Childhood-Diagnosed ADHD, Symptom Progression, and Reversal Learning in Adulthood

McCarthy, Hazel; Trinity College Dublin, Psychiatry
Stanley, Jessica; Trinity College Dublin, Institute of Neuroscience
Piech, Richard; Trinity College Dublin, Institute of Neuroscience
Wetterling, Friedrich; Trinity College Dublin, Institute of Neuroscience
Skokauskas, Norbert; Centre for Child and Youth Mental Health and Child Protection, Faculty of Medicine, Medicine
Mulligan, Aisling; University College Dublin, Department of Child and Adolescent Psychiatry, School of Medicine and Medical Science,
Donohoe, Gary; Trinity College Dublin, Psychiatry
Mullins, Diane; Trinity College Dublin, Psychiatry
Kelly, John; Trinity College Dublin, Psychiatry
Johnson, Katherine; University of Melbourne, School of Psychological Sciences
Fagan, Andrew; St. James's Hospital Dublin, Centre for Advanced Medical Imaging
Meaney, James; St. James's Hospital Dublin, Centre for Advanced Medical Imaging
Frodl, Thomas; Otto von Guericke University of Magdeburg, Psychiatry and Psychotherapy

Corresponding Author:
Thomas Frodl, Department of Psychiatry and Psychotherapy, Otto von Guericke University of Magdeburg, Leipziger Str. 44, 39120 Magdeburg, Germany. Email: Thomas.Frodl@med.ovgu.de
Abstract Objective: ADHD persists in up to 60% into adulthood, and the reasons for persistence are not fully understood. The objective of this study was to characterize the neurofunctional basis of decision making in those with a childhood diagnosis of ADHD with either persistent or remitted symptoms in adulthood versus healthy control participants. Method: Thirty-two adults diagnosed with ADHD as children were split into persistent (n = 18) or remitted (n = 14) ADHD groups. Their neural activity and neurofunctional connectivity during a probabilistic reversal learning task were compared with 32 healthy controls. Results: Remitters showed significantly higher neural connectivity in final reversal error and probabilistic error conditions, and persisters depict higher neural connectivity in reversal errors than controls at a family-wise error (FWE) corrected whole-brain corrected threshold. Conclusion: Remitters may have utilized higher neural connectivity than controls to make successful decisions. Also, remitters may have utilized compensatory strategies to override any potential underlying ADHD deficits.

Keywords
ADHD, remission, persistence, functional neuroimaging
Introduction

ADHD is a debilitating childhood-onset neurobiological disorder characterized by developmentally inappropriate levels of inattention, hyperactivity, and impulsivity (American Psychiatric Association, 2013). Adults with childhood diagnoses of ADHD have been associated with disadvantageous decision making in adulthood (M. Miller, Sheridan, Cardoos, & Hinshaw, 2013), whereas adults in remission from ADHD have shown to be comparable with healthy control participants in this domain (Huntley & Young, 2014). However, the neuropathology of decision making has not been widely explored as a long-term outcome of childhood ADHD (M. Miller et al., 2013).

Impulsive decision making in ADHD has been linked to poor cognitive flexibility (Chantiluke et al., 2014). The functional magnetic resonance imaging (fMRI)–based probabilistic reversal learning task probes the neural circuitry related to decision making in ADHD by necessitating the avoidance of punishment by adapting behavior in response to feedback (Finger et al., 2008).

The reversal learning task is governed by three neural networks (Liu, Hairston, Schrier, & Fan, 2010) implicated in the psychopathology of ADHD (Cubillo, Halari, Smith, Taylor, & Rubia, 2012). First, the reward network comprises of the ventral striatal nucleus accumbens and the dorsal striatal caudate nucleus. Immediate reward is processed in the ventral striatum, and future reward is processed within the dorsal striatum (Liu et al., 2010). Inattention and impulsivity, the core features of ADHD in adulthood, have been associated with oversensitivity to immediate rather than delayed
reinforcement (Bari & Robbins, 2013; Stark et al., 2011). Poor motivation to allocate
attention to cues signaling future reward has been linked to dorsal and ventral striatal
hypoactivity among adults with persistent ADHD compared with control and remitted adults (Cubillo, Halari, Giampietro,
Taylor, & Rubia, 2011; Stoy et al., 2011). Whereas, upon receipt of reward, dorsal
and ventral striatal hyperactivity have been found in adults with persistent ADHD
relative to controls (Furukawa et al., 2014; Paloyelis, Mehta, Faraone, Asherson, &
Kuntsi, 2012; Plichta et al., 2009; Ströhle et al., 2008).

Second, the outcome valence network includes the lateral and medial orbitofrontal
cortex (OFC; Liu et al., 2010). The reward and outcome valence networks interact to
assess the values of unchosen and future choices (Liu et al., 2010). The lateral and
medial OFCs evaluate feedback and the reversal of routine responses to maximize
task performance (Liu et al., 2010). Lateral OFC damage impairs reversal learning
(Bari & Robbins, 2013), and a neuropsychological study of reversal learning found a
performance deficit that supported OFC dysfunction in ADHD (Itami & Uno, 2002).
In addition, executive control is governed by the OFC and has been found to improve
in remitted ADHD (Halperin, Trampush, Miller, Marks, & Newcorn, 2008). In
addition, risky and inflexible decision making in adult ADHD has been significantly
correlated with reduced medial OFC activity upon receipt of monetary rewards
relative to controls (Wilbertz et al., 2012).

Third, the dorsomedial prefrontal cortex (DMPFC) is the core feature of the
information integration network, which works with the outcome valence network to
enact appropriate behavioral responses during instances of response conflict (Liu et al., 2010). This network is relevant to persistent ADHD in adulthood as perseverant responding in spite of punishment is a recurrent behavioral characteristic within this population (Fischer, Barkley, Smallish, & Fletcher, 2005; Halleland, Haavik, & Lundervold, 2012; Pazvantoglu et al., 2012; Rapport, Van Voorhis, Tzelepis, & Friedman, 2002). The aim of this study was to characterize the neurofunctional basis of decision making in adults with a childhood diagnosis of ADHD with either persistent or remitted symptoms in adulthood compared with healthy control participants. This study contrasted reversal learning task conditions to measure differences in neural activation between groups (Cools, Clark, Owen, & Robbins, 2002).

Attenuation of ADHD symptoms in adolescence is dependent upon the development of orbitofrontal and prefrontal regions, resulting in improved top-down executive control. This model proposes that functioning of frontal and prefrontal regions compensates for enduring subcortical dysfunction among those with a history of ADHD irrespective of symptom remission (Halperin et al., 2008). Interestingly, because executive dysfunction may even persist when ADHD symptoms have diminished, there might be other explanations then the improved top-down executive control (Miller, Ho, & Hinshaw, 2012). Thus, in the present study, it was hypothesized that persisters would show not only reduced activation but also reduced inter-regional functional connectivity across reward, outcome valence, and information integration networks relative to remitters and healthy controls throughout the reversal learning task. There is the exception of instances in which responses are rewarded, during which persisters were expected to display oversensitivity to reward
via increased striatal activation and functional connectivity relative to remitted and healthy control adults.

Methods and Materials

Participants

Thirty-two adults diagnosed with ADHD by consultant child psychiatrists as children (M age of diagnosis = 7.94, SD = 2.9 years) were re-investigated an average of 9.97 years after taking part in the genetic and neuropsychological studies in childhood (age at first study participation = 11.87, SD = 2 years; Brookes et al., 2006; Daly, Hawi, Fitzgerald, & Gill, 1999). Also, 32 adult control participants were recruited from the community (for mean age in the present study, see Table 1).

Exclusion for the current study criteria included neurological injury or disease, comorbid psychiatric disorder (including current alcohol or substance dependency), or a history of corticosteroid medication use.

Participants’ health, diagnostic status, and eligibility for the study were verified by a psychiatrist. Comorbidity was assessed using the Hamilton Rating Scale for Depression (Hamilton, 1960), the Beck Depression Inventory (BDI; Beck, Steer, & Carbin, 1988), and the Structured Clinical Interview for DSM-IV Axis I Disorders (SCID; First, Spitzer, & Williams, 1997) which screens for lifetime and current psychiatric disorders.
The Conners’ Adult ADHD Observer Rating Scale (CAARS O:L) is a 66-item questionnaire with nine empirically derived subscales that assess Diagnostic and Statistical Manual of Mental Disorders (4th ed.; DSM-IV; American Psychiatric Association, 1994) inattentive and DSM-IV hyperactive symptoms (Conners, 1999). The CAARS O:L was completed to identify the presence and severity of significant ADHD symptoms (Conners, 1999). The ADHD index T-score is the best screen of identifying those “at-risk” for ADHD; norms are given for a population by age and gender. T-scores of 60 or above on the ADHD Index scale are at the 86th percentile and indicate an “above average risk for the presence of ADHD” (Conners, 1999). Participants with a childhood diagnosis of ADHD and a T-score of 60 or above were included in the persistent group, and those with a T-score of 59 or below were included in the remitted group. Control participants were excluded if they had an ADHD index T-score of 60 or above on the CAARS O:L (Conners, 1999). Seven participants were being treated with methylphenidate (MPH) at the time of study participation and underwent a washout period of 48 hr prior to study involvement. To investigate the potential effects of current MPH treatment upon observed results, all imaging analyses were rerun without the seven persisters who were being treated with MPH at the time of testing (see Supplementary Material for these results). As differences between analyses may also be attributed to differences in sample size, results including the seven currently MPH-treated participants will be reported in this study.

All statistical methods for determining the sample characteristics and demographics were conducted in SPSS version 20.0. Sample characteristics are summarized in Table 1.
Significant differences between groups in intelligence quotient and socioeconomic status were not included as covariates due to a rationale that some of the tasks like working memory or attention processing are altered in ADHD, and thus, a poorer performance is expected in these domains (G. A. Miller & Chapman, 2001). Ethical approval for the study was granted by the Adelaide and Meath Hospital and St. James’s Hospital, Dublin, Ireland Ethics Committee. After complete description of the study to the participants, written informed consent was obtained.

Reversal Learning Task Procedure

The individual initially learns to make a response to gain a reward; these events are known as “rewarded correct responses.” The reinforcement contingency then reverses so that the participant is punished for a response that was previously rewarded and a new response must be learned to achieve the reward (Finger et al., 2008). Errors in responding following a contingency reversal are known as “reversal errors.” The last error that a participant makes before shifting their response to the newly rewarding stimulus is known as the “final reversal error.” Final reversal errors are critical events of interest as they reflect reversal learning, which exposes the neural circuitry underlying a participant’s ability to adapt in response to changing reinforcement. The task also contains the presentation of occasionally misleading punishment, called “probabilistic error trials” that punish the participant for a correct response at random; these allow for the examination of neural activity associated with unexpected negative outcomes (Cools et al., 2002).
On each trial, participants were presented with the same two abstract fractal images, randomly assigned to the left or right side of a central fixation cross. These stimuli were presented for 2.9 s, during which time the participant was asked to choose between the two images and press the left or right button on a button box held in their right hand (Current Designs, Philadelphia, PA) to choose the image on the left or right side of the screen. The chosen image became brighter for 2.9 s, followed by feedback for 2.9 s, indicating whether the participant had won 20 cents (Euro). Rewarding feedback was indicated with a picture of a 20-cent coin in the center of the screen, whereas punishing feedback was indicated by a picture of 20-cent coin with a red X across the image. A running total of participants’ earnings during this task were presented above the 20-cent coin. Missed trials were indicated with a red X in the center of the screen and no change in the running total. The next trial immediately followed.

In the scanner, participants performed a session that included 160 task trials with 56 null events (during which the fixation cross was presented for the duration of a normal trial) randomly interspersed for a duration of 20.06 min. Responses were made using the left or right button on a button box positioned on the stomach of the participant. The task was presented using the Cogent 2000 graphics toolbox for MATLAB (www.vislab.ucl.ac.uk/cogent.php).

Task-Based fMRI Image Acquisition

Magnetic resonance imaging (MRI) data were collected on a Philips Achieva 3.0T MRI scanner at the Centre for Advanced Medical Imaging (CAMI), St. James’s...
Hospital, Dublin. The task-based functional images were collected in single runs using a gradient-echo Echo Planar Imaging (EPI) (Echo Time (TE) = 28 ms, Repetition Time (TR) = 2,000 ms, field of view = 131 mm, flip angle = 90°) sensitive to blood oxygenation level–dependent (BOLD) contrast (T2* weighting). A total of 37 contiguous 3.2-mm-thick slices were acquired parallel to the anterior–posterior commissure plane (3 mm approximately isotropic resolution), providing complete brain coverage. The fMRI run included 600 volumes acquired continuously lasting 20.06 min in total. Structural data (for definitive atlas transformation) included a high-resolution sagittal, three-dimensional T1-weighted turbo-gradient-echo sequence (TE = 3.9 ms, TR = 8.5 ms, flip angle = 8°; 256 × 240 acquisition matrix, 1 × 1 × 1 mm voxels) scan.

Preprocessing of fMRI Data

Spatial preprocessing and statistical analysis of functional images were conducted using Statistical Parametric Mapping 8 (SPM8; revision 4290; http://www.fil.ion.ucl.ac.uk/spm/) and MATLAB R2011b (version 7.13; http://www.mathworks.co.uk/products/matlab/). Each functional time series was realigned, and data were excluded if motion parameters exceeded 3 mm in any direction or 3.0° of any angular motion throughout the course of the scan. To account for movement influences, all six rotation and translation movement parameters were extracted for each participant and were included as covariates when generating functional activation and connectivity maps. Data were then slice time–corrected, coregistered to the T1 structural image, normalized to the Montreal Neurological Institute (MNI) template, and spatially smoothed with an 8-mm Gaussian kernel.
General Linear Model (GLM) Analysis

Statistical analysis on preprocessed images was performed using a standard GLM in SPM8 at two levels:

A first-level fixed-effects analysis estimated task-associated activity in each individual, which modeled each task condition. For each experimental condition, a boxcar function representing stimulus presentation was created and convolved with a canonical hemodynamic response function (HRF) to model neural responses at each voxel. The HRF was modeled to the onset of the responses, which co-occurred with the presentation of the feedback.

This first-level GLM included these convolved condition regressors, plus six regressors modeling head movement to reduce remaining movement-related variance after realignment. A high-pass filter of 126 s was used to remove low-frequency signals, and serial correlations in the fMRI time series were accounted for by an autoregressive, AR(1), model.

The second-level analysis involves the calculation of condition effects at each voxel using the following $t$ contrasts originally used by Cools and colleagues (2002): (a) final reversal errors versus correct responses, (b) reversal errors versus correct responses, (c) probabilistic errors versus correct responses, (d) final reversal errors versus reversal errors, and (e) final reversal errors versus probabilistic errors (Cools et al., 2002).
The contrast maps derived from the second-level analysis which calculated the Cools et al. (2002) contrast effects were extracted for each participant and analyzed again in SPM8 with independent-samples $t$ tests to compare the following groups: remitters and persisters, remitters and controls, and persisters and controls. The resultant whole-brain statistical maps were explored at a $p < .001$ (uncorrected) level, and clusters were considered statistically significant at a $p < .05$ level, family-wise error (FWE) corrected for multiple comparisons across the whole brain at the cluster-level extent of 10 voxels. Coordinates of results are in MNI space.

Functional Connectivity Analysis

Using CONN resting-state and task-based software (Whitfield-Gabrieli & Nieto-Castanon, 2014), the task-based functional fMRI data initially defined in SPM8 were imported into CONN for each participant. The preprocessed functional data were temporally band-pass filtered (filter range = 0.009-0.08). Several sources of spurious variance along with their temporal derivatives then were removed from the data by linear regression, such as signal from regions centered in the white matter, cerebrospinal fluid, and movement. Here, CompCor was used to further minimize influences from movement. The data were detrended to remove linear trends within each functional session and despiked which applies a squashing function to reduce the influence of any potential outlier scans.

Based on results from a meta-analysis of reward-based fMRI studies (Liu et al., 2010), the following seed regions of interest with a 5-mm radius were extracted from three decision-making networks using WFU Pickatlas software (Maldjian, Laurienti,
Kraft, & Burdette, 2003): the right caudate ($x = 20, y = 4, z = 18$), left caudate ($x = -8, y = 14, z = 2$), right nucleus accumbens ($x = 12, y = 10, z = -4$), and left nucleus accumbens ($x = -12, y = 10, z = -6$) of the reward network; the right lateral OFC ($x = 30, y = 30, z = -16$), left lateral OFC ($x = -40, y = 44, z = -16$), the right medial OFC ($x = 2, y = 48, z = -14$), and the left medial OFC ($x = -2, y = 54, z = -6$) of the outcome valence network. The left DMPFC ($x = -2, y = 24, z = 42$) and the right DMPFC ($x = 0, y = 24, z = 40$) were used for the information integration network (Liu et al., 2010). Correlation maps were produced by extracting the BOLD time course from a region of interest (ROI) during each one of the four conditions individually (i.e., rewarded correct responses, probabilistic error trials). A correlation coefficient was then computed between the time course of the ROI with the time course from all other brain voxels across the whole brain during each individual condition. The principal technique used was the computation of seed-to-voxel, whole-brain, voxelwise functional connectivity mapping.

Task-based functional connectivity differences between groups within each individual task condition were analyzed in SPM8. The beta (correlation) maps of functional connectivity generated by CONN for each ROI and each participant within each task condition, respectively, were exported from CONN and imported into SPM8. These were then used to compare differences in ROI to whole-brain functional connectivity between the same groups outlined in the previous section using independent-samples $t$ tests. The ROI to whole-brain functional connectivity maps were explored at a $p < .001$ (uncorrected) level, and clusters were considered statistically significant at a $p < .005$ level, FWE corrected for multiple comparisons across the whole brain at the cluster-level extent of 10 voxels. The $p$ threshold was reduced to .005, FWE corrected
for the whole brain because we investigated three networks in four conditions which, however, are partly depending on each other. Coordinates of results are in MNI space.

Behavioral Analysis
Separate univariate ANOVAs were conducted to observe behavioral differences in task performance between groups.

Results

Performance

Persisters accumulated significantly less rewarded correct responses than control participants ($t = -2.29, p = .026$). Also, there were a significant fewer number of final reversal errors for persisters relative to controls ($t = -3.114, p = .003$). Remitters did not differ with controls with regard to their performance (Table 2).

GLM of Whole-Brain Neural Activity Results

Within the comparison of preceding reversal errors to correct responses, remitters revealed significantly more activity in the left occipital lobe compared with persisters ($x = -22, y = -26, z = 26$, FWE-corrected $p < .05$).

Functional Connectivity Analysis Results

Significantly more functional connectivity was observed for remitters than controls as well as for persisters compared with controls, whereby persisters did not differ significantly from remitters.

Final Reversal Errors

Significant between-group functional connectivity differences were found between the right nucleus accumbens of the ventral striatum and the bilateral superior frontal
OFC for remitters compared with controls. Within the information integration network, remitters displayed significantly more functional connectivity between the left DMPFC and the left middle temporal lobe compared with controls (Figure 1, Table 3).

**Probabilistic Error Trials**

Significant between-group differences in functional connectivity were found in the information integration network only. Remitters displayed more connectivity between the bilateral DMPFC and the right precuneus than control participants (Table 3).

**Reversal Errors**

Throughout the information integration network, persisters displayed significantly more functional connectivity between the bilateral DMPFC and the left precuneus than control participants (Table 3).

**Rewarded Correct Responses**

There were no significant differences between groups across any network during the rewarded correct responses condition.

**Discussion**

The investigation of those participants who remit from a developmental psychiatric disorder such as ADHD is highly important because it might point toward compensatory mechanisms (Halperin et al., 2008).

For example, final reversal errors expose the neural circuitry underlying a participant’s ability to adapt in response to change. During this condition, remitters performed, as well as controls, behaviorally and exerted exceptional executive control
which may have overridden any potential underlying ADHD deficit (Halperin et al., 2008). Evidence of this may lie in the finding of significantly more functional connectivity between the right nucleus accumbens of the reward network and the bilateral superior OFC which are involved in executive control (Plichta et al., 2009), for remitters compared with controls. Remitters also showed increased functional connectivity between the left DMPFC of the information integration network and the left middle temporal lobe, a region involved task strategy rehearsal (Tamm, Menon, Ringel, & Reiss, 2004). These findings highlight the possibility that remitters were highly motivated to make successful decisions (Paloyelis et al., 2012).

Conversely, during probabilistic error trials, spurious negative feedback prompted participants to question their response pattern (Cools et al., 2002). During this condition, remitters displayed more functional connectivity between the bilateral DMPFC and the right precuneus compared with controls. The precuneus is a feature of the default mode network which typically emits spontaneous fluctuations at rest which are then suppressed during goal-directed tasks (Greicius & Menon, 2004). Greater default mode network suppression is associated with greater task engagement (Liddle et al., 2011). Higher reward incentives have been found to motivate suppression of default mode network connectivity during task engagement among ADHD participants (Liddle et al., 2011). This indicates that remitted participants may require a higher incentive than controls to suppress the default mode network (Liddle et al., 2011).

Contrary to our hypotheses, remitters did not display significantly less neural activation and functional connectivity across decision-making networks relative to
control participants. Evidence of this lies within the reversal errors condition; reversal errors are errors in responding following a contingency reversal. Within this condition, there was greater functional connectivity between the DMPFC of the information integration network and the left precuneus for persisters compared with controls. This finding may highlight a failure to suppress task-inappropriate networks for persisters, as the precuneus is involved in non-goal-directed processes such as self-referential thought and mind-wandering (Castellanos et al., 2008).

The whole-brain GLM of neural activity analysis showed that the comparison of reversal errors with correct responses revealed significantly more activity in the left occipital lobe for remitters compared with persisters. Functional activity here represents a different measure as functional connectivity as activity represents the response of one brain region within the tasks active condition compared with a control condition, whereas connectivity shows how different brain regions interact during the task. Moreover, during functional connectivity, brain networks are examined, and thus, regions that are not belonging to brain networks under investigation cannot show a difference. This can be the case for the occipital lobe that is not part of our investigated brain networks. Increased occipital lobe activation is associated with memorizing visual information and processing value-related stimuli (Fassbender et al., 2011). This suggests that when confronted with negative feedback, remitters may have utilized a visual strategy to adapt to the task and attain positive feedback more so than persisters (Vaidya, 2012). There were no significant differences between remitters and persisters with respect to functional connectivity, most likely showing that while neural activity differs regionally the connectivity might functionally still be very similar. In particular, the increased connectivity for remitters is interesting, and
the connectivity of persisters seems to be increased as well but not to the extent that remitters have.

The results of this study must be considered in light of limitations. First, the course of the ADHD participants was not continuously monitored from childhood to adulthood, and thus, treatment characteristics had to be assessed retrospectively. As expected, ADHD participants were exposed to varying level of MPH across the life span, which may have contributed to some of the observed results. When excluding those ADHD participants who still took MPH currently, the results did not change. Second, although statistical effects for the remitted group were highly significant and survived correction for multiple testing, the sample size of 14 participants may inhibit the power of statistical effects and highlights the need for replication of remitted group findings in a larger sample.

Despite these limitations, findings are strengthened by the inclusion of a participant group with a childhood diagnosis of ADHD who were rigorously characterized as being either persistent or remitted participants. Also, findings are fortified by the application of a seed to whole-brain FWE-corrected functional connectivity analysis using meta-analytically defined ROIs. Finally, all statistics with the exception of two findings within the final reversal error condition would survive (p < .0014, FWE whole-brain correction) when comparisons between groups (remitters, controls, and persisters) are also considered.

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Table 1. Reversal Learning Task Participants Demographic Information.

<table>
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<tr>
<th>Characteristic</th>
<th>Persisters (n = 18)</th>
<th>Remitters (n = 14)</th>
<th>Controls (n = 32)</th>
<th>Statistic</th>
<th>p value</th>
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</thead>
<tbody>
<tr>
<td>Age (SD)</td>
<td>22.2 (3.9)</td>
<td>21.0 (2.4)</td>
<td>22.2 (6.1)</td>
<td>F = 0.291</td>
<td>.748</td>
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<tr>
<td>Gender (Male/Female)</td>
<td>16/2</td>
<td>11/3</td>
<td>27/5</td>
<td>(\chi^2 =)</td>
<td>.729</td>
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<tr>
<td>Handedness (R/L)</td>
<td>15/3</td>
<td>12/2</td>
<td>28/4</td>
<td>(\chi^2 =)</td>
<td>.920</td>
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<td>Education (SD)a</td>
<td>4.6 (0.6)</td>
<td>4.9 (0.6)</td>
<td>5.0 (0.8)</td>
<td>F = 1.73</td>
<td>.185</td>
</tr>
<tr>
<td>IQ (SD)</td>
<td>103.7 (9.0)</td>
<td>103.4 (17.0)</td>
<td>113.7 (11.9)</td>
<td>F = 4.6</td>
<td>.014</td>
</tr>
<tr>
<td>MPH duration (SD)</td>
<td>7.1 (6.1)</td>
<td>2.1 (2.2)</td>
<td></td>
<td>(t = 2.78)</td>
<td>.009</td>
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<td>CAARS O:L ADHD index T-score (SD)</td>
<td>65.4 (8.3)</td>
<td>46.7 (6.9)</td>
<td>43.1 (7.1)</td>
<td>F = 50.6</td>
<td>&lt;.001</td>
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<tr>
<td>CAARS O:L inattention T-score (SD)</td>
<td>67.4 (7.7)</td>
<td>51.3</td>
<td>45.5 (7.4)</td>
<td>F = 33.6</td>
<td>&lt;.001</td>
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<td>CAARS O:L hyperactivity/impulsivity T-score (SD)</td>
<td>66.1 (8.6)</td>
<td>48.7 (9.2)</td>
<td>42.5 (6.5)</td>
<td>F = 50.9</td>
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<tr>
<td>Measure</td>
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<td>Group 2</td>
<td>t-value</td>
<td>p-value</td>
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<tr>
<td>CPRS-R:S ADHD inattention T-score (SD)</td>
<td>73.5</td>
<td>71.7 (8.7)</td>
<td>0.445</td>
<td>.660</td>
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<tr>
<td>CPRS-R:S ADHD hyperactivity/impulsivity T-score (SD)</td>
<td>82.4</td>
<td>75 (11.8)</td>
<td>1.553</td>
<td>.134</td>
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<tr>
<td>CPRS-R:S ADHD index T-score (SD)</td>
<td>75.1 (8.9)</td>
<td>73.7 (9.4)</td>
<td>0.98</td>
<td>.74</td>
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<td>Hamilton Depression Inventory total score (SD)</td>
<td>4.29 (3.3)</td>
<td>1.57 (2.2)</td>
<td>0.47 (0.8)</td>
<td>18.7</td>
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<td>Beck Depression Inventory score (SD)</td>
<td>10.8 (1.7)</td>
<td>8.6 (1.9)</td>
<td>4.6 (1.2)</td>
<td>5.4</td>
<td>.007</td>
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<td>Current socioeconomic status (SD)</td>
<td>42.7 (2.6)</td>
<td>44.7 (3.0)</td>
<td>50.4 (1.9)</td>
<td>3.064</td>
<td>.054</td>
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</tbody>
</table>

Note. F value is derived from one-way ANOVA between groups; χ2 value is derived from chi-square test for independence with variables gender and handedness; T-score is derived from independent-samples t tests. L = left handed; R = right handed; MPH = methylphenidate, mean given in years; CAARS O:L = Conners’ Adult ADHD Observer Rating Scale; CPRS-R:S = Conners’ Parent Rating Scale-Revised: Short Version. **a**Number of years in education.
Table 2. Reversal Learning Task Behavioral Data.

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<th>Rewarded correct responses (SD)</th>
<th>Probabilistic error trials (SD)</th>
<th>Errors preceding final reversal errors (SD)</th>
<th>Final reversal errors (SD)</th>
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<tr>
<td>Persistent ADHD participants (n = 18)</td>
<td>38.3 (8.9)</td>
<td>15.7 (5.1)</td>
<td>9.3 (4.3)</td>
<td>3.2 (1.9)</td>
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<tr>
<td>Remitted ADHD participants (n = 14)</td>
<td>43.3 (5.5)</td>
<td>16.2 (3.8)</td>
<td>10.0 (4.2)</td>
<td>4.0 (1.9)</td>
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<td>Controls (n = 32)</td>
<td>44.3 (8.6)</td>
<td>17.0 (3.8)</td>
<td>8.7 (4.9)</td>
<td>4.8 (1.5)</td>
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<td>Statistic</td>
<td>$F = 3.1$</td>
<td>$F = 0.593$</td>
<td>$F = 0.423$</td>
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*Note. F value is from separate one-way ANOVAs.*
Table 3. Between Group Functional Connectivity Differences.

<table>
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<tr>
<th>Condition</th>
<th>Network</th>
<th>Group</th>
<th>Network — regions</th>
<th>FWE -Corr</th>
<th>K valu</th>
<th>t valu</th>
<th>x</th>
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Note. FWE-Corr = family-wise error corrected; K = value, voxel size; x, y, z = Montreal Neurological Institute coordinates for each significant region; OFC = orbitofrontal cortex.
Figure 1. Remitters displayed more functional connectivity between the left dorsomedial prefrontal cortex (DMPFC) and the left middle temporal lobe ($x = 58, y = −8, z = −8; t = 5$) than control participants during the final reversal error condition.
Note. Color bar represents the $t$ value. All results were $p < .005$, family-wise error corrected.
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Supplemental Material

The supplementary materials are available at http://jad.sagepub.com/ supplemental