Developmentally Delayed Children and Adults

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Introduction

Epilepsy is a disorder that can arise from a variety of etiologies, such as structural brain malformations, genetic or metabolic abnormalities, birth anoxia, cerebrovascular insults, central nervous system infections, brain tumors, or moderate to severe brain injury. It is a disorder that most often begins in childhood and adolescence but can have an onset at any point during adulthood, including older adulthood. Given the heterogeneity of epilepsy, it is not surprising that patients with epilepsy can have vastly different levels of intellectual and neurocognitive functioning. Specific factors such as the underlying pathology of seizures, age of onset, seizure type, seizure frequency, as well as antiepileptic medication regimen can have an impact on intellectual and neurocognitive functioning. Additionally, intellectual disabilities are caused by a variety of neuropathological processes, including structural brain malformations, genetic or metabolic abnormalities, birth anoxia, and cerebrovascular insults, some of which overlap with the neuropathological underpinnings of seizures. Epidemiological studies have shown that epilepsy occurs much more often in people with intellectual disability than in the general population, with estimates ranging from 10 % to over 60 % of people with intellectual disability having some form of epilepsy (Forsgren, Edvinsson, Blomquist, Heijbel, & Sidenvall, 1990; Lhatoo & Sander, 2001). In those patients with intellectual impairment and epilepsy concurrently, seizures usually present before the age of 5 years, with the severity of seizures and intellectual impairment being highly correlated (Kaufman, 2007). It is well beyond the scope of this chapter to try to characterize the intellectual functioning associated with all the different seizure types and epilepsy syndromes. However, there are several epilepsy syndromes that commonly have comorbid intellectual impairment and developmental delay, and there are several common developmental syndromes that are characterized by both intellectual impairment and seizures. This chapter will briefly outline a few syndromes that most commonly present with developmental delays and seizures. More importantly, it will attempt to provide a discussion of how neuropsychological assessment can assist in the assessment and treatment of developmentally delayed children and adults with epilepsy.

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Neurocognitive Functioning in Epilepsy Syndromes and Developmental Syndromes with Comorbid Epilepsy

There are a number of different classifications of epilepsy and specific epilepsy syndromes with which patients can be diagnosed, as designated by the International League Against Epilepsy (ILAE), many of which are diagnosed in childhood. There are also a number of different developmental syndromes in which children commonly present with intellectual impairment, developmental delays, or severe learning disorders as well as a history of seizures or a chronic epilepsy diagnosis. While the following list of classifications and syndromes is not exhaustive, it highlights several of the more common types of epilepsy syndromes and developmental syndromes that have comorbid developmental delay or intellectual impairment with concurrent seizures.

Temporal Lobe Epilepsy

It has been estimated that simple and complex focal seizures make up as many as 70 % of all the diagnosed epilepsies, and half of those originate in temporal lobe structures. Thus, approximately 30 % of all epilepsies are thought to be temporal lobe epilepsy, with two-thirds of temporal lobe epilepsies having an epileptogenic focus in mesial temporal areas and the other third having an epileptogenic focus in lateral temporal lobe regions (Crawford, 2000; Hauser, Annegers, & Kurland, 1991; Panayiotopoulos, 2002; Wiebe, 2000). For the most part, temporal lobe epilepsy is not commonly associated with developmental delay or intellectual impairment (Sauerwein, Gallagher, & Lassonde, 2005). However, cognitive functioning in patients with temporal lobe epilepsy varies from individual to individual, with the occurrence and severity of status epilepticus or a series of generalized tonic-clonic seizures presenting the greatest risk factors for amnestic syndromes and neurocognitive decline in domains other than memory (Lee, Yip, & Jones-Gotman, 2002). Furthermore, it has been demonstrated that patients with chronic, uncontrolled temporal lobe epilepsy often experience a significant decline in their overall IQ after about 30 years of uncontrolled seizure activity, although those findings are also mediated by a number of factors, including the frequency and severity of the patient's seizures and premorbid cognitive and intellectual functioning (Jokeit & Ebner, 2002). It has also been demonstrated that some proportion of patients with temporal lobe epilepsy have premorbid intellectual impairment, as lesions, areas of epileptogenesis, and seizures all interfere with the maturation and development of the brain which can lead to a global impact on cognitive development and a significant decrease in overall intellectual functioning such that even "typical" mesial temporal epilepsy with hippocampal sclerosis can be associated with impaired intellectual functioning (Sauerwein et al., 2005).

Primary Generalized Epilepsy

There are a number of primary generalized epilepsies, also known as idiopathic generalized epilepsies, most of which are presumed to have multiple genetic underpinnings that are only just beginning to be elucidated. They include syndromes such as childhood absence epilepsy, juvenile absence epilepsy, juvenile myoclonic epilepsy, epilepsy with generalized tonic-clonic seizures upon awakening, and generalized epilepsies associated with febrile events (Shouse & Quigg, 2008). For the most part, these epilepsies respond well to antiepileptic medications, particularly valproic acid, lamotrigine, topiramate, levetiracetam, and ethosuximide. Additionally, many children with one of these primary generalized epilepsies are seizure-free within 14 years of their initial diagnosis and do not need to take medication chronically, with the exception of children with juvenile myoclonic epilepsy who often need to take antiepileptic medication throughout their lives (Shahar, Barak, Andraus, & Kramer, 2004; Williams & Sharp, 2000). Regarding the cognitive correlates of primarily

generalized epilepsy, studies have shown that children demonstrate average IQs with only mild cognitive weaknesses in the areas of attention, concentration, and impulsiveness, as well as a higher rate of diagnosed learning disorders (Bhise, Burack, & Mandelbaum, 2010; Shahar et al., 2004). In particular, juvenile myoclonic epilepsy is associated with a good intellectual prognosis, particularly if it is well controlled with medication (Williams & Sharp, 2000).

West Syndrome (Infantile Spasms)

West syndrome, also known as infantile spasms, begins between 4 and 6 months of life and generally involves clusters of myoclonic seizures. There are a variety of etiologies of infantile spasms, including CNS infection, CNS developmental abnormalities, head trauma, intrapartum asphyxia, metabolic disorders, and neurodegenerative disease (Williams & Sharp, 2000), thus many of the syndromes described in this chapter have West syndrome or infantile spasms as a presenting or core feature. The overall incidence of infantile spasms has been estimated at 2–7 per 10,000 live births and often has comorbid developmental delay (Hauser et al., 1991; Lee & Ong, 2001; Lúthvígsson, Olafsson, Sigurthardóttir, & Hauser, 1994), making it one of the most common epilepsy syndromes of childhood or presentation of childhood seizures that has comorbid intellectual impairment. Interestingly, the myoclonic seizures of infancy usually wane by the age of 4 years old. As many as 60 % of children with a history of infantile spasms then develop other types of seizures and go on to have chronic epilepsy that may or may not be treatable with antiepileptic medication (Murphy & Dehkharghani, 1994). In terms of long-term prognosis, up to 20 % of infants with infantile spasms will die in infancy, usually as a result of the underlying disease or complications from their medical condition (Jeavons, Bower, & Dimitrakoudi, 1973). Of those children who survive infantile spasms, one epidemiological study demonstrated that by the age of 10 years old, 83 % of children with a history of infantile spasms will be intellectually disabled (Trevathan, Murphy, & Yeargin-Allsopp, 1999). Additionally, that study also demonstrated that approximately 12 % of 10-year-old children with severe intellectual disability have a history of infantile spasms. Interestingly, when the etiology of infantile spasms is cryptogenic, approximately 50 % of the children have a normal cognitive outcome, particularly if the seizures are well controlled with medications or surgery (Murphy & Dehkharghani, 1994).

Tuberous Sclerosis

Tuberous sclerosis is characterized by smooth and firm nodules on the face that usually appear in adolescence. In a minority of children affected by tuberous sclerosis, they also present with seizures and intellectual disability due to cerebral tubers that correlate with the skin lesions. Additionally, children with CNS involvement of tuberous sclerosis often present with autistic-like symptoms (Hunt & Dennis, 1987; Kaufman, 2007). The severity of neuropsychiatric and intellectual impairment is correlated with the number and location of cortical tubers (Caplan, Gillberg, Dunn, & Spence, 2008). While approximately 50 % of children with tuberous sclerosis need to be institutionalized due to intractable seizures and deteriorating intellectual functioning, the other 50 % of children with tuberous sclerosis have only minimal cognitive impairment, and their epilepsy is easily controlled with antiepileptic medication. However, children with cerebral tubers often have several tubers. When children have several cortical tubers, that is often correlated with more severe seizures that are often intractable to antiepileptic medication, and their intellectual disability is often more severe. While not all cortical tubers are epileptogenic, the likelihood of intellectual impairment occurring in patients with tuberous sclerosis has been associated with a history of seizures, particularly infantile spasms (Joinson et al., 2003; Kaufman, 2007). Importantly, one study demonstrated that treatment of the infantile spasms with vigabatrin resulted in a very high rate of seizure control and

a commensurate improvement in behavioral and intellectual functioning, suggesting that seizures significantly contribute to the presentation of intellectual impairment and autistic-like behavior in children with tuberous sclerosis and not simply the presence of cortical tubers (Jambaqué, Chiron, Dumas, Mumford, & Dulac, 2000).

Lennox-Gastaut Syndrome

Lennox-Gastaut syndrome is characterized by the following triad of symptoms: (1) multiple types of intractable seizures that are mainly tonic, atonic, and atypical absence seizures, (2) cognitive and behavioral abnormalities, and (3) diffuse slow spike and waves and paroxysms of fast activity on EEG (Panayiotopoulos, 2002). The syndrome usually first presents between 1 and 7 years of age, with a peak incidence occurring between 3 and 5 years of age (Rantala & Putkonen, 1999; Trevathan, Murphy, & Yeargin-Allsopp, 1997). Approximately 50 % of children with West syndrome progress to Lennox-Gastaut syndrome, and conversely up to 30 % of children with Lennox-Gastaut transition to having West syndrome (Panayiotopoulos, 2002, Rantala & Putkonen, 1999). The seizures are often difficult to control and status epilepticus is common. In about 50 % of children who are eventually diagnosed with Lennox-Gastaut syndrome, cognitive and behavioral abnormalities are evident prior to the initial diagnosis of the epileptic syndrome, but eventually intellectual disability is diagnosed in up to 96 % of children with the syndrome. Additionally, the course of intellectual impairment and developmental delay is usually progressive, and many children with the syndrome eventually require significant assistance in most aspects of daily functioning if they reach adulthood (Gastaut, 1982).

Landau-Kleffner Syndrome

Landau-Kleffner syndrome, also known as acquired epileptic aphasia, is characterized by a sudden or gradual onset of verbal deficits, particularly verbal auditory agnosia, which occurs sometime between 2 and 11 years of age following a period of normal development. It is a relatively rare epilepsy syndrome but one in which neurocognitive functioning is a hallmark feature of the syndrome. Importantly, the child should have achieved age-appropriate developmental milestones, including age-appropriate speech, at the time of the initial onset of verbal auditory agnosia (Fenichel, 2001; Panayiotopoulos, 2002). The severity of verbal deficits is highly variable between children diagnosed with the syndrome, as it can simply involve verbal auditory agnosia in which children have difficulty distinguishing speech from nonspeech sounds, or children can become totally unresponsive in oral communication and eventually demonstrate a progressive deterioration of expressive speech and vocabulary. Interestingly, the course over which verbal deficits are acquired is often fluctuating with remission and exacerbation causing a waxing and waning pattern in their behavioral and neurocognitive presentation (Paquier, Van Dongen, & Loonen, 1992). Approximately 75 % of children with Landau-Kleffner syndrome have comorbid seizures, which may have an onset before, during, or after the development of verbal deficits. Most commonly, children have generalized tonic-clonic seizures and focal motor seizures (Murphy & Dehkharghani, 1994). The seizures are usually easily treatable with antiepileptic medication, with almost all children becoming seizure-free by 15 years of age. Unfortunately, seizure remittance is not associated with an improvement in aphasia or verbal deficits, although some children do spontaneously recover all language function. To date, studies have not been able to determine what contributes to long-term recovery of language in some children, although an earlier age of onset is associated with a poorer neurocognitive outcome (Gordon, 1990). Children diagnosed with Landau-Kleffner syndrome also demonstrate a variety of behavioral problems, including hyperactivity, inattention, and impulsivity. Importantly, nonverbal abilities are generally preserved and Landau-Kleffner syndrome is not usually associated with global cognitive decline or intellectual impairment (Panayiotopoulos, 2002; Williams & Sharp, 2000).

Electrical Status Epilepticus During Sleep

Electrical status epilepticus during sleep, also known as epilepsy with continuous spike and waves during slow-wave sleep, is characterized by: (1) continuous spikes and waves during more than 85 % of non-REM sleep on EEG, (2) seizures, and (3) neurocognitive decline (Panayiotopoulos, 2002). Much like Landau-Kleffner syndrome, it is a relatively rare epilepsy syndrome in which a decline in intellectual and cognitive functioning is a hallmark feature. Usually children have a period of typical development followed by the onset of continuous spike and slow waves during sleep sometime between the ages of 4 and 14 years of age, which is accompanied by neurocognitive regression, although some children demonstrate premorbid developmental delays prior to the onset of electroencephalographic changes (Williams & Sharp, 2000). Unlike Landau-Kleffner syndrome, which is thought to be a highly related syndrome (Feekery, Parry-Fielder, & Hopkins, 1993), children with electrical status epilepticus during sleep demonstrate more global neurocognitive decline (Jayakar & Seshia, 1991). Similar to Landau-Kleffner syndrome, the seizures always remit, usually at some point during adolescence. Studies have suggested that there are some recovery of neurocognitive function and improvement in behavioral problems that occur with the remission of the continuous spike and slow waves during sleep. However, less than 25 % of children with this syndrome achieve an average level of intellectual and cognitive functioning, instead presenting with some level of cognitive and adaptive disability throughout their lives (Panayiotopoulos, 2002, Paquier et al., 1992).

Down Syndrome

Down syndrome or trisomy 21 is characterized by a range of intellectual and developmental disability, along with a number of physical and medical problems. It is the most common *genetic* cause of intellectual disability and developmental delay (Kaufman, 2007). Additionally, approximately 13–57 % of patients with Down syndrome develop seizures or an abnormal EEG at some point in their lives (Romano et al., 1990; Tangye, 1979). There is commonly a bimodal distribution of seizure onset, with the highest rate of onset occurring in childhood and another spike in onset occurring in middle age (Prasher, 1995; Tatsuno, Hayashi, Iwamoto, Suzuki, & Kuroki, 1984). Additionally, patients with Down syndrome can present with a number of different seizure types, including infantile spasms (Pollack, Golden, Schmidt, Davis, & Leeds, 1978), generalized tonic-clonic seizures, complex-partial seizures (Romano et al., 1990), and Lennox-Gastaut syndrome (Tatsuno et al., 1984).

Angelman Syndrome

Angelman syndrome is a genetic disorder in which all patients present with developmental delay that becomes apparent between 6 and 12 months of age. Behavioral and cognitive features include severely impaired expressive language, an excessively happy demeanor, very poor attention span, and autistic-like symptoms (Kaufman, 2007). Additionally, seizures, abnormal electroencephalography, and microcephaly are observed in over 80 % of patients with the syndrome. In fact, it has been estimated that about 6 % of the children who present with severe intellectual disability and epilepsy have Angelman syndrome (Guerrini, Cararozzo, Rinaldi, & Bonnani, 2003). Patients with Angelman syndrome almost always develop seizures before 3 years of age. The most frequent seizure types are myoclonic, atonic, generalized tonic-clonic, atypical absence seizures (Galván-Manso, Campistol, Conill, & Sanmartí, 2005), as well as periods of insidious myoclonic status epilepticus (Viani et al., 1995). Fortunately, there are a number of medications that have been shown to effectively treat the seizures in these patients during early childhood, including valproic acid, benzodiazepines, and ethosuximide, often in combination (Guerrini et al., 2003), with additional control of seizures also being

achieved after children are 9 years of age or older with some combination of those antiepileptic medications (Galván-Manso et al., 2005).

Fragile X Syndrome

Fragile X syndrome is a sex-linked chromosomal disorder that is characterized by intellectual impairment and distinctive non-neurological physical features. It is widely considered to be the most common cause of *inherited* intellectual disability, as it is responsible for about 10 % of all cases of intellectual disability (Kaufman, 2007). Approximately 80 % of males with fragile X syndrome are moderately or severely intellectually disabled, while 10–15 % of males with fragile X syndrome are mildly intellectually disabled or have IQs in the borderline range with significant language impairment and autistic-like symptoms. Additionally, most males with this syndrome have symptoms of attention deficit hyperactivity disorder, including distractibility and impulsivity (Fryns, Jacobs, Kleczkowska, & van den Berghe, 1984). In contrast, females carrying the fragile X gene are often asymptomatic. Approximately 30 % of females with the gene present with IQs lower than 85, and those of average intellectual functioning are at increased risk for learning disabilities (de Vries et al., 1995; Kaufman, 2007). Seizures occur in approximately 10–20 % of patients, both male and female, with fragile X syndrome, with a slightly higher prevalence of seizures in males with fragile X syndrome. The seizures that occur in fragile X syndrome most resemble those of benign focal epilepsy of childhood, including a common pattern of centrotemporal spikes, which are usually easily controlled with antiepileptic medication and often remit before 20 years of age (Berry-Kravis, 2002; Sabaratnam, Vroegop, & Gangadharan, 2001).

Rett Syndrome

Rett syndrome occurs only in females and is characterized by normal birth and typical development for the first 6–18 months of life, after which time development slows and then deteriorates with a loss of language skills, a regression of motor abilities, and a decrease in cognitive capacity. Eventually, girls with Rett syndrome are considered developmentally delayed with severe to profound intellectual disability and autistic-like symptoms (Huppke, Held, Laccone, & Hanefeld, 2003; Kaufman, 2007). It has been estimated that epilepsy occurs in 80–95 % of girls with Rett syndrome (Steffenburg, Hagberg, & Hagberg, 2001), but some studies have also argued that the incidence of seizure comorbidity in Rett syndrome is overestimated due to the frequent occurrence of autonomic dysfunction and motor symptoms that are common in the syndrome, such as twitching, jerking, head turning, falling forward, and trembling, all of which can be easily mistaken for seizures (Glaze, Schultz, & Frost, 1998). When seizures are identified in girls with Rett syndrome, they are commonly complex-partial seizures with onset occurring around 4 years of age. Most often, the occurrence of seizures is highly correlated with smaller head circumference. Additionally, girls with Rett syndrome can also present with generalized tonic-clonic, absence, myoclonic jerk, atonic, and tonic seizures. The severity and incidence of seizures decrease with increasing age, and many women with the syndrome are seizure-free (Steffenburg et al., 2001).

Dravet Syndrome (Severe Myoclonic Epilepsy in Infancy)

Dravet syndrome, also known as severe myoclonic epilepsy in infancy, is a rare form of progressive epileptic encephalopathy that is thought to have genetic underpinnings. It is estimated to affect approximately 6 % of infants diagnosed with epilepsy. It is characterized by initial febrile and afebrile, generalized and unilateral clonic or tonic-clonic seizures that occur during the first year of life in an otherwise typically developing infant (Dravet & Bureau, 2008). Over time, children will then begin to have other types of seizures, including myoclonic, atypical absences, and partial seizures, with periods of absence

status epilepticus frequently occurring between 2 and 4 years of age. One hallmark feature of the syndrome is that the seizures are often refractory to treatment with antiepileptic medication (Panayiotopoulos, 2002). As the seizures progress between 2 and 4 years of age, psychomotor delays, behavioral disturbances, and cognitive impairment become apparent. Eventually, patients with Dravet syndrome go on to have persistent refractory convulsive seizures. There has been one neuropsychological study of teenagers with Dravet syndrome that demonstrated 50 % of patients with this syndrome were severely intellectually disabled, and all teenagers had significant neurocognitive deficits in motor, verbal, and visuospatial abilities. The teenagers were described as hyperactive and psychotic-like with some autistic traits (Cassé-Perrot, Wolff, & Dravet, 2001; Wolff, Cassé-Perrot, & Dravet, 2001). Approximately 15 % of children with Dravet syndrome die as a direct or indirect result of their seizures. For those patients who survive into adulthood, their seizures always remain refractory to antiepileptic medication. Additionally, they are usually intellectual disabled and present with limited language, poor fine motor functions, generalized slowing, autistic-like behaviors, and occasionally psychiatric features, all of which are severe enough that they usually cannot work or live independently (Dravet & Bureau, 2008).

Neurocognitive Effects of Antiepileptic Drugs During Pregnancy

Epilepsy can affect not only the intellectual capacity of patients with the condition but also the intellectual functioning of children born to mothers with epilepsy. It has long been established that exposure to some antiepileptic medications in utero, particularly phenobarbital and other antiepileptic medications in high doses, can lead to fetal structural malformations (Holmes, Wysznski, & Lieberman, 2004). More recent studies have also examined the effects of fetal exposure to lower doses of antiepileptic medications and have revealed behavioral and cognitive deficits, altered neurochemistry, and reduced brain weight in the children after birth (Fisher & Vorhees, 1992; Gaily & Meador, 2007). In a groundbreaking study examining the effects of fetal exposure to four different antiepileptic medications, the Neurodevelopmental Effects of Antiepileptic Drugs (NEAD) study group demonstrated that exposure to valproic acid in utero resulted in significantly lower IQs at 3 years of age compared with in utero exposure to carbamazepine, lamotrigine, and phenytoin (Meador et al., 2009). However, it is important to note that children exposed to valproic acid in utero had an average IQ of 92, with IQs ranging from 88 to 97. Thus, none of the children exposed to valproic acid met criteria for borderline intellectual functioning or intellectual impairment. While it is important to consider in utero exposure to antiepileptic medication as a possible factor when assessing patients born to mothers with epilepsy who took antiepileptic medication during their pregnancy, there has been little evidence to suggest that in utero exposure to antiepileptic medications is a single causative factor for developmental delay or intellectual impairment.

Neuropsychological Assessment of Patients with Developmental Delay or Intellectual Impairment and Concurrent Epilepsy

Developmentally delayed or intellectually impaired patients with epilepsy are referred for neuropsychological for a variety of reasons. Most commonly, they are referred by their neurologists for evaluation of their overall general intellectual functioning and their level of general adaptive functioning. In those cases, their degree of intellectual, neurocognitive, and developmental disability needs to be determined so that appropriate recommendations and referrals can be provided. A frequently asked additional referral question is whether or not the patient's current antiepileptic medication regimen is negatively impacting their degree of intellectual, neurocognitive, or developmental impairment or delay. It has been well

established that many antiepileptic medications can have a negative impact on neurocognition, particularly memory and verbal functioning (Aldenkamp, Baker, & Mulder, 2000; Martin et al., 1999; Loring & Meador, 2001; Meador, Loring, Hulihan, Kamin, & Karim, 2003; Motamedi & Meador, 2004), and it is important to determine whether a patient with intellectual impairment is being further negatively impacted by their antiepileptic medication regimen. Finally, developmentally delayed or intellectually impaired patients with epilepsy are also referred by neurosurgeons for neuropsychological assessment to assist with determining epileptogenic lateralization and location, as well as to predict the potential impact of surgery on cognitive, behavioral, and adaptive functioning. It is important for neuropsychologists to consider the referral source and referral question when assessing developmentally delayed or intellectually impaired patients with epilepsy so that they design their battery appropriately, with special consideration to the ability of the patient to participate in a comprehensive evaluation versus a shorter evaluation and the relative value of administering some tests over others.

Definition of Intellectual Disability

The *Diagnostic and Statistic Manual of Mental Disorders*, *Fourth Edition*, *Text Revision* (DSM-IV-TR, 2000) provides the following criteria for diagnosing mental retardation or intellectual disability:

1. A measured IQ of 70 or below on an administered test of intellectual functioning.
2. Concurrent age-related deficits in adaptive functioning in at least two of the following areas:
   (a) Communication.
   (b) Self-care.
   (c) Home living.
   (d) Social skills.
   (e) Use of community resources.
   (f) Self-direction.
   (g) Functional academic skills.
   (h) Work.
   (i) Leisure.
   (j) Health issues
   (k) Safety
3. An onset of deficits before the age of 18 years.

Additionally, the DSM-IV-TR specifies the criteria for defining the severity of a patient's level of mental retardation or intellectual disability into the following levels: borderline intellectual functioning (IQ 70–85), mild mental retardation (IQ of 50–75), moderate mental retardation (IQ of 35–55), severe mental retardation (IQ of 20–40), and profound mental retardation (IQ of less than 20). The *International Classification of Diseases*, *10th revision* (ICD-10, World Health Organization, 1993) denotes similar definitions of the four levels of mental retardation and also specifies that intellectual retardation is determined by both a low measured IQ and deficits in cognitive, language, motor, social, and other adaptive behavior skills. Approximately 85 % of people who are diagnosed with intellectual disability are mildly mentally retarded, which means they can usually attain at least a sixth grade level of academic achievement and lead somewhat independent lives (McLaren & Bryson, 1987). Adults with mild mental retardation often work or volunteer in their community and live in assisted living facilities where they are minimally supervised. Given that the severity of disability and a patient's needs increase with classifications of moderate, severe, or profound mental retardation, it is often helpful to accurately assess a patient's level of intellectual disability in order to best inform patients' caretakers of their expected quality of life.

Neurocognitive Functioning in Patients with Developmental Delays or Intellectual Disability

Patients with documented intellectual disability have, by definition, delays in several aspects of cognition and adaptive functioning. However, the nature and degree of impairment in various areas of cognition is highly variable from patient to patient. Studies have demonstrated that a diagnosis

of mild mental retardation does not always correlate with impairments in attention, memory, verbal comprehension, or visual perception. In fact, when patients with mild or moderate general intellectual disability have borderline to average functioning in attention, memory, or verbal comprehension, that is highly predictive of employment success (Su, Lin, Wu, & Chen, 2008). Thus, even though a patient may present with a measured IQ below 70, that does not necessarily mean that all other aspects of their neurocognitive profile will also be in the impaired range. A careful assessment of all aspects of the neurocognitive profile of patients with intellectual disability, particularly patients with mild or moderate intellectual disability, is warranted as that provides the most accurate evaluation of all aspects of their functioning. Additionally, a thorough neuropsychological assessment provides crucial information about the possible neurocognitive effects of antiepileptic medication or the possible neurocognitive outcome of surgery.

Intelligence Tests

Given that a patient's measured IQ is the foundation for a diagnosis of mental retardation or intellectual disability, it is often essential to at least attempt to obtain a measured IQ score for patients who are thought to be developmentally delayed or intellectually impaired. The most common measures used to assess overall intellectual and general cognitive functioning are the Wechsler scales, which allow for the assessment of children from the age of two and a half years old to adults aged 91 years old. The Wechsler Preschool and Primary Scale of Intelligence, Third Edition (WPPSI-III; Wechsler, 2002) is appropriate for children age 2 years, 6 months to 7 years, 3 months and provides verbal and performance indices for all children as well as a processing speed index for older children. The Wechsler Intelligence Scale for Children, Fourth Edition (WISC-IV; Wechsler, 2003) is appropriate for children aged 6–17 years old and provides subtests to assess verbal comprehension, perceptual reasoning, processing speed, and working memory. Similarly, the Wechsler Adult Intelligence Scale, Fourth Edition (WAIS-IV; Wechsler, 2008) is appropriate for adults aged 16–91 years old and provides subtests to assess verbal comprehension, perceptual reasoning, processing speed, and working memory. If the administration of a full WPPSI-III, WISC-IV, or WAIS-IV is not possible given the severity of a patient's intellectual disability, the Wechsler Abbreviated Scale of Intelligence (WASI, Wechsler, 1999) is appropriate for both children and adults aged 6–90 years old, takes only 30 min to administer, and provides verbal (estimated VIQ), nonverbal (estimated PIQ), and overall (estimated FSIQ) measures of intellectual functioning. The Wechsler scales have the advantage of being the most widely used measures that have the greatest basis for empirical validity in the research literature. Additionally, the more recent versions of the Wechsler scales have been tailored to have shorter administration times, so they are more amenable to testing patients with significant cognitive limitations. However, it is not uncommon for patients who are assessed at major epilepsy centers around the United States and in other countries to be given older versions of the Wechsler scales (i.e., WPPSI-R, WISC-III, and WAIS-III), as those centers have often invested a great deal of time and effort in collecting valuable databases that incorporate older versions of the Wechsler scales, and so they continue to gather consistent data about the performance of patients with epilepsy on those older measures.

When using the Wechsler scales to obtain a measure of IQ or to estimate general overall intellectual functioning, it is important to consider the patient's level of verbal and nonverbal abilities in the context of both their level of disability and a possible lateralization of epileptogenic areas. While it is not unusual for patients with intellectual disabilities to have bilateral or diffuse pathology, both in relation to their epilepsy and with regard to other factors contributing to their cognitive limitations, it is also possible that they may have a lateralized epileptogenic focus that will result in a significant discrepancy between their verbal and perceptual reasoning abilities and thus artificially lower

their overall measured IQ. Thus, IQ alone is not a good predictor of postoperative cognition and seizure outcome, necessitating the gathering of additional neurocognitive data (Gleissner, Clusmann, Sassen, Elger, & Helmstaedter, 2006).

Nonverbal Tests of Intelligence

Many patients with intellectual disabilities have significant verbal limitations, even when the epileptogenic focus is in the nondominant hemisphere. Frequently, their verbal limitations are so severe that administration of a Wechsler scale to measure IQ results in a significant underestimate of their abilities. It is important to consider a patient's verbal abilities before administering the comprehensive but time-consuming scales. Even if it is possible to administer a comprehensive measure of intellectual functioning, such as the aforementioned Wechsler scales, it is often useful to administer a nonverbal test of intelligence that can be used to assess the validity of the measured IQ score. For children, the most widely used nonverbal measure of intelligence is the Leiter International Performance Scale, Revised Edition (Leiter-R; Roid & Miller, 1997), which can be used for children aged 2–21 years, provides a brief measure of mental age, and covers a wide range of abilities using a simple format. Another commonly administered brief nonverbal test of intellectual function is the Test of Nonverbal Intelligence, Third Edition (TONI-3; Brown, Sherbenou, & Johnson, 1997), which can be used for patients aged 6–90 years old and allows for a very brief and completely nonverbal estimate of overall intellectual functioning. In contrast to the Leiter-R, the TONI-3 does not assess a variety of different abilities, but it is much quicker to administer.

Comprehensive Neurocognitive Screening Tests

In addition to assessing overall intellectual functioning in patients with intellectual disabilities, it is also important to assess other aspects of neurocognitive functioning. If possible, again depending on the stamina of the patient being assessed, it is preferable to administer multiple measures within each neurocognitive domain in order to assure the reliability the data obtained on a given measure within a neurocognitive domain. However, there are a number of valuable screening tests that sample a variety of neurocognitive domains in a short period of time. Probably the most widely used neuropsychological screening measure is the Repeatable Battery for the Assessment of Neuropsychological Status (RBANS; Randolph, 1998), which can be administered to adult patients aged 20–89 years old. The RBANS provides assessments of immediate memory (immediate list learning and immediate story), visuoperceptual abilities (figure copy and line orientation), language (naming and semantic fluency), attention (digit span forward and digit-symbol coding), and delayed memory (delayed list memory with recognition, delayed story memory, and delayed figure memory). More recently, the Neuropsychological Assessment Battery (NAB; Stern & White, 2003) has provided an additional neuropsychological screening measure. The NAB can be administered to patients aged 18–97 years old. The battery is made up of six modules, each of which includes a number of different tests. The modules are (1) the Screening Module, (2) the Attention Module, (3) the Language Module, (4) the Memory Module, and (5) the Executive Functions Module. Within each module are a number of different tests that assess the designated domain. The Screening Module incorporates brief versions of several of the tests from each of the five other modules. Thus, administration of the NAB Screening Module provides a brief assessment of all global, basic aspects of neurocognitive functioning, in much the same way as the RBANS does. Furthermore, the NAB then provides the option of administering more detailed measures of a specific domain of neurocognitive functioning, if the Screening Module reveals particular weaknesses or strengths within that domain.

Language

In assessing a patient's language abilities, if a full Wechsler scale measure of intellectual functioning is administered, the individual verbal subtests from the scale may be able to provide some insight into strengths and weaknesses in the verbal profile, particularly with regard to expressive (i.e., the vocabulary and similarities subtests) versus receptive (i.e., the comprehension subtest) verbal functioning. Additionally, it may be possible to administer some of the more common measures of language functioning, such as the Boston Naming Test (BNT; Kaplan, Goodglass, & Weintraub, 2001) for which there is good normative data for patients aged 5 to 90 years old (Heaton, Miller, Taylor, & Grant, 2005; Kaplan et al., 2001) and measures of phonemic and semantic verbal fluency for which there is good normative data for patients aged 8–90 years old (Heaton et al., 2005; Welsh, Pennington, & Groisser, 1991). However, it is important to recognize that the subtests of the Wechsler scales, the BNT, and verbal fluency require relatively strong verbal skills, which can be a significant limitation for patients with developmental delay or intellectual impairment. If patients perform very poorly on those measures, they provide little insight into relative strengths and weaknesses in the verbal profile. That said, it can be valuable to do a qualitative comparison of a patient's verbal output on phonemic versus semantic fluency, as that may provide insight into whether frontal or temporal language areas are more affected or involved (Troyer, Moscovitch, Winocur, Alexander, & Stuss, 2002).

For patients with significant limitations in their expressive language abilities, a valuable measure of receptive language is the Peabody Picture Vocabulary Test, Fourth Edition (PPVT-4; Dunn & Dunn, 2007), which can be administered to patients aged 2 years, 6 months to 90 years old. This test requires patients to select one picture from an array of four pictures that best represents a word that is said to them by the examiner. The test has the advantage of taking only about 15 min to administer. From the PPVT-4, it is possible to obtain an estimate of a patient's age- and grade-related receptive language abilities. Additionally, it is now possible to make direct comparisons between receptive and expressive vocabulary with the administration of the Expressive Vocabulary Test, Second Edition (EVT-2; Williams, 2007), which was normed on the same sample as the PPVT-4. The EVT-2 can also be administered to patients aged 2 years, 6 months to 90 years old and only takes about 20 min to administer. The test requires a patient to provide an acceptable one-word response when presented with a picture and a question administered by the examiner. The PPVT-4 and EVT-2 have been validated on samples with ADHD, emotional/behavioral disturbance, giftedness, hearing impairment, language/speech delay, language/speech disorder, learning disability, and intellectual impairment and thus have proven valid for assessment of both receptive and expressive language abilities in patients with developmental delay or intellectual impairment.

Finally, as mentioned before, the RBANS and the NAB also incorporate assessment of language functioning. Specifically, the RBANS has a simple naming measure, which has a low ceiling but can be sensitive in measuring naming deficits in lower functioning patients. Additionally, the RBANS has a semantic fluency measure that requires patients to name as many fruits and vegetables as they can in a 1-min period, which also has a low ceiling but can be sensitive in measuring verbal fluency deficits in lower functioning patients (Randolph, 1998). The NAB has a language module comprised of six subtests, which can be administered individually, including an oral production subtest, an auditory comprehension subtest, a naming subtest, a reading comprehension subtest, a writing subtest, and a bill payment subtest (Stern & White, 2003). These subtests, particularly the oral production and the naming subtests, have the advantage of evaluating verbal fluency and confrontation naming, respectively, with greater sensitivity for lower functioning patients than the BNT and traditional verbal fluency tests (i.e., phonemic and semantic fluency).

Visuospatial Functioning

In assessing a patient's visuospatial abilities, if a full Wechsler scale measure of intellectual functioning is administered, the individual performance subtests from the scale may be able to provide some insight into strengths and weaknesses in visuospatial abilities (i.e., the block design, matrix reasoning, visual puzzles, and picture completion subtests), particularly if both quantitative and qualitative aspects of a patient's performance can be evaluated. However, given that the subtests of the Wechsler scales are difficult, patients with intellectual impairment and developmental disability often experience floor effects on those subtests, which make meaningful interpretation of patient's performances difficult. Similarly, the administration of the Rey-Osterrieth Complex Figure Test copy trial (RCFT; Meyers & Meyers, 1995) will likely also be negatively confounded by a patient's global cognitive limitations. However, it is often still valuable to administer the copy trial of the RCFT, as a qualitative evaluation of a patient's copying of the figure may provide some information about localization or lateralization of an epileptogenic focus (Schouten, Hendriksen, & Aldenkamp, 2009).

There are several other simpler tests of visuospatial abilities that are worth administering, most of which sample a greater range of abilities and are not as susceptible to floor effects that can make their administration on patients with intellectual impairment potentially meaningless. In particular, the Beery-Buktenica Developmental Test of Visual-Motor Integration, Fifth Edition (Beery VMI; Beery, Buktenica, & Beery, 2006) can be administered to patients aged 2–100 years old. It is a simple test that involves subtests that include freehand copying of increasingly complex figures, guided motor coordination copying of tracings of the same figures, and a motor-free visuoperceptual matching of figures. The test provides both age- and grade-equivalent scores and has a relatively low floor, making it ideal for administration to patients with developmental delay and intellectual impairment. Other tests that are also simple to administer and can provide valuable information about visuospatial abilities are the Benton Judgment of Line Orientation (Benton JOLO; Benton, Sivan, Hamsher, Varney, & Spreen, 1994), which can be administered to patients aged 18–74 years old, and the Hooper Visual Orientation Test (Hooper VOT; Hooper, 1983), which can be administered to patients aged 25–69 years old.

Once again, the RBANS and the NAB also incorporate assessment of visuospatial functioning. The RBANS requires the copy of a complex figure that is much simpler than the RCFT and a judgment of line orientation subtest that is similar to but simpler than the Benton JOLO (Randolph, 1998). The NAB Spatial Module is comprised of four subtests, which can be administered individually, including a visual discrimination subtest, the design construction subtest, the figure drawing subtest, and the map reading subtest. The visual discrimination subtest has the advantage of being a motor-free test that requires matching-to-target discrimination that is relatively sensitive and has a low floor for greater sensitivity in evaluating patients with intellectual disability or developmental delay (Stern & White, 2003).

Memory

Assessment of memory functioning is particularly critical in patients with known or suspected temporal lobe epilepsy, in patients who are being considered for anterior temporal lobectomy, and in patients who self-report or whose families/caretakers report particular memory problems. If a full Wechsler intelligence scale is administered, it may also be possible to administer one of the co-normed Wechsler memory scales: the Children's Memory Scale (CMS; Cohen, 1997) for children aged 5–16 years old, the Wechsler Memory Scale, Third Edition (WMS-III; Wechsler, 1997) for patients aged 16–89 years old and useful for comparison with the WAIS-III, or the more recently released Wechsler Memory Scale, Fourth Edition (WMS-IV; Wechsler, 2009) for patients aged 16–90 years old and useful for comparison with the WAIS-IV. In addition to the

fact that these comprehensive memory batteries can be meaningfully compared to scales of overall intellectual functioning, these inclusive batteries are made up of multiple measures of verbal and visual memory functioning, which is particularly valuable when attempting to lateralize hippocampal dysfunction. However, once again it is important to recognize that the subtests of the Wechsler scales are difficult and are designed for assessment of memory abilities in higher functioning patients, thus patients with developmental delay and intellectual impairment often experience floor effects on those measures, which makes interpretation of impaired performances on the Wechsler memory scales difficult and often meaningless. Another comprehensive memory battery that also provides comparisons of verbal and visual memory, along with some measures of general memory and attention/concentration, is the Wide Range Assessment of Memory and Learning, Second Edition (WRAML2; Sheslow & Adams, 2003), which can be administered to patients aged 5–90 years old. While the WRAML2 does not provide data for a direct comparison between overall intellectual functioning and memory abilities, it does have a greater range of sensitivity, making it a more valuable for the assessment of memory functioning in patients with cognitive limitations.

One of the most commonly administered and researched measures of verbal learning and memory in populations of patients with epilepsy is the California Verbal Learning Test, Second Edition (CVLT-II; Delis, Kramer, Kaplan, & Ober, 2000), which can be administered to patients aged 16–89 years old, or the children's version of that list learning task, the California Verbal Learning Test, Children's Edition (CVLT-C; Delis, Kramer, Kaplan, & Ober, 1986), which can be administered to children aged 5–17 years old. The standard version of the CVLT-II requires five learning trials of a 16-item word list, followed by a 20-min delay period prior to delayed memory testing. For the assessment of adult patients with developmental delay or intellectual impairment, the CVLT-II has a short-form version that involves four learning trials of a 9-item word list followed by a 15-min delay period, leading to a shorter overall administration time and lower floor effects. Another list learning measure that is shorter and easier than the CVLT-II is the Hopkins Verbal Learning Test, Revised (HVLT-R; Brandt & Benedict, 2001) for patients aged 16–92 years old. The HVLT-R involves three learning trials of a 12-item word list followed by a 20–25-min delay period. It is easy to administer and score and is well tolerated even by significantly impaired individuals. Its use has been validated with brain-disordered populations (e.g., Alzheimer's disease, Huntington's disease, amnestic disorders). Additionally, six distinct forms of the HVLT-R are available, eliminating practice effects on repeated administrations.

With regard to visual learning and memory, there are significantly fewer sensitive measures in comparison with verbal learning and memory. The most commonly cited measure of visual learning and memory is the RCFT (Meyers & Meyers, 1995), but, as stated earlier, the copy trial of the RCFT is significantly confounded by intellectual functioning, making it an insensitive measure for the quantitative assessment of visual memory in patients with developmental delay or intellectual impairment. However, there are qualitative aspects of memory for the RCFT that can be valuable to observe, so administration of delayed memory trials for qualitative if not quantitative evaluation can provide valuable information, even in patients with intellectual impairment. A simpler measure of visual learning and memory is the Brief Visuospatial Memory Test, Revised (BVMT-R; Benedict, 1997) for assessment of patients aged 18–79 years old. The test involves three learning trials of an array of six line drawings presented together on a page which the patient has 10 s to observe before attempting to reproduce the line drawings. There is also a 20-min delay trial followed by a recognition trial and an optional copy trial (which can be used to roughly assess simple visuoperceptual abilities). Much like the HVLT-R, six distinct forms of the BVMT-R are available, eliminating practice effects on repeated administrations.

Once again, the RBANS and the NAB also incorporate assessment of memory functioning.

The RBANS immediate memory component is made up of a list learning task and a brief story memory task. Similar to the CVLT-II Short Form and the HVLT-II, the RBANS list learning task is made up of four learning trials of a 10-item word list, making it more sensitive to verbal memory deficits in patients with cognitive limitations. The RBANS story memory task is also relatively simple as it is a short story that is repeated twice. Additionally, the RBANS has a delayed memory component that is made up of both a free recall and recognition trial of the word list, a free recall trial of the story, and a free recall trial of the complex figure that was copied as part of the visuospatial component. Overall, both the immediate and delayed memory components of the RBANS are relatively brief and useful in measuring immediate and delayed learning and memory deficits in patients with cognitive limitations (Randolph, 1998). The NAB has a Memory Module that is comprised of four subtests, which can be administered individually, including a list learning task, a shape learning task, a story learning task, and a daily living memory task. Much like the RBANS, the NAB list learning task is brief, involving three learning trials of a 12-item word list, followed by an interference list trial, then a short delay free recall trial, a long delay free recall trial, a long delay forced-choice trial, and a recognition trial. The NAB story memory involves two learning trials of a five-sentence story with measures of both immediate and delayed free recall of a five-sentence story. The NAB shape learning task involves three learning trials and multiple-choice immediate recognition of nine visual stimuli, followed by delayed recognition and forced-choice delayed recall of the items. Finally, the daily living task involves verbal learning as well as immediate and delayed memory of information encountered in daily living, such as medication instructions, names addresses, and phone numbers, making it a unique assessment of memory for aspects of a patients adaptive functioning. Overall, the NAB Memory Module provides measures of both verbal and visual immediate and delayed memory, much like the aforementioned memory batteries such as the WMS-IV and the WRAML2, but with much briefer administrations and a low floor for greater sensitivity in evaluating patients with intellectual disability or developmental delay (Stern & White, 2003).

Adaptive Functioning

Perhaps the most important aspect of a neuropsychological assessment of patients with intellectual disabilities is an assessment of their adaptive functioning. As highlighted earlier, age-related deficits in adaptive functioning are critical aspects of developmental delay and intellectual impairment, both for diagnosis and for the purpose of empirically evaluating everyday functioning. This aspect of a neuropsychological evaluation can often be the most meaningful for families and caretakers. The most widely used measure of adaptive functioning is the Vineland Adaptive Behavior Scales, Second Edition (Vineland-II; Sparrow, Cicchetti, & Balla, 2005), which can be used to assess adaptive functioning in patients from birth to 90 years old. The Vineland-II includes the option of administering a survey interview of parents or caregivers that can take up to one hour to administer, an expanded interview of parents or caregivers that can take an hour and a half to administer, a parent/caregiver rating form that can take up to an hour for caregivers to complete, or a teacher rating form that takes approximately 20 min for teachers to complete. The measure assesses five different domains, including communication (receptive, expressive, and written language skills), daily living skills (personal, domestic, and community-related skills), socialization (interpersonal relationships, play and leisure time, and coping skills), motor skills (fine and gross motor skills), and an optional maladaptive behavior index (internalizing, externalizing, and other behaviors). Overall, the Vineland-II provides important information about everyday adaptive functioning that aids in the diagnosis of developmental delay and intellectual impairment. Additionally, the results of the measure can be used to determine a patient's eligibility for special services in schools or treatment facilities, to plan for rehabilitation or

intervention programs, and to track a patient's progress as it correlates with medical or surgical treatment of their epilepsy. An important aspect of the Vineland-II is that the interviews, both the survey interview and the expanded interview, must be administered by a trained and qualified licensed psychologist, which may increase the validity and reliability of the measure, particularly over repeated administrations that are designed to track a patient's progress over a number of years.

Another commonly used measure for the assessment of adaptive functioning is the Adaptive Behavior Assessment System, Second Edition (ABAS-II; Harrison & Oakland, 2003), which can be used to assess adaptive functioning from birth to 89 years. The measure is a behavior rating scale that is typically completed by parents, caregivers, and/or teachers. If the behavior rating scale is given to multiple raters, it can provide different perspectives on what a given patient can or cannot do in their everyday lives without the assistance of others. The measure assesses adaptive skills in ten different areas within three different domains, including conceptual (communication skills, functional academics, and self-direction), social (social skills and leisure skills), and practical (self-care, home or school living, community use, work, and health/safety) domains. Similar to the Vineland-II, the ABAS-II provides information about a patient's everyday adaptive functioning, aids in the diagnosis of intellectual impairment and developmental disabilities, and can assist with treatment recommendations. The ABAS-II has the advantage of being a behavior rating scale that does not need to be administered by a licensed psychologist and is therefore less time-consuming from an administration perspective. Additionally, given that the behavior rating scale can be given to multiple people, it can provide a more accurate profile of a patient's level of adaptive functioning in a variety of environments. The data available on the validity of the ABAS-II suggest that it is just as valid a measure of adaptive functioning as the Vineland-II, despite being simply a behavior rating scale that is completed by patients without the direct input of a psychologist or neuropsychologist (Harrison & Oakland, 2003).

If it is possible to directly evaluate a patient's abilities, the most commonly used measure of direct assessment of everyday abilities is the Independent Living Scales measure (ILS; Loeb, 1996). This test is an individually administered assessment of the degree to which adults are capable of caring for themselves and their property. Although the ILS is usually administered to patients aged 65 years old and older, there is normative data for patients with intellectual disabilities who are aged 17 years old and older. The ILS is composed of five scales: memory/orientation, managing money, managing home and transportation, health and safety, and social adjustment. The performance-based results from the 68 ILS items are more objective and reliable than third-party observations or examinees' self-reports (Loeb, 1996). Normative data are provided for the different scales so the various areas of competence can be identified and compared. Additionally, it is possible to administer individual subtests from the ILS in order to assess specific areas of everyday functioning.

Summary

When a patient with developmental delays or intellectual impairment and concurrent epilepsy is referred for neuropsychological evaluation, it is particularly important to consider the referral question and the capabilities of the patient when designing the neuropsychological test battery. As with all neuropsychological assessments, gathering information about all domains of neurocognitive functioning is important, if it is possible. However, patients with developmental delay or intellectual impairment often cannot tolerate a lengthy evaluation, and the traditionally administered neuropsychological tests often have high floor effects, making interpretation of impaired performances meaningless. Thus, it is often valuable to utilize screening measures (i.e., the RBANS or the NAB) or other tests with lower floor effects in order to gather more accurate information about neurocognitive functioning.

Additionally, the inclusion of measures of adaptive functioning may be essential for the accurate diagnosis of intellectual impairment, particularly if a patient is referred for an initial diagnosis of intellectual impairment or for qualification of specialized services. Finally, as is highlighted in the following case reports, it is often necessary for neuropsychologists to use both quantitative and qualitative observations of an intellectually impaired patient's performance in order to fully understand their neurocognitive strengths and weaknesses.

Case Examples

Case 1

G.L. was a 26-year-old female who began experiencing complex-partial seizures that secondarily generalized when she was 3 years old. G.L.'s developmental history was notable for intellectual disability and developmental delay. Her mother indicated that she began walking at 2 years old, spoke her first words at 8 years old (i.e., "Ma" and "Dad"), and began speaking in sentences at 13 years old. G.L. started taking formal special education classes in a mainstream school in sixth grade when she was 11 years old. She received a certificate of completion when she graduated high school at 21 years old. Her mother reported that upon leaving high school, G.L. was reading at a third grade level and was performing mathematics at a second grade level. Since graduating from high school, G.L. had been part of a day program service associated with a local regional center. Through this program, she spent weekdays volunteering in the community and participating in skills training classes. She lived with her mother and sister. G.L. said she enjoyed spending her free time with her family, liked reading books, and enjoyed singing.

Regarding a presurgical medical workup, an MRI of her brain revealed no evidence of an acute process but suggested "diffuse volume loss of white matter of the right cerebral hemisphere" as well as "Wallerian degeneration of the right pyramidal tract." The MRI also indicated that "the right hippocampus is smaller and diffusely hyperintense, suggesting mesiotemporal sclerosis." Finally, the brain MRI indicated an enlarged lateral ventricle and a small cerebellar hemisphere with the inferior portion of the cerebellum appearing asymmetric. An EEG conducted during a PET scan demonstrated, "an abnormal EEG on account of mild diffuse slowing of the background" which suggested, "diffuse cerebral dysfunction associated with a broad differential diagnosis." PET imaging demonstrated, "marked hypometabolism of the right cerebrum and right cortical gray matter, predominantly affecting the right temporal lobe. In the right clinical setting, this may function as a zone of epileptogenesis." During inpatient video EEG monitoring, six seizures were observed and recorded. Clinically, during a seizure, G.L. raised her arms above her head, repositioned herself in bed, and moved nonspecifically. She then extended her left arm and leg, followed by contraction and shaking of her left hand and fingers. She moaned and vocalized nonspecifically, sometimes followed commands, and often grabbed the rail of the bed or her oxygen mask. She had difficulty answering questions but recovered postictally in less than 15 s. Electrographically, her seizures were all stereotyped with development of an ictal rhythm over the right temporal lobe and then gradual slowing that became progressively more prominent over right frontal regions.

Given the results of the brain MRI, the PET imaging, and the inpatient video EEG monitoring, G.L. was thought to have right temporal lobe epilepsy and was being considered for a standard right anterior temporal lobectomy to neurosurgically treat her medically refractory epilepsy. G.L. was referred for a neuropsychological evaluation to assess her current level of neurocognitive functioning and to determine the extent of the neuropsychological risks (e.g., loss of memory or language function) involved in a neurosurgical intervention. Regarding general cognition, G.L. was unable to articulate and reflect on her overall level of intellectual functioning. Her mother and sister reported that she had demonstrated general improvement across all cognitive domains as she had gotten older. Although her family was not aware of any formal testing results, her mother indicated that G.L. was diagnosed with intellectual impairment at an early age.

The preoperative neuropsychological test results are given in Table 13.1. Given her

Table 13.1 Neuropsychological test results in Case 1, a 26-year-old mildly intellectually disabled female with right temporal lobe epilepsy who is being considered for a standard right anterior temporal lobectomy

General intellectual functioning	Raw score	Scaled score	Description
Peabody Picture Vocabulary Test-4	111	SS = 43	Impaired
WAIS-III			
Vocabulary	9	3	Impaired
Similarities	5	2	Impaired
Comprehension	5	3	Impaired
Digit span	14	8	Low average
Block design	12	4	Borderline
Matrix reasoning	6	5	Borderline

Attention and concentration	Raw score	T score	Description
WAIS-III digit span	14	ss = 8	Low average
Forward	7		
Backward	3		
Trails A (seconds)	53″	22	Impaired
Errors	0		

Language	Raw score	T score	Description
Phonemic fluency: F(2), A(2), S(2)	6	12	Impaired
Animal naming	9	15	Impaired
Stroop color	140	z = −6.49	Impaired
Errors/ self-corrections	1/2		
Stroop word	116	z = −10.60	Impaired
Errors/ self-corrections	0/2		
Boston Naming Test	35,0,4	25	Impaired
Language screening	13/24		
WRAT-3 reading (grade Eq = 2)	24	SS = 49	Impaired
WRAT-3 spelling (grade Eq = 2)	22	SS = 57	Impaired
WRAT-3 arithmetic (grade Eq = 2)	22	SS = 50	Impaired
WJ-III word attack (grade Eq = 1.7)	6	SS = 62	Impaired

Visuospatial skills	Raw score	T score	Description
WAIS-III block design	12	ss = 4	Borderline
WMS-III visual reproduction discrim	7/7		Average
Rey-O complex figure copy	14.5		Impaired

(continued)

Table 13.1 (continued)

Visuospatial skills	Raw score	T score	Description
Beery VMI (age Eq = 5.6)	15	<45	Impaired
Beery visual perception (age Eq = 6.2)	18	<45	Impaired
Beery motor coordination (age Eq = 5.6)	16	<45	Impaired

Verbal memory	Raw score	Z score	Description
WMS-III			
Logical memory I (5,3,8)	16	ss = 3	Impaired
Logical memory II (4,7)	11	ss = 6	Low average
Recognition (8,10)	18/30		Borderline
CVLT-II total = (6,7,8,12,11)	44	T = 38	Low average
List A Trial 1	6	−1.0	Low average
Trial 2	7	−1.5	Borderline
Trial 3	8	−2.0	Impaired
Trial 4	12	−0.5	Average
Trial 5	11	−1.5	Borderline
List B	7	0.0	Average
List A short delay free recall	10	−0.5	Average
List A short delay cued recall	7	−2.5	Impaired
List A long delay free recall	11	−0.5	Average
List A long delay cued recall	6	−3.0	Impaired
Recognition hits	16	0.0	Average
Recognition false positives	2	−0.5	Average
Total recognition discriminability	3.4	0.0	Average

Nonverbal memory	Raw score	T score	Description
WMS-III			
Visual reproduction I	57	ss = 3	Impaired
Visual reproduction II	0	ss = 1	Impaired
Recognition	38/48	ss = 4	Borderline
BVMT-R total = (2,2,4)	8	<20	Impaired
Trial 1	2	25	Impaired
Trial 2	2	<20	Impaired
Trial 3	4	<20	Impaired

(continued)

Table 13.1 (continued)

Nonverbal memory	Raw score	T score	Description
Learning	2	40	Low average
Delay	4	<20	Impaired
Percent retention	100		Average
Recognition	6, 1fp		Low average
Rey-O complex figure			
Immediate recall	3.5	<20	Impaired
Delayed recall	2.0	<20	Impaired
Recognition	18/24	28	Impaired
Whole figure recognition	no		
Executive functions	Raw score	T score	Description
WAIS-III similarities	5	ss = 2	Impaired
WAIS-III comprehension	5	ss = 3	Impaired
WAIS-III matrix reasoning	6	ss = 5	Borderline
Phonemic fluency: F(2), A(2), S(2)	6	12	Impaired
Trails B (s)	300″	2	Impaired
Errors	1		
Stroop interference	218	z = −3.68	Impaired
Errors/ self-corrections	0/14		

extremely low level of general intellectual functioning, there are a number of important aspects to her performance that should be considered. Her generally extremely low level of intellectual functioning, significantly slowed speed of information processing, and impaired motor coordination likely negatively impacted her performance on a number of measures on the evaluation. Therefore, in addition to the quantitative results of the current evaluation, it was important to consider qualitative aspects of her performance in order to more accurately characterize her strengths and weaknesses, in the context of her generally extremely low level of intellectual and information processing abilities.

Qualitatively, her verbal skills were slightly stronger than indicated by her impaired performance on formal measures of language functioning because she was able to converse with the examiner, and her comprehension of simple questions and basic task instructions was adequate. In contrast, however, she demonstrated considerable difficulty when required to appreciate the broad or abstract concepts and context of conversational speech. Generally, she demonstrated qualitatively weaker complex comprehension of the gestalt of speech, thus indicating weaknesses in right hemisphere contributions to complex language information processing. She demonstrated significant strengths on measures of simple auditory attention, indicating that she was able to attend to information at an almost age-appropriate level. On measures of verbal memory, she demonstrated poor learning and memory for contextual verbal information, which was likely negatively impacted by her inability to appreciate semantic and verbal contextual and gestalt cues, once again likely reflecting weaknesses in right hemisphere contributions to language. In contrast, she demonstrated a significant strength on a task of verbal list learning and memory, which was felt to be indicative of adequate left mesial temporal functioning. On measures of visual memory, she demonstrated impaired learning and memory for all visual information, even relatively simple visual information, which was felt to be indicative of impaired right mesial temporal functioning. Furthermore, her performances on a number of other measures of neuropsychological functioning implicated right hemisphere involvement in her seizures. Specifically, she demonstrated difficulty with visual perception and visual-motor integration. Qualitatively, she was unable to appreciate the gestalt of both verbal and visual information, which also suggested right hemisphere involvement in her seizures.

While her impaired performances on some of the neuropsychological tasks may have been negatively impacted by her extremely low level of general intellectual functioning, her relative strength in visual abstract reasoning indicated relatively adequate nonverbal reasoning skills and supported the idea that she was able to process visuospatial information at a level commensurate with her overall level of intellectual functioning. Thus, her qualitative weaknesses on

the current evaluation likely represented true neurological weaknesses in right hemisphere functioning, rather than simply impairments secondary to her extremely low level of general intellectual functioning. Overall, the results of the neuropsychological evaluation suggested a specific involvement of right mesial temporal areas along with general involvement of the right hemisphere, with relatively spared right frontal lobe functioning. These findings were felt to indicate an area of epileptogenic focus in right mesial temporal structures, consistent with findings from a brain MRI, PET imaging, and inpatient video EEG monitoring.

Although G.L.'s performance was in the extremely low range across most neuropsychological domains, her strong performance on a measure of verbal learning and memory suggested adequate left mesial temporal functioning. While her quantitative performances on measures of language functioning were also extremely low, there was some qualitative and behavioral evidence for relatively good functioning of left hemisphere language areas which were not reflected by neuropsychological measures that were insensitive to performances in the extremely low range. Furthermore, she demonstrated a relative strength (both qualitatively and quantitatively) in her visuospatial reasoning skills, which indicated that she can appreciate visuospatial information appropriately and has relatively good functioning of frontal lobe structures, bilaterally. Thus, her extremely low performances on measures of visual learning and memory, combined with dramatically disrupted processing of visual and verbal gestalt and contextual information, were felt to provide evidence for right mesial temporal and generalized right hemisphere inefficiencies, with relatively spared right frontal lobe functioning. It was recommended that if G.L. became a candidate for right anterior temporal resection, Wada testing be conducted to determine the ability of her relatively stronger left mesial temporal lobe to support memory postsurgically. However, the neuropsychological team noted that it would be important that the Wada procedure be thoroughly explained to G.L. at a developmentally appropriate level, to ensure that she understood what the procedure involved, as her cooperation would be essential to the validity of the results. Furthermore, when G.L. was asked about her understanding of the neuropsychological evaluation and the possibility of undergoing resection surgery, she indicated limited understanding of the process. Thus, an additional recommendation of the evaluation was that the surgical procedure and possible sequelae of the surgical intervention be explained to her at a developmentally appropriate level given her extremely low level of general cognitive functioning in order to ensure her cooperation and compliance with pre- and postsurgical management.

Case 2

B.R. was a 55-year-old mildly intellectually disabled female with left anterior temporal lobe epilepsy who had been seizure-free for 2 years following a standard left anterior temporal lobectomy and continued medication management on a relatively low level of lamotrigine. She was referred for a neuropsychological evaluation to assess her postoperative level of neurocognitive and behavioral functioning. In particular, her mother reported that B.R. had a tendency to talk about events that did not really happen, so she had concerns that B.R. was either lying or was experiencing medication-related hallucinations. Her mother also expressed concern that B.R.'s memory had worsened since the surgery.

B.R. had undergone two prior presurgical neuropsychological evaluations. The results of the first presurgical neuropsychological evaluation indicated, "This woman demonstrates intellectual abilities which fall within the range of mild intellectual disability overall with visual-spatial abilities just lightly stronger than those in the verbal area. Her level of academic knowledge is just slightly below her level of general intelligence, and academic achievement may never have been especially strong. The battery of neuropsychological tests which was administered resulted in the identification of moderate impairment in brain functions with findings implicating both

cerebral hemispheres about equally. This impairment is expected to have a substantial impact upon functioning in daily life…In terms of predictors for seizure relief following resection surgery for epilepsy, it was noted that only one of the four predictors of likely relief from seizures arising from this battery of tests were within a favorable range. While this is not a positive result, it should be noted that a full prognostic statement of likely relief from seizures following resection surgery must take into account other critical clinical and EEG data." The results of the second presurgical neuropsychological evaluation indicated, "The patient is a 53-year-old right-handed female with moderate intellectual disability. This is conferred on the current IQ assessment. The majority of neuropsychological measures completed are consistent with her overall level of cognitive function. Interestingly, an area of particular strength was seen for repeat trials of verbal learning and memory…The patient interacts at a higher level than would be anticipated based on her IQ…Oral and cognitive presentation is reflective of generalized cortical dysfunction with preservation of left temporal lobe capacity. These findings are consistent with her history of bilateral seizures and significant illness during critical development." It was concluded that improved seizure control would probably positively improve her life in terms of her personal safety and functional ability, with some risks to her verbal memory that would likely not be apparent in her day-to-day functional capacity.

Developmentally, B.R. and her husband lived with her parents. She was able to bathe and dress herself and do a few chores around the house, such as taking care of her cat, doing some of the cleaning, and folding the laundry, all of which she could do successfully with minimal supervision or guidance. She did not do the shopping or cooking, nor did she manage any finances. She was not able to manage her medications independently and relied on her mother to remind her to take her medication.

Postsurgically, B.R. was unable to provide subjective information about her cognitive difficulties. It had been well documented that she was mildly intellectually disabled and, per medical records, had limited insight into her cognitive limitations. Her mother reported that B.R.'s memory was poor prior to her undergoing the left anteromedial temporal resection but had seemed worse since the surgery. Additionally, she reported that B.R. had a tendency to confabulate and displayed some paranoid ideation. For example, 1 day B.R. could not find her cat and assumed someone had stolen it; in fact, the cat had simply wandered away for a short time. Another time, she found that money was gone from her husband's wallet and assumed someone had stolen it, but he had just put the money in his pocket. Of note, medical records prior to surgery indicated that B.R. had a tendency to talk about memory for events that did not really happen even back then. Thus, it appeared that her tendency to confabulate was not new since the surgery. Further consistent with presurgical reports, B.R. had always been easily confused and forgetful about upcoming appointments and had often misplaced items. However, her mother felt that those problems had worsened since surgery. Her mother also reported that B.R. had begun to make literal paraphasic errors in conversation, such as saying that she wanted to go to the "*feel good*" store instead of the *Goodwill* store. This was reportedly new since she had undergone surgery. Her mother expressed concerns that these perceived cognitive changes were being caused by her long-term medication regimen of lamotrigine.

The postoperative neuropsychological test results are given in Table 13.2. Consistent with previous presurgical evaluations, the postsurgical neuropsychological evaluation measured B.R.'s overall level of intellectual functioning to be mildly intellectually disabled. On testing, B.R. performed in the impaired range on most tests of neuropsychological functioning, consistent with her performances on two previous presurgical evaluations. She once again demonstrated a relative strength in her verbal learning and memory abilities, as her performances were largely borderline to low average across those tasks. Compared with the most recent previous presurgical neuropsychological evaluation, however, she demonstrated a very mild decline in her verbal list

Table 13.2 Neuropsychological test results in Case 2, a postsurgical evaluation of a 55-year-old mildly intellectually disabled female with left anterior temporal lobe epilepsy who is seizure-free following a standard left anterior temporal lobectomy

General intellectual functioning	Raw score	Scaled score	Description
WAIS-IV (standard norming)			
Verbal comprehension subtests			
Similarities	11	4	Impaired
Vocabulary	10	3	Impaired
Information	3	3	Impaired
Comprehension	8	3	Impaired
Perceptual reasoning subtests			
Block design	20	6	Low average
Matrix reasoning	5	4	Impaired
Visual puzzles	6	5	Borderline
Working memory subtests			
Digit span	13	3	Impaired
Arithmetic	6	3	Impaired
Processing speed subtests			
Symbol search	16	5	Borderline
Coding	20	2	Impaired
Index scores			
Full Scale IQ	38	SS = 59	Impaired
Verbal Comprehension Index	10	SS = 61	Impaired
Perceptual Reasoning Index	15	SS = 71	Borderline
Working Memory Index	6	SS = 60	Impaired
Processing Speed Index	7	SS = 65	Impaired
General Ability Index	25	SS = 63	Impaired
Index-level discrepancies	*Score 1*	*Score 2*	*Significance*
Verbal comp—perceptual reasoning	61	71	0.05
Verbal comp—working memory	61	60	NS
Verbal comp—processing speed	61	65	NS
Perceptual reason—working memory	71	60	0.05
Perceptual reason—processing speed	71	65	NS
Working memory—processing speed	60	65	NS
FSIQ—GAI	59	63	0.05

Academic abilities	Raw score	Std score	Description
WRAT-4			
Word reading (grade Eq = 3.7)	35	67	Impaired
Sentence comprehension (grade Eq = 2.8)	15	62	Impaired
Reading composite	129	63	Impaired
Spelling (grade Eq = 3.3)	26	68	Impaired
Math computation (grade Eq = 1.9)	20	61	Impaired

Attention and concentration	Raw score	Scaled score	Description
WAIS-IV			
Digit span	13	3	Impaired
Forward span	4		Cum % = 100.00
Backward span	3		Cum % = 97.00
Sequencing span	3		Cum % = 98.00
Arithmetic	6	3	Impaired
Symbol search	16	5	Borderline
Coding	20	2	Impaired
D-KEFS			
Trails: visual scanning	29″	8	Average
Errors	0		
Trails: number sequencing	44″	9	Average
Errors	0		
Trails: letter sequencing	64″	5	Borderline
Errors	0		

(continued)

Table 13.2 (continued)

Speech and language	Raw score	Scaled score	Description
WAIS-IV			
Vocabulary	10	3	Impaired
Similarities	11	4	Impaired
D-KEFS			
Verbal fluency: letter	9	2	Impaired
Verbal fluency: category	21	3	Impaired
CW Interfere: color naming	34″	8	Average
Errors/ self-corrections	0/1		
CW interfere: word reading	30″	6	Low average
Errors/ self-corrections	1/0		
Boston Naming Test	40,1,6	z = −5.63	Impaired
WRAT-4			
Word reading (grade Eq = 3.7)	35	SS = 67	Impaired
Sentence comprehension (grade Eq = 2.8)	15	SS = 62	Impaired
Reading composite	129	SS = 63	Impaired

Visuospatial skills	Raw score	Scaled score	Description
WAIS-IV			
Block design	20	6	Low average
Visual puzzles	6	5	Borderline
BVMT-R copy	8/12		
Rey-O complex figure copy	18.5		Borderline

Verbal memory	Raw score	Z score	Description
WMS-IV			
Logical memory I (10,4)	14	ss = 5	Borderline
Logical memory II (9,3)	12	ss = 6	Low average
Logical memory recognition (10,10)	20/30		Cum % = 3–9
Verbal paired associates I (2,4,5,5)	16	ss = 6	Low average
Verbal paired associates II	5	ss = 6	Low average

(continued)

Table 13.2 (continued)

Verbal memory	Raw score	Z score	Description
Verbal paired associates recognition	33/40		Cum % = 3–9
Auditory Memory Index	23	SS = 75	Borderline
CVLT-II Total = (4,5,7,8,8)	32	T = 31	Borderline
List A Trial 1	4	–1.5	Borderline
Trial 2	5	–2.0	Impaired
Trial 3	7	–1.5	Borderline
Trial 4	8	–2.0	Impaired
Trial 5	8	–2.0	Impaired
List B	4	–1.0	Low average
List A short delay free recall	6	–1.5	Borderline
List A short delay cued recall	5	–3.0	Impaired
List A long delay free recall	7	–1.5	Borderline
List A long delay cued recall	7	–2.0	Impaired
Recognition hits	14/16	–0.5	Average
Recognition false positives	1/32	(–0.5)	Average
Recognition discriminability	3.0	0.0	Average
Forced choice recognition	16/16		Cum % = 100

Nonverbal memory	Raw score	T score	Description
WMS-IV			
Visual reproduction I recall	21	ss = 4	Impaired
Visual reproduction II recall	8	ss = 6	Low average
Visual reproduction II recognition	0/7		Cum % ≤ 2
BVMT-R total = (1,2,1)	4	<20	Impaired
Trial 1	1	27	Impaired
Trial 2	2	<20	Impaired
Trial 3	1	<20	Impaired
Delay	3	22	Impaired
Percent retention	100 %		Average
Recognition	4, 1fp		Borderline

(continued)

Table 13.2 (continued)

Nonverbal memory	Raw score	T score	Description
Rey-O complex figure			
3′ immediate recall	6	23	Impaired
30′ delayed recall	1	<20	Impaired
Recognition	19/24	42	Low average
Whole figure recognition	Yes		

Executive functions	Raw score	Scaled score	Description
WAIS-IV			
Similarities	11	4	Impaired
Comprehension	8	3	Impaired
Matrix reasoning	5	4	Impaired
D-KEFS			
Trails: visual scanning	29″	8	Average
Errors	0		
Trails: number sequencing	44″	9	Average
Errors	0		
Trails: letter sequencing	64″	5	Borderline
Errors	0		
Trails: letter-number switching	131″	7	Low average
Errors	4		
Trails: motor speed	54″	7	Low average
Verbal fluency: letter	9	2	Impaired
Verbal fluency: category	21	3	Impaired
Verbal fluency: switching	7	3	Impaired
Verbal fluency: switching accuracy	6	4	Impaired
CW interfere: CW inhibition	82″	6	Low average
Errors/ self-corrections	2/4		
CW interfere: CW inhib/switching	154″	1	Impaired
Errors/ self-corrections	13/4		

Mood/personality	Raw score	Rating
BDI-II	15	Mild
BAI	3	Minimal

learning capacity and retention, which was not surprising given that left mesial temporal structures that support verbal learning and memory were resected. Once again, her visual learning and memory was not as good as her verbal learning and memory. Interestingly, she also demonstrated a mild decline in her visual learning and memory abilities compared with presurgical performances. Overall, the findings of the postsurgical neuropsychological evaluation were consistent with a woman who suffered generalized cortical dysfunction and who, as a result, had mild intellectual disability and significant developmental delays. As had been demonstrated on previous presurgical neuropsychological evaluations, B.R. had a few areas of relative cognitive strength, including her verbal learning and memory ability and some aspects of social and executive skills. Her verbal learning and memory abilities continued to be a relative strength for her, despite showing a mild decline from presurgical levels. It was concluded that she was a woman who had clearly led a life that had been meaningful to her, and she continued to have the capacity to participate in her life at a level that gave her a sense of accomplishment and kept her feeling happy. Given that she was now seizure-free, she was leading a healthier life, and it was likely that she would continue to lead a happy and productive life for the foreseeable future, with very minimal to no change in her cognitive abilities since the surgery. Overall, it was felt that the neurosurgical resection to treat her refractory epilepsy was successful. Furthermore, there was no evidence to suggest that her antiepileptic medication regimen was negatively impacting her cognitive functioning or causing a significant change in her psychiatric or cognitive functioning.

References

Aldenkamp, A. P., Baker, G., & Mulder, O. G. (2000). A multicenter randomized clinical study to evaluate the effect on cognitive function of topiramate compared with valproate as add on therapy to carbamazepine in patients with partial-onset seizures. *Epilepsia, 41*, 1167–1178.

American Psychiatric Association. (2000). *Diagnostic and statistical manual of mental disorders* (5th ed.). Washington, DC: Author. Text Revision.

Beery, K. E., Buktenica, N. A., & Beery, N. A. (2006). *BEERY VMI: The Beery-Buktenica developmental test of visual-motor integration* (Administration, scoring, and teaching manual 5th ed.). Los Angeles, CA: Western Psychological Services.

Benedict, R. H. B. (1997). *BVMT-R: Brief Visuospatial Memory Test – Revised: Professional manual*. Lutz, FL: Psychological Assessment Resources, Inc.

Benton, A. L., Sivan, A. B., Hamsher, K. D., Varney, N. R., & Spreen, O. (1994). *Contributions to neuropsychological assessment* (A clinical manual 2nd ed.). New York, NY: Oxford University Press, Inc.

Berry-Kravis, E. (2002). Epilepsy in fragile X syndrome. *Developmental Medicine and Child Neurology, 44*(11), 724–728.

Bhise, V. V., Burack, G. D., & Mandelbaum, D. E. (2010). Baseline cognition, behavior, and motor skills in children with new-onset, idiopathic epilepsy. *Developmental Medicine and Child Neurology, 52*, 22–26.

Brandt, J., & Benedict, R. H. B. (2001). *The Hopkins Verbal Learning Test – Revised*. Lutz, FL: Psychological Assessment Resources, Inc.

Brown, L., Sherbenou, R. J., & Johnson, S. K. (1997). *Test of nonverbal intelligence* (3rd ed.). Austin, TX: Pro-Ed.

Caplan, R., Gillberg, C., Dunn, D. W., & Spence, S. J. (2008). Psychiatric disorders in children. In J. Engel Jr. & T. A. Pedley (Eds.), *Epilepsy: A comprehensive textbook* (2nd ed., pp. 1225–1233). Philadelphia, PA: Lippincott, Williams, & Wilkins.

Cassé-Perrot, C., Wolff, M., & Dravet, C. (2001). Neuropsychological aspects of severe myoclonic epilepsy in infancy. In I. Jambaqué, M. Lassonde, & O. Dulac (Eds.), *The neuropsychology of childhood epilepsy* (pp. 131–140). New York, NY: Plenum.

Cohen, M. (1997). *Children's memory scale manual*. San Antonio, TX: The Psychological Corporation.

Crawford, P. M. (2000). Epidemiology of intractable focal epilepsy. In J. M. Oxbury, C. E. Polkey, & M. Duchowny (Eds.), *Intractable focal epilepsy* (pp. 25–40). London: WB Saunders.

de Vries, B. B., Robinson, H., Stolte-Dijkstra, I., Tjon Pian Gi, C. V., Dijkstra, P. F., van Doorn, J., et al. (1995). General overgrowth in the fragile X syndrome: Variability in the phenotypic expression of the FMR1 gene mutation. *Journal of Medical Genetics, 32*(10), 764–769.

Delis, D., Kramer, J., Kaplan, E., & Ober, B. (1986). *The California Verbal Learning Test: Children's version*. San Antonio, TX: The Psychological Corporation.

Delis, D. C., Kramer, J. H., Kaplan, E., & Ober, B. A. (2000). *CVLT-II: California Verbal Learning Test, second edition, adult version, manual*. San Antonio, TX: The Psychological Corporation.

Dravet, C., & Bureau, C. (2008). Severe myoclonic epilepsy in infancy (Dravet syndrome). In J. Engel Jr. & T. A. Pedley (Eds.), *Epilepsy: A comprehensive textbook* (2nd ed., pp. 2337–2342). Philadelphia, PA: Lippincott, Williams, & Wilkins.

Dunn, L. M., & Dunn, D. M. (2007). *PPVT-4: Peabody Picture Vocabulary Test* (4th ed.). San Antonio, TX: Pearson Assessments.

Feekery, C. J., Parry-Fielder, B., & Hopkins, I. J. (1993). Landau-Kleffner syndrome: Six patients including discordant monozygotic twins. *Pediatric Neurology, 9*, 49–53.

Fenichel, G. M. (2001). *Clinical pediatric neurology: A signs and symptoms approach* (4th ed.). Philadelphia, PA: WB Saunders.

Fisher, J. E., & Vorhees, C. (1992). Developmental toxicity of antiepileptic drugs: Relationship to postnatal dysfunction. *Pharmacological Research, 26*, 207–221.

Forsgren, L., Edvinsson, S. O., Blomquist, H. K., Heijbel, J., & Sidenvall, R. (1990). Epilepsy in a population of mentally retarded children and adults. *Epilepsy Research, 6*(3), 234–248.

Fryns, J. P., Jacobs, J., Kleczkowska, A., & van den Berghe, H. (1984). The psychological profile of the fragile X syndrome. *Clinical Genetics, 25*(2), 131–134.

Gaily, E., & Meador, K. J. (2007). Neurodevelopmental effects. In J. Engel Jr. & T. A. Pedley (Eds.), *Epilepsy: A comprehensive textbook* (2nd ed., pp. 1225–1233). Philadelphia, PA: Lippincott, Williams, & Wilkins.

Galván-Manso, M., Campistol, J., Conill, J., & Sanmartí, F. X. (2005). Analysis of the characteristics of epilepsy in 37 patients with the molecular diagnosis of Angelman syndrome. *Epileptic Disorders, 7*(1), 19–25.

Gastaut, H. (1982). The Lennox-Gastaut syndrome: Comments on the syndrome's terminology and nosological position among the secondary generalized epilepsies of childhood. *Electroencephalography and Clinical Neurophysiology, 35*, S71–S84.

Glaze, D. G., Schultz, R. J., & Frost, J. D. (1998). Rett syndrome: Characterization of seizures versus nonseizures. *Electroencephalography and Clinical Neurophysiology, 106*(1), 79–83.

Gleissner, U., Clusmann, H., Sassen, R., Elger, C., & Helmstaedter, C. (2006). Postsurgical outcome in pediatric patients with epilepsy: A comparison of patients with intellectual disabilities, subaverage intelligence, and average-range intelligence. *Epilepsia, 47*(2), 406–414.

Gordon, N. (1990). Acquired aphasia in childhood: The Landau-Kleffner syndrome. *Developmental Medicine and Child Neurology, 32*, 270–274.

Guerrini, R., Cararozzo, R., Rinaldi, R., & Bonnani, P. (2003). Angelman syndrome: Etiology, clinical features, diagnosis, and management of symptoms. *Paediatric Drugs, 5*(10), 647–661.

Harrison, P., & Oakland, T. (2003). *ABAS-II: Adaptive behavior assessment system – Second edition*. Los Angeles, CA: Western Psychological Services.

Hauser, W. A., Annegers, J. F., & Kurland, L. T. (1991). The Prevalence of epilepsy in Rochester, Minnesota: 1940–1980. *Epilepsia, 32*(4), 429–445.

Heaton, R. K., Miller, W., Taylor, M. J., & Grant, I. (2005). *Revised comprehensive norms for an expanded*

halstead-reitan battery: Demographically adjusted neuropsychological norms for African-American and Caucasian Adults. Lutz, FL: Psychological Assessment Resources.

Holmes, L. B., Wysznski, D. F., & Lieberman, E. (2004). The AED (antiepileptic drug) pregnancy registry: A 6-year experience. *Archives of Neurology, 61*, 673–678.

Hooper, H. E. (1983). *Hooper Visual Organization Test (VOT) manual*. Los Angeles, CA: Western Psychological Services.

Hunt, A., & Dennis, J. (1987). Psychiatric disorder among children with tuberous sclerosis. *Developmental Medicine and Child Neurology, 29*, 190–198.

Huppke, P., Held, M., Laccone, F., & Hanefeld, F. (2003). The spectrum of phenotypes in females with Rett Syndrome. *Brain Development, 25*(5), 346–351.

Jambaqué, I., Chiron, C., Dumas, C., Mumford, J., & Dulac, O. (2000). Mental and behavioural outcome of infantile epilepsy treated by vigabatrin in tuberous sclerosis patients. *Epilepsy Research, 38*(2–3), 151–160.

Jayakar, P. B., & Seshia, S. S. (1991). Electrical status epilepticus during slow-wave sleep: A review. *Journal of Clinical Neurophysiology, 8*, 299–311.

Jeavons, P. M., Bower, B. D., & Dimitrakoudi, M. (1973). Long term prognosis of 150 cases of "West syndrome. *Epilepsia, 14*(2), 153–164.

Joinson, C., O'Callaghan, F. J., Osborne, J. P., Martyn, C., Harris, T., & Bolton, P. F. (2003). Learning disability and epilepsy in an epidemiological sample of patients with tuberous sclerosis complex. *Psychological Medicine, 33*(2), 335–344.

Jokeit, H., & Ebner, A. (2002). Effects of chronic epilepsy on intellectual functions. *Progress in Brain Research, 135*, 455–463.

Kaplan, E., Goodglass, H., & Weintraub, S. (2001). *Boston Naming Test* (2nd ed.). Austin, TX: Pro-Ed.

Kaufman, D. M. (2007). *Clinical neurology for psychiatrists* (6th ed.). Philadelphia, PA: Saunders Elsevier.

Lee, W. L., & Ong, H. T. (2001). Epidemiology of West syndrome in Singapore. *Epilepsia, 23*(7), 584–585.

Lee, T. M., Yip, J. T., & Jones-Gotman, M. (2002). Memory deficits after resection from left or right anterior temporal lobe in humans: A meta-analytic review. *Epilepsia, 43*(3), 283–291.

Lhatoo, S. D., & Sander, J. W. (2001). The epidemiology of epilepsy and learning disability. *Epilepsia, 42*(Suppl 1), 6–9.

Loeb, P. A. (1996). *Independent Living Scales (ILS)*. San Antonio, TX: Pearson.

Loring, D. W., & Meador, K. J. (2001). Cognitive and behavioral effects of epilepsy treatment. *Epilepsia, 42*(Suppl 8), 24–32.

Lúthvígsson, P., Olafsson, E., Sigurthardóttir, S., & Hauser, W. A. (1994). Epidemiologic features of infantile spasms in Iceland. *Epilepsia, 35*(45), 802–805.

Martin, R., Kuzniecky, R., Ho, S., Hetherington, H., Pan, J., Sinclair, K., et al. (1999). Cognitive effects of topiramate, gabapentin, and lamotrigine in healthy young adults. *Neurology, 52*, 321–327.

McLaren, J., & Bryson, S. E. (1987). Review of recent epidemiological studies in mental retardation: Prevalence, associated disorders, and etiology. *American Journal of Mental Retardation, 92*, 243–254.

Meador, K.J., Loring, D.W., Hulihan, J.F., Kamin, M., & Karim, R. (2003). Differential cognitive and behavioral effects of topiramate and valproate. Neurology, *60*(9), 1483–1488.

Meador, K. J., Baker, G. A., Browning, N., Clayton Smith, J., Combs-Cantrell, D. T., Cohen, M., et al. (2009). Cognitive function at 3 years of age after fetal exposure to antiepileptic drugs. *The New England Journal of Medicine, 360*(16), 1597–1605.

Meador, K. J., Loring, D. W., Vahle, V. J., Ray, P. G., Werz, M. A., Fessler, A. J., et al. (2005). Differential cognitive and behavioral side effects of topiramate and valproate. *Neurology, 60*, 1483–1488.

Meyers, J. E., & Meyers, K. R. (1995). *RCFT: Rey Complex Figure Test and Recognition Trial: Professional manual*. Lutz, FL: Psychological Assessment Resources, Inc.

Motamedi, G. K., & Meador, K. J. (2004). Antiepileptic drugs and memory. *Epilepsy & Behavior, 5*, 435–439.

Murphy, J. V., & Dehkharghani, F. (1994). Diagnosis of childhood seizure disorders. *Epilepsia, 35*(Suppl 2), S7–S17.

Panayiotopoulos, C. P. (2002). *A clinical guide to epileptic syndromes and their treatment*. Oxfordshire: Bladon Medical Publishing.

Paquier, P. F., Van Dongen, H. R., & Loonen, C. B. (1992). The Landau-Kleffner syndrome or acquired aphasia with convulsive disorder. *Archives of Neurology, 49*, 354–359.

Pollack, M. A., Golden, G. S., Schmidt, R., Davis, J. A., & Leeds, N. (1978). Infantile spasms in Down syndrome: A report of 5 cases and a review of the literature. *Annals of Neurology, 3*(5), 406–408.

Prasher, V. P. (1995). Epilepsy and associated effects on adaptive behaviour in adults with Down syndrome. *Seizure, 4*, 53–56.

Randolph, C. (1998). *RBANS: Repeatable battery for the assessment of neuropsychological status: Manual*. San Antonio, TX: The Psychological Corporation.

Rantala, H., & Putkonen, T. (1999). Occurrence, outcome, and prognostic factors of infantile spasms and Lennox-Gastaut syndrome. *Epilepsia, 40*(3), 286–289.

Roid, G. H., & Miller, L. J. (1997). *Leiter International Performance Scale – Revised*. Lutz, FL: Psychological Assessment Resources, Inc.

Romano, C., Tiné, A., Fazio, G., Rizzo, R., Colognola, R. M., Sorge, G., et al. (1990). Seizures in patients with trisomy 21. *American Journal of Medical Genetics. Supplement, 7*, 298–300.

Sabaratnam, M., Vroegop, P. G., & Gangadharan, S. K. (2001). Epilepsy and EEG findings in 18 males with fragile X syndrome. *Seizure, 10*(1), 60–63.

Sauerwein, H. C., Gallagher, A., & Lassonde, M. (2005). Neuropsychological deficits in children with temporal lobe epilepsy. In A. Arzimanoglou, A. Aldenkamp, H. Cross, M. Lassonde, S. Moshé, & B. Schmitz

(Eds.), *Cognitive dysfunction in children with temporal lobe epilepsy* (pp. 1–12). Paris: John Libbey Eurotext.

Schouten, D., Hendriksen, J. G., & Aldenkamp, A. P. (2009). Performance of children with epilepsy on the Rey-Osterrieth complex figure test: Is there an effect of localization or lateralization? *Epilepsy Research, 83*(2–3), 184–189.

Shahar, E., Barak, S., Andraus, J., & Kramer, U. (2004). Primary generalized epilepsy during infancy and early childhood. *Journal of Child Neurology, 19*(3), 170–174.

Sheslow, D., & Adams, W. (2003). *WRAML2: Wide range assessment of memory and learning: Administration and scoring manual*. Lutz, FL: Psychological Assessment Resources, Inc.

Shouse, M. N., & Quigg, M. S. (2008). Chronobiology. In J. Engel Jr. & T. A. Pedley (Eds.), *Epilepsy: A comprehensive textbook* (2nd ed., pp. 1961–1974). Philadelphia, PA: Lippincott, Williams, & Wilkins.

Sparrow, S., Cicchetti, D., & Balla, D. (2005). *Vineland Adaptive Behavior Scales – Second edition*. San Antonio, TX: The Psychological Corporation.

Steffenburg, U., Hagberg, G., & Hagberg, B. (2001). Epilepsy in a representative series of Rett syndrome. *Acta Paediatrica, 90*(1), 34–39.

Stern, R. A., & White, T. (2003). *NAB: Neuropsychological assessment battery*. Lutz, FL: Psychological Assessment Resources, Inc.

Su, C. Y., Lin, Y. H., Wu, Y. Y., & Chen, C. C. (2008). The role of cognition and adaptive behavior in employment of people with mental retardation. *Research in Developmental Disabilities, 29*(1), 83–95.

Tangye, S. R. (1979). The EEG and incidence of epilepsy in Down's syndrome. *Journal of Mental Deficiency Research, 23*(1), 17–24.

Tatsuno, M., Hayashi, M., Iwamoto, H., Suzuki, Y., & Kuroki, Y. (1984). Epilepsy in childhood Down syndrome. *Brain Development, 6*(1), 37–44.

Trevathan, E., Murphy, C. C., & Yeargin-Allsopp, M. (1997). Prevalence and descriptive epidemiology of Lennox-Gastaut syndrome among Atlanta children. *Epilepsia, 38*(12), 1283–1288.

Trevathan, E., Murphy, C. C., & Yeargin-Allsopp, M. (1999). The descriptive epidemiology of infantile spasms among Atlanta children. *Epilepsia, 40*(6), 748–751.

Troyer, A. K., Moscovitch, M., Winocur, G., Alexander, M. P., & Stuss, D. (2002). Clustering and switching on verbal fluency: The effects of focal frontal- and temporal-lobe lesions. *Neuropsychologia, 40*(5), 562–566.

Viani, F., Romeo, A., Viri, M., Mastrangelo, M., Lalatta, F., Selicorni, A., et al. (1995). Seizure and EEG patterns in Angelman's syndrome. *Journal of Child Neurology, 10*(6), 467–471.

Wechsler, D. (1999). *Wechsler Abbreviated Scale of Intelligence: Administration and scoring manual*. San Antonio, TX: The Psychological Corporation.

Wechsler, D. (1997). *WMS-III: Wechsler Memory Scale – Third edition: Administration and scoring manual*. San Antonio, TX: The Psychological Corporation.

Wechsler, D. (2002). *Wechsler Preschool and Primary Scale of Intelligence – Third edition: Administration and scoring manual*. San Antonio, TX: The Psychological Corporation.

Wechsler, D. (2003). *Wechsler Intelligence Scale for Children – Fourth edition: Administration and scoring manual*. San Antonio, TX: The Psychological Corporation.

Wechsler, D. (2008). *Wechsler Adult Intelligence Scale – Fourth edition: Administration and scoring manual*. San Antonio, TX: NCS Pearson, Inc.

Wechsler, D. (2009). *Wechsler Memory Scale – Fourth edition*. San Antonio, TX: NCS Pearson, Inc.

Welsh, M. C., Pennington, B. F., & Groisser, D. B. (1991). A normative-developmental study of executive function: A window on prefrontal function in children. *Developmental Neuropsychology, 7*(22), 131–149.

Wiebe, S. (2000). Epidemiology of temporal lobe epilepsy. *Canadian Journal of Neurological Sciences, 27*(Suppl 1), S6–S10.

Williams, K. T. (2007). *EVT-2: Expressive Vocabulary Test, second edition*. San Antonio, TX: Pearson Assessments.

Williams, J., & Sharp, G. B. (2000). Epilepsy. In K. O. Yeates, M. D. Ris, & H. G. Taylor (Eds.), *Pediatric neuropsychology: Research, theory, and practice* (pp. 47–73). New York, NY: The Guilford Press.

Wolff, M., Cassé-Perrot, C., & Dravet, C. (2001). Neuropsychological disorders in children with severe myoclonic epilepsy. *Epilepsia, 42*(Suppl 2), 61.

World Health Organization. (1993). *International Classification of Diseases: 10th revision*. Ann Arbor, MI: Commission on Professional and Hospital Activities.