Chapter 7

Cerebrovascular Disease and Disorders

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Introduction

Brain injury due to cerebrovascular disease is a common cause of cognitive dysfunction in adults and a clinically significant cause of disability in children. Stroke, defined as brain injury due to a disruption of cerebral blood flow, has an incidence of 94/100,000 age-adjusted person-years in high-income countries and 117/100,000 age-adjusted person-years in low-middle income countries [1]. As many as 65% of adults experience new or worsening cognitive deficits following stroke [2], and cognitive deficits occur in up to 50% of children following ischemic or hemorrhagic stroke [3]. Therefore, assessment of neuropsychological function following stroke is an important part of the medical management of these patients.

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Medical Information Regarding Cerebrovascular Disorders

The two main categories of cerebrovascular disease are ischemic and hemorrhagic. Ischemic stroke is due to lack of blood flow to part of the brain. Occlusion of a cerebral artery by a blood clot that travels from the heart or another vessel (embolus) or that develops within a cerebral artery (thrombus) results in an arterial ischemic stroke. Diminished cerebral blood flow due to narrowing of a blood vessel or decreased blood pressure also may result in ischemic brain injury. Less commonly, a blood clot develops within one or more veins that drain the brain, known as cerebral venous sinus thrombosis, and leads to venous infarction. Hemorrhagic stroke occurs when a blood vessel ruptures, leading to brain injury.

Risk Factors for Cerebrovascular Disorders

In adults, arterial ischemic stroke is commonly associated with advancing age, hypertension, atrial fibrillation, smoking, and diabetes mellitus [4]. Other risk factors include obesity, cardiac disease, carotid stenosis, sickle cell anemia, recent infection, and alcohol abuse. In young adults, abnormalities of blood vessel structure such as arterial dissection, noninflammatory vasculopathies, and vasculitis are also associated with stroke [5]. In addition, hematologic abnormalities leading to hypercoagulability may play a

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role in selected cases [6]. Cerebral venous sinus thrombosis, which can result in either ischemic or hemorrhagic infarction, is associated with oral contraceptive use, infections of the head, neck, or central nervous system, malignancy, prothrombotic states, inflammation, and pregnancy [7]. In fact, the risk of both ischemic and hemorrhagic stroke is increased during pregnancy and the postpartum period [8].

A common risk factor for primary intracerebral hemorrhage in adults is hypertension. Other risk factors include amyloid angiopathy, elevated cholesterol, treatment with anticoagulants, heavy alcohol use, smoking, renal dialysis, and use of sympathomimetic drugs such as cocaine and amphetamines [9]. Vascular malformations such as aneurysms and arteriovenous malformations (AVMs) are much less common causes of hemorrhagic stroke in adults [10, 11].

Risk factors for cerebrovascular disorders in children are quite different from adults. Congenital or acquired heart disease, congenital or acquired abnormalities of arterial structure such as arterial dissection, transient cerebral arteriopathy of childhood, moyamoya disease and vasculitis, prothrombotic states, sickle cell anemia, and infection are common risk factors for arterial ischemic stroke in children [12–14]. In neonates, maternal and fetal physiologic factors associated with pregnancy likely contribute to the risk of arterial ischemic stroke, as do congenital heart disease, prothrombotic states, maternal infection, and placental abnormalities [15]. Pediatric cerebral venous sinus thrombosis has been associated with dehydration, prothrombotic states, head and neck infection, trauma, surgery, malignancy, and inflammatory conditions [16]. Hemorrhagic stroke in children is commonly associated with vascular malformations such as AVMs, aneurysms, and cavernous malformations, although hematologic abnormalities and other medical conditions can be precipitants [17]. In contrast, hemorrhagic stroke in term neonates is often secondary to ischemia, but a cause is not always identified [18, 19].

Clinical Presentation of Cerebrovascular Disorders

In the majority of patients, cerebrovascular disease results in a focal neurologic deficit with sudden onset. The nature of the deficit depends on the precise location and the specific mechanism of brain injury. Arterial ischemic stroke affecting a single blood vessel in the anterior circulation (vessels supplied by the carotid arteries) may present with contralateral weakness, numbness or loss of vision, aphasia, or neglect, while ischemic stroke affecting a vessel in the posterior circulation (vessels supplied by the vertebral arteries) may present with cranial nerve abnormalities, ataxia, dysmetria, or altered mental status, as well as contralateral weakness, numbness, or loss of vision. Symptoms are similar in children and adults, although neonates may not exhibit any focal neurologic deficits at the time of an arterial ischemic stroke. Instead, deficits due to perinatal stroke may become apparent over months to years. Seizures occur relatively rarely in adults at the time of an arterial ischemic stroke but are more common in children and very common in neonates. Ischemic stroke due to small vessel vasculitis may be associated with acute motor or sensory deficits but may also have a more indolent presentation with chronic headaches and slowly progressive cognitive or behavioral dysfunction [20]. In patients with sickle cell anemia, symptoms of cerebrovascular disease include those for acute arterial ischemic stroke, as described above. However, these patients are also at high risk for more global neurocognitive deficits as silent infarcts accumulate [21]. Similarly, vascular cognitive impairment or vascular dementia can develop in adults following a clinically apparent episode of acute neurologic dysfunction or may develop in a slowly progressive or stepwise fashion [22]. Vascular dementia is covered in greater detail in a separate chapter in this book.

Patients with cerebral venous sinus thrombosis often come to medical attention after developing severe and unremitting headache, vomiting, altered level of consciousness, seizures, blurry or double

vision. Focal motor or sensory deficits may occur, particularly in the setting of venous infarction. Patients with intracerebral hemorrhage often present with similar symptoms, although the severity of the headache may be greater and deterioration of consciousness may occur more rapidly.

Diagnosis of Cerebrovascular Disorders

Neuroimaging techniques are the mainstay of diagnosis for cerebrovascular disorders [23, 24]; see Fig. 7.1. In the acute setting, non-contrast computed tomography (CT) is used to rapidly assess for intracerebral hemorrhage and to rule out nonvascular causes of an acute neurologic deficit. While CT is quite sensitive for acute hemorrhage, it is rather insensitive for acute ischemic stroke within the first 12–48 h, especially for strokes that are small or affect subcortical structures. Magnetic resonance imaging is the gold standard imaging study for diagnosis of ischemic stroke. In particular, acute ischemia can be detected on the diffusion-weighted imaging (DWI) sequence within minutes to hours of stroke onset [25]. The movement of water in the extracellular space is measured on this sequence. As a consequence of acute ischemia cells begin to swell, which restricts the diffusion of water in the extracellular space. Therefore, this MRI sequence is exceptionally sensitive to acute ischemia since it can detect the earliest effects of ischemia on cell structure. Cerebral perfusion, a quantitative measure of blood flow to particular brain regions, is another parameter that can be assessed. Ischemia and subsequent infarction occur when cerebral perfusion drops below a critical level for some period of time. By measuring cerebral perfusion at the time of acute stroke, either with magnetic resonance perfusion or computed tomography perfusion techniques, one can identify brain tissue that is at risk for infarction but has not yet suffered permanent injury by comparing the areas of abnormal perfusion (tissue at risk for infarction) to the areas of abnormal diffusion (infarcted tissue). The mismatch between these two images reveals the vulnerable brain tissue that may benefit from acute medical interventions and has been the focus of much research in adult stroke treatment.

Venous infarction due to cerebral venous sinus thrombosis is best seen with MRI, and the presence of acute thrombus within the venous system can often be visualized. The extent of parenchymal injury associated with intracerebral hemorrhage and small or chronic areas of hemorrhage are seen better on MRI than CT, so MRI is indicated for the evaluation of intracerebral hemorrhage as well. The high resolution of MRI allows the clinician to distinguish stroke from other conditions that can mimic cerebrovascular disease clinically. This is especially important in the evaluation of children, where stroke is a less common cause of a focal neurologic deficit than in adults [26].

Visualization of cerebral blood vessels is also necessary to characterize the etiology of cerebrovascular disorders. The choice of imaging modality depends on the stroke syndrome, acuity of the patient and local expertise. Arterial and venous structures can be visualized noninvasively with MRI or CT-based techniques. Magnetic resonance angiography (MRA) and computed tomography angiography (CTA) provide high-resolution images of the cerebral arteries, while magnetic resonance venography (MRV) and computed tomography venography (CTV) do the same for cerebral veins and venous sinuses. Carotid ultrasound and transcranial Doppler (TCD) are noninvasive techniques that use ultrasound to image flow through arteries, but they do not provide the same anatomic resolution as MRA or CTA. Carotid ultrasound is commonly used to evaluate for carotid stenosis due to atherosclerosis in adults with arterial ischemic stroke, and TCD is routinely used to assess intracranial blood flow at the time of acute stroke as well as to screen for intracranial vasculopathy in patients with sickle cell anemia [27]. The gold standard study for visualization of cerebral vessels is a catheter-based angiogram. This is an invasive test in which a catheter is placed in the femoral artery and advanced into cerebral arteries. Contrast material is then injected and visualized with X-ray images. This study is necessary for the optimal evaluation of vascular malformations such as aneurysms and

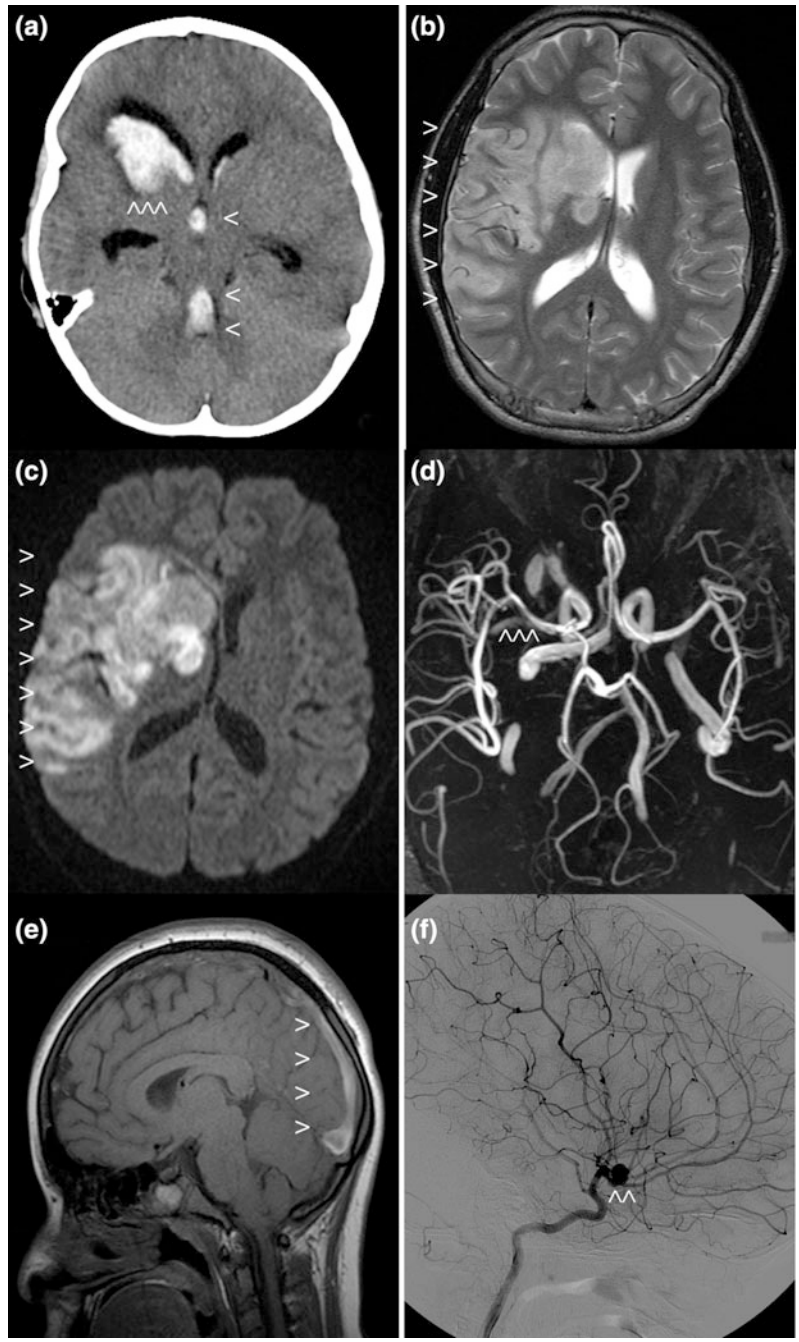

Fig. 7.1 Representative neuroimaging studies from patients with cerebrovascular disease. **a** Head CT from patient with acute intracerebral hemorrhage due to cavernous malformation. Blood is indicated by arrowheads. **b**, **c** Brain MRI from patient with right middle cerebral artery ischemic stroke. Area of infarction is indicated by arrowheads on axial T2 (**b**) and diffusion-weighted (**c**) images. **d** MRA from same patient showing narrowing and irregularity of right middle cerebral artery (arrowheads). **e** Sagittal T1 brain MRI from patient with cerebral venous sinus thrombosis. Blood clot within the superior sagittal sinus and torculum is indicated by arrowheads. **f** Cerebral catheter angiogram from patient with aneurysm affecting right anterior cerebral artery. Aneurysm is marked with arrowheads

AVMs. It is also indicated in selected cases of arterial ischemic stroke, especially when vasculitis is a diagnostic consideration.

Evaluation of heart function with an echocardiogram and electrocardiogram is another critical part of the evaluation for arterial ischemic stroke. Blood tests including serum glucose and cholesterol levels help to identify stroke risk factors in adults, while blood tests to detect a prothrombotic tendency are performed in children with ischemic stroke. In the setting of intracerebral hemorrhage, blood tests to detect a bleeding diathesis may be part of the evaluation, especially in young children.

Treatment of Cerebrovascular Disorders

The acute treatment of stroke depends on the mechanism of injury. In adults with arterial ischemic stroke, intravenous infusion of tissue plasminogen activator (tPA), a drug that lyses blood clots, is the only FDA-approved medical treatment. Widespread use of this drug is limited by the need to administer it within 4.5 h of stroke symptom onset [28], meaning that fewer than 6% of stroke patients benefit from this therapy [29]. Several studies have demonstrated improved outcome compared to medical therapy following mechanical thrombectomy in adults with large vessel occlusion in the anterior circulation. This treatment must be instituted within 6 h of stroke onset, and a greater degree of recanalization correlates with improved outcome [30]. Other acute stroke treatments include aspirin and intra-arterial administration of tPA [31]. Surgical decompression can be beneficial in patients with space-occupying infarction [32]. Ongoing studies are evaluating the optimal use of therapeutic hypothermia in the management of acute stroke [33].

To prevent future strokes, treatment with an antiplatelet or anticoagulant medication is recommended [31], in addition to treatment of stroke risk factors such as hypertension, elevated cholesterol, and diabetes. Stent placement may also be useful for secondary prevention in selected cases of arterial stenosis [34]. None of these treatments have been studied in children, although the use of antiplatelet or anticoagulant medications for secondary prevention is recommended in most cases [35]. Chronic transfusion therapy has been shown to prevent stroke in children with sickle cell anemia [36], and revascularization surgery for moyamoya disease also prevents stroke recurrence [37]. Anticoagulation is the treatment of choice for acute cerebral venous sinus thrombosis in adults and children [35, 38].

Following intracerebral hemorrhage, acute treatment may include surgical evacuation of hemorrhage or placement of a temporary ventriculostomy catheter if obstructive hydrocephalus develops. Preventative treatment of recurrent hemorrhage may include surgical clipping or endovascular coiling in the case of aneurysms, and endovascular embolization, surgical resection or treatment with stereotactic radiosurgery in the case of arteriovenous malformations [39, 40]. Supportive measures following any type of cerebrovascular insult include maintenance of cerebral perfusion pressure with intravenous fluids, avoidance of hypoglycemia or hyperglycemia, and avoidance of fever.

Mechanisms Underlying Cognitive Dysfunction in Cerebrovascular Disorders

Since cerebrovascular disease often results in circumscribed brain injury, the nature of the resulting cognitive deficits in older children and adults is generally related to the specific brain regions injured. In fact, the study of behavior in patients who experienced stroke has been one of the greatest sources of information about the functional organization of brain structure and has contributed immensely to the field of neuropsychology. Patients with focal brain injury, often due to cerebrovascular disease, have provided terrific insights into the biologic basis of behavior [41]. A comprehensive discussion of structure–function relationships in the brain is beyond the scope of this chapter, although numerous books have been devoted to this topic, especially as it relates to cerebrovascular disease (see [42, 43]). One unique aspect of brain injury resulting

from arterial ischemic stroke is that certain patterns of injury are consistently seen in different patients since the artery which supplies a particular brain region is quite consistent across patients. Knowledge of cerebrovascular anatomy allows the clinician to predict which brain regions are most likely to be affected by a stroke in the territory of a specific artery and to anticipate the deficits most likely to be seen. For example, a stroke due to occlusion of the left (language and motor dominant hemisphere) middle cerebral artery, which supplies the frontal, parietal, superior temporal lobes, and the basal ganglia, will generally result in aphasia, right hemiparesis, right hemisensory impairment, and right homonymous hemianopsia, while a stroke in the territory of the right (nondominant) middle cerebral artery will lead to spatial neglect, impaired visuospatial skills, left hemiparesis, left hemisensory disturbance, and left homonymous hemianopsia. Only some of these deficits may occur if the vascular occlusion is confined to smaller branches of the middle cerebral artery. Structure–function relationships are less consistent in patients with multifocal or progressive arterial ischemic disorders such as vasculitis, moyamoya disease, sickle cell anemia, and vascular dementia, which often result in bilateral injury and may affect white matter and subcortical nuclei to a greater degree than cerebral cortex. In patients with intracerebral hemorrhage or infarction due to cerebral venous sinus thrombosis, the deficits are largely determined by the particular brain regions that are injured, but the patterns of brain injury are more variable. In the subsequent sections, the brain regions most often associated with a particular deficit will be mentioned. While many cognitive deficits following stroke relate specifically to lesion location, deficits in attention and concentration, processing speed, and executive functioning are common following brain injury in any location. Another caveat is in the assessment of patients who experienced stroke in the newborn period or early in childhood, as anatomic localization of function and the pattern of cognitive impairment resulting from cerebrovascular disease is more variable in this population [44].

Neuropsychological Assessment Following Stroke

Neuropsychological assessment provides essential information regarding a patient's cognitive, emotional, and behavioral functioning following a stroke. An effective evaluation will provide detailed information on the patient's deficits, but will also highlight areas of strength. It is vital that all participants in the patient's care, including family members, physicians, rehabilitation therapists, and work or school personnel, understand the patient's neuropsychological profile and specifically how functioning may have changed as a result of a stroke. This will enable appropriate interventions and accommodations to be put in place in order to maximize recovery and independence.

Assessment in the Acute Phase

In the acute phases of recovery, the neuropsychologist offers pertinent information regarding patient functioning to an interdisciplinary team on inpatient units, such as establishing reliable communication with the patient (as in cases of aphasia or hemineglect), documenting the degree of cognitive impairment, assessing the patient's own judgment regarding his or her impairment and associated safety concerns (e.g., anosognosia), and contributing to prognosis and rehabilitation planning. The neuropsychologist will assess the patient's cognitive and emotional functioning following a stroke, often at repeated intervals to monitor the course of recovery.

Many challenges are presented to the neuropsychologist when conducting assessments with acutely injured patients or within inpatient settings. Prior to conducting a neuropsychological assessment in the acute period, it must be determined that the patient is oriented, alert, and capable of participating in the evaluation. This can be assessed via a standardized measure such as mini-mental status examinations, the Children's Orientation and Amnesia Test (COAT) [45], or the Galveston Orientation and Amnesia

Test (GOAT) [46]. The neuropsychologist will often need to modify standardized administration procedures to accommodate specific impairments incurred from stroke, such as hemiparesis, visual field cut, aphasia, or fatigue. Testing time may be limited on inpatient units and a comprehensive neuropsychological battery may not be practical. Therefore, a rapid screening instrument is often utilized when working on inpatient units, as they allow for brief assessment of pertinent domains, and are generally highly portable for bedside administration. Examples of these brief screening instruments include the "Cognistat" (formerly known as the *Neurobehavioral Cognitive Status Examination*) [47] and the *Repeatable Battery for the Assessment of Neuropsychological Status* (RBANS) [48] for adults, and the Comprehensive Neuropsychological Screening Instrument for Children (CNSIC) for children ages 6–12 [49][1].

It is important to note that the sensitivity of screening assessments is limited due to the possibility that relevant information may be missed because of the brevity of the evaluation [49]. Therefore, longer neuropsychological batteries may be appropriate for inpatients, depending on the patient's endurance and impairments. Full-length (typically all day) evaluations provide detailed information on a patient's strengths and weaknesses in multiple cognitive domains, assess for emotional or behavioral problems that may impact a patient's functioning, and allow for detailed recommendations. Therefore, after an inpatient stay, most patients who have suffered a stroke should return in 3–12 months for a comprehensive, follow-up neuropsychological evaluation to further identify strengths and weaknesses in their neuropsychological profile, for assessment of change, and for educational, vocational and/or treatment planning. If cognitive deficits are found, ongoing monitoring in the form of repeated neuropsychological evaluations at specified time intervals (one year is commonly recommended) may be appropriate.

It is also important to consult with the patient's neurologist and other specialists that may be involved in the patient's care before and after neuropsychological evaluations. The neurologist may identify neurologic deficits that can inform planning of a neuropsychological evaluation; however, it is important to note that subtle cognitive deficits may be present in a patient with a normal neurologic exam. Speech-language pathologists as well as occupational and physical therapists can also provide valuable information regarding a patient, and may benefit from the neuropsychologist's perspective as well. For example, since therapists work with patients frequently, they can often alert the medical team to possible deficits in attention, memory, or executive functioning, and may enjoy collaborating with the neuropsychologist on strategies to help overcome these deficits in therapy sessions. The team's psychologist and/or social worker are invaluable members of the multidisciplinary team, and can alert the neuropsychologist to psychosocial or emotional factors that may be influencing the patient's functioning and provide or link the patients to appropriate interventions. Finally, an educational or vocational coordinator can assist in re-integrating the patient into home, school, or work with appropriate accommodations and supports as recommended by the medical team as well as information gleaned from the neuropsychological evaluation.

The following sections detail domains of neuropsychological functioning commonly affected by stroke and common methods used to assess those domains. While references to specific tasks or tests are included in this section, a thorough review of assessment measures is beyond the scope of this chapter and can be found elsewhere [49, 50].

Intellectual Functioning

Assessment of intellectual functioning following a stroke is important in order to establish a

[1]The authors and copyright holders are William J. Ernst, Psy.D., University of Medicine and Dentistry of New Jersey, Robert Wood Johnson Medical School, Cooper Hospital; N. William Walker, Ed.D., James Madison University; and Gary Simpson, M.S., University of Minnesota.

comparison point by which to judge impairments or strengths in other domains and for judging relative performance among domains of intellectual functioning. In addition, performance on scales of intelligence provides clues about other neuropsychological domains that may be impaired and should be assessed further. Finally, the high prevalence rate of cerebrovascular dementia, which has been estimated to affect 25–50% of stroke patients [51], further highlights the need for the assessment of intellectual functioning following a stroke.

It is important to note that there can be a decline in performance on tests of intellectual functioning following stroke due to difficulties with task performance rather than a decline in reasoning skills. For example, hemiparesis of the dominant arm will likely result in lower performance on pencil and paper tasks, such as the Processing Speed subtests from the Wechsler scales (e.g., Wechsler Intelligence Scale for Children—Fourth Edition [52], Wechsler Adult Intelligence Scale, Third Edition [53], among others), and aphasia may result in difficulty understanding task directions and/or expressing oneself through language, as is often required for verbal reasoning tasks. In adults, left hemisphere strokes have been found to impair Verbal IQ more than Performance IQ on the Wechsler scales and the reverse is true for right hemisphere strokes [54]. In addition, brain injury in general and stroke in particular often leads to decline in attentional [54], working memory, and/or processing speed skills [55], which also may impact performance. For this reason, index, factor, and subtests analysis is particularly important when interpreting the scores of patients who have had strokes.

The neuropsychologist may determine that, due to factors that inhibit performance rather than reasoning skills, the composite score of intellectual ability may not accurately reflect the patient's potential. In this case, it may be wise to choose an index or factor score as the most likely representation of underlying cognitive ability, or choose another instrument that may allow the patient to demonstrate their reasoning skills without the need for verbal or motor output. For example, there are a select number of nonverbal tests of intelligence for children and adolescents (e.g., Leiter International Performance Scale-Revised (Leiter-R) [56], Universal Nonverbal Intelligence Test [57] (UNIT), Comprehensive Test of Nonverbal Intelligence [58] (CTONI)) and for children, adolescents, and adults (e.g., Test of Nonverbal Intelligence, Third Edition [59] (TONI-3); Raven's Progressive Matrices [60]). These tests are suitable for patients with aphasia due to lack of language demands; in some cases, even the test directions are communicated nonverbally.

In cases where it is desirable to have an estimate of premorbid intellectual functioning, there are a variety of ways in which this estimate can be obtained. Often, estimates of premorbid functioning are inferred from vocational history, educational attainment, and report from patients and families. It is also inferred with the use of tests on which performance is typically less affected by brain injury; these tests are thought to "hold" the level of premorbid function. For example, measures of crystallized intelligence [61], which is a form of intelligence based on knowledge and experiences, may reflect a patient's pre-injury level of functioning. Examples of tests of crystallized intelligence include the verbal reasoning subtests from intelligence scales, single word reading skills, and receptive vocabulary. Tests specifically developed to determine premorbid intellectual abilities include the North American Adult Reading Test (NAART) [62] and the Wechsler Test of Adult Reading (WTAR) [63] Clearly, due to the verbal aspect of most of these tasks, these tests are not good measures of premorbid functioning in patients with aphasia. It is important to note that although these measures may be good representations of pre-injury functioning, brain injury is extremely diverse and there is no one performance pattern that is diagnostic of brain injury [64].

Language

Aphasia is a common consequence of stroke, particularly left hemisphere stroke, and occurs in approximately one-third of adult stroke patients [65, 66]. Aphasia usually occurs following left

hemisphere strokes that damage the perisylvian regions of the brain, which include Broca's area, Wernicke's area, and the arcuate fasciculus [67]. Left middle cerebral artery ischemic strokes often cause damage to these perisylvian regions and result in aphasia. Damage to Broca's area, which is important for the motor programming of speech, and surrounding structures typically leads to Broca's aphasia. Broca's aphasia is characterized by word-finding difficulty, impaired repetition, agrammatism, hesitations, pauses, phonemic errors, and verbal apraxia (including phonemic errors), but with preserved language comprehension [68]. Agrammatic speech has a telegraphic quality, with omission of articles, prepositions, inflexions, and sometimes even verbs. Damage to Wernicke's area, which is important for comprehension of the spoken word, results in fluent speech characterized by paraphasias and impairment in comprehension, repetition, and naming. Reading and writing are often affected as well [68]. Damage to the arcuate fasciculus results in conduction aphasia, which is defined by poor repetition with relatively fluent speech and intact comprehension [68]. Injury to all of these regions results in global aphasia. Aphasia can also result from damage to non-perisylvian language areas, typically by damaging connections from perisylvian language regions to other brain areas; these disconnection syndromes are referred to as transcortical aphasias [67]. Transcortical motor aphasia is characterized by impaired spontaneous speech and writing with intact repetition and comprehension, while transcortical sensory aphasia is notable for fluent but paraphasic speech, intact repetition, and poor comprehension. A thorough review of aphasia subtypes can be found in Kertesz [68] and in Beeson and Rapcsak [67].

Most patients demonstrate improvement in language skills in the first year following their stroke, though in some patients milder language deficits or even continued aphasia may remain [66, 69]. For this reason, neuropsychologists working with patients who have had strokes should assess for overt aphasia as well as higher level language processing deficits.

There are a number of brief screening tools designed for quick, bedside assessment of adults suspected of having aphasia, of which the Frenchay Aphasia Screening Test (FAST) appears to be the most widely used [70]. Screening tools are designed to identify patients in need of more thorough assessments conducted by speech-language pathologists or neuropsychologists. Further evaluation for aphasia should include formal assessment of speech comprehension, repetition, naming, reading, and writing [50]. There are a number of tests that are designed to provide a comprehensive assessment of aphasia, including the Boston Diagnostic Aphasia Examination [71] and the Multilingual Aphasia Examination [72] (MAE), or the examiner can choose subtests from different tests. In addition, fluency should be assessed by qualitative observation of spontaneous speech, with attention paid to utterance length, language formulation and organization, word-finding problems or paraphasias, grammar, and syntax. Evaluating these areas will allow the examiner to appropriately categorize the subtype of aphasia.

In some stroke patients, overt aphasia improves over time but deficits in higher order language processing remain. Assessment of reading and writing skills is appropriate for children and may be appropriate for adults depending on vocation. In addition to measures of single word reading and spelling, it is useful to assess reading comprehension, fluency of reading and writing, and writing composition. It may also be useful to qualitatively assess the patient's ability to follow written directions, write to dictation, or copy a written passage [50]. Assessment of phonological and rapid naming skills, which are the core cognitive processes underlying reading acquisition [73], is particularly important to assess in children who may be at risk for developing reading problems following a stroke.

Memory

Memory impairment is one of the most common deficits experienced following a stroke.

Prevalence estimates are as high as 50% in the first few weeks following a stroke, with subsequent improvement over the ensuing months. A recent review of poststroke memory dysfunction found that deficits were observed in 13–50% of patients in the initial weeks following stroke, and this number decreased to 11–31% after one year or more [74]. Memory deficits have a negative impact on social and functional independence, can hinder progress in rehabilitation treatment programs, and can adversely impact work and school performance.

There is considerable variability in the presentation of memory deficits following a stroke. While the location of the stroke typically determines the nature of the memory impairment, memory processes are mediated by a broad network of widely distributed subcortical and cortical regions, so damage to any part of the underlying neural circuitry can disrupt memory. Knowledge of the neuroanatomic substrates of memory and acquired memory deficits from focal lesions can help guide assessment procedures in the neuropsychological evaluation. Regions within the medial temporal lobe (MTL), diencephalon, basal forebrain, and frontal lobe, and multimodal association areas of the posterior cortex are associated with memory functioning. Additionally, as memory is a higher order process that is dependent upon the general integrity of more basic perceptual functions (such as visuospatial perception or language comprehension), damage to these lower level functions can result in a memory deficit secondarily. A thorough review of the neuroanatomic underpinnings of memory deficits in stroke is beyond the scope of this chapter, and can be found elsewhere (e.g., [77]). However, a brief overview of amnestic syndromes following stroke will be summarized, with a focus on episodic memory.

Memory involves the ability to encode, store, and retrieve information, and stroke can disrupt these processes at any stage. Memory impairment can manifest in poor immediate or delayed free recall of stimulus material, in a flat learning curve despite repeated presentation of information, and with variable benefit from cueing or recognition. Intrusion errors or confabulation may be prominent. Identifying preserved aspects of memory can facilitate the process of rehabilitation and reintegration into the home or work environment.

It has been well established that damage to MTL structures can result in anterograde amnesia, or a failure to learn new information. The critical region for MTL amnesia is the hippocampal formation, although there are probable contributions from damage to adjacent parahippocampal regions. There is a lateralizing effect, in that damage to the left MTL typically results in verbal memory impairment, whereas damage to the right MTL typically results in nonverbal (visuospatial) memory deficits. MTL damage from stroke is often due to infarction in the posterior cerebral artery (PCA) and to a lesser degree the anterior choroidal artery (AChA) territories [75]. Bilateral PCA infarction involving the MTL can result in severe anterograde amnesia with retrograde amnesia likely as well. However, left PCA infarcts can appear equally severe in the acute phase, as explicit memory is language dependent [55].

Lesions within diencephalic structures have been strongly implicated in anterograde amnesia. Damage to the anterior thalamic nuclei and the mammillary bodies have been repeatedly linked with episodic memory deficits. These regions of the diencephalon have dense connections to the hippocampal formation. Damage to projections between the anterior thalamic nuclei and the mammillary bodies are a strong predictor of memory deficits following stroke. The intralaminar region of the thalamus is a critical junction from MTL structures to the mammillary bodies via the fornix. Infarctions in these regions of the diencephalon are usually from the tuberothalamic or polar arteries that arise from the posterior communicating artery.

Amnestic syndromes resulting from basal forebrain lesions are typically due to anterior communicating artery (ACoA) infarcts and often involve considerable executive impairment. Deficits are usually due to retrieval failure, and patients can benefit from recognition cues. However, both retrograde and anterograde amnesia have been documented in ACoA infarctions.

Confabulation is quite prominent in ACoA strokes, and is often related to poor awareness of memory deficit. Confabulated material can be plausible inventions to fill in gaps of missing material, or can result from intrusion or incorrectly retrieved information from a similar experience. However, confabulations are typically not intentional and tend to dissipate as the person becomes aware of memory problems. Damage to the septal nuclei in the basal forebrain can result in amnesia, due to their cholinergic connection to the hippocampus. Executive dysfunction arising from damaged frontal and subcortical regions can result in memory deficits secondarily, via impaired working memory and poor self-monitoring. Dysfunction of this nature can have considerable impact on memory formation and retrieval.

Thorough assessment of memory necessitates a comprehensive evaluation of other cognitive functions that can impact performance on standardized tests of memory, such as attention, concentration, processing speed, language, and visual-constructional abilities, all quite commonly impaired in stroke. When evaluating subjective complaints of memory deficits, it is important to ask for examples, as patients and families will often confuse dysnomia or attentional problems with memory deficits. Lezak [46] provides the following guidelines for a comprehensive memory assessment: (1) orientation to time and place (2) prose recall to determine if the patient can learn and recall meaningful information (3) rote learning ability (4) visuospatial memory (5) remote memory (6) personal-autobiographical memory. Test selection should allow the patient to engage in immediate and delayed recall trials, with both free and cued recall, recognition trials, and repetition of stimuli to facilitate learning.

Attention and Neglect

Assessment of attention is fundamental to the neuropsychological exam, as attentional deficits can mask a person's abilities in most other cognitive domains. Attention is commonly impaired in stroke, and determination of level of functioning is paramount. Furthermore, a disorder of attention (Attention-Deficit/Hyperactivity Disorder, or ADHD) is the most common psychiatric disorder following childhood stroke [76]. Deficits in attention can be expressed globally or in a limited number of areas, and can result from damage to a variety of cortical and subcortical brain systems. Subtypes of attention that can be impacted include orienting, vigilance, capacity, sustained, selective, and alternating attention. Focal lesions due to stroke may manifest in a striking attentional disturbance of neglect of stimuli contralateral to the lesion side, termed *hemineglect* or *hemi-inattention* (see below). Assessment of neglect has practical significance for treating rehabilitation professionals and caregivers, as neglect has been shown to negatively impact activities of daily living, rehabilitation success, length of hospitalization, and functional outcome [77] It is important to assess early for the presence of neglect, as it poses significant safety concerns (e.g., burns to an affected limb or falls due to neglect of surrounding space).

Assessment of attention in the neuropsychological exam should come from both behavioral observations throughout testing procedures, and from standardized measures designed to assess attention specifically or in conjunction with other cognitive skills. A multifactorial approach is necessary, as attentional impairments can occur in some domains, but not others. It is important to quantify different types of attention in stroke assessment. Sustained attention and vigilance are often assessed using a computerized continuous performance task (e.g., Conners' Continuous Performance Test-II [78] or Conners' Kiddie Continuous Performance Test [79]) or other tests of sustained attention. Attentional capacity is commonly assessed using span tests, such as Digit Span and Spatial Span from the Wechsler batteries [53].

Unilateral spatial hemineglect, characterized by decreased attention or action to stimuli in the contralesional hemifield that cannot be accounted for by sensory or motor deficits, is a well-documented phenomenon in adults with focal brain injury [80]. In adults neglect is more persistent and severe following right hemisphere injury, although it occurs with injury to either hemisphere [81]. It most commonly presents after posterior right hemisphere stroke with neglect of stimulus occurrence in the left field. Neglect can

range in severity, can vary from testing session to testing session and may be specific to a particular region of space. For example, patients may show neglect of stimuli in personal space (stimuli in contact with the body), peripersonal space (items within arm's reach) or extrapersonal space (objects beyond arm's reach) [82]. The presence of neglect may vary across spatial reference frames. Neglect can occur for objects in contralesional space with respect to the viewer (egocentric), to a stimulus (allocentric) or the environment [83]. Neglect may also be specific to a type of task (perceptual versus motor) or sensory modality (visual, tactile, auditory), and may be apparent on some tasks but not others within a given sensory modality [84].

A number of investigators have proposed theories to account for neglect in adult patients with brain injury. Neglect could result from excessive attention to one side of the world or failure to direct attention away from that side of the world. While the final result might appear the same, these are theoretically distinct possibilities and both have been suggested as the mechanism for neglect. Mesulam proposed that spatial attention relies upon a distributed network within each hemisphere, centered in the inferior parietal lobule but receiving polymodal sensory input from other parietal regions as well as information about motivational valence from cingulate cortex and basal forebrain, motor information from frontal eye fields, and general arousal modulation from the reticular activating formation. However, he suggested that the two hemispheres are not equally involved in spatial attention. Rather, the right hemisphere is more active in attentional tasks and may attend to all of extrapersonal space, while the left hemisphere only attends to right space [85]. Heilman also supported the right hemisphere as being dominant for attention, demonstrating that the right parietal lobe is active in attention to either hemifield, while the left parietal lobe only responds to stimuli in the contralateral hemifield [86]. In their views, this accounts for the greater persistence and severity of neglect following right hemisphere injury as compared to left hemisphere insults. Kinsbourne proposed asymmetric involvement of the hemispheres in attention, although he suggested that each hemisphere generates a vector of spatial attention directed contralaterally and inhibits the opposite hemisphere [87]. He accounted for the frequency of neglect after right hemisphere injury by claiming left hemisphere dominance for attention. If the right hemisphere's vector is weaker than the left, then right hemisphere injury unmasks the dominance of the left hemispheric vector.

Another way of conceptualizing neglect is a failure to disengage attention from one part of the visual world. Using this framework Posner and colleagues argued that three steps must occur, "disengaging from the current focus of attention, moving attention to the location of the target and engaging the target," and that parietal lobe injury impairs the disengage function in the contralesional visual field [88]. Numerous studies have provided support for this account of neglect using a cuing paradigm [89]. In this paradigm a subject looks at a fixation point. A highlighted cue then appears on one side, followed by a target. A valid cue appears on the same side as the target and an invalid cue appears on the side opposite the target. Subjects are consistently slower to respond to targets preceded by an invalid cue than a valid cue, and this is interpreted as a measure of the difficulty in disengaging attention from the location to which it was initially cued. However, subjects with neglect are much slower to respond to targets when the invalid cue is presented in contralesional space than ipsilesional space (for example, in left hemifield when the lesion is in the right parietal lobe), suggesting that the asymmetric disengage deficit accounts for the behavior of neglect. Overt cases of neglect can be readily observed in the patient's behaviors, such as eating food from only one side of their plate, reading only portions of a page or part of a word, or addressing persons standing in one visual field. It is important to note, however, that neglect can be subtle, and can require close observation as well as formal testing to be identified. Qualitative assessment in the neuropsychological evaluation is often obtained through object copying tasks or drawing of symmetrical figures (e.g., Clock Drawing Test [90]), in which the patient may omit details on one side of the page. Quantitative assessments of visual neglect include line bisection tests in which the patient is asked to indicate

the midpoint of a line, and cancelation tasks in which the patient is provided a page with numerous small targets and are asked to mark out a particular target stimulus.

Assessment of sensory neglect begins with unilateral presentation of stimuli and asking the patient to state the presence and location of the stimulus. For example, the examiner asks the patient to close his eyes and subsequently touches one hand or the other. Failure to detect stimulation on one side may indicate neglect or may be due to a primary sensory disturbance. For auditory modalities, the examiner stands behind the patient and provides gentle auditory stimulation (e.g., snapping or rubbing fingertips) to one ear and then another. If the patient detects unilateral stimulation accurately, the examiner should also assess for *extinction*, in which the

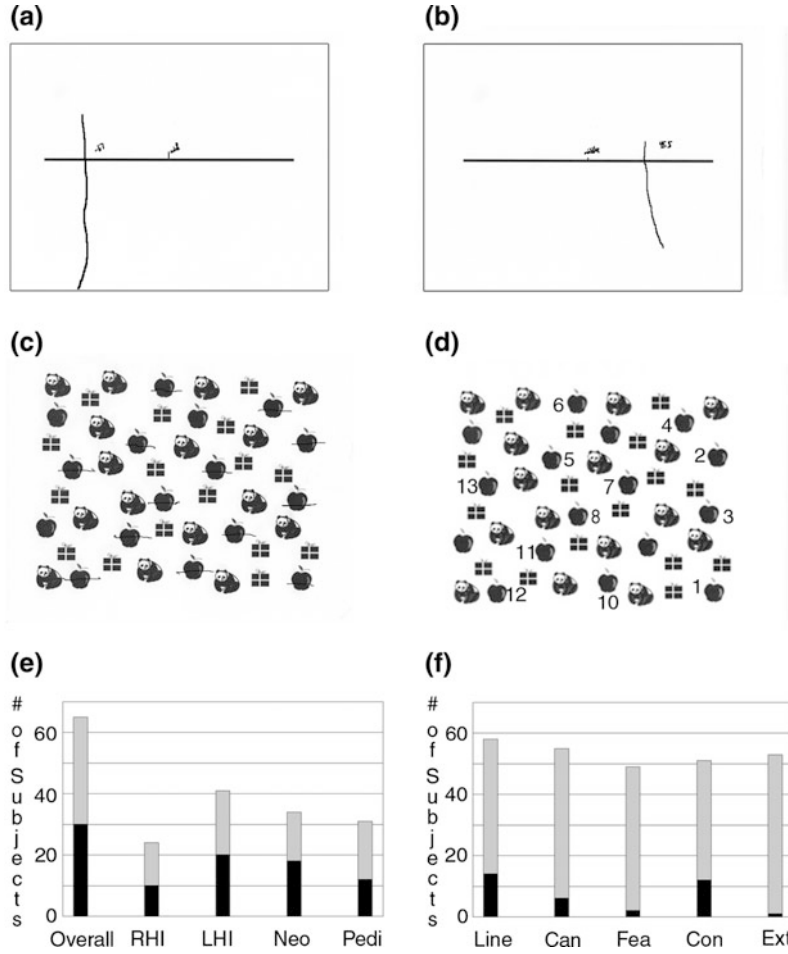

Fig. 7.2 Data from study of visuospatial neglect in children following unilateral neonatal or pediatric arterial ischemic stroke or parenchymal hemorrhage [88]. Presence of neglect was determined by comparison to normal distribution of performance by age-matched controls. **a**, **b** Examples of neglect on line bisection task from subject with left hemisphere stroke (**a**) and right hemisphere stroke (**b**). **c**, **d** Examples of neglect on cancelation task from subject with right hemisphere stroke. Subject omitted more targets from the left hemifield than the right (**c**) and canceled left-sided targets significantly later than right-sided targets (**d**). Numbers depict order in which targets were canceled. **e**, **f** Summary of performance of 65 pediatric subjects ages 2–18 years on tasks assessing for visuospatial neglect. Subjects with neglect are depicted in black and subjects without neglect are shown in gray. **e** Number of subjects showing neglect on at least one task. There was no difference in the proportion of subjects showing neglect with right hemisphere injury (RHI) as compared to left hemisphere injury (LHI), or in subjects with stroke occurring prior to one month of age (Neo) as compared to later in childhood (Pedi). **f** Number of subjects showing neglect on each of 5 tasks: line bisection (Line), cancelation (Can), featural visual search (Fea), conjunctive visual search (Con), and visual extinction (Ext)

patient fails to detect simultaneous stimulation on the side contralateral to his or her lesion but will report perception of the ipsilateral stimulus.

Visuospatial neglect has been reported in children following neonatal or pediatric stroke, but few studies have characterized this phenomenon in detail [91, 92]. In a study of 65 children who experienced unilateral arterial ischemic stroke or parenchymal hemorrhage in the neonatal period or later in childhood, chronic visuospatial neglect was assessed using 5 tasks: line bisection (Fig. 7.2a, b), cancelation (Fig. 7.2c, d), featural visual search, conjunctive visual search, and visual extinction. Almost half (30/65) of the children exhibited mild spatial neglect on at least one task, and the frequency of neglect did not differ significantly between children with right hemisphere injury as compared to left hemisphere injury, or between children with neonatal brain injury as compared to children who experienced brain injury later in childhood (Fig. 7.2e). Line bisection and conjunction search were the most sensitive tasks for the detection of neglect but did not detect neglect in all subjects (Fig. 7.2f) [93]. Overall, this study demonstrates that mild chronic visuospatial neglect is common following stroke in children and suggests that the right hemispheric dominance for visuospatial attention seen in adults is not yet consolidated in children.

Executive Functioning

Executive functions refer to a collection of higher order cognitive abilities that coordinate and regulate other mental activities. Examples of executive functions include deciding on a plan of action, sequencing steps towards a goal, regulating behaviors, selective inhibition of responding, response preparation, cognitive flexibility, set maintenance, and organizing time and space. Executive functions allow us to start and stop behaviors, monitor our performance, adapt to changing conditions and develop new strategies as needed. These functions allow an individual to engage in purposeful, goal-directed, independent behavior [50]. Aspects of attention and working memory are related to executive functioning, and successful performance of these tasks is often dependent upon these abilities.

Executive dysfunction is quite common in patients who have sustained strokes, and is considered to be a core neuropsychological deficit following cerebrovascular injury [55]. Although often described as "frontal functions," executive deficits can occur as a result of injury to non-frontal brain regions. In fact, executive dysfunction is common even in individuals whose strokes did not cause damage to the frontal lobes [55].

Behavioral manifestations of executive dysfunction can present as hypoactivity (e.g., abulia, apathy, loss of motivation, and blunted affect) or hyperactivity (e.g., distractibility, impulsivity, disinhibition, irritability, and emotional lability). Executive dysfunction can manifest cognitively as impaired response initiation and/or suppression, poor rule deduction, poor set maintenance and/or set shifting, difficulty with self-monitoring, and impaired concept formation, problem-solving, or planning abilities (see [55] for a review of these syndromes in stroke). Deficits in response rapidity are particularly common following stroke [55]. Impairments in executive functioning can be the most crippling and intractable cognitive injury, severely impacting an individual's successful reintegration at home, in the workplace, and within the community, despite relatively intact cognitive capacities in other domains. Executive functioning deficits can severely impede progress in rehabilitation of stroke, if the patient cannot benefit from feedback or generalize rehabilitation strategies into their daily living. A recent study demonstrated that executive functioning deficits are prevalent in the early phases of stroke and an excellent predictor of long-term impairment [94]. Therefore, assessment of these skills should be included in the early phases of stroke recovery.

Assessment of executive functioning should be multifaceted, and should include standardized assessment measures and qualitative observations on test-taking strategies. As Lezak notes, "A major obstacle to examining the executive functions is the paradoxical need to structure a situation in which patients can show whether and how well they can structure themselves" ([50]

p. 611). Behavioral questionnaires completed by family members can be critical in identifying poststroke behavioral change, such as the Frontal Systems Behavior Scale (FrSBe) [95]. Similarly, the Behavior Rating Inventory of Executive Function (BRIEF), which has parent, teacher, and self-report forms for children and adolescents [96], can also be useful in the assessment of executive functioning.

Formal testing of executive dysfunction following stroke can vary depending on presenting symptomatology and concerns. If possible and necessary, evaluation should include formal assessment of attention, working memory, speed of processing, response time, impulse control, planning, organization, problem solving, mental flexibility, concept formation, cognitive set maintenance, and generativity. Tests like the Rey Complex Figure Test (RCFT) [97], the Tower of London [98], and the Wisconsin Card Sorting Test (WCST) [99] can be particularly helpful in elucidating deficits in executive functioning following stroke.

Higher Order Visual Processing Skills

Stroke can impact visual processing in a variety of ways, ranging from very subtle to gross impairment. Damage to the visual cortex or portions of the visual pathway beginning at the optic nerve can lead to visual field defects or, in severe cases, cortical blindness. Higher level visual processing deficits can also occur in the absence of gross visual impairment. Impairment on higher order visual tasks is common following stroke, affecting between 34 and 75% of patients [94, 100], underscoring the need to evaluate these functions. Therefore, the neuropsychological assessment of stroke should include measurement of higher order visual processing skills.

Deficits in higher order visual processing skills are often due to posterior right hemisphere lesions; however, damage to other regions can also have an impact. Deficits can occur in the identification and localization of objects within the visual field, defined by anatomically distinct visual systems often referred to as the "what" (i.e., *visuoperception*) and the "where" (i.e., *visuospatial ability*) of higher level visual function. Object recognition ("what") is mediated by occipitotemporal structures (ventral stream), while object location ("where") is mediated by occipitoparietal structures (dorsal stream) [101]. Arterial ischemic strokes affecting the posterior cerebral artery territory can lead to visuoperceptual deficits, while strokes affecting the posterior division of the middle cerebral artery territory may also result in visuospatial deficits. Visual-constructional ability relies on these functions with a combined motor component, and is frequently included in the neuropsychological evaluation of stroke.

Cortical blindness, or complete loss of vision in both hemifields due to brain injury, is the most severe form of visual disturbance that can occur following stroke. Bilateral injury to striate cortex in the occipital lobes, as may occur with bilateral posterior cerebral artery ischemic strokes, may result in cortical blindness. Especially in the acute phase, patients may have a lack of awareness of their visual deficit and may confabulate when asked to describe their visual world, known as Anton syndrome. The mechanisms underlying this syndrome are not well understood, but the disruption of connections from primary visual cortex to brain regions necessary for conscious awareness is one possibility [102].

Visuoperceptual ability in the neuropsychological exam is often assessed through form or pattern discrimination tasks. Visual organization tests require an individual to perceive a stimulus that is fragmented, distorted or incomplete. Hierarchical form stimuli, in which a global level shape is made up of individual local level elements that differ from the global shape (e.g., the letter "M" made up of numerous "Z"s), have been used to detect hemisphere-specific visuoperceptual deficits. In adults with stroke, left hemispheric lesions have been associated with impaired local level processing while right hemispheric lesions have been associated with deficits in global processing [103]. A similar pattern of performance has also been found in children who experienced perinatal brain injury such as stroke [44].

Visual agnosia is a subtype of visuoperceptual disorders in which patients can no longer access semantic knowledge about an object in the visual field, despite intact perceptual processes. This can be further divided into *apperceptive* (impaired higher level perceptual processing) and *associative* agnosia (impaired conceptual knowledge). Modality-specific agnosia syndromes can also occur, such as *prosopagnosia* (impaired recognition of faces) and color agnosia. For a thorough description of agnosia subtypes, please refer to Bauer and Demery [104].

Visuospatial ability refers to perception of an object's orientation or location in space. Spatial neglect (discussed previously) is a common cause of impaired visuospatial skills following stroke. The inability to perform an efficient visual search is another mechanism by which stroke can impair visuospatial function [105]. Deficits in visuospatial ability can be assessed through line orientation measures (e.g., Judgment of Line Orientation; [106]).

Constructional ability, or the ability to draw or assemble an object, is a higher order visual task that requires intact perceptual/spatial skills with an additional requirement of fine motor ability. Tests of constructional ability typically involve graphomotor tasks, such as copying of figures. A popular graphomotor copying task is the Rey Complex Figure Test (RCFT) [97], which requires both visual-constructional and visual organizational skills. Tests requiring assembling and building are also somewhat common and incorporate the use of items, such as blocks or puzzle pieces. Deficits attributed to fine motor coordination in stroke patients should be considered, as they frequently confound the results of constructional tasks.

Fine Motor and Sensory Functioning

Fine motor functioning is commonly impaired following a stroke, typically on the side contralateral to the stroke [54]. It is important to assess fine motor functioning for use as an indicator of the lateralization of lesions or dysfunction [50], to aid in interpretation of other tests in a neuropsychological battery, and for treatment recommendations, such as the need for occupational therapy, school accommodations, or vocational planning.

Neuropsychologists can assess many aspects of fine motor functioning through observation, informal testing, or formal testing. Aspects of fine motor functioning to assess following stroke include apraxia, motor sequencing, assessment of motor soft signs, right–left orientation, handedness, speed, dexterity, and strength [49, 50]. Apraxia refers to the inability to understand or perform a learned skilled movement that cannot be accounted for by a primary motor or sensory deficit (for review, see [107]). While most common following strokes affecting the left parietal lobe, apraxia can occur following damage to extraparietal structures and following right hemispheric injury. Numerous subtypes of apraxia have been described, including ideomotor apraxia, characterized by impaired performance of skilled movements in response to verbal command, or pantomime and ideational apraxia, characterized by impaired use of objects. Both arms are usually affected in these apraxia subtypes, while limb-kinetic apraxia, characterized by slow, stiff, imprecise movements, affects the contralesional arm.

Handedness is particularly important to assess as many strokes, particularly those involving the distribution of the middle cerebral artery, result in hemiparesis [51]. If the dominant hand and arm are affected by the hemiparesis, handedness may be forced to shift. In some cases, a dominant hand advantage may not be present on fine motor tasks, which is another indicator of neurologic impairment. Fine motor speed, dexterity, and strength are also commonly impaired following a stroke. Speed can be assessed via a tapping test (e.g., Finger Tapping Test [108]), speed and dexterity via a pegboard test (e.g., Purdue Pegboard Test [109], Grooved Pegboard Test [110], among others), and strength via a hand dynamometer test. Difficulty with these tasks may suggest deficits in fine motor functioning, which can affect handwriting and typing – and therefore school and work performance – among other tasks. It is

important to note, however, that poor performance on speeded fine motor tasks may represent slow processing common in stroke patients rather than deficits in fine motor dexterity. For this reason, it is important to interpret the results of tests of fine motor functioning within the context of the patient's whole neuropsychological profile. Testing higher level movement control and coordination is particularly important in pediatric evaluations.

Although there is an abundance of formal tests of fine motor functioning, it is also important to observe the patient's fine motor skills during the neuropsychological evaluation. Notation should be made regarding the hand used for writing and drawing, the presence of tremors, the ability to perform skilled movements (praxis) spontaneously and during formal testing, poor coordination, mirror movements, or motor overflow.

In addition to sensory neglect discussed in a previous section, primary somatosensory functioning can be affected by a stroke [54]. Tests of tactile form recognition, graphesthesia (fingertip number writing), and finger recognition perception, among others, may be particularly useful in assessing for higher order sensory deficits [49].

Emotional and Behavioral Functioning

Emotional and behavioral changes are common occurrences following stroke [76, 111], with both neurologic and situational factors likely influencing the development of symptoms. In adults, poststroke depression is common (10–40% of stroke survivors) and is associated with impairments in executive functioning [111], poor affective modulation, and anterior lesion location [112]. Anxiety disorders, and symptoms of Post-Traumatic Stress Disorder in particular, are also common in adults following stroke [112]. Mania, associated with right hemisphere lesions, and psychosis following stroke have been documented but are rare [112]. In children, ADHD is the most common psychiatric disorder following stroke, with anxiety disorders and mood disorders also occurring at a rate higher than orthopedic controls [76].

Considering the relatively high incidence of depression and anxiety following stroke and the possibility that cognition can be impacted by the presence of psychological disturbance [113], evaluation of emotional functioning is an essential part of the neuropsychological evaluation of stroke survivors. Evaluation of behavior is also very important, particularly in light of the high rate of acquired ADHD symptomatology in children following stroke. A comprehensive evaluation of emotional and behavioral functioning requires integration of information from a variety of sources, including direct observation and the clinical interview, and may also include self-report scales, behavioral rating scales, and projective tests [113]. The patient's functional limitations following stroke should be considered in assessment choices. For example, an aphasic patient may not be able to adequately describe their emotional symptoms in a clinical interview or reliably read and comprehend questions on a self-report form. In that case, information provided by caregivers and direct observation will provide the most reliable information. Or, a patient with a new dominant arm hemiparesis may not have the motor skills to fill in answer choices on self-report questionnaires, and a clinical interview may be a better assessment choice. Interpretation of any self-report or rating scale should take into consideration the fact that some scales on these measures may be elevated due to physical symptoms related to the stroke rather than emotional factors [113].

There are a number of rating scales that may be useful in assessing the emotional and behavioral functioning of patients who have had strokes. Broad rating scales that screen a wide range of symptoms can be helpful in pinpointing domains of emotional and behavioral functioning that should be further assessed. The use of additional rating scales that specifically assess for depression, anxiety, and ADHD symptomatology may be indicated based on results of broad rating scales or on presenting concerns. When assessing for depression or anxiety following a stroke, the

clinician should consider adjustment disorder, acute stress disorder, and post-traumatic stress disorder among possible differential diagnoses. Assessment of ADHD in children following strokes should include ratings from parents, teachers, and the child if appropriate.

Long-Term Neuropsychological Outcome

The presence and degree of persistent, long-term cognitive deficits following stroke depends on a number of factors. Premorbid functioning, the age of the patient, the location and volume of the stroke, and the development of epilepsy all influence the eventual degree of cognitive impairment [114–116]. In children with ischemic or hemorrhagic stroke, parent-reported and self-reported health status were also worse in children with epilepsy or persistent hemiparesis [117]. Additionally, long-term cognitive outcome is influenced by the underlying cause of the stroke, which may independently influence neuropsychological functioning or increase the risk of future strokes, which can potentially degrade cognition. Cognitive deficits generally follow a U-shaped curve in relation to age at time of stroke, with the more persistent and severe deficits occurring in very young children and the elderly [118, 119].

Long-term outcome of stroke in adults depends on a variety of factors, such as premorbid health of the patient, demographics, comorbid conditions, and vascular risk factors. A recent literature review of stroke outcomes estimated that 70% of stroke survivors will live in rest homes or institutional care, with only 30% able to perform daily living activities independently [120]. According to this review, neuropsychological impairment in sustained attention, apraxia, pathological emotional reactions, and language deficits have been shown to be predictive of functioning and independence following discharge from the hospital. Memory impairment in the elderly significantly predicts loss of functional independence. Furthermore, recent studies have demonstrated that functional status in the months following stroke have prognostic value for long-term outcome. One study with a large cohort of patients three months post ischemic stroke found that medical and psychiatric comorbidities predicted mortality at three months, and factors such as nonwhite race, older age, not being partnered, and having periventricular white matter disease were predictive of mortality or worse functional outcomes for those that survived beyond three months [121]. Similarly, a second study demonstrated that functional status (such as dependence for ADLs) six months post stroke predicted long-term survival, with fewer than half of patients with severe disability surviving five years [122].

In children who survived ischemic stroke, the majority experience persistent neuropsychological deficits, specifically with regard to attention, concentration, and processing speed [116, 123]. In one study of children who survived hemorrhagic stroke, approximately half of the patients presented with cognitive deficits [124]. Furthermore, the majority of these patients presented with low self-esteem and/or difficulties with mood and behavior [124]. Pediatric stroke survivors are also likely to have academic difficulties and require special education services [116, 125], with one study finding that only fifty percent of patients were able to return to a regular classroom [126].

The effects of stroke on neuropsychological functioning are, in general, more extensive than the typically expected deficits associated with the specific lesion [54]. In fact, deficits in attention and concentration, processing speed, and executive functioning are common following stroke and may be somewhat independent of the location of the cerebral damage, as these functions may require integration of multiple brain regions [54, 127]. This may be particularly true for children who have had strokes, as the developing brain's plasticity allows for reorganization and the potential for "crowding" of functions. For this reason, special considerations must be made when working with children who have had strokes and their families. While cognitive deficits in adulthood are readily apparent, the effects of brain injury on young children may go unrecognized as there may not be an immediate functional loss [128]. Instead, children who have had strokes may fail to develop skills as they grow older.

Reintegration into the home, school, or work setting can be very challenging for patients following a stroke [129]. Motor, cognitive, or sensory deficits may severely limit the patient's abilities and may represent a significant change from prior functioning. Patients may no longer be able to work, drive, take care of their dependents, participate in their educational curriculum, or live independently without assistance. At the same time as their functioning decreases, demands – such as attending frequent doctors or therapy appointments or paying medical bills – may increase. The burden on family members to care for the patient can be great, and there can be significant disruptions in family life. In addition to practical demands, family members may also be emotionally affected by the changes in their loved one's functioning. Caregiver strain is considerable, with depression being a common occurrence [130]. Family-based interventions are recommended to improve these outcomes.

Treatment Approaches to Cognitive Impairment Due to Cerebrovascular Disease

For patients who develop cognitive impairment following an acute stroke, therapy targeted toward these deficits should be one part of a rehabilitation plan that may occur in an inpatient rehabilitation unit or in an outpatient setting. The benefits of cognitive therapy have been demonstrated in adults with language impairment or apraxia following left hemisphere stroke and for visuospatial neglect following right hemisphere stroke [131, 132]. The literature supporting specific cognitive interventions is described in the review by Cicerone and colleagues [131], and is treated in this volume in Sarah Raskin's chapter, "Current Approaches to Cognitive Rehabilitation". Another promising therapy is noninvasive brain stimulation. Numerous small studies have evaluated the effects of transcranial direct current stimulation (tDCS) and repetitive transcranial magnetic stimulation (rTMS) to treat deficits following stroke [133, 134].

The intensity of therapy is one factor that influences recovery from aphasia. Numerous approaches have been associated with improved function, including group communication treatment. A form of "constraint-induced" therapy, in which patients participate in massed–practice of language tasks that are particularly difficult, has been shown to improve communication skills to a greater degree than traditional therapy [135]. Small studies of medication and noninvasive brain stimulation show promise for the treatment of aphasia, but additional randomized controlled trials are needed [136]. Specific techniques for amelioration of apraxia include targeted gestural and object use therapy or strategy training (using compensations for apraxia during performance of activities of daily living as part of occupational therapy sessions) [131]. Preliminary studies suggest that noninvasive brain stimulation may have a role in the treatment of apraxia [137]. Noninvasive brain stimulation also has been used successfully to decrease neglect [138]. Visual scanning training has been used successfully in patients with neglect, although it is somewhat surprising that this top-down approach can modulate a deficit characterized by a lack of conscious awareness of stimuli [139]. As the neural mechanisms underlying cognitive dysfunction due to cerebrovascular disease are further elucidated, treatment strategies will continue to evolve. Further advances in cognitive rehabilitation will make the need for accurate neurocognitive assessment even more important, highlighting the critical role that neuropsychologists will continue to play in the rehabilitation of patients with cerebrovascular disease.

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