Introduction to Pediatric Epilepsy for Neuropsychology Students: A Literature Review

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Introduction to Pediatric Epilepsy for Neuroscientists: A Literature Review
Marc A. Silva

Abstract: A review of pediatric epilepsy is presented, with emphasis on diagnosis, taxonomy, associated psychological problems, and treatment. Epilepsy refers to a family of disorders, characterized by two or more unprovoked seizures more than 24 hours apart in a child over one month of age post birth. Epilepsy is the most common pediatric neurological disorder, effecting approximately 0.3% to 1% of patients under that age of 18. Seizures are typically classified according to (1) location of seizure onset in the brain (i.e., focal versus bilateral); (2) semiology (i.e., clinical symptoms); (3) etiology (symptomatic, idiopathic, and cryptogenic); and (4) syndrome (are epileptic disorders with specific clusters of signs and symptoms that occur together and have several typical features). Childhood epilepsy is associated with many types of cognitive and psychosocial dysfunction. Treatments aimed at reducing or eliminating epileptic seizures include pharmacotherapy, surgery, and the ketogenic diet. Psychological treatments help address the psychosocial problems associated with childhood epilepsy.

Approximately 150,000 people develop epilepsy each year in the U.S. (National Institutes of Health [NIH], 1990). Prevalence in the U.S. population is typically estimated between 0.5% and 1% (Solomon & Pfeffer, 1996) but could be as high as 5% (Novick & Arnold, 1988). Epilepsy is the most common pediatric neurological disorder (Bennett & Ho, 1997; Hagar, 2008), effecting approximately 0.3% to 1% of patients under that age of 18 (Cowan, Bodensteiner, Leviton, & Doherty, 1989; Pellock, 2004; Rutter, Graham, & Yule, 1970; Solomon & Pfeffer, 1996). Most individuals diagnosed with epilepsy experienced initial symptoms of the disorder prior to age 20 (Novick & Arnold, 1988; Solomon & Pfeffer, 1996), with median age of onset between 5 and 6 years old (Shinnar & Pellock, 2002). Each year, 20,000 to 45,000 new cases of epilepsy are diagnosed in U.S. children and adolescents (Hauser, 1994; Shinnar & Pellock, 2002). There are approximately 300,000 children in the U.S. living with epilepsy (Solomon & Pfeffer, 1996), although others indicate this number could be as high as one million (Hartlage & Telzrow, 1984). Children 1 to 12 months of age post-birth are at the highest risk for developing epilepsy (Hauser, 1994; Shinnar & Pellock, 2002). Findings about gender-related risk factors have been inconsistent (Anderson, Northam, Hendy, & Wrennall, 2001).

Definitions and explanations of terminology common in the epilepsy literature are provided in the next section (see also the glossary, Appendix A).
TERMINOLOGY

Epilepsy is a family of disorders characterized by recurrent seizures. Specifically, epilepsy (also referred to as seizure disorder) is defined as two or more unprovoked seizures more than 24 hours apart in a child over one month of age post birth (Commission of Epidemiology and Prognosis, International League Against Epilepsy [CEP/ILAE], 1993). Experiencing a single seizure, which is not entirely uncommon among children, is insufficient. Seizures must be recurrent to obtain a diagnosis of epilepsy (Bennett & Ho, 1997; Novick & Arnold, 1988; Solomon & Pfeffer, 1996).

Seizures occur when there is atypical electric activity in the brain (Hagar, 2008). In normal brain functioning, the firing of excitatory and inhibitory neurons is cooperative and balanced, which allows normal voluntary and involuntary sensory and motor movements to take place (e.g., controlled eye and limb movements). Seizures are the result of abnormal, excessive, paroxysmal, and uncontrolled discharge of neurons (CEP/ILAE, 1993; Novick & Arnold, 1988; Solomon & Pfeffer, 1996). Seizures interfere with normal functioning, with clinical manifestations that include abrupt disturbances of consciousness, speech, language, cognition, affect, sensory experiences (e.g., tingling, misperceptions), motor movement (e.g., muscle stiffening and jerking), and behavior (Bennett & Ho, 1997; Hagar, 2008; Novick & Arnold, 1988; Solomon & Pfeffer, 1996). Other epilepsy-related terminology readers should be familiar with include the following: ictal or intraictal, which refers to the period of time the epileptic seizure is experienced; postictal, which refers to the period of time just after an epileptic seizure; and interictal or interictal interval, which refers to the time period between two epileptic seizures (Novick & Arnold, 1988).

Classification

Seizures are typically classified according to location of seizure onset in the brain, semiology, etiology, and syndrome (CEP/ILAE, 1993; Hagar, 2008; Hartlage & Hartlage, 1997; Novick & Arnold, 1988; Solomon & Pfeffer, 1996). The most widely accepted classification system (as noted by Hartlage & Hartlage, 1997) is the Commission on Classification and Terminology of the International League Against Epilepsy [CCT/ILAE] (1989), which primarily classifies seizures according to whether the onset of abnormal and excessive neuronal activity is focal (thus involving one hemisphere) or bilateral (thus involving the whole brain from the start). Seizures with focal onset have traditionally been referred to as partial seizures, which will be the term primarily, used in the current paper. More
recently, researchers are using the term focal seizures because partial may inaccurately connote incompleteness.

In generalized seizures, onset is bilateral. Partial and generalized seizures are subclassified according to associated *semiology* (i.e., clinical signs and symptoms) and neuronal activity (Anderson et al., 2001; CCT/ILAE, 1989; Dreifuss, 1993; Hagar, 2008; Novick & Arnold, 1988; Solomon & Pfeffer, 1996; see Appendix B). Subclassifications of partial and generalized seizures will be explored next.

**Partial Seizures**

Seizures with focal onset are called partial seizures. There are three main types, all of which commonly occur among children (Novick & Arnold, 1988). *Simple partial seizures* (also referred to as partial elementary), are characterized primarily by disturbances in sensory-perceptual, motor, and cognitive functioning. Consciousness is preserved. *Complex partial seizures* are typically characterized by impaired or altered consciousness as well as sensory, motor, and cognitive disturbances (CCT/ILAE, 1989; CEP/ILAE, 1993; Hagar, 2008; National Society for Epilepsy, 2007; Novick & Arnold, 1988; Solomon & Pfeffer, 1996). Simple or complex seizures that begin focally and then spread to involve the whole cortex are described as *partial seizures that secondarily generalize*. These seizures often generalize into the tonic-clonic subtype (Novick & Arnold, 1988) which is described later. Secondarily generalizing seizures may originate in the brain stem or reticular activating system, which makes sense intuitively. All three partial seizure subtypes are characterized by positive symptoms and/or cessation of sensation, motor output, cognition, and consciousness.

Sensory disturbances are most characteristic of simple partial seizures. Symptoms may include visual, auditory, olfactory, gustatory, or vertiginous misperceptions or hallucinations. The experience of such sensory symptoms is sometimes referred to as an aura, particularly when first experienced as part of simple partial seizure that evolves into a complex partial or generalized seizure. Motor disturbances may include automatisms, stereotyped movements, loss of motor control, or jerking in one part of the body. Cognitive disturbances include, for example, changes in language, attention, and affect. Finally, while children are typically alert during simple partial seizures, consciousness is altered or impaired from the start during complex partial seizures (Novick & Arnold, 1988; Solomon & Pfeffer, 1996). The specific clinical symptoms experienced by the child and observed by others depend largely upon the location of abnormal electrical activity in the brain.
Although partial seizures (all subtypes) often originate in the limbic system or temporal lobe (Solomon & Pfeffer, 1996), focal onset reportedly may occur throughout the brain, with certain semiology associated with location of onset. For example, simple partial seizures arising from the mesial basal limbic or primary rhinencephalic region of the temporal lobe are associated with autonomic and/or perceptual symptoms. Seizures beginning in the uncus may be accompanied by olfactory or gustatory sensations that are often experienced by the child as unpleasant odors and bitter or salty taste (Bennett & Ho, 1997; Solomon & Pfeffer, 1996). Seizures originating from the hippocampus or amygdala may result in a rising sensation felt from the abdomen. Generally, seizures arising in the lateral temporal lobe are characterized by auditory hallucinations or visual-perceptual hallucinations. Auditory misperceptions may be experienced when seizures originate in the anterior temporal lobe, especially in the left hemisphere (Bennett & Ho, 1997). During the ictus, the child may perceive voices or sounds as being too soft or loud in volume or too low or high in pitch. Simple auditory hallucinations such as buzzing, ringing, or hissing noises may also be experienced, particularly when the seizure focus is in the primary auditory zone. Visual misperceptions are common when seizure focus is in the posterior temporal lobe. In these cases, objects may appear much smaller or larger than they actually are. As would be expected given the functional aspects of association cortex zones, complex visual hallucinations appear to arise from the temporal-parietal-occipital junction (Bennett & Ho, 1997; Solomon & Pfeffer, 1996). Other temporal lobe-related simple partial seizures include affective-perceptual symptoms such as déjà-vu (familiarity of unknown people, places, objects, or experiences), jamais-vu (unfamiliarity of known people, places, objects, or experiences), or overwhelming fear (Solomon & Pfeffer, 1996).

According to Task Force on Classification and Terminology, ILAE (2001), seizures originating in the frontal lobe feature prominent autonomic vocalizations (e.g., repetitive grunts, shrieks, or other nonlanguage utterances), and motor responses (e.g., stereotyped movements such as pelvic thrusts other repetitive body movements). Urinary incontinence and drop attacks may occur as well. When seizure focus is in the motor cortex, there may be sudden, involuntary, and repetitive contractions of muscles in a particular muscle group that spread to contiguous muscle groups progressively. This is referred to as a Jacksonian March (Task Force on Classification and Terminology, ILAE, 2001). Frontal lobe seizures may be quick to secondarily generalize (Solomon & Pfeffer, 1996).

When seizures originate in the parietal lobe, they are often accompanied by somatosensory symptoms such as numbness, tingling, or
the feeling of electricity on one side of the body (Solomon & Pfeffer, 1996). Sometimes the somatosensory symptoms will first be experienced in the hand and then spread like a Jacksonian March through the arm and throughout one side of the body. Finally, simple partial seizures originating in the occipital lobe are accompanied by visual hallucinations, such as colors, flashes, or sparks (Solomon & Pfeffer, 1996).

In contrast to the simple partial variety, complex partial seizures have an absence of aura and instead are characterized by an abrupt loss of consciousness and cessation of ongoing activity. Often, this is followed by speech-related automatisms such as shouting or screaming; affective automatisms such as laughing or crying; simple automatisms such as chewing, lip smacking, spitting, or swallowing; and complex automatisms such as drinking, running in a circle, and undressing (Novick & Arnold, 1988; Solomon & Pfeffer, 1996). Seizure duration is typically about a minute and is followed by postictal amnesia and confusion (Solomon & Pfeffer, 1996). For simple partial seizures that evolve into complex partial seizures, the aura precedes loss of consciousness.

**Generalized Seizures**

Seizures in which onset involves both hemispheres initially are referred to as generalized seizures (CCT/ILAE, 1989; Dreifuss, 1993; Hagar, 2008; Novick & Arnold, 1988; Solomon & Pfeffer, 1996). Consciousness if often impaired and motor symptoms (when they occur) are bilateral. Like partial seizures, generalized seizures are subclassified according to associated semiology and neuronal activity (See Appendix B). Generalized seizures are subclassified as absence, myoclonic, clonic, tonic, tonic-clonic, and atonic.

Of the generalized epilepsies, absence and tonic-clonic subtypes are the most frequently occurring in children (Novick & Arnold, 1988), and are described below. But first, the remaining subtypes are briefly described in order to facilitate understand terminology and semiology associated with generalized seizures. Definitions and descriptions presented here were explained in detail elsewhere (see Blume, Luders, Mizrahi, Tassinari, van Emde Boas, & Engel, 2001).

*Myoclonic* refers to brief (i.e., < 100 milliseconds) involuntary contractions of muscles or muscle groups. *Clonic* refers to regularly repetitive myoclonic contractions which involve the same muscle groups and occur at a frequency of approximately 2 to 3 seconds. *Tonic* refers to sustained increase in muscle contractions lasting seconds to minutes and is observed as a sudden seizing of muscles or muscle groups. *Tonic-clonic* refers to a sequence of tonic-clonic or sometimes clonic-tonic-clonic phases. *Atonic* refers to a sudden loss of muscle tone without apparent
preceding myoclonic or tonic phases, typically involve muscles of the head, trunk, jaw, or limbs, and last up to 2 seconds (Blume, et al., 2001).

**Absence Seizures**

Absence seizures (formerly known as petit mal seizures) are nonconvulsive (Hagar, 2008; Novick & Arnold, 1988). Absence seizures are characterized by an abrupt loss of consciousness that are usually brief (e.g., lasting approximately 10-30 seconds), and may occur dozens of times a day (Hagar, 2008; Novick & Arnold, 1988). The symptoms associated with absence seizures are typically subtle, thus the seizure may go unnoticed by others. To the observer, the individual experiencing the seizure may appear to be staring off into space. Others may perceive the child to be daydreaming. During the ictal phase, the child will not respond to the environment. The child will typically resume activities postictus with no memory for the episode. Typically, absence seizure epilepsy first occurs between the ages of 4 and 10 years of age, but may begin in adolescence. Absence seizures tend to disappear when the child reaches adulthood. However, about half of children with absence seizures later develop tonic-clonic seizures (Novick & Arnold, 1988).

**Tonic-Clonic Seizures**

Tonic-clonic seizures (formerly called grand mal seizures) are characterized by abrupt loss of consciousness and convulsive motor activity. During a tonic-clonic seizure, muscles suddenly contract and become rigid (tonic phase) and then jerk and shake violently (clonic phase). Vomiting, urination, and defecation may occur during the ictal period, followed by postictal confusion, unresponsiveness, and amnesia for the seizure (Novick & Arnold, 1988).

While location of onset is the typical classification system, it is important to note that seizures are often a symptom of some other ailment. Sometimes, epileptic seizures may be secondary to disease of the central nervous system (CNS). Seizures may have genetic determinants as well. Most often, however, no specific cause can be identified. Etiology of epilepsy is described next.

**Etiology**

Seizure etiology fall into two main categories: symptomatic and idiopathic. Symptomatic seizures result from known CNS dysfunction (e.g., focal pathology, metabolic abnormalities). That is, they are experienced as symptoms of another diagnosed disorder. Epileptic
seizures may be secondary to hypoglycemia, bacterial or viral infection, brain hemorrhage, brain contusion, or brain tumor. Seizures may result from these disorders because of intracranial pressure or metabolic changes in the surrounding neurons (CEP/ILAE, 1993; Novick & Arnold, 1998; Solomon & Pfeffer, 1996).

*Idiopathic* seizures are seizures with particular clinical signs and symptoms, but have no clear antecedent such as CNS infection or injury (Shinnar & Pellock, 2002). Although there are no detectable causes, undetected metabolic or structural abnormalities are thought to be involved (Novick & Arnold, 1988). The majority of seizures experienced by children are idiopathic.

Sometimes, family patterns can be found among children with epilepsy, thus genetic determinants are thought to be involved (Novick & Arnold, 1988). Genetic etiology appears present in absence and tonic-clonic seizures, for example.

*Cryptogenic* seizures, which have no known etiology, is another term used to classify epilepsy according to etiology. Cryptogenic seizures include both partial and generalized seizures that do not conform to criteria for the symptomatic and idiopathic categories (CEP/ILAE, 1993; Hagar, 2008). Cryptogenic seizures were presumed to be symptomatic, however over time genetic features have been identified in some variants of the subtype (CCT/ILAE, 2008).

**Epileptic Syndromes**

Epilepsy can also be classified according to syndromes, which are epileptic disorders with specific clusters of signs and symptoms that occur together and have several typical features (Solomon & Pfeffer, 1996). Approximately 50% of children with epilepsy can be classified into an epileptic syndrome (Rothner, 1992). Epileptic syndromes share similar onset ages, clinical courses, and responses to treatment, although there may be divergent etiologies. Syndrome classification is useful because it allows providers to better evaluate the patient in terms of illness course and prognosis as well as choose appropriate medication (Solomon & Pfeffer, 1996). An abridged list of epileptic syndromes, which are subclassified according to location of seizure onset and etiology can be found in Appendix C. Onset may be generalized, focal, or undetermined. Etiologies are varied. Those epileptic syndromes commonly occurring among children are described below.

*Generalized Epileptic Syndromes*
Childhood absence epilepsy and juvenile myoclonic epilepsy are generalized, idiopathic epilepsies, both of which have favorable prognoses. *Childhood absence epilepsy* (also known as pyknolepsy) typically occurs in children between 4 and 12 years of age, with the highest rate of onset occurring between 6 and 7 years of age. Childhood absence epilepsy usually remits after adolescence, although tonic-clonic seizures may develop during this time. There is a strong genetic component to this syndrome, as evidenced by EEG patterns. Seizures are characterized by brief staring and eye blinking lasting between 5 and 10 seconds, and occur several times a day. Ictal EEG shows predictable spike and wave activity. No structural lesions are present, medication helps to control seizures, and prognosis is favorable. Sodium valproate is generally prescribed for childhood absence epilepsy with additional tonic-clonic seizures. Otherwise, ethosuximide is the drug of choice (Anderson et al., 2001; Solomon & Pfeffer, 1996).

*Juvenile myoclonic epilepsy* (also known as impulsive petit mal) is characterized by brief myoclonic jerks and absence seizures as well as generalized tonic-clonic seizures that often begin during adolescence. Ictal EEG shows predictable spike and wave patterns. About one-third of patients show a photoparoxysmal response. Seizures are well-controlled with valproate, although relapse is high upon tapering or ceasing the medication (Solomon & Pfeffer, 1996).

In contrast to the prior mentioned syndromes, *Lennox-Gastaut syndrome* is a generalized epileptic syndrome that is symptomatic. Seizures typically begin between 2 and 5 years of age and are characterized by cessation of ongoing motor activity (akinetic), loss of muscle tone (atonic), and sustained muscle contractions (tonic). There is also a high incidence of tonic-clonic seizures. Sadly, prognosis of Lennox-Gastaut syndrome is less favorable. Seizures are difficult to control and there is a high incidence of associated cognitive and behavioral problems (e.g., mental retardation). Treatment for Lennox-Gastaut syndrome includes sodium valproate and benzodiazepines, as well as a ketogenic diet (Solomon & Pfeffer, 1996), which is a high fat, adequate protein, low carbohydrate diet (Freeman, Kossoff, & Hartman, 2007).

*Partial Epileptic Syndromes*

Similar to those with generalized onset, epileptic syndromes with focal onset may be idiopathic or symptomatic. Focal seizures may be simple or complex. Idiopathic syndromes common among children include benign childhood epilepsy with centrotemporal spikes and
childhood epilepsy with occipital paroxysms; they will be described first. Next, features of partial onset symptomatic syndromes are described.

**Benign childhood epilepsy with centrotemporal spikes** (also known as benign Rolandic epilepsy of childhood), typically begins in children 3 to 12 years of age. Clinical symptoms are typically atonic and akinetic, and include speech arrest, paresthesias of the mouth, and excessive drooling. Consciousness is typically preserved. There is a strong genetic component, predictable EEG spike patterns during sleep, and no evidence of underlying structural lesions. Seizures typically cease when children reach their teens. Fortunately, children typically go on to have normal intelligence and performance on neurological examinations (Solomon & Pfeffer, 1996).

**Childhood epilepsy with occipital paroxysm**, another syndrome with idiopathic focal onset, is characterized by visual symptoms such as amblyopia (i.e., blurred vision) and visual hallucinations. Often, there is a family history of epilepsy in children with this syndrome. EEG activity during sleep follows a predictable pattern. Childhood epilepsy with occipital paroxysms is said to be benign, with resolution of seizures and associated EEG abnormalities in the late teenage years (Solomon & Pfeffer, 1996).

Focal onset seizures of the symptomatic variety are classified according to anatomic location of seizure, seizure type (i.e., simple or complex partial), clinical features, and etiological factors if known. Symptomatic focal seizures often originate in the frontal lobe, temporal lobe, or limbic system. Associated ictal and interictal behavioral abnormalities are typically present and specific symptoms vary according to location of onset. Often, seizures occur unpredictably and are followed by postictal confusion. Clinical manifestations may include automatisms and other motor symptoms. If seizures are frequent, there may be associated memory problems. Cognitive and behavioral problems are associated with focal onset symptomatic syndromes. Anticonvulsant medication such as carbamazepine and phenytoin are typically prescribed. Barbiturates have been prescribed but are associated with negative cognitive side effects, thus have fallen out of favor. If medications are not effective and onset is localized to the temporal lobe, children may be good candidates for surgery to reduce or eliminate seizures (Solomon & Pfeffer, 1996).

Sometimes, it cannot be determined whether seizure onset is focal or generalized, as both types are typically present. Acquired epileptic aphasia and acquired epileptic frontal syndrome are examples of this subclass. **Acquired epileptic aphasia** (also known as Landau-Kleffner syndrome) is typically idiopathic although structural lesions in the temporal lobe have
been found on rare occasions. This syndrome is associated with predictable EEG spike and wave activity in the temporal lobe, with some children displaying continuous spike and wave activity during slow wave sleep. Seizures are often generalized and convulsive, but may also be partial with motor abnormalities. Behavioral and psychomotor problems are present in two-thirds of children. These symptoms usually begin between the ages of 2 and 10. For example, verbal-auditory agnosia and deterioration of spontaneous speech can begin as early as age 2. Seizures often remit before the age of 15, but at least one-third of children continue to have serious language disorders. Some children have responded to treatment with steroids (Solomon & Pfeffer, 1996).

Similarly, acquired epileptic frontal syndrome is also associated with continuous spike waves during slow wave sleep. Interictal EEG of the frontal lobe during both wake and sleep show predictable activity. Seizure onset is also quite early in a child’s life, typically beginning between two and a half and 5 years old. Acquired epileptic frontal syndrome is associated with subsequent deterioration of cognitive abilities and behavior. For example, children typically show impaired reasoning, impaired visual-spatial ability, and disorientation to passage of time. Treatment with ethosuximide, which is often used to treat absence seizures, was associated with improvement in children with acquired epileptic frontal syndrome (Solomon & Pfeffer, 1996).

Non-epilepsy Seizure Disorders

Certain seizures and seizure disorders appear epileptic in nature but are actually not considered as part of the epilepsy family of disorders. Febrile seizures and pseudoseizures are two examples of nonepileptic seizure disorders (CEP/ILAE, 1993; Hagar, 2008; Solomon & Pfeffer, 1996). Febrile seizures (i.e., fever-related seizures occurring in early childhood) are usually classified as symptomatic (CEP/ILAE, 1993). There are two subtypes: those associated with febrile illnesses that affect the central nervous system (e.g., respiratory illnesses) and those that are not. Febrile seizures typically occur between 6 months to 5 years of age. Febrile seizures are thought to have genetic etiology. Although frequently seen by psychologists and neuropsychologists, probably due to concerned parents, they are often not associated with later learning disorders or mental retardation (Novick & Arnold, 1988).

In contrast to epileptic and febrile seizures, pseudoseizures (also known as psychogenic seizures) are not accompanied by abnormal electrical brain activity (Hagar, 2008). Associated EEG activity appears normal (Solomon & Pfeffer, 1996). Seizures appear epileptic, but etiology is
believed to be related to stress or emotional conflict (Hagar, 2008; Solomon & Pfeffer, 1996). For example, pseudoseizures have been associated with childhood abuse and school problems. Thus, pseudoseizures are more appropriately classified as a conversion disorder (Solomon & Pfeffer, 1996).

Clinical symptoms of pseudoseizures typically include uncontrolled thrashing of the body, although incontinence and injury to the patient are typically absent (Solomon & Pfeffer, 1996). Sometimes, pseudoseizures are accompanied by a dissociative reaction or temporary amnesia which may be an unconscious attempt to "get away." Pseudoseizures are common in the pediatric population and may occur in children and adolescence, and may occur alone or alongside epilepsy (Pakalnis, Paolicchi, & Gilles, 2000; Paolicchi, 2002; Solomon & Pfeffer, 1996), making accurate diagnosis difficult.

As noted by Solomon and Pfeffer (1996), provocative EEG testing has assisted neurologists with diagnosing pseudoseizures. The provocative EEG test entails securing the patient’s permission to induce a seizure using an innocuous method, such as a cold pack placed on the head or an intravenous saline injection, which are essentially placebos. The patient is told the procedure will likely induce a seizure. The procedure was followed by a pseudoseizure response in many patients with uncontrolled seizures (Cohen, 1982). Thus, provocative EEG testing may help, but should not be used exclusively, to differentiate children with pseudoseizure from those with true epilepsy.

Notably, frontal lobe seizures are sometimes confused for pseudoseizures because of the unusual behavioral presentation and short ictal and postictal period (Solomon & Pfeffer, 1996). However, unlike frontal seizures, pseudoseizures do not occur during sleep and they are unresponsive to antiepileptic medication.

Diagnosis

Epilepsy is diagnosed and treated primarily by neurologists (Novick & Arnold, 1988). Diagnosis is based on a variety of data, including (1) detailed information about seizure activity; (2) a comprehensive patient history; (3) findings from medical and neurological examinations; and (4) results from laboratory studies (Hagar, 2008; Novick & Arnold, 1988). Tests for metabolic disorders or infections may be included. Electroencephalogram (EEG) is probably the most frequently used technology to aid physicians with diagnosis (National Society for Epilepsy, 2006; Novick & Arnold, 1988; Solomon & Pfeffer, 1996). EEG records alternating excitation and inhibition of neuronal electrical activity, and
assists with identifying the origin of seizures in the brain. However, a negative EEG does not necessarily refute the presence of seizures, as false negative results occur. Other assistive devices include neuroimaging techniques such as computerized transaxial tomography (CT), magnetic resonance imaging (MRI), and positron emission tomography (PET) scanning, which assist in locating lesions in the brain that may be associated with seizure activity (Solomon & Pfeffer, 1996).

In addition to technology-based tests, neuropsychological assessment is an important part of epilepsy diagnosis. Neuropsychological assessment aids in establishing severity of impairment (e.g., cognitive, behavioral, psychosocial) and monitoring the effects of treatment on dysfunction. For example, neuropsychological testing before and after medication treatment or after medication change can assist in finding a practical balance between seizure control and adverse cognitive, behavioral, and psychosocial consequences. Neuropsychological testing can also aid in determining focal onset of seizures, level of cognitive impairment, and whether patients are good candidates for surgery (Bennett & Ho, 1997). Skill in evaluating and tracking the children’s cognitive and psychosocial problems associated with epilepsy is probably the greatest asset of neuropsychologists.

Dysfunction Associated with Epilepsy

Children with epilepsy experience a range of problems associated with cognitive and psychosocial functioning (Novick & Arnold, 1988). Cognitive concerns are discussed first.

Cognitive Concerns

While cognitive deficits have been reported among some children with epilepsy, not all demonstrate cognitive impairment. Children with epilepsy may in fact have normal or superior intelligence. One study found that the distribution of intelligence scores in children with epilepsy was comparable to that of the general population (Rutter et al., 1970). Lennox and Lennox (1960) indicated that in a study of 1905 patients with epilepsy, two-thirds had normal intelligence while only 14% clearly showed cognitive impairment. Still others suggested that children with epilepsy have mean IQs ranging up to a standard deviation lower than average (Hartlage & Hartlage, 1997). In contrast, Bennet and Ho (1997) noted that most children with epilepsy have normal intelligence, although variance is positively skewed toward the low end of average. Discrepant findings in intellectual ability could be due to uncontrolled variables that may differentially affect cognitive functioning, such as age of onset, duration of
the seizure disorder, seizure type (i.e., focal or generalized), seizure frequency, medication effects, and whether seizures were symptomatic or idiopathic. It has also been noted that the exclusive use of the IQ score as a measure of cognitive function may be inadequate in assessing various cognitive abilities and deficits associated with brain dysfunction (Bennet & Ho, 1997), as IQ is theorized as relatively stable and research suggested it may be insensitive to cognitive changes associated with epilepsy. More recent research has investigated cognitive processes such as sensory processes, attention, concentration, learning, memory, receptive and expressive language ability, reasoning, and motor skills (Bennet & Ho, 1997).

When considering moderator variables, subgroups of epileptic children appear to be more at risk for cognitive impairment. Etiology, onset, and syndrome classifications have been examined in this regard. For example, children with underlying CNS disease (i.e., they have symptomatic epilepsy) performed worse on tests of intelligence, while idiopathic epilepsies were less often associated with intellectual compromises (Solomon & Pfeffer, 1996). For example, IQ was found to be 4-11 points lower in those with symptomatic versus idiopathic epilepsy (Tarter, 1972). Bennet and Ho (1997) reported that children with symptomatic seizures were more likely to be mentally retarded (73%) compared to those with idiopathic seizures (22%).

Seizure frequency was positively correlated with greater intellectual deficit (as noted in Hartlage & Hartlage, 1997), however this finding was inconsistent. In fact, the affects of seizures on intelligence are more homogenous within a given seizure classification than across epilepsies. For example, childhood absence seizures are unlikely to show intellectual deficits despite occurring several times a day (Farwell et al., 1985; Hartlage & Hartlage, 1997). Children with minor motor, atypical absence, or absence plus generalized tonic-clonic seizures showed mild impairments on the age appropriate Halstead-Reitan Neuropsychological Battery (Farwell et al., 1985). Children with minor motor and atypical absence seizures are more likely to show aphasia-related deficits and lower IQ scores compared to children with other types of epilepsies (Bennet & Ho, 1997; Hartlage & Harlage, 1997). Those with generalized seizures in general and tonic-clonic seizures in particular appear to be at higher risk for cognitive impairment compared to those with focal onset, regardless if the seizures were idiopathic or symptomatic (Bennett & Ho, 1997). Finally, Tarter (1972) indicated that individuals with generalized tonic-clonic seizures show the greatest intellectual deficit, those with simple partial seizures showed the least deficit, and those with partial complex seizures had intermediate levels of intellectual impairment.
Epileptic syndromes appear more predictive of cognitive impairment than seizure type. For example, children with benign Rolandic epilepsy and juvenile myoclonic epilepsy rarely show decline in intellectual functioning regardless of the number of seizures (Holmes, 1991). In contrast, progressive mental retardation was observed in 75% to 95% of children with Lennox-Gastaut syndrome (Chevrie & Aicardi, 1972). Differences in IQ are probably related to an interaction of a host of variables. IQ tends to be lower in children with earlier onset and multiple seizure types, longer and more frequent seizures, less seizure control while on medication, toxic drug levels due to medication, and multiple drug toxicity (Solomon & Pfeffer, 1996). Farwell et al. (1985) reported that three variables accounted for the variance in IQ scores, specifically years with seizure disorder (38%), followed by seizure duration (16%) and age of onset (9%).

Other cognitive problems found among children with epilepsy include, for example, problems with information processing speed, sustained and focused attention, motor fluency, vigilance, and alertness. There appears to be different cognitive problems associated with hemispheric location of seizure activity. For example, epilepsy with focal onset in the left hemisphere in general, and more the left temporal lobe specifically, is more often associated with verbal processing and immediate memory problems. In contrast, right hemisphere onset is more often associated with problems with visuospatial reasoning, attention, modulation of affect, paralinguistic aspects of communication, and parallel information processing (Solomon & Pfeffer, 1996). In a small study that compared (right and left) temporal lobe epileptic patients without a history of brain damage or neurological disease with healthy controls, no lateralizing deficits were observed, although there was a trend found for deficits in psychomotor speed, selective attention, and reasoning among the epileptic group (Haynes & Bennett, 1991).

As noted by Bennett and Ho (1997), impaired sustained attention appears related to generalized seizures more so than focal seizures, possibly because generalized seizures are more likely to involve subcortical structures responsible for maintaining attention. In contrast, those with cortically-based focal seizures appear more likely to be impaired on tests of selective attention.

Evidence for memory deficits is strongest in patients with complex partial seizures with temporal lobe foci (Bennett & Ho, 1997). Most research has focused on verbal memory, which is more likely to be impaired in those with seizures originating in the left temporal lobe. Nonverbal deficits have been observed in those with right temporal lobe onset. Long term memory appeared more affected than short term
memory. Results persisted after controlling for age of onset, duration of epilepsy, and seizure frequency. It should be noted that most studies examined surgical candidates with little attention given to patients with complex partial seizures who were not surgical candidates.

Language deficits have also been noted (Bennett & Ho, 1997). Dysnomia was reportedly prominent in patients with complex partial seizures with left temporal lobe foci. Other observed problems included circumstantiality in speech and writing, and hyperplasia (i.e., the tendency toward excessive and compulsive writing). In addition, Bennett and Ho noted that children with epilepsy perform poorer on tests of perceptual-motor skills. Finally, those with epilepsy demonstrated reduced reaction time, processing speed, and psychomotor speed (Bennet & Ho, 1997; Hagar, 2008).

To summarize, the precise cause of cognitive changes is unclear, and a variety of factors appear involved. Those with symptomatic epilepsy, generalized seizures, longer duration or seizure disorder, and certain epilepsy subtypes appear to be at greater risk. Cognitive changes could be due to alterations in the CNS because of recurrent seizure, or due to an underlying degenerative disease of which epileptic seizures area symptom (Bennett & Ho, 1997). Seizures may be secondary to head injury, infectious disease such as encephalitis, brain tumor, or cerebrovascular disease, all of which are associated with cognitive deficits in their own right (Bennett & Ho, 1997). Contributing factors may include physiological abnormalities of the limbic system, brain damage secondary to repeated and uncontrolled seizures, the presence of an underlying degenerative disease that is associated with the epilepsy, effect of the pharmacological treatment, disturbed psychological response of the patient toward societal stigma, and negative reactions by others toward the illness (Solomon & Pfeffer, 1996).

Frequency of seizures was negatively correlated with cognitive ability in adults with tonic-clonic seizures as well as children across seizure classes. At the same time, earlier age of onset and longer duration of the disorder are associated with greater risk for cognitive impairment in children age 9 to 15 as well as adults (Bennett & Ho, 1997). Notably, these findings do not take into account the effects of antiepileptic medication of cognitive dysfunction, which are discussed later. It is important to note that there are no specific cognitive deficits common among across the epilepsies, although children with epilepsy have higher incidence of cognitive problems compared to the general population (Solomon & Pfeffer, 1996).

**Associated Psychosocial Problems**
Many children with epilepsy experience myriad psychosocial problems. For example, poor academic performance has been observed most notably in arithmetic, followed by spelling, reading comprehension, and word recognition (Hagar, 2008; Novick & Arnold, 1988; Solomon & Pfeffer, 1996). In fact, children with epilepsy have been found to be 12-28 months behind nonepileptic peers in reading and 28 months behind in comprehension (Bennett & Ho, 1997). Learning problems occur in approximately 5-20% of children with epilepsy (Solomon & Pfeffer, 1996). As noted in a review by Hagar (2008), epileptic children are also at risk for vocational difficulties in adulthood, and children frequently present with comorbid depression, anxiety, and suicide ideation. During adolescence, issues related to self-esteem and peer acceptance may arise, and experiencing violent seizures that occur during school may exacerbate such feelings. Epilepsy is often associated with psychosocial problems such as parental over-protection, peer teasing and bullying, and fear of seizures (Solomon & Pfeffer, 1996). Experiencing seizures at school, learning problems, and imposed limitations on participation in sports, playground activities, and driving (a right of passage) may further limit normal peer interaction and social development (Hartlage & Hartlage, 1997).

Psychosocial disturbances are associated with age of onset, type of epilepsy, and EEG patterns. For example, childhood epilepsy is often associated with memory, attentional, and analytic deficits, reading comprehension problems, dyslexia, dyscalculia, and academic underperformance. For some epileptic children, poor reading ability is associated with specific EEG abnormalities. Adolescent onset is often associated with psychological disturbances. Children and adolescents with epilepsy have a higher prevalence of comorbid psychiatric symptoms such as inattention, hyperactivity, aggressiveness, and anxiety compared to children in the general community (Solomon & Pfeffer, 1996). Among epileptic children, 33% had psychiatric disorders, compared to 7% of the general population and 12% of children with physical illness not involving the brain (Rutter et al., 1970). Psychiatric symptoms are most often associated with partial (focal) seizures originating in the left hemisphere (specifically in the temporal lobe), with generalized seizures, with multiple types of seizures, and early age of onset (Solomon & Pfeffer, 1996). Psychosis is often associated with temporal lobe focal onset and with focal seizures that secondarily generalize (Solomon & Pfeffer, 1996).

While data on children was not readily available, adults with epilepsy appear to be at 4 to 5 times higher risk for attempting suicide compared to
the general population (Solomon & Pfeffer, 1996). Suicide attempts were associated with poor seizure control.

Social competence is positively associated with good seizure control. Externalizing behavior involving aggression, hyperactivity, and delinquent antisocial behavior was associated with male gender, disrupted parental marriage, younger age of onset, and poor seizure control. Internalizing behavior problems such as depression and fearful and inhibited behavioral was associated with good seizure control, intact parental marriage, and male gender (Solomon & Pfeffer, 1996). Given the myriad psychological problems associated with epilepsy, it is imperative that neuropsychologists develop appropriate treatment recommendations aimed at reducing or eliminating factors within control of the child, their family, and medical providers. Medical and behavioral treatments are discussed in the next section.

Treatment

Treatments for epilepsy mainly include medication, surgery, and diet. Psychotherapy may be indicated to treat associated behavioral problems. Pharmaceutical treatments are discussed first, followed by surgical treatment. Finally, behavioral techniques are discussed.

Pharmacological Treatment

Anticonvulsant medication is the primary treatment for controlling seizures. Commonly prescribed medications include phenytoin, phenobarbital, carbamazepine, primidone, ethosuximide, and valproic acid. Appropriate medication selection can be difficult, as the various seizure disorders respond differentially to different medications (Novick & Arnold, 1988). In addition, there may be individual differences in terms of absorption rates and medication tolerance. Although they differ by medication type, common side effects include drowsiness, ataxia, lethargy, intellectual dulling, nausea, dizziness, headache, tremor, and appetite changes, among others (Novick & Arnold, 1988). There appears to be a relationship between certain medications and performance on specific tests of cognitive abilities (for a review, see Hartlage & Harlage, 1997). Specific medications and their side effects are discussed next.

Phenobarbital was associated with a variety of cognitive problems, such as intellectual, attentional, information processing, and psychomotor speed deficits (Solomon & Pfeffer, 1996). Intellectual deficits were also observed in children using phenobarbital (Hagar, 2008). Concentration and short term memory was also negatively affected (Hartlage & Harlage,
Phenobarbital was also linked to psychological problems such as depression, anxiety, irritability, hyperactivity, aggression, psychosis, and sleep disturbances (Solomon & Pfeffer, 1996). Similarly, primidone was negatively associated with attention, information processing speed, and psychomotor speed (Hartlage & Harlage, 1997).

Phenytoin was associated with similar types of cognitive and psychological disturbances (Solomon & Pfeffer, 1996). For example, phenytoin use was related to intellectual impairment, memory problems, depression, confusion, and psychosis. Phenytoin may also lead to encephalopathy (Solomon & Pfeffer, 1996).

Another commonly used medication, sodium valproate, has been associated with reduced reaction time, encephalopathy, aggression, and drowsiness (Solomon & Pfeffer, 1996). The medication has also been associated with liver toxicity and decreased social competence. Interestingly, research suggested that sodium valproate may also have some positive side effects, such as improved alertness, mood, and sociability, which seem to contradict findings about the negative side effects (Solomon & Pfeffer, 1996). Research by Hartlage and Hartlage (1997) found no significant relationships between use of sodium valproate and performance on several tests of cognition.

Similarly, carbamazepine has been associated with both negative and positive side effects. Negative side effects include aggression, hyperactivity, delinquent antisocial behavior, and in rare cases, psychosis. At the same time, carbamazepine was found to improve reaction time, eye-hand coordination, and manual dexterity (Solomon & Pfeffer, 1996). Another study found no significant effects of carbamazepine on performance on a variety of cognitive tests (Hartlage & Hartlage, 1997).

Benzodiazepines have been used less frequently, probably due to a combination of negative side effects and short duration of therapeutic effectiveness (Solomon & Pfeffer, 1996). Benzodiazepines in general and clonazapam in particular were associated with memory problems and increased likelihood of aggression, irritability, emotional instability, sedation, and disinhibition of behavior. The medicine also has limited utility regarding seizure control. Tolerance builds quickly; it loses its effectiveness after only a few months, after which seizure breakthrough may occur. Finally, ethosuximide may improve cognitive performance but may increase risk for psychotic behavior (Solomon & Pfeffer, 1996).

Another aspect of pharmacological treatment worthy of discussion concerns single versus multiple medication treatment and drug serum levels. In general, a single medication (monotherapy) is preferable to treatment using multiple medications (polypharmacy) in order to reduce the likelihood of toxicity in the liver (Bennett & Ho, 1997; Solomon &...
Pfeffer, 1996), in which most drugs are metabolized. Many patients experience good seizure control while on a single antiepileptic medication (Hagar, 2008). However, as many as 25% to 30% of patients may be refractory to drug treatment (Bebin, 2002) and thus may require multiple medications. Unfortunately, polypharmacy increases the risk of toxicity, and this risk is amplified in children (Solomon & Pfeffer, 1996).

In addition to damaging one’s organs, toxic levels of antiepileptic drugs have been associated with cognitive and behavioral dysfunction (Bennett & Ho 1997). Polypharmacy increases the risk of such problems. Particularly concerning is that adverse effects have also been noted even when serum levels were within the therapeutic range. For example, patients with higher serum levels of phenytoin or phenobarbital, compared to patients with lower levels, showed intellectual deterioration, psychomotor slowing, psychiatric illness, and personality change. Serum levels were in the therapeutic range and patients exhibited no cerebral lesions or drug toxicity (Reynolds & Travers, 1974). Similarly, Trimble and Corbett (1980) found that children who experienced a decline in IQ of 10-40 points over the course of a year had higher serum levels of phenytoin and primidone compared to those with lower levels. Moreover, discontinuation of phenytoin was association with improved motor speed, attention, and concentration (Bennett & Ho, 1997). Cessation of other drug use was also correlated with improved cognitive functioning. For example, in a double-blind study, discontinuation of sodium valproate and carbamazepine was associated with improved motor speed.

Finally, the number of drugs discontinued appears to be just as important as drug type. Bennet and Ho (1997) indicated that reducing polytherapy to monotherapy resulted in improvements in alertness, concentration, drive, mood, and sociability in 50% of patients. For most patients, medication treatment effectively controls seizures to the degree that patients are able to function in life. However, approximately 30% of patients continue to have uncontrolled seizures. For these patients, other forms of treatment such as surgery or behavioral interventions may be considered.

**Surgical Treatment**

Surgical treatment for epilepsy has been in existence for over half a century (Hartage & Hartlage, 1997). Children who do not respond to medications and have definable lesions in the anterior temporal lobe or clearly focal onset are potential surgical candidates. Neuroimaging is used to determine focal onset of seizure activity and have improved the accuracy of locating the focus of epileptic seizures in the brain (Bennet...
and Ho, 1997). CT, MRI, PET, and SPECT technology if frequently used to aid in determining epileptic focus. Neuropsychological testing, however, remains the gold standard of determining patient functioning and has contributed to improving the efficacy and safety of epilepsy surgery (Hartage & Hartage, 1997). Surgical success rates have been reported as high as 75%, with success defined as remaining seizure free for at least five years post-surgery (Bennett & Ho, 1997). In a 39-year longitudinal study of patients with partial seizures, in which surgical with medically treated patients were compared, seizure frequency was found to be better controlled with surgery. However, neurological deficits were also more frequent. Thus, neurologists and neuropsychologists should work together with patients to determine the most appropriate treatment option to optimize functioning and minimize impairment. The NIH Consensus Development Conference on Surgery for Epilepsy (1990) recommends that, at minimum, specialized epilepsy treatment centers that provide evaluative and treatment services for those with intractable seizures should include both neurologists and neuropsychologists, as well as other medical staff. Moreover, specialized epilepsy treatment centers should minimally include EEG, MRI, and neuropsychological testing to assist with evaluating surgical candidacy.

Behavioral Techniques

The Ketogenic Diet

A treatment option that may sound unorthodox is the ketogenic diet, which involves massive consumption of fats in proportion to calories with minimal intake of protein and carbohydrates (Bennet & Ho, 1997). While it may seem as if such a diet would cause inordinate weight gain, actually the individual’s weight is maintained on the ketogenic diet. Moreover, the diet has consistently been associated with successful control of epileptic seizures.

In a study of 58 children with refractory epilepsy and who experienced seizures at least three times per day despite proper medication adherence, 67% demonstrated improved seizure control on the ketogenic diet. Improvement was defined as a 50% or more reduction in seizures for a minimum of four weeks. An additional 28% of the total sample experienced complete seizure control. Sixty-four percent were able to reduce one or more antiepileptic medication while 10% were able to discontinue all medications. Changes occurred quickly, with improvement usually occurring within the first two weeks of starting the diet (Kinsman, Vining, Quaskey, Mellits, & Freeman, 1992).
The ability of the ketogenic diet was commonly used to reduce seizures prior to the 1920s, and while over 70 years of research has shown the diet to be effective, the exact mechanisms of action remain unclear (Bennett & Ho, 1997). Medical research indicates that the ketogenic diet mimics fasting, in which the body first burns up glucose in the bloodstream for energy. Once the glucose is depleted, the body begins to burn fat deposits. The body’s ketogenic state (i.e., the depletion of glucose and burning of fat deposits) can be medically monitored via identification of ketone bodies that are present in urine. A major downside to this intervention is that the diet must be followed precisely. Even mild deviations such as not finishing a meal or consuming a few more grams of protein can lead to seizure reoccurrence.

Psychological Treatments

A psychologist may possibly be the first provider to identify potential seizure disorder and then facilitate referral to a neurologist. For example, parents may take their child to a psychologist suspecting that the child is exhibiting a behavioral problem. Thus it is important for psychologists to be familiar with the differential presentations of epilepsy as well as referral sources in the community (Novick & Arnold, 1988).

Psychologists in general and neuropsychologists in particular are called upon to assess the cognitive and emotional problems that are frequently experienced by children with epilepsy. For example, psychologists are asked to conduct differential diagnosis of the child’s learning, emotional, and behavioral problems (Novick & Arnold, 1988). Thus, it is imperative that psychologists be familiar with the potential effect of epilepsy on children’s cognitive and emotional development, as well as normal growth and development and typical performance on tests of cognitive abilities and personality (Novick & Arnold, 1988).

Psychologists and neuropsychologists also assist children and families in dealing with the emotional and social repercussions of having epilepsy and any associated cognitive and behavioral problems. Psychologists and neuropsychologists are in a position to educate children and families about the disorder and provide counseling for issues regarding, for example, risks and benefits of drug therapy, medication compliance, and adjustment to living with a chronic condition (Solomon & Pfeffer, 1996). Psychologists and neuropsychologists can also provide treatment in the form of traditional group and individual therapy to children and their families as well as serve as an educational resource to help children and families deal with psychosocial stressors, help families and teachers devise ways to manage the disorder, and provide stress management or...
biofeedback training as a behavioral method for reducing seizure frequency (Bennett & Ho, 1997).

Finally, psychologists and neuropsychologists recognize that in order to facilitate social development, the epileptic child should be permitted to participate in school-related activities such as class trips and recreational activities. While participation in sports is associated with small risk, children and their parents should weight the risks of feeling restricted and isolated from peers. Seizure control varies across the epilepsies, and decisions and recommendations should be handled on a case-by-case basis. For less controlled seizures, other hobbies can be encouraged such as photography and music (Solomon & Pfeffer, 1996).

RESEARCH IMPLICATIONS

Many clinical concerns have been discussed, such as identification and treatment of epilepsy. The final topic mentioned briefly here concerns research. There are many problems associated with research on epilepsy. Heterogeneity of epileptic disorders make systematic study of associated cognitive and behavioral deficits difficult, and caution should be taken when applying research results across seizure classes. Spurious variables, such as brain injury, CNS disease, seizure type, seizure frequency, duration of the disorder, drug dosages, absorption rates, and compliance should be adequately controlled for in research studies. Also, treatment efficacy and potential harmful side effects of drug treatment must also be carefully considered. For example, after just one year on the market, felbamate was found to cause liver and bone marrow failure, and was subsequently taken off the market. Since that time, guidelines for new drug trials include careful monitoring of cognition and behavior (Commission on Antiepileptic Drugs of the International League Against Epilepsy, 1994). While living with seizures is a huge burden for many patients, epilepsy also remains a challenge for interventionists and researchers working to attenuate the negative effects of this often violent and unpredictable chronic condition.

REFERENCES


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