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Spontaneous activity in the waiting brain: A marker of impulsive choice in attention-deficit/hyperactivity disorder?

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A B S T R A C T

Background: Spontaneous very low frequency oscillations (VLFO), seen in the resting brain, are attenuated when individuals are *working* on attention demanding tasks or *waiting* for rewards (Hsu et al., 2013). Individuals with attention-deficit/hyperactivity disorder (ADHD) display excess VLFO when *working* on attention tasks. They also have difficulty waiting for rewards. Here we examined the *waiting* brain signature in ADHD and its association with impulsive choice.
Methods: DC-EEG from 21 children with ADHD and 21 controls (9–15 years) were collected under four conditions: (i) *resting*; (ii) choosing to *wait*; (iii) being "forced" to *wait*; and (iv) *working* on a reaction time task. A questionnaire measured two components of impulsive choice.
Results: Significant VLFO reductions were observed in controls within anterior brain regions in both *working* and *waiting* conditions. Individuals with ADHD showed VLFO attenuation while *working* but to a reduced level and none at all when *waiting*. A closer inspection revealed an increase of VLFO activity in temporal regions during *waiting*. Excess VLFO activity during *waiting* was associated with parents' ratings of temporal discounting and delay aversion.
Conclusions: The results highlight the potential role for *waiting*-related spontaneous neural activity in the pathophysiology of impulsive decision-making of ADHD.

1. Introduction

Attention-deficit/hyperactivity disorder (ADHD) is an impairing childhood-onset psychiatric condition characterized by symptoms of inattention, hyperactivity and impulsivity with associated patterns of functional impairment (Sonuga-Barke and Taylor, in press). Pathophysiologically ADHD is a complex and heterogeneous disorder implicating multiple brain networks which regulate active engagement during cognitive, motivational and emotional operations (Cortese and Castellanos, 2012). Recently, functional magnetic resonance imaging (fMRI) studies have identified atypical patterns of spontaneous brain activity, reflected in very low frequency (VLF: e.g. <0.1 Hz) blood-oxygen-level dependent (BOLD) signals, in ADHD patients during wakeful rest when no specific task externally oriented is being undertaken (Castellanos et al., 2008; Sripada et al., 2014; Tian et al., 2008). Much of the focus of this work has been on a set of widely distributed, but functionally connected, brain regions including the posterior cingulate cortex (PCC), precuneus (PrC), medial prefrontal cortex (mPFC) and inferior parietal lobes (IPL)

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– termed the Default Mode Network (DMN) (Cao et al., 2009; Castellanos et al., 2008; Fair et al., 2010; Uddin et al., 2008). Functionally, DMN activity is a "double edged sword"; on the one hand, it is a neural substrate for important introspective cognitive processes such as meditation (Hasenkamp et al., 2012) and self-related thoughts about the personal past and future (Buckner and Carroll, 2007; Spreng et al., 2009): Dysfunction during rest, seen in ADHD, may disrupt processes of prospection and undermine effective decision making (Sonuga-Barke and Fairchild, 2012). On the other hand, DMN attenuation following the onset of goal-directed tasks appears to be necessary for effective switching from resting to working brain states (Fox et al., 2005; Greicius et al., 2003; Raichle and Snyder, 2007): Excess DMN activity when individuals are working on laboratory information processing tasks during fMRI studies is associated with performance deficits (Sonuga-Barke and Castellanos, 2007; Weissman et al., 2006). Individuals with ADHD fail to effectively suppress the DMN activity during cognitive task performance (Fassbender et al., 2009; Peterson et al., 2009), which may explain patterns of ADHD-related periodic attentional lapses and intra-individual reaction time variability (Helps et al., 2011).

Compared to fMRI BOLD signals, which map neural activity by imaging haemodynamic responses, DC-EEG offers a more direct measure of spontaneous VLF oscillations (VLFOs), albeit with relatively limited spatial resolution. While the functional significance of VLFOs and its relation to BOLD signals continue to be debated, recent DC-EEG studies have also identified a temporally and spatially stable resting VLF EEG network in healthy young adults with maximal power distributed across midline frontal and posterior scalp regions (Helps et al., 2008). The attenuation of VLF EEG power within this network following the transition from rest to the performance of cognitive demanding tasks has been replicated a number of times (Helps et al., 2009). The intra-cranial sources of this scalp activity have been localized and appear to overlap to some degree with DMN brain regions (Broyd et al., 2011). Moreover, children and adolescents with ADHD display reduced attenuation when working on attention demanding tasks with this reduction correlated with their attentional performance (Helps et al., 2010).

In an apparently unrelated way, individuals with ADHD also have difficulty waiting for future outcomes and prefer to choose smaller sooner (SS) over larger later rewards (LL) even when this leads to less reward overall (Marco et al., 2009). Explanations for this "impulsive choice" in ADHD (Robbins et al., 2012) have focused on: (i) a reduced ability to resist temptation linked to executive dysfunction (Barkley et al., 2001); (ii) increased discounting of the value of future rewards (Scheres et al., 2010), reflecting hypo-activation of reward brain centres (e.g., ventral striatum; Plichta and Scheres, 2014), and; (iii) negative affect generated by the experience of delay (i.e. delay aversion; Sonuga-Barke, 2002) mediated by hyper-activation within the brain's emotion centres (e.g. insula and amygdala; Lemiere et al., 2012; Plichta et al., 2009; Wilbertz et al., 2013). Interestingly, the potential role of intrinsic brain activity during the process of waiting in individuals with ADHD has not been investigated. A lot is known about the resting brain in ADHD; but nothing about the waiting brain.

Hsu and colleagues recently drew a parallel between waiting and resting brain states – highlighting some similarities and also some important differences (Hsu et al., 2013). In particular, they pointed out how both states involve the experience of a period of idle time. In other ways, they argued, these states are different, as waiting is always directed to a specified outcome in the future while the goal of resting may be purely recuperative. In this sense, waiting and resting can be seen as similar activities framed motivationally in different ways. Interestingly a comparison of EEG activity, made by the authors, revealed that in typically developing adults the VLFO signature for waiting, especially when this was freely chosen and rewarded, was more similar to that displayed while working (on a simple cognitive task) than during resting – with VLFO power attenuation seen in anterior and posterior medial scalp regions in both states (Hsu et al., 2013).

In the current study we analyzed scalp VLF EEG and localized its intracranial sources to; (i) test whether individuals with ADHD, relative to controls, fail to attenuate spontaneous VLFOs during waiting compared to the resting state, as shown typically by them in the working state; and; (ii) examine whether the resultant excess intrinsic waiting state activity is associated with parental ratings of two components of impulsive choice (i.e. delay aversion and increased temporal discounting). We predicted that: (i) ADHD individuals, compared to controls, would demonstrate a failure to attenuate VLFO power during the switch from resting to both working and waiting states with excess neural activity in these states localized to DMN-related regions and; (ii) this excessive waiting-related VLFO neural activity would be associated with higher levels of delay aversion and temporal discounting.

2. Materials and methods

The study was approved by the University of Southampton Psychology Ethics Committee and the Southampton and South West Hampshire Research Ethics Committee A. All parents and participants gave written informed consent and children gave assent.

2.1. Participants

Twenty-one children aged between 9 and 15 years with both a clinical and a research diagnosis of ADHD and 21 typical developing controls participated. Individuals with ADHD were recruited from local clinics through the South Hampshire ADHD Register (SHARe, http://www.southampton.ac.uk/share). They all completed the standard SHARe assessment battery, including Wechsler Intelligence Scale for Children (WISC-IV), a semi-structured psychiatric diagnostic interview (NIMH DISC-IV; Shaffer et al., 2000); and parent and teacher versions of the Conner's Comprehensive Behavior Rating Scale (CBRS; Conners, 2008). Exclusion criteria were; (a) the presence of other developmental or psychiatric disorders (except oppositional defiant disorder and conduct disorder because those disruptive behavior disorders