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Effects of methylphenidate on EEG coherence in Attention-Deficit/Hyperactivity Disorder

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Abstract

This study investigated the effects of methylphenidate on intrahemispheric and interhemispheric EEG coherence in children with Attention-Deficit/Hyperactivity Disorder (AD/HD). Twenty boys with AD/HD Combined type and 20 age- and sex-matched control subjects, aged 8 to 13 years, participated in this study. EEG was recorded from 21 sites during an eyes-closed resting condition. Wave-shape coherence was calculated for eight intrahemispheric electrode pairs (four in each hemisphere), and eight interhemispheric electrode pairs, within each of the delta, theta, alpha and beta bands. AD/HD children were tested both off and, 6 months later, on a therapeutic dose of methylphenidate. In intrahemispheric comparisons, AD/HD children had lower theta coherences at long inter-electrode distances, and reduced lateralisation at both long and short–medium inter-electrode distances than controls. For interhemispheric comparisons, AD/HD children showed increased coherences in the frontal regions for the low frequency bands (delta and theta), and reduced coherences in the alpha bands in all other regions. These EEG coherences suggest reduced cortical differentiation and specialisation in AD/HD, particularly in the frontal regions. Methylphenidate did not produce any changes in coherence values. The lack of sensitivity of coherence measures to methylphenidate in the present study suggests that eyes-closed resting EEG coherence measures are associated with structural connectivity of the underlying regions of the brain rather than the degree of functionality of these regions. These results suggest the existence of structural as well as functional brain dysfunction in AD/HD.

Keywords: Attention-Deficit/Hyperactivity Disorder; Children; EEG; Coherence; Medication

1. Introduction

Attention-Deficit/Hyperactivity Disorder (AD/HD) is a persistent problem currently affecting 4% to 6% of school-age children (Lindgren et al., 1990; Pelham et al., 1992; APA, 1994). AD/HD interferes with many aspects of normal development and functioning in a child's life, and if untreated, may predispose the child to psychiatric and social pathology in later life. In Australia and North America, stimulant medications are widely used in the treatment of AD/HD, with numerous controlled trials indicating that approximately 80% of patients have clinically significant benefits (Wilens and Biederman, 1992; Swanson et al., 1993).

The EEG of children with AD/HD has been extensively studied using power analysis, with most studies finding very similar results (see Barry et al., 2003a for a review). Typically, AD/HD children have increased theta activity (Satterfield et al., 1972, 1973a,b; Janzen et al., 1995; Clarke et al., 1998, 2001a,b) which occurs primarily in the frontal regions (Mann et al., 1992; Chabot and Serfontein, 1996; Lazzaro et al., 1998), increased posterior delta (Matousek et

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al., 1984; Clarke et al., 1998, 2001a,b) and decreased alpha and beta activity (Dykman et al., 1982; Callaway et al., 1983), also most apparent in the posterior regions (Mann et al., 1992; Clarke et al., 1998, 2001a,b; Lazzaro et al., 1998), compared to children without AD/HD. A number of studies have also investigated changes in the EEG due to stimulant medications (Chabot et al., 1999; Swartwood et al., 1998; Lubar et al., 1999; Loo et al., 1999; Clarke et al., 2002, 2003). While there are some inconsistencies within these studies, the majority have reported a degree of normalisation of the EEG produced by stimulant medications (Chabot et al., 1999; Loo et al., 1999; Clarke et al., 2002, 2003).

The coherence of the EEG activity between two sites, conceptualised as the correlation in the time domain between two signals in a given frequency band (Shaw, 1981), is believed to provide information about the degree of connectivity between structures underlying the pair of electrodes used to calculate the coherence measure. Normal brain development involves periods of both synaptic proliferation and pruning, hypothesised to cause systematic fluctuations in coherence (e.g., Thatcher et al., 1987; Thatcher, 1994) which appear to overlay a general increase attributable to increasing myelination (e.g., Barry et al., 2004). Thatcher et al. (1986) proposed a two-process model of cortico-cortical associations in which short and long neuronal fibres contribute differentially to coherence as a function of inter-electrode distance. At longer distances, coherence is mainly dependent on the longer fibres. Coherence falls off systematically with increasing inter-electrode distance, and increases with increases in longer fibre density and development. In contrast, increased density and development of short fibres, in specialised regions of the cortex, reduces coherence by increasing the complexity and competition of interactions within the cell population. This two-compartment model has wide currency in the literature, as it seems to accommodate much of the existing coherence data from normal and atypical children.

Compared to studies using traditional power measures, EEG coherence has not been thoroughly investigated in children with AD/HD, nor have the effects of stimulant medication on coherence measures. Montague (1975) found hyperkinetic children had significantly elevated intrahemispheric coherences compared to control subjects. Chabot and Serfontein (1996) and Chabot et al. (1996) reported that a mixed group of attention disorder patients had increased interhemispheric and intrahemispheric hypercoherence in frontal and central regions, and reduced parietal coherence compared to a normative database (John et al., 1980). Barry et al. (2002), using the same bands and electrode pairs as the Chabot studies, found that at shorter inter-electrode distances, children with AD/HD had elevated intrahemispheric coherences in the theta band and reduced lateral differences in the theta and alpha bands. At longer inter-electrode distances, AD/HD children had lower intrahemispheric alpha coherences than controls. Frontally, AD/HD children also had interhemispheric coherences elevated in the delta and theta bands, and reduced in the alpha band. An alpha coherence reduction in temporal regions, and a theta coherence enhancement in central/parietal/occipital regions, were also apparent. Collectively, in the context of Thatcher's coherence model, the increased coherence in the delta and theta bands, especially at short inter-electrode distances, suggests the presence of a maturational lag in CNS development in children with AD/HD, although this has not been conclusively demonstrated. Unfortunately, most previous studies in this area have focussed on the existence of coherence anomalies rather than their meaning in the AD/HD context.

To date, no studies have specifically investigated changes in EEG coherence in AD/HD as a result of stimulant medications. This is of interest as it may provide further information on how stimulants produce their therapeutic effect. Lubar et al. (1999) did suggest that methylphenidate "may influence functional linkages in the brain by normalizing their speed of conduction or by normalizing their functional differentiation" (p. 636). This would suggest that methylphenidate might normalise coherences in AD/HD, providing a global hypothesis for this study. Hence we aimed to investigate changes in EEG coherence as a result of the administration of methylphenidate in children with AD/HD.

2. Materials and method

2.1. Subjects

Two groups of 20 boys aged between 8 and 13 years participated in this study. These subjects are a subset of children included in a previous study of 50 subjects, on the effects of methylphenidate on EEG power measures (Clarke et al., 2002). The first 20 subjects recruited in the previous study were used in this study. All subjects were right handed and footed, and had a full-scale WISC-III IQ score of 85 or higher. The groups used were children diagnosed with AD/HD Combined type, and a control group. The AD/HD subjects were drawn from new patients presenting at a Sydney-based paediatric practice for an assessment and treatment of AD/HD. The AD/HD patients either had not been diagnosed previously as having AD/HD and had no history of medication use for the disorder, or had previously been assessed by another clinician and treated with medication but were medication-free for a minimum of five half-lives at the initial assessment. The control group consisted of children from local schools and community groups who were medication-free.

The AD/HD diagnosis was based on a clinical assessment by a paediatrician and a psychologist, and children were included only when both agreed on the diagnosis. DSM-IV criteria were used and children were included only if they met the full diagnostic criteria for AD/HD Combined type. Clinical interviews incorporated information from as many sources as were available, including a history given by a parent or guardian, school reports for the past 12