematic replications.

Although there is a substantial body of ABA efficacy research that demonstrates the generality of behavioral principles and processes across target behaviors, populations, and settings, the amount of efficacy research differs across specific populations with neuropsychological disorders. An ABA approach to intervention has been best practice for decades for individuals with intellectual disability, especially for those with more severe disability. Since the 1960s beginning with Lovaas' seminal work, efficacy of an ABA approach to treat young children with autism has been demonstrated and earned support by the US Surgeon General (1999) and others. A recent meta-analysis of behavioral treatments for attention-deficit/hyperactivity disorder supported the efficacy of ABA for that population (Fabiano et al., 2009).

Outcome Measurement

The primary method of measuring treatment outcomes in ABA is direct and systematic observation of the objectively defined behavioral topography of interest (e.g., its frequency, duration, intensity). That measurement could be either continuous (i.e., each event) or sampled from the individual's universe of behavior (e.g., by interval or time sampling recording). Observers should be reliability trained and observe and record independently of each other. Some ABA programs include self-observation by a client, preferably to supplement objective observation by others.

Behavior should be analyzed at its most microscopic level (e.g., trial or session data for an individual) initially before aggregating across more macroscopic levels (e.g., trial blocks, days, persons). Most often, data are plotted in a figure (e.g., line graph) and analyzed visually. For research purposes, data are typically collected in the context of the requirements of a single subject experimental design. For routine clinical practice, it is advisable to have at least baseline and treatment data.

Since ABA-based treatment programs should address socially valid goals for an individual, outcome measurement largely relies on a consideration of whether treatment effects have attained those goals. Most often, that determination can be made by visual inspection of the data. Behavior analysts are interested in clinically meaningful (i.e., visually obvious on a figure) results and not less impressive improvement, even if it is unlikely to have occurred by chance.

The social or clinical significance of outcomes can be measured more formally either by social comparison or subjective evaluation techniques (Kazdin, 1977) as previously described. For example, does the out-of-seat behavior of a child with hyperactivity after treatment compare favorably to that of his classmates who serve as the social comparison criterion? Does the teacher who serves as the subjective evaluation criterion rate the child's out-of-seat behavior as acceptable after treatment?

Since the goal of ABA research and treatment is to produce socially significant outcomes for individuals and not for samples from a population, the role of statistical analysis as a decision making tool is rather limited. Descriptive statistics are sometimes used to supplement visual analysis and social validation. Descriptive statistics can serve as an aide by summarizing certain key characteristics of the data set (e.g., measures of central tendency, variability, trend, effect size). When inferential statistics are used, they are employed to make inferences from a sample of an individual's behavior (i.e., data collected) to the universe of that individual's behavior, and not to population parameters.

Another outcome evaluative criterion is theoretical significance. Are treatment outcomes consistent with the behavioral conceptualizations that underlie treatment selection for the target behaviors? For example, is behavior reduction treated by extinction (i.e., withdrawing reinforcement from a previously reinforced response) consistent with what we know about extinction as a basic behavioral process? Because of the idiographic nature of ABA treatment, standardized instruments based on

normative data for measuring treatment outcome are generally eschewed in favor of individualized measurement as previously described. Nevertheless, individualized rating scales, logs, and standardized tests are sometimes used as secondary measures.

Qualifications of Treatment Providers

The principal credential for applied behavior analysts is national certification that is administered by The Behavior Analyst Certification Board, a nonprofit corporation. There are two levels of professional certification. The Board Certified Behavior Analyst (BCBA): (a) holds a master's or doctoral degree, (b) has had the required number of coursework hours in certain core content areas of behavior analysis (i.e., ethics, behavioral principles, behavioral assessment and selecting interventions, experimental evaluation, behavioral measurement, and behavioral change procedures), (c) has had the required number of supervised clinical training hours, and (d) has passed a written test. The Board Certified Assistant Behavior Analyst (BCABA) holds a Baccalaureate degree, has passed a written test, and has had similar coursework and supervised clinical experience as the BCBA but to a lesser degree. BCBAs and BCABAs can hold their required academic degrees in any discipline as long as they meet the other requirements. Psychologists can be certified in Behavioral Psychology, with a concentration in ABA by the American Board of Behavioral Psychology, an affiliate of the American Board of Professional Psychology.

Cross References

- ▶ Behavior Management
- ▶ Behavior Modification
- ▶ Behavioral Analysis
- ▶ Behavioral Assessment
- ▶ Behavioral Therapy
- ▶ Behaviorism
- ▶ Conners Comprehensive Behavior Rating Scales
- ▶ Errorless Learning
- ▶ Extinction
- ▶ Inter Rater Reliability
- ▶ Learning
- ▶ Stimulus Bound Behavior
- ▶ Stimulus Control
- ▶ Stimulus Generalization

References and Readings

Amari, A., Grace, N. C., & Fisher, W. W. (1995). Achieving and maintaining compliance with the ketogenic diet. *Journal of Applied Behavior Analysis, 28*, 341–342.

Baer, D. M., Wolf, M. M., & Risley, T. R. (1968). Some current dimensions of applied behavior analysis. *Journal of Applied Behavior Analysis, 1*, 91–97.

Baker, J. C., Hanley, G. P., & Mathews, M. R. (2006). Staff-administered functional analysis and treatment of aggression by elder with dementia. *Journal of Applied Behavior Analysis, 39*, 469–474.

Buchanan, J. A., & Fisher, J. E. (2002). Functional assessment and noncontingent reinforcement in the treatment of disruptive vocalization in elderly dementia patients. *Journal of Applied Behavior Analysis, 35*, 99–103.

Cooper, J. O., Heron, T. E., & Heward, W. L. (2007). *Applied behavior analysis* (2nd ed.). Upper Saddle River, NJ: Pearson.

Fabiano, G. A., Pelham, W. E. Jr., Coles, E. K., Gnagy, E. M., Chronis-Tuscano, A., & O'Connor, B. (2009). A meta-analysis of behavioral treatments for attention-deficit/hyperactivity disorder. *Clinical Psychology Review, 29*, 129–140.

Feliciano, L., Vore, J., LeBlanc, L. A., & Baker, J. C. (2004). Decreasing entry into a restricted area using a visual barrier. *Journal of Applied Behavior Analysis, 37*, 107–110.

Friman, P. C. (2007). The fear factor: A functional perspective on anxiety. In P. Sturmey (Ed.), *Functional analysis in clinical treatment* (pp. 335–355). Burlington, MA: Elsevier.

Fyffe, C. E., Kahng, S. W., Fittro, E., & Russell, D. (2004). Functional analysis and treatment of inappropriate sexual behavior. *Journal of Applied Behavior Analysis, 37*, 401–404.

Hayes, S. C., Barnes-Holmes, D., & Roche, B. (2001). *Relational frame theory.* New York: Plenum.

Horner, R. D. (1971). Establishing use of crutches by a mentally retarded spina bifida child. *Journal of Applied Behavior Analysis, 4*, 183–189.

Kazdin, A. E. (1977). Assessing the clinical or applied importance of behavior change through social validation. *Behavior Modification, 1*, 427–451.

Kern, L., Mauk, J. E., Marder, T. J., & Mace, F. C. (1995). Functional analysis and intervention for breath holding. *Journal of Applied Behavior Analysis, 28*, 339–340.

Melin, L., & Gotestam, K. G. (1981). The effects of rearranging ward routines on communication and eating behaviors of psychogeriatric patients. *Journal of Applied Behavior Analysis, 14*, 47–51.

Novak, G., & Peláez, M. (2004). *Child and adolescent development: A behavioral systems approach.* Thousand Oaks, CA: Sage.

Sidman, M. (1994). *Equivalence relations: A research story.* Boston: Authors Cooperative.

Simer, N., & Cuvo, A. J. (2009). Training vision screening behavior to children with developmental disabilities. *Research in Autism Spectrum Disorders, 3*, 409–420.

Skinner, B. F. (1938). *The behavior of organisms.* New York: Appleton-Century-Crofts.

Skinner, B. F. (1948). *Walden two.* New York: Macmillan.

Skinner, B. F. (1953). *Science and human behavior.* New York: Free Press.

Skinner, B. F. (1957). *Verbal behavior.* New York: Appleton-Century-Crofts.

Skinner, B. F. (1968). *The technology of teaching.* New York: Appleton-Century-Crofts.

Thompson, G. A. Jr., Iwata, B. A., & Poynter, H. (1979). Operant control of pathological tongue thrust in spastic cerebral palsy. *Journal of Applied Behavior Analysis, 12*, 325–333.

U. S. Department of Health and Human Services. (1999). *Mental health: A report of the surgeon general*. Rockville, MD: Department of Health and Human Services, Substance Abuse and Mental Health Services Administration, Center for Mental Health Services, National Institute of Mental Health.

Wilder, D. A., Masuda, A., O'Connor, C., & Baham, M. (2001). Brief functional analysis and treatment of bizarre vocalizations in adult with schizophrenia. *Journal of Applied Behavior Analysis, 34*, 65–68.

Applied Behavioral Analysis

► Behavior Modification

Apprehension Span

► Span of Apprehension

Apraxia

Douglas I. Katz
Boston University School of Medicine
Braintree, MA, USA

Definition

The inability to correctly carry out a learned, skilled motor act despite the preserved capability of the sensorimotor system to produce the intended movement.

Current Knowledge

Apraxia is thought to involve a loss of representations or the inability to adequately access representations of learned movements and motor skills in the damaged brain. This may lead to a loss of recall of the concept or configuration of the movement, or the inability to transform or implement the representational knowledge of the movement into a well-coordinated, properly configured, and sequenced gesture. The diagnosis of apraxia requires the exclusion of cognitive and sensorimotor impairments that may affect the ability to carry out the motor skill, such as arousal, attention, intention, language deficits or weakness, discoordination, movement disorders, and sensory loss.

Assessment: Assessment for apraxia involves asking a patient to carry out pantomimes of movements (e.g., "show me how you would salute . . . brush your teeth with a toothbrush. . . blow out a candle"). If the response in not correct, the examiner may evaluate the patient's response to imitation of the movement or ability to produce the movement using actual objects or tools. The patient may also be tested for recognition of skilled movements produced by the examiner.

Classification of Apraxia: Apraxias may be differentiated by the body elements involved in the impaired movement, using the terms *limb apraxia*, *oral or buccofacial apraxia*, *trunk* or *axial apraxia*. These disorders have different neuroanatomical underpinnings and may occur separately in different individuals. For instance, patients with oral apraxia may demonstrate normal function on tests of limb praxis.

Apraxia has been subclassifed into *ideational apraxia*, *ideomotor apraxia*, and *limb-kinetic apraxia* (Liepmann, 1900). *Ideational apraxia* is a loss of the conception of a gesture or skilled movement. In this form, the patient does not seem to know what to do, and the motor activity is not facilitated by the use of actual objects. *Ideomotor apraxia* affects the implementation of the movement, producing spatial and timing errors. The patient seems to know what to do but cannot carry the movement out properly. *Limb-kinetic apraxia* is the inability to make finely graded, precise limb movements. It has been difficult to separate this form of apraxia from motor dysfunction related to elemental motor disturbance, and it remains controversial that this is actually an apraxic disorder of learned skilled movement.

Neuropathological localization: Apraxias are almost always associated with lesions in the dominant hemisphere. The left parietal lobe is most often implicated in limb apraxia in right-handers. Portions of the frontal lobes, including the supplementary motor area, have been implicated in some forms of apraxia. Lesions in and around Broca's area are most often implicated in cases of oral apraxia. Lesions affecting transmission of information between the cerebral hemispheres, including lesions of the corpus callosum, may lead to apraxia of just the left limbs because of disconnection of movement engrams in the left hemisphere from motor control areas in the right hemisphere (*callosal apraxia*).

Other disorders: A number of disorders have labels that include the term "apraxia" but have no relationship with apraxia according to the usual definition. These include: *Dressing apraxia* – difficulty orienting clothes to the body,

often associated with left neglect, and usually occurring with superior parietal right hemisphere lesions; *constructional apraxia* – difficulty drawing or copying pictures or designs; *gait apraxia* – difficulty initiating or maintaining a normal gait pattern as can be seen in normal pressure hydrocephalus; *apraxia of gaze* – difficulty directing eye movements as seen in Balint's syndrome. *Apraxia of speech* is a disorder that affects the sequencing of sounds in words and syllables. It can be developmental or acquired and people with this disorder have difficulty coordinating articulatory motor activities necessary for speech. It is controversial whether this represents an apraxia consistent with the definitions described above, or a subtype of language or elemental motor disorders affecting articulatory sequencing.

Cross References

- ▶ Balint's Syndrome
- ▶ Broca's Aphasia
- ▶ Frontal Lobes
- ▶ Movement Disorders
- ▶ Supplementary Motor Area

References and Readings

De Renzi, E. (1990). Apraxia. In F. Boller & J. Grafman (Eds.), *Handbook of neuropsychology* (Vol. 2, pp. 245–263). New York: Elsevier.

Heilman, K. M. (1997). Disorders of skilled movements: limb apraxia. In T. E. Feinberg & M. J. Farah (Eds.), *Behavioral neurology and neuropsychology* (pp. 227–235). New York: McGraw Hill.

Liepmann, H. (1900). Das Krankheitsbild der Apraxie (motorische Asymbolie) auf Grund eines Falles von einseitiger Apraxie. *Monatschrift Psychiatrie und Neurologic, 8*, 15–44,

Rothi, L. J. G., & Heilman, K. M. (1997). *Apraxia: The neuropsychology of action*. East Sussex: Psychology Press.

Apraxia of Speech

Julie L. Wambaugh
Veterans Affairs Salt Lake City Healthcare System
and University of Utah
Salt Lake City, UT, USA

Synonyms

Historically, acquired apraxia of speech (AOS) has been known under a variety of terminological designations (e.g., aphemia, phonemic disintegration, cortical dysarthria, dyspraxia of speech). Currently, there are no acceptable synonyms in use. The descriptor, "stroke induced" (SI), has occasionally been used to specify AOS resulting from stroke (e.g., SI-AOS).

Short Description or Definition

AOS is a neurologic, motoric disorder of speech production that is characterized by slowed rate of speech, difficulties in sound production, and disrupted prosody. AOS is not a disorder of language, although it rarely occurs without aphasia. Consequently, there is no impairment of comprehension or production of language in pure AOS.

Categorization

AOS is not divided into categories. Childhood Apraxia of Speech (CAS) is a related disorder, but not a category of AOS.

Epidemiology

Duffy (2005) reported that AOS was the primary communication disorder in 7.6% of 6,101 cases of neurologic motor speech disorders. As a secondary diagnosis (e.g., accompanying aphasia), AOS can be expected to occur more frequently.

Natural History, Prognostic Factors, Outcomes

The establishment of AOS as a distinct clinical entity is typically credited to Dr. Fredrick Darley, who in the late 1960s stimulated much of the early discussion and research concerning the nature and characteristics of this disorder. Since that time, the definition and descriptors of AOS have continued to evolve, with continuing research efforts being likely to result in further refinement of our knowledge concerning this disorder.

The most frequent cause of AOS is cerebral vascular accident involving the language-dominant hemisphere. Other causes of focal brain damage (e.g., penetrating head injury, neoplasm resection) may also result in AOS. Areas of injury that have been most often associated with AOS include the regions in the premotor cortex (notably, the left posterior, inferior frontal

gyrus), parietal lobe, and insula (see Wambaugh and Shuster, 2008 for a review).

Little objective evidence exists concerning the natural course of AOS, including the factors affecting prognosis. Duffy (2005) indicates that mutism associated with AOS rarely lasts beyond 2 weeks unless other speech, language, or cognitive deficits are also present.

Treatment can be expected to result in the improvement in symptoms of AOS, even when AOS is chronic. Treatment guidelines for AOS have been developed, which provide effectiveness ratings for different types of treatment based on the existing published evidence (see below; Wambaugh, Duffy, McNeil, Robin, and Rogers, 2006a, 2006b).

Neuropsychology and Psychology of AOS

AOS is a neurogenic, motoric speech disorder that is characterized by reduced rate of speech, disrupted production of speech sounds, and disordered prosody. These symptoms may be accompanied by behaviors such as articulatory groping (silent and/or audible), speech initiation difficulties, increasing number of sound errors with increasing word length or phonetic complexity, awareness of speech errors, and motoric perseverations. Its severity ranges from a total inability to speak to negligible speech disruptions (McNeil, Robin, and Schmidt, 2009; Wambaugh et al., 2006a).

AOS is thought to be caused by difficulties in the process of converting correctly selected and ordered sounds into previously learned movement information necessary for the implementation of intended speech movements. That is, it is assumed that sounds are correctly selected and sequenced at a linguistic level of processing. However, there is difficulty in accessing stored movement plans/programs needed to articulate those chosen sounds. These difficulties cause disruptions in the selection, positioning, and movement timing of the articulators (e.g., tongue, lips, etc.). Consequently, sound productions may be inaccurate, transitions between sounds may be disrupted, and prosody may be abnormal. Sound durations as well as the intervals between sounds, syllables, and words tend to be prolonged. Sound production errors are relatively consistent in location and invariable in type across repeated productions (McNeil, Robin, and Schmidt, 2009).

AOS typically occurs with aphasia and rarely occurs without it. The symptoms of AOS, however, are not attributable to disruptions in language. AOS may also occur with another motor speech disorder, dysarthria. Unlike the dysarthrias, AOS is not associated with problems with muscle tone, weakness, reflexes, or sensory processing.

Evaluation

Diagnosis of AOS requires that the primary symptoms of reduced rate of speech, distorted sound production, and disrupted prosody be present. Behaviors such as difficulties with speech initiation or articulatory groping (see above) may also be observed, but should not be used alone for purposes of differential diagnosis (Wambaugh et al., 2006a). Screening for AOS typically involves eliciting a variety of speech samples and determining the presence or absence of AOS symptoms. For example, Duffy (2005) provides a tool that may be used to evaluate speech production across tasks such as sound, monosyllabic word, multisyllabic word, and sentence repetition; repeated word productions; alternate and sequential motion rates, reading aloud; and connected speech production. The Apraxia Battery for Adults – second edition (Dabul, 2000) also provides tasks that may be used for examining speech production in adults with suspected AOS. However, the criteria for diagnosis of AOS provided by this test will not differentiate AOS from phonemic paraphasia.

Treatment

Behavioral treatment has been demonstrated to have positive outcomes for persons with AOS. An AOS practice guidelines report revealed four general approaches to AOS treatment: (1) articulatory-kinematic treatments (techniques focused on improving articulation of sounds), (2) rate/rhythm control treatments (therapies involving manipulating rate of speech production or imposing an external rhythm on speech), (3) alternative/augmentative communication approaches (therapies involving training the use of methods/devices for supplementing or replacing speech), and (4) intersystemic facilitation/reorganization treatments (therapies utilizing a relatively intact system/modality such as singing or gesturing to facilitate speech production) (Wambaugh et al., 2006b). On the basis of objective evaluation of the existing evidence, the AOS guideline developers determined that articulatory-kinematic approaches were "probably effective" rate/rhythm control approaches and intersystemic approaches were "possibly effective"; and AAC approaches had insufficient support to warrant a rating.

There are currently no published reports of restorative neurological treatments applied specifically to AOS

(e.g., neuropharmaceutical treatment, electrical cortical stimulation, transcranial magnetic stimulation), but such reports are likely to be available in the future.

Cross References

- ▶ Aphasia
- ▶ Dysarthria
- ▶ Phonemic Paraphasia

References and Readings

Dabul, B. (2000). *Apraxia battery for adults* (2nd ed.). Austin, TX: Pro-ed.

Duffy, J. R. (2005). *Motor speech disorders: Substrates, differential diagnosis, and management* (2nd ed.). St. Louis, MO: Elsevier Mosby.

McNeil, M. (2002). Apraxia of speech: From concept to clinic. *Seminars in Speech and Language, 23*(4), 221–222.

McNeil, M. R., Robin, D. A., & Schmidt, R. A. (2009). Apraxia of speech: Definition and differential diagnosis. In M. R. McNeil (Ed.), *Clinical management of sensorimotor speech disorders* (2nd ed., pp. 249–268). New York: Thieme.

Wambaugh, J. L., & Shuster, L. I. (2008). The nature and management of neuromotor speech disorders accompanying aphasia. In R. Chapey (Ed.), *Language intervention strategies in aphasia and related neurogenic communication disorders* (5th ed., pp. 1009–1042). Philadelphia, PA: Lippincott Williams & Wilkins.

Wambaugh, J. L., Duffy, J. R., McNeil, M. R., Robin, D. A., & Rogers, M. (2006a). Treatment guidelines for acquired apraxia of speech: A synthesis and evaluation of the evidence. *Journal of Medical Speech Language Pathology, 14*(2), xv–xxxiii.

Wambaugh, J. L., Duffy, J. R., McNeil, M. R., Robin, D. A., & Rogers, M. (2006b). Treatment guidelines for acquired apraxia of speech: Treatment descriptions and recommendations. *Journal of Medical Speech Language Pathology, 14*(2), xxxv–ixvii.

Apraxic Agraphia

- ▶ Agraphia

Aprosodia

Kate Krival
Kent State University
Kent, OH, USA

Definition

Aprosodia is a deficit in comprehending or expressing prosody, i.e., variations in pitch, loudness, or rhythm of speech used in addition to words to convey specific meaning and emotional information (Leon & Rodriguez, 2008; Wymer, Lindman, & Booksh, 2002). Aprosodia is traditionally characterized as *linguistic* or *affective* (Wymer et al., 2002). Linguistic prosody aids meaning, e.g., *con*vict vs. con*vict* or *the dog and the cat in the cage are mine* vs. *the dog, and the cat in the cage, are mine* allow unambiguous discrimination of the semantic target. Affective prosody conveys attitude, e.g., incredulity, sadness, or anger, e.g., depending on the prosodic intonation, *oh, yeah, I'm just great* may be a sincere expression of a good feeling, or an equally sincere communication that the speaker is angry or frustrated. Linguistic aprosodia is associated with both left and right hemisphere lesions; affective aprosodia is more consistently associated with lesions of the right hemisphere (Baum & Pell, 1999; Pell, 2006; Ross & Monnot, 2008). Additionally, the basal ganglia appear to play a key role in processing and further distributing the meaning associated with the prosodic characteristics (Cancelliere & Kertesz, 1990; Pell & Leonard, 2003).

Clinically, aprosodia is most often considered in terms of whether receptive, expressive, or both aspects of prosodic ability are diminished in an individual. However, Ross and various colleagues have proposed a categorization system for the aprosodias, which is similar to that used to categorize aphasia types. The system is based on a combination of deficit profile and site-of-lesion information: *motor* (in the area of the frontal operculum), *sensory* (posterior temporal operculum), *conduction* (arcuate fasciculus), *transcortical* (anterior or posterior watershed), or *global* deficits (Ross, 1981, 2000; Ross & Monnot, 2008). For example, an individual with motor aprosodia might not express affective or emotional prosody when speaking; one with sensory aprosodia might not recognize the affective meaning of prosodic signals in another's speech. These nondominant hemisphere anatomic correlates of prododic deficits do have modest empirical support (see Ross & Monnot, 2008 for a summary of related investigations). Ross' *motor aprosodia* should not be confused with prosodic production impairments that arise from deficits in speech production due to dysarthria (Duffy, 2005).

Assessment of aprosodia is generally accomplished through careful observation; however, the Florida Affect Battery (Bowers, Blonder, & Heilman, 1998) and the Aprosodia Battery (Ross, Thompson, & Yenkosky, 1997) may be useful additions to standard testing regimes. Management of aprosodic impairments has received little attention in the literature; however, emerging evidence suggests that behavioral therapies may have some effect (Bornhofen & MacDonald, 2008; Leon et al., 2005; Rosenbek et al., 2004). Future work that will focus on the design

and implementation of treatment for both expressive and receptive aprosodia is anticipated.

Cross References

- ▶ Apraxia of Speech
- ▶ Dysarthria
- ▶ Prosody

References and Readings

Baum, S. R., & Pell, M. D. (1999). The neural bases of prosody: Insights from lesion studies and neuroimaging. *Aphasiology, 13*, 581–608.

Bornhofen, C., & McDonald, S. (2008). Comparing strategies for treating emotion perception deficits in traumatic brain injury. *Journal of Head Trauma Rehabilitation, 23*(2), 103–115.

Boutsen, F. R., & Christman, S. S. (2002). Prosody in apraxia of speech. *Seminars in Speech and Language, 23*, 245–255.

Bowers, D., Blonder, L., & Heilman, K. M. (1998). *The Florida affect battery.* Gainesville, FL: University of Florida Brain Institute.

Cancelliere, A. E. B., & Kertesz, A. (1990). Lesion localization in acquired deficits of emotional expression and comprehension. *Brain and Cognition, 13*(2), 133–147.

Duffy, J. R. (2005). *Motor speech disorders: Substrates, differential diagnosis, and management.* St. Louis, MO: Mosby.

Emmorey, K. D. (1987). The neurological substrates for prosodic aspects of speech. *Brain and Language, 30*, 305–320.

Karow, C. M., & Connors, E. C. (2003). Affective communication in normal and brain-damaged adults: An overview. *Seminars in Speech and Language, 24*(2), 69–91.

Leon, S. A., & Rodriguez, A. D. (2008). Aprosodia and its treatment. *Perspectives on Neurophysiology and Neurogenic Speech and Language Disorders, 18,* 66–72.

Leon, S. A., Rosenbek, J. C., Crucian, G. P., Heiber, B., Holiway, B., Rodriguez, A. D., et al. (2005). Active treatments for aprosodia secondary to right hemisphere stroke. *Journal of Rehabilitation Research and Development, 42*(1), 93–102.

Monrad-Krohn, G. H. (1948). Dysprosdy or altered 'melody of language'. *Brain, 70*, 405–415.

Pell, M. D. (2006). Cerebral mechanisms for understanding emotional prosody in speech. *Brain and Language, 96*(2), 221.

Pell, M. D., & Leonard, C. L. (2003). Processing emotional tone from speech in Parkinson's disease: a role for the basal ganglia. *Cognitive, Affective, & Behavioral Neuroscience, 3*(4), 275–288.

Rosenbek, J. C., Crucian, G. P., Leon, S. A., Hieber, B., Rodriguez, A. D., Holiway, B., et al. (2004). Novel treatments for expressive aprosodia: A phase I investigation of cognitive linguistic and imitative interventions. *Journal of the International Neuropsychological Society: JINS, 10*(5), 786–793.

Ross, E. D. (1981). The aprosodias: Functional-anatomical organization of the affective components of language in the right hemisphere. *Archives of Neurology, 38*, 561–569.

Ross, E. D. (2000). Affective prosody and the aprosodias. In M. M. Mesulam (Ed.), *Principles of behavioral and cognitive neurology.* New York: Oxford University Press.

Ross, E. D., & Monnot, M. (2008). Neurology of affective prosody and its functional–anatomic organization in right hemisphere. *Brain and Language, 104*(1), 51–74.

Ross, E. D., Thompson, R. D., & Yenkosky, J. P. (1997). Lateralization of affective prosody in brain and the callosal integration of hemispheric language functions. *Brain and Language, 56*, 27–54.

Wymer, J. H., Lindman, L. S., & Booksh, R. L. (2002). A neuropsychological perspective of aprosody: Features, function, assessment and treatment. *Applied Neuropsychology, 9*(1), 37–47.

Arachnoid Cyst

Barbara Spacca[1], Andrew Brodbelt[2]
[1]Children's Hospital "Anna Meyer"
Florence, Italy
[2]The Walton Centre for Neurology and Neurosurgery
Lower lane, Liverpool, UK

Synonyms

Temporal lobe agenesis

Short Description or Definition

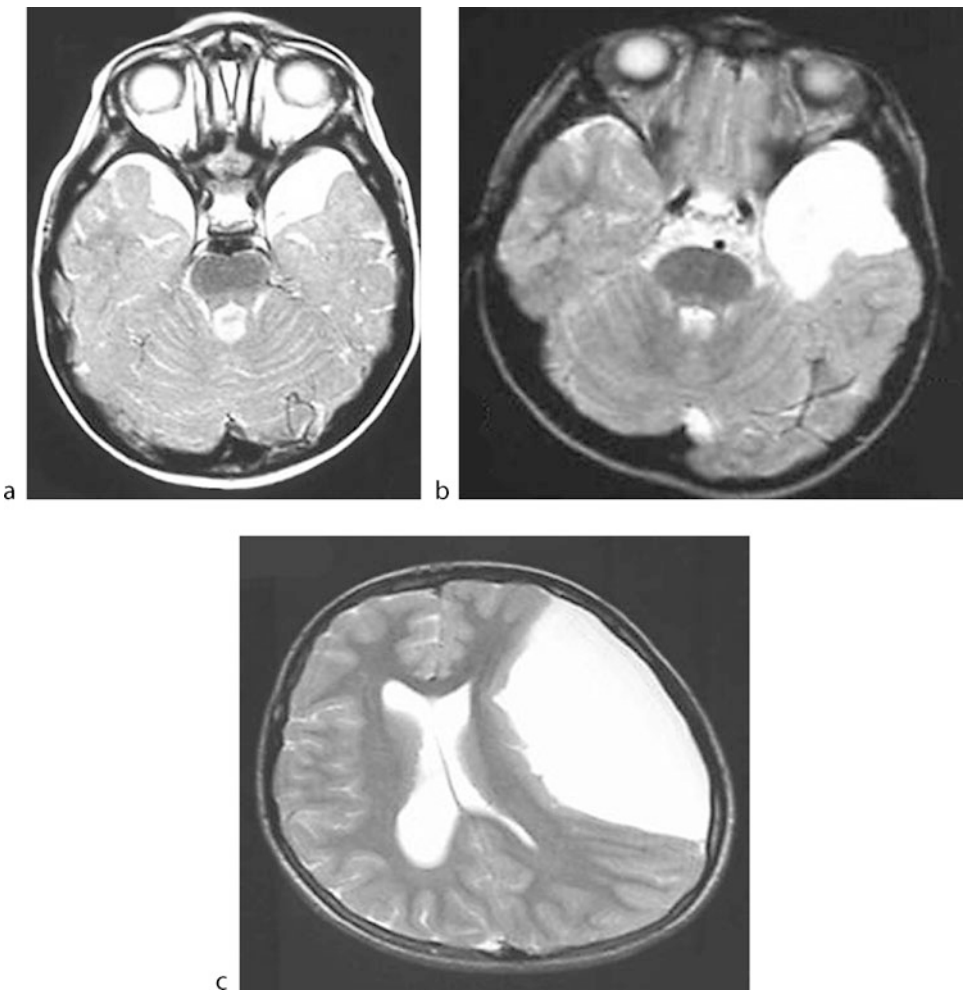
Arachnoid cysts are benign intracranial space occupying lesions. An arachnoid membrane surrounds a collection of clear fluid, identical to cerebrospinal fluid (CSF). Arachnoid cysts present due to mass effect, sudden hemorrhage, or incidentally.

Categorization

Arachnoid cysts are classified according to their location as intracranial or spinal. Intracranial arachnoid cysts can be further subclassified (Table 1). Middle fossa cysts (MFAC) can also be classified according to their size and distortion of surrounding structures based on Galassi classification (Galassi et al., 1982). Type I cysts are small, biconvex, and have no mass effect (Fig. 1a); type II cysts have a rectangular shape and involve proximal and intermediate segments of the Sylvian fissure (Fig. 1b); type III cysts entirely involve the Sylvian fissure and can produce midline shift (Fig. 1c). Arachnoid cysts may also be classified as primary congenital or acquired (Di Rocco, 1990;

Arachnoid Cyst. Table 1 Frequency and distribution of intracranial arachnoid cysts (Rengachary, Watanabe, & Brackett, 1978)

Position	Incidence (%)	Position	Incidence (%)
Supratentorial	76.8	Infratentorial	23.2
Middle cranial fossa	38.6	CerebelloPontine Angle	15.7
Sellar, intrasellar, suprasellar	13.3	Vermal	6.3
Convexity	11.5	Clival	1.2
Interemispheric fissure	8.3		
Quadrigeminal plate	5.1		



Arachnoid Cyst. Figure 1 Classification of middle fossa arachnoid cysts. (**a**) bilateral type I middle fossa arachnoid cyst demonstrating small size, biconvex appearance, and absence of mass effect; (**b**) type II middle fossa arachnoid cysts are rectangular; (**c**) type III middle fossa arachnoid cyst are large and often have significant mass effect

Oberbauer, 1999). Midline posterior fossa arachnoid cysts must not be confused with the Dandy–Walker complex. The Dandy–Walker complex describes hypoplasia or agenesis of the cerebellar vermis, associated hydrocephalus, structural anomalies such as agenesis of the corpus callosum (occurring in 68% of patients), and a post fossa arachnoid cyst- like structure that is not a true arachnoid cyst (Wilkinson & Winston, 2008).

Epidemiology

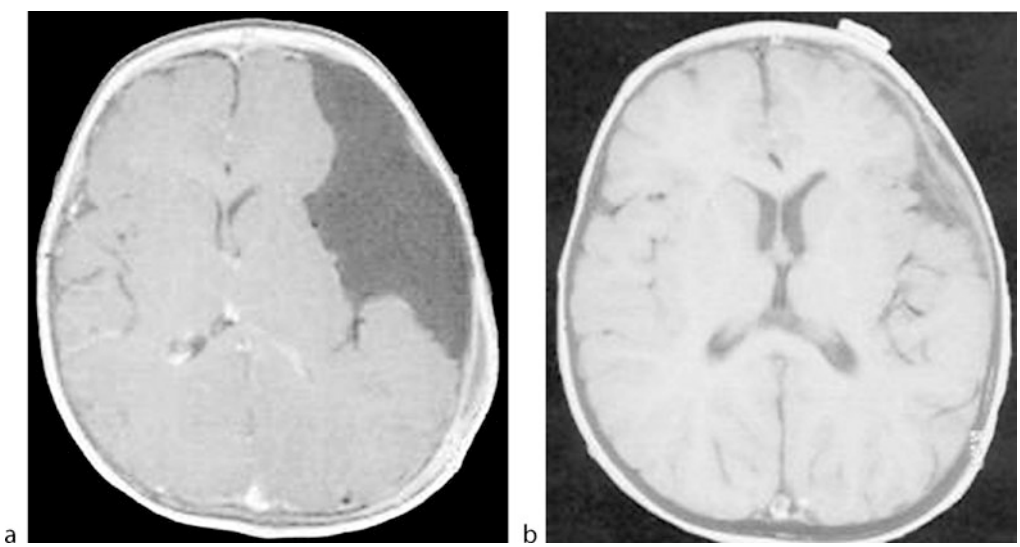
Arachnoid cysts are estimated to account for 1% of all nontraumatic intracranial lesions and are incidentally found in 1 per 1,000 autopsies (Boop & Teo, 2000; Di Rocco, 1990; Oberbauer, 1999; Wilkinson & Winston, 2008). They present in the first 2 decades of life, with a mean age at diagnosis of 6 years. There is a male predominance (2–3:1). Arachnoid cysts are mainly localized to one side, but case reports of bilateral cysts have been described (Ziaka, Kouyalis, Boviatsis, & Sakas, 2008). Familial presentations occur (glutaric aciduria type I) (Jamjoom, Okamoto, Jamjoom, al-Hajery, & Abu-Melha, 1995).

Etiology/Pathology

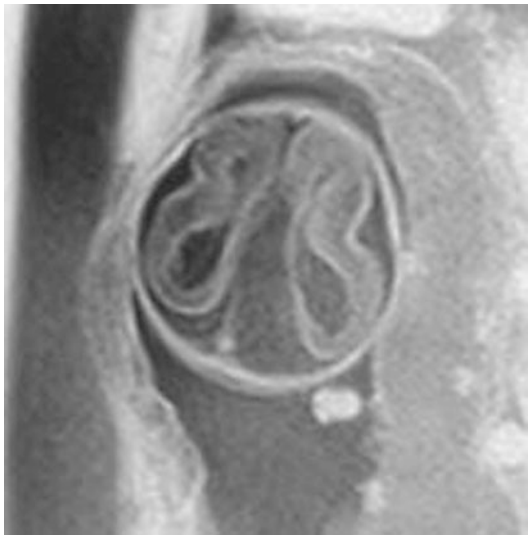
Microscopic examination demonstrates splitting of the arachnoid membrane at the margin of the cyst, a thick layer of collagen, hyperplastic arachnoid cells, and numerous blood vessels in the cyst wall, and an absence of traversing trabeculae although fine blood vessels may be present (Miyajima et al., 2000; Rengachary & Watanabe, 1981). Arachnoid cysts can communicate or be separate from the subarachnoid space (SAS), but appear to contain fluid similar in composition to CSF (Miyajima et al.; Rengachary & Watanabe; Yildiz et al., 2005).

Originally thought to be due to congenital hypoplasia of the brain (e.g. ▶ temporal lobe agenesis), this concept has been questioned, as postoperative imaging confirms that the brain expands after cyst decompression (Fig. 2). Most arachnoid cysts are now considered to be the result of a defect in early fetal development. Between the 6th and the 8th week of gestation, the meninx primitiva differentiates into the pia and arachnoid mater. Congenital duplication or splitting of the arachnoid layer at this time is thought to lead to formation of primary congenital arachnoid cysts (Bright, 1831; Gosalakkal, 2002; Miyajima et al., 2000; Rengachary & Watanabe, 1981; Schachenmayr & Friede, 1978, 1979) (Fig. 3).

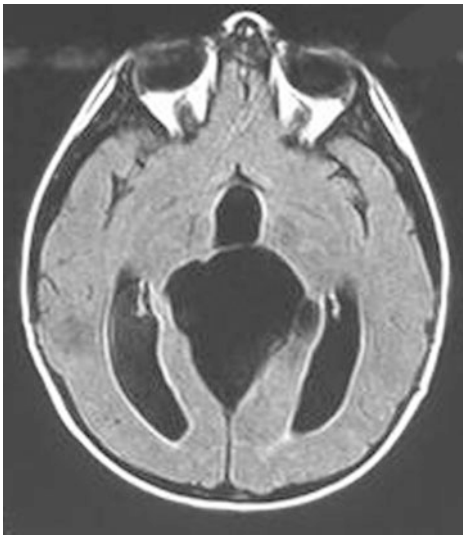
Imaging and endoscopic evidence exists demonstrating that at least in some arachnoid cysts, enlargement is due to a unidirectional valve type mechanism (Gosalakkal, 2002; Miyajima et al., 2000; Santamarta, Aguas, & Ferrer, 1995; Schroeder & Gaab, 1997). A secretory mechanism from the cyst wall has been suggested, although others have disputed this because of a lack of microscopic evidence of secretion including pineocytosis (Go, Houthoff, Blaauw, Havinga, & Hartsuiker, 1984; Gosalakkal, 2002; Schachenmayr & Friede, 1979). Water movement along an osmotic pressure gradient due to repeated small intracystal hemorrhage has also been suggested (Di Rocco, 1990). Arachnoid cysts can also be acquired following hemorrhage, head injury, or surgery (Kutlay, Colak, Demircan, & Akin, 1998).



Arachnoid Cyst. Figure 2 Middle fossa arachnoid cyst both before (**a**) and after (**b**) surgery. Note the significant brain re-expansion, an observation used to refute the suggestion of a congenital hypoplastic origin



Arachnoid Cyst. Figure 3 Foetal magnetic resonance image demonstrating an interemispheric arachnoid cyst

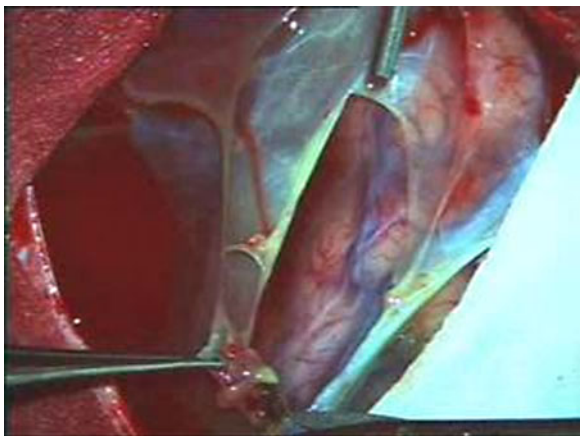


Arachnoid Cyst. Figure 4 Quadrigeminal Plate arachnoid cyst

Natural History, Prognostic Factors, Outcomes, Symptoms, and Signs

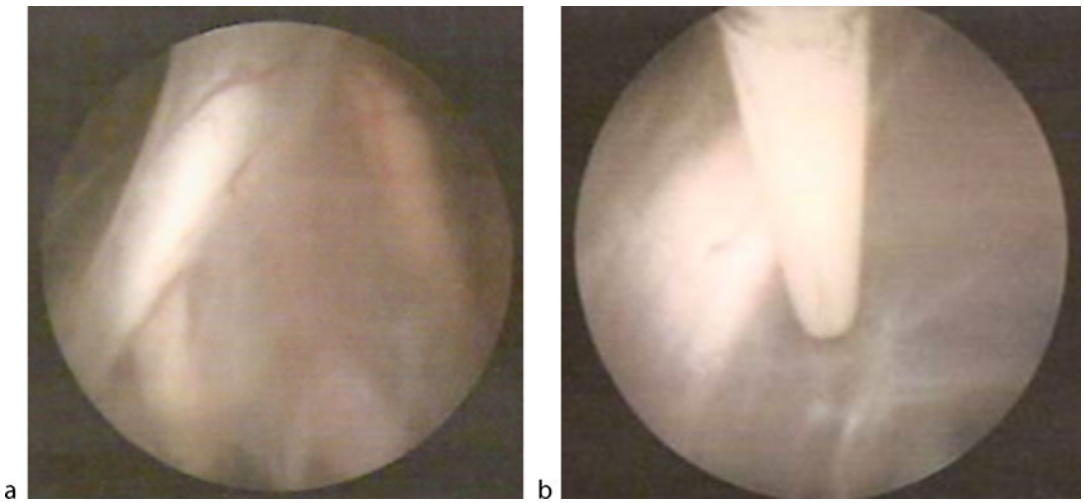
The natural history of arachnoid cysts is unpredictable. Cysts can grow in size, remain stable, rarely reduce, or disappear completely. Spontaneous hemorrhage or hemorrhage occurring after minor head injury have been described. In patients with middle fossa arachnoid cysts, the annual risk of symptomatic hemorrhage is less than 0.1% (Parsch, Krauss, Hofmann, Meixenberger, & Roosen, 1997). Hemorrhage can be asymptomatic, or, at worst, present as a life-threatening acute subdural hematoma. Subdural hygromas can also develop due to rupture of the cyst wall. Symptomatic patients may complain of symptoms related to raised ICP or specific to the cyst location. Described symptoms and signs include irritability, lethargy, headache, nausea, vomiting, diplopia, papilledema, cranial nerve dysfunction, and in infants, macrocrania, a tense fontanelle, displayed sutures, failure to thrive, or to reach developmental milestones.

In MFAC, bone deformities are common with large cysts and usually consist of macrocrania, temporal bone thinning, and bossing. Less commonly, downward displacement of the temporal floor and upward and forward displacement of the lesser wing of the sphenoid may lead to proptosis, and in extreme cases visual loss, facial numbness, and ocular palsies. Long tract compression can lead to sensory and motor limb signs. Seizures are common, occurring in up to 40% of patients. Developmental delays, behavioral disorders, memory, and attention dysfunction have also been described (Boop & Teo, 2000; Di Rocco, 1990; Oberbauer, 1999; Wilkinson & Winston, 2008).



Arachnoid Cyst. Figure 5 Intraoperative photograph demonstrating microsurgical fenestration of an arachnoid cyst

Patients with sellar and suprasellar cysts typically present with endocrine dysfunction, manifesting as failure to thrive or precocious puberty. Optic pathway compression can result in loss of visual fields or acuity, while hypothalamic pressure can produce eating and behavioral disorders. Thinning and displacement of the floor of the sella turcica and an empty sella can be observed with intrasellar cysts. Rarely, Suprasellar Cysts compressing the third ventricle present with "bobble-head doll" syndrome, whose pathogenesis is unknown, consisting in involuntary movement of the head forward and backward at a rate



Arachnoid Cyst. Figure 6 Appearance before (**a**) and during (**b**) endoscopic fenestration of a middle fossa arachnoid cyst

of 2–3 times/s (Hagebeuk, Kloet, Grotenhuis, & Peeters, 2005). Cerebral convexity cysts often present with cranial deformity and asymmetry alone. Quadrigeminal Plate Cysts (Fig. 4) can present with obstructive hydrocephalus or upward gaze palsies. Spinal arachnoid cysts usually present with myelopathy or nerve root compression (Di Rocco, 1990).

Neuropsychology and Psychology of Arachnoid Cysts

Large arachnoid cysts may present with failure to reach developmental milestones and psychomotor delay. Cases of dementia in adults have been reported (Harsh, Edwards, & Wilson, 1986). Cerebellar signs may be misdiagnosed as motor delay. MFAC and convexity cysts can be associated with cognitive problems, developmental delay, behavioral disorders, and memory and attention deficits in up to 7.8% of patients (Arai, Sato, Wachi, Okuda, & Takeda, 1996). Symptoms can be potentiated with antiepileptic drugs and sedatives. The relationship between arachnoid cysts and developmental and behavior problems is poorly understood. Functional magnetic resonance imaging demonstrates no alterations in Blood Oxygen Level Dependant responses (BOLD) yet Single Photon Emission Computed Tomography (SPECT) images can demonstrate reduced cerebral blood flow and glucose metabolism even in the contralateral hemisphere (Wilkinson & Winston, 2008). Pre- and postoperative cognitive testing, in small series, demonstrate improved performance in specific tasks after treatment, suggesting that arachnoid cysts may suppress cognitive and cortical function (Baroey Raeder, Helland, Hugdahl, & Wester, 2005; Wester & Hugdahl, 2003). However, larger series do not support significant clinical improvement after surgery in patients with severe developmental and behavior problems (Arai et al.; Levy, Wang, Aryan, Yoo, & Meltzer, 2003). In patients with developmental delay, behavioral disorders, and an arachnoid cyst, or in very young patients with large cysts, preoperative neuropsycological testing, EEG, and/or SPECT may have a role in supporting surgical intervention (Wilkinson & Winston).

Evaluation

Diagnosis and follow-up are based on clinical evaluation and imaging. Arachnoid cysts appear as cavities filled with fluid with the same characteristics as CSF, surrounded by a thin wall that is not calcified and does not enhance after contrast. Magnetic resonance imaging (MRI) is the diagnostic tool of choice because of image resolution for the cyst and surrounding anatomy (Wilkinson & Winston, 2008).

Treatment

Indications

Arachnoid cysts causing a focal neurological deficit, raised ICP, or enlarging should be treated. The management of asymptomatic patients or patients with functional

symptoms, such as seizures and developmental delay, is controversial. Asymptomatic cysts without mass effect may have a lower risk of bleeding if treated (Wilkinson & Winston, 2008; Parsch et al., 1997). Seizure control may be improved, but a causal link is not always apparent. Currently, treatment in patients with severe developmental delay does not appear to confer a significant functional improvement (Arai et al., 1996; Levy et al., 2003).

Surgical Options

Three surgical options exist. These include shunt insertion, open exploration, or endoscopic fenestration (Lena et al., 1996, Kaufman & Park, 2000). Commonly, a cystoperitoneal shunt is placed, although revision rates due to infection or system failure remain at 20–40% at 8 years (Arai et al., 1996; Oberbauer et al., 1992). Cyst fenestration consists of opening a window in both the superficial and deep walls of the cyst to allow communication between the cyst and the subarachnoid space (Figs. 5 and 6). Both microsurgical and endoscopic approaches demonstrate improvement in up to 90% of patients (Karabatsou et al., 2007; Levy et al., 2003; Spacca et al., 2009). Endoscopic fenestration is less invasive, and series suggest reduced morbidity (Karabatsou et al., 2003; Spacca et al., 2009). Treatment of an associated subdural hemorrhage or hygroma may lead to resolution of the arachnoid cyst (Parsch et al., 1997).

References and Readings

Arai, H., Sato, K., Wachi, A., Okuda, O., & Takeda, N. (1996). Arachnoid cysts of the middle cranial fossa: Experience with 77 patients who were treated with cystoperitoneal shunting. *Neurosurgery, 39*(6), 1108–1113.

Baroey Raeder, M., Helland, C. A., Hugdahl, K., & Wester, K. (2005). Arachnoid cysts cause cognitive deficits that improve after surgery. *Neurology, 64*, 160–162.

Boop, F. A., & Teo, C. (2000). Congenital intracranial cysts. In D. G. McLane (Ed.), *Pediatric neurosurgery* (pp. 489–498). Philadelphia: W.B. Saunders.

Bright, R. (1831). Reports of medical cases selected with a view of illustrating the symptoms and cure of diseases by a reference to morbid anatomy. In Longman, Rees, Orme, Brown, Green, Paternoster-Row, et al. (Eds.), *Diseases of the brain and nervous system* (pp. 437–439), London: W.B. Saunders.

Di Rocco, C (1990). Arachnoid cysts. In *Youmans: Neurological surgery* (pp. 1299–1323). Philadelphia, PA: WB Saunders Company.

Galassi, E., Tognetti, F., Gaist, G., Fagioli, L., Frank, F., & Frank, G. (1982). CT scan and medtrizamide CT cisternography in arachnoid cysts of the middle cranial fossa: Classification and pathophysiological aspects. *Surgical Neurology, 17*(5), 363–369.

Go, K. G., Houthoff, H. J., Blaauw, E. H., Havinga, P., & Hartsuiker, J. (1984). Arachnoid cysts of the sylvian fissure. Evidence of fluid secretion. *Journal of Neurosurgery, 60*(4), 803–813.

Gosalakkal, J. A. (2002). Intracranial arachnoid cysts in children: A review of pathogenesis, clinical features, and management. *Pediatric Neurology, 26*(2), 93–98.

Hagebeuk, E. E., Kloet, A., Grotenhuis, J. A., & Peeters, E. A. (2005). Bobble-head doll syndrome successfully treated with an endoscopic ventriculocystocisternostomy. Case report and review of the literature. *Journal of Neurosurgery, 103*(3 Suppl), 253–259.

Harsh, G. R., Edwards, M. S. B., & Wilson, C. B. (1986). Intracranial arachnoyd cysts in children. *Journal of Neurosurgery, 64*, 835–842.

Jamjoom, Z. A., Okamoto, E., Jamjoom, A. H., al-Hajery, O., & Abu-Melha, A. (1995). Bilateral arachnoid cysts in the Sylvian region in female siblings with glutaric aciduria type I. *Journal of Neurosurgery, 82*, 1078–1081.

Karabatsou, K., Hayhurst, C., Buxton, N., O'Brien, D. F., & Mallucci, C. L. (2007). Endoscopic management of arachnoid cysts: An advancing technique. *Journal of Neurosurgery, 106*(6 Suppl Pediatrics), 455–462.

Kaufman, B. A., & Park, T. S. (2000). Treatment of arachnoid cysts. In D. G. McLane (Ed.), *Pediatric neurosurgery* Philadelphia, PA: WB Saunders.

Kutlay, M., Colak, A., Demircan, N., & Akin, O. N. (1998). Iatrogenic arachnoid cyst with distinct clinical picture as a result of bone defect in the floor of the middle cranial fossa: Case report. *Neurosurgery, 43*(5), 1215–1218.

Lena, G., Erdincler, P., Van Calenberg, F., Genitori, L., & Choux, M. (1996). Arachnoid cysts of the middle cranial fossa in children. A review of 75 cases, 47 of which have been operated in a comparative study between membranectomy with opening of cisterns and cystoperitoneal shunt. *Neurochirurgie, 42*(1), 29–34.

Levy, M. L., Wang, M., Aryan, H. E., Yoo, K., & Meltzer, H. (2003). Microsurgical keyhole approach for middle fossa arachnoid cyst fenestration. *Neurosurgery, 53*(5), 1138–1145.

Miyajima, M., Arai, H., Okuda, O., Hishii, M., Nakanishi, H., & Sato, K. (2000). Possible origin of suprasellar arachnoid cysts: Neuroimaging and neurosurgical observations in nine cases. *Journal of Neurosurgery, 93*(1), 62–67.

Oberbauer, R. W. (1999). Intracranial and intraspinal cysts. In M. Choux, C. Di Rocco, A. D. Hockley, & M. L. Walker (Eds.), *Pediatric neurosurgery* (pp. 137–149). London: Churchill Livingstone.

Oberbauer, R. W. Haasa, J., & Pucher, R. (1992). Arachnoid cysts in children: A European co-operative study. *Child's Nervous System, 8*, 281–286.

Parsch, C. S., Krauss, J., Hofmann, E., Meixensberger, J., & Roosen K. (1997). Arachnoid cysts associated with subdural hematomas and hygromas: Analysis of 16 cases, long-term follow-up and review of the literature. *Neurosurgery, 40*(3), 483–490.

Rengachary, S., Watanabe, I., & Brackett, C. (1978). Pathogenesis of intracranial arachnoid cysts. *Surgical Neurology, 9*, 139–144.

Rengachary, S. S. & Watanabe, I. (1981). Ultrastructure and pathogenesis of intracranial arachnoid cysts. *Journal of Neuropathology and Experimental Neurology, 40*(1), 61–83.

Santamarta, D., Aguas, J., & Ferrer, E. (1995). The natural history of arachnoid cysts: Endoscopic and cine-mode MRI evidence of a slit-valve mechanism. *Minimally Invasive Neurosurgery, 38*(4), 133–137.

Schachenmayr, W., & Friede, R. L. (1978). Fine structure of arachnoid cysts. *Journal of Neuropathology and Experimental Neurology, 38*, 434–446.

Schachenmayr, W., & Friede, R. L. (1979). Fine structure of arachnoid cysts. *Journal of Neuropathology and Experimental Neurology, 38*(4), 434–446.

Schroeder, H. W., & Gaab, M. R. (1997). Endoscopic observation of a slit-valve mechanism in a suprasellar prepontine arachnoid cyst: Case report. *Neurosurgery, 40*(1), 198–200.
Spacca, B., Kandasamy, J., Mallucci, C. L., & Genitori, L. (2009). Endoscopic treatment of middle fossa arachnoid cysts: a series of forty patients treated in two centres. Child's Nerv Syst Epub ahead of print.
Wester, K., & Hugdahl, K. (2003). Verbal laterality and handedness in patients with intracranial arachnoid cysts. *Journal of Neurology, 250*, 36–41.
Wilkinson, C. C., & Winston, K. R. (2008). Congenital arachnoid cysts and the Dandy-Walker complex. In A. L. Albright, I. F. Pollack, & P. D. Adelson (Eds.), *Principles and practice of pediatric neurosurgery* (pp. 162–186). New York: Thieme.
Yildiz, H., Erdogan, C., Yalcin, R., Yazici, Z., Hakyemez, B., Parlak, M., et al. (2005). Evaluation of communication between intracranial arachnoid cysts and cisterns with phase-contrast cine MR imaging. *AJNR American Journal of Neuroradiology, 26*(1), 145–151.
Ziaka, D. S., Kouyalis, A. T., Boviatsis, E. J., & Sakas, D. E. (2008). Asymptomatic massive subdural hematoma in a patient with bitemporal agenesis and bilateral temporal arachnoid cysts. *The Southern Medical Journal, 101*(3), 324–326.

Arachnoid Mater

► Meninges

Arbitration

Robert L. Heilbronner
Chicago Neuropsychology Group
Chicago, IL, USA

Definition

Arbitration is an alternative means of settling a dispute by impartial person(s) without proceeding to a court trial. It is sometimes preferred as a means of settling a matter in order to avoid the expense, delay, and acrimony of litigation. There is no discovery and there are simplified rules of evidence in arbitration. The arbitrator(s) are selected directly by the parties or are chosen in accordance with the terms of the contract in which the parties have agreed to use a court-ordered arbitrator(s) or an arbitrator(s) from the American Arbitration Association. If there is no contract, usually each party chooses an arbitrator and the two arbitrators select a third to comprise the panel. When parties submit to arbitration, they agree to be bound by and comply with the arbitrators' decision. The arbitrators' decision is given after an informal proceeding where each party presents evidence and witnesses. Arbitration has long been used in labor, construction, and securities regulation, but is gaining popularity in other disputes.

Cross References

► Mediation

References and Readings

The Federal Arbitration Act 9 U.S.C. Section 1 et seq., (1925).

Arcuate Fasciculus

Martin R. Graf
Virginia Commonwealth University Medical Center
Richmond, VA, USA

Definition

The arcuate fasciculus is a large bundle of nerve fibers that curves around the lateral sulcus to connect Broca's area in the frontal cortex to Wernicke's area located in the posterior portion of the temporal lobe. This white matter pathway is essential for language processing in which the arcuate fasciculus connects the region associated with the ability to produce spoken language, Broca's area, to that of the ability to process spoken words that are heard which is associated with Wernicke's area. This language loop is located in the left hemisphere in approximately 90% of the population. Lesions disrupting the arcuate fasciculus result in conduction aphasia, which is characterized by paraphasic errors in which incorrect words or sounds are substituted and word repetition is impaired, although these individuals generally show reasonably normal speech and comprehension.

Cross References

► Superior Longitudinal Fasciculus

References and Readings

LaPointe, L. L. (2005). *Aphasia and related neurogenic language disorders.* New York: Thieme.

Arcuate Fibers

► Associational Fibers

Aricept

► Donepezil

Aripirozole

John C. Courtney[1], Cristy Akins[2]
[1]Children's Hospital of New Orleans
New Orleans, LA, USA
[2]Mercy Family Center
Metarie, LA, USA

Generic Name

Aripirozole

Brand Name

Abilify

Class

Atypical Neuroleptic

Proposed Mechanism(s) of Action

Partial agonism at dopamine 2 receptors. Also inhibits 5HT2a receptors, thus increasing presynaptic release of related catecholamines.

Indication

Schizophrenia, Bipolar (mixed/manic), Adjunctive by for Major Depressive Disorder, Autistic irritability in children and teens.

Off Label Use

Other psychotic disorders, acute mania, bipolar maintenance, bipolar depression, behavioral disturbances associated with dementias, behavioral disturbances in children and adolescents, and impulse control disorders.

Side Effects

Serious

Neuroleptic malignant syndrome, seizures.

Common

Insomnia, dizziness, activation, akathisia, nausea, and vomiting.

References and Readings

Physicians' Desk Reference (62nd ed.). (2007). Montvale, NJ: Thomson PDR.
Stahl, S. M. (2007). *Essential psychopharmacology: The prescriber's guide* (2nd ed.). New York, NY: Cambridge University Press.

Additional Information

Drug Interaction Effects: http://www.drugs.com/drug_interactions.html
Drug Molecule Images: http://www.worldofmolecules.com/drugs/
Free Drug Online and PDA Software: www.epocrates.com
Gene-Based Estimate of Drug interactions: http://mhc.daytondcs.com:8080/cgi bin/ddiD4?ver=4&task=getDrugList
Pill Identification: http://www.drugs.com/pill_identification.html

Arithmetic Reasoning

Zheng Zhou
St. John's University
Queens, NY, USA

Synonyms

Numerical reasoning; Quantitative reasoning

Definition

Mathematical reasoning is the mathematical methodology of axiomatic reasoning, logical deduction, and formal inference.

Current Knowledge

Research in evolutionary genetics and neuroscience suggests important neurological differences between mathematical capacities that are evolutionary primitive (e.g., counting) and those (e.g., arithmetic) that are more culturally taught (Geary, 1995). Empirical data demonstrate that mathematical reasoning and language are functionally and neuroanatomically independent, suggesting (a) there is a common and domain-general syntactic mechanism that underpins both language and mathematics, but that mathematical expressions can gain direct access to this system without translation into a language format, and (b) autonomous, domain-specific syntactic mechanisms exist for language and mathematics (Varley, Klessinger, & Romanowski, Siegal, 2005). Studies on sex differences provide evidence that math reasoning develops from a set of biologically based cognitive capacities that males and females share (Spelke, 2005). Male infants show no advantage in the processing of objects, space, or number. Highly selected male and female students show equal abilities to learn mathematics. However, other studies found male advantage in arithmetical reasoning mediated by male advantages in both computational fluency and spatial cognition.

Cross References

- ▶ Abstract Reasoning
- ▶ Academic Competency
- ▶ Academic Skills
- ▶ Problem Solving

References and Readings

Geary, D. C. (1995). Reflections on evolution and culture in children's cognition: Implications for mathematical development and instruction. *American Psychologist, 50*(1), 24–37.

Spelke, E. (2005). Sex differences in intrinsic aptitude for mathematics and science? *American Psychologist, 60*(9), 950–958.

Varley, R. A., Klessinger, N. J. C., Romanowski, C. A. J., & Siegal, M. (2005). Agrammatic but numerate. *Proceedings of the National Academy of Science of the United States of America, 102*, 3519–3524.

Zhou, Z. (in press). Mathematical reasoning. In J. S. Kreutzer, J. Deluca, & B. Caplan (Eds.), *Encyclopedia of clinical neuropsychology*. New York: Springer.

Arousal

Ronald A. Cohen
Brown University
Providence, RI, USA

Synonyms

Cortical activation; Cortical arousal; Delirium; Wakefulness

Definition

The psychological and physiological state of wakefulness, excitement, and/or activation enables readiness for action, increased sexual desire, and readiness. From a neuropsychological perspective, arousal refers to the tonic state of cortical activity elicited by subcortical reticular formation that results in increased wakefulness, alertness, muscle tone, and autonomic response (e.g., heart rate and respiration).

Historical Background

The concept of arousal played a key role in many of the earliest psychological theories. Physiologists of the nineteenth century, such as Brücke, focus on the basis of bioenergetics as they attempted to understand the basis of cell function. This influenced Freud who posited that bioenergetics were the driving forces underlying psychological experience and behavior and accounted for his construct of "Id." William James proposed that emotional experience involved the labeling of arousal and behavioral response associated with affective stimuli. Classical conditioning theory was also routed in Pavlov's observations of autonomic and behavioral unconditioned response to stimuli, such as foods that have appetitive value (i.e., unconditioned stimuli). His concept of the orienting response was one of the first constructs that directly linked arousal and learning to an attentional response. Subsequently, the arousal became a key construct in the development of the field of psychophysiology in its efforts to characterize the relationship between psychological experience and physiological response. The

demonstration by Moruzzi and Magoun (1949) shows that the brain-stem reticular formation plays a key role in generating brain activation as evident by electroencephalography. This spurred subsequent neurophysiological inquiry into the factors underlying arousal and their mediation of higher order cognitive functions. Early efforts to understand the actions of neurotransmitters in the brain were closely linked to the concept of arousal, based on the effects of norepinephrine on the sympathetic nervous system response and wakefulness. Pribram and McGuinness (1975) posited dissociations between arousal, activation, and effort in the control of attention, an important theoretical neuropsychological work that tied these processes to underlying brain mechanisms. Heilman and Valenstein's (1979) attention-arousal hypothesis proposed that the arousal associated with reticular activation interacted with a number of distinct cortical and subcortical systems involved in the control of attention, and that unilateral brain lesions across these brain systems occur in patients with hemineglect syndrome.

Current Knowledge

The concept of arousal has evolved substantially from its original conception. Some neuroscientists argue that the concept has outlived its usefulness because the term arousal is used to refer to a broad range of different behavioral and physiological phenomena with very different underlying mechanisms. This has led to overgeneralization of the construct. Yet, arousal continues to have an important role in neuropsychological theories. There is compelling evidence that brain stem and subcortical activity influences cortical activity and also autonomic response. At a behavioral and phenomenological level, arousal provides a construct that links the more primitive bioenergetic responses of the brain with higher cortical functions. This is most obvious when considering levels of consciousness that can range from deep sleep or coma to normal wakefulness to states of extreme excitement, hyperactivity, or agitation. Altered arousal is a key feature of delirium that can occur due to transient disruptions in brain function due to metabolic or drug influences.

Stimulation of the sympathetic nervous system and an increase in the secretion of epinephrine and norepinephrine increase the brain activity on EEG, along with behavioral response toward greater wakefulness, where drugs like barbiturates and alcohol have the opposite effect. The task that requires intense focused attention to perform cognitive challenges that are stressful or that require rapid response for adequate performance tend to result in increased fast wave EEG activity as well as autonomic nervous system responses such as increased heart rate and respiration, metabolic activity, and a diversion of blood from the gastrointestinal system to skeletal muscle. These responses are associated with a readiness to respond, a key element of attention, the specific nature of this attention response depends on whether the task demands involve passive vigilance or more effortful directed attention.

There is now strong evidence that multiple neural systems are involved in the maintenance, control, and allocation of arousal throughout the cortex. At least four neurotransmitter systems (acetylcholine, norepinephrine, dopamine, and serotonin) mediate the energetic state of the brain, though a variety of peptides influence the neural response across specific brain systems. While hierarchically the arousal originates in the brainstem, the nuclei of the hypothalamus play a critical role in the specificity of arousal relative to specific appetitive behaviors. For example, while damage to the reticular system of the brain stem often results in coma, hypothalamic nuclei such as the suprachiasmatic nucleus exert control over wakefulness, by maintaining circadian rhythm. Furthermore, the arousal associated with drives such as eating and sexual response are directly governed by hypothalamic functions, with higher level limbic (e.g., ▶ amygdala) and cortical control.

The most obvious clinical manifestations of disordered arousal occur in conjunction with delirium. However, factors that influence the level of arousal have direct effects on performance, as described at the turn of the last century in the Yerkes–Dodson law. There are data from a wide range of cognitive, behavioral, and neuropsychological studies demonstrating supporting the principle that task performance varies as a function of arousal, with optimal performance occurring at some intermediate level. Pathological states that cause lethargy usually reduce attentional performance. Similarly, drugs, anxiety, or other factors that lead to excessive arousal also have detrimental consequences on performance. Disturbances of arousal are commonly associated with both intoxication as well as withdrawal from drugs like alcohol and barbiturates, electrolyte imbalances, trauma to brain from closed head injury, and various neurological disorders including encephalitis, tumors, advanced Alzheimer's disease, and stroke. Conditions that affect the brain stem, hypothalamus, thalamus, limbic areas (e.g., ▶ amygdala), and frontal and temporal lobes are most likely to alter arousal, and thereby affect attention too.

From a neuropsychological perspective, arousal is an important factor influencing the intensity of attentional focus and also the ability of people to sustain attention. Kahneman (1973) proposed that arousal is a governing factor underlying attentional capacity. Cohen's (1993) four-factor attention framework and other neuropsychological theories of attention posit that capacity limitations associated with the overall level of behavioral and physiological arousal constrain attention by influencing the intensity of focus that is possible, which in turn affects other aspects of attention, most notably sustained performance.

Future Directions

Arousal appears to be a necessary and durable construct within neuropsychology. Yet, some of the concerns of neuroscientists regarding the overuse and overgeneralization of the term have merit. As knowledge increases regarding the functional neuroanatomy of specific white-matter pathways projecting from subcortical to cortical regions, there will be a need for further refinement of the arousal construct. Efforts to more clearly demonstrate the linkage between behavioral and physiological arousal in the clinical context are needed, given that they are not always coupled. The example of decreased frontal lobe activation associated with hyperactivity and impulsivity in attention deficit disorder illustrates this fact. At this point in time, arousal is typically not directly assessed as part of neuropsychological evaluations, except through behavioral observation. However, with advances in the functional neuroimaging, it is possible to demonstrate both activation as well as deactivation of particular brain regions, and to observe how these responses change in association with not only momentary task demands but also tonic state of arousal. Accordingly, in the future physiological measurement of arousal and activation across brain systems, it is likely to be a more common element of standard neuropsychological assessment.

Cross References

- ▶ Attention
- ▶ Consciousness
- ▶ Orienting Response
- ▶ Reticular Activating System
- ▶ Yerkes–Dodson Law

References and Reading

Cohen, R. A. (1993). *Neuropsychology of attention.* New York: Plenum Publishing.

Heilman, K. M., & Valenstein, E. (1979). Mechanisms underlying hemispatial neglect. *Annals of Neurology, 5*(2), 166–170.

Kahneman, D. (1973). *Attention and effort.* Englewood Cliffs, NJ: Prentice-Hall.

Moruzzi, G., & Magoun, H. W. (1949). Brain stem reticular formation and activation of the EEG. *Electroencephalography and Clinical Neurophysiology, 1*(4), 455–473.

Pribram, K., McGuinness, D. (1975). Arousal, activation, and effort in the control of attention. *Psychological Review, 82*(2), 116–149.

Arteriography, Cerebral

▶ Angiography, Cerebral

Arteriosclerotic Vascular Disease or ASVD

▶ Atherosclerosis

Arteriovenous Malformation (AVM)

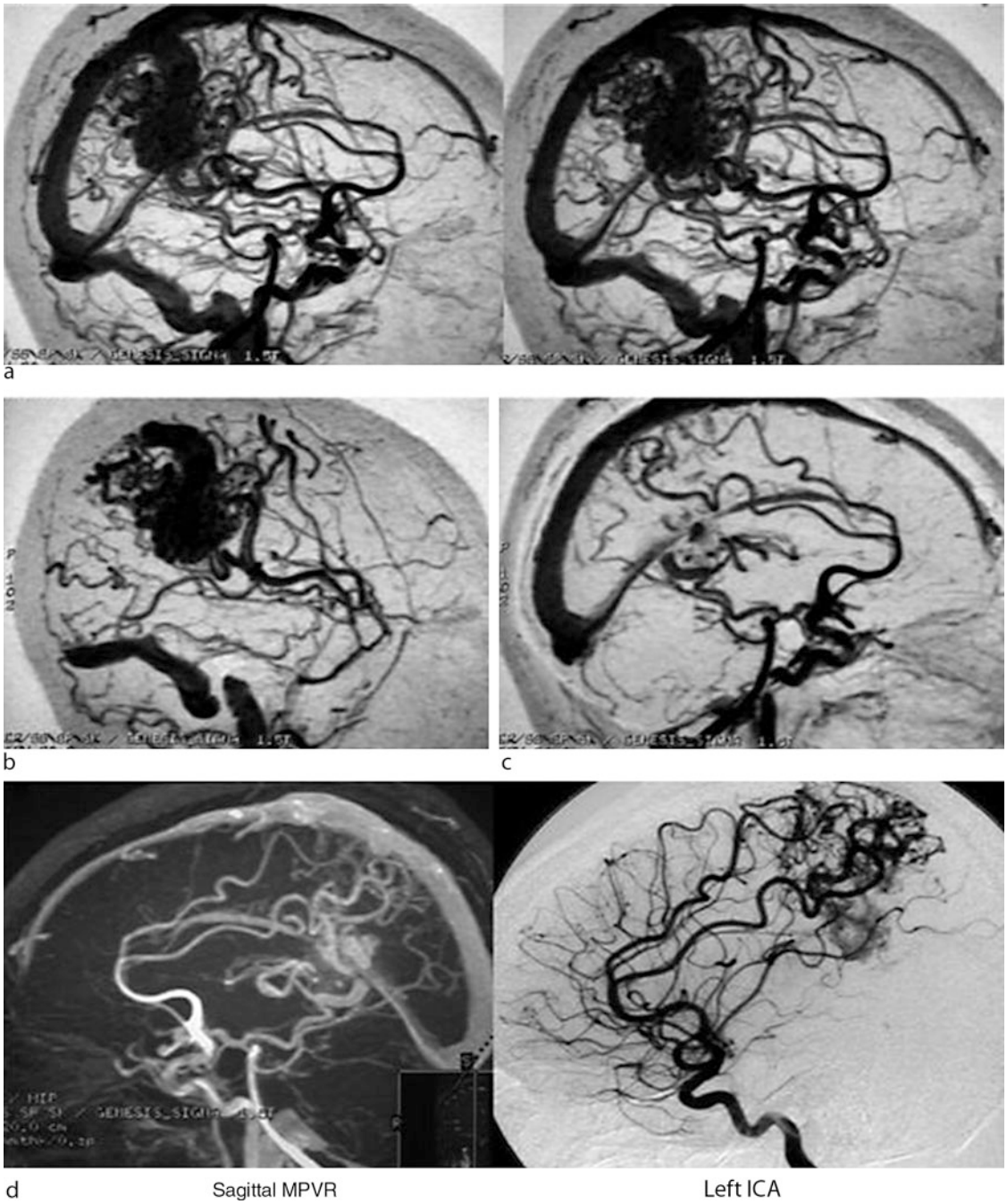
Bruce J. Diamond, Joseph E. Mosley
William Paterson University
Wayne, NJ, USA

Synonyms

Brain arteriovenous malformation; Cerebral malformation; Vascular malformation

Short Description or Definition

Arteriovenous malformation (AVMs) are irregular, anomalous, abnormal, or faulty formations or structures connecting the arteries and veins (Webster's New Explorer Medical Dictionary, 2006). AVMs have been associated with aneurysms in 10–50% of patient groups, depending on the type of angiographic techniques employed (Al-Shahi & Warlow, 2001).



Arteriovenous Malformation (AVM). Figure 1

Etiology

AVMs arise about 3 weeks after conception at the time when blood vessels are dividing into veins and arteries (Stein & Wolpertson, 1980). Recent studies have suggested that AVMs are dynamic and have the ability to grow, regress, and regenerate following obliteration by surgery or radiosurgery (Moftakhar, Hauptman, Malkasian, & Martin, 2009). Currently, it is thought that the altered expression of more than 900 genes is involved in the pathogenesis of AVMs (Moftakhar et al., 2009).

Epidemiology

AVMs are the most common type of clinically significant vascular malformation, occurring exclusively within the brain or involving extension of vessels from the subarachnoid space into brain parenchyma (Frosch, Anthony, & De Girolami, 2005). AVM sizes may vary from a few millimeters to several centimeters (Warlow, 2001), with males being affected twice as frequently as females.

Mechanisms

Cognitive improvements have been attributed to improved cerebral blood flow and reduction of hypoperfusion (Lantz & Meyers, 2008). Surgery may result in severe neuropsychological complications for some patients, including executive dysfunction and aphasia (Lantz & Meyers, 2008; Zhao et al., 2005).

Neuropsychological and Psychological Outcomes

The actual occurrence of cognitive deficits in AVM is difficult to determine (Lantz & Meyers, 2008) because much of the data have been pooled from patients with ruptured and unruptured AVMs. Patients with AVM may exhibit below normal performance on tests of intelligence, attention, and memory (Lantz & Meyers, 2008). Some research has demonstrated postsurgical improvement in patient's neuropsychological functioning, including better performance on tasks requiring executive function (Lantz & Meyers, 2008).

Recently, researchers have demonstrated brain reorganization of language function in patients with AVM by using selective Wada testing (intracarotid amobarbital sodium and xylocaine procedure), magnetic resonance imaging, and functional magnetic resonance imaging (Lantz & Meyers, 2008). Other research has demonstrated structural reorganization involving the motor cortex (Lantz & Meyers, 2008). Patients with AVM are more likely to report developmental learning disorders than patients with tumors or aneurysms, with AVM patients reporting four times the rate of learning disability compared to the normal population (Lantz & Meyers, 2008; Lazar et al., 1999). This finding may suggest that disorders of learning and intellectual function may serve as a marker for early cerebral dysfunction in patients with AVMs (Lazar et al., 1999).

Assessment and Treatment

The AVM is often recognized clinically between the ages of 10 and 30, presenting as a seizure disorder, an intracerebral hemorrhage, a subarachnoid hemorrhage, a nonspecific or migraine headache, and less frequently as pulsatile tinnitus (Al-Shahi & Warlow, 2001; Frosch et al., 2005; et al., 2005; Warlow, 2001).

The most commonly affected site is the middle cerebral artery, particularly its posterior branches, but AVMs may occur anywhere along the midbrain, cerebellum, or spinal cord (Frosch et al., 2005). Because the presence of an AVM exposes patients to the risk of permanent neurological deficits or death, surgical intervention is usually necessary (Zhao et al., 2005). The preferred treatment method is generally surgical excision (Ropper, Brown, Adams, & Victor, 2005; Zhao et al., 2005). However, advances in interventional neuroradiology and stereotactic radiosurgery (SRS) have allowed for the development of alternatives to traditional microsurgery, such as gamma knife SRS and proton beam radiosurgery (Ropper et al., 2005; Zhao et al., 2005). In addition, the treatment of giant cerebral AVMs (>6 cm in diameter) may require endovascular embolization as an adjunct to surgical intervention (Zhao et al., 2005).

Cross References

- ▶ Anterior Communicating Artery
- ▶ Gamma Knife
- ▶ Intracarotid Sodium Amytal Test
- ▶ Radiosurgery, Stereotactic Radiation Therapy
- ▶ Shunts
- ▶ Wada Test

References and Readings

Al-Shahi, R., & Warlow, C. (2001). A systematic review of the frequency and prognosis of arteriovenous malformations of the brain in adults. *Brain, 124*, 1900–1926.

Aminoff, M. J., Greenberg, D. A. & Simon, R. P. (2005). *Clinical neurology.* New York: McGraw-Hill.

Frosch, M. P., Anthony, D. C., & De Girolami, U. (2005). The central nervous system. In V. Kumar, A. K. Abbas, & N. Fausto (Eds.), *Pathologic basis of disease* (pp. 1347–1420). Philadelphia: Elsevier.

Lantz, E. R., & Meyers, P. M. (2008). Neuropsychological effects of brain arteriovenous malformations. *Neuropsychology Review, 18*, 167–177.

Lazar, R. M., Connaire, K., Marshall, R. S., Pile-Spellman, J., Hacein-Bey, L., Solomon, R. A., et al. (1999). Developmental deficits in adult patients with arteriovenous malformations. *Archives of Neurology, 56*, 103–106.

Moftakhar, P., Hauptman, J. S., Malkasian, D., & Martin, N. A. (2009). Cerebral arteriovenous malformations. Part 1: cellular and molecular biology. *Neurosurgical Focus, 26*(5), 1–15.

Ropper, A. H., Brown, R. H., Adams, R. D., & Victor, M. (2005). *Adams & Victor's principles of neurology.* New York: McGraw-Hill.

Stein, B. M., & Wolpertson, S. M. (1980). Arteriovenous malformations of the brain. I: Current concepts and treatments. *Archives of Neurology, 37*, 69–75.

Warlow, C. (2001). Stroke, transient ischemic attacks, and intracranial venous thrombosis. In M. Donaghy (Ed.), *Brain's diseases of the nervous system* (pp. 775–896). New York: Oxford University Press.

Webster's new explorer medical dictionary (New Ed.). (2006). Springfield, MA: Merriam-Webster.

Zhao, J., Wang, S., Li, J., Qi, W., Sui, D., & Zhao, Y. (2005). Clinical characteristics and surgical results of patients with cerebral arteriovenous malformations. *Surgical Neurology, 63*, 156–161.

Arteriovenous Malformations

► Vascular Malformations

Arteritis

► Vasculitis

Articulation

Janet Patterson
California State University East Bay
Hayward, CA, USA

Definition

Articulation is (1) the juncture between bones or cartilages in the skeleton of a vertebrate; (2) the movement pattern and relationship of oral structures such as the tongue and lips, to produce the sounds of speech. Articulation develops gradually and consistently across children of all cultures, and the earliest sounds made by infants are undifferentiated. As a child matures and motor control becomes increasingly well-coordinated, the child's speech becomes intelligible within the linguistic community.

Articulation is evaluated through tests of single sounds and words, and in contexts such as oral reading and conversation. Articulation disorders can disrupt speech intelligibility temporarily or for extended periods of time.

Cross References

► Apraxia of Speech
► Articulation Disorder
► Ataxia
► Dysarthria
► Dystonia
► Phoneme
► Phonics
► Speech-Language Pathology

References and Reading

Hulit, L. M., & Howard, M. R. (2005). *Born to talk: an introduction to speech and language development* (4th ed.). Boston: Pearson A & B.

Plante, E., & Beeson, P. M. (2008). *Communication and communication disorders: a clinical introduction* (3rd ed.). Boston: Pearson A&B.

Articulation Disorders

Pamela G. Garn-Nunn
University of Akron
Akron, OH, USA

Short Description or Definition

An articulation disorder is a failure to acquire a speech sound or sounds of a particular language by the expected normative age due to some type of motoric problem. Speech sound errors in articulation disorders include

Substitutions: replacing a standard speech sound with a different standard speech sound e.g., *Wabbit* for *rabbit*, *thpoon* for spoon, or *bery* for *very.*

Omission: omission of a standard speech sound e.g., *ba* for bat, *gin* for *green.* (Widespread omissions often indicate a phonological disorder, however.)

Distortions: replacement of a standard speech sound by a nonstandard sound e.g., *s* in *soup* sounds "slushy."

Additions: addition of a sound or syllable e.g., *cart* for *car* or *chiminey* for *chimney.* Additions are the least commonly occurring type of articulation error.

While some of these sound changes are common for toddlers and early preschoolers, children should master the speech sounds of English by the age of 8.

NOTE: However, individuals whose sound substitutions or omissions reflect a dialectic variation or acquisition of

English as a second language are not considered to have an articulation disorder.

Categorization

An articulation disorder is a type of speech sound disorder. It is associated with a motoric inability to produce a speech sound or sounds (rather than a failure to acquire the speech sound rules of a particular language) by the expected normative age. (► Phonological Disorder.) Articulation and phonological disorders can co-occur.

Epidemiology

Incidence figures are available for speech sound disorders, of which articulation disorders are one type. Figures cited for preschoolers are 8–9% with approximately 5% still demonstrating a speech sound disorder by first grade. Incidence of speech sound disorders in children is higher than in adults. Some children will outgrow their errors, while others will require treatment from a speech-language pathologist to develop understandable speech (see Evaluation).

During the process of speech development, articulation disorders occur more often in children with

- Genetic syndromes such as Down syndrome or other syndromes associated with cognitive delays
- Childhood apraxia of speech
- Neurological disorders such as cerebral palsy
- Orofacial anomalies such as cleft palate
- Myofunctional disorders (sometimes referred to as tongue thrust disorders)

In some cases, no definitive etiological factor will be found.

For school-aged children, articulation disorders can be a continuation of an earlier phonological or articulation problem or the result of some type of neurological injury. Similarly, in adults, a speech sound disorder can consist of residual errors of an earlier disorder or a new disorder due to a variety of neurological causes. ► Dysarthria and ► apraxia for further information on these adult causes of speech sound disorders.

Natural History, Prognostic Factors, Outcomes

A child's acquisition of the speech sounds is a gradual process. Correct articulation can depend not only on motor skills and perceptual development but also the sound make-up and length of a word. Nevertheless, research indicates that the following sounds should be mastered by the ages indicated:

Articulation Disorders. Table 1

By age 3:	p m h w b (emerging between ages 1½ and 3)
By age 3 ½:	k g d t f y (girls only) (emerging between ages 2 and 3 ½)
By age 4:	y (boys)
By age 5:	s-blends (emerging between ages 3½ and 5)
By age 5 ½:	v
By age 6:	sh ch j (girls)
By age 7:	sh ch j (boys) th (as in *th*at)
By age 8:	r s ng l z th (as *in* thumb) zh (as in mea*s*ure)

- Vowels: should all be acquired by age 3 with the exception of the *er* sound in words like *bird* and *hammer*.
- Consonants: these represent ages of *mastery*; prior to these ages, correct production will vary

For children who do not meet these milestones, testing and possible treatment by a certified speech-language pathologist is required. A person who continues to exhibit articulation errors past age 8 should also be evaluated unless their sound usage is characteristic of a dialect or first language.

Neuropsychology and Psychology of Disorder

In some cases, an articulation disorder may be associated with damage to the central or peripheral nervous system. Specific neurological correlates usually are not found except in cases of dysarthria or apraxia. When misunderstood, some children may react by refusing to speak or withdrawing from others. Children who are unable to communicate due to an articulation disorder can become frustrated and act out because they cannot make basic needs and wants known. The child's family can also become frustrated at their inability to communicate with their child. However, this type of behavior is much more likely to occur in conjunction with phonological disorders rather than articulation disorders. For adults with speech sound disorders due to apraxia or dysarthria, the effect on communication will depend on the number of sounds affected, the degree of speech understandability, and the patient's reaction to the communication problem.

Evaluation

Evaluation of articulation disorders is designed to determine:

1. Existence of a problem
2. Nature of the problem (sounds in error, patterns intelligibility)
3. Possible etiology(ies) of the problem, e.g., structural problem or neurological disorder
4. Probable course of treatment
5. Prognosis

To meet these goals, the following components should be included in an evaluation for speech sound disorders:

1. Case history
2. Hearing screening
3. Oral mechanism evaluation
4. Phonemic sound-by-position tests
5. Language testing
6. Other tests as appropriate

Treatment

For patients with simple articulation disorders, a traditional, phonetic approach can be successful. ► Phonological Disorders and ► Articulation Disorders for more information on treatment.

Cross References

► Apraxia
► Articulation Disorder
► Dysarthria
► Phonological Disorder
► Phonology

References and Readings

American Speech-Language-Hearing Association. (2007). *Speech sound disorders: Articulation and phonological disorders,* from www.asha.org/public/speech/disorders/SpeechSoundDisorders.

American Speech-Language-Hearing Association. (2008). *Incidence and prevalence of communication disorders and hearing loss in children* (2008 Ed.), from www.asha.org/members/research/reports/children.

AS

► Ashworth Spasticity Scale (and Modified Version)

ASEBA

► Child Behavior Checklist

ASHA-FACS

► American Speech-Language-Hearing Association Functional Assessment of Communication Skills for Adults

Ashworth Spasticity Scale (and Modified Version)

Kari Dunning
University of Cincinnati
Cincinnati, OH, USA

Synonyms

AS; MAS

Description

The Ashworth Scale (AS) and Modified Ashworth Scale (MAS) measure spasticity. During the administration of both AS (Ashworth, 1964) and MAS (Bohannon & Smith, 1987), the examiner passively moves the joint being tested and rates the perceived level of resistance in the muscle groups opposing the movement. Both scales are single-item measures ranging from 0 to 4, where 0 indicates no increase in muscle tone and 4 indicates that the affected part is rigid in flexion or extension. The AS is considered an ordinal scale, whereas the MAS is considered a nominal scale due to ambiguity created by the addition of the 1+ grade between 1 and 2 (Pandyan, Johnson, Price, Curless, Barnes, & Rodgers, 1999).

Historical Background

The AS was first described by Ashworth in 1964 (Ashworth, 1964) and was subsequently modified with the addition of a 1+ grade by Bohannon in 1987 with the intent to increase sensitivity (Bohannon & Smith, 1987). However,

this addition may have decreased the reliability of the MAS for heavier limbs (see below) (Ansari, Naghdi, Arab, & Jalaie, 2008; Pandyan et al., 1999; Platz, Eickhof, Nuyens, & Vuadens, 2005).

Psychometric Data

Inter- and intra-rater reliability of the AS and MAS show wide variation (Pandyan et al., 1999; Platz et al., 2005), which cannot be attributed to any one factor (Platz et al., 2005), although some evidence suggests that the inter-rater reliability of the MAS is lower for heavier limbs (Ansari et al., 2008; Pandyan et al., 1999; Platz et al., 2005). Both scales have demonstrated responsiveness to treatment (Platz et al., 2005).

Spasticity is characterized by an involuntary muscle activity (Pandyan et al., 2005) and has been traditionally defined as a velocity-dependent increase in muscle tone due to a hyperactive stretch reflex (Lance, 1980). The construct validity of the AS and MAS as spasticity assessments is inadequate because they do not address velocity dependence. Rather, these scales measure passive resistance to movement (hypertonia), which is influenced by spasticity but also altered by biomechanical factors unrelated to involuntary muscle activation (Fleuren, Voerman, & Erren-Wolters, 2009; Pandyan et al., 1999; Platz et al., 2005). Thus, AS and MAS scores are only moderately associated with reflexes (Platz et al., 2005) and electromyographic assessments (Fleuren et al., 2009; Pandyan et al., 1999; Platz et al., 2005) and more strongly associated with objective measures of resistance (Fleuren et al., 2009; Pandyan et al., 1999; Platz et al., 2005).

Clinical Uses

Despite the fact that the AS and MAS are actually only valid assessments of hypertonia (Fleuren et al., 2009; Pandyan et al., 1999; Platz et al., 2005), these scales are the most commonly used clinical tools to assess spasticity (Pandyan et al., 1999; Platz et al., 2005). Both scales have been used to describe treatment response for persons with a wide range of upper motor neuron disorders, including traumatic brain injury, stroke, multiple sclerosis, cerebral palsy, and spinal cord injury (Platz et al., 2005).

Cross References

► Severe Brain Injury
► Spinal Cord Injury

References and Readings

Ansari, N. N., Naghdi, S., Arab, T. K., & Jalaie, S. (2008). The interrater and intrarater reliability of the Modified Ashworth Scale in the assessment of muscle spasticity: Limb and muscle group effect. *NeuroRehabilitation, 23*(3), 231–237.

Ashworth, B. (1964). Preliminary trial of carisoprodol in multiple sclerosis. *Practitioner, 192*, 540–542.

Bohannon, R. W., & Smith, M. B. (1987). Interrater reliability of a modified Ashworth scale of muscle spasticity. *Physical Therapy, 67*(2), 206–207.

Fleuren, J. F., Voerman, G. E., Erren-Wolters, C. V., et al. (2009). Stop using the Ashworth Scale for the assessment of spasticity. *Journal of Neurology, Neurosurgery, and Psychiatry, 81*(2), 46–52.

Lance, J. W. (1980). Symposium synopsis. In R. G. Feldman, R. R. Young, & W. P. Koella (Eds.), *Spasticity: Disordered motor control* (pp. 485–494). Chicago, IL: Year Book Medical Publishers.

Pandyan, A. D., Gregoric, M., Barnes, M. P., et al. (2005). Spasticity: Clinical perceptions, neurological realities and meaningful measurement. *Disability and Rehabilitation, 27*(1–2), 2–6.

Pandyan, A., Johnson, G., Price, C., Curless, R., Barnes, M., & Rodgers, H. (1999). A review of the properties and limitations of the Ashworth and modified Ashworth Scales as measures of spasticity. *Clinical Rehabilitation, 13*(5), 373–383.

Platz, T., Eickhof, C., Nuyens, G., & Vuadens, P. (2005). Clinical scales for the assessment of spasticity, associated phenomena, and function: A systematic review of the literature. *Disability and Rehabilitation, 27*(1–2), 7–18.

ASIA (American Spinal Injury Association) Exam

► ASIA Impairment Scale

ASIA Impairment Scale

Amitabh Jha
Craig Hospital
Englewood, CO, USA

Synonyms

ASIA (American Spinal Injury Association) exam; Frankel scale; International standards for the neurological classification of spinal cord injury

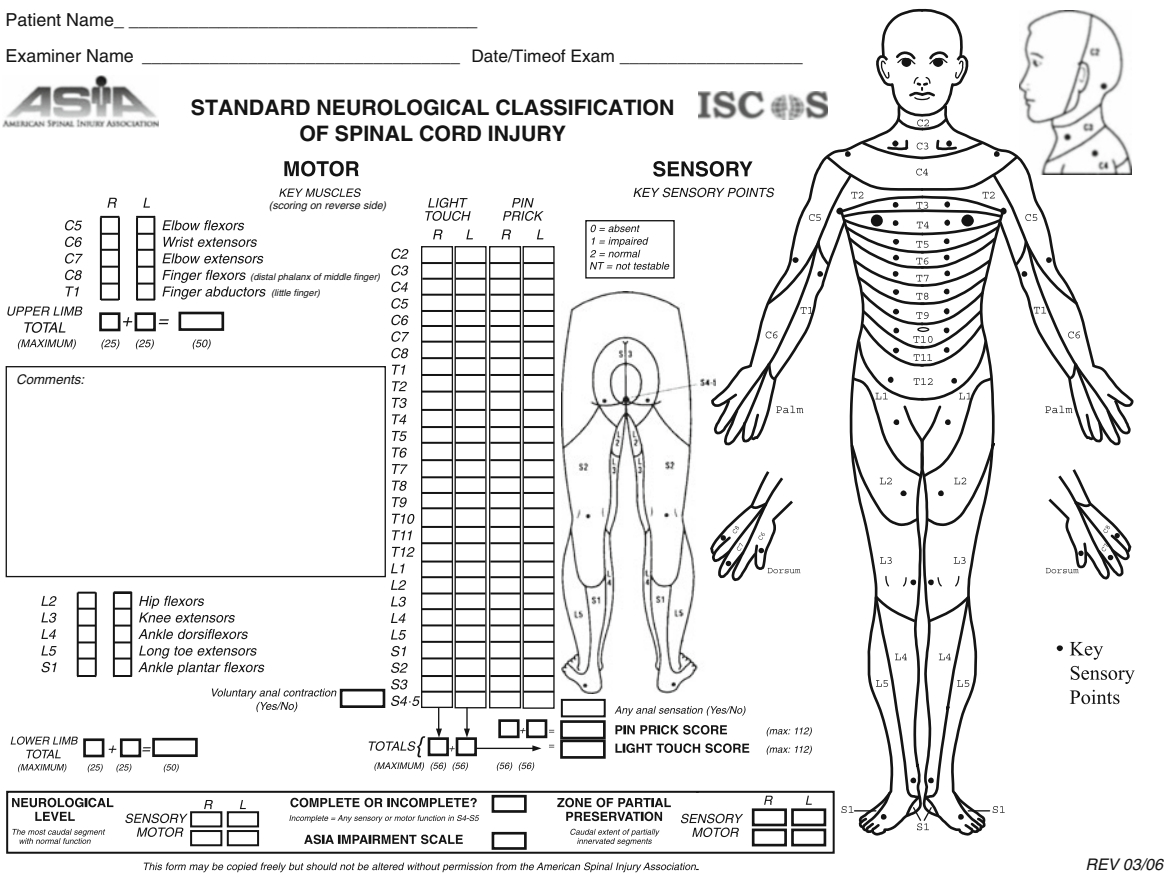
Description

The *International Standards for Neurological Classification of SCI (ISNCSCI)* is a widely accepted and readily

administered guide to document neurological function after spinal cord injury (SCI) and is intended to be a standard for measuring neurological outcomes in both clinical and research settings. Briefly, these standards utilize a two-step process consisting of a specific neurological examination followed by a classification procedure based on the results of the exam. The systematic neurological examination assesses sensory and motor function of each spinal segmental level. Sensation of light touch and pinprick (PP) stimuli is scored as 0 for absent, 1 for impaired, and 2 for normal. Motor function is scored on a scale of 0 for total paralysis to 5 for normal strength. All 28 dermatomes are tested bilaterally for sensory function, and ten key muscles are tested bilaterally for motor function, yielding sensory/light touch (LT) and sensory/pinprick (PP) summed scores ranging from 0 to 112 and motor summed scores ranging from 0 to 100. The neurological level is assigned as the lowest level with normal neurological function. In addition, the ASIA Impairment Scale (AIS) grade classification, an indicator of injury "completeness" similar to the Frankel scale, is assigned based on this information. AIS A denotes a complete injury with no sensory or motor function below the level of injury. Incomplete injuries are graded as AIS B if there is sensory but no motor function below the injury level, AIS C if there is some motor sparing, AIS D for substantial motor sparing, and AIS E for normal neurological examination (Fig. 1).

Historical Background

ISNCSCI has been used extensively in clinical practice and research since 1982. The standards and accompanying reference manual have undergone sequential revisions, most recently in 2000 and 2003, respectively.



ASIA Impairment Scale. Figure 1 International Standards for Neurological Classification of Spinal Cord Injury (ISNCSCI)

Psychometric Data

Published studies have found total motor score ICCs from 0.98 to 0.99 for intra-rater reliability and 0.97 for inter-rater reliability. Total sensory scores intra-rater reliability has ranged from 0.76 to 0.98, and 0.88 to 0.96 for inter-rater. One study reported agreement on individual muscles with Kappas ranging from 0.3 to 0.89 for each myotome, 0.02 to 0.83 for dermatome assessment using pinprick, and 0.17 to 1 when assessed using light touch.

Clinical Uses

The exam is used to document sensory and motor function after SCI. It has been used to diagnose SCI, as an outcome measure in studies to treat spinal cord pathology, as well as a tool to predict outcomes such as independence with activities of daily living, employment, life satisfaction, and life expectancy.

Cross References

- ► Sensorimotor Assessment
- ► Spinal Cord Injury

References and Reading

American Spinal Injury Association. (2002). *International standards for neurological classification of spinal cord injury* (Revised 2002). Chicago: American Spinal Injury Association.

American Spinal Injury Association. (2003). *Reference manual for the international standards for neurological classification of spinal cord injury* (Revised 2003). Chicago: American Spinal Injury Association.

Furlan, J. C., Fehlings, M. G., Tator, C. H., & Davis, A. M. (2008). Motor and sensory assessment of patients in clinical trials for pharmacological therapy of acute spinal cord injury: Psychometric properties of the ASIA standards. *Journal of Neurotrauma, 25*(11), 1273–1301.

Kirshblum, S. C., Memmo, P., Kim, N., Campagnolo D., & Millis, S. (2002). Comparison of the revised 2000 American spinal injury association classification standards with the 1996 guidelines. *American Journal of Physical Medicine & Rehabilitation, 81*(7), 502–505.

Mulcahey, M. J., Gaughan, J., Betz, R. R., & Johansen, K. J. (2007). The international standards for neurological classification of spinal cord injury: Reliability of data when applied to children and youths. *Spinal Cord, 45*(6), 452–459.

Asomatognosia

John E. Mendoza
Tulane University Medical Center
New Orleans, LA, USA

Synonyms

Disturbance of body schema

Definition

Disturbance in the normal awareness of one's own body, typically characterized by one or more of the following symptoms: (1) a tendency to ignore or neglect one side of the body, (2) a failure to recognize or difficulty in identifying a specific part of the body (usually a limb or part of a limb), (3) difficulty in differentiating the right from the left side of the body, or (4) recognizing an impairment in a part of the body (*anosognosia*).

Current Knowledge

Asomatognosia most commonly results from acute or subacute brain lesions and may affect one or both sides of the body. Unilateral neglect generally involves an entire side of the body, more commonly the left. This might be reflected in a failure to shave the affected side of the face, putting a glove only on one hand, or reduced use of the involved limb for certain activities, even though it is physically capable of doing so. If a limb is paralyzed, the patient may either deny or minimize the impairment (*anosognosia*), or may even deny ownership of the affected limb. If the affected side or a part of the body is stimulated, the individual may report that the homologous area on the intact side was touched (*allesthesia*). Patients may also have difficulty localizing or identifying parts of their own body (*autotopagnosia*). This is most commonly expressed as difficulty naming or identifying individual fingers (especially the three middle digits) either of their own hands or those of others (*finger agnosia*). This deficit is usually expressed bilaterally. *Right–left disorientation* is generally also considered a form of asomatognosia. Here, the individual has difficulty reliably identifying the right

and left sides of his or her own body or those of the examiner.

Although asomatognosia strictly refers to impaired awareness or attention to parts of one's own body, personal neglect often extends into extrapersonal space. Thus, a patient may fail to attend to visual or auditory stimuli on the affected side, despite intact visual fields or the fact that auditory stimuli enter both ears. This can be very disconcerting for family members if they are not made aware of these phenomena, perhaps believing the patient is purposely ignoring their presence.

Unilateral neglect or anosognosia type disorders are most commonly found, following acute lesions (such as strokes) of the right hemisphere. Although improvement is typically seen over time, subtle degrees of deficit may persist indefinitely. By contrast, those deficits that present bilaterally (such as finger agnosia and right–left disorientation) are usually the result of posterior left-hemispheric lesions.

Cross References

- ▶ Allesthesia
- ▶ Anosognosia
- ▶ Autotopagnosia
- ▶ Finger Agnosia
- ▶ Right–Left Disorientation

References and Readings

Hecaen, H., & Albert, M. L. (1978). *Human neuropsychology* (pp. 303–330). New York: Wiley.

Heilman, K. M., Watson, R. T., & Valenstein, E. (2003). Neglect and related disorders. In K. Heilman & E. Valenstein (Eds.), *Clinical neuropsychology* (pp. 296–346). New York: Oxford University Press.

Kortte, K. B., & Wegener, S. T. (2004). Denial of illness in medical rehabilitation populations: Theory, research and definitions. *Rehabilitation Psychology, 49*, 187–199.

Prigatano, G. P., & Schacter, D. L. (1991). *Awareness of deficit after brain injury: Clinical and theoretical issues*. New York: Oxford University Press.

Asperger Syndrome

- ▶ Asperger's Disorder

Asperger's Disorder

Stephen M. Kanne, Micah O. Mazurek
Thompson Center for Autism and Neurodevelopmental Disorders
Columbia, MO, USA

Synonyms

Asperger syndrome

Short Description or Definition

Asperger's disorder is a neurodevelopmental disorder that is associated with impairment in social relatedness and repetitive or restricted behaviors and interests. Social difficulties that are characteristic of Asperger's disorder include nonverbal aspects of social interaction (e.g., eye contact, gestures, and facial expressions) as well as social and emotional reciprocity (e.g., sharing interests, taking turns, demonstrating empathy). Behaviorally, individuals with Asperger's often exhibit intense and narrow circumscribed interests, insistence on sameness or routine, and behavioral rigidity (American Psychiatric Association, 1994). While overall level of intellectual functioning (i.e., IQ) is not impaired in individuals with Asperger's disorder, their cognition is often compromised in other areas such as executive functioning (see Neuropsychology and Psychology of Asperger's Disorder below).

Categorization

Asperger's disorder is currently classified in the DSM-IV as one of five separate pervasive developmental disorders (which also include autistic disorder, Rett's disorder, childhood disintegrative disorder, and pervasive developmental disorder NOS). Asperger's disorder is a fairly recent addition to the DSM, first appearing only in the latest version, the DSM-IV (1994). According to the DSM-IV, to meet criteria for Asperger's disorder, an individual must demonstrate impairment in social interaction (exhibiting at least two out of four possible symptoms) and restricted and repetitive patterns of behaviors or interests (exhibiting at least one out of four possible symptoms). In addition, an individual must *not* have a history of developmental delays in language, cognition, or adaptive functioning. Of note, the criteria

for Asperger's disorder are identical to those for autistic disorder (i.e., autism) in the areas of social impairment and restricted and repetitive behavior. However, autistic disorder requires an additional criterion of impairment in communication (i.e., delays in language development, impairment in conversation, stereotyped language, or lack of pretend play). Additionally, there is not a requirement in the criteria for autistic disorder that cognitive, language, and adaptive development fall within the normal range in childhood (as is the case in Asperger's disorder) (American Psychiatric Association, 1994).

Epidemiology

Prevalence estimates have varied widely from 0.3/1,000 to 6/1,000 (see Mattila et al., 2007 for review). Based on a review of the literature, Fombonne (2003, 2005) estimated the prevalence rate for Asperger's disorder to be approximately 2/10,000. Such wide variations in prevalence rates are likely due to differences in diagnostic procedures and operational definitions used in each study. In fact, recent rates from the same study varied from 1.6/1,000 to 2.9/1,000 depending on the specific criteria used for diagnosis (Mattila et al., 2007). In terms of sex differences, males are overrepresented in Asperger's disorders, with an estimated sex ratio of 4:1 (see Schopler, Mesibov, & Kunce, 1998 for review).

Natural History, Prognostic Factors, Outcomes

Asperger's disorder takes its name from the Austrian physician, Hans Asperger, whose 1944 paper on "autistic psychopathy" described a group of children who showed deficits in social behaviors, insistence on sameness, a lack of nonverbal communication, repetitive movements, and average intelligence. Asperger (in 1944) and Leo Kanner (in 1943), although unaware of one another's work, were the first to describe this cluster of symptoms. While Leo Kanner's seminal work describing autistic behaviors was the subject of much discussion and resulted in the eventual inclusion of autism in the DSM (in 1980), Asperger's paper did not receive wide attention after publication and was not translated into English until 1991 (see Frith, 1991). After the appearance of autism in the DSM-III, it became apparent that there was a group of individuals who did not meet the criteria for the narrowly defined definition of infantile autism, but who demonstrated deficits in social interaction and repetitive behaviors. As a result, Wing (1981) published an influential paper reintroducing Asperger's original ideas and arguing for broadening the definition of autism to include Asperger's disorder on the autism continuum. Eventually, a separate diagnosis of Asperger's disorder was added to the fourth edition of the DSM (1994). Since that time, debate has continued as to whether or not Asperger's disorder should remain a separate diagnosis from autism. The prevailing current view is that Asperger's disorder and autism are not distinctly different, and that Asperger's disorder may simply represent the milder end of the autism spectrum. As a result, Asperger's disorder is often used synonymously with the term "high-functioning autism" (which typically refers to individuals meeting criteria for Autistic Disorder whose IQ levels are above 70).

With regard to developmental course, Asperger's disorder is generally diagnosed much later than autistic disorder, with an average age of diagnosis being 11 years (possibly due to the lack of early developmental delays). It follows a continuous course throughout the lifespan, although for some individuals symptoms remit as a result of early intervention (see Frith, 2004 for review). Research into prognostic factors and outcome in Asperger's disorder is sparse, particularly since it has only been recognized as an official diagnosis for little over a decade; however, IQ and language ability have been found to be strong predictors of outcomes in autism spectrum disorders in general.

Neuropsychology and Psychology of Asperger's Disorder

By definition, social interactions are impaired in Asperger's disorder. However, the underlying processes by which social interactions are disrupted have been the source of recent attention. First, there is clear evidence that individuals with Asperger's disorder have impairments in their ability to understand complex emotions and a resulting inability to recognize and empathize with others' feelings. Individuals with Asperger's disorder (as well as autistic disorder), also have impairments in what is known as "theory of mind." As such, they have difficulty automatically attributing mental states to others. Although there are no formal criteria concerning communication skills for Asperger's disorder, clinical and research accounts highlight the presence of social communication difficulties. Specifically, difficulties with pragmatic language and difficulties with turn-taking in conversation are common (see Klin, Volkmar, & Sparrow, 2000 for review).

Asperger's Disorder. Table 1 DSM-IV criteria for Asperger's disorder

Social impairment (2 or more)	Restricted and repetitive behavior (1 or more)	Lack of delays in
1. Impaired nonverbal behavior	1. Abnormal and intense preoccupation with stereotyped or restricted interest	Language
2. Impaired peer relationships	2. Inflexible and nonfunctional routines or rituals	Cognitive development
3. Lack of seeking to share enjoyment, interests, or achievements	3. Stereotyped and repetitive motor mannerisms	Self-help skills
4. Lack of social or emotional reciprocity	4. Preoccupation with parts of objects	Adaptive behavior (other than social)
		Curiosity about the environment

Source: From Diagnostic and Statistical Manual of Mental Disorders, fourth edition, by American Psychiatric Association, 1994, Washington, DC

Asperger's disorder is also associated with cognitive features that affect functioning outside the social domain. Studies have shown that individuals with Asperger's disorder have very uneven cognitive profiles. One explanation for this common finding is that these individuals have "weak central coherence." That is, they are more likely to process information as discrete units rather than processing them as a unified whole. There is some evidence that bottom-up processing occurs without accompanying top-down control. As a result, high levels of details are perceived, while global information may be missed (see Frith, 2004). Studies have also shown consistent deficits in overall executive function among individuals with Asperger's disorder (as is also the case in autistic disorder). Specifically, poor performance has been shown on both the Wisconsin Card Sorting Test and the Tower of Hanoi. Particular deficits have been noted in the ability to shift response set and in overall planning. Consistent with this, individuals with Asperger's disorder are often described as having difficulty adjusting to changes in routine or task demands, and as having a strong need for sameness (see Klin et al., 2000).

Some studies, including Wing's (1981) original description, have found significantly higher verbal IQ scores than performance IQ scores among individuals with Asperger's disorder (the reverse of which is typically found in autistic disorder). Motor clumsiness has also been observed among children with Asperger's disorder since Hans Asperger's original paper, although it has never been a part of the formal diagnostic criteria (see Frith, 1991). As a result, researchers have been interested in potential similarities between Asperger's disorder and nonverbal learning disorders (NVLD) or right hemispheric dysfunction. These profiles are marked by relative strengths at rote verbal skills, with deficits in social understanding and motor coordination. While there is a great deal of overlap among these conditions, empirical findings have been equivocal. Some studies have found visual-spatial impairments (with strengths in Verbal IQ) in Asperger's disorder, while others have not demonstrated this pattern (see Klin et al., 2000). Further work with more stringent diagnostic criteria is needed in this area.

Coexisting Conditions

In addition to the core symptoms, Asperger's disorder may also be accompanied by co-occurring disorders. Studies have shown that a large percentage of children with Asperger's disorder also exhibit problems with attention and impulse control (similar to those found in ADHD). However, the DSM-IV prevents an additional diagnosis of ADHD when there is an existing pervasive developmental disorder diagnosis. In adolescence and adulthood, case studies indicate relatively high rates of depression, anxiety, and bipolar disorder among individuals with Asperger's disorder (see Ghaziuddin, 2002 for review). Recent evidence has also demonstrated that individuals with Asperger disorder have significant adaptive impairments as well (see Saulnier & Kim, 2007).

Evaluation

Diagnostic assessment of Asperger's disorder is best conducted using multiple methods and observers. Due to the complexity of the disorder, and its effects on broad areas of functioning, interdisciplinary assessment is recommended. First, because Asperger's is a neurodevelopmental disorder, parent report of early history and development, as well as structured observations of current behavior, are essential. Currently, the two "gold-standard"

tools for diagnosis of autism spectrum disorders are the Autism Diagnostic Interview – Revised (ADI-R) and the Autism Directed Observation Schedule (ADOS). These are the most widely studied measures in the field, and reliability and validity have been well established. The ADI-R is a comprehensive interview that assesses past and current functioning in the areas of communication, social interaction, and restricted or repetitive behavior. The Autism Directed Observation Schedule (ADOS) is another diagnostic tool that allows for clinic-based observations across various structured activity- and conversation-based interactions. Despite their advantages, however, neither tool was designed to measure Asperger's disorder specifically, or to differentiate between Asperger's disorder and other PDDs. A number of other scales have been developed to assess Asperger's disorder, but systematic research is lacking as of yet (see Matson & Boisjoli, 2008; Mesibov, Shea, & Adams, 2001 for review).

In addition to assessing the core symptoms of Asperger's disorder, assessment should focus on cognitive, adaptive, and communication skills. General measures of intelligence, such as the *Wechsler Scales* and the *Stanford Binet Intelligence Scales* are useful in assessing overall functioning as well as particular strengths and weaknesses. Additionally, it is helpful to include measures of visual-spatial and visual-motor processing, particularly since these areas are typically weaker in Asperger's disorder. Given common deficits in executive function and attention, neuropsychological assessment of these functions is recommended. Measures of social communication and pragmatic language, and adaptive skills, also add information to the clinical picture and help inform intervention recommendations (see Klin et al., 2000 for review).

Treatment

There is, as of yet, no available treatment that provides a "cure" for the core impairments of Asperger's disorder. However, there are a number of interventions that target specific symptoms. In addressing social deficits in Asperger's disorder, there have been several promising studies of social competence interventions among children and adolescents with Asperger's disorder and autism. Such interventions can be delivered in educational or outpatient clinic-based settings, and typically include cognitive and behavioral components (including direct instruction, modelling skills, and skills practice) (see Klin et al., 2000).

Educationally, students with Asperger's disorder often benefit from modifications and supports provided through special education. Although services vary widely based on the region, they may range from specialized schools designed to serve students with Asperger's disorder to modifications within general education classrooms. Some students may get benefit and support from paraprofessional aides in the classroom, while others may require only slight academic modifications. Most students with Asperger's disorder benefit greatly from communication interventions aimed at improving pragmatic and social skills (see Klin et al., 2000; Mesibov et al., 2001 for review).

Family support, parent training, and instruction on behavior management strategies can also be helpful when disruptive behaviors accompany the clinical picture. For adolescents and adults, there are emerging data showing that both individual and group-based cognitive behavioral therapy are promising in the treatment of co-occurring symptoms of depression and anxiety. Individual work with counsellors or mental health professionals could also focus on social and communication skills training as well as bolstering adaptive functioning. In addition, medications may be prescribed to treat associated symptoms (particularly inattention, depression, and anxiety).

Cross References

- ▶ Autistic Disorder
- ▶ Nonverbal Learning Disabilities
- ▶ Pervasive Developmental Disorder NOS

References and Readings

American Psychiatric Association. (1994). *Diagnostic and statistical manual of mental disorders* (4th ed.). Washington, DC: American Psychiatric Publishing, Inc.

Fombonne, E. (2005). The changing epidemiology of autism. *Journal of Applied Research in Intellectual Disabilities, 18*, 281–294.

Fombonne, E., & Tidmarsh, L. (2003). Epidemiologic data on Asperger disorder. *Child and Adolescent Psychiatric Clinics of North America, 12*, 15–21.

Frith, U. (Ed.). (1991). *Autism and Asperger syndrome*. Cambridge: Cambridge University Press.

Frith, U. (2004). Emanuel Miller lecture: Confusions and controversies about Asperger syndrome. *Journal of Child Psychology and Psychiatry, 45*, 672–686.

Ghaziuddin, M. (2002). Asperger syndrome: Associated psychiatric and medical conditions. *Focus on Autism and Other Developmental Disabilities, 17*, 138–144.

Klin, A., Volkmar, F. R., & Sparrow, S. (Eds.). (2000). *Asperger syndrome*. New York, NY: The Guilford Press.

Matson, J. L., & Boisjoli, J. A. (2008). Strategies for assessing Asperger's syndrome: A critical review of data based methods. *Research in Autism Spectrum Disorders, 2*, 237–248.

Mattila, M., Kielinen, M., Jussila, K., Linna, S., Bloigu, R., Ebeling, H., et al. (2007). An epidemiological and diagnostic study of Asperger syndrome according to four sets of diagnostic criteria. *Journal of the American Academy of Child & Adolescent Psychiatry, 46*, 636–646.

McLaughlin-Cheng, E. (1998). Asperger syndrome and autism: A literature review and meta-analysis. *Focus on Autism and Other Developmental Disabilities, 13*, 234–245.

Mesibov, G. B., Shea, V., & Adams, L. W. (2001). *Understanding Asperger syndrome and high-functioning autism.* New York, NY: Kluwer Academic/Plenum Publishers.

Saulnier, C. A., & Klin, A. (2007). Brief report: Social and communication abilities and disabilities in higher functioning individuals with autism and Asperger syndrome. *Journal of Autism and Developmental Disorders, 37*(4), 788–793.

Schopler, E., Mesibov, G. B., & Kunce, L. J. (Eds.). (1998). Asperger syndrome or high-functioning autism? New York, NY: Plenum Press.

Wing, L. (1981). Asperger's syndrome: A clinical account. *Psychological Medicine, 11*, 115–130.

Assessment of Consent

► Informed Consent

Assessment of Life Habits (LIFE-H)

Jessica Fish
Medical Research Council Cognition & Brain Sciences Unit
Cambridge, UK

Synonyms

The abbreviation LIFE-H is consistent, but version numbers are often appended (e.g., LIFE-H 1.0, 2.0, 3.0, 3.1)

Description

The Assessment of Life Habits (LIFE-H) is a self-report measure of social participation of people with disabilities. The original version of the scale consisted of 298 items; later versions have reduced the number of items to 240 (version 3.0). Various short forms are also available (55–77 items), with the most recent being the 77-item version 3.1. The long form is said to take between 20 and 120 min to complete, and the short form, 20–60 min. In the short form (version 3.1), items are organized into 12 categories: nutrition, fitness, personal care, communication, housing, mobility (classified as activities of regular living) and responsibilities, interpersonal relationships, community life, education, employment, and recreation (classified as social roles). The long form includes 31 subsections, essentially covering the listed domains with a greater degree of specificity. Each item is rated on a 4-point "level of accomplishment" scale (with an additional option to state "not applicable"), a 5-point "level of satisfaction" scale, as well as a rating regarding the type and level of assistance required (i.e., no assistance, assistive device, adaptation, human assistance). A score for each item is obtained with reference to a scoring template included in the manual, grading according to the level of difficulty and level of assistance. Item scores range from 0 (not accomplished) to 9 (performed with no difficulty and no assistance), with mid-scale examples being 3 (performed with difficulty and human assistance), and 6 (performed with difficulty and technical aid or adaptation). Scores can then be weighted by the number of applicable activities to obtain domain-level scores, or a simple formula can be used to obtain an overall score.

Historical Background

Noreau, Fougeyrollas, and Tremblay (2005) stated that the LIFE-H was developed to assess social participation in people with disabilities, regardless of the nature of those disabilities, and based upon the Disability Creation Process model, which views handicap as "the situational result of the interaction of two causal dimensions: the characteristics of the individual and those of the environment." Version 2.0 of the scale was developed following a content validity study that involved 12 experts in rehabilitation medicine evaluating the scale (in terms of clarity and pertinence of content, classifications used in the measurement scales, etc.); modifications included reversing the scoring of the accomplishment section such that higher scores reflected the competence in the activity. Version 3.0 incorporated a greater number of items within particular domains and added additional filter questions to some sections (e.g., if you are not currently employed, skip to section *x*). Version 3.1 is a short form based upon version 3.0.

Psychometric Data

Fougeyrollas et al. (1998) reported that the LIFE-H v1.0 demonstrated acceptable internal consistency in adults and children (Intra-class Correlation (ICCs) > 0.5 for each life habit), and good test–retest reliability in children and adults with spinal cord injury (ICC children $r = 0.73$,

and adults $r = 0.74$). Inter-rater reliability was examined in a group of 20 stroke patients (Beaulieu et al., 1996; Cited in Noreau et al., 2002), with ICCs for 6/12 "accomplishment" ratings of life habits above 0.6, and 10/12 "satisfaction" ratings for life habits above 0.6. Similar findings have been reported for inter-rater reliability of LIFE-H scores for people with physical disabilities, with ICCs of $r > 0.75$ for 7/10 categories, and $r = 0.89$ for the whole scale (Noreau et al., 2004).

Several studies have examined the predictive validity of the LIFE-H. Desrosiers et al. (2003) presented evidence of the convergent validity of the LIFE-H in the form of high correlations with the Functional Autonomy Measurement System (SMAF), and moderate correlations with the Functional Independence Measure (FIM). Further, LIFE-H scores were lower in stroke patients than neurologically healthy controls. A comprehensive review of the psychometric properties of the LIFE-H is available online (http://www.medicine.mcgill.ca/Strokengine-assess/module_lifeh_indepth-en.html#section3).

Clinical Uses

The LIFE-H is available in Dutch, English, and French versions. Adapted forms suitable for use with children aged 0–4 and 5–13 are available (for which a proxy respondent is required). The LIFE-H has been used to evaluate social participation in many patient groups, including children with cerebral palsy, adults with Spinal Cord Injury, Traumatic Brain Injury, and stroke.

Cross References

- ► Functional Autonomy Measurement System
- ► Functional Independence Measure

References and Readings

More information is available on http://www.medicine.mcgill.ca/Strokengine-assess/module_lifeh_indepth-en.html#section3. Accessed 12 May 2009.

Desrosiers, J., Rochette, A., Noreau, L., Bravo, G., Hébert, R., & Boutin, C. (Sept.–Oct. 2003). Comparison of two functional independence scales with a participation measure in post-stroke rehabilitation. *Archives of Gerontology and Geriatrics, 37*(2), 157–172.

Desrosiers, J., Noreau, L., Rochette, A., Bravo, G., & Boutin, C. (2002). Predictors of handicap situations following post-stroke rehabilitation. *Disability & Rehabilitation, 24*(15), 774–785.

Fougeyrollas, P., Noreau, L., Bergeron, H., Cloutier, R., Dion, S. A., & St-Michel, G. (1998). Social consequences of long term impairments and disabilities: Conceptual approach and assessment of handicap. *International Journal of Rehabilitation Research, 21*(2), 127–141.

Noreau, L., Desrosiers, J., Robichaud, L., Fougeyrollas, P., Rochette, A., & Viscogliosi, C. (March 18, 2004). Measuring social participation: Reliability of the LIFE-H in older adults with disabilities. *Disability & Rehabilitation, 26*(6), 346–352.

Noreau, L., Fougeyrollas, P., & Tremblay, J. (2005). *The measure of life habits (LIFE-H) user's manual.* RIPPH. http://www.ripph.qc.ca/?rub2=4&rub=15&lang=en. Accessed 23 Apr 2010.

Noreau, L., Fougeyrollas, P., & Vincent, C. (2002). The LIFE-H: Assessment of the quality of social participation. *Technology and Disability, 14*(3), 113–118.

Rochette, A., Desrosiers, J., & Noreau, L. (2001). Association between personal and environmental factors and the occurrence of handicap situations following a stroke. *Disability & Rehabilitation, 23*(13), 559–569.

Assessment of Motor Process Skills

Kelli Williams Gary
Virginia Commonwealth University
Richmond, VA, USA

Synonyms

AMPS

Description

The Assessment of Motor Process Skills (AMPS) is a standardized observational assessment widely used by occupational therapists to measure the quality of performance in activities of daily living (ADL) of persons across the age spectrum beginning at 3 years. Specifically, the AMPS tests functions that relate to purposeful, goal-oriented daily life tasks that a person wants, needs, and is expected to perform; it does not evaluate neuromuscular, biomechanical, cognitive, and psychosocial impairments (Fisher, 2006). The current version of the assessment contains 83 calibrated ADL tasks that permit evaluation of 36 skills (16 motor, 20 process); AMPS-trained raters must observe two or more specific tasks in 10–20 min increments.

A multi-perspective approach is used to rate each task by observing various motor and process skills in terms of physical effort, efficiency, safety, and independence. The 16 motor skills reflect the ability to use body positions, obtain and hold objects, move self and objects, and sustain performance during ADL task performance. The 20 process skills

pertain to sustaining performance, applying knowledge, temporal organization, organizing space and objects, and adapting performance. Scores are based on observation of the client from certified raters. Motor and process skills are rated simultaneously utilizing a 4-point ordinal criterion referenced rating scale with the highest score denoting competent performance, followed by questionable, inefficient, and markedly inefficient performance. AMPS computer scoring software converts ordinal raw scores of easy skill items for persons of low ability and hard skill items for persons of high ability along a single common equal-interval linear scale (Fisher, 1994).

Historical Background

The genesis of the AMPS is found in the psychiatric assessment of clients with schizophrenia and depression in Halifax, Canada (Fisher & Bernspång, 2007). In 1994, the basic idea was further developed and a specific tool was standardized by Anne G. Fisher, ScD, OTR and colleagues from the Division of Occupational Therapy, Umeå University in Umeå, Sweden. Currently, the AMPS is used in at least 20 countries. In 2006, the most recent version (sixth version) was published to increase applicability across populations, diagnoses, disabilities, cultural background, nationality, and age groups by adding additional tasks (Fisher, 2006).

Psychometric Data

The AMPS has robust psychometric properties. Interrater and intrarater reliability are high with 95% of calibrator raters demonstrating goodness-of-fit to the many-faceted Rasch model. Test–retest reliability is high on a diagnostically heterogeneous sample of older adults with r = 0.90 to 0.91 for AMPS process scale and motor scale, respectively (Fisher, 2006). Studies have found good validity of the AMPS when applied to groups of different racial, ethnic, and cultural backgrounds, across gender, and with multiple diagnoses.

Clinical Uses

Fisher (2006) states: "the AMPS provides occupational therapy practitioners with a powerful and sensitive tool that can assist with planning effective ADL interventions and documenting change." Because of the AMPS' unique and innovative design, occupational performance is evaluated based on the familiarity and relevance of the tasks to the client's daily life needs. Therefore, the environment should be naturalistic and approximate the conditions in which the client can comfortably perform tasks. Settings for AMPS observation can vary based on the space available and can include fully equipped clinic kitchens, laundry rooms, outdoor, and the client's own room in the hospital or nursing home.

The primary advantage of the AMPS is that it can be used with persons of virtually any age, diagnosis, or disability. However, the scope and breadth of evidence for AMPS use is limited in psychiatric, neurologic, and pediatric settings. Geriatric settings have offered the most research evidence for those with cognitive impairments and dementias, followed by a sizable proportion of research for people with learning disabilities (Hitch, 2007).

Cross References

- ▶ Activities of Daily Living
- ▶ Instrumental Activities of Daily Living
- ▶ Occupational Therapy

References and Readings

Fisher, A. G. (1994). Development of a functional assessment that adjusts ability measures for task simplicity and rater leniency. In M. Wilson (Ed.), *Objective measurement: Theory into practice* (Vol 2, pp. 145–175). Norwood, NJ: Ablex.

Fisher, A. G. (2006). *Assessment of motor and process skills. Vol. 1: Development, standardization, and administration manual* (6th ed.). Fort Collins, CO: Three Star.

Fisher, A. G., & Bernspång, B. (2007). Response to: A critique of the Assessment of Motor and Process Skills (AMPS) in mental health practice. *Mental Health Occupational Therapy, 12*, 10–11. (Available from http://www.ampsintl.com/documents/MHOT%20March%202007.pdf)

Hitch, D. (2007). A reply from Danielle Hitch to the Fisher and Bernspång response to: A critique of the Assessment of Motor and Process Skills (AMPS) in mental health practice. *Mental Health Occupational Therapy, 12*, 14. (Available from http://www.ampsintl.com/documents/MHOT%20March%202007.pdf)

Assisted Living

Jay Behel
Rush University Medical Center
Chicago, IL, USA

Synonyms

Domiciliary care; Residential care

Definition

Assisted living is a care arrangement that provides supervision and assistance to individuals who are unable to live independently but do not require the level of care provided in conventional nursing homes.

Current Knowledge

Assisted living arrangements may take place in structured assisted living facilities, small group homes, or an individual's own home or the home of a family member. These arrangements have as their goal the preservation of a degree of autonomy and privacy at home or in a home-like setting. When sited in one's home, assistance may be provided by a combination of paid caregivers, family members, and other paid or unpaid assistants to help with housekeeping, laundry, cooking, and transportation. Assistance provided may include supervision for safety, medication management, meal preparation, and accompaniment and assistance during community-based activities. Assisted living facilities may also offer social activities and specialized services for individuals with cognitive impairment. Basic Activities of Daily Living (BADL) such as hands-on bathing, dressing, and feeding are usually not considered as a part of an assisted living arrangement as the consistent need for such basic care is often seen as an indication that nursing home or a home-based parallel thereof is the more appropriate level of care.

Assisted living typically is not covered by private insurance or Medicare, and access to such care may be limited by an individual's finances. Moreover, there is a considerable variability in how care facilities, clinicians, and professional literature define and discuss assisted living. Consequently, the appropriate role of assisted living in the continuum of care remains unclear, and refinement and redefinition of this role likely will be ongoing for some time.

Cross References

► Life Care Planning

References and Readings

Stone, R. I., & Reinhard, S. C. (2007). The place of assisted living in long-term care and related service systems. *Gerontologist, 47*(Spec. No. 3), 23–32.

Assistive Technology

Diane Cordry Golden
Association of Assistive Technology Act Programs
Delmar, NY, USA

Definition

Assistive technology (AT) is a term used to refer to both AT devices and AT services. A formal, legal definition of AT devices and services was first published in the Technology-Related Assistance for Individuals with Disabilities Act of 1988 as follows:

- assistive technology device means any item, piece of equipment, or product system, whether acquired commercially, modified, or customized, that is used to increase, maintain, or improve functional capabilities of individuals with disabilities
- assistive technology service means any service that directly assists an individual with a disability in the selection, acquisition, or use of an assistive technology device

AT devices include a vast array of items such as wheelchairs, eyeglasses, hearing aids, Braille printers, electronic note-takers and organizers, augmentative communication systems, text-to-speech software, speech synthesizers, adaptive keyboards, alternative pointing devices, voice recognition software, aids for daily living, etc. AT services include evaluation/assessment services, selecting, fitting, customizing, and repairing devices, delivering training and technical assistance supports, and coordinating funding and other necessary interventions to support device acquisition and use.

The definition of AT devices and services has remained unchanged through numerous reauthorizations of the Assistive Technology Act and has been adopted in other statutes, such as the Individuals with Disabilities Education Act. The same definition has also been used in promulgating federal rules, such as the Electronic and Information Technology Accessibility Standards developed pursuant to Section 508 of the Rehabilitation Act (http://www.access-board.gov/sec508/standards.htm).

Historical Background

A precise history of AT is difficult to depict because of the diversity of devices and services included in the definition

of AT. The history of hearing aids can be traced back to Alexander Graham Bell's pioneering work on development of the telephone. Modern wheelchairs are patterned after the first folding, tubular steel wheelchair developed in the 1930s; while the first dedicated wheelchair (called an invalids chair) is thought to have been invented 4 centuries ago for Phillip II of Spain. Some devices were developed as AT and evolved into mainstream technology. For example, in 1948 the National Bureau of Standards developed specifications for a low-cost reliable talking-book machine for the blind that became the tape recorder. Conversely, some items developed as mainstream technology became AT such as voice recognition software originally developed for dictation that is used by individuals with motor disabilities who are unable to use a keyboard for computer access.

In recent years, technology use has become more commonplace for everyone. Similarly, AT use is now more frequent across the disability spectrum, addressing deficits in hearing, vision, motor, social, organizational, cognitive, speech, language, information processing, etc. Especially critical today is the use of information technology (IT), including telecommunications. IT use is now critical to success in education, employment, independent living, and community integration and AT is the interface that makes IT accessible (http://www.albritton.us/AThistory.html).

Rationale or Underlying Theory

Today, AT intervention is rooted in the disability rights movement and self-determination efforts of individuals with disabilities and their advocates. These initiatives helped to delineate the difference between the medical/rehabilitation and independent living models of intervention for individuals with disabilities. The medical model identifies a physical or mental impairment or lack of certain skills and treatment is delivered to remediate the deficit(s). With the medical model the locus of the problem lies with the individual and the goal is to "fix" the individual in some way through professional treatment. Under the independent living model the problem is defined as a lack of supports and accommodations, inaccessibility, and/or autonomy – the problem lies with the environment or the interaction with the environment, rather than within the person. In this model, AT plays a major role in addressing/ameliorating interaction difficulties, typically without overtly attempting to "fix" the disability itself (DeJong, 1979; Pelka, 1997).

Goals and Objectives

AT goals and objectives begin with a primary focus on ameliorating and/or compensating for a specific functional deficit. For example, electronic organizers can be used to address memory or information processing problems; text-to-speech software can be used to address reading deficits; augmentative communication systems can be used to address communication limitations, etc. In most cases, secondary goals are also targeted for outcomes including increasing academic success, fostering gainful employment, supporting independent community living, decreasing inappropriate behaviors, etc. With expanding legal mandates for integration of individuals with disabilities into all societal settings (Individuals with Disabilities Education Act, Section 504 of the Rehabilitation Act, and the Americans with Disabilities Act), AT goals and objectives continue to expand into new outcome areas.

Treatment Participants

AT is an appropriate intervention option to consider when functional limitations are encountered. Candidacy for AT is not limited by age, disability diagnosis, or severity/combination of deficits. There are no prerequisites for AT consideration and AT should not be relegated to a "last resort" intervention after all other interventions have been tried and abandoned.

AT can address a variety of human functions and is frequently grouped into areas such as vision, hearing, communication, daily living, computer access, learning/cognition, environmental adaptations, mobility/seating/positioning, vehicle modifications, and recreation/leisure. For almost all functional limitations, there is a range of AT intervention that can be considered as a treatment option (Cook & Hussey, 2001).

Treatment Procedures

Consideration for AT begins with assessment by a qualified team of individuals who are knowledgeable about the individual, their strengths and limitations and the range of potential AT options available to address the individual's functional needs. Best practice includes conducting structured device trials with various AT devices in the environment(s) in which the individual will be using the technology (e.g., home, school, work, community, etc.). This allows for comparative analysis of different device

features and functions to determine which best addresses the individual's needs.

Once AT has been acquired for an individual, training and support must be provided for the user, their family, and other critical individuals such as teachers, therapists, etc. More complex AT (computer-based software applications, assistive listening systems, augmentative communication devices, etc.) frequently requires significant investment of time and resources in initial programming, fitting, and set-up, in addition to training on device use (Galvin & Scherer, 1996).

Efficacy Information

Efficacy research on AT includes basic documentation of changes in functional skill areas (those the AT is intended to address) and potential secondary improvements in academic, social, behavioral, and other areas. Much of this efficacy is self-evident and is reported by the AT users themselves (Scherer, 1993).

No discussion of AT efficacy would be complete without addressing the issues of device abandonment and cost/benefit. For many types of AT, consumer discontinuing use of the device after acquisition has been a historic problem (Wessels, Dijcks, Soede, Gelderblom, & De Witte, 2003). Factors shown to mitigate abandonment include active consumer and family involvement in the selection and implementation of AT and the relative advantage of AT within the array of intervention options available (Alper & Raharinirina, 2006; Riemer-Reiss & Wacker, 2000).

As technology continues to improve, the problem of device abandonment steadily abates. Today the greater challenge is in justifying the cost/benefit of AT to secure funding from private insurance, local, state, federal, and other funding sources. Some types of AT, such as durable medical equipment, have a longer history of cost/benefit data including prevention of secondary disabilities making funding more readily available. Other types of AT, such as electronic organizers used to remediate/compensate for cognitive limitations, are relatively new with little cost/benefit data making funding difficult to secure (Gillette & DePompei, 2004; Hart, Buchhofer, & Vaccaro, 2004).

Outcome Measurement

The field of AT outcomes is quite young with most published work emerging in the 1990s. Two of the first focused articles on evaluating AT outcomes posed the questions "Are we ready to answer the tough questions?" and "Do we understand the commitment?" (DeRuyter, 1995; Trachtmann, 1994). In these articles, the authors postulated that stakeholders and AT providers must be prepared to show how their devices/services make a difference in the lives of individuals who receive an AT intervention.

Today, outcome measurement is occurring in all AT service areas (medicine, education, employment/vocational rehabilitation, and independent living) through a variety of interdisciplinary activities. Some are driven by policy needs, in particular, accountability for public dollars spent on AT (e.g., Medicare, Medicaid, special education, vocational rehabilitation, etc.) and justification for private insurance expenditures on AT. Others are driven by an overarching goal of quality service delivery and continuous program improvement.

The most direct outcome measure for AT intervention is demonstration of functional skills, independence, well-being, and quality of life. Administration of standardized assessments in the aided condition (using AT) can be useful in measuring outcomes in discreet skill areas (e.g., auditory discrimination, memory, expressive communication, etc.). In addition, some global assessment of AT outcomes can be helpful such as the Psychosocial Impact of Assistive Devices Scales (PIADS) (Jutai & Day, 2002), the Quebec User Evaluation of Satisfaction with Assistive Technology (QUEST) (Demers, Weiss-Lambrou, & Ska, 1996), and similar instruments. A number of online resources are also available with extensive data on AT outcome tools and research such as the Adaptive Technology Resource Center (http://atrc.utoronto.ca/index.php?option=com_content&task=view&id=175&Itemid=69), the Assistive Technology Outcomes Measurement System (ATOMS) Project (www.uwm.edu/CHS/atoms), the Consortium for Assistive Technology Outcomes Research (www.atoutcomes.org), and the Quality Indicators for Assistive Technology Services (www.qiat.org).

Qualifications of Treatment Providers

AT intervention can be provided by an extensive list of professionals, usually specialists in the type of the AT provided. For example, hearing aids are typically provided by audiologists or hearing instrument dispensers, eyeglasses by optometrists and ophthalmologists, etc. However, as the AT becomes less "prescriptive" in nature, the range of providers expands. Electronic note-takers and organizers can be provided by a whole host of providers, special educators, rehabilitation counselors, behavior therapists, occupational therapists, AT practitioners, etc.

The Rehabilitation Engineering and Assistive Technology Association of North America (RESNA) administers a certification program for Assistive Technology Professionals (ATPs) with associated standards of practice (http://www.resna.org/assets/240_standardsofpracticefinal1.pdf).

Cross References

- ▶ Americans with Disabilities Act of 1990
- ▶ Augmentative and Alternative Communication
- ▶ Independent Living Centers
- ▶ Individuals with Disabilities Education Act
- ▶ Section 504 of the Rehabilitation Act of 1973

References and Readings

Alper, S., & Raharinirina, S. (2006). Assistive technology for individuals with disabilities: A review and synthesis of literature. *Journal of Special Education Technology, 21*(2), 47–64.

Cook, A., & Hussey, S. (2001). *Assistive technologies: Principles and practice* (2nd ed.). California: Mosby Year-Book, Inc.

DeJong, G. (1979). Independent living: From social movement to analytic paradigm. *Archives of Physical Medicine and Rehabilitation, 60*, 435–446.

Demers, L., Weiss-Lambrou, R., & Ska, B. (1996). Development of the Quebec user evaluation of satisfaction with assistive technology (QUEST). *Assistive Technology, 8*, 3–13.

DeRuyter, F. (1995). Evaluating outcomes in assistive technology: Do we understand the commitment? *Assistive Technology, 7*(1), 3–16.

Galvin, J. C., & Scherer, M. J. (1996). *Evaluating, selecting and using appropriate assistive technology.* Gaithersburg, MD: Aspen Publishers, Inc.

Gillette, Y., & DePompei, R. (2004). The potential of electronic organizers as a tool in the cognitive rehabilitation of young people. *NeuroRehabilitation, 19*(3), 233–243.

Hart, T., Buchhofer, R., & Vaccaro, M. (2004). Portable electronic devices as memory and organizational aids after traumatic brain injury: A consumer survey study. *Journal of Head Trauma Rehabilitation, 19*(5), 351–365.

Jutai, J., & Day, H. (2002). Psychosocial impact of assistive devices scale (PIADS). *Technology and Disability, 14*(3), 107–111.

Pelka, F. (1997). ABC-CLIO companion to the disability rights movement. Santa Barbara, CA: ABC-CLIO, Inc.

Riemer-Reiss, M. L., & Wacker, R. R. (2000). Factors associated with assistive technology discontinuance among individuals with disabilities. *Journal of Rehabilitation, 66*(3), 44–50.

Scherer, M. J. (1993). *Living in the state of stuck: How technology impacts the lives of people with disabilities.* Cambridge, MA: Brookline Books.

Trachtmann, L. (1994). Outcome measures: Are we ready to answer the tough questions? *Assistive Technology, 6*, 91–92.

Wessels, R., Dijcks, B., Soede, M., Gelderblom, G. J., & De Witte, L. (2003). Non-use of provided assistive technology devices, a literature overview. *Technology and Disability, 15*(4), 231–238.

Association Areas

Maryellen Romero
Tulane University Health Sciences Center
New Orleans, LA, USA

Synonyms

Association cortex

Definition

It is recognized that the brain is neither holistic nor rigidly localized with respect to cognitive functions. However, higher-order cognitive capabilities depend on specialized regions within the brain that process, *link* or *integrate* elementary or new, as well as stored information into increasingly complex wholes. Such regions are termed *association areas* and are thought to be the neuroanatomical substrate for such higher functions as memory, emotion, perception, language, spatial and problem-solving skills, as well as the planning and execution of behavioral responses.

Three major association areas are recognized:

(1) *Frontal association cortices*, as the name implies, are located in the more anterior aspects of the frontal lobes and include dorsolateral, orbitofrontal, and premotor areas. While various feedback loops are likely involved including those from the posterior and limbic association areas, conceptually, the initial decisions and planning regarding executive or motor responses to a given situation are generally thought to flow from the prefrontal (most anterior) cortices to the premotor cortex that organizes, coordinates, and sequences the actions essential to the successful completion of the response. From there, commands are believed to be forwarded to the primary motor area (precentral gyrus) that then actually executes the motor response. The orbitofrontal cortex is shared with *limbic association cortex* (see below) that underscores the importance of the integration of emotion, memory, and behavior. Lesions to prefrontal association cortices often affect self-monitoring, planning, and executive functions, including behavioral inhibition.

(2) The *limbic association cortex* includes ventromedial frontal lobe, medial parietal lobe, temporal pole, and cingulate and parahippocampal areas. Integration of information from the hypothalamus, other limbic or paralimbic structures, and secondary sensory

association areas is received and projected to other areas of the cortex, including the prefrontal cortex discussed above, again permitting the integration of emotions, cognition and perceptions, and memory. Dysfunction is often expressed as emotional/behavioral dysregulation and memory impairment.

(3) The locations of the *parieto-temporal-occipital association cortices* are described by their names and are typically divided into secondary and tertiary areas. The former are *unimodal* in nature (respond more or less exclusively to a single sensory modality) and lie adjacent to their respective primary cortical sensory projection areas. They are thought to be responsible for further integrating and processing sensory input into potentially meaningful percepts. Hence, lesions of these secondary association areas will commonly result in modality-specific perceptual disturbances or agnosias. By contrast, the tertiary or heteromodal association areas receive input from all sensory modalities. Because of this and their central location, they are sometimes referred to as the PTO (parietal-temporal-occipital) cortex. Because of their crossed or multimodal inputs, these latter areas, which are very highly developed in man, are thought to represent the foundations for higher-order conceptual and intellectual abilities, including abstraction, language, and visual-spatial and mathematical problem solving, any or all of which can be adversely affected by lesions to these areas.

Cross References

- ▶ Association Pathways
- ▶ Heteromodal Cortex
- ▶ Secondary Cortex
- ▶ Unimodal Cortex

References and Readings

Kupermann, I. (1991). Localization of higher cognitive and affective functions: The Association cortices. In E. R. Kandel, J. H. Schwartz, & T. M. Jessel (Eds.), *Principles of neural science* (3rd ed., pp. 823–838). East Norwalk, CT: Appleton & Lange.

Mendoza, J. E., & Foundas, A. F. (2008). *Clinical neuroanatomy: a behavioral approach.* New York: Springer.

Mesulam, M.-M. (2000). *Principles of behavioral and cognitive neurology.* New York: Oxford University Press.

Pandya, D. N., & Seltzer, B. (1982). Association areas of the cerebral cortex. *Trends in Neurosciences, 5*, 385–390.

Pandya, D. N., & Yeterian, E. H. (2003). Cerebral cortex: architecture and connections. In *Encyclopedia of the neurological sciences* (pp. 594–604). USA: Elsevier Science.

Association Cortex

- ▶ Association Areas
- ▶ Homotypic Cortex

Association for Postdoctoral Programs in Clinical Neuropsychology (APPCN)

Jacobus Donders
Mary Free Bed Rehabilitation Hospital
Grand Rapids, MI, USA

Address (and URL)

APPCN
P.O. Box 69037, Pleasant Ridge, MI 48069
www.appcn.org

Membership

The Association of Postdoctoral Programs in Clinical Neuropsychology (APPCN) is an organization of approximately 50 member programs that offer comprehensive, integrated postdoctoral residencies.

Major Areas or Mission Statement

The mission of APPCN is to foster the provision of advanced specialty education and training to promote the competencies that are necessary for practice in the specialty of clinical neuropsychology (Boake, Yeates, & Donders, 2002).

Landmark Contributions

Formally incorporated in 1992, APPCN contributed to the Houston Conference, which established that completion of two years of formal postdoctoral residency training is a uniform requirement for entry into the professional practice of clinical neuropsychology (Hannay, Bieliauskas, Crosson, Hammeke, Hamsher, & Koffler, 1998). In more recent years, APPCN has been a key representative to inter-organizational groups like the Clinical Neuropsychology Synarchy, and the Inter-Organizational Summit on Education and Training.

Major Activities

APPCN is not an accrediting organization, a role which is left to the Commission on Accreditation of the American Psychological Association (APA). However, a growing number of the APPCN members are currently accredited by APA as a postdoctoral specialty program in clinical neuropsychology. Details about individual APPCN member programs, including focus on adult *v.* pediatric neuropsychology, accreditation status, primary diagnostic groups served, and other characteristics, are available on the APPCN website.

The major standards for program membership in APPCN include the following: (1) the duration of training is for a minimum of 2 years, or for an equivalent time on no less than a half-time basis, at a fixed site with regular, on-site supervision; (2) the program includes an organized and integrated combination of at least 50% clinical service, at least 10% didactic/educational activities, and at least 10% research or other scholarly activities; and (3) the program director is board-certified in Clinical Neuropsychology through the American Board of Professional Psychology (ABBP–CN). One of the major accomplishments of APPCN is the development and implementation, in collaboration with National Matching Services, of a computerized system for matching of applicants for postdoctoral residency training in clinical neuropsychology to programs that offer such training. This electronic system, instituted in 2001, is the most fair to applicants, and the most efficient for programs, with all APPCN programs that have open positions in any given year taking part in this electronic match. Postdoctoral programs that are not members of APPCN are also allowed to participate as long as they meet APPCN standards #1 and #2 above, and if they agree to respect all other conditions of the match, including prohibition of pre-emptive offers, and adherence to the binding nature of the match outcomes. Further details are available at http://www.natmatch.com/appcnmat/.

APPCN is dedicated to education of aspiring neuropsychologists about what it takes to become a competitive candidate for postdoctoral residency training. For this purpose, several educational seminars are offered on a regular basis, some in collaboration with other organizations, such as Division 40 (► Clinical Neuropsychology) of the APA and the Association of Neuropsychology Students in Training (ANST). Over the past several years, APPCN program directors have also consistently provided a "special topic presentation" about postdoctoral residency training at the annual meeting of the National Academy of Neuropsychology (NAN).

APPCN has also strived to make the process of education and evaluation as part of postdoctoral residency training in clinical neuropsychology more standardized. For this purpose, a 50-item written examination has been developed by APPCN to be used with residents who are near completion of their first postdoctoral training year, to evaluate their knowledge of major content areas like functional neuroanatomy, adult and pediatric syndromes, psychometrics, etc. This exam is not intended to give residents a "grade"; rather, it is to be used as an educational tool, to identify relative strengths and weaknesses in the residents' working knowledge base, so that the relative lacunae can be addressed during the subsequent training year. During that second year, APPCN member programs also have the opportunity to start preparing residents for board certification, by means of ethics vignettes and mock oral "fact finding" case materials that are very similar in format and level of difficulty to those used by ABPP–CN.

Finally, the most recent initiative of APPCN has involved advocacy with the United States Department of Veterans Affairs for the development of more postdoctoral training programs in clinical neuropsychology, primarily because of the high number of traumatic brain injuries among US service personnel involved in the combat in Iraq. When more than a dozen of these training programs became available in the Fall of 2007, APPCN contacted the programs, provided mentoring as needed, and waived their first-time participation fee in the electronic match. APPCN has also continued to offer assistance to new programs as they seek specialty accreditation through the APA. APPCN will continue to embrace additional organized and integrated postdoctoral training programs in clinical neuropsychology.

Cross References

► American Board of Clinical Neuropsychology (ABCN)
► American Board of Professional Psychology (ABPP)
► American Psychological Association (APA)

References and Readings

Boake, C., Yeates, K. O., & Donders, J. (2002). Association of Postdoctoral Programs in Clinical Neuropsychology: update and new directions. *The Clinical Neuropsychologist, 16*, 1–6.

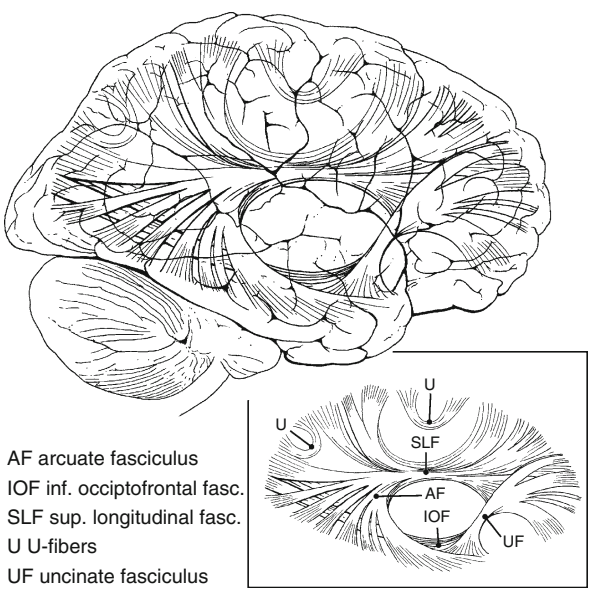
Hannay, H. J., Bieliauskas, L., Crosson, B. A., Hammeke, T. A., Hamsher, K., & Koffler, S. P. (1998). The Houston Conference on specialty education and training in clinical neuropsychology. *Archives of Clinical Neuropsychology, 13*, 157–250.

Association Pathways

John E. Mendoza
Tulane University Medical Center
New Orleans, LA, USA

Definition

Fiber pathways that lie within the cerebrum that connect one part of the cerebral cortex with another *within the same hemisphere*. Association pathways are thus contrasted with *commissures* that generally interconnect homologous areas of the two halves of the brain, and *projection pathways* that are fiber tracts interconnecting cortical and subcortical structures. They may be very long (typically termed "*fasciculi*") or very short. The latter may consist of "U"-shaped fibers connecting one gyrus with an adjacent one or horizontal connections within a gyrus itself (e.g., *bands of Baillarger*). These various pathways allow different areas of the brain to communicate with one another. Some of the major association pathways are shown in Fig. 1.



Association Pathways. Figure 1

Cross References

- ▶ Commissures, Cerebral
- ▶ Projection Pathways

Associational Fibers

Melissa J. McGinn
Virginia Commonwealth University School of Medicine
Richmond, VA, USA

Synonyms

Arcuate fibers

Definition

Associational fibers are white matter fibers that connect various cortical regions within the same cerebral hemisphere. Being the most prevalent type of neuronal tracts found in the cortex, associational fibers permit bidirectional communication between different cortical areas, allowing the cortex to function as a coordinated whole. Associational fibers arise from cortical layer II/III pyramidal neurons and can be classified as either short associational fibers, which connect adjacent gyri within the same lobe, or long associational fibers, interconnecting more distant regions located in different lobes. The major long associational fibers tracts in the brain include the superior longitudinal fasciculus, arcuate fasciculus, uncinate fasciculus, and cingulum.

Cross References

- ▶ Arcuate Fasciculus
- ▶ Association Pathways
- ▶ Cerebral Cortex
- ▶ Cingulum
- ▶ Superior Longitudinal Fasciculus
- ▶ White Matter

Associative Aphasia

- ▶ Conduction Aphasia

Associative Memory

► Paired-Associate Learning

Associative Visual Agnosia

John E. Mendoza
Tulane University Medical Center
New Orleans, LA, USA

Definition

Regardless of modality, an associative agnosia implies that although perception is intact, the particular stimulus has no meaning ("associative" value) to the individual. The stimulus can neither be named nor linked to other personal or sensory experiences. Hence, *associative visual agnosia* refers to the inability to identify or categorize a visually presented stimulus despite adequate visual perception.

Current Knowledge

Individuals with this disorder should be able to match the visual stimulus to a sample and copy or draw what is seen, thus distinguishing *associative* from *apperceptive* visual agnosia. In the latter condition, visual object recognition is also impaired, but primarily as a result of a disturbance of perception. In addition to having difficulty naming visually presented objects, a patient suffering from associative visual agnosia would likely be unable to describe their use or purpose, or indicate to which category of objects they may belong. However, in pure visual associative agnosia, identification should be possible if the patient were allowed to hold the object(s) (tactile recognition).

An associative visual agnosia may differentially affect recognition of objects, words, colors, or faces. In visual agnosia for words (also known as *pure alexia* or *pure word blindness*), visual word recognition is impaired. But the individual may be able to "read" if allowed to trace the letters with a finger, thus permitting tactile or kinesthetic recognition of individual letters. In associative color agnosia, the individual may be able to match colors, but neither name them nor identify objects with which they might be associated (such as cherries or apples for the color red). Facial agnosia (*prosopagnosia*) is a bit complex in that one may differentiate the inability to make discriminations among unfamiliar faces (thought to be more of a perceptual problem) from an inability to recognize familiar faces (generally considered an associative problem). Thus, in the latter instance, while the patient might be able to match the face or picture of a familiar person to one within an array of pictures, he would not be able to identify the face or the picture as that of his wife, his daughter, or other famous person with whom he might be familiar.

While the specific lesions causing specific associative visual agnosias are not well defined, they are generally thought to represent a disconnection type syndrome involving the temporal, occipital, and/or parietal regions of the left hemisphere with some disruption of fiber pathways or connections between the unimodal (visual) and heteromodal cortices.

Cross References

► Alexia
► Apperceptive Visual Agnosia
► Color Agnosia
► Color Anomia
► Disconnection Syndrome
► Heteromodal Cortex
► Prosopagnosia
► Unimodal Cortex

References and Readings

Bauer, R. M., & Demery, J. A. (2003). Agnosia. In K. Heilman & E. Valenstein (Eds.), *Clinical neuropsychology*, (4th ed., pp. 236–295). New York: Oxford University Press.

DeRenzi, E., & Spinnler, H. (1966). Visual recognition in patients with unilateral cerebral disease. *Journal of Nervous and Mental Disease, 142*, 513–525.

DeRenzi, E., Scotti, G., & Spinnler, H. (1969). Perceptual and associative disorders of visual recognition. Relationship to the side of the cerebral lesion. *Neurology, 19*, 634–642.

Astasia-Abasia

Douglas I. Katz
Braintree Rehabilitation Hospital
Braintree, MA, USA
Boston University School of Medicine
Boston, MA, USA

Synonyms

Blocq's disease

Definition

An inability to stand and walk in a normal and coordinated manner. Astasia means inability to maintain standing and abasia refers to impaired coordination of gait. The term is usually applied to unusual, often bizarre patterns of gait and stance that appear to have no neuropathophysiologic basis. Conversion disorder is frequently the underlying cause. Patients may sway in a staggering, unstable manner, often catching themselves before falling. This syndrome is also referred to as Blocq's disease.

Cross References

- ▶ Abasia
- ▶ Gait Disorders
- ▶ Psychogenic Disorder

References and Readings

Morris, J.G., Mark de Moore, G., Herberstein, M. (2006). Psychogenic Gait: An example of Deceptive Signaling. In: C.R. Cloninger, & M. Hallett (Eds.), *Psychogenic movement disorders: neurology and neuropsychiatry.* Philadelphia: Lippincott Williams & Wilkins.

Okun, M.S., & Koehler, P.J. (2007). Paul Blocq and (psychogenic) astasia abasia. *Movement Disorder, 22*, 1373–1378.

Astereognosis

Melissa Amick
VA Boston Healthcare System
Boston, MA, USA

Synonyms

Object agnosia; Tactile agnosia

Short Description or Definition

Astereognosis is defined as the inability to identify objects through touch without visual input.

Categorization

Astereognosis has been subdivided into primary and secondary recognition deficits. Primary recognition deficits, also called morphognosia, reflect impairments in recognizing the physical features of the object (e.g., weight or texture). Secondary recognition deficits reflect a specific impairment in object recognition with spared primary recognition (for review see De Renzi, 1982).

Epidemiology

Astereognosis can be common after stroke with one report indicating that up to 90% of patients demonstrate astereognosis (Connell, Lincoln, & Radford, 2008). Damage to the cortical regions important for haptic input integration can cause astereognosis. This disorder, therefore, is common and can occur in the presence of many neurological disorders including brain (e.g., Knecht, Kunesch, & Schnitzler, 1996), or spinal cord tumors (Lesoin, Rousseaux, Martin, Petit, & Jomin, 1986), and traumatic brain injury (Hom & Reitan, 1982).

Natural History, Prognostic Factors, Outcomes

Connell et al. (2008) followed 58 stroke survivors over a period of 6 months (baseline, 2, 4, and 6 months) and at each time period participants completed the Nottingham Sensory Assessment (see below). Stereognosis significantly improved during the observation period, with the greatest changes occurring within the first 4 months (baseline relative to 4-month performance). Regression analyses indicated that stroke severity and motor performance of the upper limb were predictive of the presence of impaired stereognosis at the baseline assessment.

Neuropsychology and Psychology of Astereognosis

Astereognosis can occur after injury to either the left or right hemisphere. A specialized role for the right hemisphere in stereognosis has been proposed, however this finding has not been consistently observed (for review see Zaidel, 1998 and De Renzi, 1982). Initially astereognosis was thought to be due to damage to the primary somatosensory cortex; however, posterior parietal lesions have also been associated with this impairment (Knecht et al., 1996).

Evaluation

Astereognosis is often examined with non-standardized methods. In the typical neurological examination, astereognosis is assessed by asking the patient to identify an object through touch without visual input. Common objects used for identification can include coins, keys, paper clips, or screws. For patients with hemiparesis, the examiner may manipulate the patient's hand to assist in object identification. Standardized assessments of astereognosis do exist. The Tactile Form Recognition Test from the Halstead–Reitan Neuropsychological Test Battery (Reitan & Wolfson, 1993) requires participants to manipulate a flat plastic shape with one hand obscured from vision, while the other hand points to the same shape mounted on a board with three other potential distractors. In the Benton Stereognosis Test (Benton, 1969), 10 cards with fine grain, sandpaper figures pasted on top are felt by the participant out of view. The participant has 30 s to explore the card and 45 s to respond. Responses are made by pointing to the corresponding line drawing mounted in full view of the respondent. The Nottingham Sensory Assessment includes an assessment of astereognosis (Gaubert & Mockett, 2000). In this task the participant is blindfolded and asked to name the object placed in their hand. Presentation of the objects is time limited. Objects to be identified include coins, comb, sponge, pencil, scissors, a cup, and a glass. Responses are scored on a scale of 0-2 depending upon the quality of the verbal response.

Treatment

Astereognosis has been observed to spontaneously improve over time (Connell et al., 2008). One study has found that stereognosis improves following systematic hand retraining in stroke survivors who were at least 2 years post stroke. Yekutiel & Guttman (1993) had 25 participants receive three, 45-min hand-retraining sessions weekly for a period of 6 weeks. The therapy was customized for each participant but everyone received education to improve insight about their impairment and exercises were intended to be appropriately challenging, designed to promote self-efficacy, used vision and the less affected hand to aid sensory function, and provided frequent breaks and novel stimuli. Unlike the control group, the patient group showed a statistically significant improvement on the stereognosis assessment. These findings suggest that functional gains through therapy can occur in the years following stroke.

Cross References

- ▶ Ahylognosia
- ▶ Amorphognosis
- ▶ Parietal Lobe
- ▶ Somatosensory Cortex
- ▶ Stereognosis
- ▶ Tactile Agnosia
- ▶ Tactile Form Recognition
- ▶ Tactual Performance Test

References and Readings

Benton, A. L. (1969). *Stereognosis test; Manual of instructions.* Neuropsychology Laboratory, Department of Psychology, University of Victoria.

De Renzi, E. (1982). *Disorders of space exploration and cognition.* New York: Wiley.

Connell, L. A., Lincoln, N. B., & Radford, K. A. (2008). Somatosensory impairment after stroke: Frequency of different deficits and their recovery. *Clinical Rehabilitation, 22*, 758–767.

Gaubert, C. S., & Mockett, S. P. (2000). Inter-rater reliability of the Nottingham method of stereognosis assessment. *Clinical Rehabilitation 14*(2), 153–159.

Hom, J., & Reitan, R. M. (1982). Effect of lateralized cerebral damage upon contralateral and ipsilateral sensorimotor performances. *Journal of Clinical Neuropsychology 4*(3), 249–268.

Knecht, S., Kunesch, E., & Schnitzler, A. (1996). Parallel and serial processing of haptic information in man: Effects of parietal lesions on sensorimotor hand function. *Neuropsychologia, 34*, 669–687.

Lesoin, F., Rousseaux, M., Martin, H. J., Petit, H., & Jomin, M. J. (1986). Astereognosis and amyotrophy of the hand with neurinoma of the second cervical nerve root. *Neurology, 233*, 57–58.

Lincoln, N. B., Crow, J. L., Jackson, J. M., Waters, G. R., Adams, S. A., & Hodgson, P. (1991). The unreliability of sensory assessment. *Clinical Rehabilitation, 5*, 273–282.

Reitan, R. M., & Wolfson, D. (1993). *The Hasltead-Reitan neuropsychological test battery: Theory and clinical interpretation.* Tucson, AZ: Neuropsychology Press.

Yekutiel, M., & Guttman, E. J. (1993). A controlled trial of the retraining of the sensory function of the hand in stroke patients. *Journal of Neurology, Neurosurgery, and Psychiatry, 56*, 241–244.

Zaidel, E. (1998). Stereognosis in the chronic split brain: Hemispheric differences, ipsilateral control and sensory integration across the midline. *Neuropsychologia, 36*, 1033–1047.

Asthenia

- ▶ Adynamia

Astrocytoma

Robert Rider
Drexel University
Philadelphia, PA, USA

Definition

Astrocytomas are the most frequently diagnosed tumors, are usually slow-growing, and may develop a cystic component. Arising in astrocytic cells anywhere throughout the central nervous system, they may occur in any age group, but are most frequently diagnosed in middle-aged males. The highest incidence of brain stem astrocytomas is found in children. Grading systems focus on the degree of resemblance to normal astrocytes, with higher grades associated with more rapid growth and greater likelihood of metastasis. Three common types of astrocytomas are: low-grade astrocytomas, which are often benign and tend to occur in the cerebellum (especially in children) but may also occur in the cerebrum in adults; anaplastic astrocytomas, which are malignant; glioblastoma multiforme, which are thought to arise from astrocytomas and are the most malignant. The specific symptoms associated with astrocytomas depend on the region of the CNS that is affected.

Cross References

- ▶ Fibrillary Astrocytoma
- ▶ Oligoastrocytoma
- ▶ Pilocytic Astrocytoma
- ▶ Xanthroastrocytoma

References and Readings

Louis, D., Ohgaki, H., Cavenee, W., & Wiestler, O. (2007). *WHO classification of tumours of the central nervous system* (4th ed.). World Health Organization.

Astrocytosis

- ▶ Gliosis

Asymmetry

Maryellen Romero
Tulane University Health Sciences Center
New Orleans, LA, USA

Synonyms

Hemispheric specialization

Definition

Asymmetry is the discordance between the right and left sides of the brain in respect to structure and/or function.

Current Knowledge

Although not initially linked to brain asymmetry, the first behavioral asymmetry that was likely noted was the superiority of motor skills exhibited by one hand, most commonly the right, over the other. The next real breakthrough with regard to asymmetry is generally thought to have occurred in the nineteenth century with the discovery that acquired language deficits (aphasia) were typically associated with lesions of the left hemisphere. Since then, other asymmetries, both functional and structural, have been identified with regard to the two cerebral hemispheres.

Structural Asymmetries

Structural asymmetries of the brain were first noted around the beginning of the twentieth century, but it was not until the late 1960s that these were first strongly correlated with functional differences between the hemispheres. In a study of 100 postmortem brains, Geschwind and Levitsky (1968) noticed that the planum temporale, located in the temporal operculum, was larger in 65% of the brains studied as compared with only 11% in which the right was larger. They concluded that this difference was likely related to the left hemisphere's association with the production of language in most individuals. Subsequent studies have demonstrated that this asymmetry can be shown to present even prior to birth, reinforcing the genetic predisposition to left-hemispheric dominance for language.

Since the advent of more sophisticated imaging techniques that allow for large-scale in vivo studies of the brain, other structural differences have been documented. The inferior frontal gyrus in the left hemisphere,

corresponding to Broca's area, has been shown to be more highly developed on the left side for most individuals. The gyri and sulci associated with the motor strip (Brodmann's area 4) are more prominent in the left hemisphere of right-handers. Fairly consistent differences in the lateral fissure have been found, with the posterior ascending ramus of this sulcus making a more abrupt upward turn in the right hemisphere as compared with the left. This would suggest likely differences in the distribution of the supramarginal and angular gyri in the inferior parietal lobules of the two hemispheres. Even on a more microlevel, differences in the size and organization of individual cells or cell columns have been identified in the two hemispheres.

It is reasonable to speculate that some structural differences likely relate to functional differences between the two hemispheres, particularly behaviors such as language and handedness. However, functional asymmetries have either been demonstrated or are suspected well beyond those which can currently be explained by structural differences. The following represent a sampling of some of the functional differences that have been observed.

Functional Asymmetries

It has been well established that language expression and comprehension are normally mediated primarily, if not exclusively, by the left hemisphere, even among left-handers. However, the right hemisphere has also been shown to play an important role in communication. Verbal communication is not just about using words in sentences or paragraphs; emotional tone or nuances of the speaker often convey important meaning. In some communications, such as those with a sarcastic intent, the real message is carried by the tone rather than by the words, which, if interpreted literally, might actually convey a very different message. The ability to use as well as interpret these emotional components of speech, known as prosody, is primarily mediated by the right hemisphere; damage to this side of the brain may produce various forms of *aprosodia*. With regard to using or interpreting the language of others, the right hemisphere is also believed to play an important role in identifying the central theme or point of the discourse of others and being able to stay on point when speaking or writing. It appears to be important in appreciating verbal (as well as nonverbal) humor and in detecting meaning from the differential inflections given to individual words in speech.

In addition to words, numbers also have their own symbolic meaning. Hence, as might be expected, the ability to use numbers is thought to be a function normally carried out by the left hemisphere, the disturbance of which following a lesion to the left hemisphere may be defined as *acalculia* (*dyscalculia*). However, most complex arithmetical operations also have a spatial component. For example, precise alignment of rows and columns of numbers is critical in mathematical operations, whether completed mentally or on paper. These spatial relations can be disturbed following right-hemispheric lesions, resulting in what has been termed *spatial dyscalculia*.

It is known that the hemisphere contralateral to the hand being used to carry out some motor tasks is immediately responsible for the execution of these movements. However, the motor programs or engrams for overlearned motor skills are believed to reside in the left hemisphere, certainly for the vast majority of right-handers, as well as many left-handers. Thus, any lesion that either directly interferes with those engrams or the ability of that information to reach the premotor cortex of either hemisphere can result in an impaired performance, especially if the individual is asked to demonstrate the action in the absence of the actual object. This latter condition is referred to as an *ideomotor apraxia*.

Perceptual abilities appear to be differentially distributed between the two hemispheres. It has already been noted that the left hemisphere is normally the leading hemisphere in interpreting verbal (semantic) information, while the right appears to be better adapted to processing certain types of emotional cues. It seems that the right hemisphere is also the more proficient in processing many types of visual-spatial or visual-gestalt information. Thus, the right hemisphere has been found to be generally superior in carrying out certain constructional tasks, making judgments regarding the orientation of lines in space, in making discriminations regarding *unfamiliar* faces, and in recognizing familiar tunes or environmental sounds. On the other hand, the left hemisphere appears to be the leading hemisphere when it comes to perception of certain aspects of one's own body. Problems of right–left orientation and difficulty recognizing individual fingers of one's hands (*finger agnosia*) are typically associated with lesions of the left inferior parietal lobule. Functional MRI studies have demonstrated consistent activation of right hemisphere structures during tests of *vigilance* and *directed* attention. However, *divided* attention tasks have been shown to selectively activate left prefrontal cortex. PET imaging studies have demonstrated increased blood flow in the right prefrontal and superior parietal cortex during tasks requiring *sustained* attention, regardless of the type of stimulus (verbal, visual, etc.) or where it is introduced (left vs. right).

Differences between the two hemispheres have also been demonstrated in learning and memory tasks and other cognitive domains. Of the two, the left hemisphere has been more strongly associated with learning verbal information. While many studies have shown that the right hemisphere is perhaps better at learning certain "nonverbal" or "visual-spatial" type information, the findings are generally less robust compared to the left hemisphere and verbal memory. One frequent explanation for this is that when faced with any memory task, humans have a natural tendency to try to verbally encode the stimulus, thus bringing the left hemisphere into play.

It has also been suggested that the two hemispheres play different roles in attention. The much more frequent association of disorders such as *unilateral neglect* and *anosognosia* with right hemispheric lesions have led to the hypothesis that while, as might be expected, the left hemisphere attends to the right side of space (both personal and extrapersonal), the right hemisphere focuses on both right and left space.

Finally, the association of the right hemisphere and emotional expression would appear to go beyond the affective intonations of speech as described above. It is commonly observed, both by health-care professionals as well as the spouses and other family members of persons with brain injury that individuals with right hemisphere lesions often behave differently than those with left-sided lesions. While the latter seem to remain emotionally attached, even if that emotion is often one of anger, frustration, or sadness, right hemispherically damaged patients are more likely to be described as apathetic, indifferent, emotionally flat, both in terms of their verbal and facial expressions and their interpersonal relationships.

Cross References

- ▶ Anosognosia
- ▶ Directed Attention
- ▶ Dominance, Cerebral
- ▶ Ideomotor Apraxia
- ▶ Language
- ▶ Unilateral Neglect
- ▶ Wada Test

References and Readings

Corballis, P. M. (2003). Visuospatial processing and the right-hemisphere interpreter. *Brain and Cognition, 53*, 171–176.

Davidson, R. J. (1992). Emotion and affective style: Hemispheric substrates. *Psychological Science, 3*, 39–43.

Davidson, R. J., & Hugdahl, K. (Eds.). (1996). *Brain asymmetry.* Cambridge, MA: Bradford Books.

Gazzaniga, M. S. (2000). *The new cognitive neurosciences.* Boston: MIT Press.

Gazzaniga, M. S., Ivry, R. B., & Mangun, G. R. (2002). *Cognitive neuroscience: The biology of the mind.* New York: W.W. Norton & Company.

Geschwind, N., & Levitsky, W. (1968). Left-right asymmetry in temporal speech region. *Science, 161*, 186–187.

Good, C. D., Johnsrude, I., Ashburner, J., Henson, R. N. A., Friston, K. J., & Frackowiak, R. S. J. (2001). Cerebral asymmetry and the effects of sex and handedness on brain structure: A voxel-based morphometric analysis of 465 normal adult human brains. *Neuroimage, 14*, 685–700.

Kinsbourne, M. (Ed.). (1978). *Asymmetrical function of the brain.* New York: Cambridge University Press.

Mendoza, J. E., & Foundas, A. L. (2008). *Clinical neuroanatomy: A neurobehavioral approach.* New York: Springer.

Ross, E. (2000). Affective prosody and the aprosodias. In M. Mesulam (Ed.), *Principles of behavioral and cognitive neurology.* New York: Oxford University Press.

Walsh, K. (1994). *Neuropsychology: A clinical approach.* New York: Churchill Livingstone.

Ataxia

Anna DePold Hohler[1], Marcus Ponce de Leon[2]
[1]Boston University Medical Center
Boston, MA, USA
[2]William Beaumont Army Medical Center
El Paso, TX, USA

Synonyms

Clumsiness

Definition

Ataxia describes a lack of coordination while performing voluntary movements. It is associated with damage to the cerebellum or its afferent or efferent pathways. It may appear as clumsiness, inaccuracy, or instability. It may affect any part of the body. When ataxia affects the arms and hands, it may cause tremor due to overcorrection of inaccurate movements. It may produce dysmetria or an inability to gauge distance correctly. It may cause past-pointing when an attempted reach overshoots the target. It may also cause dysdiadochokinesia or poor performance of regular, repeated movements. Cerebellar injury may contribute to nystagmus, hyper and hypometric saccades, scanning speech, titubation, and difficulties with gait and balance.

Current Knowledge

There are a number of different types of damage to the cerebellum. These range from fixed damage (e.g., stroke, trauma, hypoxic injury) to chemical and metabolic, and degenerative. Cerebellar injury related to vitamin deficiency (e.g., E, B12, and thiamine) may be reversible and should be identified and treated. Metabolic diseases such as Hartnup's, Refsum's, and the mitochondrial disorders are less treatable. A deficiency of Coenzyme Q10 has been described in patients with cerebellar ataxia, usually with childhood onset and often associated with seizures. The symptoms may respond to Coenzyme Q10 treatment. There are a number of hereditary cerebellar ataxias. Most of the autosomal recessive and autosomal dominant ataxias have no treatments. An exception is vitamin E deficiency, which is an autosomal recessive disorder. It is due to a mutation in the gene coding for the alpha tocopherol transfer protein located on the long arm of chromosome 8. It is characterized by childhood onset of ataxia, dysarthria, areflexia, proprioceptive deficits, extensor plantar responses, and skeletal deformities.

The episodic ataxias, which are inherited in an autosomal dominant fashion, may also have some symptomatic treatment regimens. Episodic Ataxia Type 1 is related to a chromosome 12 mutation in the potassium channel gene. Clinically, the disease manifests with episodes of ataxia lasting seconds to minutes. Patients may also suffer from myokymia during and between attacks of ataxia. The ataxia may be induced by startle or exercise. Episodic Ataxia Type 2 is related to a defect located on chromosome 19. It is due to a mutation in a voltage-dependent calcium channel. Clinically, patients present with nystagmus. Attacks last minutes to hours and may be induced by a change in posture. Patients may also complain of vertigo. As the disease progresses, ataxia becomes permanent.

Epidemiology

Ataxia is a common sign associated with inherited, acquired, toxic, and traumatic events.

Natural History

The genetic syndromes that are associated with ataxia tend to be progressive. Individuals with static insults such as strokes or trauma may show improvement in function over time.

Neuropsychology

Cerebellar syndromes may be associated with cognitive slowing.

Evaluation includes a detailed neurological examination, magnetic resonance imaging, and laboratory investigation for reversible or genetic causes.

Treatment depends on the underlying insult.

Cross References

- ▶ Cerebellum
- ▶ Dysdiadochokinesia

References and Readings

Gilman, S. (2004). Clinical features and treatment of cerebellar disorders. In R. L. Watts & W. C. Koller (Eds.), *Movement disorders* (2nd ed., pp. 723–736). New York: McGraw-Hill.

Atheromatous Plaque

▶ Atherosclerosis

Atherosclerosis

Elliot J. Roth
Northwestern University
Chicago, IL, USA

Synonyms

Arteriosclerotic vascular disease or ASVD; Atheromatous plaque; Hardening of the arteries

Definition

Atherosclerosis is the progressive pathological process of buildup of plaque inside the blood vessels, resulting in blockage of blood flow through the vessels.

Current Knowledge

The plaque that causes atherosclerosis is comprised of fatty substances, cholesterol, cells, calcium, and fibrin, a

stringy material found normally in the blood to help clot the blood. The plaque formation process stimulates the cells of the artery wall to produce substances that then accumulate in the vessel wall. Fat builds up within these cells and around them, and they form connective tissue and calcium. The artery wall thickens, the artery's diameter is reduced, and blood flow and oxygen delivery are decreased. Plaques can rupture or crack open, causing the sudden formation of a blood clot (thrombosis). Atherosclerosis can cause angina or myocardial infarction if it blocks the blood flow in the coronary arteries that supply the heart muscle, stroke if it blocks the carotid arteries that supply the brain, kidney disease if it blocks the renal arteries or gangrene possibly leading to amputation if it blocks the peripheral arteries that supply the limbs.

Atherosclerosis may be asymptomatic for many years. Risk factors for this disease have been well studied. It is thought that atherosclerosis is caused by a response to damage to the endothelium from high cholesterol, high blood pressure, and cigarette smoking. A person who has all three of these risk factors is eight times more likely to develop atherosclerosis than is a person who has none. Physical inactivity, diabetes, and obesity are also risk factors for atherosclerosis. Heredity, advancing age, and racial background are less-significant risk factors.

Treatment options include lifestyle changes, use of lipid-lowering and other drugs, angioplasty, and various surgical procedures, depending on the location of the plaque. Many lifestyle changes that prevent disease progression also prevent the onset of the disease; these include a low-fat, low-cholesterol diet, weight loss, exercise, blood pressure control, diabetes management, and smoking cessation.

Cross References

- ▶ Angioplasty
- ▶ Anticoagulation
- ▶ Antiplatelet Therapy
- ▶ Atherosclerosis
- ▶ Cerebrovascular Disease
- ▶ Cholesterol
- ▶ Coronary Disease
- ▶ Ischemic Stroke
- ▶ Myocardial Infarction
- ▶ Peripheral Vascular Disease
- ▶ Stent
- ▶ Thrombolysis
- ▶ Thrombosis

References and Readings

Stary, H. C., Chandler, A. B., Dinsmore, R. E., Fuster, V., Glagov, S., Insull, W., et al. (1995). A definition of advanced types of atherosclerotic lesions and a histological classification of atherosclerosis: A report from the Committee on Vascular Lesions of the Council on Arteriosclerosis, American Heart Association. *Circulation, 92*, 1355–1374.

Atherosclerotic Dementia

- ▶ Vascular Dementia

Atherosclerotic Heart Disease

- ▶ Coronary Disease

Atherothrombotic Brain Infarction

- ▶ Ischemic Stroke

Athymia

- ▶ Abulia

Atkins v. Virginia

Robert L. Heilbronner
Chicago Neuropsychology Group
Chicago, IL, USA

Synonyms

Mental retardation defense

Historical Background

Daryl Atkins and William Jones abducted Eric Nesbitt from a convenience store and after finding only $60 in

his wallet, Atkins and Jones used Nesbitt's vehicle to drive to an ATM and forced him to withdraw $200. Thereafter, Atkins and Jones drove Nesbitt to an isolated location where he was shot eight times and subsequently died. Atkins and Jones were quickly tracked down by police and in custody, it was determined that Jones' story claiming that Atkins pulled the trigger was more coherent than Atkins' story implicating Jones as the shooter. Thus, Atkins was charged and convicted of abduction, armed robbery, and capital murder. This took place despite the results of an IQ test completed by a clinical psychologist, in which Atkins' score of 59 placed him in the mildly mentally retarded range. Nonetheless, he was sentenced to death.

The Supreme Court of Virginia was in agreement with the judgment of the trial court and the appeal was taken to the U.S. Supreme Court. In July of 2002, the U.S. Supreme Court reversed the judgment of the trial court and the Supreme Court of Virginia and referred the case back to the sentencing court to render a sentence other than the death penalty. The U.S. Supreme Court ruled that the punishment was excessive and thus prohibited by the eighth Amendment as cruel and unusual if it is not "graduated and proportioned to the offense". An excessive judgment is judged by current societal standards. Thus, society's standards of decency, albeit subject to change, must prove that they are influenced by "objective factors to the maximum possible extent." Furthermore, it was ruled that mental retardation does not preclude a person's capability to discriminate right from wrong, though mental retardation does lead to a diminished capacities to process and comprehend information, reduces communication abilities, and decreases one's ability to learn from mistakes and experiences, reason logically, inhibit impulses, and understand the emotions and behaviors of others. The U.S. Supreme Court concluded that mentally retarded individuals are not exempt from criminal sanctions, though a decrease in personal culpability is warranted. Thus, due to the conclusions that the purposes of retribution and deterrence are not accomplished in the execution of mentally retarded individuals, coupled with the increased risk that the death penalty will be imposed erroneously; the U.S. Supreme Court ruled that the eighth Amendment precludes execution of mentally retarded persons.

Despite the court's ruling, in July of 2005 a Virginia jury determined that Atkins was intelligent enough to be executed due to the fact that another IQ score had been recorded at above 70. Moreover, the prosecution claimed that his poor performance in school was related to use of alcohol and drugs and that earlier assessments of his IQ were "tainted". Thus, Atkins was set to be executed on 2 December 2005. However, the decision was recently reversed again by the Virginia Supreme Court, as a result of state procedural grounds.

Current Knowledge

Forensic psychological and neuropsychological assessments of mentally retarded individuals being considered for the death penalty are highly important. Specifically, the U.S. Supreme Court did not specify the degree of mental retardation required to circumvent the death penalty and instead left such determinations up to the discretion of the states. It is important to note that sub-average intelligence alone does not warrant a label of mental retardation. Impairments in adaptive functioning and evidence of mental retardation prior to the age of 18 years are needed for a diagnostic determination of mental retardation.

Cross References

- ▶ Intellectual Disabilities
- ▶ Intelligence

References and Readings

Atkins v. Virginia, 153 L. Ed 2d 335 (2002).

Cunnningham, M. D., & Goldstein, A. M. (2003). Sentencing determinations in death penalty cases. In A. Goldstein (Ed.). *Forensic psychology (Vol 11). Handbook of psychology.* New Jersey: Wiley.

Denney R. L. (2005). Criminal responsibility and other criminal forensic issues. In G. Larrabee (Ed.). *Forensic neuropsychology: a scientific approach.* New York: Oxford University Press.

Melton, G. B., Petrila, J., Poythress, N. G., & Slobogin, C. (2007). *Psychological evaluations for the courts: A handbook for mental health professionals and lawyers* (3rd ed.). New York: Guilford Press.

Atomoxetine

John C. Courtney
Children's Hospital of New Orleans
New Orleans, LA, USA

Generic Name

Atomoxetine

Brand Name

Strattera

Class

Norepinephrine reuptake inhibitor

Proposed Mechanism(s) of Action

Inhibits the presynaptic reuptake of norepinephrine and theoretically increases dopamine in the prefrontal cortex via the same mechanism.

Indication

Attention Deficit Hyperactivity Disorder.

Off Label Use

Treatment resistant depression and anxiety.

Side Effects

Serious

Increased cardiac rate, potential hypertension, orthostatic hypotension, rare liver damage, potential for induction of mania, and suicidal ideation.

Common

Sedation in children, decreased appetite, dry mouth, constipation, nausea, vomiting, dysmenorrhea, erectile dysfunction, and impaired libido.

References and Readings

Physicians' Desk Reference (62nd ed.). (2007). Montvale, NJ: Thomson PDR.

Stahl, S. M. (2007). *Essential psychopharmacology: The prescriber's guide* (2nd ed.). New York, NY: Cambridge University Press.

Additional Information

Drug Interaction Effects: http://www.drugs.com/drug_interactions.html
Drug Molecule Images: http://www.worldofmolecules.com/drugs/
Free Drug Online and PDA Software: www.epocrates.com
Gene-Based Estimate of Drug interactions: http://mhc.daytondcs.com:8080/cgi bin/ddiD4?ver=4&task=getDrugList
Pill Identification: http://www.drugs.com/pill_identification.html

Atrophy

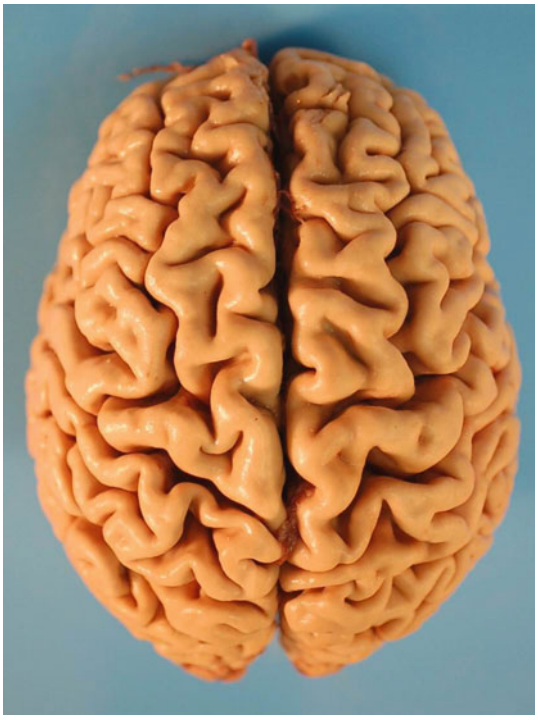
JoAnn T. Tschanz
Utah State University
Logan, UT, USA

Synonyms

Degenerative; Wasting

Definition

Atrophy refers to loss of cells of any tissue. In the brain, atrophy refers to a loss of neurons that may be generalized (e.g., diffuse atrophy) or focal, reflecting



Atrophy. Figure 1 Display of diffuse atrophy of the cerebral hemispheres. Note the shrunken gyri and prominent, widened sulci (Photo courtesy of Steven S. Chin, M.D., Ph.D., University of Utah Health Sciences Center)

circumscribed regional cell loss. With atrophy, there is also a corresponding loss of neural connections (synapses). Features of atrophy include sulcal widening, shrunken gyri, and enlarged ventricles. Focal atrophy may occur as a result of trauma or cerebrovascular lesions, for example. Generalized atrophy may occur with neurodegenerative conditions such as Alzheimer's disease. Atrophy may be viewed on gross inspection of the brain postmortem or antemortem with structural imaging techniques such as MRI or CT scan. Figure 1 displays diffuse brain atrophy of the cerebral hemispheres viewed from the top.

Attendant Care

Amy J. Armstrong
Virginia Commonwealth University
Richmond, VA, USA

Definition

Attendant care involves the provision of services to assist individuals with mental and/or physical disabilities in the performance and/or conduct of activities of daily living in order to maximize community inclusion and independent living. The intent of attendant care is to promote independence, participation, and quality of life of the individual while also preventing medical problems. Typically, the individual receiving attendant services is unable to perform such tasks independently, or may perform them with great difficulty. Attendant services include, but are not limited to activities such as: bathing, dressing, feeding, toileting, transferring, mobility, cooking, cleaning, laundering, cognitive assistance and monitoring. Services may also relate to sustaining health such as dispensing medications etc.

Attendant care may be provided by a family member such as a spouse, partner, sibling or parent, or by a hired employee. Typically, attendant care is provided by persons who have been trained to provide the service/s within the home and/or community. The independent living model of attendant care contends that individuals with disabilities should be empowered, to the highest degree possible, to recruit, screen and hire, train and terminate their respective personal attendants, thereby ensuring self-determination and choice. Additional considerations related to the provision of attendant care include where and how to locate and access quality service providers, adequate training of an attendant, and financial issues including paying a competitive wage to personal attendants. Funding sources of attendant care may include private resources such as: Health Insurance; Auto Insurance; and Worker's Compensation; or public resources such as: Medicaid; Department of Vocational Rehabilitation; Department of Veterans Affairs; Crime Victims Compensation and/or other State-funded programs.

Cross References

► Assisted Living

References and Readings

Rodriguez-Banister, K. (2006). *The Personal Care Attendant Guide: The Art of Finding, Keeping, or Being One.* New York: Demos Medical Publishing.

Attention

Ronald A. Cohen
Brown University
Providence, RI, USA

Synonyms

Concentration; Focus; Vigilance

Definition

Cognitive processes that enable the selection of, focus on, and sustained processing of information. The object of attention can either be environmental stimuli actively being processed by sensory systems, or associative information and response alternatives generated by ongoing cognitive activity.

Historical Background

Attention is subjectively self-evident to all people, and terms that referred to attention-type experiences have been described by philosophers through the ages. The concept of attention is strongly linked in the philosophy

to the nature of consciousness, self-awareness, and most theories of the "mind." Accordingly, attention has been the subject of psychological inquiry from the beginning of this scientific discipline. The writings of William James captured this fact, as evident from this well-known excerpt from his *Principles of Psychology* (1898).

> Everyone knows what attention is. It is the taking possession by the mind, in clear and vivid form, of one out of what seem several simultaneously possible objects or trains of thought. Focalization, concentration, of consciousness are of its essence. It implies withdrawal from some things in order to deal effectively with others

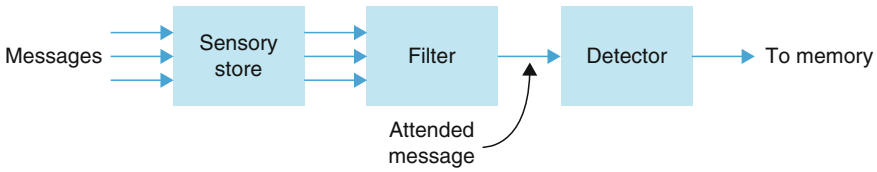
While written over 100 years ago, this description very succinctly captures essential aspects of the phenomena of attention, and remains apropos even today. The understanding of cognitive, behavioral, and neuropsychological bases, influences, and effects of attention have dramatically evolved since the time of William James. Yet, the underlying subjective and behavioral experiences characterized by James and the other psychologists of his time remain largely consistent with current phenomenology of attention. Different types of attention were described, such as directed, divided, focused, sustained, selective, and volitional attention, many of which continue to be used to describe the varieties of attentional experience. The primary limitation of these early efforts was the lack of experimentation that would have enabled operationalizing of these constructs and understanding of the processes underlying them.

Following the initial efforts of early psychologists to study attention from perspectives of structuralism and functionalism, a rather long period ensued dominated by behaviorism during which cognitive processes, like attention, were largely viewed as outside of the realm of empirical psychological inquiry. Attention was considered to be a construct that could be explained by more basic behavioral principles, such as discrimination learning, cue dominance, anticipation, and expectation. Classical conditioning theory provided an essential framework for behavioral analysis of attention, as the orienting response to novel stimuli, and its subsequent habituation, provided the behavioral and neural building blocks for simple forms of attention, in the absence of long-term memory formation (i.e., conditioning). The concepts of motivation and drive which played a major role in neobehaviorism, also helped to bridge attention theory and learning principles.

Information theory (Shannon & Weaver, 1949), which evolved out of technological advances in radio communication and also radar detection during World War II, was a major impetus for the subsequent re-emergence of cognitive science. In particular, the application of information processing models and signal detection methods to the study of communication led to a resurgence of research interest in attention. This is not surprising considering the fact that signal detection and selection, the basic elements of almost all theories of selective attention, are also central to information and communication theory. This approach emphasized the probabilistic nature of information detection and selectivity, a conceptual departure from earlier psychophysical methods used to study perception. The application of information processing approaches to the study of attention was a logical step, as one of the primary problems for any communication or information processing system is reducing the total amount of incoming signal to manageable levels to enable subsequent processing of this information.

Broadbent (1958) proposed the first formal model of selective attention based on the information processing theory. He maintained that attention occurs because there is an information "bottleneck" as the large quantity of environmental information that is available during parallel processing is subject to channel capacity limitations later in the stream of processing due to serial processing constraints. Broadbent posited that the primary requirement for attention to occur was a filtering process (as shown in Fig. 1) that occurred soon after sensory registration and served to separate relevant from irrelevant signals in order to enable meaningful information to be available for subsequent serial processing through limited capacity information channels. This model presumed a somewhat passive system by which this filtering occurred, with selection driven by the salience of the stimuli themselves. However, the nature of this filtering process was not fully operationalized in this initial model. In the years that followed, a number of variations on this model of attention were proposed by other investigators working in the newly emerging field of cognitive psychology.

Most notably, Treisman proposed an attenuation theory of attention, which was similar to Broadbent's model in which he postulated a single process that occurred early in the information processing stream, soon after sensory registration (Treisman & Gelade, 1980). According to attenuation theory, selective attention requires distinguishing between messages on the basis of their physical characteristics, such as location, intensity, and pitch, as well as content. In this model of attention, stimuli naturally differ in their threshold for activating awareness of a stimulus, and the process of attention effectively decreases (i.e., attenuates) the strength (e.g., loudness) of irrelevant stimuli. This attenuation process was considered to occur in conjunction with a feature integration process that enabled



Attention. Figure 1 Model depicting filtering process as proposed by Broadbent (1958)

perceptual experience. This line of research was noteworthy for the use of dichotic listening paradigms in which attention is divided between the two ears, and information must be selected from one of the two channels of input.

The bottleneck models proposed by Broadbent and Treisman proposed that selection occurs at a very early stage of processing soon after sensory registration, thereby linking attention squarely with sensory selection. Essentially, selective attention filters inhibits focus on information occurring in the unattended ear in dichotic listening experiments before semantic analysis and other cognitive processes have time to occur. Other investigators (e.g., Deutch and Deutch (1963) argued that attention is strongly influenced by the response demands of a situation and that it likely occurred at a later stage of processing, and that in reality both ears analyze incoming information semantically, though response demands creates a bias toward one ear over the other. This led to heated debates in the 1960s and 1970s over the location of the bottleneck. While considerable experimental evidence indicated that early sensory selection occurs prior to a point in time when semantic information has been processed, there is also other paradigms that demonstrate that in most situations selection is greatly influenced by semantics and the response requirements that exist.

Subsequent researchers took this a step further by demonstrating that capacity limitations constrain attention and the intensity of attentional focus that is possible at any given point in time. Kahenman's (1983) capacity theory of attention proposed that people's capacity for attentional focus is not static, but instead varies as a function of factors such as the reward characteristics of the task, arousal level, and other biological determinants. This theory of attention was extremely important in that it brought to the forefront the fact that attention should not be conceptualized in purely mechanical terms as was the case in early attention models based solely on information processing theory. Rather attention needed to be viewed in the context of the biological factors that drive it. This helped to catalyze an emphasis on the study of focused attention, a shift that coincided with information coming from psychophysiological studies that showed linkages between arousal, activation, and effort in the control of attention (Pribram & McGuinness, 1979).

A large body of cognitive studies of attention followed this pioneering work. Several of these are particularly important in a historical context. Posner (1979) made an important distinction between overt and covert shifts of attention that occur in the context of visual selective attention. Overt attention is characterized by the act of intentionally directing attention (i.e., looking) toward a stimulus, whereas covert attention occurs without intention when focus is drawn to a particular stimulus or location, typically as a result of cues or other types of information of which the person may have little conscious awareness. Posner also refined the use of chronometric methods to demonstrate the costs associated with these attention shifts. His research also made a distinction between two primary processes, selection and focus, that were necessary to account attention's intensity and spatial distribution.

Shiffrin and Schneider (1979) conducted seminal studies that distinguished automatic from controlled attention. They varied the number of targets to be detected and the consistency of target location based on either fixed or variable memory demands. By creating greater variability in task characteristics, subjects could not rely on memory to facilitate performance, which slowed their response time. Under these conditions, automaticity was no longer feasible. Besides demonstrating the distinction between automatic and controlled attention, these findings also illustrated the relationship between attention and memory, and set the stage for a long line of research examining working memory in relationship to attention.

Neuropsychological Models and Frameworks

Over the past 2 decades, research efforts have been directed at organizing these varieties of attention into coherent frameworks. Furthermore, researchers have proposed neuropsychological models of attention that seek to characterize the functional neuroanatomic systems involved in attention, the processes for which these systems are

responsible, and also how these functional brain areas interact. The models described below are not meant to be an exhaustive review of the literature in this regard, but rather highlights some of the key elements of current theoretical frameworks and the extent to which there is consistency across models.

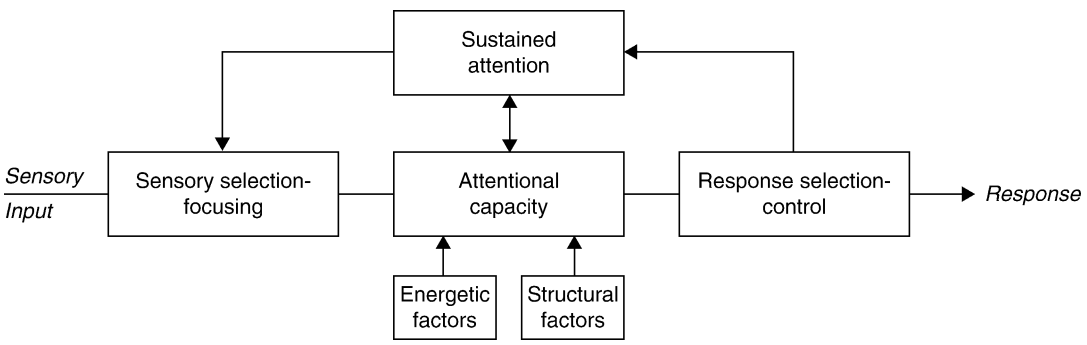
Alan Mirsky provided one of the first neuropsychological frameworks to account for what he described as the "elements" of attention. This framework proposed five elements of attention: (1) selection, (2) focus, (3) execute, (4) switch, and (5) sustain. This theoretical framework was derived from factor analyses of neuropsychological test results obtained from a large sample from his clinical practice.

Cohen (1993) proposed a similar component process framework of attention that hypothesized four primary components of attention (Fig. 2): (1) sensory selective attention; (2) response intention, selection, and control; (3) capacity-focus; and (4) sustained attention. A primary goal of Cohen's model was to include components reflecting similar levels of analysis. The components of this framework were also derived from factor analysis of clinical neuropsychological data with efforts made to retain only the minimum number of factors necessary to account for maximum variance in the data, with an effort to make conservative interpretation of the component processes associated with each factor. Each component was hypothesized to be a function of other more basic subcomponent processes. This model posits that these four components of attention are not completely orthogonal or functionally independent, but instead rather share common component subprocesses, processes depending on the task at hand. A simplified version of the model is shown.

In everyday situations, attention depends on the interaction of all four of these component processes. However, for some tasks, the primary demand may be for sustained attention or vigilance, whereas for another task it may be efficient use of available attention capacity and the intensity of focus. Similarly, some tasks that are weighted more demand for sensory selective attention, while others place greater demand on response intention and selection. In other words, while these four components need to be accounted for in explaining attention across all situations, particular tasks may require minimal demands for sustained attention, but intense demands on capacity and focus. Validation efforts directed at this framework have shown the principal factors to be highly reliable, internally consistent, and valid with respect to their weighting relative to specific brain disorders and conditions. For example, patients with attention-deficit disorder have greatest impairment on tasks requiring sustained attention, whereas patients with diminished speed of processing have greatest problems on tasks requiring capacity and focus. It is noteworthy that the analyses conducted by both Mirsky and Cohen yielded very similar factor structures and validity data, providing strong evidence that four to five primary components processes exist that account for most varieties of attention. These attentional component processes are described in greater detail below.

Selective Attention

A fundamental aspect of all attentional processes is that it is selective. Attention enables the selective deployment of cognitive resources for the processing of information from either the external environment or internal cognitive processes or associative representations. Attention also requires a shift from less salient information. Processes that enable or facilitate the selection of salient information for further cognitive processing are collectively referred to as *selective attention* (Treisman, 1969; Triesman & Geffen, 1967). Individuals are constantly flooded with an infinite number of signals from both outside and within. By reducing



Attention. Figure 2 Simplified neuropsychological model of the components of attention

the amount of information that will receive additional processing, attention constrains incoming information to the individual's available capacity at a given point in time, thereby keeping the level of information to be processed at a manageable level. While selective attention is necessary and beneficial for cognitive function, there are costs associated with selectively attending. By attending to a particular stimulus, the likelihood of detecting other potentially relevant stimuli or choosing an alternative response strategy is reduced. Optimal selective attention depends on the system being flexible and adaptive, with the capacity to select and focus on certain stimuli, but then to shift to other stimuli or cognitive processing when task conditions change. Selective attention thereby serves as a gating mechanism for the flow of information processing and the control of behavior.

Response Selection and Control

Attention has traditionally been viewed as a process closely related to perceptual processing. It prepares the individual for sensory intake, perceptual analysis, and integration with other cognitive processes. Yet, there are many situations in which attention is not directed at incoming sensory information, but rather selection response alternatives, and the control of responding once a selection has been made. Even when a task primarily requires selective attention, there are usually coexisting response demands. While sensory selection may be automatically elicited by the occurrence of salient external stimuli, more often than not the act of attending is linked to a planned, goal-directed course of action. In this regard, attention and responding are directed to obtain information that will optimize behavior.

The processes associated with response selection and control range from simple behavioral orienting, such as turning one's head in response to a sound source to more complex cognitive processes involving intention, planning, and decision making. Response selection and control form the basis for what humans typically experience as volitional action. Before responding, individuals generate a large number of response alternatives. These response alternatives are evaluated prior to making an actual motor response, leading to response bias, that is, the probability of selecting specific responses.

The attentional processes involved in response selection and control are related to a broader class of cognitive processes, commonly referred to as *executive functions* (Fuster, 1989; Luria, 1966). Several processes associated with response generation underlie executive control: intention, selection, initiation, inhibition, facilitation, and switching. Not only do these processes account for the control of simple motor responses, they also provide the foundation for more complex cognitive processes, such as planning, problem solving, and decision making, as well as conceptual processes such as categorization, organization, and abstraction. Executive control is strongly dependent on the actions of prefrontal-subcortical systems. Executive control is dependent on the ability of the system to act with intention, to initiate responding, to inhibit responding based on new information, and to efficiently shift from one response alternative to another in accordance with changing environmental demands.

Focused Attention and Capacity Limitations

Attention is also characterized by having intensity and by the extent to which it is allocated in either a focal or diffuse manner. The intensity of attentional focus is a function of both situational and task demands and organismic factors, such as motivation and drive. Focused attention is constrained by capacity limitations (Kahneman, 1973) that limit the intensity of focus that is possible on a moment-by-moment basis. Attentional capacity is influenced by both structural and energetic factors (Cohen, 1993). Energetic capacity limitations tend to be state dependent and reflect the changing energetic conditions of the brain, including motivation, and the incentives to attend that are present in the situation. Structural factors tend to be more stable and dependent on each person's intrinsic information processing capacity. Factors that influence structural capacity include the processing speed capacity that is a function of the integrity of neural transmission, memory encoding, storage and retrieval limitations, and temporal–spatial processing dynamics that vary across people. Given these factors that limit attentional capacity, focused attention varies relative to the cognitive demands and type of information to be processed, and situational incentive. Focused attention can occur relative to either sensory selective attention, or intention and response selection, and in fact often involves the coordination of sensory and response selection. Such coordination is quite effortful (Pribram & McGuinness, 1975). Arousal and activation vary as a function of the existing demands for focused attention, with greater activation occurring when there is more utilization of available capacity because of the need to focus.

Automatic Versus Controlled Attention

An important distinction exists between automatic and controlled attentional processing (Schneider & Shiffrin, 1977;

Hasher & Zacks, 1979). Automaticity occurs most commonly in the context of sensory selective attention, particularly for tasks requiring simple detection of a target from a set of stimuli, and also on tests of attention span. With automaticity, there is usually relatively little demand placed on attentional capacity, and often attention can occur without much awareness or subjective effort (e.g., attending to other cars while driving on an empty highway). Automaticity can be interfered with increase in size and complexity of the environment to be attended to. Spatial selective attention is particularly well suited for automatic attentional processing since visual information typically occurs in parallel with a vast array of information reaching the brain almost instantaneously. Automaticity is more difficult to achieve for tasks that require sequential cognitive operations, though some degree of automaticity may be attainable through practice. Controlled attention is typically required for tasks in which there are working memory demands, or other requirement of other cognitive processes, such as memory encoding and retrieval, rapid processing speed, or executive control. The demand for focused intensity varies as a function of requirements for controlled attention that exist for a particular task. Generally, response intention, selection, and control are not very amenable to automatic attentional processing, as behavioral responding typically requires complex motor sequencing with executive control demands. However, the fact people are able to perform certain tasks such as typing or playing a musical instrument with considerable automaticity illustrates that automaticity is attainable for well-learned motor programs.

Sustained Attention

Attention varies as a function of the temporal dynamics of the task to be performed and the situation, and all humans experience some degree of performance variability, particularly when long periods of sustained performance are required. Sustained attention refers to processes that enable the maintenance of performance over time. Compared to other cognitive processes, such as language and visual perception, attention is inherently variable by necessity, as it must be responsive to changing stimulus conditions, task demands, and motivational and energetic states. Problems with sustained attention commonly occur on tasks requiring attentional persistence for long durations when there are high levels of demand for effortful processing. All people have limits in their capacity for sustained attention. Sitting in a 1-hour lecture is not a problem for most bright college students, but even the brightest students would encounter tremendous difficulties sustaining their focus for a lecture that lasted 12 consecutive hours.

Vigilance refers to sustained attention directed toward specific targets, in which a state of readiness is required to detect and respond to stimuli occurring at variable and often infrequent intervals (e.g., Colquhoun & Baddeley, 1967; Corcoran et al., 1977). Detecting rare targets with lengthy intervals between responses can be difficult. This type of sustained attention is quite common in everyday life. For example, a watchman may spend the entire night attending to the possibility of an intruder without this event ever occurring. Attention to low-frequency events has different processing requirements than responding to high-frequency events and, for many people, is more difficult. Vigilance and sustained attention are under the influence of sustained motivational level, boredom, and fatigue, which are sensitive to the dynamics of temporal tasks.

Current Clinical and Experimental Evidence

Neuropsychological Studies

Twenty years ago the clinical and experimental neuropsychological literature on impairments of attention associated with neurological and psychiatric disorders affecting the brain was quite limited. Much of the neuropsychological focus on attention was on the assessment of attention span in the context of psychometric analysis of performance on tests such as digit span. This probably reflected the fact that adequate attention was once viewed more as a necessary condition for other cognitive functions to occur optimally, but not particularly important in its own right in considerations of brain–behavior relationships. This attitude has changed dramatically, and attention is now widely regarded as a critical cognitive process that reflects not only the interface between both the external environment and internal cognitive functions, but also moment-by-moment information processing. A literature review conducted about 2 decades ago revealed less than 500 studies focused on the neuropsychology of attention. Recent literature reviews suggest that this number is now over 40, 000. This increase in interest in attention reflects the fact that: (1) attention disturbances are one of the most common by-products of brain, (2) attention is closely tied to the human experiences of consciousness, awareness, and cognitive control, (3) major advances have occurred in the methodology for studying and assessing attention, and (4) for a number of reasons, there has been an increased societal interest in

attention disturbances, perhaps in part because of the intense information processing demands and pace of life that people now experience.

Impairments of attention may be either specific or nonspecific. Specific impairments occur when only aspect of attention is affected. Often this occurs when impaired attention is directly associated with a particular type of cognitive operation, such as spatial processing. These impairments are often associated with focal brain disturbances affecting specific cortical or subcortical systems necessary for the cognitive operation. Nonspecific disturbances of attention are much more common, often occurring due to disorders that affect arousal, motivation, or other factors that reduce attentional capacity, and as a result of more diffused nonlocalized brain disorders. Both types of attentional disturbance provide insights into the cognitive processes of attention and the brain mechanisms that underlie these processes. Though localized lesions provide the best vehicle for analysis of the role of specific brain structures in attentional control, nonspecific attentional impairments illustrate the influence of metabolic and neurotransmitter abnormalities on information processing rate, arousal, and other energetic and structural factors that may affect attentional capacity and focus. Attentional capacity is a direct function of level of consciousness, making this an essential part of the clinical assessment of attention. Levels of consciousness range from normal states of alertness and awareness to coma.

A brief summary of the attentional disturbances associated with several common neurological and psychiatric conditions is provided below. For more detailed consideration see Cohen (1993).

Stroke and Neglect Syndrome

Unilateral stroke affecting the nondominant cortex often causes hemi-neglect syndrome, perhaps the most well known and dramatic form of attention disturbance. The defining feature of neglect syndrome is the failure to attend to, respond to, or be aware of stimuli on one side of space. Many variants of neglect syndrome may be observed clinically. Most patients with neglect exhibit impairments of sensory selective attention, although some may have primary problems with hemi-spatial response selection and control. Experimental investigations have confirmed the role of attention in hemi-neglect syndrome. Manipulation of attentional parameters demonstrates that symptoms of hemi-neglect change as attentional demands are modified (Kaplan et al., 1989). Regardless of which attentional process is most affected, all patients with neglect syndrome have a fundamental disorder involving the spatial distribution and allocation of attention.

Alzheimer's and Neurodegenerative Dementias

Attention disturbance is usually not described as a primary feature of Alzheimer's disease (AD) and historically tended to be viewed as one cognitive function that was largely spared. This conclusion is misleading. While patients with early-stage AD typically do not show overt symptoms of severe inattention, they frequently have marked difficulty with focused attention and executive control, particularly when tasks required controlled attentional processing. This reflects a distinction between performance on tests of simple and complex attention, as conclusions about spared attention in AD have often been based on the observation of preserved attention span on tests such as digit span. Patients with early AD are often usually alert, energetic, and able to maintain their general focus on the assessment process. Yet, most will have considerable difficulty on tasks requiring focused and divided attention, suppression of interference (e.g., Stroop), information processing speed and efficiency (e.g., Symbol Coding), and working memory. As the disease progresses, performance becomes impaired on most tasks requiring effortful attentional processing. Pervasive disturbance eventually develops affecting all aspects of attention, including self-awareness.

Multiple Sclerosis

Multiple sclerosis (MS), one of the most common neurologic in young adults, often affects learning, memory, and executive control. Given the fact that the disease affects the myelin of the white matter, deficits in these areas are often strongly associated with attentional impairments and slowed inefficient information processing. Attentional capacity is typically reduced with performance decrements usually evident under conditions of increased informational load. Fatigue is the most common of all symptoms in MS and is associated not only with motor effort but also with attending to and performing cognitive tasks. Patients with MS experience difficulty maintaining consistent effort on tasks.

HIV

Similar to MS, HIV-infected patients who have not developed severe AIDS dementia typically show primary impairments in the areas of psychomotor and information processing speed, focused and sustained attention, and executive functioning. This reflects the fact that when not adequately treated, HIV tended to initially have greatest effects on subcortical systems, including the basal ganglia.

Closed Head Injury

The most common effects of closed head trauma are diffuse axonal damage due to shearing forces and frontal lobe disturbances. Consequently, attention and executive dysfunction are among the most common associated cognitive problems. Persistent distractibility, poor concentration, apathy, and fatigability are prominent sequelae. Deficits of arousal and poor performance on measures of selective, focused, divided and sustained attention, processing speed, and executive functioning tend to occur, which may contribute to associated learning and memory retrieval problems as well.

Epilepsy

Transient changes in the level and quality of consciousness, common in seizure disorder, typically cause marked alterations in attention around the time of the seizure. During the time between seizures, patients with epilepsy may have greater problems than healthy individuals on tests of focused and divided attention. These deficits appear to be related in part to slowed speed of processing and its effects on attentional capacity. Pharmacological effects associated with anticonvulsant therapy likely contribute in part to these attentional effects.

Metabolic Disturbances

Factors that affect the metabolic function often cause delirium, or more subtle alterations in attention and arousal. Accordingly, metabolic disturbance is one of the most common reasons for transient alterations in attention among people without other neurological or psychiatric illness. Metabolic disturbances that affect the brain can be the result of a wide variety of factors, including drug effects and systemic illnesses, such as liver and kidney disease, and diabetes.

Psychiatric Disorders

Difficulties with focused and sustained attention are extremely common among patients with psychiatric disorders, including affective disorders (major depression and bipolar disturbance) and schizophrenia. Severe anxiety states can also interfere with attention. A strong relationship exists between expenditure of effort and performance on tests of attention and other demanding cognitive functions for patients with major affective disorders. Impairments tend to be somewhat proportional to severity of depression, with performance improving when the depression resolves. Diminished attentional capacity is particularly evident on tasks that require psychomotor speed, attentional focus, and effortful demands for mental control. Abnormal attention is also a central feature of schizophrenia, as filtering of irrelevant stimuli and thoughts has long been considered to be a major element of the disorder, which has been linked to the dopamine system. Schizophrenics often encounter difficulties on tests of sensory selective attention because of their susceptibility to distraction. Slowed reaction time and processing speed also contribute to problems with attentional capacity, and both focused and sustained attention (Nuechterlein, 1977).

Attention-Deficit Disorder (ADD)

A developmental disorder of attention, ADD is the most widely recognized of all attention disturbance. Problems with sustained attention and distractibility are key features of the disorder, along with hyperactivity among a subset of children. While there is general agreement regarding the existence of ADD, there continues to be considerable debate about its manifestations and pathophysiology, particularly in light of the fact that ADD tends to occur along with other comorbid conditions.

Primate Studies

Understanding of the neural substrates of attention was greatly enhanced by the use of neurophysiological methods in primates. The value of these studies is that they provided directed recording of electrical activity from brain areas implicated in attention both by past clinical studies of patients with neurological disorders and also ablation studies involving laboratory animals. In the 1970s, Robert Wurtz, Michael Goldberg and their colleagues (1982) began electrophysiological studies from the brain of monkeys trained on specific attention paradigms. The earliest of these studies showed that the superior colliculus exhibits increased firing rates during visual attention, providing the first direct evidence of the involvement of a neural area in this process. Subsequently, a large number of studies were conducted that showed the contribution of other brain regions, particularly in posterior visual areas to specific aspects of visual selective attention. This work both confirmed the role of areas like the inferior parietal cortex that had been suspected of being involved in visual selective attention based on studies of hemi-neglect syndrome. Over time, there has been increasing emphasis on the role of frontal brain systems in relationship to these posterior brain areas. There is now a large body of research on this topic, supporting to general conclusions about selective attention: (1) Visual selective attention is controlled by multiple interacting brain areas that comprise a functional system. (2) Selective attention involves not only

posterior visual brain areas, but also frontal–striatal systems that provide executive response control. Active investigation continues using primate models with particular emphasis on source analysis of how particular types of neurons are tuned to optimize attention to particular types of signals. This research has been instrumental in characterizing the functional brain systems governing attention in humans.

Functional Neuroimaging

Attention was one of the first cognitive functions to be demonstrated through the use of functional imaging methods, such as functional MRI and PET. The fact that attentional parameters can be easily manipulated in the context of the scanner and that attention reflects the moment-by-moment information processing of the brain makes it very conducive to study through functional brain imaging. These efforts have largely confirmed the involvement of inferior parietal and frontal brain systems in attention, with studies showing the relative contribution of specific areas in selective, focused, and sustained attention. This is a rapidly growing area of neuropsychological inquiry. To date, results of functional neuroimaging experiments have largely supported evidence from earlier cognitive, neuropsychological, psychophysiological, and primate studies with respect to the neural substrates of attention.

Clinical Assessment Considerations

Although an essential cognitive process, attention is more difficult to directly observe or measure than other cognitive functions like language, visual perception, or memory. Attention fluctuates in accordance with changes in task demands and the processing capacity of the patient over time. Unlike other cognitive functions, performance may be quite different across different points in time, and it is this variability that in fact defines attention. Attention is often situation specific. This accounts for why some children with ADD perform well in a controlled laboratory setting, despite reports of gross problems with inattention in school or the home.

Unlike most other cognitive processes, attention primarily serves a facilitative function. Attention enhances or inhibits perception, memory, motor output, and executive functions, including problem solving. Yet, attention is always measured as a function of performance on tasks that also loads on one or more of these other cognitive domains. Therefore, pure tests of attention do not exist, and attention usually must be assessed within the context of performance on tasks that load on one or more these other domains. Attentional performance is often assessed as derived measure obtained by comparing performance across tasks that control for key attentional parameters (e.g., target–distractor ratio). Absolute performance often provides less informative measures of performance inconsistencies in the assessment of attention. For example, how performance varies as a function of time, spatial characteristics, or memory load provides more information about attentional dynamics than simply considering total errors on a visual detection task. Since attention is not the by-product of a unitary process, or a single sensory modality, it cannot be adequately assessed on the basis of findings from one specific test. For example, conclusions based on digit span performance are misguided. Attentional assessment requires a multifactorial approach. The specific attention measures used in an evaluation depends on the overall level of functioning of the particular patient. For patients with global cognitive dysfunction, it may be difficult to use certain tasks that require overly complex responses. For patients with relatively high overall cognitive abilities, tasks should be chosen that require multiple component processes. If the patient is able to perform well on these tasks, then severe attention disturbance involving specific attentional component processes can be ruled out. The Stroop and Trail-Making tests are examples of tasks that require multiple attentional processes. If impairments are found on such tasks, then more extensive testing of specific component processes can be conducted. When possible, efforts should be made to use tasks that incorporate signal detection methods, even when not evaluating sensory selective attention per se. This methodology provides the best means of accurately summarizing performance relative to all types of possible errors, and easily integrates with response time measures.

Attentional parameters that should be considered. A thorough assessment of attention should be based on analysis of data from a comprehensive battery of attentional tests that sample underlying component processes (Cohen, 1993). Accordingly, tasks should be used that are differentially sensitive to the following attentional parameters: (1) spatial characteristics, (2) temporal dynamics, (3) memory demands, (4) processing speed requirements, (5) perceptual complexity, (6) demands for response sequencing and control, (7) cognitive complexity of the task, (8) effort required to complete task, and (9) task salience, relevance, and reward value.

While multifactor neuropsychological assessment provides the best means of evaluating attentional

impairments, a comprehensive attentional evaluation may not be feasible in everyday clinical practice, because of time constraints, the patient's overall severity of cognitive impairment, or the fact that other cognitive functions must be assessed in greater detail because of the referral questions. Consequently, clinicians should be aware of the information that can be obtained from different levels of attentional assessment. A few primary tests of attention should be included in all neuropsychological evaluations. The continuous performance test (CPT) paradigm provides an excellent measure for assessing sustained attention and other related indices. Tests of focused and selective attention are also now widely available. Several attention batteries have also been developed that may facilitate the comprehensive assessment of the elements of attention.

Future Directions

Real-time functional brain-imaging methods will enhance the ability of neuropsychologists in the future to assess moment-by-moment variations in attention associated with task performance. There continues to be the need to attentional batteries that are theoretically coherent and provide assessment of the component processes that govern attention.

Cross References

- ▶ Attention-Deficit Disorder
- ▶ Automaticity
- ▶ Consciousness
- ▶ Directed Attention
- ▶ Divided Attention
- ▶ Effort
- ▶ Focused Attention
- ▶ Habituation
- ▶ Hemi-Inattention Syndrome
- ▶ Intention
- ▶ Orienting Response
- ▶ Selective Attention
- ▶ Sustained Attention

References and Readings

Cohen, R. A. (1993) *Neuropsychology of Attention.* New York: Plenum.

Cohen, R. A., Meadows, M. E., Kaplan, R. F., & Wilkinson, H. (1994) Habituation and sensitization of the OR following bilateral cingulate damage. *Neuropsychologia, 32*(5), 609–617.

Colquhoun, W. P., & Baddeley, A. D. (1967). Influence of signal probability during pretraining on vigilance decrement. *Journal of Experimental Psychology, 73*, 153–155.

Desimone, R., & Gross, C. G. (1979). Visual areas in the temporal cortex of the macaque. *Brain Research, 178*, 363–380.

Deutsch, J. A., & Deutsch, D. (1963) Attention: Some theoretical considerations. *Psychological Review, 70*, 80–90.

Fuster, J. M. (l989). *The prefrontal cortex: Anatomy, physiology, and neuropsychology of the frontal lobe.* New York: Raven.

Goldberg, M. E., & Bushnell, M. D. (l981). Behavioral enhancement of visual response in monkey cerebral cortex. II. Modulation in frontal eye fields specifically related to saccades. *Journal of Neurophysiology, 46*, 783–787.

Hasher, L., & Zacks, R. T. (1979). Automatic and effortful processes in memory. *Journal of Experimental Psychology: General, 108*, 356–388.

Heilman, K. M., Watson, R. T., & Valenstein, E. (l993). Neglect and related disorders. In K. M. Heilman & E. Valenstein (Eds.), *Clinical neuropsychology* (3rd ed., pp. 279–336). New York: Oxford University Press.

Heilman, K. M., Bowers, D., Coslett, H. B., & Watson, R. T. (l983). Directional hypokinesia in neglect. *Neurology, 2(*33), 104.

Heilman, K. M., Watson, R. T., Valenstein, E., & Goldberg, M. E. (1988). Attention: Behavior and neural mechanisms. *Attention, 11*, 461–481.

James, W. (1890). *The principles of psychology.* (Vol. 1., pp. 403–404). New York: Henry Holt.

Kahneman, D. (1973). *Attention and effort.* Englewood Cliffs, NJ: Prentice-Hall.

Kahneman, D., & Treisman, A. (1984). Changing views of attention and automaticity. In R. Parasuraman & D. R. Davies (Eds.), *Varieties of attention.* New York: Academic.

Kaplan, R. F., Verfaellie, M., DeWitt, L. D., & Caplan, L. R. (1990). Effects of changes in stimulus contingency on visual extinction. *Neurology, 40*(8), 1299–1301.

Mattingley, J. B., Bradshaw, J. L., Bradshaw, J. A., & Nettleton, N. C. (1994). Residual rightward attentional bias after apparent recovery from right hemisphere damage: Implications for a multi-component model of neglect. *Journal of Neurology, Neurosurgery & Psychiatry, 57*(5), 597–604.

Mesulam, M. A. (1981). A cortical network for directed attention and unilateral neglect. *Archives of Neurology, 10*, 304–325.

Parasuraman, R. (1984). Sustained attention in detection and discrimination. In R. Parasuraman & D. R. Davies (Eds.), *Varieties of attention.* (pp. 243–289). New York: Academic.

Pardo, J. V., Fox, P. T., Raichle, M. E. (1991). Localization of a human system for sustained attention by positron emission tomography. *Nature, 349*(6304), 61–64.

Posner, M. I., Walker, J. A., Friedrich, F. A., & Rafal, R. D. (l987). How do the parietal lobes direct covert attention? *Neuropsychologia, 25*(lA), 135–145.

Posner, M. I., & Cohen, Y. (1984). Facilitation and inhibition in shifts of visual attention. In H. Bouma & D. Bowhuis (Eds.), *Attention and performance X.* Hillsdale, NJ: Erlbaum.

Pribram, K. H., & McGuinness, D. (1975). Arousal, activation, and effort in the control of attention. *Psychological Review, 82*, 116–149.

Schneider, W., & Shiffrin, R. M. (1977). Controlled and automatic human information processing: I. Detection, search, and attention. *Psychological Review, 84*, 1–66.

Shannon, C. E., & Weaver, W. (1949). *The mathematical theory of communication.* Urbana, Illinois: The University of Illinois Press.

Treisman, A., & Gelade, G. (1980). A feature-integration theory of attention. *Cognitive Psychology, 12*, 97–136.

Verfaellie, M., Bowers, D., & Heilman, K. M. (1988). Attentional factors in the occurrence of stimulus-response compatibility effects. *Neuropsychologia, 26*, 435–444.
Watson, R. T., Heilman, K. M., Cauthen, J. C., & King, F. A. (1973). Neglect after cingulotomy. *Neurology, 23*, 1003–1007.
Wurtz, R. H., Goldberg, M. E., Robinson, D. L. (1982). Brain mechanisms of visual attention. *Scientific American, 246*(6), 124–135.

Attention Deficit Disorder

► Attention Deficit, Hyperactivity Disorder

Attention Deficit, Hyperactivity Disorder

Kevin M. Antshel, Russell Barkley
State University of New York - Upstate Medical University NY, Mount Pleasant, SC, USA

Synonyms

ADD; ADHD; ADHD, combined; ADHD, predominantly hyperactive-impulsive type; ADHD, predominantly inattentive type; Attention deficit disorder; Hyperkinetic disorder

Short Description or Definition

Attention deficit/hyperactivity disorder (ADHD) is characterized by developmentally inappropriate degrees of inattention, impulsiveness, and/or hyperactivity that most often arise in early to middle childhood, result in functional impairment across multiple domains of daily life activities, and remain relatively persistent over time.

Categorization

DSM-IV-TR defines three ADHD subtypes: Predominantly Inattentive type (ADHD-I), Predominantly Hyperactive/Impulsive type (ADHD-H/I) and Combined type (ADHD-C). ADHD-C is the most prevalent subtype in clinically-referred samples yet the true population prevalence of ADHD-C and ADHD-I is likely comparable, each accounting for roughly half of the ADHD cases. ADHD-H/I is far less common, is most often observed in preschool and early elementary school aged children, and is probably just the earlier developmental stage to the C-type in many instances. In general, hyperactive-impulsive symptoms decline more steeply as children age (although feelings of restlessness may persist), but inattentive symptoms remain relatively constant.

Children with ADHD-H/I and ADHD-C are at higher risk for conduct problems. Youth with ADHD-I are at higher risk for learning disorders, anxiety and possibly depression. While some argue that ADHD-I is a distinct disorder from ADHD-C and ADHD-HI, others have not found consistent differences between the subtypes on neuropsychological or laboratory measures. Though diagnosed as a categorical disorder, ADHD may actually represent an extreme end along a normal continuum for the traits of attention, inhibition and the regulation of motor activity.

Epidemiology

The population prevalence of ADHD is estimated to be 3–9% of school-age children and 4–5% of adults. ADHD is more prevalent in males and those with chronic health problems, family dysfunction, low socioeconomic status, presence of a developmental impairment, or urban living. ADHD is a worldwide disorder found in most countries with rates similar to if not higher than those found in North America. Differences across ethnic groups within the North America are sometimes found but seem to be more a function of social class than ethnicity.

Natural History, Prognostic Factors, Outcomes

The syndrome of attention difficulties, impulsive behavior and overactivity has been known since the late 1700s and certainly since the early 1900s. Numerous attempts have been made at definition and nomenclature, including Strauss syndrome, minimal brain dysfunction or damage, hyperkinetic child syndrome (or hyperkinesis), and attention deficit disorder with and without hyperactivity.

ADHD can exist without other psychiatric disorders in 25–30% of ADHD cases (MTA Collaborative Group, 1999) but is more often associated with co-morbidity. Oppositional defiant disorder (45–65%) is the most common psychiatric co-morbidity in ADHD. As many as half of these oppositional children will progress to early onset

conduct disorder such as lying, stealing, fighting and otherwise violating the rights of others. Major depressive disorder (20–30%) and anxiety disorders (10–30%) are also relatively common co-morbid conditions in pediatric ADHD.

Longitudinal research following children with ADHD into adulthood suggests that 50–86% of children with ADHD continue to show impairing symptoms as they age. The fact that some children *do not* continue to have an ADHD diagnosis may be due in part to the finding that ADHD symptoms decline as a function of age in typically developing populations. However, it may also simply reflect that DSM symptoms and symptom thresholds may be developmentally inappropriate and too restrictive, respectively, to be applied to outside of childhood. For example, DSM-IV inattentive symptoms are more common in adolescents than DSM-IV hyperactive/impulsive symptoms. While this may infer that inattention persists at higher levels than hyperactivity/impulsivity, it may also simply reflect the developmental insensitivity of the DSM-IV symptoms.

Genetics also appear to be a large factor in those who continue to demonstrate clinically significant ADHD post-childhood versus those whose symptoms are in remission. For example, prevalence rates of ADHD among the relatives of children with persistent ADHD are significantly higher than rates in relatives of children with remitted ADHD. In addition, a history of major depressive disorder before age 13 is a predictor of the syndromic persistence of ADHD into adolescence as is having a below average IQ.

By definition, individuals with ADHD need to be functionally impaired in two or more domains of major life activities. In children, academic, social and family functioning domains are the most frequently impaired (MTA Collaborative Group, 1999). Educational impairments including academic underachievement and learning disabilities are well documented in the pediatric ADHD literature.

In adolescents and young adults, academic impairments continue to persist; young adults with ADHD completed fewer years of education, with nearly 1/4 failing to complete high school. Others have similarly reported that relatively few young adults with ADHD attempt college (20%) and even fewer graduate (5%) from college. Compared to children with ADHD who are followed into adulthood, clinically diagnosed adults with ADHD appear to have higher intellectual levels, have graduated from high school and have at least attempted college.

In addition to educational impairments, impairments in domains such as occupational, dating/marital relations, financial management, driving, child-rearing, managing a household and maintaining health are also consistently reported in adults with ADHD. For example, employer ratings are lower for adults with ADHD and adults with ADHD have more part-time employment and change jobs more often.

There are some data to suggest that ADHD is *more* functionally impairing than most other outpatient psychiatric disorders in these domains. While the relationship between ADHD symptoms and impairment in children with ADHD is modest ($r = 0.3$), these relationships may be more robust in adults ($r = 0.7$).

Neuropsychology and Psychology of ADHD

A meta-analysis suggested that children with ADHD have an IQ about nine points lower than typically developing peers. Similar data have been reported in adults with ADHD. Lower performance on the WAIS-III Arithmetic and Digit Symbol may account for a substantial portion of the IQ differences noted between adults with ADHD and community controls.

Controlled processing deficits are commonly observed in pediatric ADHD. Children with ADHD perform less well on laboratory tasks that assess vigilance, motoric inhibition, organization, planning, complex problem solving, and verbal learning and memory. Adults with ADHD are impaired on these same cognitive domains.

Both children and adults with ADHD perform less well on tasks that require vigilance, or the ability to sustain attention. There is also some evidence that "rare target" paradigms (few targets, many non-targets) such as the Gordon Diagnostic System appear to be more difficult for adults with ADHD than those paradigms with higher signal probabilities.

Response inhibition has been hypothesized to play a central role in pediatric ADHD. Continuous performance test (CPT) commission errors are a common laboratory measure of this construct. Unlike attention deficits (which seem to emerge more reliably in rare target CPT's), response inhibition deficits emerge more reliably in higher signal probabilities such as the Conners CPT. Several studies have reported that adults with ADHD make more errors of commission on high signal CPT's relative to both clinical and community control participants.

Executive functioning deficits are present in both pediatric and adult ADHD. Thus, it is surprising that performance on one of the most well established tests of executive functioning, the Wisconsin Card Sorting Test is not impaired in adults with ADHD. Multiple studies have failed to report a

significant difference between adults with ADHD and community controls on WCST categories completed and number of errors, both perseverative and non-perseverative.

Verbal fluency is impaired in adult ADHD. The most widely used verbal fluency task in adult ADHD populations has been the Controlled Oral Word Association Test. Multiple studies have reported significant differences between community controls and adults with ADHD.

Given the importance of attention and working memory to memory encoding and storage, it is not surprising that adults with ADHD have been demonstrated to have memory deficits. They also appear to have more difficulty managing auditory/verbal information relative to visual information. Although differences emerge between adults with ADHD and community controls on the WAIS-III Digit Span, the effect size of the differences are much larger on the California Verbal Learning Test. For example, adults with ADHD perform less well on overall rates of learning, recall, recognition and semantic clustering. The weaker performance on the semantic clustering index may indicate failure to adopt a strategy.

Evaluation

The American Academy of Child and Adolescent Psychiatry (Pliszka, 2007) has established guidelines for the assessment and treatment of ADHD. No neurological, genetic, neuropsychological or behavioral tests have sufficient positive and negative predictive power to accurately classify ADHD cases with sufficient success to recommend them for clinical diagnosis. Clinical diagnosis is based largely on careful history taking, use of structured interviews containing DSM-IV criteria for ADHD and related disorders, and the expert knowledge of the clinician in the differential diagnosis among childhood mental disorders. Paramount in the evaluative process is the time to listen to parental concerns, probe for details concerning nature, onset, and course, elaborate the specific impairments resulting from these concerns, and place them in the larger framework of the clinical taxonomy of mental disorders. The clinical interview is then supplemented with the use of parent and teacher behavior rating scales to assess developmental deviance of symptoms, screening of intelligence and academic achievement skills by standardized testing, brief observation of the child during unstructured and structured activities, contact with school personnel concerning classroom functioning and compilation of prior school and mental health records available on the child.

Other sources of information essential for the diagnostic process are behavioral rating scales or checklists on which normative data are available. These include "broad band" questionnaires, such as the Behavioral Assessment System for Children – 2nd edition or Child Behavior Checklist for screening the major dimensions of childhood psychopathology (e.g. anxiety, depression, attention, hyperactivity, aggression, etc.). "Narrow band" questionnaires specifically evaluate the symptoms of ADHD as set forth in DSM-IV. Rating scales can reliably, validly and efficiently measure *DSM-IV*-based ADHD symptoms. Some examples of instruments demonstrating appropriate psychometric properties with a strong normative base include the ADHD Rating Scale IV and the Conners Rating Scales – 3rd edition.

A number of specific tests have been devised to provide objective measures of a subject's vigilance and impulse control, such as the Gordon Diagnostic System, Conners Continuous Performance Test or the Test of Variables of Attention, among others. Research suggests, that these tests are not especially accurate at classifying children as ADHD; while the presence of abnormal scores on such tests indicates the presence of a disorder in as many as 90% of children who perform poorly, such scores cannot indicate the specific disorder present. Moreover, the ecological validity of these tests is low thus precluding the ability to predict from the test scores how the child will function in more natural settings, such as home and school. These tests are therefore not recommended for routine diagnostic evaluations of children with ADHD, although they may be used in clinics specializing in ADHD as part of research or drug trials. More useful information is likely to be obtained from the parent and teacher rating scales discussed above.

Treatment

Treatment for ADHD in children typically involves three components: parent and child education and support, classroom accommodations, and medication. Substantial evidence exists to show that training parents in child behavior management skills can be of significant benefit in the reduction of parent–child conflict and improvement in child success within the home (MTA Collaborative Group, 1999). The school setting frequently requires adjustment to meet the special needs of the child with ADHD. School interventions often include alterations to the curriculum and work load to better mesh with the limited attention, persistence, and disorganization of the child with ADHD; increases in sources of positive reinforcement for work productivity; occasional use of immediate and systematic negative consequences for disruptive or inappropriate behavior; implementation of a daily

school behavior report card (the ratings on which are linked to a home token economy).

The mainstay of treatment for many children with ADHD is medication, frequently psychostimulants. Three classes of medication appear to be useful for management of ADHD, these being: psychostimulants (methylphenidate, amphetamines), noradrenergic reuptake inhibitors (atomoxetine), and antihypertensive medications (clonidine, guanfacine).

Stimulant medications, especially extended release formulations, are a front-line management strategy in pediatric ADHD; approximately 70% of children with ADHD will show an efficacious response to stimulant medications such as Methylphenidate or mixed-salt amphetamines. The side effects of stimulants are fairly benign, short-lived, dose related, and often managed through dose or timing adjustments, or by switching to a different delivery system or stimulant.

Atomoxetine is a nonstimulant approved for management of ADHD. Atomoxetine is an exclusive noradrenergic reuptake inhibitor and is the first drug indicated for ADHD that is not a Schedule II controlled substance with low potential for abuse, making it more convenient than the stimulants for sampling, prescribing, and titrating. Clonidine and guanfacine are alpha$_2$-noradrenergic agonists that have some effectiveness for the management of hyperactive-impulsive ADHD symptomatology. They are also considered "off-label" for treatment of ADHD as they have not as yet been specifically approved by the FDA for treatment of ADHD. An extended release form of guanfacine received FDA approval in 2009.

In adults, stimulant medications are effective in approximately 70% of individuals with ADHD. Atomoxetine may be particularly effective for adults with ADHD and co-morbid depression or for those with a co-morbid substance use disorder.

Managing psychiatric co-morbidity is a significant component of pediatric ADHD. The same dictum appears central to managing ADHD in adults. While "uncomplicated" ADHD exists in about 25% of the adults with ADHD, most adults with ADHD have significant psychiatric co-morbidity that requires clinical attention and management. One aspect in which the psychiatric co-morbidity is evident in treatment strategies is pharmacotherapy. Although the evidence for the efficacy of polypharmacy is limited at this time, multiple researchers have asserted that polypharmacy may be more likely in adult ADHD than pediatric ADHD.

Similar to pediatric ADHD, a psychosocial treatment component is typically recommended in adult ADHD. What constitutes the psychosocial component, however, appears to be somewhat different in adult ADHD relative to pediatric ADHD. For example, neither cognitive behavioral therapy (CBT) nor cognitive therapy has much research support in pediatric ADHD. Nonetheless, there are some data to suggest that CBT may be more efficacious in adults with ADHD. For example, in the adult ADHD literature, there is some evidence that CBT is efficacious for reducing functional impairments in adults concurrently treated with stimulants.

Cross References

- ▶ Americans with Disabilities Act
- ▶ Attention; Attention/Executive Functions
- ▶ Atomoxetine; Behavior Assessment System for Children (BASC)
- ▶ Cognitive Behavioral Therapy
- ▶ Conners 3rd edition
- ▶ Continuous Performance tests
- ▶ D-amphetamine
- ▶ Executive Functioning
- ▶ Individuals with Disabilities Education Act
- ▶ Learning Disability
- ▶ Metacognition
- ▶ Methylphenidate
- ▶ Section 504 of the Rehabilitation Act of 1973
- ▶ Stimulants
- ▶ Working Memory

References and Readings

Barkley, R. A. (2006). *Attention deficit hyperactivity disorder: A handbook for diagnosis and treatment* (3rd ed.). New York: Guilford Press.

Barkley, R. A., & Murphy, K. R. (2006). *Attention deficit hyperactivity disorder: A clinical workbook* (3rd ed.). New York: Guilford.

MTA Collaborative Group. (1999). A 14-month randomized clinical trial of treatment strategies for attention-deficit/hyperactivity disorder. The MTA Cooperative Group. Multimodal treatment study of children with ADHD. *Archives of General Psychiatry, 56* (12), 1073–1086.

Nigg, J. (2006). *What causes ADHD: Understanding what goes wrong and why.* New York: Guilford.

The ADHD Report, a bimonthly newsletter for clinicians edited by Dr Barkley with contributions from leading clinicians and researchers. Guilford Publications, New York.

Pliszka, S. (2007). Practice parameter for the assessment and treatment of children and adolescents with attention-deficit/hyperactivity disorder. *Journal of the American Academy of Child and Adolescent Psychiatry, 46*(7), 894–921.

Attention Network Test (ANT)

Michael S. Worden
Brown University
Providence, RI, USA

Attention is often subdivided by researchers into a number of separate systems. Although there is certainly some interaction between them, these systems play different roles in terms of their effect on information processing and the control of behavior. Further, there is evidence that different attentional systems are associated with different, largely nonoverlapping brain regions and rely to a large extent on different neurotransmitter systems. One such framework advanced by Michael Posner and colleagues defines three separate attention systems or networks: alerting, orienting, and executive control.

The *alerting system* is responsible for helping the organism reach and maintain an alert state. This state, which is separate from arousal, is characterized by a readiness to perceive and process incoming stimuli. The alerting system has been associated with superior parietal, right frontal, and thalamic brain regions and the norepinephrine neurotransmitter system.

The *orienting system* is responsible for selecting and giving preference to specific sensory information, often in terms of spatial location. Attentional orienting in space may be done overtly by, for example, moving the head or covertly, that is, without moving the eyes or head. For example, a football player might look down the field with his eyes while attending covertly to the location and movements of other players in his peripheral vision. Attended items are generally processed faster and more accurately than nonattended items. Brain areas that have been linked to the orienting system include areas of the parietal cortex and the frontal eye fields, and the cholinergic neurotransmitter system appears to play an important role.

The *executive attention system* is involved in monitoring one's performance in the context of current task demands and providing control signals that help other systems adapt to changing contexts and conflicting information. Executive attention is especially important for detecting and responding to situations in which there is stimulus–response conflict. Such conflict arises when two or more stimuli or two or more aspects of the same stimulus are associated with different behavioral responses. A common example is the Stroop task in which subjects are presented with printed words and they must name the color of the ink in which the word is printed (e.g., red ink) when the word itself spells out a different color (e.g., BLUE). Brain areas implicated in the executive attention system include frontal midline regions such as the anterior cingulate cortex and the lateral prefrontal cortex. The neurotransmitter dopamine is important in the functioning of this network.

The *Attention Network Task* (*ANT*) was developed by Jin Fan, Michael Posner, and colleagues at the Sackler Institute for Developmental Psychobiology. Using subtractive methodology, the ANT is designed to assess each of these three attentional networks using a single reaction-time paradigm. The fundamental task of the participant is simple. On each trial, the participant looks at a small *fixation cross* in the center of a computer screen and a small arrow, called the *target*, is briefly displayed either above or below the fixation. The participant is required to respond by pressing one of two buttons as quickly and accurately as possible indicating whether the arrow is pointing to the left or right. On some presentations, the target is preceded by a briefly presented cue stimulus while on other trials it is presented with no advanced warning. These cues are either predictive or non-predictive. *Orienting cues* are presented either above or below the central fixation and indicate the location at which the upcoming arrow will be shown. *Non-orienting cues* are presented either at the center of the screen or else both above and below fixation simultaneously. Both types of cues indicate that the target is about to appear but only orienting cues provide information regarding the location of the impending target. Finally, in some cases, the target arrow is flanked on either side by other stimuli. These *flanking stimuli* may be arrows pointing in the same direction as the target (called congruent trials) or they may be arrows pointing in the opposite direction as the target (called incongruent trials).

The efficiency of the three attention networks may be assessed independently for each participant by use of the subtractive method. Both reaction time and accuracy may be examined. To assess the alerting network, scores from trials in which no cue was presented are compared to scores from trials in which there was a cue presented. The difference in mean reaction times between these two trial types constitutes an *efficiency score* for the alerting network and is indicative of the extent to which the alerting network was able to use the information provided by the cue to improve behavioral performance. In a similar manner, an efficiency score for the orienting network may be derived by subtracting mean scores from trials with orienting cues from the scores for trials with non-orienting cues. Both of these trial types include a cue so there should be no difference in terms of a

contribution from the alerting network. The difference in scores measures the degree to which the orienting system could take advantage of the predictive cues to orient to a specific spatial location. In the case of the non-orienting cues, the participant could not predict whether the target would appear above or below the fixation point and therefore could not improve performance by orienting to one or the other spatial location. An efficiency score is derived for the executive attention system by comparing scores on trials with congruent flankers to trials with incongruent flankers. Subjects will tend to be slower and less accurate for incongruent trials than for congruent trials, and the size of these differences indicates the extent to which the individual is able to suppress conflicting response tendencies.

A number of intriguing findings have come from studies that have utilized the ANT. Supporting the notion that the three attention networks assessed by the ANT constitute independent systems, a large-scale study of over 200 individuals found that there was very little correlation in efficiency scores among the three networks. In other words, the particular score of an individual on any one of the three attention networks does not tend to predict that individual's scores on the other two networks. A high efficiency score for the alerting network, for example, does not suggest what one's scores are likely to be for either the orienting or executive attention networks. Using electroencephalographic (EEG) recordings from the surface of the scalp, it was found that each of these three attention systems is associated with distinct patterns of neural oscillations. A number of variations on the original ANT have been developed to address specific questions and for the study of special populations. For example, child-friendly versions of the ANT that use cartoon pictures of fish instead of arrows have been used to study the development of attention systems.

Attentional deficits are a hallmark of many psychiatric and neurological disorders. The ANT has been used to assess the relative impact of many disorders on the different attention systems and to help distinguish between or establish subtypes of particular disorders. Among others, variations on the ANT have proven useful in the study of attention deficit hyperactivity disorder, Alzheimer's disease, autism, borderline personality disorder, traumatic brain injury, substance abuse, and schizophrenia.

References and Readings

Fan, J., McCandliss, B. D., Sommer, T., Raz, A., & Posner, M. I. (2002). Testing the efficiency and independence of attentional networks. *Journal of Cognitive Neuroscience, 14*(3), 340–347.

Fan, J., McCandliss, B. D., Fossella, J., Flombaum, J. I., & Posner, M. I. (2005). The activation of attentional networks. *Neuroimage, 26*(2), 471–479.

http://www.sacklerinstitute.org/users/jin.fan/

Posner, M. I., & Rothbart, M. K. (2007). Research on attention networks as a model for the integration of psychological science. *Annual Review of Psychology, 58*, 1–23.

Attention Process Training

► Attention Training

Attention Span

► Span of Apprehension

Attention Training

McKay Moore Sohlberg
University of Oregon
Eugene, OR, USA

Synonyms

Attention process training, direct attention training, process training

Definition

Attention training is based on the premise that attentional abilities can be improved by activating particular aspects of attention through a stimulus drill approach. The repeated stimulation of attentional systems via graded attention exercises is hypothesized to facilitate changes in attentional functioning. Most attention training programs assume that aspects of cognition can be isolated and discretely targeted with training exercises.

Current Knowledge

The aspects of attention that are trained vary widely among interventions and frequently depend upon a theoretical model of attention. Attention models,

regardless of their operational framework, appear to include functions related to sustaining attention over time (vigilance), capacity for information, shifting attention, speed of processing, and screening out distractions. Some attention efficacy studies evaluate attention interventions that focus on particular attention components such as reaction time and sustained attention for visual information (e.g., Ponsford and Kinsella, 1988). Other efficacy studies use attention training programs that include hierarchical tasks to address a continuum of attention components from basic sustained attention to more complex mental control (e.g., Park, Proulx, & Towers, 1999; Sohlberg, McLaughlin, Pavese, & Heidrich, 2001).

Evidence supports the effectiveness of attention training beyond the effects of nonspecific cognitive stimulation for patients with traumatic brain injury or stroke during the postacute phase of recovery and rehabilitation (Butler, 2008; Cicerone et al., 2000). Evidence-based practice guidelines for attention training were generated from examination of the intervention research literature (Sohlberg et al., 2003). Analysis of nine Class I and Class II studies suggested that certain aspects of attention training are helpful in improving attention performance in some adults with traumatic brain injury. Treatment parameters found to influence positive outcomes included high frequency of attention training, combining attention training with metacognitive training (e.g, self monitoring and strategy training), and individualizing training to match the client's attention profile. The effects of attention training may be relatively small or task-specific, and the research encourages clinicians to actively facilitate and monitor the impact of attention training on functional, everyday activities.

Cross References

- ► Attention
- ► Attention/Executive Functions
- ► Neuropsychological Rehabilitation
- ► Plasticity
- ► Process Training

References and Readings

Butler, R. W., Copeland, D. R., Fairclough, D. L., Mulhern, R. K., Katz, E. R., Kazak, A. E. et al. (2008). A multicenter, randomized clinical trial of a cognitive remediation program for childhood survivors of a pediatric malignancy. *Journal of Consulting and Clinical Psychology, 76*(3), 367–378.

Cicerone, K. D., Dahlberg, C., Kamar, K., Langenbahn, D. M., Malec, J. F., Bergquist, T. F. et al. (2000). Evidence-based cognitive rehabilitation: Recommendations for clinical practice. *Archives of Physical Medicine & Rehabilitation, 81*, 316–321.

Galbiati, S., Recla, M., & Pastore, V. (2009). Attention remediation following traumatic brain injury in childhood and adolescence. *Neuropsychology, 23*(1), 40–49.

Park, N. W., & Ingles, J. L. (2001). Effectiveness of attention rehabilitation after acquired brain injury: A meta-analysis. *Neuropsychology, 15*, 199–210.

Park, N. W., Proulx, G., & Towers, W. M. (1999). Evaluation of the attention process training programme. *Neuropsychological Rehabilitation, 9*, 135–154.

Sohlberg, M. M., Avery, J., Kennedy, M., Ylvisaker, M., Coelho, C., Turkstra, L., & Yorkston, K. (2003). Practice guidelines for direct attention training. *Journal of Medical Speech Language Pathology, 11*(3), xix–xxxix.

Sohlberg, M. M., McLaughlin, K. A., Pavese, A., Heidrich, A., & Posner, M. (2001). Evaluation of attention process training and brain injury education in persons with acquired brain injury. *Journal of Clinical and Experimental Neuropsychology, 22*, 656–676.

Attentional Response Bias

Ronald A. Cohen
Brown University
Providence, RI, USA

Definition

Attentional response bias refers to the tendency to respond to the targets of attention on a particular task or in a given context. This tendency is often operationalized using signal detection theory based on possible error types that can occur; that is, either misses (errors of omission) or false positive (errors of commission). The proportion of these types of errors can be expressed as an index corrected relative to the total number of errors of all types made (β: beta). A person who makes a much larger number of errors of commission than errors of omission (misses) is exhibiting a response bias toward responding by indicating they detected the target even when it was not presented, which in many cases reflects excessive impulsivity or inhibitory control problems. Conversely, a tendency to miss targets, but to rarely make false positive efforts, suggests that the patient may be trying hard to never make an error, which in turn results in not responding when they should. This is often observed in patients who lack motivation, are depressed, or who experience problems because of slowed processing speed. In healthy individuals, response bias can be influenced by

instructional set, reward, or other factors that shift the likelihood of responding or not responding.

Cross References

► Continuous Performance Test
► Signal Detection Theory

Attention-Deficit/Hyperactivity Disorder (ADHD)

► Minimal Brain Dysfunction

Attorney

Moira Dux
Rosalind Franklin School of Medicine
Baltimore, MD, USA

Definition

An attorney is defined as one who is legally appointed on another's behalf. An attorney-at-law is an individual who has achieved the necessary educational requirements (J.D.) and is licensed to practice law by the highest court of a state or some other form of jurisdiction. In civil cases (e.g., personal injury, medical malpractice), there are plaintiff and defense attorneys. The plaintiff attorney represents the injured party (e.g., plaintiff) in an action against the party they allege to be responsible for the damages; the defense attorney represents the defendant (e.g., insurance company, hospital, and doctor). In criminal matters, there are prosecution and defense attorneys. The prosecuting attorney represents the party (e.g., Federal, State, or local government) who has accused and wants to convict the offender of some type of criminal action (e.g., murder, assault). The defense attorney represents the party (e.g., defendant) who has been accused of committing the crime.

Cross References

► Litigation

References and Readings

Larrabee, G. (2005). *Forensic neuropsychology: A scientific approach.* New York: Oxford University Press.
Stern, B. H., & Brown, J. (2007). *Litigating brain injuries.* New York: Thomson Reuters.

Atypical Antipsychotic

► Neuroleptics

Atypical Autism

► Pervasive Developmental Disorder NOS

Atypical Teratoid/Rhabdoid Tumor (AT/RT)

Jennifer Tinker
Drexel University
Philadelphia, PA, USA

Definition

Atypical Teratoid/Rhabdoid Tumor (AT/RT) is a rare, highly malignant tumor of early childhood, most commonly diagnosed in infants who are less than 2 years. First described by Rorke and colleagues in 1987 (Lefkowitz, Rorke, & Packer, 1987), the AT/RT received its designation because of its complex histological components. Prognosis is extremely poor with a median survival of 6–11 months. Over half of AT/RTs identified are located within the posterior fossa (brainstem, cerebellum, and predominantly the cerebello-pontine angle) (Rorke, Packer, & Biegel, 1996). Clinical presentation varies largely by tumor location and size. Infants, in particular, may present with nonspecific symptoms, including lethargy and failure to thrive. Older children (>3 years of age) may demonstrate more specific problems, including head tilt, cranial nerve palsy, headache, and hemiplegia (Rorke & Biegel, 2000). Often histologically confused with PNET/medulloblastoma.

Cross References

► Medulloblastoma
► Primitive Neuroectodermal Tumor

References and Readings

Lefkowitz, I. B., Rorke, L. B., & Packer, R. J. (1987). Atypical teratoid tumor of infancy: definition of an entity. *Annals of Neurology, 22*, 56–65.

Rorke, L. B., & Biegel, J. A. (2000). Atypical teratoid/rhabdoid tumour. In P. Kleihues & W. K. Cavenee (Eds.), *World health organization classification of tumours. Pathology & genetics. tumours of the nervous system* (pp. 145–148). Lyons, France: IARC Press.

Rorke, L. B., Packer, R. J., & Biegel, J. A. (1996). Central nervous system atypical teratoid/rhabdoid tumors of infancy and childhood: definition of an entity. *Journal of Neurosurgery, 85*, 56–65.

Atypicals (antipsychotics)

► Antipsychotics

Auditory Agnosia

John E. Mendoza
Tulane University Medical Center
New Orleans, LA, USA

Synonyms

Auditory-sound agnosia; Auditory-verbal agnosia; Pure word deafness

Definition

Rare condition in which sounds, although heard, are not properly interpreted and thus have little or no meaning for the patient.

Current Knowledge

When present, auditory agnosia, is usually primarily limited to impaired recognition of either language sounds or nonlanguage (environmental) sounds. The former is known as *auditory-verbal agnosia* or *pure word deafness*. No commonly used term is applied to the latter. In either condition, appreciation of certain aspects of musical sounds might also be compromised (*amusia*). For this syndrome to be diagnosed, other higher order deficits that might more readily explain the deficit (such as aphasic disorder) should be ruled out. In auditory-verbal agnosia there is impairment of one's ability to process, interpret, or comprehend speech sounds or spoken language. Patients may report that it is like hearing someone speaking in a foreign language. Reading, writing, and speaking are intact, although speaking may be slightly problematic due to the distortions in auditory feedback heard as speech is attempted. In auditory-verbal agnosia (pure word deafness), the ability to match nonspeech or "environmental" sounds (e.g., a barking dog, the ringing of a bell, or a train whistle) to corresponding pictures may remain intact. Conversely, one may have difficulties identifying or matching nonspeech sounds, while retaining the ability to process and interpret spoken language. Some degree of impairment in one's ability to recognize musical sounds is commonly, but not invariably, present in these disorders. Select patients may have difficulty recognizing familiar tunes or melodies, while retaining their ability to produce them spontaneously. Others may be impaired at matching tones, rhythms, or timbre, for example, identifying the sound of a particular musical instrument.

Auditory agnosia is thought to result from either (1) unilateral or bilateral lesions of the unimodal (secondary) auditory association cortex in the middle portions of the superior temporal gyrus and/or (2) a disconnection syndrome involving the primary auditory cortex (Heschl's gyrus) of one hemisphere and the subcortical projections from the opposite hemisphere to the unimodal auditory association cortex on that same side. Such lesions would allow elementary sounds to be heard (as one or both of Heschl's gyri are intact), but would produce impaired higher level processing due to damage or inaccessibility to the unimodal cortex. With critically placed bilateral lesions of the superior temporal gyri, an agnosia for all types of complex auditory input may be present. Auditory-verbal agnosia is more likely to result from left-sided lesions as described above, while auditory agnosia for nonspeech sounds is more likely to be associated with right hemispheric lesions. Agnosia for musical sounds may also be differentially affected, but in an even less consistent manner.

Cross References

► Agnosia
► Amusia
► Disconnection Syndromes

References and Readings

Bauer, R. M., & Demery, J. A. (2003). Agnosia. In K. Heilman & E. Valenstein (Eds.), *Clinical neuropsychology* (4th ed., pp. 236–295). New York: Oxford University Press.

Auditory and Visual Evoked Potentials

► Event-Related Paradigms

Auditory Brainstem Response Audiometry

► Brainstem Auditory Evoked Responses

Auditory Brainstem Responses (ABR)

► Brainstem Auditory Evoked Responses

Auditory Cortex

John E. Mendoza
Tulane University Medical Center
New Orleans, LA, USA

Definition

That portion of the cerebral cortex devoted exclusively to the processing of input from the medial geniculate nuclei (auditory information).

Current Knowledge

Located in the superior portion of the temporal lobe of each hemisphere, the auditory cortex consists of both primary (*idiotypic*) and secondary (*unimodal homotypic*) cortices. The former is located in the temporal operculum (Brodmann's area 41 and part of 42) and is referred to as Heschl's gyrus. The primary auditory cortex receives direct input from the medial geniculate nuclei of the thalamus, which it is thought to process auditory input at a very basic level with little, if any, distinction between the right and left hemispheres. The secondary auditory cortex (primarily Brodmann's area 22) surrounds the primary cortex and, for the most part, is located in the lateral portion of the superior temporal gyrus. The posterior portion of this secondary cortex in the left hemisphere constitutes *Wernicke's area*. These secondary cortices are thought to be responsible for the further refinement of auditory input, organizing it into meaningful or potentially meaningful percepts. Lesions of Wernicke's area (left hemisphere) are associated with severe comprehension and other language-related deficits, whereas comparable lesions in the right hemisphere may be associated with difficulty recognizing or interpreting nonlanguage sounds. Such lesions in the right hemisphere might help account for the inability of some patients to comprehend or interpret the emotional tones or inflections in spoken language, which may convey more meaning than the actual words themselves (i.e., receptive aprosodia).

Cross References

► Aprosodia
► Auditory Agnosia
► Homotypic Cortex
► Idiotypic Cortex

Auditory Discrimination

Beth Kuczynski[1], Stephanie A. Kolakowsky-Hayner[2]
[1]University of California
Davis, CA, USA
[2]Santa Clara Valley Medical Center,
Rehabilitation Research Center
San Jose, CA, USA

Synonyms

Auditory processing

Definition

Auditory discrimination is the ability to recognize differences in phonemes (the smallest unit of sound in a

language), including the ability to identify words and sounds that are similar and those that are different. Auditory discrimination tests are performed to measure a person's phonological awareness, such as the ability to focus on and manipulate phonemes within spoken words. Impaired auditory discrimination should be addressed early in child development as it is pertinent to learning and development.

Cross References

- ▶ Language
- ▶ Phonological Disorders
- ▶ Phonology

References and Readings

Gordon-Brannan, M. E., & Weiss, C. E. (2008). *Clinical management of articulatory and phonologic disorders* (3rd ed.). Philadelphia, PA: Lippincott Williams & Wilkins.

Moller, A. R. (2000). *Hearing: Its physiology and pathophysiology.* San Diego, CA: Academic Press.

Warren, R. M. (1999). *Auditory perception: A new synthesis* (2nd ed.). New York: Cambridge University Press.

Warren, R. M. (2008). *Auditory perception: An analysis and synthesis* (3rd ed.). New York: Cambridge University Press.

Auditory Evoked Response (AER)

- ▶ Brainstem Auditory Evoked Responses

Auditory Pathway

Woon Chow
Virginia Commonwealth University
Richmond, VA, USA

Definition

The auditory neural pathway in the central nervous system transmits and processes sound signals from the ear to the cortex. The configuration of the pathway is multisynaptic and bilaterally projecting.

Current Knowledge

From the Outer Ear to the Cochlear Nuclei

Sound is transmitted through the air as longitudinal waves, enters the outer ear, and vibrates the tympanic membrane. The three ossicles (malleus, incus, and stapes) amplify and transmit these vibrations to the oval window, producing waves in the scala vestibuli, a fluid-filled compartment within the coil-shaped cochlea of the inner ear. These fluid waves distort the stiff basilar membrane. Residing on the membrane, hair cells within the organ of Corti transduce the minute movements of the membrane into the graded release of glutamate onto the peripheral processes of bipolar afferent fibers, whose cell bodies are located in the spiral ganglion. The central processes exit the base of the cochlea, form the auditory trunk of the vestibulocochlear nerve (eighth cranial nerve, CN VIII), and project ipsilaterally to the ventral and dorsal cochlear nuclei in the brainstem.

From the Cochlear Nuclei to the Superior Olivary Nuclei

Fibers from the dorsal cochlear nucleus decussate to the contralateral inferior colliculus via the lateral lemniscus. Fibers from the ventral cochlear nuclei project ipsilaterally to the superior olivary nucleus and also decussate via the trapezoid body to the contralateral superior olivary nucleus. This circuit provides temporal and intensity differences in the horizontal plane between right and left ear to aid in sound source localization. Because of the bilateral nature of these afferent projections, central lesions rarely result in total unilateral hearing loss.

From the Superior Olivary Nuclei to the Medial Geniculate Nuclei

Afferent fibers from the superior olivary nuclei merge with other audition-associated ascending fibers and project via the lateral lemniscus to the inferior colliculus. The inferior colliculus receives bilateral inputs from almost all audition-related nuclei and acts as a nearly obligatory relay in the ascending auditory pathway. It is here that horizontally oriented and vertically oriented sound source localization data is fully and finally integrated. Ascending fibers from the inferior colliculus project ipsilaterally to

the last subcortical relay station, the medial geniculate nucleus.

Located in the posteroinferior portion of the thalamus, the medial geniculate nucleus is a relay between the inferior colliculus in the brainstem and the auditory cortex. The medial geniculate nucleus plays a role in directing and maintaining attention.

From the Medial Geniculate Nuclei to Heschl's Gyri

Outputs from the medial geniculate nucleus project via the internal capsule to the ipsilateral primary auditory cortex located in the posterior portion of the superior temporal gyrus of Heschl. At the cortical level, detected sound is finally perceived. Bilateral lesions of the auditory cortex remove the conscious perception of sounds, but because of extensive subcortical processing, an individual may still react reflexively to a sound without actually "hearing" it.

Tonotopic Mapping

One idea of note is tonotopy, which is the spatial arrangement of where particular frequencies of sound are relayed and processed within the auditory system. In the cochlea, high frequency sounds are detected by hair cells at the base and low frequency sounds at the apex. This tonotopic organization is preserved systematically all the way up to the primary auditory cortex, where higher frequency sounds are mapped to a more medial location on the superior temporal gyrus whereas lower frequency sounds are mapped to a more anterolateral location.

Cross References

- ▶ Auditory Cortex
- ▶ Auditory System
- ▶ Cochlea
- ▶ Cochlear Nuclei (Dorsal and Ventral)
- ▶ Heschl's Gyrus
- ▶ Inferior Colliculi
- ▶ Internal Capsule
- ▶ Lateral Lemniscus
- ▶ Medial Geniculate Nuclei
- ▶ Trapezoid Body
- ▶ Vestibulocochlear Nerve

Auditory Perceptual Disorder (APD)

▶ Central Auditory Processing Disorder

Auditory Processing

Scott L. Decker, Jessica A. Carboni
Georgia State University
Atlanta, GA, USA

Definition

Auditory processing is a term used to describe the process in which sound waves are transduced into neurological impulses and decoded by the primary auditory cortex in the temporal lobe of the brain. Further processing involves general sound detection and language sounds.

Object vibration causes molecules of air surrounding it to condense and pull apart, producing waves that travel away from the object. Receptor cells within our ears will be stimulated if the vibration ranges between approximately 30 and 20,000 times per second (Carlson, 2007). These waves will then be perceived as sound.

There are three dimensions of sound: pitch, loudness, and timbre. The pitch of an auditory stimulus is determined by the frequency of vibration or cycle per second (Hertz). Intensity of sound is a function of loudness, whereas vigorous vibrations of an object produce more intense sound waves thus producing louder sounds. Information regarding the nature of sound is produced through timbre.

Our ears are able to detect stimuli, determine the spatial location of those stimuli, and recognize the identity of such stimuli.

Cross References

- ▶ Auditory Discrimination
- ▶ Auditory Pathway

References and Readings

Carlson, N. R. (2007). *Physiology of behavior* (8th ed.). Boston: Pearson.

Auditory Processing Disorder (APD)

► Central Auditory Processing Disorder

Auditory Sensory Memory

► Echoic Memory

Auditory Spatial Processing

► Spatial Processing

Auditory System

Maryellen Romero
Tulane University Health Sciences Center
New Orleans, LA, USA

Structure

The structure and function of the human auditory system was first postulated by the physicist George Ohm more than 100 years ago. Dr. Ohm theorized that the auditory system's main function was to translate complex sound material into highly specialized vibratory signals that could then be processed in the brain and recoded as recognizable entities. At a very basic level, the auditory system might be considered as being composed of three primary structures and their interconnections. The first of these is the ear, which itself is typically divided into three components. The outer or external ear is that which is visible, the *pinna* and the *auditory meatus* or ear canal which terminates at the *tympanic membrane* or ear drum. Next is the middle ear which primarily consists of a linked series of three small bones, the *malleus*, *incus*, and *stapes*, which act together as a system of levers. The former is attached to the tympanic membrane and the latter to the oval window of the inner ear. The middle ear is connected to the oral cavity by the eustachian tube which allows for equalization of pressure on either side of the tympanic membrane. The semicircular canals, the vestibule, and the cochlea comprise the inner ear. The first two constitute the end organs for the vestibular system, whereas the *cochlea* and *organ of Corti* contained within it represent the origin of the nerve impulses that eventually are translated into sounds.

The second set of structures in the auditory system is the brainstem nuclei associated with hearing. The *dorsal* and *ventral cochlear nuclei* located in the region of the pontine–medullary junction represent the origin of the second-order auditory fibers. Next in line are the *superior olivary nuclei*, which lie in the pons and are the first nuclear group to receive auditory input from both ears. The next and final *major* nucleus concerned with hearing in the brain stem is the *inferior colliculus*, a paired structure in the dorsal portion of the midbrain.

The brain itself might be considered the third portion of the auditory system. The two most critical structures here are the medial geniculates of the thalamus, and Heschl's gyri (Brodmann's area 41) which lie in the temporal operculum (within the lateral fissure) of each hemisphere. It is this last structure, in conjunction with its adjacent secondary auditory cortices, which is responsible for processing the auditory input into meaningful information.

Finally, there are the major pathways that interconnect these various structures. The auditory portion of the vestibulo-cochlear nerve (CN VIII) is the first-order neuronal pathway in the auditory system. It has its origins in the organ of Corti and terminates in the dorsal and ventral cochlear nuclei. The *acoustic stria* (dorsal, ventral, and intermediate) form the second-order neurons of the auditory system. What is important to note is that while most fibers cross the midline, some remain ipsilateral, thus at a very early stage there is bilateral input from each ear. The *trapezoid body* of the pons represents one such major crossing of these auditory fibers (primarily those from the ventral acoustic stria). Most of these second-order fibers synapse in the superior olivary nuclei, although some proceed directly to the inferior colliculi. The *lateral lemniscus*, again consisting of both crossed and uncrossed fibers, interconnects the superior olivary nuclei with the inferior colliculi. From there, the *brachium of the inferior colliculi* carries auditory signals to the medial geniculates which, in turn, project ipsilaterally to the primary auditory cortices. It should be noted that, due to the arrangement of the auditory pathways, by the time these signals reach the cortex they are derived from both ears, with approximately 60% coming from the contralateral ear and 40% from the ipsilateral one.

Function

Joseph Fourier, a French mathematician, identified the physical and mathematical properties of sound waves and described the transformation of such stimuli into frequency, amplitude, and phase, which govern discrete elements of sound such as loudness and pitch. In its raw, unprocessed state, sound exists in the form of vibration that results in alterations in the pressure of the air in the immediate environment. These alterations in pressure take the form of waves that have a specific *frequency* or combination of frequencies as well as intensity. The *frequency* of the sound wave, as measured by hertz (Hz) is the major determinant of the *pitch* of the resulting sound, experienced by the listener as high or low. The *amplitude* of the wave, or its height, is the major determinant of the *loudness* of the resulting sound, measured in *decibels (dB)*. The human ear is capable of capturing sound over a considerable frequency range, approximately 20–20,000 Hz.

The transduction of sound waves into the perception of sound is complex. Vibrations entering the *external auditory meatus* strike the *tympanic membrane*, causing it to vibrate. This vibration is transferred directly to the *ossicles*; first the *malleus*, which is attached to the *tympanic membrane*, followed by the *incus* and then the *stapes* which sets the oval window of the inner ear in motion. The vibration is then picked up by the fluids (perilymph and endolymph) of the cochlea, first setting the perilymph of the scala vestibuli and then the endolymph of the organ of Corti and basilar membrane upon which its rests, and finally the perilymph of the scala tympani from where it is dissipated via the round window of the inner ear. In the course of this activity, the basilar membrane is differentially affected depending on the frequency of the waves causing the hair cells along its length to be stimulated, initiating patterns of nerve impulses that correspond to the particular pitch. This very discrete information is picked up by the *auditory nerve* (CN VIII) in the form of bioelectrical nerve impulses, which then are propagated through the various pathways described above until eventually reaching the cerebral cortex where they are eventually interpreted as speech or other sounds.

Illness

Damage to any part of the auditory system, from cerumen (wax) in the auditory canal to bilateral cortical lesions (exceedingly rare) can result in hearing deficits. Because of the multiple crossings and ipsilateral connections within the system, hearing loss which is confined to one ear normally implies damage no higher than the cochlear nuclei. Pure word deafness (intact hearing with the inability to understand spoken language without other major aphasic deficits) can result from a relatively rare occurrence of damage to Heschl's gyrus on the left and a dissociation of input to the secondary association areas from the non-dominant hemisphere. Damage at intermediate levels may result in poor localization of sounds. Aside from ponto-medullary strokes, unilateral (or bilateral) hearing loss is most commonly the result of damage to the middle or inner ear or the nerves that emanate from the latter. Any of many causes could be the problem, from prolonged exposure to loud noises, trauma, infections, medications, and, of course, simply aging. While formal assessments of hearing loss are best left to audiologists, a gross assessment of hearing acuity is important to better understand why a particular patient may be having difficulty either on examination of mental status or coping at home or on the job. Given a hearing loss, neurologists will often try to differentiate its particular nature. Two types of peripheral hearing loss (i.e., not due to a lesion of the brain stem or above) are typically identified, conductive and sensorineural. The former, which is generally more amenable to treatment, is a result of a problem with the external or middle ear, while the latter implies damage to the inner ear. These can often be distinguished by a couple of procedures using a tuning fork (preferably 512 Hz). In the first, the ability of the patient to hear the vibration is tested by comparing air to bone conduction (*Rinne test*). Here the base of the vibrating tuning fork is applied to the mastoid process just behind the ear. When the sound is said to have dissipated, the ends of the fork are immediately moved near the auditory canal (air conduction). If the problem is in the middle ear, the sound will not be heard. Conversely, if the sound is heard better via air than bone conduction, a sensorineural (inner ear) deficit is suspected. It should be noted that for normals, air conduction will be superior to bone conduction, but one should be looking for relative differences in acuity, not absolute auditory thresholds as the latter will likely lowered in the affected ear. A second procedure is to press the base of the tuning fork on the middle of the forehead. If there is a sensorineural loss, the sound will be localized to the unaffected ear, while it will be localized (sound louder) in the affected ear in a conductive hearing loss. This latter procedure is referred to as the *Weber test*.

Another common problem associated with hearing is *tinnitus*, a buzzing, ringing, or other repetitive noxious sound in one or both ears. It can be relatively brief or chronic. If the latter, it can be very disturbing to the patient. The causes can be multiple, including certain

drugs (e.g., aspirin), aftereffects of exposure to loud noises, infections, or occasionally may represent the initial symptoms of a more serious condition such as a brainstem tumor. Unfortunately, treatment options for this condition are quite limited. Having background noise, such as music, is often helpful.

Cross References

- ► Aphonia
- ► Auditory Cortex
- ► Auditory Pathway
- ► Cochlea
- ► Pure Word Deafness
- ► Tinnitus
- ► Weber Test

References and Readings

Bradley, W. G., Daroff, R. B., Fenichel, G. M., & Jankovic, J. (2004). *Neurology in clinical practice: Principles of diagnosis and management – Fourth Edition.* Philadelphia, PA: Butterworth-Heineman.

Wilson-Pauwek, L., Akesson, E. J., Stewart, P. A., & Spacey, S. D. (2002). *Cranial nerves in health and disease.* Hamilton, ONT: B.C. Decker, Inc.

Auditory Verbal Learning

Judy Creighton[1], H. Allison Bender[2]
Stephanie Assuras[1], Jennifer Woehr[3]
Joan C. Borod[1,3], Nancy S. Foldi[1,4]
[1]Queens College and The Graduate Center of the City University of New York
Flushing, NY, USA
[2]New York University Langone Medical Center
New York, NY, USA
[3]Mount Sinai School of Medicine
New York, NY, USA
[4]State University of New York, Stony Brook School of Medicine
Mineola, NY, USA

Description

An auditory verbal learning task typically requires individuals to hear a list of items, learn those items, and recall and/or recognize them at a later time. These tasks assess acquisition and retrieval components of memory, including encoding, learning characteristics, storage, consolidation over short- or long-time intervals, and subsequent access to the information either by free retrieval or recognition. The nature of the test composition, the instructions to the individual, and the scoring dictate what conclusions are drawn from the task.

Auditory verbal learning tasks (AVLTs) are used in both clinical and research settings, and are a hallmark of memory assessment. Recent versions of these tests include the California Verbal Learning Test-II (CVLT-II; Delis, Kaplan, Kramer, & Ober, 2000), Hopkins Verbal Learning Test-R (HVLT-R; Brandt & Benedict, 2001), World Health Organization/UCLA Auditory Verbal Learning Test (WHO/UCLA AVLT; Maj et al., 1993), Rey Auditory Verbal Learning Test (RAVLT; Schmidt, 1996), Neuropsychological Assessment Battery (NAB; Stern & White, 2003), and List Learning in the Center to Establish Registry for Alzheimer's Disease (CERAD; Morris et al., 1989; Welsh, Butters, Hughes, Mohs, & Heyman, 1991). Other commonly used list-learning tasks (e.g., ADAS-COG; Rosen, Mohs, & Davis, 1984), like the Free and Cued Selective Reminder Task (FCSRT; Buschke, Sliwinski, Kuslansky, Katz, Verghese, & Lipton, 2006; Grober, Merling, Heimlich, & Lipton, 1997), are not solely auditory, adding visual words or picture presentations of items.

List-learning tasks share many design features. The number of words in the to-be-learned list (e.g., 12–16 items) has been designed to exceed the typical vigilance span of seven items and to stress learning demands. The learning phase is the presentation of the list across several trials. Following each trial, the examinee is asked to recall as many items as possible. Once the learning is complete, a short time interval elapses, usually including interference tasks designed to prevent rehearsal of the list items. The examinee is then asked to recall items from the list, constituting a short term recall. After another longer interval, again containing some distraction, a recall is requested. These short- and long-term retrieval assessments capture the examinee's ability to store, consolidate, and maintain information, as well as to retrieve it on command. Tests can include a subsequent multiple- or forced-choice task to facilitate access, capturing the items that were encoded but could not be accessed on free retrieval.

Despite commonalities, instruments vary in content and administration. List construction on some tests (e.g., ► CVLT-II, ► HVLT-R, WHO/UCLA ► AVLT, and

► NAB) incorporates semantic categories, whereas others do not (e.g., ► RAVLT, ► CERAD, and ADAS-COG). Examinees are not initially informed of these categories in order to determine whether they can exploit semantic information to their advantage and to facilitate their ability to organize, encode, and learn more items. To ensure and document that any particular item is fully encoded with semantic knowledge, the FCSRT adopts an alternate use of semantic organization by cueing examinees with the semantic category while the word is being learned and by prompting the category immediately afterward. Another variation among tests is the use of interference lists. For instance, after the initial learning phase of the target lists in the CVLT-II and NAB, an alternate list is administered, designed to share some but not all of the semantic categories of the target list. This helps to address susceptibility to interference and source learning. Other tests (e.g., ► HVLT-R and FCSRT) do not have prescribed interference tasks, although other word-list or naming tasks should not be used during the delay. Delayed recall is commonly tested after a 20–30-min interval. There are various methods to assess the recognition memory of the target list. Examinees can identify target-list words among a list of distracters (CVLT-II, HVLT-R, and NAB) or identify targets in forced- (CVLT-II) or multiple-choice (FCSRT) recognition trials. While most tasks use recognition after short- (NAB) or long-term (CVLT-II and HVLT-R) free recall, one test (ADAS-COG) relies exclusively on the immediate recognition to assess learning.

AVLTs reveal significant information about learning and memory processes. The multiple trial exposure generates an individual's learning curve, indicating whether information learned on an earlier trial is maintained and appended with new information. Learning characteristics, particularly serial position effects (i.e., primacy and recency effects), provide insight about how learning occurs. For instance, the dual storage model (Raaijmakers & Shiffrin, 1981) suggests that items from primacy and middle regions of the lists are thought to reflect long-term storage, whereas recent items remain in immediate working memory. The position of an item in the list, known as the distinctiveness feature, can also aid in later recall, with the distinct first or last items having preference. Susceptibility to proactive and/or retroactive interference of the interference list or shared semantic categories of target items are analyzed. Long-term retention of verbal information can be parsed into storage and retrieval components via examination of free-recall versus recognition scores.

Historical Background

Word lists have been used to assess learning and memory for over a century. Ebbinghaus (1885) was early to observe and describe the serial position phenomenon. Eduoard Claparède (Boake, 2000) assessed learning and memory in his work on child pedagogy in 1916 using a 15-item word list, which was adapted by André Rey to develop the RAVLT in 1941. The RAVLT, first published in France, has been adapted since its development and modified for use in multiple languages. In 1996, the RAVLT manual (Schmidt, 1996) was published, providing standard instructions on administration, scoring, and interpretation. The original CVLT, published in 1987 (Delis, Kramer, Kaplan, & Ober, 1987), incorporated semantic categories, scorings of learning characteristics, use of semantic strategy, and contrast measures of learned and retrieved items. The CVLT-II revision (Delis et al., 2000), published in 2000, adopted new norms.

The CVLT–Children's Version (Delis, Kramer, Kaplan, & Ober, 1994) is appropriate for children in the age group of 5–16 years. The HVLT (Brandt, 1991) was introduced with six alternate forms designed for longitudinal, repeated testing, and the revised version (Brandt & Benedict, 2001) incorporated delayed recall and recognition trials. The newest list-learning task from the NAB (Stern & White, 2003) has been normed on individuals up to 97 years of age. The WHO/UCLA AVLT was designed by the WHO in 1993 to better evaluate examinees worldwide (Maj et al., 1993). When designing this instrument, the authors were careful to select words that were familiar across multiple cultures. Similar to the CVLT-II, the words comprising the WHO/UCLA AVLT can be classified into categories. However, the categories of the WHO/UCLA AVLT are universally familiar (i.e., body parts, animals, tools, household objects, and transportation vehicles). Of note, the WHO/UCLA AVLT is a component of the Neuropsychological Screening Battery for Hispanics (Ponton et al., 1996).

Psychometric Data

Normative data for AVLTs span an age range of 7–97 years. Groups used in normative data include healthy adults, men, women, and Hispanic individuals. Stratified norms according to age, sex, ethnicity, educational level, and region of the country (e.g., Northeast) are also available. Many tests (e.g., ► CVLT-II and ► CERAD) have been normed for European, Asian, and Southeast Asian groups.

Direct translation of word lists into other languages should be avoided, as words may have been selected to accommodate word frequency within a language or appropriateness within a culture. Some AVLTs are targeted for certain populations using shorter versions and more age-appropriate word lists (e.g., ▶ CVLT-C). Shorter forms have also been adopted for more impaired individuals (e.g., ▶ CVLT-II, Short Form; Delis et al., 2000).

Verbal learning tests are used to evaluate memory performance over time. Test–retest reliability using the same version of the test has been evaluated for 1-month as well as 1-year intervals. Many tests have adopted alternate or multiple forms. Whereas alternate versions can reduce practice effects, there is evidence that these effects are not completely eliminated (Houx et al., 2002) due to procedural learning. Therefore, examiners must be very cognizant of practice effects. Even after 2 years, healthy older adults showed practice effects on the CVLT-II (Blasi, Zehnder, Berres, Taylor, Spiegel, & Monsch, 2009).

Construct validity of adult and child versions of the CVLT in assessing learning and memory has been examined in several studies. Attention span, learning efficiency, delayed recall, and inaccurate recall represent one example of a four-factor model that was identified by a factor analysis in a sample of children with traumatic brain injury (Mottram & Donders, 2005). Variability across studies may be a result of methodological differences, demographic differences, severity of patient population, and/or time elapsed between disease onset and assessment.

In terms of inter-test relationships, tests are not interchangeable, as word lists and administrations vary significantly. However, the RAVLT correlates moderately with the CVLT-II. The CVLT-II is now incorporated into the Wechsler Memory Scale – IV as a valid component of the memory indices. The HVLT-R also shows a high correlation with the CVLT-II, although it may be more appropriate for greater disease severity.

Clinical Uses

Verbal learning tests are ubiquitous in assessments of memory-impaired populations. Amnesic disorders, degenerative dementias (including Alzheimer's, Parkinson's, and Huntington's disease), temporal lobe epilepsy, traumatic brain injury, depression, and focal stroke are diseases that have not only benefited from these tests, but also have promoted refinements and further development to extend our knowledge of the neuropsychological underpinnings of memory function. These instruments evaluate both quantitative and procedural aspects of verbal learning, providing detailed information about an individual's capacity to acquire, consolidate, store, and retrieve information, thus revealing significant aspects of the learning and retrieval processes. Learning characteristics, particularly primary and recency serial position effects (Foldi, Brickman, Schaefer, & Knutelska, 2003), are highly informative in differentiating clinical populations and provide insight about how learning is occurring. A detailed step-by-step exploration of each individual's learning process enables the clinician or researcher to identify specific areas of vulnerability and can guide intervention strategies.

Auditory verbal learning tasks have been instrumental in assessing change in memory over time. The auditory verbal learning paradigm has been very sensitive in discriminating between healthy and memory-impaired groups. A vast literature demonstrates the sensitivity of these tests to the detection of prodromal Alzheimer's disease.

Cross References

▶ California Verbal Learning Test-II
▶ California Verbal Learning Test-II, Children's Version
▶ Consortium to Establish a Registry for Alzheimer's Disease (CERAD)
▶ Hopkins Verbal Learning Test – Revised
▶ Memory
▶ Neuropsychological Assessment Battery
▶ Rey Auditory Verbal Learning Test

References and Readings

Blasi, S., Zehnder, A. E., Berres, M., Taylor, K. I., Spiegel, R., & Monsch, A. U. (2009). Norms for change in episodic memory as a prerequisite for the diagnosis of mild cognitive impairment (MCI). *Neuropsychology, 23*, 189–200.

Boake, C. (2000). Edouard Claparède and the Auditory Verbal Learning Test. *Journal of Clinical and Experimental Neuropsychology, 22*, 286–292.

Brandt, J. (1991). The Hopkins Verbal Learning Test: Development of a new memory test with six equivalent forms. *The Clinical Neuropsychologist, 5*, 125–142.

Brandt, J., & Benedict, R. (2001). *Hopkins Verbal Learning Test-Revised.* Lutz, FL: Psychological Assessment Resources.

Buschke, H., Sliwinski, M. J., Kuslansky, G., Katz, M., Verghese, J., & Lipton, R. B. (2006). Retention weighted recall improves discrimination of Alzheimer's disease. *Journal of the International Neuropsychological Society, 12*, 436–440.

Delis, D. C., Kaplan, E., Kramer, J. H., & Ober, B. A. (2000). *California Verbal Learning Test – II* (2nd ed.). San Antonio, TX: The Psychological Corporation.

Delis, D. C., Kramer, J., Kaplan, E., & Ober, B. A. (1994). *California Verbal Learning Test – Children's Version.* San Antonio, TX: Pearson.

Delis, D. C., Kramer, J. H., Kaplan, E., & Ober, B. A. (1987). *California Verbal Learning Test: Adult Version.* New York: The Psychological Corporation.

Ebbinghaus, H. (1885). *Memory: A contribution to experimental psychology* (H. A. Ruger & C. E. Bussenenues, Trans., 1913). New York: Teachers College, Columbia University.

Foldi, N. S., Brickman, A. M., Schaefer, L. A., & Knutelska, M. E. (2003). Distinct serial position profiles and neuropsychological measures differentiate late life depression from normal aging and Alzheimer's disease. *Psychiatry Research, 120*, 71–84.

Grober, E., Merling, A., Heimlich, T., & Lipton, R. B. (1997). Free and cued selective reminding and selective reminding in the elderly. *Journal of Clinical and Experimental Neuropsychology, 19*, 643–654.

Houx, P. J., Shepherd, J., Blauw, G. J., Murphy, M. B., Ford, I., Bollen, E. L., et al. (2002). Testing cognitive function in elderly populations: The PROSPER study. *Journal of Neurology, Neurosurgery, and Psychiatry, 73,* 385–389.

Maj, M., D'Elia, L., Satz, P., Janssen, R., Zaudig, M., Uchiyama, C., et al. (1993). Evaluation of two new neuropsychological tests designed to minimize cultural bias in the assessment of HIV-1 seropositive persons: A WHO study. *Archives of Clinical Neuropsychology, 8*, 123–135.

Morris, J. C., Heyman, A., Mohs, R. C., Hughes, J. P., van Belle, G., Fillenbaum, G., et al. (1989). The Consortium to Establish a Registry for Alzheimer's Disease (CERAD). Part I. Clinical and neuropsychological assessment of Alzheimer's disease. *Neurology, 39*, 1159–1165.

Mottram, L., & Donders, J. (2005). Construct validity of the California Verbal Learning Test-Children's Version (CVLT-C) after pediatric traumatic brain injury. *Psychological Assessment, 17*, 212–217.

Ponton, M. O., Satz, P., Herrera, L., Ortiz, F., Urrutia, C. P., Young, R., et al. (1996). Normative data stratified by age and education for the Neuropsychological Screening Battery for Hispanics (NeSBHIS): Initial report. *Journal of the International Neuropsychological Society, 2*, 96–104.

Raaijmakers, J. G. W., & Shiffrin, R. M. (1981). Search of associative memory. *Psychological Review, 88,* 93–134.

Rosen, W. G., Mohs, R. C., & Davis, K. L. (1984). A new rating scale for Alzheimer's disease. *American Journal of Psychiatry, 141*, 1356–1364.

Schmidt, M. (1996). *Rey Auditory Verbal Learning Test: A handbook.* Los Angeles: Western Psychological Services.

Stern, R. A., & White, T. (2003). *Neuropsychological Assessment Battery.* Lutz, FL: Psychologial Assessment Resources.

Welsh, K., Butters, N., Hughes, J., Mohs, R., & Heyman, A. (1991). Detection of abnormal memory decline in mild cases of Alzheimer's disease using CERAD neuropsychological measures. *Archives of Neurology, 48*, 278–281.

Auditory-Sound Agnosia

► Auditory Agnosia

Auditory-Verbal Agnosia

► Auditory Agnosia

Augmentative and Alternative Communication (AAC)

Diane Cordry Golden
Association of Assistive Technology Act Programs
Delmar, NY, USA

Definition

Augmentative and alternative communication (AAC) is a set of procedures and processes by which an individual's communication skills can be maximized for functional and effective communication. AAC approaches supplement or replace natural speech with aided options that incorporate the use of some type of device ranging from simple picture communication systems to complex speech generating devices and/or unaided options that involve only the individual's body, such as sign language. AAC may be used to augment understanding as well as written or oral expression. A "multimodal" approach that includes both devices and unaided strategies may be most effective in meeting the individual's communication needs.

Historical Background

Prior to about 1970, AAC was not a widely accepted intervention technique and could even be described as contraindicated in the professional literature. At that time, it was thought that the act of vocal production was a critical building block of human language development. As a result, interventionists believed that providing an alternative to speech production would deter speech (and thus language) development because the child would choose to use the "easier" alternative mechanism (Bates, 1976; Fourcin, 1975).

In the late 1960s and in the 1970s, research evidence indicated speech was actually a secondary component to language function and that robust receptive and expressive language could be developed without vocal production. In many cases, the use of alternatives to speech production was found to actually support (and in no way deter) vocal production (Schlosser & Wendt, 2008; Silverman, 1980; Zangari, Lloyd, & Vicker, 1994). In 1980, the American Speech-Language-Hearing Association (ASHA) established an Ad Hoc Committee on Communication Processes and Nonspeaking Persons that developed a position statement outlining the concept of AAC as a set of intervention techniques using a variety of

symbol sets and communication interaction behaviors. This became the framework for the field of AAC today.

At about the same time, new computer technologies were exploding onto the scene creating previously unimaginable opportunities for AAC device development. The Trace Research and Development Center, part of the College of Engineering at the University of Wisconsin-Madison, was formed in 1971 to address the communication needs of people with severe disabilities who were nonspeaking. The Center was an early leader and innovator in the augmentative communication field and pioneered development of electronic communication aids in the 1970s and 1980s that became prototypes for the speech generating devices (SGDs) of today (Vanderheiden, 1978; Vanderheiden & Grilley, 1976).

Rationale or Underlying Theory

Today the widespread acceptance of AAC is a valid intervention option to develop viable means of effective communication for any individual with limited "natural" speech, as well as to enhance comprehension for those who are not hearing impaired, but who have difficulty understanding spoken language. In 1992, the National Joint Committee for the Communication needs of Persons with Severe Disabilities issued a Communication Bill of Rights that unequivocally states, "All persons, regardless of the extent or severity of their disabilities, have a basic right to affect, through communication, the conditions of their own existence." A set of 12 specific rights are described in the Bill of Rights including, "the right to have access at all times to any needed augmentative and alternative communication devices and other assistive devices and to have those devices in good working order."

Goals and Objectives

Most of the early history of AAC focused on individuals with neuromotor impairments that limited oral-motor skills such as cerebral palsy and amyotrophic lateral sclerosis. However, with the passage of landmark legislation such as the Education of Handicapped Children's Act (P.L. 94–142), Section 504 of the Rehabilitation Act, and later the Americans with Disabilities Act, individuals with all types of disabilities have become more integrated into education, employment, community living, and society in general. This change created a widespread need for individuals with all types of disabilities to have an effective, functional communication system. More complex and efficient AAC systems have been developed to meet this need with some specifically focused on individuals with neuropsychological disabilities such as autism (Glennen & DeCoste, 1997). While the core goal of AAC is to provide effective communication, related objectives can include decreasing problem behaviors and increasing successful education, employment, and community living outcomes.

Treatment Participants

Early in the history of AAC, two misconceptions thrived regarding candidacy for AAC – that a set of prerequisite skills (usually cognitive and motor) was required before AAC could be considered and AAC should only be implemented after all traditional forms of speech therapy had failed. Both have been proven unsubstantiated as many successful AAC users have severe motor and/or cognitive impairments, and research has shown no justification for waiting to implement AAC as it can support speech development (Shane & Bashir, 1980). As a result, candidacy for AAC is not limited by age, disability diagnosis or prerequisite cognitive or motor skills. Individuals who can benefit from AAC may be of all ages, including infants and toddlers with disabilities, and may have diagnoses including apraxia, dysarthria, aphasia, autism, ALS, cerebral palsy, multiple sclerosis, Parkinsons, mental retardation, etc.

Treatment Procedures

The challenges for those providing intervention are maintaining current knowledge of the vast array of available AAC device options, appropriately matching the skill sets of individuals with disabilities to available AAC systems, securing funding to acquire the system, improving communication opportunities and environments, and providing supports sufficient to ensure effective use of the system.

Consideration for aided AAC intervention begins with assessment by a qualified team of individuals who are knowledgeable about the individual and his other strengths and limitations especially in the areas of speech, language, and motor skills. One or more team members should be knowledgeable about the range of potential AAC alternatives available and those that are viable options to meet the individual's communication needs. Appropriate practice in assessment includes conducting structured device trials with various AAC devices in the environment(s) in which the individual will be using the technology (e.g., home, school, community, etc.). This allows for comparative analysis of different device

features and functions to determine which best address the individual's functional communication needs.

The result of an AAC assessment is identification of the system features appropriate for an individual including specification of device input features (selection techniques), message characteristics, and output features. Once an appropriate AAC system has been acquired, training and support for the user, their family, and others (e.g., teachers, therapists, etc.) must be implemented. More complex AAC systems frequently require initial programming and device setup as part of user support services. Short and long-term communication goals should be developed using the AAC system and therapy services implemented to support goal achievement (Beukleman, Garrett, & Yorkston, 2007; Beukelman & Mirenda, 2005; www.aac-rerc.com).

Efficacy Information

Efficacy research on AAC ranges from observation of changes in functional communication skills to potential secondary improvements in academic, social, behavioral, and other areas. For individuals with limited or no functional communication, an AAC system that delivers basic communication ability can be deemed effective by self-verification of communication occurring (Fried-Oken & Bersani, 2000). Beyond this basic gauge of AAC efficacy, research has been done on a variety of specific outcomes such as decreasing problem behaviors through the use of AAC (Vaughn & Horner, 1995), enhancing the rate of AAC communication, (Venkatagiri, 1993), and even nuances such as speech synthesizer intelligibility (Mirenda & Beukelman, 1990) all in an effort to support AAC efficacy.

Seminal work on AAC efficacy done by Ralf Schlosser (2003) addressed a wide range of AAC efficacy issues including the role of AAC in facilitating or hindering natural speech development, literacy development in AAC users, and the effects of speech output (use of speech generating devices). In 2001, Medicare began coverage of speech generating devices (SGDs) based on acceptance of AAC efficacy research. Since then, a number of private insurance carriers have followed suit and now cover SGDs as do most state Medicaid programs.

Outcome Measurement

The most direct outcome measure for AAC intervention is demonstration of effective and efficient communication. Any number of standardized communication measures can be used to document communication efficacy using the AAC system. In addition, the Adaptive Technology Resource Center had identified a variety of outcome measurement tools that focus on the functional efficiency and functional gains achieved through the use of assistive technologies including AAC, see http://atrc.utoronto.ca/index.php?option = com_content&task = view&id = 178&Itemid = 69.

Qualifications of Treatment Providers

AAC intervention is typically provided by speech-language pathologists (SLPs) who are licensed by states as health care providers, educated at the graduate level in the study of human communication, its development and its disorders. Medicare requires an SLP who provides AAC assessments or treatment to hold the Certificate of Clinical Competence (CCC) in speech-language pathology from the American Speech-Language-Hearing Association. In addition to SLPs, some other types of professional providers may be members of the intervention team providing AAC services, especially in the educational environment, e.g., special educators, occupational therapists, assistive technology practioners, etc. (ASHA, 2002; ASHA, 2004; ASHA, 2005).

Cross References

- ▶ Articulation
- ▶ Articulation Disorder
- ▶ Assistive Technology
- ▶ Speech
- ▶ Speech/Communication Disabilities
- ▶ Speech-Language Pathology
- ▶ Speech-Language Therapy
- ▶ Speech Sound Disorders

References and Readings

American Speech-Language-Hearing Association. (1981). Position statement on non-speech communication. *ASHA, 23*, 577–581.

American Speech-Language-Hearing Association. (2002). *Augmentative and alternative communication: Knowledge and skills for service delivery* [Knowledge and Skills]. Retrieved from www.asha.org/policy

American Speech-Language-Hearing Association. (2004). *Roles and responsibilities of speech-language pathologists with respect to augmentative and alternative communication: Technical report* [Technical Report]. Retrieved from www.asha.org/policy

American Speech-Language-Hearing Association. (2005). *Roles and responsibilities of speech-language pathologists with respect to augmentative and alternative communication: Position statement* [Position Statement]. Retrieved from www.asha.org/policy

Bates, E. (1976). *Language and context: The acquisition of pragmatics.* New York: Academic Press.

Beukleman, D., Garrett, K., & Yorkston, K. (2007). *Augmentative and alternative communication strategies for adults with acute or chronic medical conditions.* Baltimore: Paul H. Brookes Publishing Company.

Beukelman, D., & Mirenda, P. (2005). *Augmentative and alternative communication: Management of severe communication disorders in children and adults* (3rd ed.). Baltimore: Paul H. Brookes Publishing Company.

Fourcin, A. J. (1975). Language development in the absence of expressive speech. In E. H. Lenneberg & E. Lenneberg (Eds.), *Foundations of language development* (Vol. II). New York: Academic Press.

Fried-Oken, M., & Bersani, H. (2000). *Speaking up and spelling it out: Personal essays on augmentative and alternative communication.* Baltimore: Paul H. Brookes Publishing Company.

Glennen, S. L., & DeCoste, D. C. (1997). *Handbook of augmentative and alternative communication.* San Diego: Singular Publishing Group.

Mirenda, P., & Beukelman, D. (1990). A comparison of intelligibility among the natural speech and seven speech synthesizers with listeners from three age groups. *Augmentative and Alternative Communication, 6*, 61–68.

National Joint Committee for the Communication Needs of Persons with Severe Disabilities. (1992). Guidelines for meeting the communication needs of persons with severe disabilities. *ASHA*, *34*(Suppl. 7), 1–8. Retrieved from www.asha.org/policy or www.asha.org/njc

Schlosser, R. W. (2003). *The efficacy of augmentative and alternative communication: Toward evidence-based practice.* San Diego: Academic Press.

Schlosser, R. W., & Wendt, O. (2008). Effects of augmentative and alternative communication intervention on speech production in children with autism: A systematic review. *American Journal of Speech-Language Pathology, 17*, 212–230.

Shane, H., & Bashir, A. S. (1980). Election criteria for the adoption of an augmentative communication system: Preliminary considerations. *Journal of Speech and Hearing Disorders, 45*, 408–414.

Silverman, F. (1980). *Communication for the speechless.* Englewood Cliffs, NJ: Prentice-Hall.

Vanderheiden, G. C. (1978). *Non-vocal communication resource book.* Baltimore: University Park Press.

Vanderheiden, G. C., & Grilley, K. (1976). *Non-vocal communication techniques and aids for the severely physically handicapped.* Austin, TX: Pro-Ed.

Vaughn, B., & Horner, R. (1995). Effects of concrete versus verbal choice systems on problem behavior. *Augmentative and Alternative Communication, 11*, 89–92.

Venkatagiri, H. S. (1993). Efficiency of lexical prediction as a communication acceleration technique. *Augmentative and Alternative Communication, 9*, 161–167.

Zangari, C., Lloyd, L. L., & Vicker, B. (1994). Augmentative and alternative communication: A historic perspective. *Augmentative and Alternative Communication, 10*, 27–59.

Aura

Kenneth Perrine
Northeast Regional Epilepsy Group
Hackensack, NJ, USA
Weill-Cornell College of Medicine
New York, NY, USA

Definition

An *aura* is a *paroxysmal* episode that occurs before several types of neurologic events. It is a type of warning heralding the onset of the *ictal* event such as a migraine or an epileptic seizure. Auras usually last longer in migraines (up to minutes) than in seizures (typically several seconds). Episodes longer in duration or more remote from the *ictus* in both migraine and seizures are called *prodromes*. In both disorders, auras can represent any disruption of neurologic function, the specific phenomena of which arise from the localization of their onset in the brain.

Current Knowledge

Auras can consist of disruptions or activations of primary sensory modalities (touch, hearing, smell, taste, vision), including paresthesias (somatosensory hallucinations that feel like tingling or "pins and needles") or numbness, unformed (noises, distortions) or formed (voices, songs, commercial jingles) auditory hallucinations or transient deafness, and olfactory or gustatory hallucinations (usually noxious, such as burned rubber). Visual hallucinations are especially common in migraine, and can include loss of vision such as blind spots or hemianopsia (loss of vision on one side), positive phenomena such as "scintillating scotoma" (flickering spots of light that may begin centrally and extend to arcs of flickering white or colored lights), or zig-zag or other geometric lines or patterns. Formed visual hallucinations can occur (especially in epilepsy), which are usually described as animals or cartoon characters. Visual distortions can also occur, such as macropsia/micropsia (seeing objects larger/smaller) and telescopia/micropsia (seeing objects farther away/closer). In epilepsy, more complex somatosensory auras can occur, such as a rising epigastric sensation (feeling the stomach rising up to the mouth) or ineffable "feelings" that the patient cannot elucidate. Complex experiential psychic auras can also occur (especially in epilepsy), such as déjà vu, out-of-body experiences, depersonalization,

derealization, bizarre perceptual phenomena, etc. Psychological symptoms such as anxiety, panic, and fear are also common. In migraines, auras are thought to be caused by the vascular phenomena causing the headache. Of note, migraine auras can occur without any subsequent headache. In epilepsy, auras are actually *simple partial seizures* produced by epileptiform electrical discharges that affect one brain region alone; they do not disrupt consciousness, and can be recalled by the patient after the ictus.

Cross References

► Epilepsy
► Partial Seizures

References and Readings

Allan Ropper, A. H., & Samuels, M. (2009). *Adams and Victor's principles of neurology* (9th ed.). New York: McGraw-Hill.

Engel, J., & Pedley, T. A. (Eds.). (2008). *Epilepsy: A comprehensive textbook* (2nd ed.). New York: Lippincott Williams & Wilkins.

www.epilepsyfoundation.org

Authoritative Reference

► Learned Treatise

Autism

► Autistic Disorders

Autism Diagnostic Interview, Revised

So Hyun Kim, Catherine Lord
University of Michigan Autism
and Communication Disorders Center (UMACC)
Ann Arbor, MI, USA

Synonyms

ADI-R

Description

The current edition of the *Autism Diagnostic Interview-Revised* (ADI-R; Rutter, Le Couteur, & Lord, 2003) is a standardized, semistructured, and investigator-based interview for parents or caregivers of individuals with autism. It provides a diagnostic algorithm for the ICD-10 definition of autism (World Health Organization [WHO], 1992) and DSM-IV (American Psychiatric Association [APA], 1993). The interview is appropriate for the diagnostic assessment of any person within the age range extending from early childhood to adult life, provided that they have a non-verbal mental age above 2 years. The ADI-R includes 93 items in three domains of functioning – language/communication, reciprocal social interactions, and restricted, repetitive, and stereotyped behaviors and interests, as well as other aspects of behaviors. Up to 42 of the interview items are systematically combined to produce a formal, diagnostic algorithm for autism as specified by the authors, or a general diagnosis of autism spectrum disorders (ASD) as used in several collaborative studies (Risi et al., 2006). All items in the ADI-R are coded in terms of whether the behavior is "currently" occurring, and whether it "ever" occurred, or occurred during a specifically defined period in preschool years. The diagnostic algorithm is based on the "ever/most abnormal" codes in preschool years, but current scores can be used to facilitate a clinical diagnosis.

Most of the ADI-R pertains to behaviors that are rare in individuals who do not have ASD and/or who do not have profound intellectual disabilities. Thus, numerical estimates of the typical scores of general population have not been obtained. Researchers have used scores in the domains or overall as estimates of severity of autistic symptoms. However, the validity of this approach has not been directly tested. Scores have been published for many research populations but not yet systematically dimensionalized.

Historical Background

The WPS Edition of the ADI-R (2003) is a modified version of the 1994 version (Lord, Rutter, & Le Couteur, 1994), which was based on the original Autism Diagnostic Interview (ADI; Le Couteur et al., 1989). The 1994 version was somewhat shorter than the original in order to make the interview more appropriate for clinical, as well as research, usage. The diagnostic algorithm developed for the 1994 version remains unaltered (apart from minor changes in age cutoff).

Psychometric Data

Psychometric properties for the original ADI were provided for a carefully selected, blindly interviewed and coded, sample of 16 autistic and 16 mentally handicapped children and adults covering a range of IQs and chronological ages. Inter-rater reliability was assessed for a sample of ten children with autism and ten without, with multirater kappas ranging from 0.55 to 0.94 for each item and intraclass correlations above 0.94 for all subdomain and domain scores. The majority of individual items showed good discriminative validity showing diagnostic differences across autistic and mentally handicapped groups (Le Courteur et al., 1989).

Psychometric properties for the current ADI-R were provided for a carefully selected, blindly interviewed and coded, sample of 25 autistic and 25 mentally handicapped children ranged in chronological age from 36 to 59 months, with mental ages ranging from 21 to 74 months. Inter-rater reliability was assessed, with multirater kappas ranging from 0.63 to 0.89 for each item and intraclass correlations above 0.92 for all subdomain and domain scores. Following the initial standardization study of the ADI-R, a further study was undertaken of a separate sample of 53 children with autism and 41 nonautistic children with mental handicap or language impairments (Lord et al., 1993). Inter-rater reliability was as high as the initial study, with multirater kappas ranging from 0.62 to 0.96 for individual items. Test-retest reliability was very high, with all coefficients being in the 0.93–0.97 range. Majority of individual items showed good discriminative validity showing diagnostic differences across autistic and mentally handicapped groups (see Lord et al., 1994). The algorithm cutoffs were determined by identifying the point within each area that yielded the best combination of sensitivity and specificity both exceeding 0.90.

Clinical Uses

The ADI-R offers a profile of a child in different areas including language/communication, reciprocal social interactions, and restricted, repetitive, and stereotyped behaviors and interests based on the parents' detailed descriptions of the history and behaviors of the child. It can provide a comprehensive description of a child both currently and in earlier ages, but must be used in conjunction with observations and/or direct testing in making a diagnosis of ASD. The ADI-R can provide a useful structure to obtain history and understand a parent's perspective on their children's symptoms associated with ASD, but requires approximately two hours to administer and substantial practice to do so reliably.

The *Diagnostic Algorithms* are sets of rules that allow classification of patterns of behavior according to whether or not they meet the current DSM-IV or ICD-10 diagnostic criteria of autism and nonautistic ASD. One caveat for clinical users is that they should be aware that diagnostic algorithm result and a true clinical diagnosis are not the same. Clinical diagnosis is based on multiple sources of information, including direct observation. Thus, even though the ADI-R provides broader contexts including the information about history or functioning of a child than observations, ADI-R alone cannot be used to make a complete standard diagnosis.

Current Behavior Algorithms can be used to assess the participant's current behavior. This can be used in clinical settings to assess changes brought about by intervention or changes reflecting increasing developmental maturity or changing life circumstances.

The ADI-R should only be used by appropriately experienced clinicians. Interviewers must be familiar with the concepts of ASD and relevant behaviors. Training workshops and videotapes are available to help clinicians understand the scoring and administration of the ADI-R.

Cross References

- ▶ Autism Diagnostic Observation Schedule
- ▶ Autistic Disorder
- ▶ Childhood Autism Rating Scales
- ▶ Modified Checklist for Autism in Toddlers (M-CHAT) also CHAT

References and Readings

American Psychiatric Association. (1993). *Options book for DSM-IV.* Washington, DC: Author.

DiLavore, P., Lord, C., & Rutter, M. (1995). The pre-linguistic autism diagnostic observation schedule (PL-ADOS). *Journal of Autism and Developmental Disorders, 25*, 355–379.

Le Couteur, A., Rutter, M., Lord, C., Rios, P., Robertson, S., Holdgrafer, M., et al. (1989). Autism diagnostic interview: A semistructured interview for parents and caregivers of autistic persons. *Journal of Autism and Developmental Disorders, 19*, 363–387.

Lord, C., Rutter, M., & Le Couteur, A. (1994). Autism diagnostic interview-revised: A revised version of a diagnostic interview for caregivers of individuals with possible pervasive developmental disorders. *Journal of Autism and Developmental Disorders, 24*(5), 659–685.

Risi, S., Lord, C., Gotham, K., Corsello, C., Chrysler, C., Szatmari, P., et al. (2006). Combining information from multiple sources in the

diagnosis of autism spectrum disorders. *Journal of the American Academy of Child and Adolescent Psychiatry, 45*, 1094–1103.

Rutter, M., Le Couteur, A., & Lord, C. (2003). *Autism diagnostic interview-revised.* Los Angeles: Western Psychological Services.

World Health Organization. (1992). *The ICD-IO classification of mental and behavioral disorders: Clinical descriptions and diagnostic guidelines.* Geneva: Author.

Autism Diagnostic Observation Schedule

So Hyun Kim, Catherine Lord
University of Michigan Autism and Communication Disorders Center (UMACC)
Ann Arbor, MI, USA

Synonyms

ADOS

Description

The *Autism Diagnostic Observation Schedule* (ADOS; Lord, Rutter, DiLavore, & Risi, 2001) is a semistructured, standardized assessment of communication, social interaction, and play or imaginative use of materials for individuals who have been referred because of possible autism spectrum disorders (ASD). As part of the schedule, planned social occasions, referred to as "presses" (Lord, Rutter, Goode, & Heemsbergen, 1989) are created in which a range of social initiations and responses is likely to appear. In the same way, communication opportunities are designed to elicit a range of interchanges. Play situations are included to allow observation of a range of imaginative activities and social role-play. A variety of structured activities and materials, and less structured interactions, provide standard contexts within the ADOS in which the social, communicative, and other behaviors relevant to the understanding of ASD are observed.

The ADOS consists of four modules. Each module is appropriate for children and adults at different developmental and language levels, ranging from no expressive or receptive use of words, to fluent, complex language in an adult. Only one module, lasting about 30 minutes, is administered to any individual at a given point of time. In the ADOS, the examiner uses the module that best matches the expressive language skills of the individual child or adult in order to make judgments about social and communicative abilities as independent as possible from the effects of absolute level of language delay. Each module has its own protocol, which contains a schedule of activities designed for use with children or adults at particular developmental and language levels. Recently, the Toddler Module of the ADOS was developed for use in children between 12 and 30 months of age in addition to the original four modules (Lord, Luyster, Gotham, & Guthrie, in press).

Module 1 is intended for children who do not use spontaneous phrase speech consistently. It consists of 10 activities with 29 accompanying ratings. Module 2 is intended for children with some flexible phrase speech who are not verbally fluent. It consists of 14 activities with 28 accompanying ratings. Module 3 provides 13 activities and 28 ratings. It is intended for verbally fluent children for whom playing with toys is age-appropriate. The operational definition of verbal fluency is the spontaneous, flexible use of sentences with multiple clauses that describe logical connections within a sentence. It requires the ability to talk about objects or events not immediately present. Module 4 contains the socioemotional questions, along with interview items about daily living and additional tasks. It is intended for verbally fluent adults and for adolescents who are not interested in playing with toys such as action figures (usually over 12–16 years). This module consists of 10–15 activities with 31 accompanying ratings. The difference between Modules 3 and 4 lies primarily in whether information about social communication is acquired during play or through a conversational interview. It is important to note that adolescents or adults may feel uncomfortable when presented with the toys for young children that are available in modules 1 and 2; suggestions for modifying the earlier modules to be appropriate for older children or adults who are less verbal are available from the authors. In addition to the four modules, the Toddler Module is intended for children between 12 and 30 months of age who should have a nonverbal age equivalent of at least 12 months and be walking independently. It consists of 11 activities with 41 accompanying ratings (Lord et al., in press).

The ADOS provides the diagnostic algorithms that are sets of rules that allow classification of autism or ASD. Separate diagnostic algorithms for each module can be generated using subsets of items in each module. Items and the thresholds for the classification of autism and of ASD in the algorithms differ for each module. However, the general principles and procedures for computation are the same across modules and similar to the DSM-IV (American Psychiatric Association, 1993) and ICD-10 (World Health Organization, 1992). The algorithms for

Module 1, 2, and 3 were recently revised from the previous algorithms (Gotham, Risi, Pickles, & Lord, 2007). Reflecting recent research, the revised algorithms now consist of two new domains, Social Affect and Restricted, Repetitive Behaviors, combined to one score to which thresholds are applied, resulting in generally improved predictive validity compared to the previous algorithms. The module 1 consists of no words and some words algorithms by language level. The module 2 includes "Younger than 5" and "Greater or Equal to 5" algorithms by chronological age. Module 3 includes a single algorithm. All items appearing on the new algorithms contribute to a single score with two classification thresholds, one for autism and another for ASD. There are the Toddler Module algorithms for children between 12 and 30 months, who do not have phrase speech; once children have developed phrase speech, they should be administered module 2. Since differential diagnosis can be challenging especially in toddlers, the toddler module algorithms generate range of concern (little-or-no concern; mild-to-moderate concern; moderate-to-severe concern) rather than strict classifications.

Most of the ADOS pertains to behaviors that are rare in individuals who do not have ASD and/or who do not have profound intellectual disabilities. Thus, numerical estimates of the typical scores of general population have not been obtained. Scores from module 1 to 3 have now been calibrated for children with ASD to yield a standard severity score based on a large sample (see below; Gotham, Pickles, & Lord, in press).

Historical Background

In its present form, the current WPS Edition of the ADOS (Lord et al., 2001) is a combination of two similar diagnostic instruments: the 1989 version of the ADOS (Lord et al., 1989) and the *Pre-Linguistic* ADOS (PL-ADOS; DiLavore, Lord, and Rutter, 1995). The ADOS was first introduced in the 1980s as a method of standardizing direct observations of social behavior, communication, and play in children suspected of having autism. It was intended to be administered to children between the ages of 5 and 12, who had expressive language skills at least at the 3-year-old level. It was proposed as a complementary instrument to the Autism Diagnostic Interview (ADI; Le Couteur et al., 1989), an investigator-based parent or caregiver interview that yielded a description of history, as well as current functioning, in areas of development related to autism. Because children under age five constitute the bulk of referrals for a first diagnosis of autism, there was a need to extend the age and verbal limits of the ADOS to be appropriate for younger and nonverbal children. The PL-ADOS was then created based on the growing interest in using the instruments in clinical settings, which addressed the concerns of parents and fit the abilities of children functioning at infant and toddler levels. As a result, it included more flexible, briefer activities and greater use of play materials for nonverbal young children that served as a downward extension for the ADOS, rather than a replacement. The PL-ADOS was effective in discriminating 2–5-year-old-children with autism from children with non-autism spectrum developmental delays (DiLavore et al., 1995). However, it tended to be underinclusive for children with autism who had some expressive language. Thus, a tool was required to address the needs of children who fell between the PL-ADOS and ADOS in language skills. Furthermore, the ADOS consisted primarily of activities intended for school-age children. Additional or alternative tasks were needed for adolescents and adults. The current edition of the ADOS was designed in response to these factors. The current ADOS differs from the preceding instruments in a way that it is aimed at providing standard contexts for the observation of behavior for a broader developmental and age range of individuals suspected of having autism. Thus, the current ADOS includes additional items developed for verbally fluent, high-functioning adolescents and adults as well as younger and nonverbal children.

However, even though this updated version of the ADOS did indeed extend the usefulness of the original ADOS below a language level of 3 years, research has indicated that it remained of limited value for children with nonverbal mental age below 16 months. Thus, a standardized diagnostic measure applicable for infant and young toddlers was also needed for early identification (Gotham et al., 2007). The recent development of the Toddler Module of the ADOS reflects this need for the measure to be applicable to very young children from 12 to 30 months.

The original algorithms included two domains, social interaction and communication. Recently, Gotham et al. (2007) revised algorithms for module 1, 2, and 3, and the existing social and communication domains were merged, and the domain of Restricted Repetitive Behaviors (RRB) was newly included. The revised algorithms resulted in increased specificity and sensitivity proving increased diagnostic validity compared to the previous algorithms. Furthermore, even though the inclusion of the RRB domain did not improve predictive value of the ADOS in differentiating individuals with autism from those with pervasive developmental disorder – not otherwise specified (PDD-NOS; also referred as ASD), it

aided in distinguishing PDD-NOS from non-spectrum cases.

Psychometric Data

Psychometric properties for the original ADOS were provided for a carefully selected, blindly interviewed and coded, sample of 223 children and adults with autistic disorder (autism), pervasive developmental disorder – not otherwise specified (PDD-NOS) or non-spectrum (NS) diagnoses. Inter-rater reliability was assessed, with mean multirater kappas of all items for each module ranging from .65 to .78 and intraclass correlations above .82 for all subdomain and domain scores. Test-retest reliability varied by subdomain ranging from .59 to .82. In the original sample, the ADOS algorithms generally achieved 94% correct classification. The exceptions were the ASD versus non-spectrum (NS) module 2 specificity of 87% and module 3 sensitivity of 90%, and the PDD-NOS versus NS Module 2 specificity of 88% and sensitivity of 89% and module 3 sensitivity of 80% (Lord et al., 2001).

Psychometric properties for the newly revised algorithms were provided for a sample of 1,139 different participants. The revised algorithms resulted in increased specificity in classifying non-autism ASD in lower functioning populations, evidenced by the 12–31% increase in specificity for children without any words (depending on nonverbal mental age) and the modest gain in specificity for older children who have not progressed beyond phrase speech. During module 1, no words improved in each diagnostic comparison (e.g., from the sensitivity of 19% to 50% for children with nonverbal mental age of 15); the specificity of both module 2 groups improved for non-autism ASD versus NS (e.g., from 77% to 83% for children greater or equal to 5). For autism versus non-spectrum and for ASD versus NS, the new and old algorithms performed approximately equally well in terms of sensitivity. For non-autism ASD versus non-spectrum, sensitivity of the new algorithm was somewhat lower in module 1, no words (as was necessary to raise specificity; e.g., 100% in old algorithm versus 97% in new algorithm for children under nonverbal mental age under 15), but it showed improvement from the old algorithm in the higher-functioning modules 1 (AUT versus NS; from 88% to 97%) and module 2 (ASD versus NS; from 76% to 84%) cells. Inter-rater reliability on the ADOS was monitored through joint administration and scoring by two different examiners for at least 1 in 10 cases and, in some cases, through scoring of videotapes. Agreement remained at greater than 85% (Gotham et al., 2007).

Psychometric properties for the Toddler Module were provided for a sample of 182 different participants. The sensitivity of each algorithm ranged from 83% to 91% and specificity from 86% to 94%. Inter-rater item and domain reliability was greater than .71, and inter-rater algorithm reliability ranged from .60 to .90. Intraclass correlations ranged from .74 to .99 for all algorithm domains and total scores (Lord et al., in press).

Clinical Uses

Use of the ADOS is related to the examiner's clinical skills and experience with the instrument. Examiners need to be sufficiently familiar with the ratings and the activities so that they can focus their attention on observation of the individual being assessed, rather than on administration of tasks. The examiner should have sufficient practice in observation of ASD symptoms and scoring of the ADOS items, as well as in administering the activities. Examiners are encouraged to attend workshops, use videotapes, or work with colleagues to obtain inter-rater reliability before administering the ADOS for clinical or research purposes (Lord et al., 2001). Examiners should note that the Toddler Module and module 1 are always administered with parents or caregivers in the room, which provides an opportunity to show a parent, examples of behaviors that define ASD, and get information from a parent about the validity of the child's behaviors during the testing session. Because the ADOS consists of codings made from a single observation, it does not include information about history or functioning in other contexts. This means that the ADOS alone cannot be used to make a complete standard diagnosis, but used in conjunction with other testing.

Lord and her colleagues suggested several strategies that clinicians or researchers may take to measure how behaviors of individual may have changed over time by using the ADOS item and domain scores (Lord et al., 2000). If an individual has been administered the same module more than once, raw scores on individual items and on algorithm domains can be compared. If an individual has changed modules, raw scores on items that remain constant across modules (about two thirds of each contiguous module) can be compared, yet comparison of raw domain scores is not meaningful. However, the ADOS calibrated scores recently developed by Gotham et al. (in press) can be used in this case to compare assessments across modules and time. The calibrated scores have more uniform distributions across age- and language-groups compared to raw totals, which make it possible to compare children's scores longitudinally across

distinct algorithms. Thus, calibrated scores can be useful in clinical settings to test treatment responsiveness and other clinical outcomes in individuals with ASD.

In addition, it was suggested that more detailed coding of communication samples or particular behaviors (e.g., pragmatics, sentence structure, gestures) may also be carried out from videotapes of the ADOS. Other observational coding schemes that address specific aspects of behavior in more detail may also be applied using the ADOS as a way of obtaining a discrete sample of behavior in standard contexts. Often, clinicians carrying out diagnostic assessments may wish to make programming suggestions for parents/caregivers, therapists, or teachers. Many of the activities and codes of the earlier modules have fairly straightforward implications both for how to teach an individual child and for the content of appropriate goals. For example, module 1 provides opportunities for children to make requests in a number of circumstances, including requests for action (i.e., the examiner to blow a balloon), requests for food, requests to continue a social game, and requests for an object or activation of that object (i.e., operating a bubble gun). Noting how children make requests and in what circumstances they are most easily able to communicate their interest or needs, allows the clinician to create goals to teach new request behaviors and to help the children generalize existing behaviors across contexts. Generating programming goals from modules 3 and 4 may be somewhat more complex, because fewer codes describe specific behaviors that may be usefully taught in a direct fashion. Realizing the degree to which adults with autism have limited insight into the nature of social relationships, or having the opportunity to observe adolescents describing the emotions of the main characters in a story, can be helpful in representing the strengths they may have and difficulties they experience in social interaction.

Cross References

- ▶ Autism Diagnostic Interview-Revised (ADI-R)
- ▶ Autistic Disorder
- ▶ Childhood Autism Rating Scales
- ▶ Modified Checklist for Autism in Toddlers (M-CHAT) also CHAT

References and Readings

American Psychiatric Association. (1993). *Options book for DSM-IV.* Washington, DC: Author.

DiLavore, P., Lord, C., & Rutter, M. (1995). Pre-linguistic autism diagnostic observation schedule (PL-ADOS). *Journal of Austism and Developmental Disorders, 25*, 355–379.

Gotham, K., Pickles, A., & Lord, C. (in press). Standardizing ADOS scores for a measure of severity in autism spectrum disorders. *Journal of Autism and Developmental Disorders.*

Gotham, K., Risi, S., Pickles, A., & Lord, C. (2007). The autism diagnostic observation schedule: Revised algorithms for improved diagnostic validity. *Journal of Autism and Developmental Disorders, 37*, 613–627.

Le Couteur, A., Rutter, M., Lord, C., Rios, P., Robertson, S., Holdgrafer, M., et al. (1989). Autism diagnostic interview: A semistructured interview for parents and caregivers of autistic persons. *Journal of Autism and Developmental Disorders, 19*, 363–387.

Lord, C. E., Luyster, R., Gotham, K., & Guthrie, W. J. (in press). *Autism diagnostic observation schedule – toddler module.* Los Angeles, CA: Western Psychological Services.

Lord, C., Risi, S., Lambrecht, L., Cook, E. H., Leventhal, B. L., DiLavore, P., et al. (2000). The autism diagnostic observation schedule–generic: A standard measure of social and communication deficits associated with the spectrum of autism. *Journal of Autism and Developmental Disorders, 30*(3), 205–223.

Lord, C., Rutter, M., DiLavore, P. C., & Risi, S. (2001). *Autism diagnostic observation schedule.* Los Angeles, CA: Western Psychological Services.

Lord, C., Rutter, M., Goode, S., & Heemsbergen, J. (1989). Autism diagnostic observation schedule: A standardized observation of communicative and social behavior. *Journal of Autism and Developmental Disorders, 19*(2), 185–212.

Lord, C., Rutter, M., & Le Couteur, A. L. (1994). Autism diagnostic interview-revised: A revised version of a diagnostic interview for caregivers of individuals with possible pervasive developmental disorders. *Journal of Autism and Developmental Disorders, 24*(5), 659–685.

World Health Organization. (1992). *The ICD-IO classification of mental and behavioral disorders: Clinical descriptions and diagnostic guidelines.* Geneva, Switzerland: Author.

Autism Spectrum Disorder

- ▶ Pervasive Developmental Disorder NOS

Autistic Disorder

Fred R. Volkmar
Yale University
New Haven, CT, USA

Synonyms

Childhood autism; Infantile autism; Kanner's syndrome

Short Description/Definition

Autistic disorder is a neurodevelopmental condition characterized by marked problems in social interaction, communication/play, and a set of unusual behaviors related to difficulties in tolerating change in the environment. The condition is of early onset. In most cases, it appears to be congenital, but perhaps in 20% of cases, a period of normal development is observed. The condition always appears before 3 years of age.

Categorization

Autism was first described by Leo Kanner in 1943 (Kanner, 1943). Early controversy centered around the idea that autism might be a form of schizophrenia, but several lines of evidence suggest this is not the case. Changes in approaches to the definition of autism have occurred over time. Currently, both the American Psychiatric Association (DSM-IV-TR) (World Health Organization, 2000) and International (ICD-10) (World Health Organization, 1994) categorization systems define autistic disorder in essentially the same way. Autistic disorder is one or a group of conditions referred to as the pervasive developmental disorders (PDD). Other conditions in that class include Aspeger's disorder (in which marked social deficits are observed but some aspects of language are relatively preserved); Rett's disorder (a condition largely confined to girls and characterized by marked deterioration in motor, cognitive, and communicative skills); childhood disintegrative disorder (a rare condition where at least 2 years of normal development precedes the emergence of an 'autistic like' illness); and PDD-NOS (not otherwise specified) – a term reserved for cases exhibiting some features of autism but not the full syndrome.

Epidemiology

A number of epidemiological studies have been undertaken around the world. Their interpretation is complicated by methodological differences including case finding and definitions used. The earliest studies reported rates on the order of 1 in 2,000 children, but more recent work suggests that a figure of 1 in 800–1,000 children is probably more accurate; the broader PDD spectrum is much more ambiguously defined and probably affects as many as 1 in 150 children (Fombonne, 2005). Much debate has centered on whether autism is increasing in frequency, but this issue remains unclear despite better methods of case detection and greater public awareness (Fombonne, 2005).

Rates of autistic disorder are typically three to four times higher in boys than in girls. The nature of this gender difference remains unclear, but speculation has centered on lower thresholds for expression of the condition in boys. An early impression of increased rates in better educated families appears to have been due to referral bias and has not been supported by later work.

Natural History, Prognostic Factors, Outcomes

Issues of diagnosis can be complex in infants as not all required features may be exhibited until around age 3 (Lord & Venter, 1992). After that time, diagnostic agreement increases substantially. By school age, autistic children become more sociable and may make significant academic gains although behavioral difficulties are prominent. During adolescence, some children make substantial gains and others lose skills. There is increased risk for development of epilepsy throughout the developmental period, with peak frequencies of new onset of epilepsy in early childhood and adolescence (Volkmar & Nelson, 1990).

The first studies of long-term outcome in children with autism were relatively pessimistic with only 2–3% of cases being able to achieve adult independence and self-sufficiency. Several factors appear to significantly improve prognosis: cases are now detected at early ages (when intervention may be more effective (National Research Council, 2001), and in many countries, educational services are now mandated). It appears that at least 20% or more of children with autism are capable of self-sufficiency in adulthood with at least another 15–20% able to be largely independent (Howlin, 2005). Major predictors of long-term outcome include nonverbal cognitive ability and the capacity to use language to communicate only around age 5. Adaptive abilities (the ability to cope with real world situations) are also important particularly as the person becomes older.

Neuropsychology and Psychology of Autistic Disorder

The first attempts to develop psychological models of autism centered around the notion that experiential factors might be involved. As evidence of brain involvement accumulated, theories shifted to focus on neurocognitvie and brain-based mechanisms.

Several neurocognitive models/theories have been proposed. One approach posits difficulties in executive functioning skills; this model would account for some of the problems with shifting set and perseveration typical of individuals with autism (Ozonoff et al., 2005). However, deficits in these areas are not specific to autism and are not strongly related to the extent of social vulnerability. Another approach has focused on difficulties in what is termed 'Central Coherence' or the capacity to integrate information into coherent or meaningful wholes (Happe, 2005). This model centers on problems resulting from difficulties in selective attention and appreciation of social meaning. Another approach posits difficulties in understanding and empathizing with others (Baron-Cohen, 1989). This Theory of Mind hypothesis has been very productive for research. It presumes that difficulties arise as a result of an inability to understanding feelings, intention, and social meaning. Weaknesses of this approach include the fact that more able individuals with autism can solve usual theory of mind type problems; a second problem arises because many of the first features of autism appear before usual theory of mind skills are established in typically developing infants. A relatively newer approach, Enactive Mind, has attempted a synthesis of insights from studies of social cognitive information processing in autism with normal developmental perspectives (Klin, Jones et al., 2003) (Fig. 1).

A focus on specific brain mechanisms was suggested by high rates of epilepsy and various neurological signs and symptoms (e.g., persistence of 'primitive' reflexes, delayed development of hand dominance, etc.). A range of abnormalities has been found in post-mortem studies. Lesion studies, e.g., of the amygdala or hippocampus, have produced some behaviors in monkeys similar to some of those seen in autism (Bachevalier, 1996). Other studies have focused on abnormalities in the cerebellum and overall brain size which appears to be increased in autism (Courchesne et al., 2004).

Other approaches have focused on specific neuropsychological processes. For example, Scultz and colleagues (Schultz et al., 2000) used fMRI techniques to demonstrate that more cognitively able individuals with autism process faces differently than typical controls; essentially they fail to activate the fusiform 'face area'. This observation is of interest given a large body of experimental work on differences in face processing in autism. Another work, e.g., using eye tracking technology, has revealed marked differences in scanning of the environment during social situations with more able individuals with autism tending to focus on the lower half of the face or objects, thus losing a considerable amount of social-affective information (Klin, Jones et al., 2002).

Autistic Disorder. Figure 1 Visual focus of an autistic man and a normal comparison subject showing a film clip of a conversation. Typically developing person (top line) goes back and forth between the eyes in viewing a social scene, a high functioning person with autism goes back and forth between the mouths of the speakers. Reprinted with permission from Klin, Jones, Schultz, Volkmar, and Cohen (2002)

Beginning with the first twin studies of autism in the late 1970s a considerable body of work has strongly implicated genetic factors in the pathogenesis of autism. There are significantly increased rates of autism in identical twins and a higher risk in siblings both of autism and a range of other developmental problems. It appears that multiple genes are involved and several candidate genes are now being studied (Rutter, 2005).

Evaluation

Evaluation of the child with autism typically involves the efforts of members of several different disciplines – psychology, speech-language pathology, medicine, occupational and physical therapy, and special education. Goals for evaluation include clarification of the diagnosis and establishment of patterns of strengths/weakness that have implications for programming. Medical evaluations are indicated to look for conditions like Fragile X syndrome and seizures sometimes associated with autism (Volkmar et al., 1999).

Treatment

Over the past decade a considerable body of work on intervention has become available. In its influential 2001

review a panel from the US National Research Council systematically evaluated ten treatment programs for younger children with autism. Although differing in some respects these programs shared many similarities including intensive individualized programs and structured teaching. Many, although not all, of these programs make extensive use of applied behavior analytic principles to teach basic skills which can then be expanded. Increasing social and communication abilities are important goals. Psychotherapy is not a mainstay of treatment but is sometimes used in older and more able individuals but is to be problem-focused in nature.

Drug treatments can be helpful relative to certain symptoms (e.g., agitation, stereotyped mannerisms) but do not address the core social deficit (Scahill & Martin, 2005).

Cross References

- ▶ Adaptive Behavior
- ▶ ADI
- ▶ ADOS
- ▶ Applied Behavior Analysis
- ▶ Asperger Disorder
- ▶ Behavior Modification
- ▶ Epilepsy
- ▶ Executive Functioning
- ▶ Intellectual Disability
- ▶ TEACCH
- ▶ Vineland II

References and Readings

American Psychiatric Association. (2000). *Diagnostic and statistical manual* (4th ed., Text Rev.). Washington, DC: APA Press.

Bachevalier, J. (1996). Brief report: Medial temporal lobe and autism: A putative animal model in primates. *Journal of Autism and Developmental Disorders, 26*(2), 217–220.

Baron-Cohen, S. (1989). The theory of mind hypothesis of autism: A reply to Boucher [comment]. *The British Journal of Disorders of Communication, 24*(2), 199–200.

Courchesne, E., Redcay, E., Kennedy, D. P. (2004). The autistic brain: Birth through adulthood. *Current Opinion in Neurology, 17*(4), 489–496.

Fombonne, E. (2005). Epidemiological studies of pervasive developmental disorders. In F. R. Volkmar, A. Klin, R. Paul, & D. J. Cohen (Eds.), *Handbook of autism and pervasive developmental disorders* (Vol. 1, pp. 42–69). Hoboken, NJ: Wiley.

Happe, F. (2005). The weak central coherence account of autism. In F. R. Volkmar, A. Klin, R. Paul, & D. J. Cohen (Eds.), *Handbook of autism and pervasive developmental disorders* (Vol. 1, pp. 640–649). Hoboken, NJ: Wiley.

Howlin, P. (2005). Outcomes in autism spectrum disorders. In F. R. Volkmar, A. Klin, R. Paul, & D. J. Cohen (Eds.), *Handbook of autism and pervasive developmental disorders* (Vol. 2, pp. 201–222). Hoboken, NJ: Wiley.

Kanner, L. (1943). Autistic disturbances of affective contact. *Nervous Child, 2*, 217–250.

Klin, A., Jones, W., Schultz, R., Volkmar, R., & Cohen, D. (2002). Visual fixation patterns during viewing of naturalistic social situations as predictors of social competence in individuals with autism. *Archives of General Psychiatry, 59*(9), 809–816.

Klin, A., Jones, W., Schultz, R., & Volkmar, F. (2003). The enactive mind, or from actions to cognition: Lessons from autism. *Philosophical Transactions of the Royal Society of London, Series B: Biological Sciences, 358*(1430), 345–360.

Klin, A., Jones, W., Schultz, R., Volkmar, F., & Cohen, D. (2002). Defining and quantifying the social phenotype in autism. *American Journal of Psychiatry, 159*, 895–908.

Lord, C., & Venter, A. (1992). Outcome and follow-up studies of high-functioning autistic individuals. In E. Schopler & G. B. Mesibov (Eds.), High-functioning individuals with autism current issues in autism (Vol. xviii, pp. 187–199; 316). Plenum: NY.

National Research Council. (2001). *Educating young children with autism.* Washington, DC: National Academy Press.

Ozonoff, S., South, M., & Provencal, S. (2005). Executive functions. In F. R. Volkmar, A. Klin, R. Paul, & D. J. Cohen (Eds.), *Handbook of autism and pervasive developmental disorders* (3rd edn, pp. 606–27). New York: Wiley.

Rutter, M. (2005). Genetic influences and autism. In F. R. Volkmar, A. Klin, R. Paul, & D. J. Cohen (Eds.), *Handbook of autism and pervasive developmental disorders* (Vol. 1, pp. 425–452). Hoboken, NJ: Wiley.

Scahill, L., & Martin, A. (2005). Psychopharmacology. In F. R. Volkmar, A. Klin, R. Paul, & D. J. Cohen (Eds.), *Handbook of autism and pervasive developmental disorders* (Vol. 2, pp. 1102–1122). Hoboken, NJ: Wiley.

Schultz, R. T., Gauthier, I., Klin, A., Fulbright, R. K., Anderson, A. W., Volkmar, F. (2000). Abnormal ventral temporal cortical activity during face discrimination among individuals with autism and Asperger syndrome. *Archives of General Psychiatry, 57*(4), 331–340.

Volkmar, F., Cook, E. Jr., Pomeroy, J., Realmuto, G., Tanguay, P. (1999). Summary of the practice parameters for the assessment and treatment of children, adolescents, and adults with autism and other pervasive developmental disorders. *Journal of the American Academy of Child and Adolescent Psychiatry, 38*(12), 1611–1616.

Volkmar, F. R., & Nelson, D. S. (1990). Seizure disorders in autism. *Journal of the American Academy of Child and Adolescent Psychiatry, 29*(1), 127–129.

World Health Organization. (1994). *Diagnostic criteria for research.* Geneva: World Health Organization.

Autobiographical Memory

Katherine Tyson
University of Connecticut
Storrs, CT, USA

Synonyms

Memory; Personal memory; Recollective memory

Definition

Autobiographical memory (AM) is the memory of events or information involving the self. Researchers generally conceptualize AM as episodic, as opposed to semantic. AMs are temporally defined (e.g., by the date of the remembered event) and involve a sense of "recollection or reliving" of the original event (Greenberg & Rubin, 2003).

Historical Background

Levin, Benton, and Grossman (1982) are sometimes credited with originating the term AM. However, AM research dates back to Francis Galton's 1879 study of his own recall of events in his personal past. Galton sampled his own episodic memories by finding associations between words and events from his past and dating those events. In 1974, Crovitz and Schiffman modified Galton's technique to create what became a widely used method for studying AM (see Rubin, 1999). Their revised technique involved asking participants to think of memories associated with words presented to them. In 1983, Nigro and Neisser pioneered studies examining the effect of point of view on AM in their studies of field memories (viewed from the same viewpoint as originally experienced) and observer memories (viewed from an observer's perspective). They found that older memories were more often viewed from the observer point of view than recent memories (see Rubin, 1999). Current research has spanned a variety of areas, including examining AM's functional mechanisms, studying psychopathology's potential effects on AM, and investigating AM's neuropsychological underpinnings through imaging studies.

Current Knowledge

Phenomenology

Much of the recent research on AM has concentrated on AM's function. Pillemer (1992) posited that AM has three basic functions: self-related, communicative (social), and directive (planning for present and future events) (Bluck, 2003). In serving the self, AM helps people to develop a sense of coherence and continuity in defining who they are through memories. In its communicative role, AM provides the content of conversations and facilitates building intimacy in social relationships. Sharing of AMs can also inform and teach others about the sharer's world. As a directive tool, AM can help people solve problems as they examine lessons from past events and think about how future events and behavior might turn out.

As a cultural mechanism, in particular, AM helps not only to shape the individual self, but also to provide the individual with a sense of identity in relation to a wider community (Bluck, 2003). In Euro–American societies, AM appears to emerge around three-and-a-half years of age, as adults begin to share memories with their children. Some cultural differences have emerged in the nature of AM. Asian societies, for example, may report fewer AMs and have fewer and later memories from earlier childhood compared to Euro–Americans. Whereas collective identity may be the focus in these societies, Americans tend to focus on creating a unique identity; AM is essential to this development of a self.

In its role of aiding self-development, AM may also drive positive perceptions of self and emotion regulation. Research by Wilson and Ross (Bluck, 2003) has shown that remembering positive events often brings about a positive mood. Furthermore, the third person, observer's perspective from which people often remember negative life events gives them distance from those events, which may also promote well-being. Sharing of AMs with others may aid emotion regulation.

As a facilitator of social interaction AM helps people to reflect on and share recollections of the past with one another. Fivush et al. (Bluck, 2003) have suggested that in mother–child relationships, sharing of AMs may help children to learn how to deal with and express emotions, particularly negative ones.

In its directive function, AM guides current behavior and functioning. Both everyday and traumatic memories guide people's present decisions and actions.

Methods in AM Research

Several methods have been developed for studying AM. Given its complexity and the lack of consensus about how AM works, no single method has emerged as a gold standard; rather, these methods are often used in combination.

Open-ended methods include the *word-cue method*, similar to Galton's original method. Participants are presented with cue words or other stimuli and asked to think of memories. Typically, after the cued portion of such a study, the researcher will ask the participants to date the memories. This method has tended to provide consistent results, lending support to expected findings: childhood amnesia of early life memories, retention of the

memories of the most recent two decades, and for people over age 40, an increase in memories about adolescence and early adulthood (Wenzel & Rubin, 2005). This cueing method is most commonly applied using the *Autobiographical Memory Test*, first described in 1986 by Williams and Broadbent (Wenzel & Rubin, 2005). A second open-ended method involves simply asking a participant about his or her life. A more structured approach, the *involuntary-memory-diary method*, asks participants to keep a diary record of involuntary AMs as they occur.

Some other methods for delving into AM are more closed-ended. The *Autobiographical Memory Interview*, developed by Kopelman, Wilson, and Baddeley, was designed to be used with neuropsychological patients (Wenzel & Rubin, 2003). The interview asks for specific kinds of memories from specific time periods. The participant is not provided a choice as to the types of memories he or she will share. In the *diary recall method*, participants record events and subsequently receive a memory test for these events. Unlike the other methods, the diary recall method can provide some measure of the accuracy of memories. A final method, the *questionnaire method*, asks participants to report on a series of properties of AMs; this method is often used in conjunction with other approaches. Recently, Sutin and Robins (2007) have developed *The Memory Experiences Questionnaire*, a measure designed to assess a comprehensive range of dimensions of AM.

In developing methods to study such a multifaceted phenomenon as AM, researchers focus on several variables of interest. These variables include: whether the memory is general or specific, latency to retrieve a memory, number of omissions (i.e., when a person does not present a specific personal memory for certain stimuli presented), age of memories, and affective tone. Studies have shown that the last of these variables, affective tone, can potentially differentiate AMs of people with psychopathology from AMs of people without psychopathology (Dalgleish & Brewin, 2007).

AM and Psychopathology

In studying the relationship between psychopathology and AM, researchers have found that certain aspects of AM in clinical populations do differ from those of healthy populations. Evidence suggests that AM in patients with suicidal ideation, current or past depression, and trauma history may be overgeneral compared to the specific memories that healthy individuals recall (Hermans, Raes, Philippot, & Kremers, 2006). For example, a depressed patient might report a memory of going to lunch with her mother on Tuesdays, as opposed to remembering a specific one of those Tuesday lunches.

Research also indicates that trauma and non-trauma memories differ substantially in clinical, but not in healthy populations (Dalgleish & Brewin, 2007). While involuntary memory may be enhanced in some clinical populations, voluntary memory is often fragmented, incomplete, and disorganized, particularly in people with a trauma history. PET and fMRI studies have suggested that the retrieval of trauma memories in PTSD patients is characterized by increased activity of limbic and paralimbic areas, including the amygdala. Additionally, researchers have found deactivation of the medial prefrontal areas and Broca's area and decreased hippocampal activity in PTSD patients when they processed emotional, rather than neutral material.

In looking at depressed individuals, studies have suggested that cues reflecting personal characteristics are more likely to promote a shift to processing of information within the long-term view of the self, increasing the likelihood that self-related semantic information will be provided in response to cues on the Autobiographical Memory Test. In a different, but related line of research, euthymic individuals with a history of depression and patients with a borderline personality disorder retrieved less specific AMs in response to cue words that matched highly endorsed attitudes or schema. This finding suggests that an impaired retrieval of specific memories may be the result of certain cues activating generic, higher-order mental representations in people with both psychopathology histories and present diagnoses (Dalgleish & Brewin, 2007; Hermans et al., 2006). Generally dysfunctional attitudes, whether in an individual exhibiting psychopathology or in a healthy individual, could play a part in an individual's inability to retrieve specific memories.

Neuropsychology

Although researchers have studied the neuropsychology of AM specifically, knowledge about the neuropsychology of memory in general is much more substantial. By looking at the broad memory literature, researchers have been able to make some claims about the neuropsychology of AM and to suggest areas for future study.

AM appears to be distributed throughout the brain. Retrieval of personally experienced events has been linked to medial temporal lobe, visual cortex, posterior parietal midline, and prefrontal cortex activity (Daselaar et al., 2008; Greenberg & Rubin, 2003). AM's emotional and sensory components may involve still other brain areas.

Daselaar et al. (2008) have worked to map the time course of AM, including emotional and reliving aspects of AM. Through functional magnetic resonance imaging (fMRI), Daselaar et al. examined both initial accessing of memories and subsequent elaboration of the memories. As a person first began to recall a personal memory, hippocampal, retrosplenial, and medial and right prefrontal cortex activation occurred (Daselaar et al., 2008). As participants rated memories, brain areas associated with emotion and sensory function were activated, including the amygdala and hippocampus for initial emotion ratings, and visual cortex and ventromedial and inferior prefrontal cortex for reliving ratings. This line of research underlines AM's dynamic involvement of multiple brain areas.

The visual, auditory, and olfactory systems all appear to be potential parts of the broad AM system. Research has demonstrated that visual imagery is central to AM, especially when considering long-term visual memories (Greenberg & Rubin, 2003). The medial-temporal lobes and the frontal lobes have been implicated in case study research examining visual imagery's role in AM. Auditory imagery may also be involved in AM, but so far studies have not shown autobiographical amnesias to be related specifically to damage of the auditory cortices. As with visual imagery, further research may provide more information on this aspect of AM.

In addition to its sensory dimensions, AM also seems to be closely related to language. However, with only one exception, semantic dementia, AM impairment does not seem to be related to language-related neuropsychological impairments (Greenberg & Rubin, 2003). In semantic dementia, patients display better recall for recent memories than for older ones. A patient with semantic dementia experiences loss of AM, as well as a loss of the ability to maintain semantic memories in storage.

Future Directions

Future research on AM should concentrate on defining and specifying AM both behaviorally and through neuropsychological techniques, including functional and structural imaging. Continuing to consider and revise a conceptual model of AM, such as Pillemer's, is important to providing researchers a better, more definite way to conceptualize AM. Looking at AM cross-culturally may help to determine whether this type of memory plays distinct roles in different cultures and societies. Individual differences in AM are also an important area for study, given researchers' focus on AM as important to the formation of self. In research on psychopathology, looking at schema activation and overgeneral AMs may be important to understanding why clinical populations remember AMs differently from nonclinical populations.

Taking a closer look at the neuropsychology of AM will be necessary as we find better ways to define AM behaviorally. Correlating behavioral changes with the brain changes we can see through imaging will be a significant area for future study so that we develop a clearer idea of what structures make up the AM circuitry in the brain.

Cross References

- ▶ Declarative Memory
- ▶ Episodic Memory
- ▶ False Memory
- ▶ Forgetting
- ▶ Memory Impairment
- ▶ Remote Memory
- ▶ Working Memory

References and Readings

Bluck, S. (Ed.). (2003). Autobiographical memory: Exploring its functions in everyday life [Special issue]. *Memory, 11*.

Dalgleish, T., & Brewin, C. R. (Eds.). (2007). Autobiographical memory and emotional disorder [Special issue]. *Memory, 15*(3).

Daselaar, S. M., Rice, H. J., Greenberg, D. L., Cabeza, R., LaBar, K. S., & Rubin, D. C. (2008). The spatiotemporal dynamics of autobiographical memory: Neural correlates of recall, emotional intensity, and reliving. *Cerebral Cortex, 18*, 217–229.

Greenberg, D. L., & Rubin, D. C. (2003). The neuropsychology of autobiographical memory [Special issue]. *Cortex, 39*, 687–728.

Hermans, D., Raes, F., Philippot, P., & Kremers, I. (Eds.). (2006). *Autobiographical memory specificity and psychopathology.* New York: Psychology Press.

Levin, H. S., Benton, A. L., & Grossman, R. G. (1982). *Neurobehavioral consequences of closed head injury.* New York: Oxford University Press.

Rubin, D. C. (Ed.). (1999). *Remembering our past: Studies in autobiographical memory.* New York: Cambridge University Press.

Sutin, A. R., & Robins, R. W. (2007). Phenomenology of autobiographical memories: The memory experiences questionnaire. *Memory, 15*(4), 390–411.

Wenzel, A., & Rubin, D. C. (Eds.). (2005). *Cognitive methods and their application to clinical research.* Washington, DC: American Psychological Association.

Autoimmune Disorders

- ▶ Myasthenia Gravis

Autoimmune Thyroiditis

► Hypothyroidism

Automated Interpretation

► Test Interpretations: Computer Based

Automated Neuropsychological Assessment Metrics

Summer Ibarra
Rehabilitation Hospital of Indiana
Indianapolis, IN, USA

Synonyms

ANAM

Definition

The Automated Neuropsychological Assessment Metrics (ANAM) is a computer-based battery of tests designed to measure an individual's neurocognitive skills including areas such as sustained attention, processing speed, working memory, and visuospatial ability. It consists of 31 test modules as well as forms for recording demographic information (see Fig. 1; Center for the Study of Human Operator Performance; Reeves, Winter, Bleiberg, & Kane, 2007). The entire battery of tests can be administered or the administrator can elect to customize a subset of the ANAM tests in order to assess more specific areas of functioning (Vincent et al., 2008). The most recent version of ANAM uses a Windows platform and can be found at the Center for the Study of Human Operator Performance at the University of Oklahoma (Jones, Loe, Krach, Rager, & Jones, 2008).

Administration time can range from a few minutes for a single subtest to 90+ minutes for the entire battery (U.S. Army Medical Department, 2009). Scoring for the ANAM is computer generated. Scores for ANAM subtests can be calculated in a variety of ways, including the percentage of correct responses (accuracy score), mean response time for accurate responses (MS), and the ratio of accuracy and speed or number of correct responses per minute (throughput score) (Jones et al., 2008).

Historical Background

The ANAM was originally developed by the US Department of Defense as a means of monitoring changes in human performance when encountering environmental challenges, but has now become a common assessment instrument for use in several clinical populations (Kane, Roebuck-Spencer, Short, Kabat, & Wilken, 2007) and research applications (Vincent et al., 2008). The current ANAM is the result of 30+ years of research and is directly linked to older standardized test batteries, including the Unified Tri-Service Cognitive Performance Assessment Battery (Reeves et al., 2007).

Current Knowledge

Various combinations of ANAM subtests have been employed to investigate neurocognitive changes and impairment in medical and neurological conditions including acquired brain injury, multiple sclerosis, Parkinson's disease, systemic lupus erythematosus (Kane et al., 2007),

ANAM executive module	Participant information	Sleepiness scale	Mood scale
2-Choice reaction time	Code substitution	Logical reasoning	Matching grids
Matching to sample	Mathematical processing	Memory search	Running memory CPT
Simple reaction time	Tapping	Procedural reaction time	Spatial processing
Manikin	Switching	Tower puzzle	Standard CPT
Pursuit tracking	Stroop test	Spatial processing – delayed	Grammatical reasoning
Complex reaction time	4-Choice reaction time	Relative judgment	Symbolic reaction time
Digit reaction time	Visual vigilance	Unstable tracking	Dual task

Automated Neuropsychological Assessment Metrics. Figure 1

migraine headache (Roebuck-Spencer, Sun, Cernich, Farmer, & Bleiberg, 2007) and Alzheimer's dementia (Levinson, Reeves, Watson, & Harrison, 2005). Currently, in an effort to better identify the occurrence of traumatic brain injury (TBI), the ANAM is also being used by the US military to establish a baseline of neurocognitive functioning prior to deployment for all Service members (U.S. Army Medical Department, 2009).

Data from over nine studies suggest that varying combinations of ANAM subtest batteries are sensitive and specific in detecting neurocognitive change among individuals with neurological disorders (Kane et al., 2007). Common uses include screening and triage, monitoring of disease progression, and detection of treatment and medication effects (Kane et al., 2007).

Other uses of the ANAM include evaluation of cognitive functioning in determining fitness for duty, neurotoxicology, human factors engineering, and various fields of medicine such as aerospace, undersea, military operations, and sports (Reeves et al., 2007).

Advantages

The ANAM has been noted as an ideal instrument for assessing change in neurocognition (Roebuck-Spencer et al., 2007). Through randomization of stimuli, practice effects are minimized across numerous testing sessions (Roebuck-Spencer et al., 2007). Further, subtle changes in response time can be more precisely detected as compared to manual calculation of response time (Roebuck-Spencer et al., 2007). Other advantages include time efficiency and cost-effectiveness, both of which are helpful when attempting to triage large numbers of patients (Kane et al., 2007).

Limitations

Research findings indicate that varying combinations of the ANAM batteries are not as thorough as more extensive neurocognitive assessments.

Administration

Administration time can range from a few minutes for a single subtest to 90+ minutes for the entire battery (U.S. Army Medical Department, 2009). Scoring for the ANAM is computer generated. Scores for ANAM subtests can be calculated in a variety of ways, including the percentage of correct responses (accuracy score), mean response time for accurate responses (MS), and the ratio of accuracy and speed or number of correct responses per minute (throughput score) (Jones et al., 2008).

Psychometrics

The subtests of the ANAM were selected from previously established assessment instruments (e.g., Walter Reed Performance Assessment Battery, the Air Force Criterion Task Set, Navy Performance Evaluation Tests for Environmental Research) with research supporting their respective sensitivity, reliability, and validity (Reeves et al., 2007). As researchers have attempted to gather psychometric data for the current ANAM, many have included only subsets of the subtests in their studies rather than the entire ANAM battery.

Various combinations of ANAM subtests have been shown to be both sensitive and specific in detecting cognitive changes in a number of neurological conditions (Kane et al., 2007).

Through the process of multiple baseline administrations, test–retest reliabilities across several ANAM subtest throughput scores ranged from 0.50 to 0.91 with 9 of the 10 estimates <0.77(Short, Ivins, & Kane, manuscript in preparation).

Construct validity has been established between several of the commonly used ANAM subtests (e.g., Math, Running Memory, Code Substitution Delayed Memory, and Logical Reasoning) and more traditional measure of neurocognitive function such as Trail Making Test A&B, Animal Naming, Controlled Oral Word Association Test, and the Digits Backward and Digit Symbol subtests of the WAIS-III (Short, Cernich, Wilken, & Kane, 2007).

Future Directions

The use of the ANAM in various fields of medicine and science continues to develop as evidenced by recent studies attempting to validate specified subsets of the ANAM battery. Examples include validation of the ANAM-sports medicine battery (ASMB) designed for surveillance and management of sports related concussions (Cernich, Reeves, Sun, & Bleiberg, 2007), use of ANAM tests to assess the effects of extreme environmental stressors such as high altitude, toxins, and radiation exposure (Lowe et al., 2007), and assessment of medication efficacy and potential medication side effects, specifically for CNS-active drugs (Wilken, Sullivan, Lewandowski, & Kane, 2007).

Cross References

- ▶ Cognitive Functioning
- ▶ Concussion
- ▶ Mild Brain Injury
- ▶ Traumatic Brain Injury

References and Readings

Jones, W. P., Loe, S. A., Krach, K., Rager, R. Y., & Jones, H. M. (2008). Automated neuropsychological assessment metrics (ANAM) and Woodcock-Johnson III tests of cognitive ability: A concurrent validity study. *The Clinical Neuropsychologist, 22*, 305–320.

Kane, R. L., Roebuck-Spencer, T., Short, P., Kabat, M., & Wilken, J. (2007). Identifying and monitoring cognitive deficits in clinical populations using Automated Neuropsychological Assessment Metrics (ANAM) tests. *Archives of Clinical Neuropsychology, 22S*, S115–S126.

Reeves, D. L., Winter, K. P., Bleiberg, J., & Kane, R. L. (2007). ANAM genogram: Historical perspectives, description, and current endeavours. *Archives of Clinical Neuropsychology, 22S*, S15–S37.

Roebuck-Spencer, T., Sun, W., Cernich, A. N., Farmer, K., & Bleiberg, J. (2007). Assessing change with the automated neuropsychological assessment metrics (ANAM): Issues and challenges. *Archives of Clinical Neuropsychology, 22*, S79–S87.

References – ANAM

Center for the Study of Human Operator Performance. (nd). *ANAM tests and associated modules.* http://c-shop.ou.edu/anam4–2.htm. Retrieved on 10 March 2009.

Cernich, A., Reeves, D., Sun, W., & Bleiberg, J. (2007). Automated neuropsychological assessment metrics sports medicine battery. *Archives of Clinical Neuropsychology, 22S*, S101–S114.

Jones, W. P., Loe, S. A., Krach, K., Rager, R. Y., & Jones, H. M. (2008). Automated neuropsychological assessment metrics (ANAM) and Woodcock-Johnson III tests of cognitive ability: A concurrent validity study. *The Clinical Neuropsychologist, 22*, 305–320.

Kane, R. L., Roebuck-Spencer, T., Short, P., Kabat, M., & Wilken, J. (2007). Identifying and monitoring cognitive deficits in clinical populations using automated neuropsychological assessment metrics (ANAM) tests. *Archives of Clinical Neuropsychology, 22S*, S115–S126.

Levinson, D., Reeves, D., Watson, J., & Harrison, M. (2005). Automated neuropsychological assessment metrics (ANAM) measures of cognitive effects of Alzheimer's disease. *Archives of Clinical Neuropsychology, 20*, 403–408.

Lowe, M., Harris, W., Kane, R. L., Banderet, L., Levinson, D., & Reeves, D. (2007). Neuropsychological assessment in extreme environments. *Archives of Clinical Neuropsychology, 22S*, S89–S99.

Reeves, D. L., Winter, K. P., Bleiberg, J., & Kane, R. L. (2007). ANAM genogram: Historical perspectives, description, and current endeavours. *Archives of Clinical Neuropsychology, 22S*, S15–S37.

Roebuck-Spencer, T., Sun, W., Cernich, A. N., Farmer, K., & Bleiberg, J. (2007). Assessing change with the automated neuropsychological assessment metrics (ANAM): Issues and challenges. *Archives of Clinical Neuropsychology, 22*, S79–S87.

Short, P., Cernich, A., Wilken, J. A., & Kane, R. L. (2007). Initial construct validation of frequently employed ANAM measures through structural equation modeling. *Archives of Clinical Neuropsychology, 22S*, S63–S77.

Short, P., Ivins, B. J., & Kane, R. L. (manuscript in preparation). Reliability characteristics of select Automated Neuropsychological Assessment Metrics (ANAM) measures.

U.S. Army Medical Department (2009). *Automated Neuropsychological Assessment Metrics (ANAM).* www.medicine.army.mil/prr/anam.html. Retrieved on 10 March 2009.

Vincent, A. S., Bleiberg, J., Yan, S., Ivins, B., Reeves, D. L., Schwab, K., et al. (2008). Reference data from the automated neuropsychological assessment metrics for use in traumatic brain injury in an active duty military sample. *Military Medicine, 173*, 836–849.

Wilken, J. A., Sullivan, C. L., Lewandowski, A., & Kane, R. L. (2007). The use of ANAM to assess the side-effect profiles and efficacy of medication. *Archives of Clinical Neuropsychology, 22S*, S127–S133.

Automatic Behavior

- ▶ Automatism
- ▶ Stimulus-Bound Behavior

Automatic Language

Roberta DePompei
The University of Akron
Akron, OH, USA

Synonyms

Nonpropositional language

Definition

Automatic language is the use of nonpropositional language forms. Even if the patient is unable to converse at all, he or she may produce automatic responses. These responses may be: (a) automized sequences: counting, reciting the alphabet, saying the days of the week; (b) memorized sequences: prayers pledge of allegiance; (c) recurrent social speech: "Have a nice day," "How are you?"; (d) emotional speech: cursing or a typically stated sentence when emotionally upset. It is important to note that these types of responses are not clearly thought out and are not under the cognitive control of the patient. These responses do not

represent propositional language skill and should not be considered as a conscious attempt to participate in conversational situations. Automatic language can be found in severe aphasias and in many dementias. It may also occur in mental health problems such as schizophrenia.

Cross References

► Stereotypy

References and Readings

Alajouanine, T. (1956). Verbal realization in aphasia. *Brain, 79*, 1–28.
Blanken, G., & Marini, V. (1997). Where do lexical speech automatisms come from? *Journal of Neurolinguistics, 10*(1), 19–31.
Chapey, R. (Ed.). (2001). *Language intervention strategies in aphasia and related neurogenic communication disorders* (4th ed.). Philadelphia: Lippincott, Williams & Wilkins.

Automaticity

Anna MacKay-Brandt
Brown University Medical School
Providence, RI, USA

Definition

A mental operation that proceeds without voluntary control and without requiring capacity or processing resources.

Current Knowledge

Automatic processes are usually found in the context of stimulus information that is well integrated into the individual's memory through either a classical conditioning, an overlearned behavior (e.g., reading), or an evolutionarily adaptive response (e.g., orienting response). The Stroop effect (Stroop, 1935; MacLeod, 1992) is a good example of the influence of automaticity on behavior. Reading becomes automatic at a level of proficiency acquired by most school-aged children, such that it is out of an individual's control *not* read a presented word. This involuntary response is captured in the interference it produces when one attempts to ignore a color word and instead name the color of the stimulus. Reaction time tends to be slower when the color word and the color of the stimulus are incongruent when compared to the time to name the color of a series of Xs or a noncolor word.

Cross References

► Controlled Attention
► Orienting Response
► Reading Fluency
► Stroop Effect

References and Readings

MacLeod, C. M. (1992). The Stroop task: The "gold standard" of attentional measures. *Journal of Experimental Psychology: General, 121*, 12–14.
Stroop, J. R. (1935). Studies of interference in serial verbal reactions. *Journal of Experimental Psychology, 18*, 643–662.

Automatism

Douglas I. Katz
Boston University School of Medicine
Boston, MA, USA

Synonyms

Automatic behavior

Definition

This is a complex movement that occurs without conscious awareness or purposeful intent.

Current Knowledge

Automatisms may occur in the setting of complex-partial seizures. Typical simple movements include lip smacking, chewing, or finger rubbing. More complex automatisms include walking, running, undressing, and speaking. Emotional expressions, such as laughing or crying, may also occur as automatisms. Automatisms may occur during seizures or as post-ictal phenomena. Speech automatisms

tend to lateralize to the left hemisphere but lateralization is not predictable for other automatisms (Rasonyi, Fogarasi, Kelemen, Janszky, & Halasz, 2006). Responsiveness is usually lost when automatisms occur during seizures. Rarely, patients may have preserved responsiveness in the presence of seizure-induced automatisms, and only with seizures that arise from right hemisphere foci (Ebner, Dinner, Noachtar, & Luders, 1995).

In addition to epileptic seizures, automatisms may also be observed in other situations including intoxication, sleep walking, hypoglycemia, and psychological disorders, such as dissociative fugue states. Forensic assessments aimed at determining culpability often center around the differential diagnosis of automatisms (Fenwick, 1990).

Cross References

► Complex Partial Seizures

References and Readings

Ebner, A., Dinner, D. S., Noachtar, S., & Luders, H. (1995). Automatisms with preserved responsiveness: A lateralizing sign in psychomotor seizures. *Neurology, 45*(1), 61–64.

Fenwick, P. (1990). Automatism, medicine and the law. *Psychological Medicine. Monograph Supplement, 17*, 1–27.

Rasonyi, G., Fogarasi, A., Kelemen, A., Janszky, J., & Halasz, P. (2006). Lateralizing value of postictal automatisms in temporal lobe epilepsy. *Epilepsy Research, 70*(2–3), 239–243.

Autonomic Dysregulation

► Hemodynamic Response

Autonomic Nervous System

Scott Vota
Virginia Commonwealth University
Richmond, VA, USA

Synonyms

Internal regulation system; Involuntary nervous system; Visceral nervous system

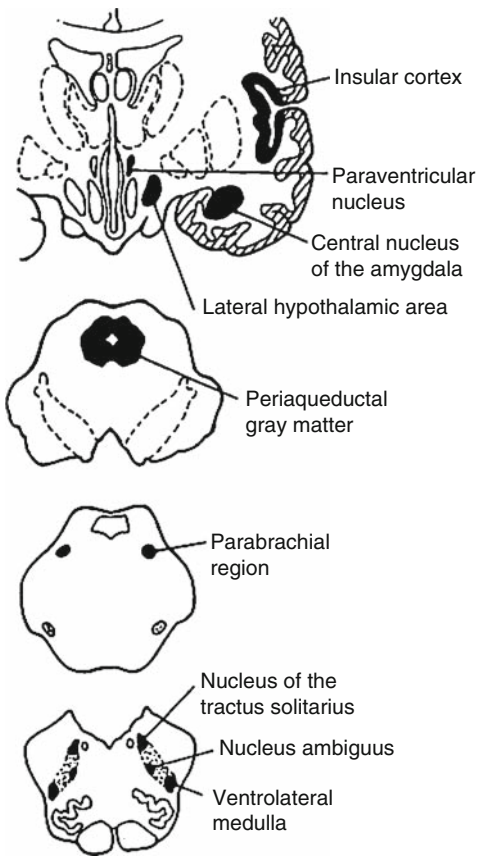
Definition

The autonomic nervous system is a complex and vital system that helps to maintain homeostasis and adaptation throughout the human body. It is composed of both central and peripheral components that provide thermoregulation, arterial blood pressure adaptation, as well as alterations in regional blood flow in response to metabolic demands, micturition, gastrointestinal motility, and sexual function.

Current Knowledge

Central Component

The central components of the autonomic nervous system are located within the cerebral cortex, thalamus, hypothalamus, hippocampus, and cerebellum. These components are integrally connected via a network of ascending and descending pathways see Fig. 1. This provides a high



Autonomic Nervous System. Figure 1 Central components of the autonomic nervous system

level of control over autonomic function. These interconnections ultimately descend to specific cells within the brainstem and spinal cord. The thoracolumbar outflow consists of fibers that arise in the intermediolateral cell column of the thoracic and first two lumbar segments of the spinal cord. This is the origin of the sympathetic division of the autonomic nervous system. The cranial outflow, arising from cranial nerve nuclei III, VII, IX, and X, and the sacral outflow, arising from cell bodies in the intermediate cell column of sacral segments 2 through 4, form the parasympathetic division of the autonomic nervous system.

Peripheral Component

The peripheral part of the autonomic nervous system is then composed of sympathetic and parasympathetic pathways. These pathways arise from two distinct anatomic portions of the brainstem and spinal cord. The parasympathetic fibers arise from the craniosacral portion, and the sympathetic fibers arise from the thoracolumbar region. Although anatomically separated, the two parts are complementary in maintaining a balance in the activities of many visceral structures and organs. The preganglionic neurons for both the parasympathetic and sympathetic divisions release acetylcholine, but the difference lies in the postganglionic neurotransmitter release. The parasympathetic postganglionic fibers release norepinephrine and epinephrine and thus are referred to as cholinergic. The sympathetic postganglionic fibers release norepinephrine and epinephrine and thus are classified as adrenergic. The terminals of sympathetic fibers on sweat glands, however, do not follow this pattern and are cholinergic (see Figs. 2 and 3).

Parasympathetic Nervous System

Parasympathetic outputs arise from the preganglionic neurons located in the nuclei of the brainstem and sacral spinal cord. Preganglionic parasympathetic axons travel a long distance before eventually reaching their target ganglia, which are typically close to, or within the target end organ.

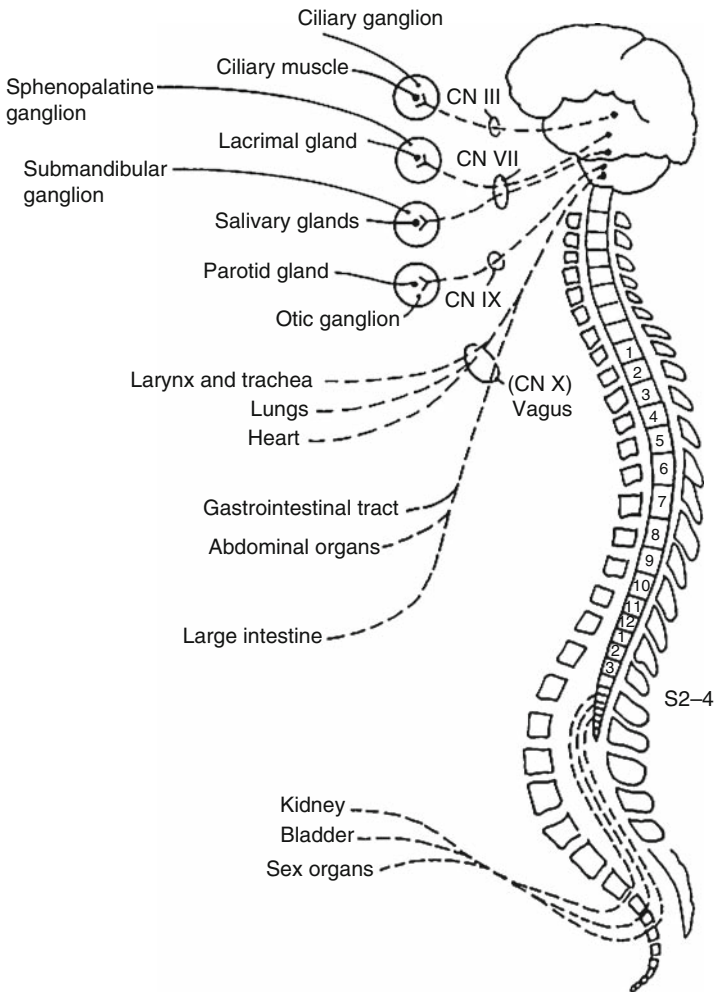
The cranial preganglionic parasympathetic nuclei (Edinger Westphal Nuclei) projects through the oculomotor nerve. These preganglionic axons synapse on neurons of the ciliary ganglion. The neurons innervate the iris and ciliary muscles, eliciting pupillary constriction and accommodation of the lens. The superior salivatory nucleus located in the pons projects via the facial nerve to the sphenopalatine ganglion. This innervates the lacrimal gland (producing lacrimation) and the cerebral and cranial blood vessels (eliciting vasodilatation). Axons also travel to the submandibular ganglion, providing secretomotor and vasodilator inputs to the corresponding salivary glands. The inferior salivatory nucleus sends axons via the glossopharyngeal nerve to ultimately synapse on the otic ganglion, stimulating parotid gland secretion. Most preganglionic parasympathetic output from the brainstem is mediated by the vagus nerve, which receives input from the dorsal motor nucleus of the vagus and the lateral portion of the nucleus ambiguus. The vagus nerve innervates the heart, respiratory tract, and the entire gastrointestinal tract with the exception of the descending colon and rectum.

The sacral preganglionic output arises from neurons of the sacral preganglionic nucleus located in the lateral gray matter of the sacral spinal cord. These axons travel to the pelvic splanchnic nerves, which join the inferior hypogastric plexus to innervate the descending colon, bladder, and sexual organs. These outputs elicit contraction of the bladder detrusor muscle and circular smooth muscle of the rectum as well as regulating vasodilatation of the cavernous tissue of the penis required for erection.

Sympathetic Nervous System

The sympathetic preganglionic neurons are primarily located in the intermediolateral nucleus in the thoracic and upper lumbar regions of the spinal cord. The preganglionic sympathetic axons exit through the ventral roots and pass on to the corresponding spinal nerve to reach the paravertebral sympathetic chain. The majority of the presynaptic fibers branch and run rostrally or caudally along the sympathetic chain and synapse on the paravertebral ganglia. The remaining fibers pass through the paravertebral chain without synapsing. These form the splanchnic nerves which innervate prevertebral ganglia.

The paravertebral sympathetic ganglia are primarily a relay station for preganglionic inputs. They innervate all tissues and organs except those in the abdomen, pelvis, and perineum. For example the superior cervical ganglion sends postganglionic axons to innervate the eye, facial sweat glands, salivary glands, pineal, thyroid, and parathyroid glands. These outputs elicit pupil dilatation, contraction of the Muller muscle of the eyelid, facial sweating, and vasoconstriction in facial and cerebral circulation. The stellate ganglion, which receives preganglionic input from the mid thoracic segment, sends postganglionic axons to innervate blood vessels and sweat glands in the upper limbs and trunk. These outputs produce either vasoconstriction or vasodilatation in the skin and muscle, sweating, or piloerection. Outputs from the stellate



Autonomic Nervous System. Figure 2 Parasympathetic Nervous System

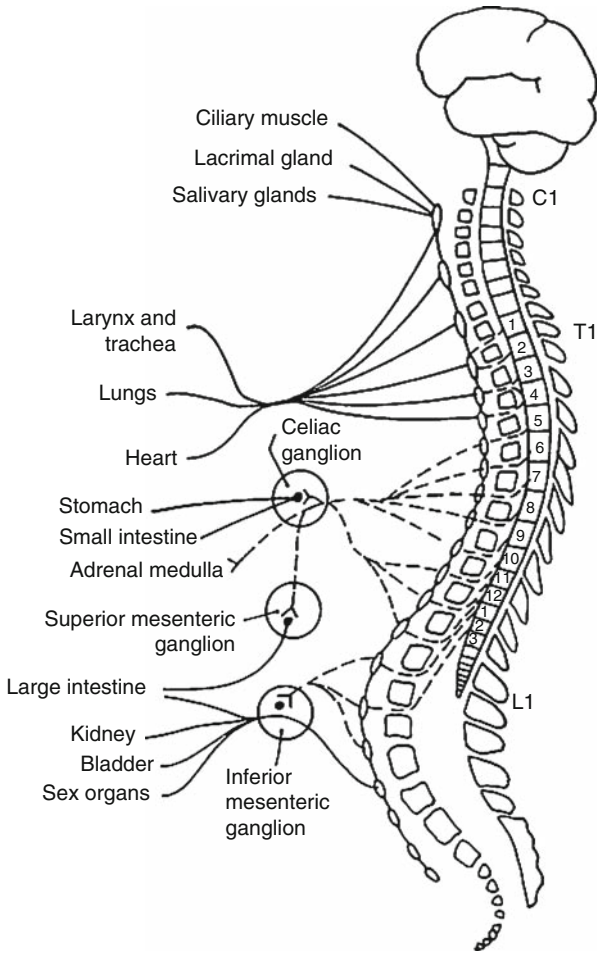
ganglion also elicit cardiac acceleration and bronchodilation. The lumbar paravertebral ganglia subsequently innervate the blood vessels and sweat glands in the lower limb.

The prevertebral ganglia are located anterior to the abdominal aorta. Preganglionic input from the lower thoracic segments is carried by the splanchnic nerves to the celiac and superior mesenteric ganglia and provides postganglionic fibers to the celiac plexus that innervates all abdominal viscera, with the exception of the descending colon. These outputs produce vasoconstriction and inhibition of the gastrointestinal tract motility. Preganglionic axons from the lumbar spinal segments travel via the lumbar splanchnic nerves to synapse in the inferior mesenteric ganglion. These axons innervate the descending colon, rectum, bladder, and sexual organs eliciting vasoconstriction, smooth muscle relaxation of the bladder and rectum, constriction of the internal sphincter of the bladder and rectum, and ejaculation.

Diagnosing Autonomic Dysfunction

Medical History

As the autonomic nervous system innervates all organ systems, a detailed medical history and physical examination is paramount. This will help develop a proper differential diagnosis and laboratory evaluation. The goals of the clinical evaluation are to identify the presence, location, and time course of autonomic dysfunction. This will help to determine which part(s) of the autonomic nervous system may be involved: sympathetic noradrenergic,



Autonomic Nervous System. Figure 3 Sympathetic Nervous system

sympathetic cholinergic, parasympathetic cholinergic, or adrenomedullary. Specific questions should be asked to determine if the patient may have symptoms of orthostatic hypotension, anhydrosis, weight change, constipation, sexual dysfunction, sialorrhea, or urinary retention. Questions related to aggravating and relieving factors need to be considered. Examples include: relationship to meals; environmental temperature; and diurnal variation. A complete listing of all prescribed medications, as well as over the counter herbal and dietary supplements need to be reviewed.

Examination

An exam should start with a general overview of the patient making note of facial expression, posture, and height. Vital signs should be checked in the supine, seated, and standing positions. A thorough skin examination making note of acrocyanosis, pallor, mottling, diaphoresis, alopecia, or erythema should be performed. An eye exam can also be valuable. Attention should be given to pupillary shape, size, and the response to light and accommodation.

Diagnostic Testing

A workup to uncover an etiology for autonomic dysfunction should begin with routine serologic testing. This includes serum electrolytes, glucose, hepatic function tests, protein electropheresis, and a complete blood count. Further serologic testing may include cortisol levels, paraneoplastic autoantibodies, and plasma catecholamines. An EKG and echocardiogram should also be performed.

A variety of more specialized tests, both invasive and noninvasive, may also need to be considered. These include, but are not limited to the following: deep breathing

and valsalva ratio, isometric handgrip and cold pressor tests, thermoregulatory sweat and skin sympathetic tests, quantitative sudomotor axon reflex testing, power spectral analysis of heart rate variability, tilt table testing, and neuroimaging such as PET scanning.

Treatment

Both nonpharmacologic and pharmacologic treatments are available to treat patients with autonomic dysfunction. For certain disorders, surgical intervention may be needed. The goal is to ameliorate all symptoms while avoiding side effects.

Nonpharmacologic measurements start with patient education. Symptoms such as rising slowly from a seated position, or modifying sodium intake may be enough in some autonomic disorders to provide patients with a symptom free life.

Pharmacotherapy may include medications to increase central blood volume, such fludrocortisones, vasopressin analogues, acetylcholinesterase inhibition, or caffeine.

Cross References

- ▶ Anticholinergic
- ▶ Arousal
- ▶ Cerebellum
- ▶ Cholinergic System
- ▶ Hippocampus
- ▶ Hypothalamus
- ▶ Thalamus

References and Readings

Benarroch, E. E., Westmoreland, B. F., Daube, J. R., Reagan, T. J., & Sandok, B. A. (1999). *Medical neurosciences: An approach to anatomy, pathology, and physiology by systems and levels* (4th ed.). Philadelphia: Lippincott Williams and Wilkins.

Bradley, W. G., Daroff, R. B., Fenichel, G., & Jankovic, J. (2004). *Neurology in clinical practice* (4th ed.). Boston: Butterworth-Heinemann.

Gilman, S., Newman, S. W., Manter, J. T., & Gatz, A. J. (2003). *Manter and Gatz's essentials of clinical neuroanatomy and neurophysiology* (10th ed.). Philadelphia: F.A. Davis Company.

Netter, F. H. (1991). *Nervous system, Part 1: Anatomy and physiology* (Vol. 1) (Ciba collection of medical illustrations). Summit, NJ: Ciba-Geigy Corporation.

Ropper, A. H., & Brown, R. H. (2005). *Adams and Victor's principles of neurology* (8th ed.). New York: McGraw-Hill.

Rowland, L. P. (2005). *Merritt's neurology* (11th ed.). Philadelphia: Lippincott Williams and Wilkins.

Autoreceptor

Beth Kuczynski[1], Stephanie A. Kolakowsky-Hayner[2]
[1]University of California
Davis, CA, USA
[2]Santa Clara Valley Medical Center,
Rehabilitation Research Center
San Jose, CA, USA

Synonyms

Heteroreceptor; Receptor

Definition

An autoreceptor is a receptor located on the neuron (terminals, soma, and/or dendrites), and the function is to bind a specific ligand (such as neurotransmitters or hormones) released by that same neuron. The autorecpter is mainly used as a feedback mechanism to monitor neurotransmitter synthesis and/or release. Dopaminergic neurons can have autoreceptors that regulate the release of dopamine. Autoreceptor regulation is very effective in modulating neurotransmission and is of interest for pharmacological intervention.

Cross References

- ▶ Hormones
- ▶ Neurotransmitters

References and Readings

Carey, R., DePalma, G., Damianopoulos, E., Müller, C., & Huston, J. (2004). The 5-HT_{1A} receptor and behavioral stimulation in the rat: Effects of 8-OHDPAT on spontaneous and cocaine-induced behavior. *Psychopharmacology, 177*(1/2), 46–54.

Meltzer, H. (1980). Relevance of dopamine autoreceptors for psychiatry: Preclinical and clinical studies. *Schizophrenia Bulletin, 6*(3), 456–475.

Autotopagnosia

John E. Mendoza
Tulane University Medical Center
New Orleans, LA, USA

Definition

Disturbance of body schema involving the loss of ability to localize, recognize, or identify the specific parts of one's body.

Current Knowledge

While some reported cases exhibit impaired knowledge of most body parts, autotopagnosia is most frequently manifested as difficulty in identifying or naming specific fingers (*finger agnosia*), especially the three middle fingers. The problem extends to identifying comparable body parts on the examiner or graphic representations of body parts. The deficit usually involves both sides of the body, thus distinguishing it from unilateral neglect. While not typically classified as such, *right-left disorientation* likely reflects another form or subtype of autotopagnosia. In this condition, patients are unable to reliably identify the right and left sides of their bodies or those of others. Both finger agnosia and right-left disorientation are frequently present at the same time, particularly following lesions of the left angular gyrus and may be a part of what has been defined as Gerstmann's syndrome. The latter would also include deficits in writing (agraphia) and arithmetical operations (acalculia).

Cross References

- ▶ Finger Agnosia
- ▶ Gerstmann's Syndrome
- ▶ Right-Left Disorientation

References and Readings

Benton, A. L., & Sivan, A. B. (1993). Disturbances of the body schema. In K. M. Heilman & E. Valenstein (Eds.), *Clinical neuropsychology* (pp. 123–140). New York: Oxford University Press.

Denberg, N. L., & Tranel, D. (2003). Acalculia and disturbances of the body schema. In K. M. Heilman & E. Valenstein (Eds.), *Clinical neuropsychology* (pp. 161–184). New York: Oxford University Press.

AVMs

- ▶ Vascular Malformations

Avolition

Irene Piryatinsky, Paul Malloy
Butler Hospital and Alpert Medical School of Brown University
Providence, RI, USA

Synonyms

Apathy

Definition

Avolition is a severe problem with initiation, volitional, or willed action, and production of goal-directed behavior. It may reflect a general lack of motivation and drive. Avolition is commonly seen as one of the negative symptoms in patients with schizophrenia, and is also common in frontal lobe disorders affecting medial frontal systems.

Cross References

- ▶ Abulia
- ▶ Apathy
- ▶ Cingulate Gyrus

References and Readings

Foussias, G., & Remington, G. (2008). Negative symptoms in schizophrenia: Avolition and Occam's Razor. Schizophrenia Bulletin Advance Access 10.10.1093/schbul/sbn094.

Liddle, P. F. (1994). Volition and schizophrenia. In A. S. David & J. C. Cutting (Eds.), *The neuropsychology of schizophrenia* (pp. 39–48). Hillside, UK: Lawrence Erlbaum.

Rummel, C., Kissling, W., & Leucht, S. (2005). Antidepressants as add-on treatment to antipsychotics for people with schizophrenia and pronounced negative symptoms: A systematic review of randomized trials. *Schizophrenia Research, 80*, 85–97.

Avonex®

- ▶ Beta-Interferons

Awareness

- ▶ Alertness
- ▶ Consciousness

Awareness of Illness

- ▶ Insight, Effects on Rehabilitation

Awareness, Social Awareness

Terisa Gabrielsen, Elaine Clark
University of Utah
Salt Lake City, UT, USA

Synonyms

Social cognition; Theory of mind

Definition

Social awareness is defined as the ability to recognize another person's thoughts and feelings, predict and understand another's behaviors based on the perception of another's mental state, and empathize with others.

Current Knowledge

Social awareness is required for people to live successfully in complex social groups and requires the ability to perceive and process subtle social signals (e.g., recognition and interpretation of facial expression and vocal tone). Areas of the brain that are thought to be involved in social awareness include: right temporal lobe (facial recognition and expression), superior temporal sulcus (biological motion), and orbitofrontal and prefrontal cortex, amygdala, and possibly insular cortex (social cognition) (Kolb & Whishaw, 2003; Winston, Strange, O'Doherty, & Dolan, 2002). Core skills for social awareness include perspective taking and the ability to read the emotions of others using nonverbal cues. Deficits in social awareness are often found among individuals with various developmental disorders, including autism and nonverbal learning disabilities. Social awareness skills are key components in social learning and social skill interventions (e.g., Bellini, 2006).

References and Readings

Beland, K. (2007). Boosting social and emotional competence. *Educational Leadership, 64*(7), 68–71.

Bellini, S. (2006). *Building social relationships.* Shawnee Mission, KS: Autism Asperger Publishing Co.

Kolb, B., & Whishaw, I. Q. (2003). *Fundamentals of human neuropsychology* (5th ed.) New York: Worth.

Markova, G., & Legerstee, M. (2006). Contingency, imitation, and affect sharing: Foundations of infants' social awareness. *Developmental Psychology, 42*(1), 132–141.

Sperry, R. W., Zaidel, E., & Zaidel, D. (1979). Self recognition and social awareness in the deconnected minor hemisphere. *Neuropsychologia, 17,* 153–166.

Winston, J. S., Strange, B. A., O'Doherty, J., & Dolan, R. J. (2002). Automatic and intentional brain responses during evaluation of trustworthiness of faces. *Nature Neuroscience, 5,* 277–283.

Axon Sheath

► Myelin