26 Neuropsychology

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Abnormalities in brain structure and/or function are common in developmental, psychiatric, and neurological disorders, including intellectual disabilities. These abnormalities are central to defects in cognitive processing in these conditions, which, in concert with other factors, impact an individual's academic achievement, functional independence, and vocational outcome (Yeates, Ris, Taylor, & Pennington, 2009). A central focus in clinical neuropsychology is to identify and describe the fundamental cognitive processing deficits in brain-based disorders and to explain these deficits in terms of brain structure and function (Lezak, Howieson, Bigler, & Tranel, 2012). As such, neuropsychology is essential to the understanding of intellectual disabilities, and neuropsychological assessment is a key component of patient care (Yeates et al., 2009).

This chapter will discuss defining features of neuropsychology, assumptions made by neuropsychology, essential methods in neuropsychological research, approaches to clinical neuropsychological assessment, and core domains of cognitive functioning assessed in neuropsychology. Finally, this chapter will discuss emerging research areas in neuropsychology that have great potential to advance our understanding of brain-behavior relationships in normal and clinical populations.

What Is Neuropsychology?

Neuropsychology can be defined as the study of brain-behavior relationships (Kolb & Whishaw, 2009). Behavior, in this definition, can be understood in a broad sense to include cognition, emotion, and behavioral responses; however, traditionally, cognitive processing has been the main focus of neuropsychology (Ogden, 2005). The central aim of neuropsychology is to develop a science of cognition, emotion, and behavior that explains these three phenomena in terms of the function of the human brain (Kolb & Whishaw, 2009). As the name implies, neuropsychology is an inherently trans-disciplinary field, drawing from a diverse set of research areas, including anatomy, biology, biophysics, ethology, pharmacology, physiology, physiological psychology, neurosurgery, psychometrics, cognitive psychology, and philosophy, among others (Kolb & Whishaw, 2009).

Neuropsychology itself is composed of two distinct but partially overlapping sub-disciplines. Cognitive neuropsychology attempts to understand and characterize normal cognitive function through the study of brain-damaged patients. Cognitive neuropsychology is often less inter-

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ested in brain localization of cognitive processes and instead emphasizes the implications of brain damage-induced cognitive changes for theories of normal cognitive information processing (Ward, 2006). In contrast, clinical neuropsychology places greater emphasis on the behavioral expression of central nervous system dysfunction (Lezak et al., 2012). Accordingly, the focus in clinical neuropsychology is on brain pathology and the associated signs and symptoms of this pathology. This chapter principally focuses on clinical neuropsychology. It should be noted, however, that the research questions, methods, and findings of these two sub-disciplines overlap to a significant extent.

Although described as a clinical discipline, clinical neuropsychology has both research and applied clinical branches. Clinical neuropsychological research is aimed at characterizing cognitive phenotypes, identifying cognitive markers of disease states, describing longitudinal trajectories of cognitive deficits, and developing measures to facilitate diagnosis, cognitive profile characterization, and evaluation of response to intervention. As a clinical practice, neuropsychology attempts to infer brain functioning and characterize lesion location, clarify cognitive strengths and weaknesses, predict functional difficulties, contribute to the determination of legal competency, and inform intervention targets and measure intervention outcomes (Heaton & Marcotte, 2000).

Foundational Assumptions of Neuropsychology

An important aspect of any discipline is the assumptions made by practitioners within that discipline. The discipline of neuropsychology rests on three key assumptions, which serve as the preconditions for investigation. The first of these assumptions is the brain hypothesis. The brain hypothesis maintains that the brain is the source of behavior (Kolb & Whishaw, 2009). This assumption commits neuropsychology to materialism, which maintains that behavior can be explained by the complex interaction of physical entities and events. However, neuropsychology typically does not embrace a reductive materialism, in which behavior, such as memory, can be reduced to individual neurons. Instead, it is more commonly assumed that behavior is an emergent property of the complex interactions among numerous neurons and neuronal networks (Pennington, 2009). Moreover, the influence between the brain and behavior is typically assumed to be bidirectional. In this sense, the brain is both the source of behavior and in turn is shaped and molded by one's learning history and experience. There is now a wealth of evidence demonstrating synaptic plasticity-driven changes in neural wiring due to unique experience histories, such as those found among musicians, blind readers of Braille, and the congenitally deaf, among others (Galaburda & Pascual-Leone, 2003).

The second assumption provides more specificity to the brain hypothesis. This second assumption is the cerebral localization hypothesis (also termed domain specificity), which maintains that specific cognitive functions can be localized to regions or circuits within the brain. The cerebral localization hypothesis consists of three key claims: (1) the brain has a modular organization; (2) each module is specialized for a particular cognitive process; and (3) these modules can be reliably localized to specific brain regions (Greiffenstein, 2014). Notably, cerebral localization does not entail that these brain-behavior modules are isolated and independent of one another. Instead, efficient performance of a behavior, such as speech production, requires the orderly integration of multiple modules. In addition, many of these modules are localized to distinct regions of the brain, with information processed both simultaneously and sequentially in these modules. Taken together, a more nuanced view of cerebral localization entails not only that cognitive functions are localized but also that they are distributed in multiple regions of the brain, operate in parallel to one another, and are integrated in a hierarchical fashion, with more complex modules built on simpler ones (Kolb & Whishaw, 2009).

Finally, the third assumption of neuropsychology is the psychological or cognitive assumption. This assumption holds that the use of psychological or cognitive constructs to explain normal or abnormal behavior is more parsimonious than a wholesale inventory of correlated behavioral abnormalities or a reduction of behavior to neurophysiology (Morton & Frith, 1995; Pennington, 2009). While some may interpret this assumption as maintaining that single cognitive deficits underlie specific disorders, such as phonological processing for dyslexia or theory of mind for autism, a more nuanced and scientifically plausible understanding of this assumption is that these disorders are characterized by multiple cognitive deficits acting in combination with one another. A key task of neuropsychology is to identify these fundamental cognitive constructs and explain how their interactions explain characteristic behavioral abnormalities within specific disorders (Pennington, 2006).

Clinical Neuropsychology: The Key Role of Psychometrics

One of the defining features of clinical neuropsychology is the emphasis placed on strong psychometric theory to inform clinical assessment. In fact, this focus on psychometrics distinguishes clinical neuropsychology from the closely related discipline of behavioral neurology. While both clinical neuropsychology and behavioral neurology specialize in the behavioral expression of brain dysfunction, behavioral neurology evaluates and characterizes this behavioral expression in terms of pathological signs, which are either present or absent. In contrast, clinical neuropsychology is firmly grounded in the psychometric tradition of empirical psychology, emphasizing the measurement of continuously distributed behavioral variables with known acceptable reliability and validity (Horton & Puente, 1986; Rourke & Brown, 1986). Thus, psychometrically informed measurement of behavior is an essential feature of clinical neuropsychology.

Several core psychometric considerations in neuropsychology warrant discussion. The first of these considerations is the reliance on continuously distributed variables. Continuously distributed variables are preferred in neuropsychology because their frequency distributions often conform to a normal curve (also known as a normal distribution or bell curve). The normal curve reflects the probability of obtaining a score or range of scores when randomly sampled from the population. This probability is often described in terms of percentile ranks or their associated deviate scores. A percentile rank indicates the percentage of individuals from the population who score at or below a given test score. Deviate scores, which include z, T, scaled, and standard scores, are standardized expressions of raw scores and reflect the number of standard deviation units from which a score differs from the mean of the distribution. Deviate scores thus function to convert raw scores into percentile ranks. Conceptually, deviate scores and percentile ranks are used to characterize the degree of abnormality of an obtained score, with abnormal scores reflecting poor test performance interpreted as indicative of neuropsychological impairment (Slick, Strauss, Sherman, & Spreen, 2006). There is considerable debate over optimal cutoffs for defining abnormality/neuropsychological impairment, but most definitions range from ≥ 1 standard deviation below the mean (16th percentile or below) to ≥ 2 standard deviations below the mean (0.4th percentile or below) (Heaton & Marcotte, 2000).

The use of percentile ranks and deviate scores to detect neuropsychological impairment relies on the use of a comparison sample to derive a standard normal distribution. This process is often referred to as norming and the data resulting from this process as normative data. Conceptually, normative data should reflect the distribution of test scores in the general population. Creation of normative data for test score interpretation therefore requires a large (greater than at least 200 cases) sample in order to avoid sampling error and to increase the representativeness of the sample to the general population

(Nunnally & Bernstein, 1994). In addition, the demographic composition of the normative sample should be comparable to the general population. Recognizing that demographic factors, such as age, education, gender, and race/ethnicity, can affect neuropsychological test scores independent of brain dysfunction, demographic corrections are commonly applied to normative data in neuropsychology. In general, there are two main approaches to normative comparisons in clinical neuropsychology: (1) comparing individual test scores to normative data that approximates as closely as possible the general population and (2) comparing individual test scores to normative data that matches as closely as possible the unique subgroup to which the examinee belongs (e.g., non-Hispanic Caucasian males with 14 years of education) (Mitrushina, Boone, & D'Elia, 2005; Strauss, Sherman, & Spreen, 2006). Notably, adaption of either of these approaches may be dictated by the purposes of the evaluation. For instance, in attempting to diagnose intellectual disability or learning disability, comparison to all other persons of the same age in the general population is most appropriate. However, if the purpose of the evaluation is to characterize cognitive strengths and weaknesses to inform diagnostic considerations and/or plan classroom accommodations, comparison to the examinee's unique subgroup may be more apposite (Strauss et al., 2006). Ultimately, availability of appropriate normative data is crucial to rendering informed clinical decisions based on neuropsychological test performance (Heaton & Marcotte, 2000).

In addition to the availability of adequate normative data, the reliability of neuropsychological tests and the validity of the interpretations based on neuropsychological test scores are important psychometric considerations. Reliability reflects the degree to which a test consistently measures a given construct. There are several types of reliability, including internal consistency reliability (which indicates the extent to which items on a test measure the same construct), test-retest reliability (which reflects the temporal stability of a measure), alternate forms reliability (which denotes the similarity of scores across two measures of the same construct), and inter-rater reliability (which indicates the similarity of scores across two raters of the same test). The greater the reliability of a test, the more confidence an examiner can have in the precision of a score based on performance on that test. In contrast, validity refers to the extent to which a test actually measures what it intends to measure. Similar to reliability, there are multiple types of validity evidence that include, at a minimum, content-related validity (i.e., the degree to which the content of the test is relevant, representative, and of high technical quality), construct-related validity (i.e., the extent to which a test measures what it intends or purports to measure), criterion-related validity (i.e., the extent to which a test is related to an external outcome), and response process validity (i.e., the degree to which the response processes implemented by examinees are consistent with measurement on the intended construct) (although for further types of validity information, see American Educational Research Association, 1999; Messick, 1995). Adequate validity is essential to the interpretation of a test score as indicative of a specific construct. A considerable amount of research is dedicated to evaluating the reliability and validity of neuropsychological measures and deriving appropriate normative data in order to facilitate test selection, administration, and interpretation.

Essential Research Methods in Neuropsychology

There are several essential methods used in neuropsychology to identify brain-behavior relationships. Historically, the lesion study has been the most important method to neuropsychology. Lesion studies evaluate the impact of brain damage on patient behavior. These types of studies were central to the development of the cerebral localization hypothesis and remain key in the determination of brain-behavior relationships. The central premise of the lesion study is that the function of a given brain region can be inferred on the basis of impaired and spared abilities resulting from lesions to that area. Lesion studies can be described in terms of single dissociation studies or double dissociation studies. In single dissociation studies, a patient with brain damage exhibits impairment on one task (task A), but a relatively normal performance on a separate task (task B). This type of finding suggests that task A and task B utilize different cognitive processes that rely on separate neural regions. However, a key shortcoming of single dissociation studies is the possibility that tasks A and B require the same cognitive processes/neural regions but that task B requires more of this cognitive process than task A. Conclusions about brain-behavior relationships can be strengthened through demonstration of a double dissociation. In a double dissociation, one patient with brain damage exhibits impairment on task A, but relatively normal performance on task B, while another patient with a lesion in a different brain region is impaired on task B, but normal on task A. Double dissociations provide strong evidence for the distinctness of closely related cognitive processes and their neural correlates (Ward, 2006).

Neuroimaging represents another essential research method in neuropsychology. Neuroimaging can be classified as structural or functional neuroimaging. Structural neuroimaging refers to brain imaging methods that produce static images of the spatial configuration of different types of brain tissue. Obtaining static images of the brain is based on the fact that different types of brain tissue (e.g., the skull, gray matter, white matter, cerebrospinal fluid, etc.) have different physical properties. Correlation of a structural abnormality with specific impairment on neuropsychological testing yields valuable information on the potential causal role of that region to that neuropsychological ability. Structural imaging modalities include computerized tomography and magnetic resonance imaging, which differ in their method of measuring physical properties of different tissue types (Ward, 2006).

In contrast to structural imaging, functional imaging creates dynamic images of changes in physiological characteristics of the brain that may be correlated with task-related cognitive processes. Most functional imaging modalities are based on the fact that additional regional blood flow is needed to supply oxygen and glucose to meet the metabolic demands of carrying out specific cognitive tasks. Comparison of this task-related physiological response to a baseline level of physiological activity during a control condition can thus shed light on brain region recruitment for that cognitive task, which suggests specialization of that region for the specific cognitive function under investigation. Selection of a baseline condition is a complex process, however, and requires isolating the specific cognitive process under investigation from other cognitive processes that may be involved in the task. There are several experimental designs that have been used for this comparison, which include cognitive subtraction, factorial designs, and parametric designs (see Friston, 1997, for a review of these designs and their relative advantages and disadvantages and Kosslyn, 1999, for a discussion of the difficulties of functional neuroimaging interpretation). Positron emission tomography and functional magnetic resonance imaging are the two most common functional imaging modalities (Huettel, Song, & McCarthy, 2014).

Additional methods of neuropsychological investigation include electroencephalography (EEG), single cell recordings, transcranial magnetic stimulation, computational modeling, and animal models; however, discussion of these other methods is beyond the scope of this chapter.

Approaches to Neuropsychological Assessment

A typical assessment in neuropsychology involves the administration of a multitude of cognitive and behavioral tasks. Through integration of the qualitative and quantitative data obtained by these measures, a neuropsychologist can clarify key deficits in cognitive processing, identify syndrome-level patterns of these deficits, and surmise most likely etiologies for these syndromes (Heaton & Marcotte, 2000). Historically, several distinct assessment approaches have been followed to achieve these ends. This section provides a brief description of four of the most common assessment approaches.

Qualitative Approach (Luria)

The qualitative approach to neuropsychological assessment is most often associated with the Russian neuropsychologist A.R. Luria (Glozman, 2007). Luria assumed that mental and behavioral functions were complex constellations of more fundamental component parts and that it was the neuropsychologist's role to ascertain whether and which of these fundamental components was impaired in a patient (Lezak et al., 2012). To write, for instance, involves, at a minimum, skilled movement, spatial organization, word selection, and grapheme sequencing. Impairment in any one of these fundamental cognitive processes can result in a disturbance in writing ability. Moreover, impairment in one of these fundamental abilities is likely to impact performance on other tasks. For instance, impaired word selection may also emerge as word finding problems in spontaneous speech and difficulty identifying the names of pictures and objects. Detection and characterization of neuropsychological impairment for Luria and his followers in the qualitative approach primarily involved assessing qualitative aspects of patient behavior, placing particular emphasis on the nature of deviations or errors, while the use of psychometric instruments was considerably less common. Assessment for Luria was highly individualized, following a hypothesis-driven approach in which the particular behaviors assessed were selected by the neuropsychologist based upon the neuropsychologist's working hypothesis regarding the underlying fundamental deficits from which the patient suffered (Ardila, 1992).

The qualitative approach is not without its critics. For one, several authors have questioned whether this method can be properly classified as clinical neuropsychology, preferring instead to place Luria in the tradition of behavioral neurology. As discussed above, in contrast to clinical neuropsychology, which relies on the measurement of continuously distributed variables within a psychometric tradition, behavioral neurology emphasizes dichotomous classification based on pathological signs (Horton & Puente, 1986; Rourke & Brown, 1986). For another, given the non-standardized nature of the assessment and the lack of emphasis on quantitative measurement, the qualitative approach of Luria has been criticized for being subjective, occasionally obscure and resulting in conclusions of questionable validity (Reitan, 1976). Nonetheless, Luria's emphasis on breaking down complex mental and behavioral functions into component parts and his attention to the nature of errors were highly influential to future neuropsychological developments (Ardila, 1992).

The Fixed Battery Approach (Halstead-Reitan)

In contrast to the qualitative approach, the fixed battery approach involves administration of the same comprehensive set of tests to all examinees, regardless of presenting complaints, purposes of the evaluation, or diagnostic considerations. This approach is most commonly associated with Ward Halstead and Ralph Reitan and their battery of tests, the Halstead-Reitan neuropsychological battery (HRNB), although a number of other fixed batteries exist. Historically, the HRNB emerged from the recognition that no single neuropsychological test could accurately detect and characterize the effects of brain damage. Instead, Halstead and subsequently Reitan noted that there was considerable heterogeneity in presentation, functional ability, and test performance among individuals with brain damage (Hom & Nici, 2015). Halstead initially developed a small battery of ten tests designed to measure the complex operations of higher-level mental functions of the central nervous system. Reitan further evaluated these ten tests, as well as dozens of others, to empirically determine their ability to reliably detect the presence of brain damage, lateralization of brain damage, recovery potential, and type of lesion or disease. Tests that contributed to the accurate detection and localization of brain lesions were retained and compiled to create the Halstead-Reitan neuropsychological battery (Goldstein, 2015; Hom & Nici, 2015; Reitan & Wolfson, 2009).

The fixed battery approach has both advantages and disadvantages. In terms of advantages, fixed batteries tend to yield more information on the performance of specific tests across a wide range of clinical populations. As a result, there is often a greater wealth of empirical research to ground interpretation of test scores using fixed batteries, including better norms, greater knowledge of the psychometric properties of tests, and greater knowledge of how to integrate test data across the battery (Heaton, Grant, Anthony, & Lehman, 1981; Reitan, 1964). On the other hand, however, fixed batteries can be unnecessarily lengthy and expensive and cause examinee stress and/or exhaustion due to over testing. In addition, fixed batteries are more likely to become outdated over time as the field develops and may inadequately assess certain cognitive domains, thus requiring administration of supplemental tests (Heaton & Marcotte, 2000). Nonetheless, the fixed battery approach is common in research contexts where a premium is placed on the use of a uniform set of tests and procedures so as to facilitate comparison across study participants.

The Flexible Battery Approach (Iowa-Benton)

The flexible battery approach involves the administration of a tailor-made set of tests to assess patients in a highly individualized manner, with test selection guided by the neuropsychologist's working hypothesis about the condition(s) the examinee is known or suspected to have. This approach is most typically associated with the work of Arthur Benton at the University of Iowa. The development of this approach was based on observation of clinical examinations conducted by psychiatrists and neurologists, which were noted to be highly flexible and efficient. These examinations began with a broad mental status exam, from which the clinician pursued diagnostic possibilities through diverse questions. Exams could last from anywhere between 15 min to over an hour, depending on the degree of diagnostic uncertainty involved in the exam. Benton was impressed by the flexibility and hypothesis-driven nature of these examinations and believed that neuropsychological assessment should follow this model. In this view, neuropsychological assessment should consist of standardized objective tests, similar to Halstead-Reitan, but these tests should be implemented in a highly flexible, hypothesis-testing-driven manner, more akin to Luria (Tranel, 2009).

Benton's approach to assessment consisted of a small, core battery of between two and six standard tests administered to every patient. Then, based on the referral question and the patient's performance on the core battery, additional tests were administered to explore diagnostic possibilities. This approach might be better conceptualized as a fixed-flexible approach, given that a standard set of batteries was always administered and a large set of additional measures were implemented to pursue the remaining diagnostic hypotheses. More recently, the Iowa-Benton school has undergone subtle revision in its approach. In particular, the core battery has expanded in length, and additional information has been incorporated to guide the flexible, hypothesis-testing-driven component of the assessment, including the patient's complaints, impressions gained from an initial clinical interview, the patient's medical history, neurological findings, and neuroimaging data (Tranel, 2009).

The flexible and fixed-flexible battery approach has much to recommend it. These approaches avoid unnecessary testing and allow the neuropsychologist to probe more precisely into the nature of a patient's deficits. However, there is often less psychometric and clinical information available on how tests should be interpreted in conjunction with one another. In addition, flexible and fixed-flexible battery approaches tend to be more reliant on patient- and informant-report of cognitive symptoms to guide test selection, which may lead to imprudent test selection if patient and/or informants lack accurate knowledge of cognitive deficits (Heaton & Marcotte, 2000).

Boston Process Approach (Kaplan)

The final approach to neuropsychological assessment reviewed in this chapter is the Boston Process Approach, which is most commonly associated with the work of Edith Kaplan. At its core, the Boston Process Approach has three main aims: (1) to understand the qualitative nature of behavior assessed by clinical psychometric instruments, (2) to reconcile descriptive richness with reliable and valid assessment, and (3) to incorporate recent insights from cognitive neuroscience and experimental psychology into clinical neuropsychological assessment (Delis, Kramer, Fridland, & Kaplan, 1990). This approach stemmed from the realization that there was considerable variability in the manner in which patients exhibited the loss of one and the same specific cognitive function and that this variability often correlated with lesion size and location. For instance, performance on Wechsler Adult Intelligence Scale-IV Block Design test reliably differs among individuals with left vs. right hemisphere lesions. Patients with right hemisphere lesions are more likely to exhibit configural processing errors, in which they fail to retain the 2 × 2 or 3 × 3 configural structure of produced block constructions. In contrast, patients with left hemisphere lesions are more likely to produce internal block rotation errors while retaining the configural structure of the design. This pattern of performance is consistent with accounts of hemispheric specialization, in which the right hemisphere is dominant for global processing and the left hemisphere for local processing (Delis, Kiefner, & Fridlund, 1988; Delis, Robertson, & Efron, 1986; Robertson & Delis, 1986). Thus, in the Boston Process Approach, the emphasis is placed on the manner in which a patient solves, or fails to solve, items on a neuropsychological test, rather than just their final quantitative score on that test. Over the past two decades, there have been a growing number of tests and methods developed to provide standardized ways of scoring these process outcomes, such as those implemented in the California Verbal Learning Test-II (Delis, Kramer, Kaplan, & Ober, 2000). The Boston Process Approach is most typically associated with a flexible assessment approach, although it can be used with a fixed battery as well.

Core Domains of Neurocognition in Neuropsychology

Neuropsychological assessment involves the administration of a battery of cognitive tasks across several domains of cognition. Assessment with numerous tasks across domains is necessary because neuropsychological tasks are multi-determined, such that poor performance on any given task can be the result of several cognitive and/or non-cognitive factors. To tease apart these potential contributing factors and identify underlying spared and impaired abilities and processes requires the evaluation of the pattern of performance across tasks. In addition to the evaluation of cognition, neuropsychological assessment should include, at a minimum, a global measure of intellectual functioning; an estimate of adaptive, social, behavioral, and emotional functioning; and evaluation of academic achievement in reading and math. As other chapters in this handbook are more specifically devoted to assessment of intelligence (Chaps. 2 and 22), adaptive behavior (Chap. 23), and emotional functioning (Chaps. 8, 24, 47, 48, and 49), this section will cover issues specific to the assessment of core cognitive domains in neuropsychology. Core cognitive domains include attention, memory, executive functions, language, and visuospatial ability.

Attention

Attention refers to a set of processes that enable efficient allocation of cognitive resources to the task at hand (Cohen, Malloy, Jenkins, & Paul, 2014). Unlike other cognitive domains, attention is not a fundamental substrate of cognition, but instead governs the flow and processing of information within other cognitive domains, such as memory, language, and visuospatial abilities (Cohen et al., 2014). This ability is achieved through at least four distinct attentional processes

(Cohen et al., 2014; Mirsky, Anthony, Duncan, Ahearn, & Kellam, 1991).

The first of these processes is sensory selective attention. As the name implies, sensory selective attention involves the selection of sensory input for additional cognitive processing. This selection process occurs outside of conscious awareness and at a very early stage of information processing. In order to successfully selectively attend to sensory stimuli, three subprocesses must be integrated: the ability to filter out irrelevant information, the ability to enhance the processing of relevant/filtered information, and the ability to remain engaged on a stimulus or to disengage from a stimulus and selectively orient/attend to a new stimulus.

The second attentional process is referred to as intention. Intention is important for the selection and control of behavioral responses. Unlike sensory selective attention, intention is a controlled, effortful process that requires conscious awareness. Given its controlled, effortful nature, intention partially overlaps with aspects of executive functioning (see the executive function section below for further detail).

Third, attention is constrained by an individual's attentional capacity. Attentional capacity refers to the amount of information to which an individual can allocate additional cognitive resources at any one time. Attentional capacity is impacted by state factors, such as fatigue, and trait factors, including neural transmission and processing speed, working memory capacity, and spatial and temporal processing constraints.

The fourth core attentional process is sustained attention. Sustained attention refers to the ability to maintain levels of attention across time. Individuals with sustained attention difficulties will often exhibit variability in performance over extended periods of time, often due to loss of interest and/or susceptibility to distraction.

The neuroanatomy of attention is complex and cannot be localized to a single brain system. Instead, multiple brain systems interact as a coherent network to control attention. These regions include the inferior parietal cortex, frontal cortex, limbic system, thalamus, basal ganglia, and the midbrain (Cohen et al., 2014).

Neuropsychological assessment of attention is challenging for a number of reasons. For one, as mentioned above, it is not a fundamental cognitive substrate, but rather functions to enhance other cognitive processes. As such, pure measures of attention do not exist. For another, attention by definition varies over time and may be situation specific. Thus, attention is usually assessed on tasks that load on more than one cognitive domain and may be best evaluated by examining performance across tasks that differ with respect to attentional parameters (e.g., attentional capacity load, time on task, etc.). For sensory selective attention, key tests include letter and symbol cancellation tasks, which involve searching an array of stimuli to identify targets from distractors (Lezak et al., 2012). Intention, on the other hand, is often assessed qualitatively through tasks such as double alternating movements, alternating graphic sequences (e.g., Rampart figures), and motor impersistence (Royall, Mahurin, & Gray, 1992). Attentional capacity is most often measured with the digits forward subtest of, for instance, the Wechsler Adult Intelligence Scale-IV (Wechsler, 2008). More complex tasks of attentional capacity that also require focus typically involve varying both the amount of information attended to and the complexity of effortful processing necessary to perform some operation on that information. A popular measure of attentional capacity and focus is the paced auditory serial addition test (PASAT; Gronwall, 1977). Finally, tests of sustained attention evaluate the temporal characteristics of performance on tasks that involve detecting targets among distractors. The most common of these measures are continuous performance tests (CPT), such as the Connors CPT-II (Connors, 2000).

Memory

Memory is a remarkably complex cognitive domain composed of several distinct memory systems. These memory systems differ in both their time course and the type of information for which they are specialized. Regarding time course, there are three distinct stages of memory.

The first of these stages is the sensory storage (or sensory registration). This stage refers to the point in time in which sensory information (e.g., visual, auditory, gustatory, etc.) is initially registered. This stage is very short in duration, lasting milliseconds to seconds. If no additional processing is conducted, this sensory information quickly dissipates. The second stage of memory processing is referred to as short-term or working memory. Short-term memory has a duration of up to approximately 30 s. In addition, short-term memory has a limited storage capacity in which individuals can typically only maintain 7 ± 2 distinct items (e.g., to-be-remembered words). Unless further processing is applied to items in short-term memory, such as rehearsal or organization, these items will be forgotten. Information that has been sufficiently processed in short-term memory will be transferred into the third and final stage of memory, long-term memory. Long-term memory is relatively permanent and with unlimited capacity (Scott & Schoenberg, 2011d).

There are several different types of long-term memory, which differ in the nature of the information for which they are specialized. Squire and Zola (1996) proposed the most influential taxonomy of long-term memory. In their model, memory can be divided into declarative and non-declarative types. Declarative (explicit) memory refers to long-term memories that can be retrieved and reflected on consciously, including memory for names, people, places, events, and facts. Within declarative memory, there are two further subtypes. The first subtype of declarative memory is semantic memory. Semantic memory is memory for facts and general world knowledge, such as the name of 17th President of the United States and the day of the year on which Christmas falls. This is in contrast to episodic memory, which refers to memory for personally experienced and remembered events, such as what you ate for breakfast today. As opposed to semantic memory, episodic memory requires the active recall of the learning event. Episodic memory is the more important type of memory in neuropsychological assessment (Scott & Schoenberg, 2011d). Episodic memory can be further characterized by whether it involves verbal or visual material, whether it is learned intentionally or incidentally, and whether the episodic memory is for a recent or remote event. In addition, episodic memory can be subdivided into three subprocesses, encoding, consolidation, and retrieval. Encoding refers to the process of learning material, consolidation refers to the process of transferring new material from short- to long-term memory, and retrieval is the process of activating information from long-term memory back to short-term memory for conscious recollection (Scott & Schoenberg, 2011d).

In contrast, non-declarative (implicit) memory refers to information that can influence thought and behavior without conscious awareness. Non-declarative memory includes memory for skills, priming, classical conditioning, and nonassociative learning. Non-declarative memory is seldom evaluated in neuropsychological assessment (Squire & Zola, 1996).

Given the complexity of long-term memory, it is perhaps unsurprising that the functional neuroanatomy of this cognitive domain is similarly complex. Episodic memory is subtended by two functional neurocircuits, a medial circuit (often referred to as the Papez circuit) involving the hippocampus, fornix, mammillary bodies, anterior medial nucleus of the thalamus, and the cingulate, and a lateral circuit (often referred to as the amygdaloid circuit) involving the amygdala, thalamic nuclei, orbitofrontal cortex, piriform cortex, insula, hypothalamus, limbic striatum, and nucleus basalis of Meynert (Mishkin, 1982). Amnestic syndromes are most commonly associated with damage to three distinct regions. First, damage to the medial temporal lobe (hippocampus, parahippocampal gyrus, and entorhinal cortex) often leads to an anterograde amnesia characterized by preserved insight into memory difficulties, increased rate of forgetting, limited retrograde amnesia, and lack of confabulation. Second, patients with damage to the diencephalic regions, especially the medial thalamus region and the mammillary bodies, exhibit anterograde amnesia, but with normal rates of forgetting. Due to disruption of frontal areas, patients with damage to this are may also present with limited insight and a tendency to confabulate. Third, damage to the basal forebrain region results in profound attention difficulties that adversely impacts encoding and retrieval processes, but may leave consolidation intact. Patients with damage to this area have poor insight into their memory difficulties and demonstrate a tendency to confabulate (O'Connor & Race, 2013).

Multiple aspects of episodic memory should be evaluated in order to comprehensively characterize this domain. In particular, memory testing should include measures of verbal (e.g., list learning, story passage recall) and nonverbal (e.g., figure recall) memory. In addition, memory for these stimulus types should be conducted immediately after learning trials (i.e., immediate recall), over the course of multiple repetitions of the stimuli (i.e., learning over trials), following an approximately 20–30 min delay (i.e., delayed recall), and using a yes/no recognition testing format (i.e., recognition) (Scott & Schoenberg, 2011d).

Based on the performance on these learning and memory tasks, one can characterize the episodic memory subprocesses impaired in a patient. For instance, a patient exhibiting poor immediate recall and limited improvement over multiple repetitions of to-be-learned material but who retains most information over a delay likely has a primary deficit in encoding. A patient with poor immediate recall, but some learning over multiple repetitions of information, as well as severely impaired delayed recall that only slightly improves with recognition likely has a primary deficit in consolidation. Finally, a patient with normal immediate recall and learning, impaired delayed recall, and normal recognition likely has a primary deficit in retrieval. Of course, patients can also have deficits in multiple episodic memory processes, leading to even greater specificity in memory profile characterization and neuroanatomical lesion localization (Scott & Schoenberg, 2011d).

Multiple memory tests are available for administration. Representative tests of episodic memory include the Wechsler Memory Scale-IV (Wechsler, Holdnack, & Drozdick, 2009), California Verbal Learning Test-II (Delis et al., 2000), California Verbal Learning Test-Children's Version (Delis, Kramer, Kaplan, & Ober, 1994), and Children's Memory Scale (M. Cohen, 1997).

Executive Functions

Executive functions are a heterogeneous collection of cognitive processes. Fundamentally, executive functions are involved in integrating other cognitive domains to make decisions and initiate complex actions. There are several component processes involved in executive functions. These processes include planning, problem-solving, concept formation (i.e., identify abstract concepts), set shifting, verbal fluency, inhibitory control, and working memory. Certain aspects of memory, especially encoding strategy use and memory retrieval, also involve executive operations. These processes rely principally on the integrity of the frontal lobes. Notably, executive functions undergo rapid change during development. As such, greater inter-individual variability in executive function performance is expected among children and adolescents (Floden, 2014; Scott & Schoenberg, 2011b).

One popular model of frontal lobe functioning divides the prefrontal cortex into three functional regions. The first of these regions involves the dorsolateral prefrontal cortex. Dysfunction in this region is characterized by difficulty carrying out complex goal-directed behavior due to difficulties with organization, planning, sequencing, and selecting and implementing strategies, comprising a so-called dysexecutive syndrome. Individuals with damage to the dorsolateral prefrontal cortex may also appear mentally inflexible and perseverate on incorrect strategies and exhibit poor working memory, especially with regard to mental manipulation of information. In addition, this region supports complex aspects of attention, including selective attention and attention shifting. As such, individuals with damage to the dorsolateral prefrontal cortex may appear highly distractible. The dorsolateral prefrontal cortex is also important for implementing encoding strategies (e.g., semantically categorizing to-be-remembered material) and retrieving items from episodic long-term memory (Floden, 2014; Scott & Schoenberg, 2011b). There is some suggestion of hemispheric specialization for these operations, with the left dorsolateral prefrontal cortex specialized for encoding strategy use and the right dorsolateral prefrontal cortex for retrieval (Habib, Nyberg, & Tulving, 2003).

The second important region of the prefrontal cortex is the orbital/ventromedial region. Damage to this region often results in a "disinhibition syndrome," characterized by lack of impulse control and social filter, inability to delay gratification, and emotional dysregulation. Individuals with damage to this region often exhibit poor judgment, with their behavior governed by the pursuit of immediate reinforcers. In addition, these individuals are often hyperverbal and hyperactive, have difficulties with sustained attention, and have little insight into their behavior (Floden, 2014; Scott & Schoenberg, 2011b).

The third important functional region of the prefrontal cortex is the medial frontal region. Damage to this area results in an "apathetic syndrome." Patients often exhibit lethargy, lack of spontaneous initiation of behavior, and appear disengaged from their environment. They may also appear to be emotionally indifferent, dull, and unmotivated and to lack curiosity (Floden, 2014; Scott & Schoenberg, 2011b).

A variety of measures are available for executive function assessment. Planning can be measured with Tower tests (Delis, Kaplan, & Kramer, 2001) or through more qualitative methods such as inspection of complex figure copying strategy (Meyers & Meyers, 1995). Verbal fluency is often measured with phonemic (Benton, Hamsher, & Sivan, 1983) or semantic (Lezak et al., 2012) word generation tasks. The Wisconsin Card Sorting Test is one of the most popular measures of executive functions, measuring abstract concept formation, set maintenance and set switching, and novel problem-solving (Heaton, 1981). Complex attention can be measured in a variety of ways. The Trail Making Test is a popular measure of task set switching of attention (Reitan, 1958), and the Stroop Test (Golden, 1976) is a class measure of selective attention and the ability to suppress a prepotent response. There are considerably fewer measures available for assessment of the disinhibition syndrome. The Iowa Gambling Task is a commonly administered measure of orbital and ventromedial prefrontal cortex function and involves the ability to learn and adapt behavior to response-reward contingencies (Bechara, Damasio, Damasio, & Anderson, 1994). Assessment of the apathetic syndrome is often achieved through self- or informant-report instruments, rather than performance-based measures. Finally, the Frontal Systems Behavior Inventory evaluates common symptoms resulting from frontal lobe damage and provides separate scales for dysexecutive, disinhibited, and apathetic symptoms. This measure provides both self- and informant-report forms, enabling evaluation of discrepancies across raters, which may shed additional light on patient insight into executive deficits (Grace & Malloy, 2001).

Language

Language is arguably the most distinctly human of all cognitive abilities. While other animals are able to communicate, the scope and complexity of human language is unparalleled. At its core, language refers to the use of arbitrary symbols to convey meaning and involves the ability to comprehend, formulate, and produce spoken, written, and gestural symbolic representations. These abilities are distinct from speech, which involves the ability to control the articulatory movements necessary to produce oral expression. Most language functions are mediated by the dominant (often left) hemisphere, although the ability to comprehend and produce prosody in language involves the non-dominant (often right) hemisphere. Due to the relative importance of non-prosodic aspects of language function, this section will focus only on dominant hemisphere language abilities (Sabsevitz & Hammeke, 2014; Schoenberg & Scott, 2011; Scott & Schoenberg, 2011c).

The ability to use language depends on several constituent processes, including orthographic processing (grouping individual letters into words), phonological processing (deciphering, mentally maintaining, and retrieving the articulatory movements and sound structure of speech), and semantic processing (storing and accessing word meanings). These three fundamental language processes rely on distinct neuroanatomical regions. Orthographic processing is subserved by the left inferior temporal-occipital region. Individuals with damage to this area often exhibit adequate language production, comprehension, writing, and identification of single letters, but their reading of words is slow and effortful (Sabsevitz & Hammeke, 2014). In contrast, phonological processing involves a broader network of brain regions in the dominant hemisphere, including the supramarginal gyrus, superior temporal gyrus and sulcus, and the inferior frontal gyrus. Damage to this area can lead to difficulties selecting and sequencing phonemes during speech production and/or difficulties maintaining or manipulating phonological information in working memory (Sabsevitz & Hammeke, 2014). Semantic processing is widely distributed throughout the temporal and parietal lobe, especially the lateral temporal lobe and angular gyrus. Impairments in semantic processing can result in difficulties with spoken word comprehension, semantic categorization, and object naming (Binder, Desai, Graves, & Conant, 2009).

Language functions are typically divided into two major groups, receptive and expressive language, which both rely on varying degrees of the three abovementioned language processes. Receptive language consists of the ability to comprehend language, both written and spoken, and is localized to the posterior dominant hemisphere. Language comprehension requires processing the phonological elements of speech sounds, retaining phonological information long enough to enable processing of semantic content, and deciphering the semantic content of words and sentences. The dominant hemisphere temporal-parietal area including Wernicke's area is central to comprehension of spoken and written language (Scott & Schoenberg, 2011c). This region is located adjacent to the primary auditory cortex and is key to isolating specific phonemic characteristics of sound into known phonemic systems (Kolb & Whishaw, 2009).

In contrast, expressive language deficits involve difficulties in producing speech. To produce speech, an individual must use multiple language subprocesses, including those involved in semantics (to conceptualize the intended communication), syntax (to order the intended communication), phonology (to map semantic knowledge onto speech sounds), and motor planning (to activate the appropriate motor programs for the intended communication). These processes depend on the posterior inferior frontal lobe as well as the dorsal prefrontal cortex (Sabsevitz & Hammeke, 2014).

Assessment of expressive language should involve at a minimum an analysis of spontaneous speech for output fluency, accuracy of word retrieval, integrity of grammar/syntax, length of utterances, omission of words, meaningfulness of content, and articulatory precision of word production. In addition, tests of picture naming, verbal fluency, phrase repetition, story description, and a writing sample should be administered as part of an assessment of expressive language. Measures of auditory comprehension are key to the assessment of receptive language. Measures of auditory comprehension include simple and complex command following, word-picture matching, yes/no questions, word reading, and sentence comprehension (Sabsevitz & Hammeke, 2014; Schoenberg & Scott, 2011; Scott & Schoenberg, 2011c). Several language-specific batteries have been developed to assess each of these areas of language functioning, including the Boston Diagnostic Aphasia Examination (Goodglass, Kaplan, & Barresi, 2000) and the Western Aphasia Battery Revised (Kertesz, 2006).

Visuoperceptual, Visuospatial, and Visuoconstructional Abilities

Visuoperceptual and visuospatial abilities are central to competent everyday functioning. Most of these abilities occur automatically and outside of awareness, thus obscuring their importance. However, when the brain regions that underlie these functions are damaged, a number of deficits may occur. These deficits may include an inability to process basic aspects of stimuli (e.g., color, form, and orientation), recognize familiar objects, find one's way in the environment, copy or draw designs, or attend to objects in the left hemispatial field. The nature of these deficits and their corresponding functional neuroanatomy are the topic of this section.

Visuoperceptual and visuospatial functional anatomy involves two separate streams of visual information processing that occur in parallel, despite the unitary nature of conscious experience of the visual world. Initial analysis of visual information occurs in the primary visual cortex in the occipital lobe. Primary visual cortex is responsible for extracting very basic visual information from stimuli, including orientation, spatial frequency, and direction of visual stimulus movement. This information is then sent to brain regions involved in higher levels of visual processing, which integrate these initial visual perceptual features into integrated wholes. These higher-level visual functions are predominantly processed in the right hemisphere and involve two separate pathways, a ventral stream involved in visuoperceptual analysis for object recognition and a dorsal stream involved in visuospatial analysis to guide movement in relation to visual information (Scott & Schoenberg, 2011a).

The ventral stream runs from the occipital to temporal lobe. These regions are involved in the perception of form, color, and shape. Damage to this stream can result in difficulties discriminating between colors (termed achromatopsia), defects in form discrimination, problems with matching identical stimuli, and difficulties mentally synthesizing fragmented pictures into complete wholes. Bilateral damage to the fusiform gyrus can result in a more specific inability to recognize faces (termed prosopagnosia). More extensive damage to the occipitotemporal region can result in visual agnosias, which are characterized by an inability to recognize visually presented objects. Two types of visual agnosias have been identified. Apperceptive visual agnosia involves an inability to group together visual stimulus elements into a whole object, despite accurate perception of attributes of the object. Associative visual agnosia consists of accurate perception of a whole, integrated object, but a failure to link semantic knowledge to that perception (Bauer, 2014; Scott & Schoenberg, 2011a).

The dorsal stream runs from the occipital cortex through the superior temporal gyrus and into the parietal lobe. This region is involved in visuospatial processing and visuomotor interaction. Damage to the dorsal, visuospatial stream also results in a range of deficits, including difficulties attending to the left hemispatial field (termed attentional neglect), an inability to localize objects in space, difficulties finding one's way in the environment with respect to the self (termed egocentric disorientation), and problems with judging the relative orientation of lines. Deficits in visuoconstructional abilities, such as putting blocks together to construct designs or drawing complex figures, can result from damage to either ventral or dorsal streams, although the nature of deficits may differ depending on the region of damage (Bauer, 2014; Scott & Schoenberg, 2011a).

A variety of measures are available to assess visuoperceptual and visuospatial abilities. As a first step, sensory functioning, including visual acuity, oculomotor ability, and visual field deficits, should be evaluated (Scott & Schoenberg, 2011a). Commonly administered measures of visuoconstruction include the WAIS-IV Block Design task (Wechsler, 2008) and the Rey-Osterrieth Complex Figure Test (Meyers & Meyers, 1995). Visuospatial ability can be measured with the Judgment of Line Orientation test (Benton, Varney, & Hamsher, 1978) and hemispatial neglect by line bisection and cancellation tasks (Lezak et al., 2012). Finally, measures of visuoperceptual ability include the Benton Visual Form Discrimination test (Benton, Sivan, & Hamsher, 1983) and the Hooper Visual Organization Test (Hooper, 1983).

Future Directions in Neuropsychology

Clinical neuropsychology is a rapidly advancing field. Technological developments as well as increasing recognition of the limitations of neuropsychological assessment to nonmainstream cultural groups have led to some of the most exciting and important new research areas in neuropsychology. This section discusses three of these emerging research areas: cultural neuropsychology, connectomics, and the integration of genomics with neuropsychology.

Cultural Neuropsychology

The United States is currently undergoing a dramatic demographic shift that is changing the composition of the country (Bureau, 2011). This, among other factors, has led to growing interest on the impact of culture on neuropsychological test performance. Traditionally, neuropsychology has struggled to account for cultural contributions to test performance, leading to reduced diagnostic specificity with examinees from nonmainstream cultural groups (Cagigas & Manly, 2014). This has largely been due to a mismatch between normative standardization samples and culturally diverse examinees, with most standardization samples consisting of well-educated, English-speaking, US-born, culturally mainstream Whites. Cultural neuropsychology is an attempt to improve the discipline of neuropsychology by exploring the effects of and pathways by which cultural experiences impact brain-behavior relationships. In this way, cultural neuropsychology may be defined as the study of brain-behavior relationships that emerge out of the manner in which human being engage in culture-specific practices that shape the organization, development, and revision of their cognition and behavior (Cagigas & Manly, 2014).

There are several important strains of cultural neuropsychological research. First, a considerable amount of research has explored the causes of test sore differences across cultural groups. In the aggregate, individuals from nonmainstream cultural backgrounds typically score lower on neuropsychological tests than their culturally mainstream counterparts. This may be due to one or more of the following factors: (1) improper translation of tests, including culturally inappropriate wordings and use of inappropriate norms (van der Vijver & Hambleton, 1996); (2) discrepancies in the quality of education across cultural groups, despite similar number of years of education (Manly & Jacobs, 2002); (3) low levels of acculturation to the culture in which the tests were developed and normed (Artiola, Fortuny, Heaton, & Hermosillo, 1998); and (4) reduced comfort and confidence during the test session due to racial socialization (Cagigas & Manly, 2014). In addition, bilingualism has also been shown to affect neuropsychological test performance, leading to poorer scores on measures of vocabulary (Bialystok, Luk, Peets, & Yang, 2009), picture naming (Gollan, Fennema-Notestine, Montoya, & Jernigan, 2007), and semantic fluency (Gollan & Ferreira, 2009; Gollan, Montoya, & Werner, 2002). However, some research suggests that bilingualism confers advantages on executive functioning tasks, presumably due to greater familiarity with managing and switching between two competing representations of language among bilinguals (Bialystok, Craik, & Luk, 2008).

Second, cultural neuropsychological research has explored approaches to developing more culturally sensitive approaches to neuropsychological assessment. Chief among these efforts has been the development of separate norms for racial/ethnic or language groups. This approach has been shown to improve diagnostic accuracy (Miller, Heaton, Kirson, & Grant, 1997). However, some have noted that there is still considerable variability within racial/ethnic and language groups that remains unaccounted for. Ultimately, it has been argued that race and ethnicity may more accurately be considered proxies for, and thus confounded by, other more meaningful variables, such as language proficiency, educational quality, or socioeconomic status (Cagigas & Manly, 2014). In addition, in developing culturally sensitive neuropsychological measures, it is important not to simply assume that the validity of the measure demonstrated in the culturally mainstream group generalizes to a new cultural group. Thus, a growing body of research has sought to evaluate the construct validity of neuropsychological measures across cultural groups (Cagigas & Manly, 2014).

Third, some research has demonstrated differences in cognitive processes across individuals from different cultures. Studies have found that culture can impact a number of cognitive processes, ranging from facial (Goh et al., 2010) and visual object processing (Gutchess, Welsh, Boduroglu, & Park, 2006) to semantic categorization use to facilitate free recall (Gutchess et al., 2006). In fact, culturally specific cognitive information processing has long been recognized in neuropsychology. Luria studied remote rural communities in Uzbekistan and noted that individuals from these communities did not categorize objects based on abstract rules, like their educated adult counterparts, but rather did so based on the relationship of the stimulus objects to their everyday lives (Nell, 1999, 2000). Nonetheless, evaluation of the culture-specific nature of cognition has largely been overlooked in subsequent years. An exciting new area of research has begun to explore the manner in which cultural practices shape cognition, emotion, and behavior as well as brain structure and function (Cagigas & Manly, 2014)

Connectomics

Historically, most neuroimaging research in clinical populations has focused on regional abnormalities in brain structure and/or functioning. However, recent advances in neuroimaging and network modeling have led to growing interest in the dynamics of large-scale brain networks within normal populations and abnormalities within and between these networks in clinical populations (Menon, 2011). A central goal of this research is to provide a comprehensive characterization of the structural pathways connecting remote brain regions and the functional interactions between these remote regions. The study of these large-scale networks is referred to as connectomics and the descriptions derived therefrom as the human connectome (Sporns, 2013). Emerging findings from connectomics suggest that the human brain consists of several distinct functional networks and that these networks are organized in a modular fashion, with networks interlinked through sub-networks or core hub regions, which enable global information flow and integration (Sporns, 2013).

Adopting a network-level analysis of brain-behavior relationships has led to novel findings among several clinical populations. For instance, traditional neuroimaging studies evaluating regional abnormalities in brain structure and function among individuals with autism have often reported abnormalities in the frontal lobes, amygdala, and cerebellum (Amaral, Schumann, & Nordahl, 2008). However, many of these findings have been inconsistent across studies. Moreover, descriptions of regional abnormalities may be insufficient to characterize the distributed nature of a disorder like autism, especially given the heterogeneity of the cognitive and behavioral phenotype of this disorder. As such, evaluation of the structure, integrity, and integration of distributed functional networks may be more revealing of brain-behavior relationships in autism.

Recent research on network functional connectivity in autism has revealed important findings. For one, autism is most consistently characterized by underconnectivity between the prefrontal cortex and posterior brain regions and regional overconnectivity within the extrastriate cortex, frontal lobe, temporal lobe, amygdala, parahippocampal gyrus, and temporo-thalamic regions (Maximo, Cadena, & Kana, 2014; Murphy, Foss-Feig, Kenworthy, Gaillard, & Vaidya, 2012; Noonan, Haist, & Muller, 2009; Shih et al., 2010; Shih et al., 2011; Uddin et al., 2013; Welchew et al., 2005). These findings have been taken to suggest inefficient brain network integration, with overabundant connectivity occurring in nonessential regions, leading to poor distributed network coordination in the midst of high levels of regional noise. It remains to be determined whether regional overconnectivity in autism is a cause or an effect of observed underconnectivity across distributed brain regions (Maximo et al., 2014). For another, emerging research has shown that irregularities in specific networks are associated with distinct behavioral abnormalities. For instance, overconnectivity within specific nodes in the default mode network has been associated with lower verbal and nonverbal communication ability, more severe repetitive behaviors, and restricted, repetitive behaviors (Agam, Joseph, Barton, & Manoach, 2010; Monk et al., 2009; Weng et al., 2010). In this sense, brain network abnormalities may serve as promising intermediate phenotypes linking genes to behavior (Sporns, 2013).

Genetics and Neuropsychology

Another promising avenue is the integration of genomics with neuropsychology. Genomic research is focused on identifying genetic contributions to normal and pathological phenotypes and has been made possible by rapid advances in human genome sequencing and techniques for identifying single nucleotide polymorphisms and quantifying gene expression. Cognition has emerged as an important phenotype in these investigations, due to the contribution of cognition to functional outcomes (e.g. vocation, academic achievement) and the presence of cognitive impairment in pathological conditions as diverse as autism, schizophrenia, Parkinson's disease, and Alzheimer's disease. Neuropsychology specializes in teasing apart the multiple cognitive processes contributing to performance on cognitive tasks and linking these specific processes to brain structure and function. As such, neuropsychology is well positioned to assist in genomic research on cognitive phenotypes (Kremen, Panizzon, & Cannon, 2016).

For instance, Panizzon et al. (2011) explored performance on the California Verbal Learning Test-II (Delis et al., 2000), a word list learning episodic memory task, among twin pairs. These authors found that while the same set of genes contributed to short- and long-delay free recall, a different set of genes was associated with performance during learning trials. Short- and long-delay free recall as well as learning trials involve free recall; however, only learning trials additionally involve acquisition of to-be-remembered content. As such, these authors reasoned that there are separate genetic influences on recall and acquisition processes. This implies that episodic memory tests are not interchangeable at the genetic level. Studies that fail to take into consideration this specificity of the multiple cognitive processes contributing to a particular cognitive domain may thus obscure the genetic contribution to these processes.

Exploration of gene-environment interactions is an especially exciting area of genetic and neuropsychology research. Gene-environment interactions deal with the manner in which the response to an environmental factor varies as a function of one's genotype (Kremen et al., 2016). These interactions are important insofar as they indicate the mutability of one's genetic endowment and indicate the potential for psychosocial or behavioral intervention. For instance, Ferencz et al. (2014) created a genetic risk score based on several genes previously associated with episodic memory among individuals differing in levels of physical activity. These authors reported that the effect of the risk score on episodic memory differed across individuals with high vs. low physical activity. In particular, the genetic risk score was associated with episodic memory impairment only among individuals in the low physical activity group. In other words, physical activity was protective against genetic effects on episodic memory. Incorporation of these and other gene-environment interactions has the potential to improve interventions for cognition and can assist in the development of individualized treatment recommendations, a main goal of the emerging field of precision medicine (Collins & Varmus, 2015).

Conclusion

Neuropsychology is an expansive and rapidly developing field. Neuropsychological investigations have deepened our understanding of brain-behavior relationships in the normal brain and the manner in which these relationships are disrupted in a variety of developmental, psychiatric, and neurological disorders. Technological developments in brain imaging and genetics and the expansion of neuropsychology to previously understudied populations promise to yield further transformative insights into brain structure and function.

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