Until quite recently, the seizure disorders of childhood were broadly associated with generalized disruptions in brain maturation and, by association, the complete range of behavioral and intellectual deficits common in children with epilepsy. This concept of pediatric epilepsy as a cause of diffuse cognitive problems was supported by several lines of evidence as well as by clinical experience. However, recent refinements in clinical and psychological testing indicate that the epilepsies of childhood are distinct neurologic entities with equally distinct psychological outcomes. As researchers continue to explore the complicated links between seizure activity and psychosocial and neurologic traits, clinicians will be in a better position to make treatment decisions.

This article describes the evolving view of pediatric epilepsy as clusters of specific impairments often amenable to specific interventions rather than a sweeping age-related diagnosis associated with a high likelihood of inevitable behavioral and cognitive problems.

**The Traditional View: Children with Epilepsy Tend to Have Generalized Cognitive and Psychosocial Difficulties**

A generally accepted theory is that as many as half of all children who develop chronic epilepsy will display academic difficulties, behavioral disorders, psychiatric dysfunction, or lower quality of life.\(^1\,2\) One seminal study found that behavioral disorders were 2 to 3 times more frequent in children with epilepsy than in the general population.\(^3\) The characteristics evaluated included impulsivity, irritability, aggressiveness, hyperactivity, and opposition. Adults with childhood-onset epilepsy have also shown rates of psychiatric complications about 2 to 3 times greater than that seen in a control population.\(^4\)

Other studies have documented that the school performance and intellectual quotient (IQ) of children is significantly lower than in the general population.\(^5\,6\) In fact, 12% to 14% of children with epilepsy have an IQ lower than 70.\(^7\) Conversely, a high percentage of mentally deficient children are found to have epilepsy.

Often harder to measure, but no less recognized, are epilepsy-related psychological problems such as anxiety, depression, lack of motivation, poor self-
esteem, and at times, autistic behavior and even psychotic episodes. Socially, these children may also be withdrawn and display subtle academic problems. While some psychosocial problems may be attributable to the epilepsy itself or to the anticonvulsant medications, many of these impairments may stem from the child's emotional reaction to the illness. For example, dealing with “differences” in social settings, the possibility of peer rejection, and the lack of control over seizures often can produce tremendous psychosocial pressure for a child. Similarly, because of frequent hospitalizations and anxiety over seizure-related injuries, family conflicts may also be an issue, such as siblings reacting adversely to overprotectiveness granted to the child with epilepsy.

**THE EVOLVING VIEW: NOT ALL EPILEPTIC CHILDREN HAVE THE SAME COGNITIVE DEFECTS**

While no one questions that children with epilepsy are, overall, at an increased risk for developing psychological, intellectual, and social problems, considering all children with epilepsy as a single group with a single disorder is becoming increasingly difficult. Instead, as in adults, specific sets of clinical and electrophysiological characteristics are becoming clear. As the distinctions between various pediatric epilepsies grow sharper, the expectations for psychological outcomes are shifting, and different clinical entities are now seen as having their own unique cognitive expressions. For instance, generalized convulsions and epileptogenic encephalopathies can produce specific cognitive deficits. This may happen when the underlying epileptogenic process occurs at the precise time of the myelogenetic or synaptogenetic development of a neural structure.

As an example, because the myelination process for the occipital, frontal, and temporal lobes occurs so late in development, typically from 6 to 12 months of age through puberty, the functions of these areas are at risk from any epileptic event during this phase. In West's syndrome, with a known onset between 4 and 7 months of age, one long-term consequence is visual agnosia. Individuals who have difficulties recognizing visual objects and faces may in turn develop autistic features. These visual defects may be related to a disruption in the development of the posterior associative cortex during the exact period of disease onset. In fact, studies in children with West's syndrome have documented perfusion defects in the parieto-occipital regions by single photon emission computed tomography (SPECT) studies.

Another example of epileptic events impinging on specific epochs of brain development can be seen in the rare Landau-Kleffner syndrome. The onset of this condition is typically between 3 and 7 years, corresponding to an important period of language development. A common long-term consequence of this syndrome is receptive aphasia.

Another aspect of brain development vulnerable to epileptic disruption is synaptogenesis. Several lines of research suggest that mammals have a period of significant synapse creation between the ages of 0 and 2 years. The extra synapses are progressively eliminated until they reach a plateau stage in middle age.
then progressively decline after 60 to 70 years of age (Figure 1).11

When epileptic activity was induced in the occipital cortex of month-old rabbits, immature and nonspecific projections that are normally eliminated during development were maintained in the mature animals; the conclusion of this study was that the epileptic activity stabilized the immature, and aberrant, callosal projections.12 Current views suggest that increasing cognitive capacities during childhood may coincide with the gradual loss, rather than formation, of new synapses.13 If such a loss is prevented by an epileptic event, cognitive deficits may arise.

**Psychological Consequences After One Episode of Status Epilepticus**

To pursue the question of whether or not the brain can avoid cognitive impacts after a single episode of status epilepticus (SE), a pilot study was recently initiated involving 20 children with idiopathic SE. The 9 girls and 11 boys had experienced 1 SE episode of more than 30 minutes’ duration when they were a mean age of 12.9 months. Preliminary results with cognitive testing 3 months after the episode revealed several significant differences between these children with SE and a control group of 34 children (13 girls, 21 boys) with the same socioeconomic status but no history of epilepsy (Figure 2).

In this ongoing study, the differences in the developmental scale scores were still evident after 9 months. Although a group of 9 children (3 girls, 6 boys) with 1 episode of febrile convulsions (lasting less than 20 minutes) had consistently lower scores on the same Griffith’s developmental scale tests, the differences were not statistically different. Thus, preliminary results from clinical trials and some animal data indicate that even a single episode of SE in infancy may have long-lasting consequences on brain development and cognitive performance.

**Neuropsychology of Focal Epilepsies**

In the search for a more precise characterization of the developmental and psychological sequelae of childhood epilepsies, much research attention has turned to the focal epilepsies. As described in the remainder of this article, this line of research has been increasingly successful in correlating several well-defined partial epilepsies of childhood with distinct neuropsychological profiles.

**Temporal Lobe Epilepsy**

While not typically associated with subnormal intelligence,14 temporal lobe epilepsy with early onset can produce increased risk for severe retardation15 and developmental language disorders.16 Basic reading skills such as comprehending fillies or segmenting syllables may be compromised.

The eventual patterns of lateralized brain function seen in adults may be foreshadowed in the type of memory or reading deficits seen in these children...
with focal seizures of the temporal lobes. For example, poor reading performance in school-age children has been associated with left temporal lobe epilepsy.16 In these children, the loss of verbal memory may reduce the ability to learn words and stories. While these verbal memory deficits are greater in those with left temporal foci, children with right temporal lobe seizures exhibit greater impairment of visual-spatial memory, such as remembering the location or appearance of an object.17

In terms of psychiatric problems, autistic regression has been noted in some children with temporal lobe seizures.18 Psychopathological traits, such as rage outbursts and increased aggressiveness, have also been noted to occur at higher rates in these children.19 Although the involvement of the temporal circuits in emotions may explain such a high frequency of psychopathology, the impact of temporal lobe laterality on such behavioral disorders is uncertain.

FRONTAL LOBE EPILEPSY
Epilepsy in the frontal lobes, which are intimately associated with motor function, speech, and regulation and organization of behavior, may be associated with a broad range of psychological deficits. Based on case studies, frontal lobe epilepsy in children appears to produce a syndrome including disinhibition, physical and verbal aggression, and cognitive defects, including difficulty with divided attention and planning.20 Many of these features parallel findings in adults with frontal lobe epilepsy.

PARIETO-OCCIPITAL LOBE EPILEPSY
Epilepsies of the parieto-occipital lobe are rare in children. When they occur, they may produce subjective sensations (eg, tingling and numbness), ideomotor apraxia (eg, the inability to move a body part even though paralysis is not present), and visual disturbances. Many of these clinical phenomena are rare in most patients with seizures and likely reflect the epileptogenic activity in the sensory-rich parieto-occipital region. Seizures are also sometimes provoked by specific activities such as mathematical or spatial activities that may preferentially trigger parietal lobe functions or by watching television, video, or computer screens, which may trigger occipital lobe functions.

MOVING TOWARD A NEUROPSYCHOLOGICAL PROFILE
In our clinic, we set out to explore the possible connections between distinct epilepsy types and performance on tests of important but often difficult to measure mental and behavioral characteristics such as motor coordination, attention span, memory, visual perception, and planning ability. Our goal was to determine whether the neuropsychological profiles of common childhood epilepsies could be defined.

The study group consisted of 16 children with frontal lobe epilepsy, 8 children with temporal lobe epilepsy, and 8 children with generalized absence seizures. All 3 groups were within the average range of global IQ and were also comparable in terms of age, age at seizure onset, and duration of epilepsy. The tests administered included: The Wechsler Intelligence Scale for Children, version III (WISC-III), the California Verbal Learning Test for Children, the Continuous Auditory Performance Test, the Purdue Pegboard Test, Thurstone’s Unit and Bimanual Performance Test, Luria’s Motor Sequences, Wisconsin Card Sorting Task, Self-Ordered Pointing Task, Verbal Fluency Test, and the Tower of London test.

Results from these and other tests, plus teachers’ ratings on the Achenbach’s Child Behavior Checklist, indicate that children with frontal lobe epilepsy have deficits that are commonly seen in adults with frontal lobe epilepsy. These include problems with motor coordination, planning abilities, mental flexibility, and behavioral control (eg, thought disorder, social problems) as well as divided attention.

When the Tower of London test results from the 3 groups were plotted against the results from a large normative group of 200 children who do not have epilepsy, many children with frontal lobe epilepsy were at least 2 standard deviations beyond the average (Figure 3). The test measures both planning time and execution time required for moving labeled balls from an initial position to one of several goal positions. As shown in the results, those children with frontal lobe seizures exhibit a very slow low planning time, which translates into a relatively high execution time because they have to readjust their strategy while performing the task. Children in the other groups are more often within 1 standard deviation of the norm.
Other tests can reveal qualitative differences in underlying neuropsychological damage between the epilepsy seizure types. For instance, in the Complex Figure Drawing Test, the child with temporal lobe epilepsy can often competently copy a figure as requested, but he or she typically cannot clearly reproduce the figure from memory—an indication that visual-spatial memory has been affected. The child with frontal lobe epilepsy, on the other hand, will produce a very poor first copy of the figure but, when the original figure is taken away, reproduce a very similar poor copy from memory. The impulsiveness and lack of organization is revealed by the first part of the test, but the intact spatial memory is displayed by the second half of the test.

Such profiles of neuropsychological traits in children with a history of focal epilepsy—if they can be refined and repeated—may soon allow improved pre- and postsurgical assessment. Much work remains to be done. As the distinct cognitive expressions of pediatric epilepsy are revealed, improvements in the timing and methods of intervention in childhood epilepsy will be possible.

Figure 3. Children With 1 of 3 Different Types of Epilepsy: How They Perform on the Tower of London Test

PLE = frontal lobe epilepsy (n=16); TLE = temporal lobe epilepsy (n=8); GEA = generalized epilepsy (absence) (n=8).
QUESTIONS & ANSWERS

Previous studies suggest that at least 4 grand mal seizures were necessary before cognitive problems developed. This presentation suggests even a single epileptic seizure in children can produce such problems. Why the difference?

Dr Lassonde: Possibly because earlier studies included patients with mixed etiologies; for example, status epilepticus patients with meningitis, with tumors, or who were symptomatic. Our studies included only asymptomatic children who had a single episode and no recurrences. The new animal data are also indicating that disturbances may be related to 1 single episode of epileptic seizures.

Is the pediatric brain more resistant to epileptic injury than the adult brain?

Dr Riviello: This is an old idea that may be incorrect. In many of the older studies of status epilepticus, for example, the duration of a seizure in adults that were left with deficits was often longer than the duration of seizure in children. The neuropsychological data presented by Dr. Lassonde also support the idea that the pediatric brain is actually more sensitive to injury.

Dr Lassonde: The concept of neural plasticity in childhood is still valid in certain settings, such as neurosurgery. In split-brain surgery, for example, children do not develop the disconnection symptoms seen in adults. The developing brain can reorganize itself. But with epilepsy, which is an ongoing process occurring during key developmental steps, plasticity is a less applicable concept.

Are the cognitive and behavioral problems described in this presentation caused by the seizures, an underlying lesion, or perhaps even the medication?

Dr Lassonde: We don’t know for sure, although none of the children tested had a seizure in the 2 months prior to testing. Also, only a few of the children had an identifiable lesion. Overall, we believe that the seizures impact development of the brain, which is reflected in the specific cognitive deficits.

Dr Bourgeois: This question is made even more difficult to answer by the additional unknown role of subclinical discharges. Some patients with so-called postictal aphasia may have ongoing epileptiform discharges, detectable only by depth electrodes. This transient cognitive impairment is underrecognized and underrated. However, the cognitive disorders are probably not associated with medication because the deficit types vary while the patients are probably all on the same mix of medications.

Are children with bitemporal epilepsy more severely impaired?

Dr Duchowny: Some case reports indicate that bilateral hippocampal involvement is associated with autism. In our experience, children with independent temporal lobe discharges are unusual, but this is uniformly associated with severe impairment and major illness such as autism, psychotic thought disorders, or cognitive and behavioral disorders.

Dr Lassonde: In our small study, we saw no differences between children with unilateral focal epilepsy and those with bilateral epilepsy. But we are aware of the possible connection with autism. The pattern of the unilateral seizures, and whether or not they are truly independent or spreading via the corpus callosum, needs to be studied.

REFERENCES