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Topical Review

Current Advances in Childhood Absence Epilepsy

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ABSTRACT

BACKGROUND: Childhood absence epilepsy is an age-dependent, idiopathic, generalized epilepsy with a characteristic seizure appearance. The disorder is likely to be multifactorial, resulting from interactions between genetic and acquired factors, but the debate is still open. We review recent studies on different aspects of childhood absence epilepsy and also to describe new concepts. **METHODS:** Data for this review were identified using Medline and PubMed survey to locate studies dealing with childhood absence epilepsy. Searches included articles published between 1924 and 2013. **RESULTS:** The diagnosis comprises predominant and associated seizure types associated with other clinical and electroencephalographic characteristics. Many studies have challenged the prevailing concepts, particularly with respect to the pathophysiological mechanisms underlying the electroencephalographic seizure discharges. Childhood absence epilepsy fits the definition of system epilepsy as a condition resulting from the persisting susceptibility of the thalamocortical system as a whole to generate seizures. This syndrome, if properly defined using strict diagnostic criteria, has a good prognosis. In some cases, it may affect multiple cognitive functions determining risk for academic and functional difficulties; the detection of children at risk allows tailored interventions. Childhood absence epilepsy is usually treated with ethosuximide, valproate, lamotrigine, or levetiracetam, but the most efficacious and tolerable initial empirical treatment has not been well defined. **CONCLUSIONS:** We review recent studies and new concepts on the electroclinical features and pathophysiological findings of childhood absence epilepsy in order to highlight areas of consensus as well as areas of uncertainty that indicate directions for future research.

Keywords: childhood absence epilepsy, idiopathic generalized epilepsy, system epilepsy, thalamocortical system, neuropsychological aspects, treatment

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Introduction

Childhood absence epilepsy (CAE) is a common form of pediatric idiopathic generalized epilepsy, accounting for 10% to 17% of all cases of epilepsy diagnosed in school-aged children.[1] It is characterized by multiple typical absence seizures, accompanied with bilateral, symmetrical, and synchronous discharges of 3-Hz generalized spike and waves on electroencephalography (EEG). There is a new increased interest in the cognitive, behavioral, and genetic aspects, but also in the neuroimaging studies in these patients.

The purpose of this report is to review recent studies on clinical features of CAE. Data for this review have been identified on Medline and PubMed survey for studies dealing with CAE, references from relevant articles, and searches of the authors' file. Searches were done by considering articles published between 1924 and 2013. We considered reports in English, French, and Spanish. Specific review articles, systematic reviews, textbooks, and case reports were examined for any further publications, as were the reference sections of all articles identified by the literature search.

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Epidemiology

CAE has been variously reported to occur between 5.8 and 7.1 times per 100,000 persons.[2,3] In children's cohorts, the prevalence has been estimated to range from 0.4 to 0.7 per 1000 persons.[4] CAE, with some exceptions, is clearly more frequent in girls than in boys (11.4% vs. 2.5%).[5] CAE usually begins between 4 and 10 years with a peak at 5-7 years.[6]

Clinical and EEG presentation

Clinical presentation

CAE is characterized by very frequent (often dozens per day) absence seizures. Information from retrospective studies might be a source of confusion, and many authors have incorrectly classified as CAE any type of epilepsy with onset of absences seizures during childhood. The striking impairment of consciousness is the essential feature of absence seizures in CAE, with loss of awareness, unresponsiveness, and behavioral arrest.[7] Most children have a complete arrest of their activity, but a few can continue activities in an altered fashion.[8] In the periods immediately before and after seizures, mild impairment has been reported, but transient peri-ictal deficits are still debatable.[9] Another important feature of absence seizures is variation in consciousness deficits from one seizure to another, within and between patients.[10] Other associated ictal clinical features in CAE consisted of staring, 3-Hz regular eyelid movement, and eye opening that usually occur in an inconsistent manner during seizures in which eyes are initially closed.[8] Automatisms occur frequently in CAE and are more likely to be observed in longer seizures and during hyperventilation; they are predominantly oral and similar for the same child. However, these repetitive motor activities are not present in all absence seizures even in the same child, and their presence is not influenced by age or state of alertness.[11] Mild clonic or tonic movements often occur during the first seconds of the absence seizure, whereas atonic falls never occur. Pallor is common. Incontinence of urine is exceptional.[12] Some studies report perioral myoclonia and single or arrhythmic myoclonic jerking of limbs, head, or trunk during seizure in a small number of children with CAE.[8,13]

Seizure duration is influenced by factors such as provocation (hyperventilation and intermittent photic stimulation), state of arousal, sleep deprivation, medication, and individual factors.[14,15] Seizure duration of less than 4 seconds or more than 30 seconds is not typical of CAE.[16] However, all children with absence seizures with focal onset also had other seizures with generalized onset.[8,17] Therefore, exclusion criteria have been proposed[16]: the presence of seizures other than typical absence seizure such as generalized tonic-clonic seizure (GTCS) or myoclonic jerks before or during the active stage of absences. Eyelid and perioral myoclonia and single violent jerks may also be an exclusion criterion.[18]

Furthermore, the International League Against Epilepsy (ILAE), by accepting myoclonic absence epilepsy and juvenile myoclonic epilepsy as separate syndromes, probably excludes absence seizures with myoclonic and mild typical absence seizures from CAE; ILAE also defines reflex absence seizures that are, triggered by specific stimuli (such as photic stimulation), as a distinct category, indicating that these also may not be part of CAE.[19] Other precipitating or facilitating factors are emotional, intellectual, nyctohemeral, and metabolic stimuli.[20]

EEG aspects

The typical pattern is a bilaterally synchronous and symmetrical discharge of rhythmic 3-Hz spike-wave complexes that start and end abruptly; often, a recovery of functions can be observed toward the end of the seizure and sometimes functions can be initially spared.[7]

Sadleir and colleagues detailed the electroclinical features of absence seizures and analyzed the video monitoring of characteristics of 339 absence seizures in a cohort of 47 children with newly diagnosed, untreated CAE.[8] These authors showed that an average seizure duration was 9.4 seconds (range, 1 to 44 seconds), a bit shorter than the 12.4 seconds previously reported.[21]

In 50% of seizures in CAE, the initial generalized discharge consisted of typical spike-wave morphology, whereas in others it consisted of single spike, polyspikes, or an atypical, irregular generalized spike wave. Seizures without regular spike-wave discharges are rare. The majority of the discharges consisted of spike-wave complexes with one or two spikes per wave; however, children with a photoparoxysmal response are more likely to have three or four spikes per wave. The discharge can develop some degree of irregularity at the end of the seizure, particularly during drowsiness, sleep, and hyperventilation. In these circumstances, slow waves or complexes of different frequency and/or morphology or brief, transient interruptions of seizure discharges can disrupt the regular ictal discharges.[22] Hyperventilation and intermittent photic stimulation induce absence seizures in 83% and 21% of patients, respectively.[8] The interictal EEG in CAE is characterized by a normal background activity, but an interictal paroxysmal activity consisting of fragments of generalized spike-wave discharges can be documented in up to 92% of patients. Focal epileptiform interictal discharges may be present not only in the bicentral areas, but also in the frontal, temporal, and parietal areas.[8,22] Occipital intermittent rhythmic delta activity, described also as rhythmic posterior bilateral delta activity, is another interictal abnormality of CAE. It is characterized by rhythmic bursts at 2.5-4 Hz over the occipital regions, which is enhanced by hyperventilation and drowsiness and attenuated by eye opening and deep stages of sleep.[8,22]

Multiple spikes (more than three), 3-4 Hz spike-wave paroxysms of less than 4 seconds, or ictal discharge fragmentations are not typical of CAE and may suggest a worse prognosis.[16]

Neuropsychological/cognitive aspects

Neuropsychological studies have demonstrated that, even during childhood and at diagnosis, patients affected by CAE have cognitive and linguistic impairment as well as behavioral disorders.[23,24] The cognitive difficulties involve particularly the attentional domain and the executive