Performance monitoring is altered in adult ADHD: A familial event-related potential investigation

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Abstract

Background: Attention deficit hyperactivity disorder (ADHD) is a common neurodevelopmental disorder that starts in childhood and frequently persists into adulthood. Electrophysiological studies in children with ADHD provide evidence for abnormal performance monitoring processes and familial association of these processes with ADHD. It is not yet known whether these processes show the same abnormalities and familial effects in adults.

Method: We investigated event-related potential (ERP) indices of performance monitoring in adults with ADHD compared to age matched control participants. We subsequently investigated whether the ERP indices showed a familial association with ADHD by investigating these processes in first degree relatives of children with ADHD. This was achieved using an arrow flanker task presented to 21 adults with ADHD, 20 fathers of children with ADHD and 20 control participants.

Results: Compared to the control group, both adults with ADHD and fathers of children with ADHD displayed significantly weaker error and conflict monitoring, as indexed by the smaller error negativity (Ne) and the N2 components. These two components were highly correlated within each of the three groups ($r = 0.53–0.65$). The groups did not differ on the error positivity (Pe).

Conclusions: These findings closely resemble those previously found in children with ADHD, suggesting that conflict monitoring and early error processing are also abnormal in adults with ADHD; and share familial influences with ADHD throughout the lifespan. The relationship between different indices of performance monitoring may suggest partly common underlying mechanisms or modulators.

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1. Introduction

Attention deficit hyperactivity disorder (ADHD) is a childhood-onset, neurodevelopmental disorder, which frequently persists into adulthood, with around 15% meeting full criteria for ADHD at the age of 25 years (Faraone, Biederman, & Mick, 2006). ADHD is highly heritable with twin studies indicating that approximately 76% of phenotypic variance is accounted for by genetic influences (Faraone et al., 2005). Further evidence comes from family studies (Faraone et al., 2005; Thapar, Holmes, Poulton, & Harrington, 1999), which show increased rates of ADHD in all first degree relatives of affected probands, including siblings (Biederman et al., 1992; Faraone, Biederman, Keenan, & Tsuang, 1991) and parents (Biederman et al., 1992; Biederman, Faraone, Keenan, & Tsuang, 1991).

Functional candidate gene studies focusing on dopamine and related neurotransmitter pathways find convincing evidence for association with genetic variants within or close to the dopamine D4 and D5 receptor genes (Li, Sham, Owen, & He, 2006) and suggestive evidence for a number of other genes, including the dopamine transporter (Thapar, Langley, Owen, & O’Donovan, 2007). Taken together with the results of genomewide scans for genetic variants associated with ADHD these data indicate a complex genetic inheritance with multiple alleles of small effect contributing to the risk for ADHD (Neale et al., 2008).

The relationship from genes to brain to behaviour in ADHD is therefore complex, with the effect of any single gene on behaviour expected to be small. The search for associations with neurobiological intermediate phenotypes or endophenotypes, which reflect more closely the underlying neurobiological mechanisms, has two potential advantages. First, it is feasible that specific genes may show greater effects in endophenotypes than behavioural phenotypes, providing improved measures for new gene discovery. Second, the study of endophenotypes is an essential step in eluci-
dating the cognitive and neurobiological mechanisms that mediate genetic effects on behaviour (Gottesman & Gould, 2003; Tsuang & Faraone, 2000).

The main requirements for cognitive or neurobiological endophenotypes are first that they must be associated with the diagnosis by showing case–control differences, and second they should be present in first degree relatives of affected individuals with levels significantly higher than in the general population (Gottesman & Gould, 2003; Kuntsi, McLoughlin, & Asherson, 2006). In ADHD, interest in performance monitoring as a potential candidate endophenotype emerged, as it has been associated with ADHD in numerous studies (see Kuntsi et al., 2006 for a review) and is linked to dopaminergic functioning (de Bruijn, Hulstijn, Verkes, Ruigt, & Sabbe, 2004; de Bruijn, Sabbe, Hulstijn, Ruigt, & Verkes, 2006; Frank, D’Lauro, & Curran, 2007; Holroyd & Coles, 2002; Kramer et al., 2007; Zirnheld et al., 2004) in prefrontal–cingulate pathways that have been implicated in ADHD (Carter et al., 1998; Gehring & Knight, 2000; Paloyelis, Mehta, Kuntsi, & Asherson, 2007).

The process of performance monitoring is an essential prerequisite for adaptively altering behaviour and decision making, and comprises error detection and conflict monitoring, functions that can be measured by their neurophysiological correlates (event-related potentials or ERPs). An ERP component that is associated with performance monitoring is the N2, a fronto-central negative amplitude that occurs between 200 and 400 ms after stimulus onset. The N2 was originally thought to index response inhibition as there is an N2 enhancement during inhibition of the go response in go/no-go tasks (Falkenstein, Hohnsbein, & Hoormann, 1999). More recent studies suggest that the N2 reflects a more general performance monitoring process, independent of response inhibition (Donkers & van Boxtel, 2004; Nieuwenhuis, Yeung, van den, & Ridderinkhof, 2003). Studies using continuous performance or go/no-go-tasks in children and adults with ADHD did not find differences in N2 between participants with ADHD and controls (Banaschewski et al., 2004; Fallgatter et al., 2004; Overtoom et al., 1998). Yet tasks requiring a higher level of conflict monitoring, such as the stop task and flanker task, have elicited diminished N2 amplitudes or topographic N2 alteration in children with ADHD (Albrecht, Banaschewski, Brandeis, Heinrich, & Rothenberger, 2005; Albrecht et al., 2008; Brandeis et al., 1998; Pliszka, Liotti, & Woldorf, 2000). The abnormality in conflict monitoring processes, as indexed by the N2, is therefore only elicited when there are increased demands on these processes. A familial association between ADHD and the N2 in children was indicated in a recent study, suggesting that the processes reflected by the N2 may mediate genetic effects on ADHD behaviours (Albrecht et al., 2008). To date this has only been explored in relation to childhood ADHD, so it is not yet clear whether there are familial influences on the N2 in older individuals with ADHD.

An erroneous response, in healthy individuals, is associated with a component called the error-related negativity (ERN) (Gehring, Goss, Coles, Meyer, & Donchin, 1993) or the error negativity (Ne) (Gehring, Coles, Meyer, & Donchin, 1990). The specific functional significance of the Ne is still under debate. It may reflect mismatch (Gehring et al., 1993) or response conflict between error and required responses (Carter et al., 1998). A number of studies have investigated the functional relationship between the Ne and the N2: while some suggest that they represent distinct neurophysiological processes (Falkenstein et al., 1999; Ridderinkhof et al., 2002), others suggest they represent the same process of conflict monitoring (Yeung & Cohen, 2006). An additional component associated with error monitoring, the error positivity (Pe), has a more posterior distribution and is elicited after the Ne (Falkenstein, Hoormann, & Hoormann, 1995). Although far less research has addressed the function of the Pe, it is elicited, unlike the Ne, only after full errors of which the subject is aware, which suggests that it represents conscious error-recognition processes (Hajcak, McDonald, & Simons, 2003; Nieuwenhuis, Ridderinkhof, Blom, Band, & Kok, 2001; O’Connell et al., 2007).

Recent ERP studies of the Ne and Pe in childhood ADHD have indicated abnormalities in these processes in children with ADHD (Albrecht et al., 2008; Liotti, Pliszka, Perez, Kothmann, & Woldorf, 2005; van Meel, Heslenfeld, Oosterlaan, & Sergeant, 2007), but this has not yet been investigated in adult ADHD. Further, a recent study indicated that siblings of ADHD probands have altered Ne components in comparison to controls, which must be due to shared genes and/or the environment (Albrecht et al., 2008). Some inconsistency has emerged in the findings of the Ne and Pe in childhood ADHD (Burgio-Murphy et al., 2007; Jonkman, van Melis, Kemner, & Markus, 2007; Wiersema, van der Meere, & Roeyers, 2005) but this has been attributed to the sensitivity of the Ne and Pe components to task-specific factors, such as task difficulty, the definition of an error in each of the studies and differences in the number of error trials used in computation of these components.

The overall aim of this study was to investigate ERP indices of performance monitoring in adult ADHD. Using the same arrow flanker task that was used to investigate the familiarity of performance monitoring in childhood ADHD, we studied the key processes in a sample of adults with ADHD, first degree relatives of ADHD probands (fathers of children with an ADHD diagnosis) and healthy adult controls to obtain meaningful results. First, we predict that, based on the previous findings in children using an identical arrow flanker task (Albrecht et al., 2008), adults with ADHD will have attenuated Ne but normal Pe components. This would indicate the presence of the same deficits in adults with ADHD as that seen in children with ADHD when investigated under identical conditions. Further, we predict that the N2 component will be enhanced in the incongruent compared to the congruent conditions of this task and that this enhancement will be reduced in the ADHD participants compared to the control group, suggesting that conflict monitoring is abnormal in adult ADHD. Second, as parents of children with ADHD share 50% of their genetic variance with their affected offspring (to the same degree as siblings), we hypothesise that the parents of children with ADHD will be significantly different from controls in these cognitive–neurophysiological parameters, indicating a familial association between these parameters and ADHD in adults. Additionally, given the uncertainty regarding the extent to which the N2 and the Ne may reflect distinct or common underlying mechanisms (Falkenstein et al., 1999; Ridderinkhof et al., 2002; Yeung & Cohen, 2006), we aimed to investigate the relationship between these components for the task used here.

2. Methods and materials

2.1. Sample

Twenty-one male adults with ADHD, 20 fathers of children with combined subtype ADHD and 20 healthy control adults participated in this study. On the basis of informed consent. The joint South London and Maudsley and the Institute of Psychiatry NHS Research Ethics Committee approved this study (086/05). Age range was 18–56 years, with a mean age of 32.51 (SD = 8.64) for the ADHD group, 45.90 (SD = 4.15) for the parent group and 30.00 (SD = 6.51) for the control group. A one-way ANOVA indicated a significant main effect of age [F(1, 59) = 18.03, p < 0.001] with post hoc analyses showing no significant difference between the probands and controls [p = 0.48] but significant differences between the probands and fathers [p < 0.001] and controls and fathers [p < 0.001]. Controls were age matched primarily to the proband group, because the primary aim of the study was to show case–control differences for the cognitive–physiological parameters. It was not however possible to identify an age matched sample for the fathers of children with ADHD. All participants had an IQ of 80 or above on the Wechsler Adult Intelligence Scale (WAIS-II) (Wechsler, 1997), with mean IQs of 118 (SD = 10.00) for the ADHD group, 121 (SD = 13.37) for the parent group and 122 (SD = 12.10) for the control group, with no main effect of group on IQ [F(2, 58) = 0.67, p = 0.52].
Adults with ADHD were recruited from the National Adult ADHD Clinic at the Maudsley Hospital, where they received a diagnosis of ADHD from a consultant psychiatrist who specialises in adult ADHD, following an in-depth clinical and psychopharmacological assessment. For the purposes of the study, diagnostic criteria from the DSM-IV were applied. The psychopharmacological data available had been obtained from each of the 18 ADHD symptom items in childhood and adulthood. In addition, individuals were only included if either the proband or an informant reported six or more DSM-IV items for both the hyperactive-impulsive and inattentive sub-scales in childhood, using the Barkley Adult ADHD rating scale for retrospective recall of childhood (Barkley & Murphy, 2005) and, in addition, six or more inattentive items from the Barkley Adult ADHD rating scale for current symptoms (Barkley & Murphy, 2005). ADHD cases included in the study fulfilled criteria for DSM-IV combined subtype ADHD in childhood and either combined type (n = 17) or inattentive type (n = 4) as adults, due to the reduction in the number of hyperactive-impulsive symptoms compared to the inattentive symptoms in one of these cases. Several symptoms of combined type ADHD (Asherson, Chen, Craddock, & Taylor, 2007) were present here. The exclusion criteria for the ADHD group included the presence of an Axis I or II co-morbid psychiatric diagnosis and taking any psychoactive medication other than stimulant medication for treatment of ADHD. A minimum of 48 h medication-free period was required prior to the assessments. All participants were right-handed, as determined by preferred writing hand, and had normal or corrected-to-normal vision.

The parent group was recruited from a database of families who had previously participated in the International Multicenter ADHD genetics project (IMAGE). All of the participating fathers had a biological child who received a research diagnosis of DSM-IV combined subtype ADHD (Chen, et al., 2008). This ensured matching of the childhood subtype of ADHD, since the adult ADHD group had combined subtype ADHD as children, similar to the subtype of the offspring of the fathers included in the study. None of the fathers had a major psychiatric condition, history of substance abuse, or previous head injury. Self-report data were collected on current and retrospective ADHD symptoms, using the Barkley Adult ADHD rating scales, based on the rating scale data, one of the control participants had above-threshold symptoms for the inattentive subtype in the current ratings and two had symptoms sufficient to qualify for combined subtype from the retrospective ratings. These individuals were not excluded from the analysis as they were only above threshold on self-report scales, they had never sought treatment for their symptoms and did not consider themselves impaired. Furthermore, as stated above, the use of unselected samples enables a more accurate estimate of the familial association between ADHD and secondary measures (Andreou, et al., 2007). Control participants were selected from a database of volunteers at the Institute of Psychiatry. They were selected if they had no major psychiatric conditions, substance abuse or previous head injury, and were matched with ADHD participants on age. Self-report data were collected on current and linearly interpolated return movements using the Gratton and Coles method (Gratton, Coles, & Donchin, 1983). Trials with remaining artifacts exceeding ±100 μV in any channel were rejected from the digitally lowpass-filtered (0.1–30 Hz, 24 dB/dec) data before averaging. All trials were inspected visually to detect additional subtle artifacts. Segments were averaged separately for each participant in three different response conditions: (1) stimulus-locked incorrect trials, (2) stimulus-locked congruent correct trials, and (3) response-locked incorrect trials. All averages were free from residual artifacts and contained a minimum of 20 accepted sweeps. The ERPs were transformed to the average reference for all subsequent computations (Lehmann, 1987). Maps of the topographical scalp distribution of electrical brain activity were produced by 16 lateralsite electrodes and a single reference electrode placed between the electrode locations. Calibrated zero baselines were used (instead of prestimulus-baseline corrections) to avoid distorting the map topographies (Brandeis & Lehmann, 1986; Lehmann, 1987).

Control participants had no major psychiatric conditions, substance abuse or previous head injury, and were matched with ADHD participants on age. Self-report data were collected on current and retrospective ADHD symptoms, using the Barkley Adult ADHD rating scales. Based on the rating scale data, one of the control participants had above-threshold symptoms for the inattentive subtype in the current ratings and two had symptoms sufficient to qualify for combined subtype from the retrospective ratings. These individuals were not excluded from the analysis as they were only above threshold on self-report scales, they had never sought treatment for their symptoms and did not consider themselves impaired. Furthermore, as stated above, the use of unselected samples enables a more accurate estimate of the familial association between the cognitive–electrophysiological data and ADHD.

If tested, the two controls and one father with possible ADHD were not outliers on any of the ERP or performance variables and excluding them from analyses did not alter any of the results. We have therefore included them in the main analyses presented here. The mean score for the control group on the ADHD behaviour rating was 8.70 (SD = 8.30) for current and 5.90 (SD = 5.11) for retrospective symptoms. For the ADHD group, the mean scores were 16.55 (SD = 7.62) for current (Fz, FCz) and 13.63 (SD = 5.32) for retrospective symptoms. For the fathers, the mean scores were 12.10 (SD = 8.81) for current and 7.90 (SD = 6.84) for retrospective symptoms. The small difference in ADHD symptom scores between the fathers and controls was not significant for either the current (F1, 39) = 1.58, p = 0.22) or retrospective (F1, 39) = 1.10, p = 0.30) ratings.

2.2. Task and stimuli

The flanker task was based on the Eriksen flanker paradigm (Eriksen & Schultz, 1979) (Fig. 1) and consisted of ten blocks of 40 trials. Columns of black arrowheads (equilateral triangles with 18 mm edge length at 3 positions with 23 mm distance centrality) were presented in the center of the screen in grey background at 120 cm viewing distance. On every trial, the fixation mark in the centre of the screen was replaced by the stimulus. The flankers (two arrowheads pointing to the same direction above and below the position of the fixation mark) were presented 100 ms before the target arrowhead appeared between the flankers (for another 150 ms). Participants were seated in an adjustable chair (eyes protected from light) and not exposed to stimuli; and in the parent group 183.40 (SD = 19.40) for congruent stimuli and 156.75 (SD = 42.87) for incongruent stimuli and 134.86 (SD = 39.83) for incongruent stimuli; and in the parent group 183.40 (SD = 19.40) for congruent stimuli and 156.75 (SD = 18.93) for congruent stimuli. The N2 latency data were skewed and no transformations were successful (cubic, square, identity, square root, 1/root square, inverse, 1/square, 1/cubic); as such, these data were analysed with generalized estimating equations (GEE) in a repeated measures design (group × congruency). GEE models estimate averages rather than the entire distribution of values, and hence are less restricted by distributional assumptions than other approaches to repeated measures analysis. This approach accounts for the correlation in performance on the two conditions; specifically, an exchangeable correlation structure was assumed to account for the within-subject correlation. This allowed the implementation of a group by congruency interaction to test whether group differences for latency of the ERP components are larger in the incongruent condition, as predicted. GEE provides unbiased estimates of the marginal effects, even if the assumed correlation structure is misspecified (Liang & Zeger, 1986; Rabe-Hesketh & Skrondal, 2005). To safeguard a possible misspecification against the variance/covariance matrix, a robust Hubert White sandwich estimator was used to adjust standard errors and hence confidence intervals and p-values (Williams, 2000). In order to test overall effects of group and interaction terms, we used the Wald chi² test. We calculated effect sizes (d) for these data between ADHD and control participants using the difference of the marginal means from the GEE model, divided by the pooled standard deviation of the raw data. It should be noted, however, that these effect sizes might be inaccurate due to the skewness of the data.
3. Results

3.1. Performance data

Repeated measures analyses of variance indicated no overall group effect in terms of errors committed \( F(2,57) = 1.10, p = 0.34 \). The data showed a significant effect of congruency \( F(1,57) = 434.75, p < 0.0001 \), with more errors being committed in incongruent than congruent trials \( t = 12.12 \) for the parent group, \( t = 22.09 \) in the control group, \( t = 18.43 \) in the ADHD group and \( t = 12.14 \) in the parent group. As IQ did not differ between groups, we did not include it in subsequent analyses. However, as age significantly differed between the father compared to the control and proband groups, we initially included age as a covariate in all analyses and only report it when it was significant, as we dropped it from the analyses otherwise.

We adopted a significance level of \( p < 0.05 \) (two-tailed) throughout the analyses and report trends \( p < 0.09 \). All statistical analyses were performed using Stata (Stata Statistical Software, 1997).

Table 1

<table>
<thead>
<tr>
<th></th>
<th>Controls (n = 20)</th>
<th>Parents (n = 20)</th>
<th>ADHD (n = 21)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Errors, mean (SD)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Congruent trials</td>
<td>4.35 (4.61)</td>
<td>3.30 (3.53)</td>
<td>5.15 (5.51)</td>
</tr>
<tr>
<td>Incongruent trials</td>
<td>35.70 (9.29)</td>
<td>30.55 (12.55)</td>
<td>35.10 (17.94)</td>
</tr>
<tr>
<td>MRT, mean (SD)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Congruent trials</td>
<td>285.35 (34.53)</td>
<td>311.09 (31.38)</td>
<td>327.42 (78.40)</td>
</tr>
<tr>
<td>Incongruent trials</td>
<td>373.09 (42.13)</td>
<td>405.52 (38.84)</td>
<td>410.60 (74.87)</td>
</tr>
<tr>
<td>SD-RT, mean (SD)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Congruent trials</td>
<td>65.45 (22.88)</td>
<td>70.59 (31.23)</td>
<td>95.12 (55.43)</td>
</tr>
<tr>
<td>Incongruent trials</td>
<td>63.00 (20.52)</td>
<td>71.79 (23.34)</td>
<td>93.99 (47.89)</td>
</tr>
<tr>
<td>CV, mean (SD)</td>
<td>0.23 (0.06)</td>
<td>0.23 (0.08)</td>
<td>0.28 (0.09)</td>
</tr>
<tr>
<td>MRT: mean reaction time in ms.</td>
<td></td>
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<tr>
<td>SD-RT: within-subject variability in RTs in ms.</td>
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<tr>
<td>CV: coefficient of variation (SD-RT/MRT).</td>
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</table>
Fig. 2. Response-locked error-related components at latencies of maximal amplitude for control participants (red border), parents (green border) and ADHD participants (black border) with maps of error negativity (top) and error positivity bottom, plus t-maps for group comparisons (Controls versus ADHD participants and fathers, respectively). (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of the article.)
3.2.2. Ne and Pe

ANOVA indicated no significant group effects on the latency of the Ne [$F(2, 45) = 1.01, p = 0.37$] (Table 2 and Fig. 2). A Kruskal–Wallis test indicated a main group difference in Ne amplitude measured as a peak-to-peak difference [$H(2) = 11.08, p = 0.004$]. Mann–Whitney post hoc tests indicated a significant difference between ADHD cases and controls [$U = 44.00, p = 0.001$]; a significant difference between fathers and controls [$U = 81.00, p = 0.03$] but no difference between cases and fathers [$U = 122.00, p = 0.32$]. Further, no main group effect on the amplitude of the Pe component [$H(2) = 2.65, p = 0.27, d = 0.11$] or no significant differences in latency between groups emerged [$H(2) = 3.96, p = 0.14, d = 0.44$; Table 2].

3.2.3. N2 and Ne

Spearman’s nonparametric correlation, with age partialled out, indicated significant relationships between the Ne and the N2 for controls [$r = 0.65, p = 0.003$], ADHD participants [$r = 0.53, p = 0.02$].

![Fig. 3. Stimulus-locked N2 to incongruent correct responses. Stimulus-locked averages of control (red), ADHD (black) participants and parents (green). Scalp maps show topography at the mean latency of the N2 peak for each group, plus t-maps for group comparisons (Controls versus ADHD participants and fathers, respectively). (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of the article.)](image-url)

Table 2

<table>
<thead>
<tr>
<th></th>
<th>Controls (n = 19)</th>
<th>Parents (n = 16)</th>
<th>ADHD (n = 16)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean (SD)</td>
<td>Mean (SD)</td>
<td>Mean (SD)</td>
</tr>
<tr>
<td>Error negativity at FCz</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PNe</td>
<td>−1.09 (11.03)</td>
<td>−10.50 (33.20)</td>
<td>−19.79 (33.39)</td>
</tr>
<tr>
<td>Ne</td>
<td>79.36 (25.91)</td>
<td>96.19 (14.75)</td>
<td>85.42 (16.23)</td>
</tr>
<tr>
<td>Amplitude (µV)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PNe</td>
<td>−0.11 (1.94)</td>
<td>0.85 (2.36)</td>
<td>−0.22 (2.36)</td>
</tr>
<tr>
<td>Ne</td>
<td>−9.05 (5.62)</td>
<td>−5.46 (4.61)</td>
<td>−5.05 (2.74)</td>
</tr>
<tr>
<td>Error positivity at Cz</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Latency (ms)</td>
<td>266.65 (86.11)</td>
<td>288.82 (63.75)</td>
<td>275.52 (76.32)</td>
</tr>
<tr>
<td>Amplitude (µV)</td>
<td>8.36 (4.34)</td>
<td>5.71 (2.76)</td>
<td>6.60 (3.57)</td>
</tr>
</tbody>
</table>

PNe: positive peak preceding Ne.
In addition, as in the previous study of children with ADHD, we investigated neurophysiological parameters of performance monitoring. The findings indicate an association between adult ADHD and abnormal performance monitoring, which is strikingly similar to those reported in children with ADHD using the same measures analysed in precisely the same way (Albrecht et al., 2008). In addition, as in the previous study of children with ADHD and their siblings (Albrecht et al., 2008) we found evidence for the familial association between the measures of abnormal performance monitoring and ADHD, but this time in a sample of adults.

As predicted, Ne but not Pe was attenuated in the ADHD group compared to controls, which indicates abnormal initial error detection processes in adult ADHD. This is the first investigation, to our knowledge, into error monitoring in adult ADHD. It is in agreement with similar investigations in childhood ADHD (Liotti et al., 2005; van Meel et al., 2007) in addition to the study of Albrecht et al. (2008) that used identical procedures. Conversely, we did not observe a reduction of the Pe in adults with ADHD. The similarity in the pattern of findings to those obtained by Albrecht et al. (2008) provides some evidence that the inconsistencies of previous findings in error monitoring in ADHD may be due to the sensitivity of these components to task-specific factors, such as emphasis on speed versus accuracy and error rate. We also observed the predicted group differences for conflict monitoring: an N2 enhancement for incongruent stimuli was highest in the control group with attenuated amplitude in the ADHD group.

Fathers of children with ADHD, although not significantly different from the control group in their self-rated behaviour in this study, were significantly different from the control participants in impairment in their error processing, as indexed by the Ne. The significant difference between fathers and the control group on the ERP variables, indicates the presence of shared familial factors that link ADHD and error monitoring at an aetiological level. Furthermore the lack of a significant difference between these two groups for some of the behavioural measures suggests that the ERP variables are more sensitive to the underlying familial liability for ADHD than behaviour itself. The familial association between ADHD and ERP variables could arise from either genetic or shared environmental factors; although the lack of common environmental influences reported for ADHD from the analysis of numerous twin samples (Faraone & Doyle, 2000) strongly suggests that these familial effects are primarily genetic in origin. We therefore conclude that, as in children with ADHD, the Ne appears to index a genetically influenced endophenotype of adult ADHD. Similarly, the parent group was attenuated in the amplitudes of the N2, suggesting that the N2 may also represent an informative endophenotype for ADHD in adults, as well as for childhood ADHD (Albrecht et al., 2008).

The adaptive feedback procedure used in this version of the arrow flanker task kept response accuracy constant at a predetermined level; as such we were able to avoid confounds with speed-accuracy trade-off and equalise error rates between groups. A congruency effect emerged for both errors and RT, with more errors and slower RTs in the incongruent condition. Under the incongruent condition significant differences were observed in the comparison of the adult ADHD probands compared to both the fathers of ADHD children and the control groups. The fact that in our data the performance measures was not significantly different between the group of fathers and the group of controls, while suggesting that there is no familial association of the error and RT variables with adult ADHD, could arise from lack of power to detect relatively small familial effects. In contrast, as discussed above, the significant difference between the father and control groups for the Ne and N2, suggests that these are more sensitive to the underlying familial liability for ADHD than the cognitive performance measures from the same task. This could be explained by behavioural adaptation at the task performance level, where individuals are trying to complete the task to the best of their ability, which is not however reflected in the underlying neuronal activity which better reflects impaired neuronal function associated with the familial risks for ADHD. This closely relates to one of the criteria for an endophenotype, which is the presence of abnormal biological processes, among 'unaffected' first degree relatives of affected cases (Gottesman & Gould, 2003).

The high correlations between the Ne and N2 indicate the possibility of common aetiological influences on these processes. The Ne and the N2 components share sources in the anterior cingulate cortex (ACC) (Carter et al., 1998; Gehring & Knight, 2000), an area previously associated with both adult and childhood ADHD (Bush et al., 1999; Seidman et al., 2006). Although this area is functionally and structurally complex, it is involved in reward-based decision making (Bush et al., 2002) and is thought to be part of a lower level arousal system (Critchley, Melmed, Featherstone, Mathias, & Dolan, 2002). In light of the inconsistencies in the findings on performance monitoring in ADHD and the evidence of a possible common mechanism underlying both Ne and N2, we need also to consider the possibility that error and conflict monitoring deficits in ADHD could both be dependent on motivational and arousal states, which can be modified by task-specific conditions. Previous research has shown that factors that increase motivation or arousal, such as event rate (the presentation rate of stimuli) or rewards, can improve the performance of children with ADHD (Andreou et al., 2007; Konrad, Gauggel, Manz, & Scholl, 2000; Slusarek, Velling, Bunk, & Eggers, 2001). There is evidence that the Ne is subject to influences by monetary incentives (Hajcak, Moser, Yeung, & Simons, 2005; Pailing & Segalowitz, 2004) but further research is required into separating the effects of these factors on performance monitoring in ADHD.

Since the Ne is linked to dopaminergic functioning (Holroyd & Coles, 2002; Kramer et al., 2007), these findings suggest a pos-
sible underlying neural mechanism for the familial influences on abnormal error monitoring in ADHD. Preliminary evidence for such effects comes from the report that the 7-repeate allele of the dopamine D4 receptor (DRD4), a known risk allele for ADHD (Li et al., 2006; Thapar et al., 2007), has shown distinct effects on error monitoring processes (Kramer et al., 2007). The N2 has been linked to the COMT polymorphism (Kramer et al., 2007), previously identified as a possible risk allele for ADHD (Bellgrove et al., 2005) and, similar to the Ne, is related to dopaminergic functioning (Kramer et al., 2007).

To ensure the homogeneity of the sample and minimise the impact of potential confounding conditions, the participants with ADHD were selected to have no major comorbidities and we included males only. This highly selected group had slightly higher than expected IQs, yet they were well matched with the control and parent groups for IQ. Future studies are required to confirm these findings in more typical ADHD samples. Yet another potential limitation in this study was the poor match for age between the fathers of children with ADHD and the proband and control groups. However we do not see an effect of age on any of the cognitive or electrophysiological variables used in this study. Further, if the cognitive processes associated with ADHD improve with age, reflecting the general tendency for reduced ADHD symptoms in adults as compared to children, we would expect any bias due to the age differences in the sample to lead to an overall reduction in Father-control differences. Since we find significant differences between these two groups we conclude that we are indeed detecting true familial effects between ADHD in adults and the Ne and N2, except in the unlikely situation that the Ne and N2 show increasing age dependent differences between the ages of 30 and 45. Although age was not significant as a covariate for any measure, the results indicating familiality on these processes should be replicated in age matched samples to ensure the accuracy of these findings. Another key question that this research does not test is whether these ERP abnormalities are specific to ADHD. Further studies are needed to investigate if they distinguish this ADHD from other conditions, including overlapping neurodevelopmental disorders such as autism spectrum disorder, and behavioural problems such as conduct disorder.

In conclusion, in an investigation of ERP indices of performance monitoring in adult ADHD, we found a similar profile of altered processing deficits as previously identified in children with ADHD using the same procedures and methods of analysis (Albrecht et al., 2008). This suggests that similar group differences for the underlying deficits indexed by the ERP indices appear across the lifespan in ADHD. Further studies should test explicitly the question of whether there is developmental stability with similar findings observed within individuals when measured at different developmental ages, and the association between such potential stability of the underlying processes associated with ADHD, and persistence of the behavioural symptoms into adult life in a proportion of patients with childhood ADHD. We also obtained evidence of familial influences on these processes in adults, as fathers of children with ADHD also had altered indices of performance monitoring, in comparison to controls. As with the case-control differences, these familial effects are therefore seen in groups of adults with ADHD and their the adult relatives of ADHD probands, across the lifespan. Future research should include the longitudinal follow-up of these measures from childhood to adulthood in adult siblings as well as probands, to specifically map the trajectory of the familial effects. Finally, further research is also required to investigate the possibility of a common underlying neural mechanism affecting both the Ne and N2 and their relationship to other cognitive and neural processes implicated in ADHD, as well as investigating the role of specific genes in the association between ADHD and performance monitoring deficits.

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