

Psychiatric Aspects of Childhood Epilepsy

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Abstract

Childhood epilepsy is a chronic, recurrent disorder of unprovoked seizures. The onset of epilepsy in childhood has significant implications for brain growth and development. Seizures may impair the ongoing neurodevelopmental processes and compromise the child's intellectual and cognitive functioning, leading to tremendous cognitive, behavioral and psychosocial consequences. Children with epilepsy are at increased risk for emotional and behavioral problems. In addition to the direct effects of epilepsy, there are multiple contributory factors including the underlying neurological abnormalities and adverse effects of medication. This review discusses the current understanding of various psychiatric aspects of childhood epilepsy, including the neuropsychological, behavioral and psychosocial concomitants of childhood epilepsy.

Keywords: Childhood epilepsy; Psychiatric aspects; Psychosocial aspects

Introduction

Childhood epilepsy is a chronic, recurrent disorder with a prevalence rate of 4-8 cases per 1000 children, of which nearly one-third are associated with a developmental disability (1-3). As childhood epilepsy involves the brain during an active period of growth and development, it may interfere with the cognitive process of the brain (4). Recurrent seizures may lead to tremendous behavioral and psychological consequences (5,6). Living with epilepsy can be quite challenging for the young patients and their families, posing a considerable psychosocial burden.

The review discusses the current understanding of psychiatric aspects of childhood epilepsy, focusing on the neuropsychological, behavioral and psychosocial concomitants of childhood epilepsy. The psychiatric considerations in the evaluation and management of children with epilepsy have been discussed. We begin with a brief overview of childhood epilepsy.

Childhood Epilepsy: An Overview

Childhood epilepsy is considered as a heterogeneous condition resulting from various causes, mostly idiopathic and comprises of various syndromes and seizure types. The Commission on Epidemiology of the International League Against Epilepsy published a diagnostic scheme based on the following five axes: (a) behavior during the seizure, (b) types of seizures (generalized like tonic-clonic, absence, myoclonic or focal with/without secondary generalization), (c) detailing specific syndromes (such as Lennox-Gestalt syndrome), (d) causes and (e) resultant impairments (7). Generalized epilepsy/syndrome types are more often seen in children 0-6 years of age and partial/localization-related in the age period of 6 to 15 years (8). Nearly

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80% of cases with epilepsy have an onset in childhood, and if untreated, epilepsy tends to follow a chronic and recurrent course extending into adulthood. Nearly two-thirds of children with epilepsy respond favorably to treatment and of these, 70% are able to discontinue medication after a few years (9). Nearly 10-15% have intractable seizures defined as failure of trial with two or more anti-epileptic drugs (8,10). Surgical treatment is usually considered for children with disabling intractable epilepsy or localized seizure activity. Although long-term seizure outcomes are generally favorable, the patients may continue to experience adverse long-term psychiatric and psychosocial outcomes.

Neuropsychological Function

The onset of epilepsy in children has significant implications for brain growth and development. Seizures may impair the ongoing neurodevelopmental processes and compromise the child's intellectual and cognitive functioning (4). Earlier studies primarily focused on intellectual quotient (IQ) tests in children with epilepsy; however, more recent studies have tested a wide range of neuropsychological functions including attention and concentration, learning and memory, and executive functions.

General Intellectual Functioning

The famous Isle of Wight study had indicated that although the mean IQ score of children with epilepsy was comparable to healthy controls, it displayed a higher variability than the control group, with several children scoring above average and many others in the mentally handicapped range (11). While a vast majority of children with epilepsy fall within normal limits of IQ scores, a sub-group of children appears to have subnormal intellectual functioning. Subsequent research suggests that children with epilepsy have a three times higher risk for mental retardation and academic underachievement or failure. The frequent co-occurrence of neurological abnormalities such as tuberous sclerosis, chromosomal abnormalities may be a contributing factor towards lower IQ, as intellectual impairments are less prominent in children with idiopathic childhood epilepsy (12). Certain clinical characteristics such as early onset, high seizure frequency and history of status epilepticus

are associated with lower IQ scores. It is likely that different seizure types are associated with distinct IQ profiles, with an earlier study showing mean score of 106 in classic absence seizures, 99 in generalized tonic-clonic, 94-96 in focal and 70 in minor motor or atypical absence seizures (13). More recent studies also found differences in full-scale IQ across various seizure types. Children with generalized symptomatic epilepsy scored significantly lower than temporal lobe epilepsy and generalized idiopathic epilepsy (14). The delineation of epileptic syndrome may have important implications for the intellectual potential of the child.

Cognitive Impairments

Studies show that nearly one in four children with epilepsy have a subnormal cognitive functioning (15). The cognitive deficits are commonly seen in attention, working memory and executive functions like planning, organization and mental flexibility. Visual spatial functions and concept formation are also affected, as are language abilities and fine motor skills (5,15). Children with cryptogenic localization related epilepsy experience cognitive difficulties in alertness, mental speed and memory and these deficits are more prominent at a younger age (16). Hemisphere-specific disruptions of cognitive skills have been found in temporal lobe epilepsy, with left-sided lesions showing lower performance on verbal memory tasks and right-sided lesions having decreased visual memory functioning (17). The cognitive deficits in idiopathic generalized epilepsy are less prominent compared to focal epilepsy with specific deficits pertaining to the area of origin. Cognitive profiles in epilepsy are as heterogeneous as the epileptic syndromes themselves and are possibly related to the clinical characteristics of epilepsy, such as age at onset, multiple seizures, medication status, presence of subclinical EEG activity, the underlying cause and type of epilepsy. (15,18). Some studies did not find a difference in cognitive functions across the seizure types and instead, suggested a diffuse effect reflected in a pattern of decreased attention skills (17). It has also been suggested that although chronic epilepsy generally impairs cognition, but it also induces processes of functional reorganization and behavioral compensation (19).

The link between childhood epilepsy and cognition is complex, and depends on varying interactions between the underlying cause of epilepsy (such as physiologic disturbance, genetic defect), direct effects of seizure activity on brain structure and function, and/or the medications used to treat seizures. The adverse familial and psychosocial factors often seen in cases with childhood epilepsy may also contribute to cognitive dysfunction. Some new onset cases of childhood epilepsy display cognitive deficits pointing to the presence of antecedent anomalies in cognitive development. The varying interactions between multiple factors make it highly unlikely to have a single unified neuropsychological picture of childhood epilepsy (20). Most recent literature is trying to link the cognitive abnormalities directly to indices of structural, functional, metabolic, and other neurobiological markers of cerebral integrity, independent of their association with clinical epilepsy characteristics (21). The possibility of a progressive neuropsychological decline has been raised in cases of childhood-onset temporal lobe epilepsy as evident by a reduced hippocampal and total brain volume compared to adult-onset cases (22). It has been proposed that childhood-onset epilepsy is associated with an adverse neurodevelopmental impact on the brain, which represents an early acquired vulnerability, effectively reducing cerebral reserve and placing children at risk for progressive cognitive decline in the context of chronic and unremitting epilepsy.

Cognitive Adverse Effects of Medication

While treatment with antiepileptic drug may improve cognition by reducing the number of seizures, the negative side-effects of sleepiness, slower reaction time and deficits in attention may contribute to impairments in learning and cognitive performance. Unlike adults, cognitive side effects in children occur against the backdrop of ongoing cognitive and psychosocial development, and treatment decisions made in childhood may have lifelong implications. Common side effects of anti-epileptic medication are slowed motor and psychomotor speed, poorer attention and mild memory impairment. Phenobarbital and traditional benzodiazepines are associated with the greatest risk of cognitive side effects. Children on phenobarbital may fail

to catch up and compensate in educational achievement even after 3-5 years of discontinuation, pointing to a more complex effect than simply interfering with new learning ability.

The cognitive side effects of carbamazepine, phenytoin and valproate sodium are comparable and associated with modest psychomotor slowing accompanied by decreased attention and memory. Lamotrigine is associated with little or no objective cognitive impairment, while topiramate may have significant cognitive side-effects (23).

Emotional and Behavioral Problems

Epidemiological studies have shown that behavioral disturbances are five-fold higher in children with epilepsy (28%) compared to children from the general population and 2.5 times higher compared to children with other chronic conditions like diabetes and asthma (11,24,25). Characteristics common to chronic illnesses such as strict medication regimen, frequent hospitalizations, and limitation of activities are present in childhood epilepsy. However, the higher prevalence of psychopathology cannot be solely attributed to the chronicity of disease, and it appears that specific epilepsy-related factors such as underlying brain dysfunction may have a role. This is in accordance with the general finding that children with neurological disorders are at higher risk for psychopathology than children with non-neurological diseases. Even a limited period of seizures in childhood may lead to long-term effects extending into adulthood (9).

A meta-analysis of 46 studies (n=2,434) showed medium to large effect sizes for an increased risk of behavioral problems, both internalizing and externalizing, in children with epilepsy (5). Children with epilepsy are at increased risk for the whole range of psychopathology, especially attention/hyperactivity problems, mood and somatic symptoms.

Nearly 20-35% of children with epilepsy have clinical attention-deficit hyperactivity disorder, mostly inattention type, compared to 3% to 7% of the general pediatric population (26, 27). Even newly diagnosed cases of childhood epilepsy have an increased risk for inattentiveness and hyperactivity (28, 29). Children with complex partial seizures have an elevated risk

of internalizing symptoms, including depression and anxiety (30). The mood symptoms are seen more often in older children and adolescents with epilepsy rather than young children. Psychosis is rare in childhood epilepsy and in case of occurrence, is usually in association with complex partial seizures. Sleep disturbances appear to be common in children with epilepsy and have been associated with behavioral problems (27).

Some clinical variables; namely, seizure control or seizure frequency, type of epilepsy, age of onset, duration and localization may have a possible association with behavioral problems, though results have been mixed (31). It is unclear whether the behavioral changes are specific to epilepsy type. While some studies found no difference between seizure types, others have reported higher behavioral problems in partial seizures compared to other seizure types (31,32). Recent research has suggested that unlike adults, foci in the right hemisphere led to worse emotional and social functioning, demonstrating that seizures impact the brain differentially during development (33). Age of onset is a complex confounding variable in behavioral studies of epilepsy because young age is more likely to be associated with mental retardation or neurological abnormalities, difficult-to-control seizures and multiple anti-epileptic drugs, all of which may be associated with behavioral problems. The anti-epileptic drugs may also be associated with a wide range of behavioral symptoms, particularly in children on polytherapy (34). The etiological framework proposed by Noeker and colleagues highlights four major causes that have to be differentiated when considering the origin of behavioral dysfunction in epilepsy: (a) effects of underlying CNS damage and dysfunction, (b) the impact of epileptic activity, (c) effects and side-effects of antiepileptic drugs and (d) psychological coping reactions in the patient and in the family. These variables act within the biological context of the developing brain structure and the psychosocial context of child development (35).

Familial and Psychosocial Adjustment

Population-based studies show that nearly 70-75% of children with epilepsy have some type of disability or handicap affecting their daily life and choices for the future (36). Epilepsy can result in many psychological

difficulties in children, at onset or on realization of being different from other children. The unpredictability of seizure episodes, social embarrassment, feelings of lack of control and helplessness may lead to negative impact on self-esteem and self-confidence during the growing years. The child may feel social isolation and have poor social adaptation which can result from perceived stigma or over-dependency caused by parental overprotection. There may be a reluctance to engage in social interaction, with concomitantly low self-esteem and under-achievement. Children with epilepsy have a poorer health-related quality of life. The epilepsy related factors such as presence of co-morbid impairments and being on multiple anti-epileptic drugs were the best predictors for a poor health-related quality of life in children (37).

Children with epilepsy did not succeed in passing the normal comprehensive school in comparison to healthy controls (20% v 2%), had left school at the secondary level (53% v 46%) and remained without any vocational education (27% v 11%) to empower them (38). A combination of childhood epilepsy and poor cognitive development is more likely to be associated with adverse long-term outcomes such as under-employment and being unmarried or single as an adult. Significant social deficits were found in children with epilepsy in rural India (39). The boys had limited peer group activities, and parents conferred fewer responsibilities to school age and adolescent children compared to controls. In preschoolers parental overprotection was reported. The nature of the social deficits was beyond the constraints imposed by the neurological impairments. The parental criticism and psychological control was associated with higher behavioral problems, whereas parental acceptance was associated with lower levels of externalizing behavior problems in children with epilepsy (5). This suggests the complex nature of interaction between the child's behavioral problems and parental reactions, also providing a window for opportunity for family interventions.

Epilepsy poses a significant psychosocial stressor for the entire family and is associated with negative impact on the mental health of other family members. Parents of children with new-onset epilepsy spent more time in health care, had less recreational activities and had

more life stress compared to controls (40). Epilepsy in children presents an ongoing demand on the family's ability to adapt and function, challenging the coping resources of parents. Parents, especially mothers have significant more worries and stress around the epilepsy diagnosis, comorbidities, and treatments (e.g. effect of seizures on the brain, behavior problems) and management of disease (e.g., future seizures, lifestyle changes) which continued to be present over time (41). Studies indicate that 45-65% of parents of children with intractable epilepsy experience significantly elevated levels of parenting stress. The increased parenting stress caused by having a child with epilepsy has been found to adversely affect parent-child interaction, leading to behavioral and emotional problems (42).

Siblings of children with chronic epilepsy also have increased behavioral issues, mostly in externalizing behaviors. Siblings of children with epilepsy report a higher level of concern (a) that people will make fun of them because of their sibling's seizures; (b) not knowing how to help during a seizure; (c) feeling left out; and (d) injury and death as a result of a seizure (43).

Findings have been consistent that family-related psychosocial variables are associated with child behavior. In general, greater family stress, fewer family adaptive resources (e.g., low family esteem and communication), more negative perceptions about the epilepsy (e.g., stigma), more negative parent-child interactions, and poorer family adjustment were associated with more child behavior problems. Often, family variables remained significantly associated with child behavior even after variance for seizure variables had been controlled (31).

Academic Difficulties

Children with epilepsy are more likely to experience academic difficulties and school-related problems. They are also at an increased risk for continued underperformance and underemployment after reaching adulthood (29). A subgroup of children with epilepsy (those who not only have neuropsychological deficits but also disorganized/unsupportive home environments) are particularly at risk for adverse academic outcomes. Learning disorders and attention-deficit hyperactivity disorders are more common in children with epilepsy

than in the general population, which may contribute to academic difficulties (27,44). The risk for educational problems is highest with symptomatic epilepsy associated with structural brain changes or genetic syndromes. Fastenau and colleagues proposed a model to explain academic underachievement, where neuropsychological deficits played an integral role, mediating the effects of structural and electrophysiologic abnormalities, with contribution from seizure-related, demographic and psychosocial risk factors (45). Educational underachievement appears to be multifactorial in etiology, with contribution from cognitive deficits, behavioral problems and psychosocial stressors.

Need to Develop Integrated Etiological Framework

Epilepsy is a complex phenomenon and the behavioral concomitants are the product of a complex interaction among neurological, drug-related and psychosocial variables. An integrated model to explain child psychopathology would include familial and psychosocial stress, illness and drug-related variables, and the subtle to severe cognitive and language deficits, all of which may increase vulnerability to behavioral problems in children with epilepsy (46). The child's behavioral problems may in turn pose more stress on familial coping resources. The burden of epilepsy may generate negative effects on the family, which may affect parent-child interactive behavior and consequently, lead to higher internalizing and externalizing behavior problems. The recurrent and unpredictable nature of seizures, family burden and social stigma associated with epilepsy are assumed to influence the psychosocial development of children, making them vulnerable to psychopathology (47, 48). The psychosocial context may vary across cultures and some Asian cultures attach stigmatizing beliefs to epilepsy or may simply, consider it as a form of insanity. The perceptions of child and family largely depend on the sociocultural context and social attitude towards epilepsy.

Psychiatric Considerations in Evaluation and Management

Most of pediatricians and child neurologists are unaware of the need for mental health referrals in children with epilepsy, and report a lack of collaboration with mental

health providers (49). The majority of children with epilepsy do not receive mental health care despite having a diagnosable psychiatric disorder. As not every child with epilepsy needs mental health and educational assessment or intervention, clinicians are encouraged to adopt standardized screening tools to identify the children who are most in need of mental health interventions (50). This will allow the mental health clinician to convey important psychiatric considerations and be alert to important changes in the course and physical treatment of the child's epilepsy. There is a need of psychiatric referrals prior to surgery for all cases of childhood epilepsy. The psychiatrist should be involved early on and continue to collaborate in post-surgical care especially as the patients may be prone to experience depression and occasionally psychotic disorders in the post-surgical period.

Need for Psychiatric Assessment

There is a growing recognition to provide a multidisciplinary care with the involvement of various professionals, including mental health professionals, in the evaluation and long term care of children and families with epilepsy. Psychiatrists may be involved at the time of making the diagnosis, especially if there is a co-occurrence of pseudoseizures or the clinical features of seizures are discordant with the electrophysiological profile. Such children need careful observation, evaluation for psychosocial stressors and clinical delineation of pseudoseizures, if present.

There is a need to involve a mental health professional in the detailed assessment of children with diagnosed epilepsy. The comorbidity with other neuropsychiatric conditions is quite common in childhood epilepsy, and a thorough history, including developmental details and mental state examination should be conducted to assess psychiatric comorbidity such as autism, or behavioral consequences such as hyperactivity and depression. Children who experience social or academic difficulties are a candidate for a detailed neuropsychological assessment for sustained attention, memory and executive functioning. This can bring out the severity and pattern of deficits, and could guide the psychological and educational interventions to improve the child's functioning. The feedback to parents and teachers can

focus on providing support and encouragement to the child in the areas of better functioning to boost his/her confidence.

Since behavioral disturbances can occur in both new-onset and chronic epilepsy, the monitoring for emotional and behavioral difficulties should begin as soon as the diagnosis is made. The full assessment may require multiple interviews over a period of time with informants from several settings like parents, peers or teachers. Several instruments are available for screening and assessment. The Child Behavior Checklist (CBCL) and the Child and Adolescent Symptom Inventories are general behavioral screening questionnaires used in children with chronic health problems (51, 52). Quality of life scales specific to childhood epilepsy are available which assess the physical, psychological, social and academic functioning such as Quality of Life in Childhood Epilepsy (53) and the Impact of Pediatric Epilepsy Scale (54).

The familial and psychosocial impact of the disorder on children and families is often neglected in the clinical settings and should be focused in the psychiatric assessment. The burden of parents should be assessed in various areas such as emotional burden, psychological health, impact on daily routine and financial burden. The coping skills and resources of the family should be assessed, and any maladaptive patterns of coping should be identified. The familial and societal response to the child's illness should be understood in subjective terms, and the child should be interviewed to explore for possible bullying in school or issues pertaining to stigma in social settings. The psychiatric evaluation must be conducted at regular intervals, especially after changes in seizure frequency and medications, as the psychiatric and psychosocial problems may evolve or change over time and therefore, may need a continued monitoring.

Psychiatric Management: Approach and Strategies

Psychoeducation regarding common emotional and behavioral problems experienced in childhood epilepsy should be routinely incorporated in clinical care, and benefits of psychoeducational sessions have been documented. Parents who participated in group psychoeducational sessions showed increased understanding of epilepsy and less anxiety, and children

who participated felt more competent and needed fewer restrictions compared to children in the control group (55). Researchers attempted to provide telephonic interventions for information and support needs and found reductions in concerns and improved family relationships (47). The mental health clinician must provide psychoeducation and guidance to parents regarding neuropsychological correlates of their child's epilepsy from a thorough evaluation of potential cognitive weaknesses to explaining the role of neuropsychologists and educational advocates in the community or school (20).

Psychotherapy (individual, group or family) is an important treatment that should be considered for emotional and behavioral problems in children with epilepsy. Effective psychotherapy can help patients understand the meaning of and responses to their illness, improve treatment adherence, impart adaptive coping skills and enhance psychosocial functioning. Specific issues that might be addressed are the initial reactions of grief, anxiety, or anger related to the diagnosis of epilepsy, decreased competence and autonomy in the preschool child, attention and learning problems in the school-age child, and self-esteem and social issues in the adolescent (20, 56). However, there continues to be a paucity of empirical evidence that supports the efficacy of any psychotherapeutic modality in children with epilepsy (20).

In a review of the existing intervention programs for children and families facing epilepsy, the treatment goals were delineated as reducing the children's concerns and fears, problem behaviors, minimizing associated stress, increasing epilepsy knowledge and decision-making skills; improving attitudes toward epilepsy; and improving epilepsy management, independence, coping skills and efficient communication (57). These interventions were delivered through a variety of modalities including individual meetings, parent groups, phone interviews/conferences, video conferencing and summer camps. Both individual and group cognitive behavioral intervention strategies, including relaxation and biofeedback, predominated as the treatment approach.

The pharmacological considerations involve a review of the anti-epileptic drugs the child is taking and the various cognitive and behavioral adverse-effects of the

drug (s) needs to be carefully evaluated. In case of severe behavioral concerns of an epileptic drug, a discussion can be done with the child neurologist focusing on the issues related to dosage, use of alternate effective drugs and the risk versus benefit ratio in relation to seizure control and behavioral problems. Initiation of psychopharmacology may be the option for emotional and behavioral problems interfering with academic and social functioning. The choice of the pharmacologic agent will depend on (a) the safety and efficacy profile in the pediatric population (b) potential interactions between psychotropic and antiepileptic drugs, and (c) the likely effect on the seizure threshold.

Stimulants are the first line of treatment in patients with comorbid ADHD and epilepsy. With regard to the efficacy of methylphenidate, multiple studies have shown improvement in nearly 70% of children with the dual diagnosis of epilepsy and ADHD. Atomoxetine, a potent specific norepinephrine reuptake inhibitor, may also be used as an alternative safe option (20). Selective serotonin reuptake inhibitors are the agents of choice for treating depression and anxiety in children. They may cause inhibition of the cytochrome P450 enzyme system, resulting in an increase in phenytoin, carbamazepine and valproate levels. The antipsychotic agents have been used for children with psychosis, pervasive developmental disorders and tics. The newer atypical antipsychotics are safe and an effective option and are not known to significantly lower the seizure threshold. Haloperidol also has little effect on seizure threshold; however, other typical agents like chlorpromazine and clozapine are potentially seizurogenic. The enzyme-inducing antiepileptic agents like carbamazepine may cause a decrease in serum concentration of most of the antipsychotic medications and dose titrations may be required.

Psychiatric Issues in Epilepsy Surgery

Surgery considered as the main treatment option for intractable cases of epilepsy is being increasingly performed for children with intractable epilepsy. While it may be seen as an extreme step, recurrent seizures may incapacitate the child and independent daily functioning may not be possible. The benefits of removing the epileptogenic brain tissue in such cases may outweigh

the risks of surgical resection. It is important to address any fear or anxieties of the child or parents during the pre-surgical period. A mental health professional should be involved prior to surgery to evaluate the psychopathology, if any. The degree of neuropsychological deficits should be documented in the pre-surgical period to facilitate a comparison after surgery. The comorbid psychiatric symptoms may improve or may maintain status quo after surgery, with little evidence for deterioration. Children may suffer from adjustment disorder, depression, or anxiety symptoms, commonly seen in the post-surgical period. Even psychosis may occur in a few cases especially after temporal resection (58). Surgery may lead to seizure control; however, the child may continue to feel social isolation and stigma. The difficulties in establishing and maintaining personal relationships may persist in adulthood (59). Long term psychosocial care and support is needed to attain the maximum possible level of functioning.

Future Directions

The psychiatric problems in children with epilepsy have remained under-recognized and under-treated in clinical settings. All children with epilepsy should be routinely screened for academic and behavioral problems. Children with epilepsy and psychopathology should receive a collaborative multidisciplinary care, especially focusing on psychoeducation, psychopharmacologic treatment, psychosocial interventions and school or educational support, aiming to promote the quality of life in children and families living with epilepsy. As cognitive development in preschool children is progressive and dynamic, large-scale prospective follow-up studies will facilitate understanding of the cognitive profiles of children. Recent research on the lifetime perspective of cognitive functioning in children needs to be built on understanding the long term course and impact. Research should aim to identify the groups which are at high risk for behavioral and psychosocial problems in order to initiate preventive interventions. The etiological framework needs to be investigated further to explain the behavioral symptoms in childhood epilepsy. The frequent comorbidity with cognitive deficits, learning disabilities and academic difficulties underscores the need for interventions at school level.

Research should adequately be focused on psychosocial and stigma-related issues and suitable public health interventions should be designed to reduce stigma and to promote mental health of children with epilepsy.

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