EEG Abnormalities In ADHD: How Should We Treat?

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Attention deficit hyperactivity disorder (ADHD) has been described as the most common neurodevelopmental disorder in childhood. ADHD is characterized by symptoms of inattention, hyperactivity, and impulsivity occurring in 3-8% of school-aged children in the general population [1,2]. Several studies have drawn attention to the frequent occurrence of epileptic seizures [3] and electroencephalographic abnormalities in children with ADHD [4]. At least 20% of children with epilepsy have symptoms of ADHD as comorbidity [5,6]. Hughes et al. [4] reported that the occurrence of focal paroxysmal abnormality (PA) during sleep recording in 24% of 176 children with ADHD [4]. Thus, the proportion of children with ADHD who also have PA on a routine electroencephalogram (EEG) is significantly greater than that in the general population. Despite the evidence for this bidirectional relationship between ADHD and epilepsy, however, performance of a routine EEG in the evaluation of children with suspected ADHD is not usually recommended [7].

Psychostimulants such as methylphenidate (MPH) and noradrenergic potentiation such as atomoxetine (ATX) are generally the most effective medication for children with ADHD [8]. However, MPH or ATX is not effective in approximately 20-30% of children with ADHD [9]. Moreover, there have been reports of psychostimulants inducing or exacerbating seizure disorders in patients with ADHD, particularly with EEG PA. On the other hand, the presence of PA in the EEG of children with behavior disorders may be related to outcome. Some children show transient behavioral and learning difficulties correlated with PA but without clinical epilepsy [10]. In another study, 80% of adult patients with PA but without clinical epilepsy showed improvement in cognitive function after taking antiepileptic drugs (AEDs) [11]. Transitory cognitive impairment describes subtle momentary cognitive deficits in patients with PA, either without overt seizures or interictally [12]. In opinions from these investigations, whether PA warrants treatment continues to be debated.

Subclinical PA may be accompanied by subtle impairments of attention shown by changes in reaction time during simultaneous EEG [13]. The few observations of increased prevalence of EEG PA in children with ADHD and the experience of using AEDs as a spike suppressor in childhood epilepsies with increased prevalence of focal EEG PA and the scarce experience of using AEDs in children without epilepsy. In previous study, Gordon et al. [14] reported that a cognitive-enhancing effect of valproate sodium (VPA), likely to be related to reductions in PA [14]. Recently, several studies have been investigated to explore the usefulness of AEDs in ADHD patients who had EEG PA but no clinical seizures. Bakke et al. reported that a more than 50% reduction in spike index was found in 22/35 children (63%) using levetiracetam (LEV) [15]. Out of these an improved behavior was noticed in 13 children (59%). They concluded that study described the benefit of LEV in children with ADHD with and without epilepsy on the occurrence of EEG PA as well as on behavior. In another study by Miyazaki et al. VPA administration notably decreased clinical symptoms of ADHD with frontal spikes [16]. In our current research, we investigated the usefulness of AEDs such as VPA in ADHD patients who had PA but no clinical seizures. In addition, we also investigated the relationships between neuropsychological disturbance, localized PA, and treatment with VPA [17]. This study showed that the EEG improved with VPA treatment in 5 of 8 patients with frontal PA and 3 of 5 patients with roladic PA. While 83.3% of patients with improvements in both assessments had frontal PA, only 16.7% had roladic PA. Patients with frontal PA showed a significantly higher correlation between PA frequency and improvement in ADHD-rating scale (ADHD-RS). In this study of children with ADHD, EEG improvement with AED treatment showed a high correlation with behavioral improvements as shown by ADHD-RS and global assessment of functioning (GAF) scores. Frontal PA showed a strong correlation with ADHD-RS and GAF scores, and that treatment with VPA was effective both in decreasing PA and in improving behavioral problems in at least some of the patients with ADHD with frontal PA [17].

Prevailing opinion characterizes ADHD as a disorder of executive function attributable to abnormal dopamine transmission in the frontal lobes and frontostriatal circuitry. Thus, ADHD can be characterized by frontal lobe dysfunction. The onset of paroxysmal electrical activity was closely related in time with the development of a neuropsychological and behavioral pattern characterized by inattention, impulsiveness, mood swings and perseveration, with deficits in time orientation, reasoning and learning strategies, which shared many features with adult frontal syndrome [18]. In ADHD with EEG abnormalities, paroxysmal activity affects the frontal area and results in those impairments. Damage to the prefrontal cortex has been associated with an inability to organize and carry out goal-directed behaviors. In our previous 3-dimensional MRI volumetric studies, frontal and prefrontal lobe volumes revealed growth disturbance in epilepsy patients with frontal lobe dysfunction compared with those of normal subjects [19,20]. Moreover, in the patients with shorter seizure durations and EEG abnormalities periods, ratios were soon restored to a more normal growth ratio, whereas growth disturbances of the prefrontal lobes were persistent in the patients with longer seizure durations and EEG abnormalities periods. These findings suggest that the duration of EEG paroxysmal anomalies may be associated with prefrontal lobe growth, which is associated with neuropsychological problems. Damage to the frontal regions during childhood may interrupt normal maturational processes and organization, resulting in impairments to neurobehavioral development. Integrative executive functions may thus rely on the health of frontal lobe tissue and connectivity with the rest of the cortex [21].

When symptoms of ADHD do not respond to MPH or ATX, some clinicians start looking for alternative explanations. Becker et al. suggested that practice parameters for the assessment and treatment of children with ADHD until puberty should include EEG, regardless lack

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of overt seizures or other neurological conditions [22]. However, in their study group only "routine EEG" was mentioned and nothing about treatment. Studies reporting an increased frequency of PA in children with ADHD and reports of ADHD-type symptoms resolving when spike activity is suppressed with AEDs have led to recommendations for performing EEGs [23]. The EEG may be of value in assisting in the management of at least some children with ADHD. In addition, urgent suppression of PA might be warranted to prevent the progression of neuropsychological impairments. Although much remains to be done, substantial advances in the management of ADHD have been made, and the prospect for significant enhancement of the lives of children with ADHD continues to improve. In these findings and our opinion, clinical work up in children with ADHD without epilepsy who do not respond to traditional ADHD drugs, should include an EEG with awake and sleep recording and in the presence of EEG PA the use of an AED such as LEV or VPA should be considered.

References