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Probabilistic reward learning in adults with Attention Deficit Hyperactivity Disorder—An electrophysiological study

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ABSTRACT

Attention Deficit Hyperactivity Disorder (ADHD) is hypothesized to be characterized by altered reinforcement sensitivity. The main aim of the present study was to assess alterations in the electrophysiological correlates of monetary reward processing in adult patients with ADHD of the combined subtype. Fourteen adults with ADHD of the combined subtype and 14 healthy control participants performed an active and an observational probabilistic reward-based learning task while an electroencephalogramm (EEG) was recorded. Regardless of feedback valence, there was a general feedback-related negativity (FRN) enhancement in combination with reduced learning performance during both active and observational reward learning in patients with ADHD relative to healthy controls. Other feedback-locked potentials such as the P200 and P300 and response-locked potentials were unaltered in the patients. There were no significant correlations between learning performance, FRN amplitudes and clinical symptoms, neither in the overall group involving all participants, nor in patients or controls considered separately. This pattern of findings might reflect generally impaired reward prediction in adults with ADHD of the combined subtype. We demonstrated for the first time that patients with ADHD of the combined subtype show not only deficient active reward learning but are also impaired when learning by observing other people's outcomes.

1. Introduction

Executive dysfunction (Schultz et al., 1997), disrupted reward learning (see Luman et al. (2010)) and associated performance monitoring problems (Miltner et al., 1997) are currently discussed as core concepts underlying the psychopathology of Attention Deficit Hyperactivity Disorder (ADHD). Children and adults with ADHD favor immediate small to delayed bigger rewards (Sonuga-Barke et al., 1992; Marx et al., 2010, 2013) and immediate rewards that may be unfavorable in the long term (Carrillo-de-la-Pena and Cadaveira, 2000; Pfabigan et al., 2011). Also, reward learning appears to lack modulation by motivational factors such as frequency or magnitude of reward in children with ADHD (Luman et al., 2009). The “reward system” relies on dopamine (DA) as a neurotransmitter (Yeung and Sanfey, 2004; Hajcak et al., 2005; Leng and Zhou, 2010; Ma et al., 2011) and involves projections to the striatum and frontal cortex, particularly the medial orbitofrontal cortex (OFC) and anterior cingulate cortex (ACC) (Yeung and Sanfey, 2004; Sato et al., 2005). Mesolimbic DA hypoactivity represents a core feature of ADHD, potentially resulting in a failure to efficiently use cues that predict future rewards or in a steeper temporal discounting slope, meaning that patients with ADHD would not be willing to wait until they get a reward (Potts et al., 2006). Stimulant medication increases DA activity and thus affects reward learning: while non-medicated adults with ADHD were impaired both when learning from positive and from negative feedback, stimulant medication was found to improve learning from positive feedback only (Frank et al., 2007). There is evidence of altered structure and function of central regions in the reward system in ADHD, such as aberrant connectivity patterns involving the OFC (Konrad et al., 2010; Cocchi et al., 2012; Tomasi and Volkow, 2012), OFC hyporesponsiveness to reward (Cubillo et al., 2012; Wilbertz et al., 2012; Edel et al., 2013), smaller ACC volumes (Makris et al., 2010; Amico et al., 2011; Bledsoe et al., 2013) and ACC hypoactivation during reward-based decision making (Ernst et al., 2003).

A prominent event-related potentials (ERPs) component, the feedback-related negativity (FRN), observed between 200 and 300 ms after presentation of the feedback stimulus (Miltner et al., 1997), has been associated with the processing of (negative) performance feedback. It resembles the response-locked error-related negativity (ERN) or error negativity (Ne) (Falkenstein et al., 1991; Gehring et al., 1993). Both components are generated in the ACC (Dehaene et al., 1994; Gehring and Willoughby, 2002), have

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been linked to the DA system, are modulated by individual preferences for positive or negative feedback learning (Frank et al., 2005) and indicate processes related to performance monitoring. The FRN appears to reflect a DA-driven teaching signal in feedback-based learning, coding a negative reward prediction error (Holroyd and Coles, 2002). Alternative accounts emphasize the role of the ACC as general action-outcome predictor (Alexander and Brown, 2011), with both unexpected negative and positive feedback eliciting large amplitude FRNs (Ferdinand et al., 2012). It is unclear in how far the P300, associated with stimulus evaluation and categorization (Ridderinkhof and van der Molen, 1995), plays a role in the context of feedback processing. There are reports of increased P300 amplitudes for positive relative to negative feedback, for unexpected relative to expected and for larger relative to smaller outcomes (Yeung and Sanfey, 2004; Leng and Zhou, 2010; Ma et al., 2011). However, feedback valence does not seem to modulate the P300 consistently. An earlier positive component, the P200, has been associated with a less specific attention-facilitating effect by salient (rewarding) stimuli (Potts, 2004; San Martin et al., 2010).

Functional magnetic resonance imaging (fMRI) studies showed activation of overlapping networks involving the dorsal ACC, the OFC, the posteriomedial frontal cortex, and supplementary motor regions in response to one's own and to other people's errors (Shane et al., 2008; Brazil et al., 2011). Both the ERN (Miltner et al., 2004; van Schie et al., 2004; Bates et al., 2005) and the FRN (Yu and Zhou, 2006; Koban et al., 2010) have also been recorded when participants observed someone else's responses and performance feedback. Compared to active responding, the peak of the observational ERN occurs later and with an attenuated amplitude. Similarly, the observational FRN is reduced in magnitude relative to the active FRN (Bellebaum et al., 2010). Observational learning places additional social, cognitive and emotional processing demands on the individual. Empathy and mentalizing may be required to infer the other person's emotional state and the consequences of the other person's performance and feedback for one's own outcomes (Thoma and Bellebaum, 2012).

Previous studies, mostly involving children and tasks that primarily tap response inhibition, yielded inconsistent results with inconspicuous (Wiersema et al., 2005, 2009; Wild-Wall et al., 2009; Zhang et al., 2009; Shen et al., 2011), more pronounced (Burgio-Murphy et al., 2007), but mostly reduced (Liotti et al., 2005; van Meel et al., 2005; Albrecht et al., 2008; Groen et al., 2008; McLoughlin et al., 2009; Herrmann et al., 2010; Senderecka et al., 2012; Groom et al., 2013) ERN amplitudes in ADHD patients (see Geburek et al. (2013)). The findings for the FRN, rarely investigated in this disorder, are similarly inconsistent. In children with ADHD, the FRN was either more pronounced in response to unfavorable performance feedback during a guessing task (van Meel et al., 2005) and to abstract performance feedback following the physical reception of actual monetary rewards (Holroyd et al., 2008), entirely absent during a time production task (van Meel et al., 2011) or did not differ from the FRN observed in controls during a flanker task (Rosch and Hawk, 2013). Regarding the P300, adults with ADHD showed reduced P300 modulation by reward magnitude during a gambling task (Ibanez et al., 2014), while children with and without ADHD showed comparable reward-associated enhancement of the P300 during a flanker task (Rosch and Hawk, 2013). The P200 in response to feedback has been reported to be inconspicuous (Groen et al., 2008, 2013) or enhanced for unfavorable performance feedback in ADHD children (van Meel et al., 2005).

The inconsistent results may be due to a number of reasons. One of them relates to task-induced reward expectations: Van Meel et al. (2005) and Holroyd et al. (2008) used guessing tasks with random presentation of reward and non-reward. Rosch and Hawk (2013) employed a flanker task with deterministic stimulus-response contingencies and van Meel et al. (2011) a time production not involving clear reward expectations as difficulty is dynamically adjusted to the participant's performance level. Feedback could not be used for the optimization of behaviour in any of the studies, but the FRN is most pronounced when a response strategy can be learned (Holroyd et al., 2009).

One further issue that might contribute to the discrepant findings relates to the clinical heterogeneity of ADHD. ERN enhancement was observed only in children with the combined but not with the inattentive subtype of ADHD (Burgio-Murphy et al., 2007). Holroyd et al. (2008) reported increased sensitivity to actual monetary rewards (in contrast to abstract representation of monetary rewards as performance feedback) in children with ADHD of the combined subtype. In a recent fMRI study, predominantly inattentive ADHD patients showed ventral striatal hyporesponsiveness during reward anticipation. However, in response to reward feedback, the OFC was underactivated in ADHD patients of the combined subtype only (Edel et al., 2013). Also, for children and adolescents with the combined ADHD subtype, steeper temporal reward discounting curves were observed than in patients with the inattentive subtype or typically developing controls (Scheres et al., 2013). Overall, evidence suggests a special role of the combined ADHD subtype for reward feedback processing.

Previous studies predominantly involved children and adolescents. During the transition from childhood to adulthood, hyperactivity is known to change to restlessness, while symptoms of inattention persist (Volkow and Swanson, 2013). Although there is evidence of normalization of brain structure in adults with ADHD, cortical maturation appears to peak at a developmentally later stage, particularly in the prefrontal cortex (Shaw et al., 2007; 2012; Onnink et al., 2014). Furthermore, different developmental trajectories have been suggested for performance-based and utilitarian (e.g. in guessing tasks) feedback: performance-based feedback and associated FRNs might continue to mature after the age of 12, while FRNs associated with utilitarian feedback appear similar in size between adults and children at the age of 10 (Groen et al., 2008; Holroyd et al., 2008; van Meel et al., 2011). It is thus conceivable that reward learning impairment is ameliorated in adult ADHD patients.

The present study investigated alterations of reward learning and processing in adults with ADHD of the combined subtype. There has been growing evidence for impaired social cognition in ADHD (see Uekermann et al. (2010)) and for reduced theory of mind and empathy (Marton et al., 2009; Maoz et al., 2014) in particular. Thus, patients with ADHD might also show altered reward learning in social contexts where they are required to learn by observing the performance of other individuals. To our knowledge, this issue, which is highly relevant to everyday life, has not been explored before. We thus analyzed the feedback-locked P200, FRN and P300 in parallel active and observational learning tasks, in which feedback could be used to optimize behaviour. We expected that in patients relative to controls, behavioral performance and feedback processing would be altered during both types of feedback learning, with the latter being primarily reflected in the (observational) FRN due to its close relationship to the DA system. In order to characterize potential feedback processing changes in ADHD in a broader performance monitoring context, we also explored the ERN and observational ERN. The N100 was assessed as a measure of early bottom-up stimulus processing and visual attention (Mangun et al., 1993; Vogel and Luck, 2000) due to N100 modulations in the context of observational feedback learning in previous studies (Kobza et al., 2011; Rak et al., 2013).

2. Method

2.1. Participants

Fourteen patients with ADHD of the combined subtype (age range 20–49 years) and 14 healthy age-matched control participants (age range 20–48 years) took part in the experiment (see Table 1 for demographic and clinical characteristics). Patients were recruited from the ADHD outpatient service of the Department of Psychiatry, LWL University Hospital, Ruhr University Bochum, and diagnosed with