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

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ABSTRACT

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

Table 1
Demographic and clinical characteristics.

	Control ($N=21$) Mean (SD)	ADHD ($N=21$) Mean (SD)	t/χ^2	p
Age	11.47 (1.69)	11.00 (1.95)	0.845	.403
Gender (male/female)	17/4	20/1	2.043	.343
Estimated IQ *(WISC-IV)*[a]	105.48 (13.16)	97.29 (12.43)	2.073	.045*
Conners comprehensive behaviour rating scale (CBRS)				
Parent report (*T* score)				
Inattentive type	54.62 (10.83)	86.43 (5.61)	−11.954	<.001***
Hyperactive-impulsive type	54.05 (11.54)	86.05 (6.93)	−10.891	<.001***
Quick delay questionnaire (QDQ)				
Parent report				
Total score	21.62 (6.48)	41.24 (6.68)	−9.659	<.001***
Delay aversion	11.14 (3.48)	21.48 (3.76)	−9.235	<.001***
Delay discounting	10.48 (3.39)	19.76 (3.51)	−8.731	<.001***
Two choice reaction time task (2CRT)				
Total errors	32.62 (20.50)	55.81 (38.00)	−2.461	.020*
Mean RT (ms)	474.82 (64.85)	484.19 (51.91)	−0.517	.608
SD of RT	105.41 (37.52)	138.07 (35.09)	−2.913	.006**

[a] WISC-IV: Wechsler Intelligence Scales for children.
* $p < .05$.
** $p < .01$.
*** $p < 001$.

commonly coexist with ADHD) as diagnosed by clinicians; (b) IQ less than 70; (c) medication use (except short acting stimulants). Medicated patients refrained from medication for at least 24 h prior to testing. The controls were recruited from local schools and clubs. They completed the short form of WISC-IV (Vocabulary and Block Design) and their parents completed the CBRS. Controls were excluded if they had an estimated IQ less than 70 or if they met clinical cut-offs on any ADHD subscale (no controls were excluded for these reasons). The two groups did not differ in terms of age and sex (Table 1). Individuals with ADHD had lower estimated IQ compared to controls.

2.2. Procedures

EEG was recorded during four conditions each lasting five minutes. In the resting condition (REST), participants were instructed to relax and focus on the fixation cross on the monitor. In the working condition (WORK), participants completed a 300 trial two-choice reaction time task (2CRT). Each trial lasted 1 s, which included stimulus presentation time for 400 ms and inter-stimulus interval for 600 ms. Participants were required to indicate the direction of an on-screen arrow by pressing the "left" or "right" button on a response box. They were asked to focus their attention and respond as quickly and accurately as possible (correct rate: control: 89%; ADHD: 81%). In the forced-to-wait (F-WAIT) condition participants were instructed to wait for 5 min before they could start the next experimental session. In the choose-to-wait (C-WAIT) condition they were given a choice to wait for 5 min to win a ticket for a £20 lottery draw, or to immediately terminate the waiting period (one patient with ADHD declined this invitation but completed the other EEG sessions which were included in the analysis). Condition order was counterbalanced using a Latin square table (Bailey, 2008). Each participant was randomly assigned to one of the following sequences: (i) REST; WORK; C-WAIT; F-WAIT; (ii) WORK; F-WAIT; REST; C-WAIT; (iii) F-WAIT; C-WAIT; WORK; REST; (iv) C-WAIT; REST; F-WAIT; WORK.

All participants' parents completed the previously validated Quick Delay Questionnaire (QDQ; Clare et al., 2010) for the assessment of participants' delay-related problems. QDQ is a Likert type scale measuring temporal discounting (5 items) and delay aversion (5 items). The whole experimental session took 2 h. Each family was reimbursed £30 for their time and travel expenses.

2.3. Electrophysiological data acquisition and processing

EEG was recorded using a Neuroscan Synamps^2 70 channel system via 24 bit A/D converter and a direct current (DC) procedure, combined with a 70 Hz low-pass filter and 500 Hz sampling rate. Participants were fitted with an electrode cap with 66 equidistant electrodes (Fig. 1a; Easycap; Hersching, Germany). Electro-oculogram (EOG) was measured using Ag/AgCl electrodes placed below the left and right eyes. Impedance was kept below 5 kΩ. Data was initially referenced to the nose electrode. The first 55 of 66 electrodes for EEG recording were set up for analysis only because the other 11 electrodes are located at the outmost circle on the cap and previous studies have shown that they were frequently contaminated with artefacts. This also allowed us to shorten the preparation time for cap setting and prevent participants becoming bored. EEG signals from those selected electrodes were re-referenced to an average reference using MATLAB (version R2010a). The linear trend caused by DC drift was removed using the 'detrend' command in MATLAB. Independent component analysis (ICA) was used to remove all artefacts and ocular movements with fast ICA algorithm (Hyvärinen, 1999). EEG signals were reconstructed by back-projection of all artefact-free

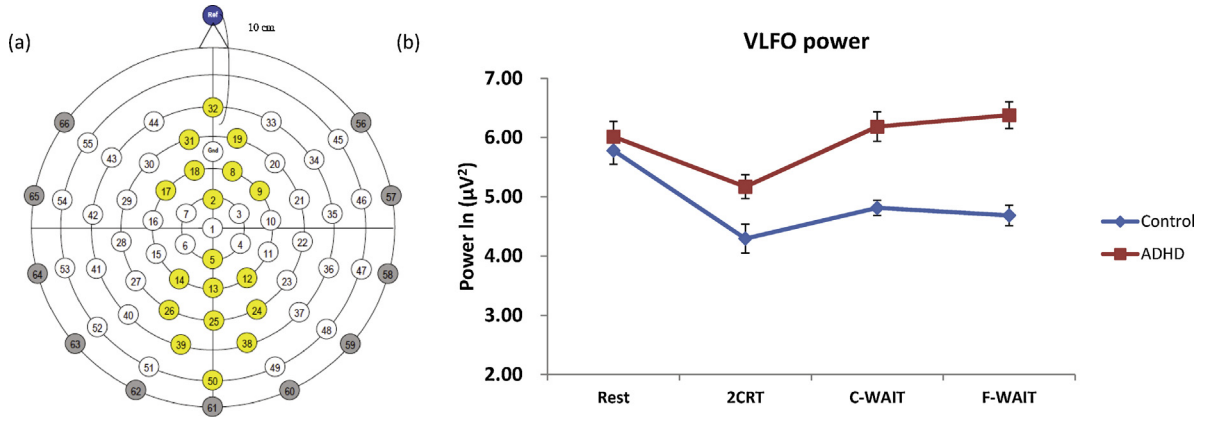

Fig. 1. (a) A priori VLF EEG network specification. Electrodes selected for the VLF EEG network are highlighted in yellow. The electrodes discarded for analysis are marked in grey. (b) The VLFO EEG power extracted from the selected electrodes within the network (yellow) during resting, working and waiting conditions. The value of power was natural log-transformed. Error bars are the standard errors of the means. 2CRT: two choice reaction time task. C-WAIT: condition when participants chose to wait. F-WAIT: condition when participants were forced to wait.

components and subjected to Fast Fourier Transformation (FFT). One minute Hamming windows overlapped by 20 s were applied. The VLFO power within the very low frequency band (0.02–0.2 Hz) was calculated (Penttonen and Buzsáki, 2003). Based on previous VLFO studies (Broyd et al., 2011; Helps et al., 2010; Hsu et al., 2013), we a priori identified a VLFO network consisting of two groups of midline electrodes (anterior and posterior clusters, see Fig. 1a). EEG power from the selected electrodes was averaged and natural log-transformed to correct for non-normality (Gasser et al., 1982). Two participants (one with ADHD) were excluded because of poor data quality which continued to obscure the EEG even after ICA artefact correction was performed. The final comparisons were conducted on two groups of 20.

2.4. Source localization

Standardized low-resolution electromagnetic tomography software (sLORETA; Pascual-Marqui, 2002) was used for source localization. Artefact-free EEG was down-sampled from 500 Hz to 25 Hz using the 'decimate' command in MATLAB to meet the computational constraints of sLORETA. The down-sampled EEG data in time series were then exported in ASCII format from MATLAB to sLORETA. Using sLORETA package we computed the cross-spectra and corresponding electric generators which contained the information of cortical three-dimensional (3D) distribution. The computed sLORETA images represented the amplitude of computed current source density in 6239 voxels, with a spatial resolution of 5 mm.

2.5. Data analysis

We tested for differences between groups in the QDQ subscales using *t*-tests. Two-way repeated measures ANOVAs assessed the differences in VLFO power with Condition (REST, WORK, C-WAIT and F-WAIT) as the within-subject factor and Group (Control vs. ADHD) as the between-subjects factor. Analyses were run with and without IQ as a covariate. Effect sizes were calculated using Cohen's *d*. Correlations between REST-to-WORK/WAIT power differences and delay-related questionnaire measures were calculated using Pearson's *r*. With regard to source localization, the within subject differences between sLORETA images for REST and each of the non-REST conditions (WORK, F- and C-WAIT) were computed for the control and ADHD groups separately using sLORETA statistics package. Follow-up testing computed the between group difference (ADHD and controls) for each of these condition contrasts. The sLORETA images were compared using non-parametric permutation tests based on the estimation of empirical probability distribution for the maximum of a *t*-statistic via 5000 randomization with a conservative significance threshold correcting for multiple comparisons (Nichols and Holmes, 2002).

3. Results

Individuals with ADHD had higher delay aversion and temporal discounting scores on the QDQ (Table 1). The levels of mean VLFO power within the network of each condition are shown in Fig. 1. There was a significant main effect of Group ($F(1, 37) = 16.92$, $p < .001$) and Condition ($F(3, 111) = 21.22$, $p < .001$) and a significant Group by Condition interaction ($F(3, 111) = 9.02$, $p < .001$). Controls displayed significantly and substantially lower levels of VLFO activity in WORK, F-WAIT and C-WAIT compared to REST (Control: Cohen's $d^{WORK} = 1.41$; $d^{C\text{-}WAIT} = 1.17$; $d^{F\text{-}WAIT} = 1.21$). In the ADHD group the VLFO power was reduced in WORK compared to REST, but not in C-WAIT or F-WAIT (ADHD: Cohen's $d^{WORK} = 0.82$; $d^{C\text{-}WAIT} = -0.16$; $d^{F\text{-}WAIT} = -0.34$). Moreover, the REST-to-WORK attenuation effect in ADHD was significantly smaller than seen in controls ($t(38) = 2.30$; $p < .03$). Adding IQ as a covariate reduced the Condition effect ($F < 1.50$; $p > 20$), but other effects remained significant ($F^{Group} > 4.84$, $p < .05$; $F^{Group\ by\ Condition} > 4.94$, $p < .05$). The correlation between the REST-to-WORK attenuation in scalp VLFO power and performance error on the 2CRT task was not significant

($r = -.14$, $p > .05$). However, the REST-to-WAIT but not REST-to-WORK difference in scalp VLFO power negatively correlated with parents' combined QDQ ratings ($r^{\text{F-WAIT}} = -.53$, $p < .01$; $r^{\text{C-WAIT}} = -.42$; $p < .01$; $r^{\text{WORK}} = -.19$, $p = .23$), suggesting the less REST-to-WAIT attenuation the higher levels of delay aversion and temporal discounting.

Fig. 2 shows the whole scalp distribution of VLFO power. At REST both groups showed maximal power along the frontal pole and midline regions. During WORK the VLFO power was lower for both groups although it remained greatest in the frontal pole and centro-parietal areas. Within the ADHD group the C-WAIT and F-WAIT VLFO signature was more similar to REST than WORK despite some evidence of focal reductions in frontal areas and temporo-parietal junction and a degree of exacerbation in temporal and centroparietal locations. In contrast, in the control group the VLFO signature during C- and F-WAIT was similar to that during WORK with suppression of EEG power across the whole scalp.

As predicted, sLORETA localized the resting VLFO for both groups to midline structures, including key DMN regions such as medial frontal gyrus (BA 6 & 8) and precuneus (BA 31) (see Appendix Fig. A.1). Fig. 3 shows the intracranial source localization for the contrast between REST and non-REST conditions. In line with the scalp distribution, sLORETA identified significant WORK and F-WAIT induced attenuations within the control group in the medial frontal gyrus (BA 6), precentral and postcentral gyrus (BA 4), as well as paracentral lobule (BA 6) (REST vs. WORK: pseudo $t = 7.48$, corrected $p = 0.03$; REST vs. F-WAIT, pseudo $t = 7.14$, corrected $p = 0.03$). For controls the REST to C-WAIT effect failed to reach significance after stringent control for multiple testing (pseudo $t = 6.76$, corrected $p = 0.07$), albeit the attenuations were localized to similar regions. The ADHD group displayed REST-to-WORK attenuation in similar regions but the effects were smaller and failed to reach significance (pseudo $t = 7.49$, corrected $p = 0.09$). Nominally significant REST to C- and F-WAIT reductions occurred in DMN-related regions, including precuneus, superior parietal lobule, postcentral gyrus and medial frontal gyrus (F-WAIT: pseudo $t = 5.07$, corrected $p = 0.20$; C-WAIT: pseudo $t = 6.16$, corrected $p = 0.15$) but these were not significant when p values were adjusted for multiple testing. Consistent with the scalp maps, within the ADHD group the VLFO activity was increased during the F-WAIT and C-WAIT compared to REST within the temporal regions including limbic lobe and insula (blue regions on Fig. 3). For the REST-to-F-WAIT contrast there was a significant group difference in insula (BA 13) and inferior frontal gyrus (pseudo $t = 3.65$, corrected $p = 0.035$). For the REST-to-C-WAIT contrast a significant group difference was identified in insula, middle and superior temporal gyrus (BA 13, 21, 22, 41; pseudo $t = 3.67$, corrected $p = 0.01$). There was no group difference in terms of the REST-to-WORK transition ($p = .42$). To explore these unpredicted temporal lobe/insula effects further, we then extracted the sLORETA generators within the local regions showing group difference when waiting and examined their correlations with the delay aversion and discounting scores on QDQ. There were highly significant positive correlations between QDQ scores and F-WAIT activity in insula (MNI[$x/y/z$] = $-35/20/5$; $r^{\text{delay aversion}} = .57$, $p < 0.001$; $r^{\text{temporal discounting}} = .57$, $p < .001$) and inferior frontal gyrus (MNI[$x/y/z$] = $-35/25/0$; $r^{\text{delay aversion}} = .51$, $p = 0.001$; $r^{\text{temporal discounting}} = .53$, $p < .001$); and C-WAIT activity in superior temporal gyrus (MNI[$x/y/z$] = $50/-20/5$; $r^{\text{delay aversion}} = .46$, $p < 0.01$; $r^{\text{temporal discounting}} = .42$, $p < 01$), middle temporal gyrus (MNI[$x/y/z$] = $60/-30/-5$; $r^{\text{delay aversion}} = .41$, $p < 0.01$; $r^{\text{temporal discounting}} = .37$, $p < 05$) and insula (MNI[$x/y/z$] = $45/-15/5$; $r^{\text{delay aversion}} = .53$, $p = 0.001$; $r^{\text{temporal discounting}} = .50$, $p = 001$).

4. Discussion

Despite considerable recent interest in the resting brain the current study is the first to examine spontaneous VLFOs during waiting states in ADHD. We set out to test two hypotheses: First, individuals with ADHD, compared to controls, would display excess spontaneous VLFO activity during waiting, similar to that observed in the past when they are working on goal-directed tasks; second, this excess activity would be related to measures of impulsive choice. There were a number of findings of note.

First, we replicated prior evidence of suppression of VLFO activity during episodes of waiting and working relative to resting in healthy children and adolescents (Hsu et al., 2013). Our study supports the view that in terms of spontaneous brain activity, waiting, despite some characteristics in common with resting, is similar to other goal-directed activities such as performing information processing tasks. Prior debates about the functional status of EEG-VLFO as a measure of real neuronal activity, and the extent to which it is functionally similar to BOLD oscillations (Demanuele et al., 2013; Vanhatalo et al., 2005), notwithstanding, the localization of sources to midline structures in the current study raises new questions about the relationship between the EEG-VLFO network and the DMN. Indeed recent studies using simultaneous EEG-fMRI recordings have identified a direct association between spontaneous BOLD signals and EEG in both infra-slow (Hiltunen et al., 2014) and higher frequency domains (Laufs et al., 2003; Mantini et al., 2007). There has also been evidence indicating an association between the increase of theta power (particularly in anterior mPFC) and Rest-to-Work BOLD signal attenuation in the DMN during cognitive task performance (Meltzer et al., 2007; Scheeringa et al., 2009). Further work should examine the functional significance of EEG-VLFO by co-registering EEG signals to structural images attained from MRI or using simultaneous fMRI-EEG recordings. Also, it is important to investigate the effect of attenuation of EEG power from resting to waiting in different frequency, including traditional frequency bands.

Second, individuals with ADHD, compared to controls, attenuated VLFO power to a lesser degree when working relative to resting but the spatial distribution of REST-to-WORK attenuation was similar between the two groups. The ADHD group also displayed a significantly elevated error rate during the performance of the attention task. Reduced rest-to-work attenuation in ADHD is consistent with previous EEG (Helps et al., 2010) and fMRI

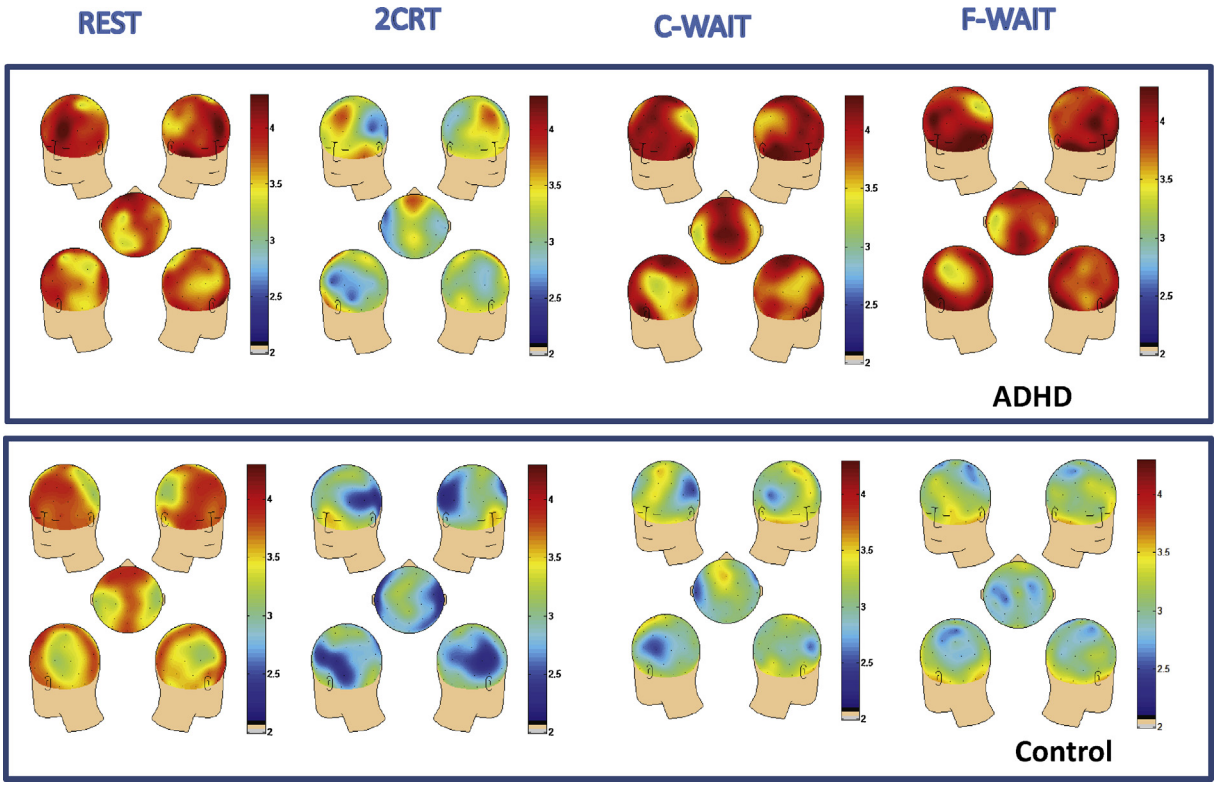

Fig. 2. Spatial distributions of scalp recorded VLFO across the whole scalp. Top row: ADHD group; bottom row: controls. 2CRT: two choice reaction time task. C-WAIT: condition when participants chose to *wait*. F-WAIT: condition when participants were forced to *wait*.

literature (Fassbender et al., 2009; Liddle et al., 2011), as well as the default mode interference hypothesis (DMI; Sonuga-Barke and Castellanos, 2007), which predicts periodic attentional lapses (e.g. periodic clusters of longer reaction time or increased performance errors) when default activity persists during a task. However, the result was not entirely consistent with the findings of Broyd et al. (2011), who observed different spatial distributions

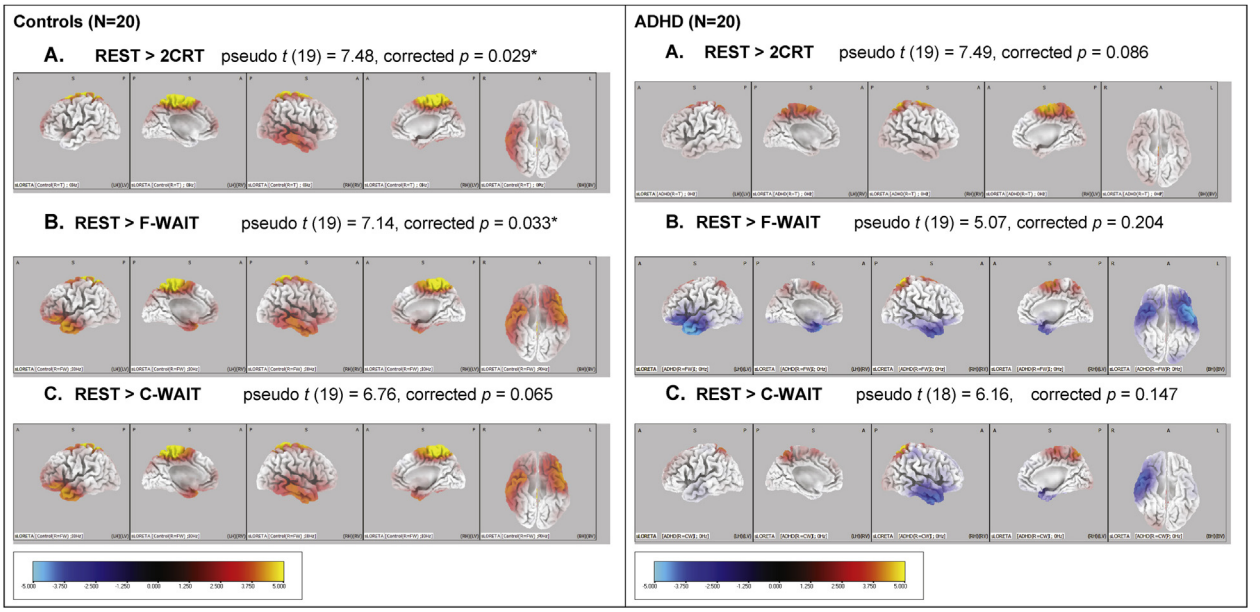

Fig. 3. The intracranial source differences between REST and WORK/WAIT conditions.

of VLFO attenuation for adults with high and low ratings of ADHD symptoms.

Third, we provided the first evidence that individuals with ADHD also display excess VLFO activity during waiting tasks – in fact the apparent lack of suppression when judged across the scalp was even more marked for waiting than for working, despite isolated and non-significant effects in a number of specific DMN regions. There are a number of possible explanations for the failure of rest-to-wait attenuation in ADHD. First, and most straight-forwardly, individuals with ADHD may simply fail to suppress the VLFO activity when transitioning from resting to waiting, as is suggested by the DMI hypothesis. This could be the result of failures in executive control (Willcutt et al., 2005) or to problems engaging brain mechanisms implicated in state-to-state switching, (i.e., salience network; Menon and Uddin, 2010). An alternative hypothesis is that, rather than a failure to suppress resting brain activity, excess VLFO activity during waiting represents a positive decision to engage in introspective and self-referential mental activity, such as mind wandering, typically associated with VLFO activity in the core DMN regions (Buckner and Carroll, 2007). In this sense excessive VLFO activity in DMN-related regions might represent a cognitive coping strategy to deal with the aversiveness of waiting – (an expression of delay aversion Marco et al., 2009; Sonuga-Barke et al., 1992). It can therefore be seen as an internalized manifestation of the common observation that children with ADHD display more distracted and hyperactive behavior when waiting in situations with low levels of stimulation.

Fourth, as predicted the level of VLFO attenuation from resting to waiting was found to be related to delay aversion and heightened temporal discounting as rated by parents. It is at present unclear what is the cause and what is the effect here – on the one hand, failure to suppress VLFO during waiting might impair individual's ability to focus on, and achieve, the goal of waiting. On the other hand, as suggested above, it may be that the more delay averse and impulsive an individual is the more they engage in self-referential processing during waiting, for the purpose of reducing negative affections arising from the period of delay (Sonuga-Barke, 2002). In some ways the latter view seems more likely, as the former appears to contradict the literature relating to the role of the DMN in setting a personally desired goal for a future event and its influence on the ability to wait (Sonuga-Barke and Fairchild, 2012).

Finally, an unpredicted increase in VLFO activity in the insula and specific temporal regions was observed in ADHD patients during the waiting periods and this was positively correlated with the level of delay aversion and temporal discounting as rated by parents. In hindsight these effects could have been predicted on the basis of previous fMRI studies supporting the idea that delay during waiting is aversive to individuals with ADHD. Specifically, research has identified elevated activation in the emotional brain centre (Dalgleish, 2004) for this clinical group during their responsiveness to a period of delay. For example, Plichta and colleagues (2009) identified increased activity in amygdala in adults with ADHD comparing to healthy controls during the choices of delayed rewards. Lemiere et al. (2012) found increased insula and amygdala activity during the anticipation of an inescapable delay. Wilbertz and colleagues (2013) reported a positive association between the activity in inferior temporal cortex and right amygdala and the length of delayed period within the ADHD but not the control group. The current results therefore provide some of the first evidence linking the EEG power in the temporal regions to delay aversion (Broyd et al., 2012) although we admit the difficulty to examine deep cortical structures using scalp recording EEG signals.

The study had a number of limitations. First, individuals in the ADHD group had lower IQ than controls; however, analyses were run with and without IQ as a covariate and this did not change the results. Second, the use of sLORETA may constrain the interpretation as the images this package produces lack precise spatial resolution. Focal activities may be over- or under-estimated. Despite this, recent evidence demonstrates deep sources can be reliably estimated from scalp-recorded electrophysiological data (Lucka et al., 2012; Michel et al., 2004), with significant correspondence to haemodynamic procedures used in the same tasks (Mulert et al., 2004). The localization of VLFO to DMN-related regions found in the current study is plausible. Third, the characterization of impulsive choice was assessed by one measure. Future research should include a broader battery of measures. Fourth, participants' behaviors during waiting conditions may affect result interpretation. Future studies should videotape participants when they are waiting, evaluate participants' behavioral responses to waiting conditions and the relation to VLFO attenuation.

5. Conclusions

In summary, the current study provides the first evidence of excessive DMN related EEG activity during waiting in ADHD and its link to parents' ratings of delay-related problems. The relationship between neural activity, impulsive choice and internalized self-referential activity should be explored in future research.

Conflict of interest

Chia-Fen Hsu and Nicholas Benikos report no potential conflicts of interest. Dr Sonuga-Barke has potential conflicts of interest in relation to Shire pharmaceuticals – speaker fees, consultancy, advisory board membership, research support and conference attendance funds. Janssen Cilag – speaker fees. Visiting chairs at Ghent University and Aarhus University. Grants awarded from MRC, ESRC, Wellcome Trust, Solent NHS Trust, European Union, Child Health Research Foundation New Zealand, NIHR, Nuffield Foundation, Fonds Wetenschappelijk Onderzoek – Vlaanderen (FWO).

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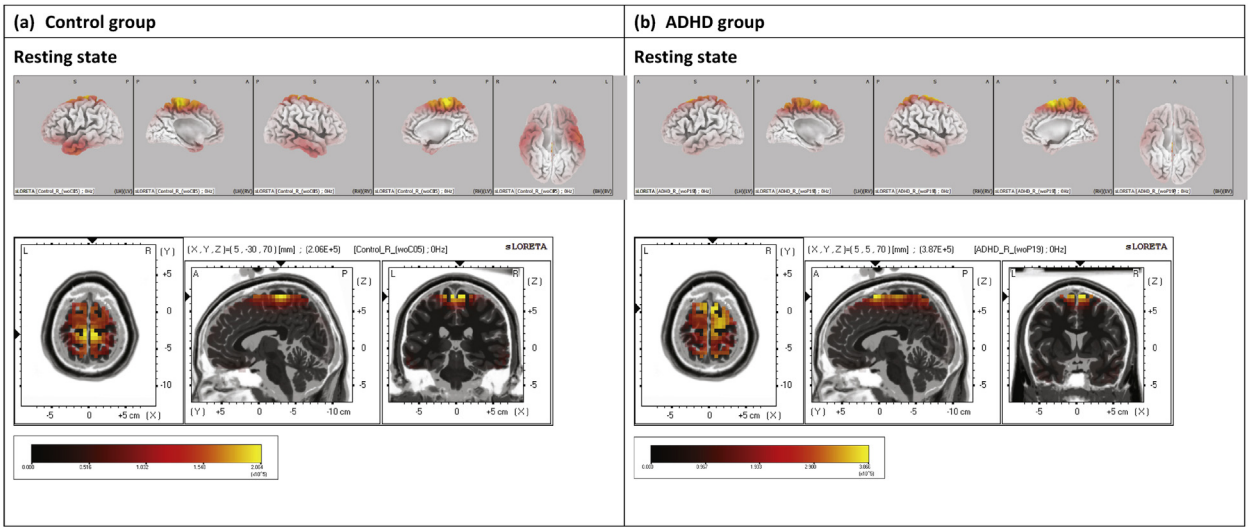

Fig. A.1. sLORETA images of the resting EEG (0.02–0.2 Hz). Left panel: typical developing controls; right panel: individuals with ADHD.

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Appendix A.

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