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EVENT-RELATED POTENTIALS IN CHILDREN WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER AND EXCESS BETA ACTIVITY IN THE EEG

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SUMMARY

Background: *This study investigated whether ERPs from an inter-modal oddball task could distinguish between two groups of children with Attention-Deficit/Hyperactivity Disorder (AD/HD) of the combined type, with and without excess beta in their EEG, and controls.*

Material/ Methods: *Three age-matched groups of male children (20 typical AD/HD without excess beta, 20 AD/HD with excess beta, 20 controls) were presented with an inter-modal oddball task in which a counter-phasing checkerboard was the non-target visual stimulus (randomly presented on 80% of trials), and a 2000 Hz tone was the auditory target (20% of trials). Stimuli were presented at a fixed rate (stimulus-onset asynchrony 1.03 s) and participants were required to silently count all targets.*

Results: *Compared with controls, the AD/HD group without excess beta showed reduced P2 and P3 to auditory targets, topographic differences in target N1 and N2, and reduced P2 and P3 to visual non-targets, replicating previous AD/HD research. The AD/HD group with excess beta showed a general reversal of these effects in the auditory target N1, P2, N2, and P3, and visual non-target N1, P2 and P3, appearing similar to the control group. However, their visual non-target P1 was more aberrant than that of the other AD/HD group.*

Conclusions: *These results suggest that the children with excess beta do not demonstrate the impaired discrimination and categorization usually noted in children with AD/HD of the combined type. Further research on the cognitive and perceptual functioning of EEG-defined subgroups of AD/HD is warranted.*

Key words: *Inter-modal oddball task, cognitive functions, perceptual functions*

BACKGROUND

Attention Deficit/Hyperactivity Disorder (AD/HD) is a prevalent disorder of childhood, which affects approximately 5% of children (American Psychiatric Association; APA, 1994). The primary symptoms of AD/HD are varying levels of inattention, hyperactivity, and impulsivity. The DSM-IV (APA, 1994) presents a two dimensional model of AD/HD, which allows the diagnosis of three types of the disorder: AD/HD of the predominantly inattentive type (AD/HDin), AD/HD of the predominantly hyperactive/impulsive type (AD/HDhyp), and AD/HD combined type (AD/HDcom). Event related potentials (ERPs) have been used to investigate the perceptual and cognitive-processing deficits in this disorder [see Kropotov & Mueller (2009) for a recent discussion of potential benefits of ERP usage in the AD/HD field in neuropsychology]. Many ERP studies have reported differences in cortical activity differentiating AD/HD patients from normal children, and between DSM-IV types of AD/HD (see Barry et al., 2003 for a review).

The visual P1 component has not differentiated AD/HD children from controls in several studies (Strandburg et al., 1996; Jonkman et al., 1997; Oades, 1998; Steger et al., 2000), but Kemner et al. (1996) reported that children with attention deficit disorder with hyperactivity (according to DSM-III criteria; APA, 1980 – similar to AD/HDcom) had smaller P1 amplitudes to standard and deviant stimuli at occipital sites.

The N1 and P2 components have differentiated AD/HD children from controls in both the auditory and visual modalities, but such findings are not consistent. Loiselle et al. (1980) reported reduced N1 amplitudes to attended stimuli in hyperactive subjects compared with controls, using a selective dichotic listening task. Johnstone and Barry (1996) reported no N1 amplitude differences to targets and non-targets in a two-tone oddball task. Oades et al. (1996) also found no amplitude differences for N1 in a three-tone oddball task. The reason for these variations in findings is unclear. In the visual modality, Kemner et al. (1996) found no N1 differences between AD/HD subjects and controls to deviant, novel or standard stimuli. Similarly, Strandburg et al. (1996) found no N1 amplitude differences during a continuous performance task. They suggest that the resource allocation for visual processing indexed by early ERPs was not dysfunctional in AD/HD.

A number of studies have reported larger P2 components in children with AD/HD compared to controls, for both auditory and visual stimuli (Holcomb et al., 1986; Robaey et al., 1992; Satterfield et al., 1994; Johnstone & Barry, 1996; Oades et al., 1996; Kemner et al., 1996). However, this difference is not always found (Prichep et al., 1976; Halliday et al., 1983; Karayanidis et al., 2000). Oades (1998) suggests that a larger P2 represents irrelevant stimuli capturing attention and therefore reflects greater resource allocation to multiple stimuli, whereas smaller P2 amplitudes may relate to impulsive behaviour "…if an inhibitory process in the transition from exogenous to endogenous processing is missing" (Oades et al., 1996, p. 165).

The N2 component, particularly in oddball tasks, is related to stimulus discrimination and is elicited by unexpected events (Näätänen & Picton, 1986). In AD/HD children it has been reported to be smaller to target and standard stimuli (Loiselle et al., 1980; Satterfield et al., 1984; Satterfield et al., 1990; Satterfield et al., 1994; Johnstone & Barry, 1996; Johnstone et al., 2001), which has been interpreted as a task relevant stimulus discrimination deficit (Satterfield et al. 1994; Johnstone & Barry, 1996; Lazzaro et al., 2001).

The P3 component to targets in AD/HD subjects is consistently smaller than in controls. However, the interpretation of this decrease has varied over different paradigms. Satterfield et al. (1990) argued that decreased P3 amplitude reflected a deficit in arousal. Loiselle et al. (1980) using a selective attention task, Satterfield et al. (1994) using a mixed modality task, and Overtoom et al. (1998) using a continuous performance task, suggested that smaller P3 amplitude reflected an attention deficit. Other laboratories have suggested that this effect reflects diminished stimulus facilitation (Holcomb et al., 1986; Satterfield et al., 1990; Kemner et al., 1996), and in both the auditory (Frank et al., 1994, 1998) and visual modalities (Holcomb et al., 1985; Strandburg et al., 1996; Frank et al., 1996; Jonkman et al., 2000) smaller P3 amplitudes have been thought to reflect a deficit in resource capacity or inappropriate allocation of resources. It is apparent that the large number of factors that mediate P3, such as probability, attention, stimulus context, task relevance, memory, processing resources and their allocation, have all been reflected in these varying interpretations over differing experimental paradigms.

Relatively few studies have examined cross-modal stimuli in relation to AD/HD. Satterfield et al. (1990, 1994) used frequent and infrequent tones and flashes concurrently, with responses required to the infrequent stimulus in a designated modality, while ignoring all other stimuli. Satterfield et al. (1990) found both intra- and inter-channel selection deficits and concluded that these resulted from insufficient facilitation of responses to attended stimuli. Satterfield et al. (1994) reported that AD/HD children had smaller N1 amplitudes with shorter latencies, and smaller N2 and P3 amplitudes, and concluded that these differences reflected preferential processing of attended stimuli. Johnstone et al. (1996b) conducted a similar study, aiming to reduce confounds in the Satterfield studies. Their primary finding was a general decrease in the auditory P2 component, which they interpreted as a deficit in processing task relevant stimuli.

Brown et al. (2005), using an inter-modal oddball task, showed that AD/HD in children had smaller N1, P2 and P3 amplitudes than controls to auditory targets and visual non-targets. These differences were attributed to a generalised deficit in stimulus processing in the AD/HDin subjects. Using the same inter-modal paradigm, Barry et al. (2006) reported a study of two groups of boys with different DSM types of AD/HD. Both types showed reduced P2 and P3 amplitudes to targets and non-targets compared with controls. In addition, boys with the combined type showed greater component equipotentiality and

increased latencies to the auditory targets than boys with the inattentive type of AD/HD. A similar but weaker pattern for the visual non-target responses was found, but only in the inattentive group. That is, apart from some type differences, both the Brown et al. (2005) and Barry et al. (2006) studies reported that children with AD/HD showed reduced P2 and P3 amplitudes to both auditory targets and visual non-targets compared with controls in an inter-modal paradigm.

In a study of normal adults comparing ERPs from this paradigm and an auditory oddball paradigm, Brown et al. (2006) noted the absence of a large N2 to targets in the inter-modal task, compared with responses to the identical target in an auditory oddball task. They concluded that early ERP components in oddball conditions are affected only by standards of the same sensory modality, while later cognitive components reflect context-specific processes, such as those involving the inter-modal visual standard. The inter-modal paradigm can thus illuminate different aspects of sensory processing compared with those commonly explored in intra-modal oddball tasks. For example, the reduced P2 noted in AD/HD children in the inter-modal oddball task, compared with the general increase reported in auditory oddball tasks, may reflect the absence of intra-modal processing in the P2 latency range.

In this context, the aim of the current study was to investigate whether this inter-modal oddball task could distinguish two groups of children with AD/HD of the combined type, differing in their resting EEG profiles. Clarke et al. (2001b) had described an atypical group of children with AD/HD of the combined type who had excess beta activity apparent in their resting eyes-closed EEG, and reported that these children were prone to moody behaviour and temper tantrums. Subsequently Clarke et al. (2001a) carried out a cluster analysis of a large group of children with AD/HD of the combined type, and reported the existence of three EEG-defined subtypes, one of which (Cluster 3) had excess beta in their EEG. The other two clusters were described as having the typical AD/HD profile of increased theta activity, and reduced beta activity, although they differed in detail – Cluster 1 had high amplitude theta with deficiencies of delta and beta, and Cluster 2 had increased slow wave and deficiencies of fast wave activity. In a later cluster study of children with the inattentive type of AD/HD (Clarke et al., 2002), Clusters 1 and 2 were again found, but not the excess beta Cluster 3. That is, there appears to be a unique subgroup of children with AD/HD of the combined type, who have excess beta in their EEG. This study investigated the ERP responses of such children to the auditory-visual oddball task, to determine whether they have processing deficits similar to children with the typical AD/HD profile of increased theta activity and reduced beta activity.

MATERIAL AND METHODS

Participants

Three groups of 20 boys between the ages of 8 and 12 years (mean age 9.8, SD 1.1 years) participated in this study. They were a subset of subjects from the EEG cluster study of Clarke et al. (2001a) who had ERP data available. There were two age-matched AD/HD groups, consisting of children diagnosed with AD/HDcom with excess beta in their EEG (AD/HD+) and without excess beta (AD/HD-), and a group of age-matched controls. The AD/HD group without excess beta showed the excess theta typical of the disorder.

The AD/HD subjects were new patients presenting to a private paediatric clinic in Sydney, Australia. These children had no diagnostic history of AD/HD, had not been treated with medication for the disorder and were tested prior to any medication administration. Inclusion of the AD/HD participants was based on a clinical assessment and agreement of both a paediatrician and a psychologist. Diagnosis was based on DSM-IV criteria and inclusion was dependent on meeting the full diagnostic criteria for AD/HDcom. The AD/HD subjects completed a psycho-educational assessment including the WISC-III, Neale Analysis of Reading and the Wide Range Achievement Test (WRAT, spelling subtest). Clinical subjects were only included if they had a full scale IQ greater than 85.

Control subjects were included if they scored within the average range or better on an assessment of reading and spelling, and had an IQ greater than 85. Control children were assessed in a clinical interview similar to that used for assessing the clinical subjects, and parents of control children completed a Child Behaviour Checklist to aid in the screening for behavioural problems.

Exclusion criteria for all groups included a history of problematic prenatal, perinatal or neonatal period, a disorder of consciousness, head injury with cerebral symptoms, history of central nervous system diseases, convulsions or a history of convulsive disorders, paroxysmal headaches or tics. Any children from the clinical or control samples demonstrating depression, anxiety, oppositional behaviour, syndromal disorders or EEG spike wave activity were also excluded.

Procedure

All subjects were tested in a single morning session that lasted approximately 2.5 hours. In this period all subjects had an electrophysiological assessment including an EEG and a visual/auditory oddball task, which is the focus of this paper. This task was performed with subjects seated in a reclined position.

EEG electrode placement was in accordance with the international 10/20 system. Activity was recorded at Fp1, Fp2, Fpz, F3, F4, F7, F8, Fz, C3, C4, Cz, T3, T4, T5, T6, P3, P4, Pz, O1, O2 and Oz, using an electrode cap with

tin electrodes referenced to linked ears. Electro-oculogram (EOG) was recorded, using a single 9 mm tin electrode, from the outer canthus of the right eye and referenced to Fpz. Activity was grounded using a 9 mm tin electrode placed on the left cheek, and impedance levels for all electrodes were set to 5 kOhm.

ERPs were generated online by a Cadwell Spectrum 32, software version 4.22, using test type cognitive, protocol M-XP300. The low frequency filter was set at 0.53 Hz, high frequency filter at 70 Hz, with a 50 Hz notch filter. The sampling rate for the ERP was set at 200 Hz. ERP epochs were recorded for the period 500 ms after stimulus presentation and averaged on line. The technician manually assessed parameters for artifact rejection based on an initial artifact-free period of the raw ERP trace. Activity that exceeded these parameters was rejected from the averaged ERP.

Stimuli

The visual/auditory oddball task consisted of 240 (80%) visual stimuli (non-targets), and 60 (20%) auditory stimuli (targets), presented at a rate of 1 stimulus every 1.03 sec. The visual stimulus consisted of a counter-phasing (reversing) checkerboard presented on a 14 in computer monitor with a fixation point in the centre. The auditory stimulus was a 2000 Hz tone (60 dB with 15 ms rise/fall times and 15 ms plateau) presented binaurally through headphones, randomly interspersed with the visual stimuli. Subjects were required to maintain gaze at the fixation point while silently counting the number of tones presented.

ERP quantification

Peak picking was carried out manually, blind to the subject group, by selecting the largest positive or negative deflection within latency ranges defined from the across-group grand means. N1, P2, N2 and P3 components were analysed for auditory target stimuli, and P1, N1, P2, N2 and P3 components were analysed for visual non-target stimuli. Latency ranges were as follows – for auditory targets: N1, 60-190 ms; P2, 100-280 ms; N2, 160-340 ms; and P3, 240-450 ms, – for visual non-targets: P1, 35-160 ms; N1, 70-195 ms; P2, 115-260 ms; N2, 170-360 ms; and P3, 260-490 ms. Following our previous studies of ERPs in this paradigm, the ERPs for both target and non-target stimuli were analysed from 9 sites (F3, Fz, F4, C3, Cz, C4, P3, Pz, and P4).

Statistical analysis

ERP data for all component amplitudes and latencies from the central 9 sites were analysed using a mixed MANOVA (O'Brien & Kaiser, 1985), with a between-subject factor of Group (AD/HD+, AD/HD-, and controls), and within-subject factors of sagittal (Frontal, Central, Parietal) and lateral (Left, Midline, Right) topographic dimensions. Within the Group factor, planned non-orthogonal contrasts compared the AD/HD- group with the control group

(to check comparability with previous literature), and the AD/HD+ group with the AD/HD – group (to establish ERP profile differences). Following Pfefferbaum et al. (1989), additional planned contrasts were included to clarify the topographic distribution of each component's amplitudes. Contrasts for the sagittal factor compared frontal vs. parietal, and central vs. the mean of frontal and parietal regions. Contrasts for the lateral factor compared left vs. right hemispheres, and midline vs. the mean of the hemispheres. As these contrasts were planned and did not exceed the degrees of freedom for effect, no Bonferroni-type adjustment of a levels was required (Tabachnick & Fidell, 1989). If there was a main effect of group, amplitude data were submitted to vector scale normalization (McCarthy & Wood, 1985) and only group by topographic interactions that remained significant after this procedure are reported. All contrasts reported had df = (1, 57). To save space, only between-group results are presented.

RESULTS

Between-group ERP comparisons

No child had less than 24 target epochs and 96 non-target epochs in their averages. The mean ERPs for the AD/HD and control groups are shown in Figure 1 in separate panels for auditory target (top) and visual non-target stimuli (bottom). The auditory target produced a fronto-central N1 around 120 ms, and a centro-parietal P3 (340 ms). Between these there is evidence of a central P2 (200 ms) and a negative-going peak corresponding to the N2 (250 ms), which are more obvious in individual data. In response to the auditory targets, the AD/HD+ group generally appears to be similar to the control group rather than the AD/HD- group.

In the response to visual non-targets, a parietal P1 (85 ms) is evident, followed by a fronto-central N1 (130 ms), centro-parietal P2 (200 ms), a fronto-central negative-going peak corresponding to the N2 (250 ms), and a parietal P3 (335 ms). With the ERPs to the visual non-target stimuli, the AD/HD+ group appears to be quite distinct from the other groups.

Target ERPs

The AD/HD- group differed from the controls in having reduced left frontal N1 amplitude ($F = 4.11$, $p < .05$). The AD/HD+ differed from the AD/HD- group in having reduced N1 at the midline ($F = 4.76$, $p < .05$), and a reduction in the right hemisphere approached significance ($F = 3.91$, $p = .053$) (see Figure 2, top left panel).

Across the scalp, the AD/HD- group had smaller auditory P2 amplitudes than the control group ($F = 7.45$, $p < .01$); see Figure 2, second left panel. In the lateral dimension, the reduction was larger in the midline than the hemispheres ($F = 9.23$, $p < .005$). This topographic difference was almost revers-

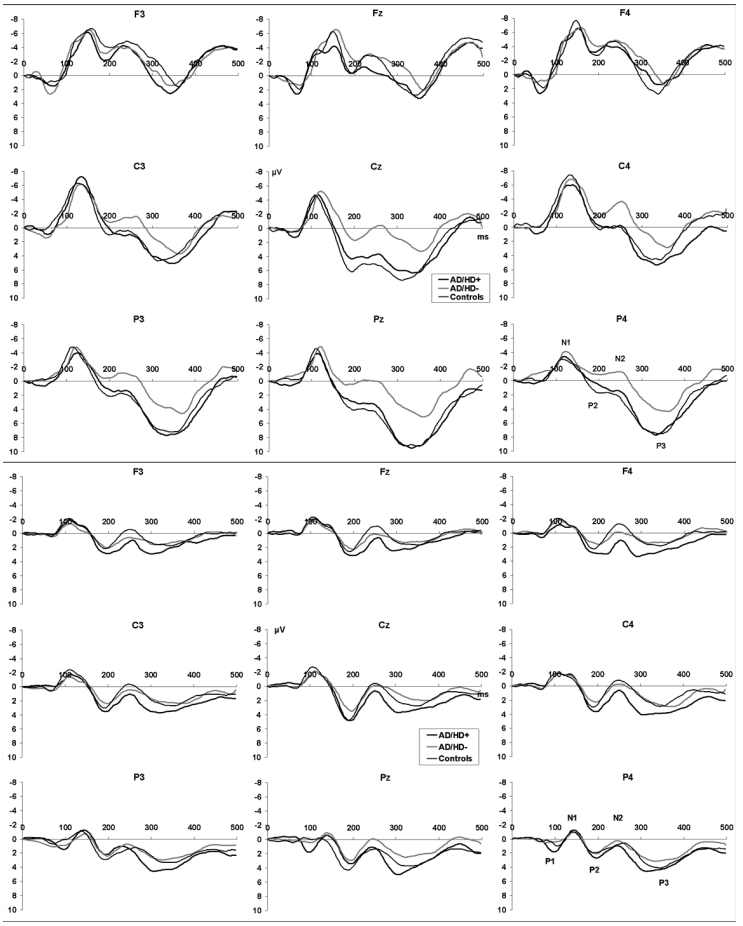

Fig. 1. Grand average ERPs at analysis sites for auditory targets (top) and visual non-targets (bottom), for the AD/HD+ (thick black line), AD/HD- (grey line) and control (thin black line) groups separately. Response peaks are indicated at P4.

ed in the AD/HD+ group, which had a more midline P2 topography than the AD/HD- group ($F = 5.92$, $p < .05$).

The AD/HD- group had a less frontal auditory N2 than the control group, with its amplitude enhanced in posterior ($F = 8.46$, $p < .005$) and central regions ($F = 11.30$, $p < .001$) (see Figure 2, third left panel). It was also relatively enhanced at the midline ($F = 8.26$, $p < .01$) and vertex ($F = 9.23$, $p < .005$). The AD/HD+ group N2 was reduced from that of the AD/HD- group in posterior (approached significance, $F = 3.03$, $p = .087$) and midline ($F = 4.33$, $p < .05$) regions, approaching the distribution of the control group.

Auditory P3 amplitudes were smaller in the AD/HD- group than controls (see bottom left panel of Figure 2), $F = 7.05$, $p < .01$), particularly in the midline ($F = 11.24$, $p < .001$), although this only approached significance in the normalised data ($F = 3.29$, $p = .05$). This midline reduction was larger in pos-

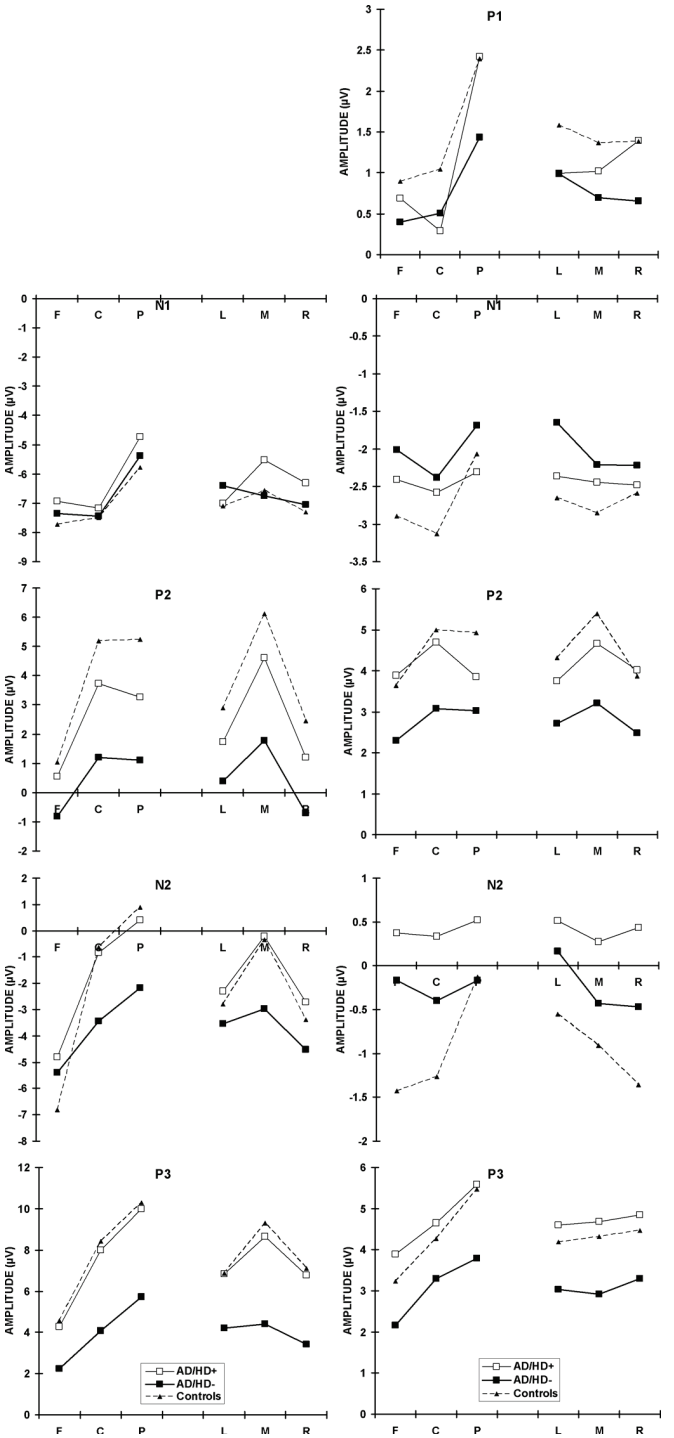

Fig. 2. Sagittal and lateral distribution of each component, separated by group, for auditory targets (left) and visual non-targets (right). Regions are labelled: F = frontal, C = central, P = parietal, L = left hemisphere, M = midline, R = right hemisphere

terior than frontal regions ($F = 4.60$, $p < .05$) and largest in central regions ($F = 12.13$, $p < .001$). These differences were substantially reversed in the AD/HD+ group compared with the AD/HD- group: P3 was larger overall ($F = 5.85$, $p < .05$).

Auditory ERP latencies tended to be longer in the patient groups compared with controls. N1 latency was significantly longer in the AD/HD- group (133.2 ms) than the control group (120.2 ms) ($F = 7.68$, $p < .01$). P2 latency was somewhat longer in the AD/HD- group (201.8 ms) than controls (187.3 ms) ($F = 3.63$, $p = .062$), as was P3 latency (346.5 ms versus 332.6 ms: $F = 3.33$, $p = .073$). No auditory latency differences between AD/HD+ and AD/HD- approached significance.

Non-target ERPs

The visual P1 was somewhat reduced in AD/HD- compared with controls, but this did not approach significance in any group or topographic comparisons. As is apparent in the top right panel of Figure 2, P1 was relatively reduced centrally ($F = 6.34$, $p < .05$), but enhanced in the right hemisphere ($F = 4.78$, $p < .05$), in the AD/HD+ group compared with the AD/HD- group.

Although apparently somewhat smaller, the visual N1 (second right panel of Figure 2) did not differ significantly in the AD/HD- group compared with the control group. The visual N1 was larger in the left central region in AD/HD+ than AD/HD- ($F = 5.99$, $p < .05$).

The visual P2 (Figure 2, third right panel) was reduced in the AD/HD- group compared with controls ($F = 6.59$, $p < .05$). This was substantially reversed in the AD/HD+ group, which had a significantly larger P2 than the AD/HD- group ($F = 4.04$, $p < .05$).

The visual N2 component (see Figure 2 fourth right panel) was relatively small, and none of the apparent topographic differences between the groups approached significance.

The fifth right panel of Figure 2 shows that the visual P3 amplitudes were reduced in the AD/HD- group compared with controls ($F = 4.10$, $p < .05$). This was reversed in the AD/HD+ group, which had a significantly larger P3 than the AD/HD- group ($F = 6.94$, $p < .05$), particularly in the midline frontal region ($F = 9.72$, $p < .005$).

Visual ERP latencies generally tended to be longer in the patient groups. P1 latency was somewhat longer in the AD/HD- group (84.1 ms) than the control group (79.2 ms) ($F = 2.95$, $p = .091$), as was N1 latency (128.5 ms compared to 119.0 ms: $F = 3.87$, $p = .054$), and P2 latency (197.9 ms compared with 190.5 ms: $F = 3.63$, $p = .062$). N2 latency was also somewhat longer in the AD/HD- group (257.7 ms) than controls (249.9 ms) ($F = 3.14$, $p = .082$). In contrast to the other visual peaks, P3 latency was significantly reduced in AD/HD+ (320.8 ms) compared with AD/HD- (342.8 ms) ($F = 6.55$, $p < .05$).

DISCUSSION

This study used an inter-modal oddball paradigm, with a counter-phasing checkerboard as the visual non-target and a tone as the auditory target, in an exploration of perceptual and cognitive processing differences in boys with AD/HD of the combined type, with and without excess beta activity in their EEG. The auditory targets produced clear N1, P2, N2 and large P3 components, with the expected morphology and topography (see Figure 1), embedded in a broad frontal negativity previously reported in children (Holcomb et al., 1986; Courchesne, 1990; Johnstone & Barry, 1996; Johnstone et al., 2001; Barry et al., 2006). As expected, the visual non-targets produced an additional parietal P1 around 100 ms. The broad frontal negativity of the auditory response was absent from the visual response, and as previously reported in this paradigm, the visual non-target response included an appreciable P3. This component to the standard stimuli in an oddball task probably reflects the wider attentional focus in children, resulting in similar components to target and standard stimuli (Friedman et al., 1984; Enoki et al., 1993; Johnstone et al., 1996a; Barry et al., 2006).

Boys with AD/HD of the combined type without excess beta (but with excess theta – essentially representing the bulk of boys within this DSM type) had significantly reduced amplitudes in many components elicited by the auditory targets, compared with the control group. N1 to targets was significantly reduced in the left frontal region. P2 was globally reduced, particularly in the midline. N2 was less frontal and relatively enhanced at the midline, indicating a more equipotential N2. Complementary effects were apparent in the target P3, together with a global amplitude reduction. That is, auditory target stimuli produced smaller P2 and P3 components, and more equipotential P2, N2 and P3 components in a typical AD/HDcom group than in control boys. All components produced by auditory target stimuli tended to have greater latencies in this group. The increased equipotentiality of auditory target components in the standard AD/HDcom group suggests less specificity/specialisation of the underlying processes and their generators. This is supported by the increased latency in the same components, together suggesting a general immaturity in perceptual/cognitive functioning. This replicates our previous findings on this group (Barry et al., 2006).

Boys with AD/HD-, compared with controls, also had reduced P2 and P3 amplitudes elicited by the visual non-targets, with generally longer latencies. Again, these results confirm previous findings (Barry et al., 2006). The reduced visual non-target P2 and P3 amplitudes in this group parallel the reduced auditory target P2 and P3 amplitudes, suggesting that they reflect a general processing deficit. In an oddball task, the P2 component probably represents inhibition of sensory input from further processing (Hegerl & Juckel, 1993) involving automatic stimulus identification/discrimination (Lindholm & Koriath, 1985), or inhibition of other channels competing for attention and further processing

(Hansen & Hillyard, 1988; Oades, 1998). P3 is generally taken to represent context updating (Donchin & Coles, 1988), and the extent to which this is activated depends upon the significance or relevance of the stimulus (Sutton & Ruchkin, 1984). Alternative perspectives have been proposed, such as context closure (Desmedt, 1981; Verleger, 1988) and event categorization (Kok, 2001). The latter seems particularly relevant here as it accommodates the P3 to the visual non-target stimuli. Hence reduced P2 and P3 together could indicate reduced discrimination and categorization of all stimuli in this paradigm. This suggestion was previously proposed in Barry et al. (2006).

The target AD/HD group with excess beta showed a general reversal of these effects, particularly in the P2 and P3 to both auditory targets and visual non-targets, making their ERPs generally similar to the control group. This suggests that they do not possess the impaired discrimination and categorization noted in typical AD/HDcom boys. However, the excess beta group did demonstrate similar latency aberrations to those noted in the AD/HD- group, suggesting that, to some extent, they suffer a general immaturity in perceptual/cognitive functioning in common with the AD/HD- group. Distinct from this was the reduced P3 latency to non-target visual stimuli, readily apparent in the mean ERPs shown in the bottom panel of Fig. 1. This could suggest an early disengagement from the non-target stimuli in this paradigm.

The AD/HD group with excess beta also displayed aberrant visual non-target P1 and N2 components (see Fig. 2), although the latter was not significant. Their P1 was reduced in central areas and had a right-hemisphere focus quite unlike that of the other groups. P1 is generally thought to reflect aspects of the initial extraction of visual information, but the implications of such aberrant topography are unknown. These visual non-target processing anomalies could be expected to impact perceptual/cognitive functioning in this group, and are worthy of further research in future studies of this EEG-defined subtype of AD/HD.

The most important finding of this study is that the EEG-defined subtypes of AD/HD children, despite both meeting DSM-IV criteria for AD/HD of the combined type, differ substantially in their ERPs elicited in this intermodal oddball paradigm. These ERP differences imply differences in their stimulus processing, which in turn can be expected to affect a range of cognitive and perceptual processing in their daily activities. It is interesting to note that the ERPs of the group with excess beta appear more normal than those of the typical AD/HD group, with many of their components almost matching those of the controls. This implies that the impact of the elevated beta in their EEG extends beyond the increased moodiness and temper tantrums noted in their symptom profile, perhaps directly producing behavioural impairments similar to those commonly attributed in the literature to the ERP anomalies found in the bulk of children with AD/HD of the combined type. Further research exploring the functioning of EEG-defined subgroups of children with AD/HD is clearly warranted by the present results.

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REFERENCES

American Psychiatric Association (APA). (1980). *Diagnostic and Statistical Manual of Mental Disorders (3rd ed.).* Washington DC: American Psychiatric Association.

APA. (1994). *Diagnostic and Statistical Manual of Mental Disorders (4th ed.).* Washington DC: American Psychiatric Association.

Barry, R.J., Johnstone, S.J. & Clarke, A.R. (2003). A review of electrophysiology in attention-deficit/hyperactivity disorder: II. Event related potentials. *Clinical Neurophysiology, 114,* 184-198.

Barry, R.J., Clarke, A.R., McCarthy, R., Selikowitz, M. & Brown, C.R. (2006). Event-related potentials in two DSM-IV subtypes of Attention-Deficit/Hyperactivity Disorder: An investigation using a combined modality auditory/visual oddball task. In: R.D. Oades (ed.), *Attention-Deficit/Hyperactivity Disorder (AD/HD) and the Hyperkinetic Syndrome (HKS): Current Ideas and Ways Forward* (229-247). New York: Nova Publishers, Inc.

Brown, C.R., Clarke, A.R., Barry, R.J., McCarthy, R., Selikowitz, M. & Magee, C. (2005). Event-related potentials in Attention-Deficit/Hyperactivity Disorder of the predominantly inattentive type: An investigation of EEG-defined subtypes. *International Journal of Psychophysiology, 58*, 94-107.

Brown, C.R., Clarke, A.R. & Barry, R.J. (2006). Inter-modal attention: ERPs to auditory targets in an inter-modal oddball task. *International Journal of Psychophysiology, 62*, 77-86.

Clarke, A.R., Barry, R.J., McCarthy, R. & Selikowitz, M. (2001a). EEG-defined subtypes of children with Attention-Deficit/Hyperactivity Disorder. *Clinical Neurophysiology, 112*, 2098-2105.

Clarke, A.R., Barry, R.J., McCarthy, R. & Selikowitz, M. (2001b). Excess beta in children with Attention-Deficit/Hyperactivity Disorder: An atypical electrophysiological group. *Psychiatry Research, 103,* 205-218.

Clarke, A.R., Barry, R.J., McCarthy, R., Selikowitz, M. & Brown, C.R. (2002). EEG evidence for a new conceptualisation of attention deficit hyperactivity disorder. *Clinical Neurophysiology, 113*, 1036-1044.

Courchesne, E. (1990). Chronology of postnatal human brain development: Event-related potential, positron emission tomography, myelinogenesis, and synaptogenesis studies. In: J.W. Rohrbaugh, R. Parasuraman & R. Johnson (eds.), *Event-Related Brain Potentials: Issues and Interdisciplinary Vantages* (210-241). New York: Oxford University Press.

Desmedt, J. (1981). P300 in serial tasks: an essential post-decision closure mechanism. *Progress in Brain Research, 54,* 682-686.

Donchin, E. & Coles, M.G. (1988). Is the P300 component a manifestation of context updating? *Behavioral and Brain Sciences, 11*, 357-427.

Enoki H., Sanada S., Yoshinaga H., Oka E. & Ohtahara S. (1993). The effects of age on the N200 component of the auditory event-related potentials. *Cognitive Brain Research, 1*, 161-167.

Frank, Y., Seiden, J.A. & Napolitano, B. (1994). Event-related potentials to an „oddball" auditory paradigm in children with learning disabilities with or without attention deficit hyperactivity disorder. *Clinical Electroencephalography, 25*, 136-141.

Frank, Y., Seiden, J.A. & Napolitano, B. (1996). Visual event related potentials and reaction time in normal adults, normal children and children with attention deficit hyperactivity disorder: Differences in short-term memory processing. *International Journal of Neuroscience, 88*, 109-124.

Frank, Y., Seiden, J.A. & Napolitano, B. (1998). Electrophysiological changes in children with learning and attentional abnormalities as a function of age: event-related potentials to an „oddball" paradigm. *Clinical Electroencephalography, 29*, 188-93.

Friedman, D., Brown, C., Vaughan, H.G., Cornblatt, B. & Erlenmeyer-Kimling, L. (1984). Cognitive brain potential components in adolescents. *Psychophysiology, 21,* 83-96.

Halliday, R., Callaway, E. & Naylor, H. (1983). Visual evoked potential changes induced by methylphenidate in hyperactive children: Dose/response effects. *Electroencephalography and Clinical Neurophysiology, 55,* 258-267.

Hansen, J.C. & Hillyard, S.A. (1988). Temporal dynamics of human auditory selective attention. *Psychophysiology, 25*, 316-329.

Hegerl, U. & Juckel, G. (1993). Intensity dependence of auditory evoked potentials as an indicator of central serotonergic neurotransmission: a new hypothesis. *Biological Psychiatry, 33*, 173-187.

Holcomb, P.J., Ackerman, P.T. & Dykman, R. (1985). Cognitive event-related potentials in children with attention and reading deficits. *Psychophysiology, 22,* 656-667.

Holcomb, P.J., Ackerman, P.T. & Dykman, R. (1986). Auditory event-related potentials in attention and reading disabled boys. *International Journal of Psychophysiology, 3*, 263-273.

Johnstone, S.J. & Barry, R.J. (1996). Auditory event-related potentials to a two-tone discrimination paradigm in attention deficit hyperactivity disorder. *Psychiatry Research, 64*, 179-192.

Johnstone, S.J., Barry, R.J. & Anderson, J.W. (2001). Topographic distribution and developmental timecourse of auditory event-related potentials in two subtypes of attention-deficit hyperactivity disorder. *International Journal of Psychophysiology, 42*, 73-94.

Johnstone, S.J., Barry, R.J., Anderson, J.W. & Coyle, S.F. (1996a). Age-related changes in child and adolescent event-related potential component morphology, amplitude and latency to standard and target stimuli in an auditory oddball task. *International Journal of Psychophysiology, 24*, 223–238.

Johnstone, S.J., Barry, R.J. & Fox, A.M. (1996b). A combined auditory and visual „oddball" ERP investigation of children with attention-deficit hyperactivity disorder. In: C. Ogura, Y. Koga & M. Shimokochi (eds.), *Recent Advances in Event-Related Brain Potential Research* (774-776). Amsterdam: Elsevier Science.

Jonkman, L.M., Kemner, C., Verbaten, M.N. & Koelega, H.S. (1997). Effects of methylphenidate on event-related potentials and performance of attention-deficit hyperactivity disorder children in auditory and visual selective attention tasks. *Biological Psychiatry, 41*, 690-702.

Jonkman, L.M., Kemner, C., Verbaten, M.N., Van Engeland, H., Camfferman, G., Buitelaar, J.K. et al. (2000). Attentional capacity, a probe ERP study: Differences between children with attention-deficit hyperactivity disorder and normal control children and effects of methylphenidate. *Psychophysiology, 37*, 334-346.

Karayanidis, F., Robaey, P., Bourassa, M., de Koning, D., Geoffroy, G. & Pelletier, G. (2000). ERP differences in visual attention processing between attention-deficit hyperactivity disorder and control boys in the absence of performance differences. *Psychophysiology, 37*, 319-333.

Kemner, C., Verbaten, M.N., Koelega, H.S., Buitelaar, J.K., van der Gaag, R.J., Camfferman, G. et al. (1996). Event-related brain potentials in children with attention-deficit and hyperactivity disorder: Effects of stimulus deviance and task relevance in the visual and auditory modality. *Biological Psychiatry. 40,* 522-534.

Kok, A. (2001). On the utility of P3 amplitude as a measure of processing capacity. *Psychophysiology, 38*, 557-577.

Kropotov, J.D. & Mueller, A. (2009). What can event related potentials contribute to neuropsychology? *Acta Neuropsychologica*, *7*, 169-181.

Lazzaro, I., Gordon, E., Whitmont, S., Meares, R. & Clarke, S. (2001). The modulation of the late component event related potentials by pre-stimulus EEG theta activity in ADHD. *International Journal of Neuroscience, 107*, 247-264.

Lindholm, E. & Koriath, J.J. (1985). Analysis of multiple event related potential components in a tone discrimination task. *International Journal of Psychophysiology, 3,* 121-129.

Loiselle, D.L., Stamm, J.S., Maitinsky, S. & Whipple, S.C. (1980). Evoked potential and behavioral signs of attentive dysfunctions in hyperactive boys. *Psychophysiology, 17*, 193-201.

McCarthy, G. & Wood, C.C. (1985). Scalp distributions of event-related potentials: An ambiguity associated with analysis of variance models. *Electroencephalography and Clinical Neurophysiology, 62,* 203-208.

Näätänen, R. & Picton, T.W. (1986). N2 and automatic versus controlled processes. In: W.C. McCallum, R. Zappoli, & F. Denoth (eds.), *Cerebral Psychophysiology: Studies in Event-Related Potentials,* EEG Suppl., 38, 169-186. Amsterdam: Elsevier.

O'Brien, R.G. & Kaiser, M.K. (1985). MANOVA method for analyzing repeated measures designs: an extensive primer. *Psychological Bulletin, 97*, 316-333.

Oades, R.D., Dittmann-Balcar, A., Schpker, R., Eggers, C. & Zerbin, D. (1996). Auditory event-related potentials (ERPs) and mismatch negativity (MMN) in healthy children and those with attention-deficit or Tourette/tic symptoms. *Biological Psychology, 43,* 163-185.

Oades, R.D. (1998). Frontal, temporal and lateralized brain function in children with attention-deficit hyperactivity disorder: A psychophysiological and neuropsychological viewpoint on development. *Behavioural Brain Research, 94*, 83-95.

Overtoom, C.C.E., Verbaten, M.N., Kemner, C., Kenemans, J.L., van Engeland, H., Buitelaar, J.K. et al. (1998). Associations between event-related potentials and measures of attention and inhibition in the Continuous Performance Task in children with ADHD and normal controls. *Journal of the American Academy of Child & Adolescent Psychiatry, 37*, 977-985.

Pfefferbaum, A., Ford, J.M., White, P.M. & Roth, W.T. (1989). P3 in schizophrenia is affected by stimulus modality, response requirements, medication status, and negative symptoms. *Archives of General Psychiatry 46,* 1035-1044.

Prichep, L.S., Sutton, S. & Hakerem, G. (1976). Evoked potentials in hyperkinetic and normal children under certainty and uncertainty: A placebo and methylphenidate study. *Psychophysiology, 13*, 419-428.

Robaey, P., Breton, F., Dugas, M. & Renault, B. (1992). An event-related potential study of controlled and automatic processes in 6-8-year-old boys with attention deficit hyperactivity disorder. *Electroencephalography-and-Clinical-Neurophysiology, 82*, 330-340.

Satterfield, J.H., Schell, A.M., Backs, R.W. & Hidaka, K.C. (1984). A cross-sectional and longitudinal study of age effects of electrophysiological measures in hyperactive and normal children. *Biological Psychiatry, 19,* 973-990.

Satterfield, J.H., Schell, A.M., Nicholas, T.W., Satterfield, B.T. & Freese, T.E. (1990). Ontogeny of selective attention effects on event-related potentials in attention-deficit hyperactivity disorder and normal boys. *Biological Psychiatry, 28*, 879-903.

Satterfield, J.H., Schell, A.M. & Nicholas, T. (1994). Preferential neural processing of attended stimuli in attention-deficit hyperactivity disorder and normal boys. *Psychophysiology, 31*, 1-10.

Steger, J., Imhof, K., Stenhausen, H.C. & Brandeis, D. (2000). Brain mapping of bilateral interactions in attention deficit hyperactivity disorder and control boys. *Clinical Neurophysiology, 111*, 1141-1156.

Strandburg, R.J., Marsh, J.T., Brown, W.S., Asarnow, R.F., Higa, J., Harper, R. et al. (1996). Continuous-processing-related event-related potentials in children with attention deficit hyperactivity disorder. *Biological Psychiatry 40*, 964-980.

Sutton, S. & Ruchkin, D.S. (1984). The late positive complex: advances and new problems. *Annals of the New York Academy of Sciences, 425*, 1-23.

Tabachnick, B.G. & Fidell L. S. (1989). *Using Multivariate Statistics*. New York: HarperCollins.

Verleger, R. (1988). Event-related potentials and cognition: a critique of the context updating hypothesis and an alternative explanation of P3. *Behavioral and Brain Sciences, 11*, 343-356.

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