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**Abstract**

**Background:** Attention-deficit/hyperactivity disorder (ADHD) has been associated with reduced resting state connectivity in the core subsystem of the default mode network (DMN; medial prefrontal cortex – posterior cingulate cortex). However, the neuropsychological consequences of this hypoconnectivity remain to be determined. Building on recent theoretical models of DMN function, we tested the association between DMN hypo-connectivity and three candidate endophenotypes of ADHD: (i) excessive task-unrelated spontaneous thought (i.e., mind-wandering); (ii) sub-optimal decision-making due to exaggerated temporal discounting; and (iii) delay aversion – a heightened emotional response to the imposition or experience of delay.

**Methods:** Twenty male adolescents with a clinical diagnosis of ADHD and 18 typically developing adolescents (all aged 11-16 years) underwent a resting-state fMRI scan to assess DMN connectivity. An experimental paradigm was used to assess temporal discounting and questionnaires were used to measure mind wandering and delay aversion.

**Results:** ADHD was significantly associated with DMN hypo-connectivity specifically in the core subsystem, elevated levels of mind-wandering, delay aversion, and temporal discounting. Mediation analysis suggested that DMN hypoconnectivity mediated the link between ADHD and delay aversion.

**Conclusion:** The results provide initial evidence that disturbances in the DMN may impair ability to regulate delay-related negative affect in adolescents with ADHD.

**Keywords:** ADHD, default mode network, fMRI, spontaneous thought, delay aversion, temporal discounting

**Introduction**

Attention-deficit/hyperactivity disorder (ADHD) is a complex and impairing neurodevelopmental condition characterised by age-inappropriate inattention and/or hyperactivity-impulsivity (Posner et al., 2020). Functional magnetic resonance imaging (fMRI) studies have demonstrated disrupted functional connectivity in a range of resting-state networks that contribute to neuropsychological processes known to be impaired in ADHD (for a review, see Castellanos and Aoki, 2016). For instance, studies have reported a distinctive pattern of reduced connectivity between components of the default mode network (DMN) in ADHD. At its core are functionally connected hubs situated in regions of the medial prefrontal and posterior cingulate cortices (Andrews-Hanna et al., 2010) which are incorporated into a wider network that includes a *dorsal medial subsystem* (dorsal medial prefrontal and lateral temporal cortices, the temporal parietal junction and the temporal pole), and a *medial temporal subsystem* (hippocampal formation, ventral medial prefrontal and retrosplenial cortices and the inferior parietal lobule; Andrews‐Hanna et al., 2014; Yeo et al., 2011). In general, the DMN is active during rest or self-referential and introspective states (Fox et al., 2015), including reflecting on the past and envisioning the future (Buckner et al., 2008). It is down-regulated during conditions and tasks requiring focused attention on the external world and stimuli (Fransson, 2006). When DMN activity is not attenuated as it should be, it interferes with task performance (Li et al., 2007). Within the broader domain of self-referential and introspective cognition, it has been proposed that the three subsystems are functionally dissociable. The dorsal medial subsystem is hypothesized to be implicated in general mentalising, conceptual and emotional processing ability (Andrews‐Hanna et al., 2014), the medial temporal subsystem supports mental scene construction (Christoff et al., 2016; Karapanagiotidis et al., 2017), while the core system co-ordinates internally-oriented thought in the other two subsystems towards personally relevant future goals (Molnar-Szakacs and Uddin, 2013; Utevsky et al., 2014) - integrating autobiographical information related to desired future states and the ability to ‘imagine’ goal-orientated outcomes (Gerlach et al., 2014; Sonuga-Barke and Fairchild, 2012).

Recent reviews have found core subsystem hypo-connectivity in both children and adults with ADHD (Castellanos & Aoki, 2016). However, the functional implications of such DMN hypo-connectivity are poorly understood. A logical place to start is to investigate associations between DMN core subsystem hypo-connectivity and neuropsychological processes known to be altered in ADHD (Christoff et al., 2016). Here we test a number of alternative hypotheses. The first hypothesis is that DMN hypo-connectivity in ADHD underpins excessive mind-wandering (task-unrelated spontaneous thought), because of a failure to attenuate DMN activity during the transition to task performance (Sonuga-Barke and Castellanos, 2007). Individuals with ADHD report elevated levels of mind-wandering (Franklin et al., 2014; Shaw and Giambra, 1993). They also show a difficulty in proactively preventing mind-wandering and/or mitigating its negative effects on task performance (Franklin et al., 2014; Schooler et al., 2011). Core DMN activity is associated with mind-wandering (Fox et al., 2015), being preferentially activated during task-unrelated compared with task-related thought (Stawarczyk et al., 2011). Artificially exciting or inhibiting components of the core subsystem using transcranial magnetic stimulation have been shown to either increase or suppress levels of mind-wandering, respectively (Kajimura et al., 2017). DMN hypo-connectivity at rest in ADHD has been suggested to reflect a dysregulated network that is unable to attenuate during the transition to a goal-directed mental state (Aboitiz et al., 2014). We predicted that DMN core subsystem hypo-connectivity in ADHD would be associated with a greater frequency of mind-wandering in ADHD. In order to examine the specificity of this prediction, we also measured the related construct of daydreaming (stimulus-independent thought that occurs outside of an attention demanding task; Mrazek et al. 2013).

The second hypothesis was that abnormal DMN connectivity impairs the ability to simulate future outcomes of different choices - leading to sub-optimal intertemporal decision-making, which in ADHD is characterised by a tendency to assign less value to future compared to immediate rewards (Marx et al., 2018). First proposed by Sonuga-Barke and Fairchild (2012; see also Sonuga-Barke et al., 2016), the hypothesis is that DMN dysregulation undermines the ability to envision future events, preventing individuals with ADHD from fully estimating the subjective utility of different choice outcomes. In a non-clinical population, Benoit et al. (2011) found that the DMN core subsystem was differentially activated when participants were imagining the value of future economic outcomes and that the degree of activation was correlated with the tendency to discount the value of delayed rewards. Based on this model, we predicted that core subsystem hypo-connectivity would mediate the link between ADHD and heightened temporal discounting.

We also examined the related construct of delay aversion (negative affect associated with delay imposition). The delay aversion hypothesis (Sonuga-Barke, 2002) postulates that aspects of ADHD – e.g., inattentive and hyperactive behaviours, are functional expressions of a desire to escape an exaggerated negative affect experienced by individuals with ADHD during periods of extended delay (e.g., during idle time or while waiting for an outcome). Support for this view comes from both behavioural studies that show increased levels of ADHD symptoms in delay rich settings (Marx et al., 2018) and neuroimaging studies that show cues predicting upcoming delay periods elicit abnormally high levels of amygdala activity in adolescents with ADHD (Van Dessel et al., 2018). It has also been shown that individuals with ADHD display elevated levels of brain activity within a very low frequency band localised to the DMN in individuals with ADHD while waiting (Hsu et al., 2015, 2013). The third prediction tested, therefore, was that delay aversion in ADHD would be mediated by alterations in DMN connectivity, although it is unclear which particular subsystem will be implicated based on prior EEG evidence which lacks the spatial resolution to discriminate between the core, dorsal medial and medial temporal subsystems (ref missing).

**Methods**

**Participants**

Sixty-one male adolescents (30 ADHD/31 controls) aged between 10-16 years participated in the study (see Table 2). The ADHD group were recruited from local clinics using the South Hampshire ADHD Register (SHARe; https://www.southampton.ac.uk/psychology/research) and the control group from local schools and youth groups. Participants were excluded from the control group if they met the criteria for any DSM-IV Axis-I diagnosis and from the ADHD group for failing to fulfil criteria for an ADHD research diagnosis in standardised interviews (see below). Additional exclusion criteria for the ADHD group were: a) the presence of any other commonly co-occurring neuropsychiatric conditions as assessed by clinicians (with the exception of oppositional defiant disorder (ODD) and conduct disorder (CD) given their high comorbidity with ADHD (Waschbusch, 2002)); b) current medication use, excluding short acting stimulants (in which case patients were asked to withhold taking medication for 24 hours prior to testing). Additional exclusion criteria for both groups were: a) an IQ <75, to exclude participants with probable intellectual disabilities; and b) standard MRI exclusion criteria (cardiac pacemaker, metal in body, claustrophobia, etc.). Twelve adolescents were excluded from the control group due to the presence of Axis-I disorders. A further 11 subjects were excluded from the ADHD group (four for not meeting diagnostic criteria for ADHD at the time of testing, five for withdrawing prior to completing the study and one for excessive head movement during the resting state scan (maximum displacement > 1 voxel)). This left a final sample of 38 adolescents (20 ADHD/18 controls; mean age (SD) = 13.27 (1.55) years). Of the 20 ADHD participants, two met criteria for ADHD, nine for ADHD + ODD and nine for ADHD + ODD + CD. The University of Southampton Ethics Committee, the NHS Research Ethics Committee and the University Hospital Southampton NHS Trust’s Research and Development office reviewed and approved this study (NHS Research Ethics Committee reference: 14/SW/1005).

**Measures**

**Screening and diagnosis:** The diagnostic assessment was performed by interviewing parents about their child’s behaviour using a fully-structured psychiatric interview (DISC-IV-P; Shaffer, Fisher, Lucas, Dulcan, and Schwab-Stone, 2000) and completing the parent and self-report versions of the Conner’s Comprehensive Behaviour Rating Scale (Conners CBRS 3rd Edition; Conners et al., 2011). The DISC-IV-P is a widely used and studied mental health interview tested for clinical and general populations (sensitivity: ADHD = 0.98, ODD = 1.00, CD =1.00; specificity: ADHD = 0.90, ODD = 0.91, CD = 0.99; (Lucas et al., 2001)). The Conners CBRS uses symptom scales to assess major depressive disorder, generalised anxiety disorder, separation anxiety disorder, social phobia, obsessive compulsive disorder, autistic disorder, and asperger’s disorder.

**Temporal discounting:** A computerised temporal discounting task was administered (see Demurie et al., 2012). Participants were instructed to choose between two hypothetical choice alternatives: a small immediate reward and a large delayed reward. Delay periods were: “today”, “tomorrow”, “the day-after-tomorrow”, “one week’s time” and “two weeks’ time”. Reward magnitudes were: £0, £5, £10 and £30. Each reward was paired four times with each delay, resulting in 100 choice trials. In the analysis, the subjective value of the delayed reward was estimated by averaging the magnitude of the small immediate reward for which the participant showed indifference in choice against the large delayed reward. For each subject and each timepoint, switch points were calculated in both ascending (large delayed reward likely to be preferred when the immediate reward is low) and descending (small immediate reward likely to be preferred when the value of the delayed reward is low) choice sequences. Subjective values were determined as the average points of indifference across ascending and descending choice sequences for the delayed outcome relative to the immediate “today” option (Critchfield and Kollins, 2001).

**Delay aversion**: The parent version of the Quick Delay Questionnaire (QDQ; Clare et al., 2010) was administered. The QDQ is a validated questionnaire consisting of five items assessing delay aversion (e.g., “hates waiting for things”). Parents responded on a 5-point Likert scale ranging from “*not at all like him*” to “*very much like him*”.

**Mind wandering**: The Mind Wandering Questionnaire (MWQ; Mrazek et al., 2013) was completed by the participants - a 5-item questionnaire validated in adolescents to measure off-task thought (e.g., “*whilst reading, I find I haven’t been thinking about the words and must therefore read it again*”). Participants responded to each item on a 6-point Likert scale ranging from “*almost never*” to “*almost always*”.

**Daydreaming:** The Day-Dreaming Frequency Questionnaire (DDFQ; Giambra, 1995) was completed by participants. This is a 12-item questionnaire that measures stimulus-independent thought occurring outside of an attention demanding task (e.g., “*On a long bus, train or airplane ride, I daydream…*”). Responses were made on a 6-point Likert scale. Scores on each of these questionnaires have been shown to correlate with DMN signal (Godwin et al., 2017; Hsu et al., 2016, 2013; Mason et al., 2007).

**fMRI Image acquisition**

Imaging data were collected on a 3-Tesla Siemens Magneton Skyra (Siemens AG, Erlangen, Germany) at Southampton General Hospital, UK using a 12-channel head coil. Structural scans were acquired using a T1-Weighted (MP-RAGE) three-dimensional dataset (voxel size=1 mm x 1 mm x 1 mm, repetition time = 2200ms, flip angle = 8°, 178 slices) with a scan acquisition time of 6 minutes and 52 seconds. These were acquired for the purposes of registration and to produce masks of white matter and cerebrospinal fluid to assist with denoising the resting-state signal. Functional scans were obtained using a T2\* -weighted EPI pulse sequence (repetition time = 2500ms, 44 slices, voxel size= 3mm x 3mm x 3mm voxels in an interleaved acquisition, flip angle = 90°, 147 volumes). After the automatic removal of the first 4 volumes to allow for magnetic stabilisation effects, the entire resting-state scan took 5 minutes and 55 seconds. During the scan, participants were instructed to look at a fixation cross that was viewed though a mirror affixed to the head coil. An eyes-open acquisition with fixation cross was selected given evidence that voxel-to-voxel correlations show the highest test-retest reliability compared with eyes closed or eyes open not staring at a cross (Patriat et al., 2013).

**Image pre-processing**

The FSL version 5 software package (http://fsl.fmrib.ox.ac.uk) and the Connectivity Toolbox version 17e (Conn; http://www.nitrc.org/projects/conn; Whitfield-Gabrieli and Nieto-Castanon, 2012) were used for image pre-processing. First rigid-body correction for head motion was applied and all scans were aligned to the Montreal Neurological Institute (MNI) space using nonlinear registration performed with 12 degrees of freedom. Functional data was spatially smoothed with an isotropic full-width half-maximum kernel of 6mm3. To reduce the effects of spurious correlations, a 36 parameter confound regression strategy was applied (Ciric et al., 2017). 24 motion parameters (consisting of 3 displacement parameters, 3 rotation parameters, 6 first order temporal derivatives of these values and 12 quadratic expansions of those derivatives), 8 physiological parameters (2 averaged white matter and cerebral spinal fluid timeseries, 2 first order temporal derivatives and 4 quadratic expansions of those derivatives) and 3 global mean signal parameters were regressed from the functional dataset. After regression the data was bandpass filtered to restrict analysis to the slow 4 and slow 5 frequency bands (0.01-0.073 Hz) thought to most optimally capture resting-state networks whilst excluding artificial signal (Xue et al., 2014). After bandpass filtering the data was de-spiked using a hyperbolic tangent function to further reduce the influence of outlier scans.

*[Insert Table 1 about here]*

**Regions of interest (ROIs)**

Following Andrews-Hanna et al. (2010), 11 ROIs overlapping left lateralised nodes of the core, dorsal medial, and medial temporal subsystems were used in this study (see Table 1 for regions and coordinates). The connectome employed was originally validated on young adults. However, we opted to use it here because by adolescence the DMN appears to be fully formed, with only limited increases in functional connectivity between DMN nodes that persist into adulthood (Sherman et al., 2014; Supekar et al., 2010). Therefore, we felt justified in using these ROIs with an adolescent population. All ROIs were 8mm radial spheres created using FSL.

Mean signal time series within each ROI were extracted and Pearson’s correlation coefficients were calculated. These correlation coefficients were normalised using Fisher’s r-to-z transformation to create an interval scale. Consistent with previous studies that have used this set of ROIs, we averaged functional connectivity within the three DMN subsystems to calculate overall measures of functional connectivity specific to each subsystem.

**Statistical analysis**

First, between subjects t-tests were used to compare control and ADHD groups in terms of average functional connectivity for each of the DMN subsystems and temporal discounting, delay aversion, mind-wandering and daydreaming scores. For temporal discounting we compared groups in terms of changes of subjective value of the delayed reward between “today” and “tomorrow”, “tomorrow” and the “day-after-tomorrow”, the “day-after-tomorrow” and “one weeks’ time” and “one weeks’ time” and “two weeks’ time”. Statistical significance was assessed at p<0.05, False Discovery Rate (FDR) correction; for the three DMN subsystems assessed. Second, the relationship between DMN connectivity in the three subsystems and the other dependent variables were examined using Pearson’s correlations for outcomes shown in Stage 1 to be associated with ADHD. Finally, mediationl models were used to test our predictions. For each hypothesis, group membership (i.e., ADHD vs. Control group) was the predictor variable, DMN connectivity the mediator variable, and either mind-wandering, daydreaming, temporal discounting or delay aversion the outcome variable. Mediationl analyses were conducted with MPLUS version 8 (Muthén & Muthén, 2017). Significance of direct and indirect effects was determined via bias-corrected bootstrapped confidence intervals, with 10,000 bootstraps.

**Results**

**Demographic and neurocognitive differences between the ADHD and control group**

Participants with ADHD and controls were of a similar age. Individuals with ADHD showed significantly lower IQ and elevated ODD and CD symptoms scores compared with controls (see Table 2). Relative to controls, individuals with ADHD showed increased levels of mind-wandering and delay aversion, but not daydreaming. Figure 1 displays the changes in subjective value of the delayed outcomes as a function of delay to its delivery for the two groups. Participants with ADHD showed higher rates of temporal discounting and group differences were driven by a significantly greater drop in subjective value between “today” and “tomorrow” in the ADHD group. The comparisons of the other time periods were not significant.

*[insert Table 2 about here]*

*[Insert Figure 1 about here]*

**fMRI resting state connectivity differences between the ADHD and control group**

Relative to controls, adolescents with ADHD exhibited significantly reduced connectivity in the DMN core (t(36)= 4.12, p(FDR)<0.001), but not the dorsal medial (t(36)= 0.95, p(FDR)=0.34) or the medial temporal subsystems (t(36)= 1.15, p(FDR)= 0.34); see Figure 1. The difference in core subsystem connectivity between the groups remained significant after controlling for IQ (F(1,38)= 16.83, p(FDR)<0.001).

**Correlations between DMN connectivity and neuropsychological performance**

There were significant correlations between delay aversion and temporal discounting scores (for the contrast “today” vs. “tomorrow”) and core subsystem hypo-connectivity; see Table 3. However, there were no correlations between core subsystem connectivity and mind-wandering or daydreaming. No neuropsychological outcomes correlated with dorsal medial or medial temporal subsystem connectivity (all p values > 0.1).

*[Insert Table 3 about here]*

**Mediation analysis**

The results of the four mediation models are displayed in Figure 3. In all four models, there was a direct effect between ADHD group status and DMN core subsystem hypo-connectivity. DMN hypo-connectivity only mediated the relationship between ADHD and delay aversion. There was no indirect effect for any of the other outcome measures across the four models. There were, however, additional direct effects, with ADHD significantly predicting mind-wandering (Model a) and day dreaming (Model b), but not temporal discounting (Model c), or delay aversion (Model d).

*[Insert Figure 3 about here]*

**Discussion**

Previous research has reported DMN core subsystem hypo-connectivity in ADHD, yet comparatively little is known about the associations between this connectivity pattern and neuropsychological functioning. In this study we tested a number of possibilities regarding the putative relationships between ADHD, DMN connectivity and neuropsychological deficits. There were a number of findings of note.

First, consistent with recent reviews of empirical findings, we found ADHD-related hypo-connectivity in the DMN core subsystem – which links the medial prefrontal and posterior cingulate cortex (Castellanos and Aoki, 2016; Posner et al., 2014). Furthermore, this was the first study to investigate overall ‘global’ connectivity in the other two dorsal medial and medial temporal DMN subsystems in patients with ADHD – the dorsal medial and medial temporal subsystems. Collectively, our results support reviews suggesting these subsystems are unaltered in individuals with ADHD (Castellanos and Aoki, 2016).

Second, ADHD was associated with elevated levels of self-reported mind-wandering and delay aversion and heightened temporal discounting of rewards on an intertemporal choice task. This is consistent with a considerable body of evidence from studies using a range of different methods. Compared to controls, the minds of individuals with ADHD wander more frequently, as evidenced by questionnaires (Biederman et al., 2017; Shaw and Giambra, 1993) and experience sampling methods (Arabacı and Parris, 2018). Individuals with ADHD also show elevated delay aversion and temporal discounting evidenced from both questionnaire-based measures (Clare et al., 2010) and conventional lab-based decision-making tasks (Marx et al., 2018). Accordingly, mind-wandering, delay aversion and excessive temporal discounting are each thought to be important neuropsychological correlates of ADHD (Arabacı & Parris, 2018; Sonuga-Barke, 2002, 2003).

Third, despite our observation of elevated levels of mind-wandering in the ADHD group, there was no relationship between mind-wandering and DMN core subsystem hypo-connectivity and DMN hypo-connectivity did not mediate the relationship between ADHD and mind-wandering. Whilst the current study is the first to investigate whether DMN connectivity is associated with mind-wandering in ADHD, a meta-analysis has reported a strong association between task-unrelated thought and DMN connectivity in healthy populations (Fox et al., 2015). The DMN interference hypothesis postulates that low frequency temporal synchrony between these task positive systems and the DMN is required to maintain DMN attenuation during task performance, with mind-wandering and increased response time variability arising as a consequence of mind-wandering thoughts intruding on task performance (Sonuga-Barke and Castellanos, 2007). Furthermore, Aboitiz et al. (2014) argued that reduced DMN connectivity contributes to the failure to attenuate DMN activity in the transition from resting to task states and to an increased risk of mind-wandering during task performance. One explanation for this inconsistency between results is that mind-wandering is not driven by within-DMN disruption per se, but that it arises out of reduced functional coupling between the DMN and other resting-state networks such as executive control networks (Christoff et al., 2016; Sonuga-Barke and Castellanos, 2007). In fact, reduced anti-correlations between the DMN and executive control systems, and not within-DMN connectivity, have been shown to correlate with poor attentional control during task performance in adolescents with ADHD (Barber et al., 2015).

Fourth, DMN core subsystem hypo-connectivity was correlated with temporal discounting - consistent with the proposal by Sonuga-Barke and Fairchild (2012) that DMN dysfunction in the form of hypo-connectivity reduces the ability to envision the future and so acts together with problems of executive control and reward evaluation to impair inter-temporal decision making. Although previous studies have found a link between DMN activation and temporal discounting (Benoit et al., 2011), this is the first study to extend these investigations by exploring intertemporal decision-making and its neural substrates in adolescents with ADHD. In this regard, we found no evidence that DMN connectivity mediates the links between ADHD and heightened temporal discounting. This suggests that other factors are likely to be driving temporal discounting in ADHD perhaps linked to aspects of reward circuits. Future studies should focus on the interplay between DMN (prospection) and dorsal (executive control) and ventral (reward) fronto-striatal circuits in determining individual differences in decision-making (Sonuga-Barke et al., 2016).

Fifth, DMN core subsystem functional connectivity fully mediated the relationship between ADHD and delay aversion. This suggests a role of the DMN core subsystem in regulating negative affective responses to waiting or the imposition of delay in ADHD – that are independent of temporal discounting effects. Consistent with this interpretation, Hsu et al. (2015) reported that children with ADHD, relative to non-ADHD controls, display elevated levels of very low frequency electroencephalography (EEG) oscillations in a network with sources overlapping the DMN during both wakeful rest and while waiting for rewards. Crucially, DMN-related neural activity also correlated with parent-reported delay aversion. Those with higher levels of low frequency DMN power also showed high levels of delay aversion. On the basis of these findings Hsu et al. (2015) predicted that engagement in self-referential thought reduces the aversiveness of periods of idle time for people with ADHD by changing the perception of time passing. In this sense, playing a role within the delay aversion model equivalent to that of the external manifestations of ADHD – i.e., inattentive and hyperactive symptoms (Sonuga-Barke, 2003, 2002). Christoff et al. (2016) suggest that the DMN core subsystem focuses spontaneous thought towards personally relevant goals when individuals are faced with a salient event. It is likely that the experience of delay in individuals with ADHD is experienced as highly emotionally aversive. Weakened functional integrity within the DMN therefore could be expected to contribute to elevated levels of unconstrained spontaneous thought, reflected in increased DMN power during waiting - as has been previously observed (Hsu et al., 2016; Hsu et al., 2013). Although beyond the scope of the current study, future investigations into how levels of spontaneous thought shift during goal-orientated waiting in patients with ADHD would be important in confirming this prediction.

To our knowledge, this is the first study to explore different neuropsychological effects of DMN dysregulation in ADHD in the same study. However, there are a number of limitations that should be taken into account when interpreting these findings. First, although comparable to much of the resting-state fMRI literature on ADHD (Castellanos and Aoki, 2016) the sample size was limited and this could have reduced our statistical power to detect associations - especially with regard to the mediational analyses. Second, given the functionally dissociable nature of the DMN, the current study focused on average connectivity within individual subsystems. Whilst this increases the sensitivity to detect network level effects, it does so at the cost of topographical specificity. There is emerging evidence highlighting the importance of individual seed level connections, to different features of spontaneous thought (Smallwood et al., 2016) and the current study may not have been able to detect these effects. Third, following previous studies that have used this set of ROIs, analyses were restricted to the left lateralised DMN (Andrews‐Hanna et al., 2010; Dodell-Feder et al., 2014). Fourth, the assessment of mind-wandering and delay aversion was based on self-report and parent-report measures, respectively. These were selected because at the time of testing, there were no alternative, validated methods of measuring either construct in adolescents. Although both questionnaires have good psychometric properties (Clare et al., 2010; Mrazek et al., 2013), future studies should use a broader set of measures including laboratory tasks*.* Fifth, although CD is likely independently associated with altered DMN connectivity (Broulidakis et al., 2016), within this study we lacked statistical power to investigate whether the observed results were driven by high levels of CD comorbidity in our sample. Finally, the data reported were all cross-sectional – the use of longitudinal data would have provided a stronger test of the mediational models.

In summary, the current study represents the first attempt to empirically link atypical DMN connectivity during wakeful rest to the network’s putative psychological and motivational functions, which are thought to be disrupted in ADHD. Core DMN subsystem hypo-connectivity was correlated with delay aversion and temporal discounting in patients with ADHD, and it fully mediated the relationship between ADHD and delay aversion. Further work needs to be undertaken to test the hypothesis that DMN hypo-connectivity is a neural expression of delay aversion in ADHD.

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Table 1**:** *Default mode network regions of interest and their respective coordinates using the Talairach system with the Montreal Neurological Institute (MNI) template*

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Subsystem/network | Region | Abbreviation | MNI coordinates | | |
|  |  |  | X | Y | Z |
| Core Subsystem | Posterior cingulate cortex | PCC | -6 | 52 | -2 |
|  | Anterior medial prefrontal cortex | aMPFC | -8 | -56 | 26 |
| Dorsal medial Subsystem | Dorsal medial prefrontal cortex | dMPFC | 0 | 52 | 26 |
|  | Temporal parietal junction | TPJ | -54 | -54 | 28 |
|  | Lateral temporal cortex | LTC | -60 | -24 | -18 |
|  | Temporal pole | TempP | -50 | 14 | -40 |
| Medial temporal lobe | Ventral medial prefrontal cortex | vMPFC | 0 | 26 | -18 |
| (MTL) Subsystem | Posterior inferior parietal lobule | pIPL | -44 | -74 | 32 |
|  | Retrosplenial cortex | Rsp | -14 | -52 | 8 |
|  | Parahippocampal cortex | PHC | -28 | -40 | -12 |
|  | Hippocampal formation | HF | -22 | -20 | -26 |

|  |  |  |  |
| --- | --- | --- | --- |
| **Clinical/neuropsychiatric assessment** | **ADHD group (n=20)** | **Control group (n=19)** | **t-test** |
| **Age (y)** | 12.86 (1.53) | 13.60 (1.43) | 1.37 |
| **Intelligence Quotient** | 98.10 (9.47) | 106.32 (10.28) | 2.68\*\* |
| **Diagnostic Interview Schedule for Children (DISC)** |  |  |  |
| ADHD symptoms | 16.65 (2.94) | 4.39 (4.39) | 12.86\*\*\* |
| ODD symptoms | 10.10 (1.83) | 3.94 (3.37) | 7.13\*\*\* |
| CD symptoms | 7.05 (5.15) | 0.63 (1.06) | 5.31\*\*\* |
| **Delay aversion (Quick Delay Questionnaire)** | 10.85 (2.01) | 8.47 (1.95) | 3.19\*\* |
| **Mind Wandering Questionnaire (MWQ)** | 4.22 (1.12) | 2.91 (1.12) | 3.68\*\* |
| **Daydreaming Frequency Questionnaire** | 38.35 (11.16) | 32.26 (8.79) | 1.88 |
| **Temporal discounting task** |  |  |  |
| Subjective value of delayed reward (now to tomorrow) | 0.77 (0.15) | 0.87 (0.07) | 2.66\* |
| Subjective value of delayed reward (day after tomorrow) | 0.72 (0.19) | 0.80 (0.14) | 1.50 |
| Subjective value of delayed reward (in 1 week’s time) | 0.63 (0.30) | 0.76 (0.19) | 1.48 |
| Subjective value of delayed reward (in 2 weeks’ time) | 0.60 (0.28) | 0.73 (0.27) | 1.36 |

Table 2: *Demographic, neuropsychiatric and clinical characteristics of the sample*

Note: \*p<0.05, \*\*p<0.01, \*\*\*p<0.001; all subjects were male; values in parenthesis are standard deviations; ADHD=Attention-deficit/hyperactivity disorder, ODD=oppositional defiant disorder, CD= Conduct disorder

Table 3: *Pearson cross-correlations between default mode network (DMN) subsystem functional connectivity and behavioural outcomes and the respective p-values for the correlations*

|  |  |  |  |
| --- | --- | --- | --- |
| Measure | Core subsystem  *r* and *p* values | Dorsal medial subsystem | Medial temporal subsystem |
| Delay aversion | -0.52 (**0.001**)\* | 0.008 (0.96) | -0.081 (0.63) |
| Temporal discounting | 0.38 (**0.018**)\*\* | 0.053 (0.75) | 0.05 (0.76) |
| Mind-wandering | -0.10 (0.55) | -0.30 (0.06) | -0.20 (0.20) |
| Daydreaming | -0.007 (0.94) | -0.03 (0.85) | -0.12 (0.53) |

Note: values in parenthesis report uncorrected p-values; \* p=0.004 (false discovery rate correction)\*\* p=0.036 (false discovery rate correction)

b)

a)

*Figure 1:* Temporal discounting and its relationship to default mode network (DMN) core subsystem functional connectivity. a) Temporal discounting curves for the two groups. Compared with controls (blue spheres), individuals with attention deficit/hyperactivity disorder (ADHD; orange spheres) show a significant drop in preference for the large reward during the shift from ‘now’ (0 days) to ‘tomorrow’ (1 day). b) A positive correlation was observed between DMN core subsystem functional connectivity and the subjective value of the large reward during the shift from ‘now’ to ‘tomorrow’. Core subsystem connectivity did not correlate with any of the other delay periods. \*p=0.012

*Figure 2:* Default mode network functional connectivity averaged across each of the three subsystems of the network. Individuals with ADHD show core subsystem hypo-connectivity compared with typically-developing controls (error bars show SEs). Results were significant at p<0.05 False Discovery Rate (FDR) correction for the three DMN subsystems examined. MTL = medial temporal subsystem; dMPFC = dorsal medial subsystem.

*p*(FDR)<0.001

![Shape

Description automatically generated with medium confidence]()

Figure 3: Mediation models with bootstrapped and bias-corrected 95% confidence intervals. DA: delay aversion, DD: daydreaming, DMN: Default mode network connectivity, ADHD: ADHD group vs. Control group, MW: mind-wandering, TD: temporal discounting. Note: Dashed lines indicate non-significant effects, solid lines indicate significant direct effects and bold lines indicate significant indirect effects