Behavioral Issues in Pediatric Epilepsy

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Epilepsy is one of the most common chronic neurological disorders of childhood. Therapy should consist of education to reduce fears and concerns, psychotherapy to decrease triggers for seizures, and careful medication monitoring to avoid those drugs that reduce seizure threshold or have excessive interactions with antiepileptic drugs.

Seizures are symptoms caused by abnormal discharges from neurons in the central nervous system. Based on the description of the episode and the results of an electroencephalogram (EEG), seizures are classified as generalized or partial. Epileptic syndromes are classified as localization-related (focal) epilepsies or generalized epilepsies. They are considered symptomatic if there is a known abnormality, cryptogenic if there is presumed but unproven damage, and idiopathic if the disorder is familial or not associated with additional CNS damage. Epilepsy is one of the most common CNS disorders affecting children, with approximately 5% to 10% of children having a seizure during the first two decades of life and 1% developing epilepsy. Childhood epilepsy is a particular concern to psychiatrists because of the frequency of associated behavioral problems. The prevalence of behavioral problems in children with epilepsy is twice that seen in children with chronic illnesses not involving the CNS and four times that seen in healthy children (Rutter et al., 1970). There are multiple risk factors for behavioral problems in children with epilepsy and a variety of behavioral problems seen in them.

Risk Factors
Demographic and biological factors have been extensively evaluated as possible risk factors for behavioral problems. An early age at onset has been a predictor for cognitive problems, but has been less reliable as a predictor of behavioral problems. Central nervous system damage is one of the most consistent risk factors. Rutter et al. (1970) and Steffenburg et al. (1996) have shown that more than half of children with epilepsy and additional evidence of CNS dysfunction have significant behavioral problems. Of the seizure variables, age of onset and seizure type and focus have been inconsistent predictors, whereas seizure frequency and severity have been better predictors of emotional trouble (Dunn and Austin, 1999). Antiepileptic drugs (AEDs) are not major determinants of risk for behavioral problems. However, both phenobarbital and the benzodiazepines have been associated with hyperactivity, and behavioral troubles have also been attributed anecdotally to many of the other AEDs (Bourgeois, 1998).
Psychosocial factors are also important in determining risk of behavioral troubles in children with epilepsy. Hoare and Kerley (1991) and Austin et al. (1992) have shown that stress within the family is associated with behavior problems. Poor communication within the family was a major risk factor for depressive symptoms in adolescents with epilepsy (Dunn et al., 1999). The child's attitude toward the illness has been associated with behavior, with a negative attitude related to poor self-concept and depression (Austin and Huberty, 1993). An attribution style in which control was thought to reside in factors unknown or beyond one's self was a predictor of depression in adolescents with epilepsy (Dunn et al., 1999).

Behavioral Problems
Children with epilepsy are at risk for certain specific diagnoses. Symptoms of attention-deficit/hyperactivity disorder (ADHD) have been found in approximately a third of the children with epilepsy. These children more often have symptoms of inattention than hyperactivity or impulsivity (Dunn, 2001). Mood disorders are also common, with approximately one-fourth of adolescents with epilepsy having symptoms of depression (Dunn et al., 1999). Anxiety has not been assessed as often as mood disturbance, although two studies have found an increased risk, especially in adolescents (Ettinger et al., 1998; Oguz et al., 2002). Approximately a third of children with autistic disorder may have seizures during their lifetime. The rare Landau-Kleffner syndrome of acquired epileptic aphasia is part of the differential diagnosis of autistic disorder. A schizophreniform psychosis has been seen in adults with epilepsy but seems to be uncommon in children, although
Caplan et al. (1997) have found illogical thinking in children with partial complex seizures.

**Education and Psychotherapy**

Treatment should include education and psychosocial therapies. The treating physician needs an understanding of both AEDs and psychotropic medications. Unfortunately, there are very few intervention studies to guide therapy.

Education for the child and parents should occur early in therapy and may prevent emergence of behavioral difficulties. In our studies of children with new-onset seizures (McNelis et al., 1998; Shore et al., 1998), we found that both children and parents had many fears and concerns. Children worried about social aspects of seizures, such as how to talk to others about their seizures and about the possibility of having a seizure in public. We found that 13% of the children with new-onset seizures were avoiding activities because of fears of having another seizure.

Of the parents, mothers reported more concerns than fathers. Six months after the first seizure, between one-third and one-half of the mothers said they worried about each of the following: brain tumors, death from seizures, cognitive decline and addiction to antiepileptic drugs. Approximately half of the children and their mothers expressed a desire for more support in dealing with seizures. Group education has been utilized for families of children with epilepsy. Lewis et al. (1990) found improved knowledge of epilepsy in children and mothers and a reduction in maternal anxiety after group education. We have used a small group approach to education (Austin et al., 2002), providing information and emotional support and assessing participants before and after the intervention. Knowledge of epilepsy increased and information and support needs decreased for both children and parents.

Both individual and group psychotherapy techniques have been used successfully in children and adults with intractable seizures. Most reported interventions have begun with assessment of seizure precipitants, looking particularly for emotionally based triggers for seizures. The therapist next taught relaxation techniques or self-control and advised family members about the value of a neutral response to seizures (Dahl et al., 1985; Puskarich et al., 1992; Spector et al., 1999; Williams et al., 1979). The outcome of these therapies included a reduction in seizure frequency and improvement in self-esteem.

**Psychopharmacology**

Decisions on diagnosis and therapy should include a review of medications used to prevent seizures and possibly modifications if the AED seems to be contributing to behavioral difficulties. For most of the currently used AEDs, behavioral side effects are minimal or infrequent. Lethargy is a side effect that has been attributed to almost all AEDs. Hyperactivity and irritability due to barbiturates and benzodiazepines have been reported, with a few anecdotal reports of hyperactivity and aggression associated with gabapentin (Neurontin), lamotrigine (Lamictal) and vigabatrin (Sabril). There are case reports of delirium with phenytoin (Dilantin) and valproate sodium (Depacon), as well as psychosis with ethosuximide (Celontin), topiramate (Topamax), levetiracetam (Keppra), zonisamide (Zonegran) and vigabatrin. Topiramate may cause inattention, confusion and delay in word-finding, particularly if the dose is increased too rapidly. It may be necessary to change AEDs to determine if a behavioral problem is a side effect of medication or a feature of the child’s illness.

Antiepileptic drugs may have positive effects on behavior (Ketter et al., 1999). Divalproex sodium (Depakote) and carbamazepine (Tegretol) are helpful in some patients with bipolar disorder, and emerging data suggest that other AEDs such as gabapentin and lamotrigine may be beneficial. Lamotrigine seems to have a positive effect on depression in patients with epilepsy, and gabapentin may be useful for anxiety. Discontinuation of AEDs has been associated with withdrawal-emergent psychopathology.

If the child has developed a significant behavioral problem, psychotropic medication may be necessary. Decisions on drug use should be based on likely effectiveness, drug interaction with AEDs, and potential effect on the seizure threshold (Barry and Huynh, 2002). Stimulants, such as methylphenidate (Ritalin, Concerta, Methylin, Metadate) and dextroamphetamine (Dexedrine) are first-choice agents for children with epilepsy and ADHD. There seems to be minimal, if any, lowering of seizure threshold with these agents. The selective serotonin reuptake inhibitors can be used as first-choice agents to treat depression or anxiety since they have minimal effect on seizure threshold. There may be inhibition of the cytochrome P450 (CYP) enzymes by SSRIs that causes an increase in phenytoin, carbamazepine and valproate levels. Similarly, nefazodone (Serzone) may inhibit CYP 3A4, thus increasing carbamazepine levels. There is an increased risk of seizures with higher dose bupropion (Wellbutrin), clomipramine (Anafranil) and maprotiline (Ludomil), and a lesser though still increased risk with imipramine (Tofranil), desipramine (Norpramin) and nortriptyline (Aventyl, Pamelor). Drug interactions with phenobarbital, phenytoin and carbamazepine may lower
tricyclic antidepressant levels. Chlorpromazine (Thorazine) and clozapine (Clozaril) are the antipsychotic medications with the highest risk for seizures. The risk is low with haloperidol (Haldol) and is probably low with the atypical antipsychotics, although less information is available. Decreased serum levels of antipsychotics have been reported when patients are receiving concomitant phenobarbital, phenytoin or carbamazepine.

**Treatment Integration**

We are not aware of any studies in the literature on the integration of psychotherapy and pharmacology for children with epilepsy. However, we are convinced that optimal care is best provided in an integrated fashion, by either a neurologically informed psychiatrist or psychologically minded neurologist. The psychotherapeutic skills that strengthen the alliance between physician, child and family should facilitate recognition of fears and concerns about epilepsy and reduction in stresses that may increase seizure frequency. A therapeutic alliance will promote adherence to consistent use of AEDs, thus reducing the risk of seizure relapse. Knowledge of pharmacology is essential for recognition of behavioral problems due to AEDs and for optimal management that requires both psychotropic and antiepileptic drugs.

Research is now moving from therapy to prevention, identifying gene locus and function for the epileptic syndromes, and increasing our understanding of developmental aspects of epileptogenesis and molecular targets for drugs. The current emphasis on quality of life assessment for the child with epilepsy should lead to earlier recognition and better therapies for the behavioral problems seen so frequently in these children.

**References: References**

17. Puskarich CA, Whitman S, Dell J et al. (1992), Controlled examination of effects of progressive


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