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Event-related potentials in children with attention deficit hyperactivity disorder: An investigation using an auditory oddball task

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ABSTRACT

The aim of the study was to investigate differences in electrophysiological brain activity between children diagnosed with attention deficit hyperactivity disorder combined type (ADHD-Com) and normally developing children, using the auditory 2-tone oddball paradigm. Forty right-handed subjects aged between 6.9 and 12.3 years participated in the present study, with 16 boys and 4 girls in each of the control and ADHD-Com groups. Children were individually age- and gender-matched. The auditory oddball task consisted of 155 standards (1 KHz, $p=.66$) and 80 targets (1.5 KHz, $p=.34$), presented randomly one at a time. Subjects were instructed to listen to the sounds and count the rare tones. Task performance in ADHD children did not differ compared to that in the control group. Event-related potentials (ERPs) elicited to target and standard stimuli were analyzed for between-group differences. The ADHD group showed enhanced P2 and reduced N2 component to both oddball stimuli, followed by reduced P3 component to attended targets compared with controls. The difference in the P3 amplitude between targets and standards was smaller in the ADHD group, particularly over the right hemisphere. These results suggest deficiencies in both automatic and controlled processing in children with ADHD. Enhanced amplitude of the P2 in ADHD children may reflect an early orienting deficit which affects later processing stages in the oddball task. Reduced amplitude of the N2 in the clinical group may be associated with stimulus discrimination impairment and inappropriate conflict monitoring. Reduced amplitude of target P3 and its asymmetrical distribution in ADHD children may reflect a deficit in higher-level executive functions, such as attention allocation and stimulus evaluation, accompanied by an impairment of global aspects of attentional processing that are under right hemisphere control.

1. Introduction

Attention deficit hyperactivity disorder (ADHD) is a prevalent developmental disorder that, according to the Diagnostic and Statistical Manual of Mental Disorders (4th edition; DSM-IV; American Psychiatric Association, 1994), is characterized by a persisting pattern of increased impulsivity, high levels of motor activity, and attention problems that impair functioning in home, school, and social settings. The DSM-IV criteria allow the diagnosis of three subtypes of the disorder: ADHD of the predominantly inattentive, hyperactive/impulsive or combined type. Children with ADHD combined type demonstrate behaviors from both the inattentive and hyperactive/impulsive dimensions. This disorder is commonly diagnosed in boys than girls, usually with the onset occurring prior to age 7, and with males being overrepresented by ratios ranging from 3:1 to 9:1 (Arnold, 1996; Gaub and Carlson, 1997).

This one of the most commonly diagnosed childhood disorder has been associated with a variety of environmental and biological risk factors, including genetic, neurochemical and neuroanatomical components (Curatolo et al., 2009). Multiple reports have documented differences in brain mass, cerebral volume, glucose metabolism, and hemispheric anomalies in individuals with ADHD (Casey et al., 1997; Castellanos et al., 1996; Filipek et al., 1997; Semrud-Clikeman et al., 1994; Zametkin et al., 1990). More recent investigations utilizing a broad range of techniques, in children, adolescents and adults, have suggested that ADHD especially involves atypical cerebral asymmetries (Bradshaw and Sheppard, 2000; Giedd et al., 2001; Hale et al., 2000, 2009; Reid and Norvilitis, 2000; Stefanatos and Wasserstein, 2001).

The behavioral symptoms of ADHD have been reported to be similar to those seen in patients with acquired right hemisphere lesions (Geeraerts et al., 2008; Heilman et al., 1986; Mesulam et al., 1976; Voeller et al., 1988). Multiple studies have shown that the right

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hemisphere plays a critical role in sustaining and shifting attention (Corbetta et al., 1993; Pardo and Raichle, 1991; Riccio et al., 2002), as well as regulating arousal (Aston-Jones et al., 1984). Reduced performance on vigilance measures in ADHD subjects has indicated sustained attention deficits (Sergeant, 1989), probably related to right-hemisphere fronto-parietal network dysfunction (Posner and Petersen, 1990).

In addition, unilateral right hemisphere damage has been associated with spatial attention deficits such as hemispatial neglect and extinction (Heilman et al., 1993; Milner and McIntosh, 2005). Some behavioral studies, using the letter cancelation and line bisection tasks, have supported a subtle right hemisphere deficit in ADHD children (Rolfe et al., 2006; Sheppard et al., 1999; Voeller and Heilman, 1988). The right hemisphere, especially the right frontal region, has also been implicated in maintaining motor behavior (Kertesz et al., 1985), which has been shown to be deficient in ADHD children (Voeller et al., 1989; Voeller and Heilman, 1988).

Structural and functional brain imaging studies have linked the behavioral symptoms of altered attentional performance among children and adults with ADHD to abnormalities in frontal, striatal and parietal areas of the right hemisphere (Booth et al., 2005; Sowell et al., 2003; Vance et al., 2007).

As already mentioned above, extensive research has shown that children with ADHD perform worse than normal control children on a wide range of attentional tasks (Douglas, 1983). Attention allocation is typically examined in the auditory, visual or mixed modality oddball task that requires the detection of target stimuli in a string of standard stimuli. Previous studies have reported that children with ADHD are impaired in target detection and discrimination, committing more errors and showing slower and more variable responses (Banaschewski et al., 2003; Brandeis et al., 2002; Jonkman et al., 2000). The attentional deficits of ADHD children have also been displayed in the amplitudes and/or latency of event-related brain potentials (ERPs) which are a useful tool for the investigation of attentional processing impairments (Barry et al., 2003). Electrophysiological oddball studies have shown abnormally increased latency and decreased amplitude in ADHD child ERPs especially in response to oddball targets.

Firstly, the previous studies have demonstrated changes in neural processing related to automatic or early attentional processing. The P2 component, peaking at around 150–200 ms over central regions, has been able to differentiate ADHD children from controls in both the auditory and visual modalities (Barry et al., 2003). A number of studies have shown that the P2 component is larger in ADHD children compared to controls for both auditory (Holcomb et al., 1985, 1986; Kemner et al., 1996; Oades et al., 1996; Satterfield et al., 1994) and visual stimuli (Kemner et al., 1996; Robaey et al., 1992). In oddball task the P2 component has been related to the inhibition of processing potentially competing stimuli (Hansen and Hillyard, 1988; Oades et al., 1996). It has been proposed that a larger P2 in ADHD subjects represents the capturing of attention by irrelevant stimuli and therefore reflects greater resources allocation to multiple stimuli (Oades, 1998).

Secondly, the N2 component, peaking at around 200–250 ms over frontal regions, has also been able to differentiate hyperactive and inattentive subjects from controls. ADHD children have been shown to display a reduced N2 component in response to target and standard stimuli in both auditory and visual modalities (Johnstone and Barry, 1996; Johnstone et al., 2001; Satterfield et al., 1990, 1994). The N2 component is believed to be functionally connected with an active process of stimulus categorisation (Oades et al., 1996). Thus, the N2 reduction in ADHD subjects may represent salient stimulus categorisation deficit, which affects later target-related information processing stages (Johnstone and Barry, 1996; Lazzaro et al., 2001; Oades, 1998; Satterfield et al., 1994).

As reviewed by Barry et al. (2003), the most consistent ERP finding in relation to ADHD is the reduced parietal P3 amplitude in the auditory oddball task (e.g., Johnstone and Barry, 1996; Johnstone et al., 2001; Kemner et al., 1998; Satterfield et al., 1990). This positive component, with a peak latency of 300–800 ms, is generally taken to mark the completion of stimulus evaluation (Oades, 1998). It has also been proposed that the P3 may reflect context closure (Desmedt, 1981; Verleger, 1988) or an updating of the working memory contents (Donchin and Coles, 1988). In the ADHD context, some previous studies have related a reduced P3 to the deficits in processing task-relevant or salient information, engaging selective attention and context updating (e.g., Satterfield et al., 1990). It is worth to stress that in the study of Oades et al. (1996), based on the passive oddball paradigm, the control group had the P3 maximum biased to the right hemipshere, whereas for the ADHD group the P3 maxima were in the midline. This result may indicate that the completion of stimulus evaluation may be deficient in the right hemisphere in ADHD children.

The present study aimed at replicating and extending the previous findings of abnormal P2, N2 and P3 component activity and their topographic distribution during the auditory oddball task in children with ADHD-Combined type. Based on prior studies, we hypothesized that children with ADHD would show altered ERP components in response to the target and standard stimuli. We also supposed that if ADHD is primarily a right hemisphere dysfunction, asymmetrical differences in electrophysiological brain activity between ADHD and control children may be particularly detectable in the active oddball task, which is one of the sustained attention paradigms.

2. Method

2.1. Participants

Forty right-handed children aged between 6.9 and 12.3 years (M = 9.2 years, SD = 1.9 years) participated in the present study, with 16 boys and 4 girls in each of the control and ADHD-Combined type groups. Children were individually age- and gender-matched. Of an initial sample of 44 subjects recruited to the study, two ADHD boys were excluded because of excessive movement artifacts resulting in low trial counts for ERPs. Two of their normal counterparts were also excluded, leaving a final sample of 40. For inclusion in the study, each child had to have an estimated IQ of 80 or greater on the Wechsler Intelligence Scale for Children-Revised (Wechsler, 1974) (M = 109.6, SD = 13.52) and report no hearing or vision problems. ADHD children were recruited through a public psychological clinic and a local support group and had significant symptoms of ADHD for at least one year. Clinical participants were diagnosed with ADHD of the combined type by a psychologist with strict adherence to the diagnostic criteria of DSM-IV. The diagnosis was subsequently confirmed by an independent experienced physician. Behavior in school was evaluated via parents' reports. Parents were asked for their opinions on the presence, severity, and duration of current ADHD symptoms as well as the level of dysfunction caused by these symptoms. Participants could not meet criteria for oppositional defiant disorder, conduct disorder or any anxiety, tic, or affective disorder. Children were excluded if they had been known to suffer an epileptic seizure, periods of unconsciousness, motor or sensory loss, serious head-injuries, or serious psychiatric condition. Eleven children from the ADHD group were taking stimulant or other treatment medication, but were required to refrain from taking it in the 24 h prior to testing. The children of the control group, without a family history of ADHD, were recruited from various local elementary schools. Healthy controls could not receive a diagnosis of ADHD on the DSM-IV rating scale and structured interview. Moreover they could not meet criteria for any psychiatric disorders or have any history of past treatment with psychotropic medication. Control children were not taking any medications at the time of the study. Ethical approval was obtained from local ethical review boards. Written informed consent from a parent and assent