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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 in adults. 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.

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-

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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, Hoormann, & Hohnsbein, 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, & Woldorff, 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, Hohnsbein, & 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, & Woldorff, 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 familiality 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. We tested two main hypotheses. 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 male 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 = 5.84) 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 [$F(1, 59) = 53.87$, $p < 0.001$] 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–electrophysiological 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 [$F(2, 58) = 0.67$, $p = 0.52$].