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Differential reward processing in subtypes of adult attention deficit hyperactivity disorder

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ABSTRACT

Objectives: Abnormalities in reward processing have been found in adolescents and adults with ADHD using the 'Monetary Incentive Delay' (MID) task. However, ADHD groups in previous studies were heterogeneous regarding ADHD subtype, gender and, in part, drug treatment status.
This study sought to compare neural activations in the ventral striatum (VS) and prefrontal regions during reward processing in homogenous ADHD subtype groups and healthy adults, using the MID task.
Methods: In total, 24 drug-naïve, right-handed male adults with ADHD (12 subjects with combined type (ADHD-ct) and 12 subjects with predominantly inattentive (ADHD-it) type ADHD), and twelve healthy right-handed male control subjects were included.
Results: Compared to ADHD-ct and healthy subjects, ADHD-it subjects showed a bilateral ventral striatal deficit during reward anticipation. In contrast, ADHD-ct subjects showed orbitofrontal hyporesponsiveness to reward feedback when compared with ADHD-it and healthy subjects.
Conclusions: This is the first fMRI study that delineates dysfunctional and subtype-divergent neural and behavioural reward processing in adults with ADHD.

1. Introduction

Attention-deficit/hyperactivity disorder (ADHD) is a common cognitive/behavioural developmental disorder in children, adolescents and adults (American Psychiatric Association, 1994; Kooij et al., 2005; Kessler et al., 2006). Studies to date confirm significant neuropsychological and neurophysiological differences between ADHD-combined type and ADHD-predominantly inattentive type (Conzelmann et al., 2009; Johnstone and Clarke, 2009; Huang-Pollock et al., 2007). Neuropsychological research and theory suggests that attention deficits, executive dysfunction and dysregulation of state, energy and motivation are pivotal characteristics of the disorder (Nigg, 2005). The 'dual pathway model' of Sonuga-Barke (2002) deals with the behavioural heterogeneity of subjects with ADHD, and suggests that executive/inhibitory dysfunction as well as motivational deficits may underlie ADHD. Sergeant (2005) introduced a 'cognitive-energetic model' of ADHD that focuses on the prevalence and interaction of three main neuropsychological factors: (1) dysfunction of executive ("top-down") control, (2) dysfunction of specific cognitive/attention processes, and (3) an energetic ("bottom-up") dysregulation (Sergeant et al., 2003; Sergeant, 2005). Sagvolden et al. (2005) sought to integrate clinical, neuropsychological, neural, and developmental aspects of ADHD, proposing altered function in three dopamine pathways, (1) the mesolimbic branch, (2) the mesocortical branch, and (3) the nigrostriatal branch. They used this proposal to explain underlying symptoms of ADHD (combined type and predominantly hyperactive-impulsive type): (1) delay aversion, hyperactivity, impulsiveness, deficient sustained attention, and failure to inhibit responses, (2) attention response deficiencies and poor behavioural planning, and (3) impaired motor functions and deficient non-declarative habit learning and memory.

These different approaches indicate the enormous challenges to unveiling the relations between clinical symptoms (e.g. concerning subtype differences), neuropsychological functioning and underlying neurobiological mechanisms in ADHD. However, knowledge of the neural foundations of neuropsychological and behavioural

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abnormalities in ADHD has been markedly enhanced by functional imaging findings in the past few years. Previous fMRI studies predominantly focused on the association of attention/executive and response inhibition deficits with dysfunctions in thalamo-cortico-striatial circuits (Bush et al., 2005). Given the dysfunction of reinforcement and extinction (Johansen et al., 2002), aversion to delayed gratification (Luman et al., 2005), and increased addiction proneness (Biederman et al., 1998) in subjects with ADHD, more recent imaging research concentrated on the neural correlates of incentive processing and motivational mechanisms. On the basis of findings such that rats with lesions in the ventral striatum displayed symptoms of impulsivity (Cardinal et al., 2001), Scheres et al. (2007) found reduced ventral striatal activation in adolescents with ADHD during reward anticipation, using a motivational fMRI paradigm (Monetary Incentive Delay task, MID) (Knutson et al., 2001a, 2001b; Juckel et al., 2006a, 2006b). Moreover, activation of the ventral striatum or nucleus accumbens, which is known as the central component of the mesolimbic dopaminergic reward system, was inversely correlated with hyperactive/impulsive symptoms in ADHD and control groups.

Ströhle et al. (2008) were the first to use the above-mentioned motivational paradigm to investigate striatal and prefrontal activation patterns during reward anticipation and feedback in adults with ADHD. They found that, compared to healthy controls, adults with ADHD showed decreased ventral striatal activation during reward anticipation, but increased activation of parts of the orbitofrontal cortex in response to feedback of gain. In contrast, a recent fMRI study using the same experimental paradigm was unable to find significant differences in striatal activation during anticipation of reward as well as alterations of the orbitofrontal cortex during reward feedback when comparing two groups of male adults with ADHD in childhood (with MPH treatment in childhood vs. no pharmacological intervention in childhood) to a healthy control group (Stoy et al., 2011). Using a similar reward anticipation task, a recent study by Stark et al. (2011) showed a significant negative correlation between ADHD-related behaviour, i.e., the inattention and the hyperactivity/impulsivity subscales of the adult ADHD self-report scale (ASRS), and the fMRI signal during different reinforcement conditions, i.e., monetary reward and punishment avoidance anticipation, located in the bilateral nucleus accumbens. In addition, a significant negative correlation between the sum ASRS score and the striatal activation in response to gain and punishment avoidance was detected (Stark et al., 2011).

However, the interpretation of the previously reported fMRI results is hindered by three major confounding variables, namely psychotropic medication, gender, and the heterogeneity concerning the ADHD subtype. Therefore, we applied the well established MID task (Knutson et al., 2001a) to homogeneous subtype groups of male and drug-naïve patients We decided for the two most frequent and contradistinctive ADHD subtypes according to DSM-IV criteria, i.e., combined type and predominantly inattentive type, thus neglecting the predominantly hyperactive-impulsive type which has the weakest evidence for validity (Willcutt et al., 2012).

On the basis of two of the abovementioned models that included motivational aspects in the psychopathology of ADHD (Sonuga-Barke, 2002; Nigg, 2005), and with respect to recent fMRI studies on reward processing in ADHD (Scheres et al., 2007; Ströhle et al., 2008; Stark et al., 2011), we expected that both investigated ADHD subtypes would show ventral striatal (and prefrontal) abnormalities under reward anticipation and feedback. Given the abovementioned negative correlations between hyperactivity/impulsivity and ventral striatal activation during reward anticipation, we particularly hypothesised, that the combined-type ADHD patients would display less striatal activation during reward anticipation than the predominantly inattentive subjects.

2. Methods

2.1. Subjects

24 drug-naïve, right-handed male adults with ADHD, twelve each with the combined subtype (ADHD-ct) and the predominantly inattentive subtype (ADHD-it) of ADHD, and twelve right-handed healthy adults (CON) were included. Right-handedness was verified by means of the Edinburgh Handedness Inventory (Oldfield, 1971). Groups did not differ significantly in age (ADHD-ct: $M = 32.7$ years, SD = 8.6; ADHD-it: $M = 33.5$ years, SD = 12.7; HC: $M = 32.4$ years, SD = 8.6; ANOVA: $F(2) = 0.04$, $p = 0.96$) and years of education (ADHD-ct: $M = 13.0$ years, SD = 1.47; ADHD-it: $M = 12.75$ years, SD = 1.86; HC: $M = 13.91$ years, SD = 2.15; ANOVA: $F(2) = 1.32$, $p = 0.28$). No group differences were found with respect to smoking ($\chi^2 = 2.36$, df = 2, $p = 0.31$), number of cigarettes smoked per day (ANOVA: $F(2) = 0.96$, $p = 0.41$), nor the interval between the last cigarette smoked prior to fMRI performance and beginning of the experiment (ANOVA: $F(2) = 0.85$, $p = 0.45$).

Patients and controls had no personal or family history of serious mental disorders (dementia, substance dependence, psychosis or bipolar disorder), and ADHD patients did not display comorbidity with any of the aforementioned psychiatric disorders. Patients were recruited from the outpatient unit for adults with ADHD of the Department of Psychiatry, Ruhr University, LWL University Hospital Bochum, and the healthy control group consisted of staff members (and relatives or friends of those) of this clinic.

In order to exclude patients with severe comorbidity, i.e., the abovementioned psychiatric comorbidity or other concomitant disease, or those being already on drug treatment, recruitment of ADHD patients was performed by screening of 48 patients with ADHD-combined type and 25 patients with ADHD-predominantly inattentive type who entered our unit for adults with ADHD. The screening procedure included consideration of SCID results, which were collected within the initial routine diagnostic procedure in our ADHD outpatient unit. Healthy control persons were merely asked about current, lifetime and familial mental disorders.

None of the selected subjects refused to take part, and all participants gave full informed consent, after all procedures had been fully explained to them. The study was approved by the ethics committee of the Ruhr University Bochum (No. 2946/2007).

2.2. Assessment of ADHD

ADHD diagnoses were established by experienced clinical experts (M.-A. E.; H. W.). The German short version of the Wender Utah Rating Scale (WURS-k) was used to retrospectively assess ADHD symptoms when patients were between six and ten years old, in order to estimate the probability of the presence of ADHD (whatever subtype) in childhood (Retz-Junginger et al., 2002), since ADHD in childhood is a sine qua non for diagnosing ADHD in adults. ADHD diagnoses were established by means of a German checklist based on the DSM-IV diagnostic criteria, ADHD Diagnostic Checklist (ADHD-DC) (Rösler et al., 2004). This brief interview allows for the assessment of the number of symptoms of inattentiveness, hyperactivity and impulsiveness. The severity of current ADHD symptoms was assessed using the German version of the Wender Reimherr Interview, WRI (Rösler et al., 2006). The WRI allows for expert rating of the severity of seven ADHD symptom domains, which are ‘inattentiveness’, ‘hyperactivity’, ‘hot temper’, ‘affective lability’, ‘stress intolerance’, ‘disorganization’, and ‘impulsivity’. The WRI scores did not contribute to ADHD subtype differentiation. Control subjects underwent all of the same procedures. The WURS-k, The WRI and the ADHD-DC are part of a German set of validated