The neurobehavioral mechanisms of motivational control in attention-deficit/hyperactivity disorder

Ahmet O. Ceceli, Joman Y. Natsheh, Daniel Cruz and Elizabeth Tricomi

A B S T R A C T

Attention-deficit/hyperactivity disorder (ADHD) poses debilitating impairments in the neurobehavioral systems governing reward-related processes—key to the control of motivated behaviors. Individuals with ADHD may rely on a motivational control system that favors cue-driven habits—rooted in the posterior putamen—over caudate and prefrontal cortex-driven goal-directed behaviors. We examined the neurobehavioral correlates of motivational control in ADHD. Twenty-five adults with ADHD and 25 neurotypicals underwent fMRI while training on two stimulus-outcome associations. A devaluation procedure followed, whereby they were selectively satiated on one of the snack outcomes, decreasing its value. A subsequent extinction test determined outcome-sensitivity (i.e., whether responses towards devalued snack diminished). Despite behavioral similarities, the ADHD group displayed a distinct neural signature marked by enhanced posterior putamen activation as a function of training. This region also displayed diminished functional connectivity with the dorsal anterior cingulate cortex, which is associated with top-down control. Our whole-brain analysis yielded ADHD-specific posterior putamen and opercular/insular cortex activity over the course of training—regions associated with stimulus-sensitivity and maladaptively rigid behaviors, respectively. Neural comparisons also identified hyper-recruitment of the hippocampus in the ADHD group. These results highlight corticostriatal discrepancies in ADHD, possibly serving as a biomarker of the disorder.
1. Introduction

Attention-deficit/hyperactivity disorder (ADHD) involves reward-related behavioral anomalies that significantly impair executive function and overall quality of life (Barkley, 1997; Castellanos & Tannock, 2002). ADHD is specifically associated with impaired reward learning (Johansen et al., 2009), difficulties adaptively processing rewards (Douglas & Parry, 1983; Luman, Oosterlaan, Knol, & Sergeant, 2008; Sethi, Voon, Critchley, Cercignani, & Harrison, 2018; Sluysken, Velling, Bunk, & Eggers, 2001), and heightened delay discounting (Antrop et al., 2006; Kessler, Adler, Barkley, et al., 2005; Kuntsi, Oosterlaan, & Stevenson, 2001; Marx, Höncke, Berger, Wandschneider, & Herpertz, 2013, 2010; Sonuga-Barke, Taylor, Semb, & Smith, 1992). The cardinal symptom of impulsivity is a well-documented contributor to maladaptive reward-related behavioral rigidities such as addictions (Cunill, Castells, Tobias, & Capella, 2015; Urcelay & Dalley, 2012). We posit that these reward-related abnormalities may also drive aberrances in the neurobehavioral mechanisms underlying the control of motivated behaviors (i.e., striking an adaptive balance between stimulus-driven habits and outcome-driven, goal-directed behaviors). Goal-directed behaviors are those executed towards valuable outcomes, and they track the value of the outcome tied to the action (e.g., checking your email app in response to the notification sound while awaiting an important message). In contrast, habits are reflexive, precipitated by salient stimuli, and inflexible, in that they are performed regardless of the value associated with the outcome (e.g., checking the email app in response to the notification sound while driving, despite the unsafe context).

A growing body of neurobiological evidence asserts that ADHD is also characterized by dysfunctions in the brain’s reward circuitry (Castellanos & Tannock, 2002). This network of cortical (e.g., anterior cingulate cortex; ACC; ventromedial prefrontal cortex; vmPFC, orbitofrontal cortex; OFC) and subcortical (e.g., striatum, amygdala, and hippocampus) brain regions regulates the process of experiencing rewarding outcomes, learning from rewards, and directing behaviors to maximize gains while minimizing losses (Daw, Gershman, Seymour, Dayan, & Dolan, 2011; Delgado, 2007; Galvan et al., 2005; Knutson, Fong, Adams, Varner, & Hommer, 2001). Compared to neurotypicals (NTs), individuals with ADHD exhibit irregularities in reward-related neural processing, such as decreased striatal signals during the anticipation of a rewarding outcome, and increased orbitofrontal cortex activation at reward receipt (Furukawa et al., 2014; Plchta et al., 2009; Plchta & Scheres, 2014; Scheres, Milham, Knutson, & Castellanos, 2007; Ströhle et al., 2008).

The compromised neural systems that regulate reward-related processes largely overlap with the corticostriatal circuits that also drive motivated behaviors. Motivated behaviors are posited to be controlled either by the pursuit of a desirable outcome, or triggered by an antecedent stimulus regardless of the outcome (i.e., deliberate and goal directed or reflexive and habitual) (Adams, 1982; Dickinson & Balleine, 1994). These components of motivational control have distinct neural representations. The dorsomedial portion of the striatum (i.e., caudate in humans) receives afferents from the prefrontal cortex to drive goal-directed behaviors that are performed in congruence with the value of a consequential reward (Tricomi, Delgado, & Fiez, 2004; Yin, Knowlton, et al., 2005; Yin, Ostlund, et al., 2005). The dorsolateral part of the striatum (i.e., putamen in humans) fosters connectivity with the motor cortex and the supplementary motor area, guiding cue-based habits that are triggered by salient, preceding stimuli, rather than by the value of contingent outcomes (Tricomi, Balleine, & O’Doherty, 2009; Yin, Knowlton, & Balleine, 2004, 2006). For instance, in the study by Tricomi and colleagues, participants from the general population exhibited heightened posterior putamen activity following extensive experience with stimulus–response–outcome (S–R–O) associations, suggesting that the posterior putamen region displays sensitivity to the strength of the S–R association (i.e., as behaviors become more stimulus-driven) (Tricomi et al., 2009). ADHD is associated with functional abnormalities in these key motivation-related regions. Attentional and motivational deficits in ADHD are correlated with disruptions in the dopaminergic reward pathways along the midbrain and striatum (Volkow et al., 2009, 2011). Importantly, ADHD is consistently associated with irregular fronto-striatal connectivity (Costa Dias et al., 2013; Rosch, Mostofsky, & Nebel, 2018; Tomasi & Volkow, 2012; von Rhein et al., 2017). Potentially, motivational control abnormalities in ADHD may present as heightened sensitivity to stimuli, making the posterior putamen and the prefrontal cortex candidate regions for aberrant signaling during associative learning and the strengthening of S–R–O associations. In support of this premise, recent investigations of a rat model of ADHD have reported habit-driven action control (i.e., persistent lever-press responses in pursuit of a devalued food) in the spontaneously hypertensive rat (SHR) strain that possesses ADHD-like symptoms (Natshel & Shiflett, 2015, 2018).

To examine the neural systems guiding habitual and goal-directed behaviors in ADHD, we administered a free-operant reward learning paradigm adapted from Tricomi et al. (2009) to individuals with ADHD and matched NTs who underwent functional MRI. In line with Tricomi et al.’s report of heightened posterior putamen engagement following extensive S–R training in the general population, we hypothesized that the ADHD group would exhibit habitual control following moderate, single-day S–R training, in that following devaluation, individuals with ADHD would diminish responses towards the still-valued snack, yet persist in responding to the stimulus associated with the devalued snack outcome. We hypothesized a more flexible control of action in NTs, in that they would maintain their responses towards the still-valued snack, and at the same time, diminish their responses towards the devalued snack. We interrogated an a priori posterior putamen region of interest (ROI) to reveal potential differences in neural processing following training, and hypothesized that the posterior putamen would display enhanced activation as a function of S–R training in the ADHD group compared to the NTs. We also used the posterior putamen as a seed region in a psychophysiological interaction (PPI) to detect potential abnormalities in corticostriatal connectivity in ADHD, which we hypothesized might be marked by diminished communication between the posterior putamen and the prefrontal cortex. Lastly, we employed a whole
brain analysis to further examine the neural signature of motivational control in ADHD following moderate S–R training, with the expectation that compared to NTs, the ADHD group would significantly recruit the a priori posterior putamen region that is used as a seed in the above analyses over the course of S–R training.

2. Materials and methods

We report how we determined our sample size, all data exclusions, all inclusion/exclusion criteria, whether inclusion/exclusion criteria were established prior to data analysis, all manipulations, and all measures in the study.

2.1. Participants

Study procedures were not pre-registered prior to the research being conducted. A meta-analysis of studies investigating brain function in ADHD reports the average sample size per study as 28, including ADHD and neurotypical (NT) groups (Lei et al., 2015). Due to the heterogeneity in ADHD symptom severity and presentation (American Psychiatric Association, 2013; Ramtekkar, Reiersen, Todorov, & Todd, 2010), we increased our sample size to the upper range of the reviewed studies. Following the recruitment criteria outlined below, 25 adults with ADHD and 25 NTs participated in the study (11 females and 14 males in each group; ADHD M_age = 22.32, SD_age = 4.69; NT M_age = 21.48, SD_age = 2.92, age range = 18–35). This sample size placed our study in the 95th percentile of studies reviewed in Lei et al. (2015). ADHD and NT groups were matched on age, gender, handedness, and working memory (WM) capacity (as described below in 2.2.2. Screening session). Participants were recruited via flyers posted in the Rutgers University-Newark area. Informed consent was obtained from all participants per the ethical principles outlined on the Declaration of Helsinki (Rickham, 1964), and experimental protocols were approved by the Rutgers University Institutional Review Board (IRB). Participants were remunerated $20 per hour of participation.

2.2. Study inclusion criteria

2.2.1. Pre-screening

Individuals interested in participating in the study were provided pre-screener questionnaires via email to determine eligibility using Qualtrics (http://www.qualtrics.com). MRI-safe individuals (i.e., those without claustrophobia or ferrous metal in or on their bodies) were invited to undergo an in-person screening session only if they confirmed the absence of the following exclusion criteria: (1) any neuropsychiatric illnesses for the NT group, and any neuropsychiatric illness other than ADHD for the ADHD group, (2) history of head injuries, (3) disqualifying psychoactive medication use (i.e., ADHD group: current or past use of non-ADHD medication with psychoactive properties such as antidepressants and anxiolytics; NT group: any current or past use of psychoactive medication), and due to the snacks to be consumed in the course of the experiment: (4) active dieting behaviors or concerns over body weight, and (5) reservations about consuming large amounts of chocolate and cheese crackers. Interested individuals who did not find eating either of the snacks to be consumed in the study pleasant were restricted from participation. Individuals previously diagnosed with ADHD less than 12 months prior to the interview session were also restricted from participating in the study, and they were not considered for the NT group. Exclusion criteria were determined prior to data analysis.

2.2.2. Screening session

All participants underwent a screening session comprising pen-and-paper questionnaires, standardized tests, and a semi-structured neuropsychiatric interview performed under the supervision of a clinician. The screening day lasted approximately 1.5 h.

To match the groups per the parameters noted above, we administered the Digit Span subtest of Wechsler's Adult Intelligence Scale (WAIS-IV; Wechsler, 2008)—a multi-trial alpha-numeric WM capacity measure. Independent samples t-tests were performed on composite Digit Span scores (derived from the sum score of Digits Forward, Backward, and Sequencing) to ascertain that there were no significant group differences in the matching parameters of age, t(48) = .76, p = .451, or WM capacity, t(48) = .40, p = .694. Additionally, measures assessing impulsivity via Barratt’s Impulsiveness Scale (BIS, Patton, Stanford, & Barratt, 1995), ADHD symptom severity via ADHD Self-Report Scale (ASRS; Kessler, Adler & Ames et al., 2005), and treatment history were collected. We used the composite scores from the BIS and ASRS scales to quantify impulsivity and symptom severity, respectively. The ADHD group scored significantly higher on measures of impulsivity, t(48) = 3.81, p < .001, and symptom severity, t(48) = 13.44, p < .001. We also matched participants on handedness; there were five left-handed participants in each group (see Table 1 for the sample profile).

Because most ADHD medications have a duration of action and half-life shorter than 12 h (Kolar et al., 2009), individuals with ADHD were instructed to refrain from medication use for at least 24 h prior to their scheduled screening session. Eighteen individuals with ADHD discontinued medication use for the study. Of the remaining participants in the ADHD group, four were previously medicated, and three were medication-naive. Stimulant medications used to treat ADHD among the sample, including both current and previous use, were as follows: amphetamines (n = 9), lisdexamfetamine (n = 4), methylphenidate (n = 2), methylphenidate and lisdexamfetamine (n = 1), methylphenidate and guanfacine (n = 1), amphetamines and lisdexamfetamine (n = 4), and amphetamines and methylphenidate (n = 1). Eight individuals with ADHD received some form of psychological therapy from a clinician; five of these individuals underwent cognitive-behavioral therapy treatment. The NT group reported no history of medication use or psychological therapy.

All participants underwent a neuropsychiatric interview conducted using the Mini International Neuropsychiatric Interview 6.0 (MINI) and the MINI Plus: Adult ADHD module (Sheehan et al., 1998), which assess individuals based on guidelines from the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV). We followed the diagnostic procedures from the MINI Plus: Adult ADHD module to confirm
ADHD diagnoses in the ADHD group, and to rule the same diagnosis in the NT group. We used the MINI 6.0 to rule out non-ADHD psychiatric disorders in the ADHD group, and all major psychiatric disorders in the NT group (Sheehan et al., 1998). Per these criteria, a childhood onset of ADHD symptomology was required to confirm the ADHD diagnosis. The psychiatric illnesses that served as exclusion criteria are as follows: major depressive disorder, manic-depressive disorder, generalized anxiety disorder, agoraphobia, social phobia, obsessive-compulsive disorder, post-traumatic stress disorder, alcohol and substance dependence/abuse, psychotic disorders, mood disorders with psychotic features, anorexia nervosa, bulimia nervosa, and antisocial personality disorder. Participants were cleared for the MRI scan only if they were deemed free of psychiatric illness per MINI 6.0 criteria, and if they were in the ADHD group, above the clinical threshold of ADHD manifestation per the MINI 6.0 Plus: ADHD module criteria. Due to the snacks to be provided during the fMRI scan session, the Eating Attitudes Test 26 (EAT-26; Garner, Olmsted, Garfinkel, 1982) was administered to screen maladaptive eating attitudes predictive of heightened risk for eating disorders. Participants with an EAT-26 score of 20 or above were excluded from the remainder of the study. Please see the Supplement for number of individuals excluded and the reasons for exclusion.

### 2.3. MRI scan session

Following the screening session, qualifying participants were scheduled for the fMRI scan. Participants were instructed to fast for at least 4 h prior to the scan session to increase the desirability of the snacks to be used as rewards throughout the study. Although participants with ADHD were instructed to refrain from taking ADHD medication for at least 24 h before the screening session, for the MRI session, we chose to increase this medication-free period to 36 h to prevent any acute effects on brain function that may remain beyond the 24-h window. The MRI session lasted approximately 2.5 h. Participants spent from 60 to 75 min inside the MRI scanner.

### 2.4. Experimental paradigm

E-prime (Psychology Software Tools, Pittsburgh, PA) was used for stimulus presentation and response collection. Prior to entering the MRI scanner, we collected subjective pleasantness ratings for each snack to be used during the free-operant task. Specifically, because the task involved rewarding actions with M&M (Mars, McLean, VA) and Goldfish cracker (Pepperidge Farm, Norwalk, CT) outcomes, participants were asked how pleasant they would find eating an M&M and a Goldfish cracker on a scale of 0 (least pleasant) to 5 (most pleasant).

Next, after completing a brief practice session outside of the scanner, participants underwent a free-operant task with food rewards during fMRI, similar to Tricomi et al. (2009). In this paradigm, two “task” fractals predicted differential snack outcomes contingent on button press responses, such that index and middle finger button presses produced either M&M or Goldfish images to indicate an earned snack. A third fractal was used to indicate unrewarded rest trials, for which participants refrained from making any response. Specifically, participants were informed that fractal images would be presented throughout the experiment, and a schematic above each fractal would indicate which button was activated for response collection for that fractal. Participants were instructed that during each trial in which a fractal was presented with an active button, they could respond via button presses as often as desired to earn the associated snacks, and that they should pay attention to the fractal—button—snack associations. Participants did not consume the snacks during the scan; rather, they were informed that a proportion of the earnings would be consumed following the completion of the scan. Each active button response produced either a gray circle (50 ms) to indicate that a response was registered but not rewarded, or a snack image corresponding to the snack earned (1 sec) below the fractal. Rewards were administered on a random interval reinforcement schedule (RI-10), meaning each second, a participant had a .1 probability of earning a reward following a button press. Thus, a reward became available on average every 10 sec, and was collected upon the first response executed by the participant following its availability (see Fig. 1 for task structure). This RI reinforcement schedule has been shown to be conducive to developing outcome-insensitivity when compared to fixed or variable-ratio reward delivery (Baum, 1993; Knowlton & Patterson, 2018). The fractal—button and button—snack associations were counterbalanced across participants. The responses towards task fractals were self-paced, and fractal onset and offset indicated the start and end of each trial. Twelve task (six of each fractal, randomly varying durations of 20, 30, or 40 sec) and eight rest trials (20 sec) comprised each 8-min run. Participants underwent a moderate amount of training (six runs) and were then taken out of the MRI scanner for the outcome-devaluation procedure. We identified our six run, 48 min training period as moderate relative to the under-trained (two runs equaling 16 min) and over-trained (12 runs equaling 96 min) groups that underwent the same free-operant task in Tricomi et al. (2009). Other paradigms that incorporate outcome-devaluation have also identified moderate training conditions as being important in the development of outcome devaluation.

### Table 1 – Study sample profile.

<table>
<thead>
<tr>
<th></th>
<th>ADHD (n = 25)</th>
<th>NT (n = 25)</th>
<th>sig.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (SD)</td>
<td>22.32 (4.69)</td>
<td>21.48 (2.92)</td>
<td>p = .451</td>
</tr>
<tr>
<td>Sex</td>
<td>F = 11, M = 14</td>
<td>F = 11, M = 14</td>
<td>individually matched</td>
</tr>
<tr>
<td>Handedness</td>
<td>R = 20, L = 5</td>
<td>R = 20, L = 5</td>
<td>individually matched</td>
</tr>
<tr>
<td>Working Memory: Digit Span (SD)</td>
<td>28.16 (3.86)</td>
<td>27.60 (5.93)</td>
<td>p = .694</td>
</tr>
<tr>
<td>Impulsivity: BIS (SD)</td>
<td>75.92 (5.89)</td>
<td>69.40 (6.19)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Symptom Severity: ASRS (SD)</td>
<td>45.76 (9.01)</td>
<td>14.24 (7.51)</td>
<td>&lt;.001</td>
</tr>
</tbody>
</table>

Note: ADHD diagnoses in the ADHD group, and to rule the same diagnosis in the NT group. We used the MINI 6.0 to rule out non-ADHD psychiatric disorders in the ADHD group, and all major psychiatric disorders in the NT group (Sheehan et al., 1998). Per these criteria, a childhood onset of ADHD symptomology was required to confirm the ADHD diagnosis. The psychiatric illnesses that served as exclusion criteria are as follows: major depressive disorder, manic-depressive disorder, generalized anxiety disorder, agoraphobia, social phobia, obsessive-compulsive disorder, post-traumatic stress disorder, alcohol and substance dependence/abuse, psychotic disorders, mood disorders with psychotic features, anorexia nervosa, bulimia nervosa, and antisocial personality disorder. Participants were cleared for the MRI scan only if they were deemed free of psychiatric illness per MINI 6.0 criteria, and if they were in the ADHD group, above the clinical threshold of ADHD manifestation per the MINI 6.0 Plus: ADHD module criteria. Due to the snacks to be provided during the fMRI scan session, the Eating Attitudes Test 26 (EAT-26; Garner, Olmsted, Bohr, & Garfinkel, 1982) was administered to screen maladaptive eating attitudes predictive of heightened risk for eating disorders. Participants with an EAT-26 score of 20 or above were excluded from the remainder of the study. Please see the Supplement for number of individuals excluded and the reasons for exclusion.
We chose to administer moderate S-R training, because we reasoned that the critical comparison point between ADHD and NT groups is when NTs potentially exhibit the most variability in motivational control processes. This would allow us to investigate whether ADHD may tip that scale towards stimulus-sensitivity.

Once out of the scanner, snack earnings accumulated throughout the task were given to participants at a ratio of 4 images to 1 snack to prevent satiety (snack consumption in grams: $M_{\text{ADHD}} = 29.28$, $SD_{\text{ADHD}} = 5.63$, $M_{\text{NT}} = 26.12$, $SD_{\text{NT}} = 4.58$). Next, in the devaluation stage, one of the snack outcomes was made available to the participant until it was no longer pleasant, effectively diminishing its value. Specifically, the participant was instructed to consume the snack until it was no longer pleasant. The experimenter remained in the room with the participant during the devaluation procedure. The snack chosen for selective satiety was counterbalanced across participants. Post-devaluation subjective ratings of snack pleasantness were collected to ensure that the now-devalued snack outcome was perceived as less valuable compared to the pre-training ratings. The experimenter offered more of the snack to the participant if these ratings did not decrease from their pre-training responses, but participants were not forced to consume more snacks to proceed with the study (snack consumption in grams: $M_{\text{ADHD}} = 81.36$, $SD_{\text{ADHD}} = 36.41$, $M_{\text{NT}} = 88.64$, $SD_{\text{NT}} = 39.30$). Following devaluation, participants re-entered the fMRI context and underwent an identical free-operant task, but unbeknownst to them, the trials were no longer rewarded. This 3-min extinction phase (20-sec valued, devalued, and rest fractals presented three times) allowed us to determine whether button presses were outcome-sensitive. For instance, diminished button press responses to the fractal associated with the now-devalued snack would indicate outcome-driven behavior, as the participant’s response rate slows down in accordance with the outcome value. In contrast, a persistent response rate to the stimulus predictive of the devalued snack would indicate stimulus-driven performance, as the participant responds at a similar rate regardless of snack value. The extinction test should provide a snapshot of previously formed associations in the training stage, without any influence of new reward delivery, hence our decision to test for habits in extinction (i.e., in absence of reward) (Balleine & Dickinson, 1998; Tricomi et al., 2009). Extinction took place during fMRI to provide similar training and testing contexts.

2.5. FMRI data acquisition

A 3 T Siemens Trio (Erlangen, Germany) MRI scanner with a 12-channel phased array coil was used to acquire structural and functional brain images at the Rutgers University Brain Imaging Center (RUBIC). High-resolution T1-weighted structural images at isotropic 1 mm voxel dimensions were obtained using a Magnetization Prepared Rapid Gradient Echo (MPRAGE) sequence. Forty-one T2*-weighted echo-planar image slices were obtained for blood oxygenation level dependent (BOLD) signal analyses using the following parameters in an interleaved order of acquisition: 3 mm isotropic voxels, TR: 2500 ms TE: 30 ms, field of view: 192 mm × 192 mm, flip angle: 90°. We acquired brain images at a 30° oblique orientation to the anterior commissure – posterior commissure axis to improve signal-to-noise ratio.
particularly in the ventral prefrontal cortex region that is most susceptible to signal dropout (Deichmann, Gottfried, Hutton, & Turner, 2003).

2.6. Behavioral data analysis

Data analysis procedures were not pre-registered prior to the research being conducted. To determine whether ADHD and NT groups exhibited differential motivational control in response to outcome devaluation, we performed a mixed-design ANOVA with the dependent variable (DV) as the change in response rate ($\Delta$Response_Rate) between training and extinction (extinction minus training responses per second), Stimulus Value (valued, devalued) as a within-subjects, and Group (ADHD, NT) as a between-subjects factor. Shapiro–Wilk tests indicated normally distributed DVs in both groups (all ps > .12). Post-hoc t-tests were used to confirm whether $\Delta$Response_Rate to valued and devalued stimuli were significantly different in each group. Pleasantness rating comparisons between pre-training and post-extinction stages were performed using paired-samples t-tests to ensure that the outcome-devaluation procedure was successful in diminishing the subjective value of the devalued snack. We also explored potential differences in response rate patterns over the course of training across groups via a mixed-design ANOVA. We used the global response rate (i.e., a combination of responses to both task fractals) as DV, Group (ADHD, NT) as the between-subjects and Time (bins of early, middle, and late stages) as within-subjects factors. We assessed global response rate, because during training, there should be no difference in value across the two snacks, rendering the valued and devalued snack differentiation trivial. This exploratory analysis aimed to confirm that the potential stimulus-sensitivity related neural results could not be attributed to group differences in motor output.

Although we matched ADHD and NT groups on a variety of individual difference measures (i.e., demographics and WM capacity), we also aimed to examine our sample’s diagnostic profile for potentially relevant factors. We had a specific interest in impulsivity, as it is a cardinal symptom of ADHD, and it has been previously linked to behavioral inflexibilities such as those that give rise to addiction (Urcelay & Dalley, 2012). We performed a multiple regression analysis with Devalued_$\Delta$Response_Rate as an index of behavioral flexibility. We used symptom severity scores obtained via the ASRS survey, impulsivity scores via BIS, WM capacity via Digit Span, and treatment history as indexed by years of medication use as regressors to detect relationships with devaluation-related changes in response rate to the devalued cue (Devalued_$\Delta$Response_Rate) in the ADHD group. A similar model using only the Symptom, Impulsivity, and WM capacity variables as regressors were used with NT data to determine whether subspecial ADHD symptom severity, impulsivity, and WM capacity predicts behavioral flexibility in the NT sample. This analysis served as an exploration of individual variability within our sample, and these variables’ potential links to motivational control. Specifically, we hypothesized that in both groups, ADHD symptomology and impulsivity would be negatively correlated, and WM capacity would be positively correlated with behavioral flexibility (Otto, Skatova, Madlon-Kay, & Daw, 2015). In the ADHD group, we hypothesized that medication history would have a protective effect on motivational control, manifesting as a positive correlation with behavioral flexibility.

2.7. FMRI data analysis

We used FSL (version 5.0; http://www.fmrib.ox.ac.uk/fsl) for fMRI data pre-processing and analysis. We skull-stripped brain images to eliminate non-brain matter from analyses and employed FMRIB’s Linear Image Registration Tool (FLIRT) to spatially transform our functional and structural images to the Montreal Neurological Institute (MNI) template (Jenkinson & Smith, 2001). We accounted for head movement via FSL’s MCFLIRT (Jenkinson, Bannister, Brady, & Smith, 2002; Jenkinson & Smith, 2001) and extracted six motion parameters to be included as regressors of no interest in the general linear model (GLM). Additionally, we identified volumes that showed spikes in translation and rotation parameters when compared to a reference volume. These outliers were determined by a typical boxplot threshold (75th percentile + 1.5 x interquartile range) using fsl_motion_outliers and regressed out in the GLM. This algorithm removed an average of 5.8% of the volumes in each run (range: 1%–16.7%). Following this outlier removal procedure, no substantial volume-to-volume movement remained, in that maximum displacement was below the voxel dimensions (mean motion: .33 mm; maximum motion: 1.26 mm). Importantly, neither the number of spikes in movement, t(295) = .52, p = .600, nor the volume-to-volume displacement, t(48) = .64, p = .525, was significantly different across ADHD and NT groups. The BOLD data we acquired in an interleaved order were slice-time corrected and spatially smoothed using a 5 mm full width at half maximum Gaussian smoothing kernel, and a high-pass filter cutoff of 100 sec was applied to ignore extraneous signal due to scanner drift. Three runs (ADHD = 2, NT = 1) were discarded due to data corruption, and the GLM was altered accordingly for these participants’ analyses. These three runs were in the middle of their respective scan sessions, such that the analyses aimed at deriving late and early S–R activation estimates were unaffected.

We generated parameter estimates from the pre-processed data for each participant using a GLM approach. “Task” onset and “rest” onset were captured via 1-sec events at each trial, and a “reward” regressor was captured as a 1-sec event at reward receipt. We chose to model 1-sec stick functions at onset, as we reasoned that these time windows may best capture the BOLD signal associated with stimulus-sensitivity. This is also a practice with precedence in the literature (Morris, Quail, Griffiths, Green, & Balleine, 2015; Tricomi et al., 2009). We did not include extinction scan data in the GLM, as these brief scans do not provide sufficient power for fMRI data analysis. Therefore, all analyses of neural data inform processes involved in moderate S–R learning, but not devaluation or extinction. These task, rest, and reward regressors, their temporal derivatives, along with the six motion parameters and motion outlier timeseries were convolved with a canonical hemodynamic response function (HRF). Linear contrasts of task versus rest onset were computed in each run to selectively determine stimulus-evoked activation patterns.
Each participant’s first-level parameter estimates were entered into a fixed-effects model to generate participant-level ‘early’, ‘mid’, and ‘late’ regressors (two runs in each bin, denoting the stage of S–R learning during the free-operant task. These learning phase regressors were parametrically weighted (−1, 0, 1 as early, mid, and late) and used in the group-level region of interest (ROI), psychophysiological interaction (PPI), and whole-brain analyses outlined below. To explore reward receipt-related signaling, we derived an average of the reward receipt event across all runs in each subject.

2.7.1. ROI analysis: posterior putamen and stimulus-sensitivity

Due to the strong a priori hypothesis centered on the role of the posterior putamen in driving stimulus-sensitivity, we created 5 mm radius spherical anatomical masks of left and right putamen (±33, −24, 0) using MNI coordinates obtained from a previous study employing the same free-operant task (Tricomi et al., 2009). We extracted percent signal change values from this posterior putamen seed region in each participant’s early, mid, and late stage, task versus rest contrast image using FSL’s Featquery tool. We performed a repeated measures ANOVA using Time (early, mid, late) as a within-subjects, and Group (ADHD, NT) as a between-subjects factor to detect posterior putamen activation differences across groups as a function of training length (i.e., a Group × Time interaction). Given the incremental recruitment of the posterior putamen over the course of extended S–R training in the general population (Tricomi et al., 2009), a similar pattern over moderate training in the ADHD group would suggest an accelerated recruitment of this region closely associated with stimulus-sensitivity.

To further examine our sample’s diagnostic profile in the context of stimulus-sensitivity-related neural signaling, we also performed a multiple regression analysis to reveal potential associations between treatment history, ADHD symptom severity, impulsivity, and WM capacity on posterior–putamen activity in each group. The regressors Medication, Symptom, Impulsivity, and WM capacity were used to predict percent signal change in the posterior putamen ROI over the course of training in the ADHD group. The regression was repeated for the NT group without the inclusion of the Medication variable. This set of analyses served as an exploration of individual variability within our sample, and these variables’ potential links to motivational control-related striatal signaling.

2.7.2. Psychophysiological interaction: posterior putamen functional connectivity

In a PPI analysis, we used our a priori posterior putamen region as a seed to identify target brain areas that exhibited functional connectivity as a result of moderate S–R training (Friston et al., 1997). This approach permitted us to assess whether corticostratial discrepancies across ADHD and NT groups exist over the course of moderate S–R learning. We concatenated our task and rest regressors into a single time course, weighted task as 1 and rest as −1 to create a “psychological” regressor which was convolved with an HRF. We also included this regressor’s temporal derivative in the GLM. Next, we extracted timeseries information from our anatomically extracted 5 mm radius left posterior putamen mask, which was transformed into each participant’s functional space, to create a “physiological” regressor. Using these two regressors, we derived a “PPI” (i.e., interaction of psychological and physiological time courses) regressor in our design matrix. Lastly, we also included in our PPI GLM regressors representing all other events throughout the fMRI scan: an HRF-convolved regressor that weighed the task and rest events equally (i.e., as they would be represented in the whole-brain GLM), an HRF-convolved reward regressor for reward receipt events, and motion outlier parameters. This method allowed us to estimate target brain regions that exhibited task-based coupling with the posterior putamen seed, while ruling out regions that may evoke continuous, non-task-specific coupling, such as anatomical connectivity (O’Reilly, Woolrich, Behrens, Smith, & Johansen-Berg, 2012).

The second-level analysis, as outlined in the fMRI data analysis section above, aggregated the first two runs to derive “early”, the middle two runs to derive “mid”, and the last two runs to derive “late” run regressors at the participant level. We assigned parametric weights to these regressors (−1, 0, 1), and performed linear contrasts of the resulting statistical maps to calculate late versus early activation patterns in each participant. For the group-level estimation of moderate S–R learning-related functional connectivity (ADHD versus NT group contrast), we entered these maps into a mixed-effects model using FLAME 1 & 2 (FMRIB’s Local Analysis of Mixed Effects), which performs Markov Chain Monte Carlo simulations to improve variance estimation and permit population inferences (Beckmann, Jenkinson, & Smith, 2003).

We employed a cluster defining threshold of p < .005, corrected to a cluster extent threshold of p < .05, which requires more than 207 contiguous voxels (a volume of at least 1,655 mm³ in the transformed data) to constitute a significant cluster.

2.7.3. Whole-brain GLM

To identify brain regions involved in moderate S–R training in ADHD, we derived parametrically weighted early, mid, and late training phase activation maps from each participant and entered them into a mixed-effects model using FLAME 1 & 2, with a cluster defining threshold of p < .005, corrected to a cluster extent threshold of p < .05, which requires more than 302 contiguous voxels (a volume of at least 2,416 mm³ in the transformed data) to constitute a significant cluster. These stimulus-driven statistical maps denoted which brain regions were significantly active over the course of moderate S–R learning, and allowed for ADHD versus NT contrasts for group-level comparisons to elucidate potential differences in the ADHD brain. Lastly, we calculated an average of the BOLD response to reward delivery across all runs in each subject to ensure that the reward indicators (i.e., the appearance of the earned snack image) in our task reliably activated regions in the brain’s reward circuitry, such as the striatum and the vmPFC. We further explored reward delivery via a group comparison to potentially reveal whether ADHD is associated with heightened sensitivity to reward receipt. We used the same whole-brain analysis parameters as above to perform these data explorations and report the findings in the supplement.
2.8. Data availability

The data that support the findings of this study (i.e., the unthresholded statistical maps of whole-brain and PPI analyses) are openly available in the repository NeuroVault, at https://neurovault.org/collections/5312/, reference number 5312 (Gorgolewski et al., 2015). The script used in experiment presentation is openly available in the Open Science Framework repository, at https://osf.io/6kw72. Participant level data are available upon request to the corresponding author via email, and approval of the request by the IRB. These participant-level data are not available in a public repository due to IRB restrictions regarding confidentiality.

3. Results

3.1. Behavioral results

We did not find a significant difference in outcome-sensitivity across ADHD and NT groups. The mixed-design ANOVA of ΔResponse_Rate revealed no main effect of Group, F(1,48) = .24, p = .629, h_p^2 < .01, a main effect of Stimulus Value, F(1,48) = 10.76, p = .002, h_p^2 = .06, and no Group × Stimulus Value interaction, F(1,48) = .02, p = .876, h_p^2 < .01, suggesting that the ADHD and NT groups did not differ in devaluation sensitivity and both performed in a goal-directed manner (see Fig. 2). Pre-versus post-devaluation comparison of pleasantness ratings confirmed that across all participants, the devaluation procedure successfully diminished the subjective value of the devalued snack, t(49) = 16.60, p < .001 (see Supplementary Fig. 1 for a depiction of pleasantness ratings). We also examined global response rates over the course of training (responses to a combination of both task fractals in early, middle, and late stages of training) and found that groups did not differ in response patterns throughout training (Group × Time interaction F(2,96) = .89, p = .415, see Supplementary Fig. 2). Thus, the neural results below cannot be attributed to motor output differences during training across groups.

We performed a multiple regression analysis in the ADHD group data, using the variables Symptom, Impulsivity, WM capacity, and Medication to predict the participant-level measure of outcome sensitivity, Devalued_ΔResponse_Rate. We had a specific interest in the impulsivity variable, given its defining role in hyperactivity and association with maladaptive behavioral rigidities (Urcelay & Dalley, 2012). None of these regressors significantly predicted outcome-sensitivity as assessed by Devalued_ΔResponse_Rate (all p-values > .291). Similarly, when this regression analysis was repeated in the NT group data to detect individual differences in sub-clinical ADHD symptom severity, impulsivity, and WM capacity, no regressor significantly predicted outcome-sensitivity (all p-values > .161). Although we did not find a link between impulsivity and response rate, these results suggest that individual variability in our sample’s diagnostic profile did not significantly contribute to behavioral flexibility.

3.2. FMRI results

3.2.1. ROI analysis: posterior putamen and stimulus-sensitivity

The posterior putamen has been shown to play a role in stimulus-sensitivity in the general population over extended (i.e., 3-day) S–R training (Tricomi et al., 2009). Specifically, in that study, participants who had undergone extended training exhibited higher posterior putamen activation. In our study, we administered moderate, single day training, and tested whether ADHD is associated with an accelerated recruitment of the posterior putamen via a mixed-design ANOVA. We extracted BOLD data from a posterior putamen mask (Fig. 3A) and used the percent signal change as DV, Group as a

Fig. 2 – Response rate pre-devaluation (Training) and post-devaluation (Extinction). ADHD and NT groups exhibit similar sensitivity to outcome value. Behavioral similarities here suggest that both groups maintained goal-directed control (i.e., diminished responses to the devalued stimulus at extinction). Error bars depict standard error of the mean. Swarm plot points represent data from individual subjects.
between-subjects, and Time as a within-subjects factor. In the left posterior putamen, we found no main effect of Group, $F(1,48) = .20$, $p = .657$, $\eta^2_p < .01$, no main effect of Time, $F(2,96) = .73$, $p = .482$, $\eta^2_p = .01$, but a significant Group $\times$ Time interaction, $F(2,96) = 5.35$, $p = .006$, $\eta^2_p = .10$ (Fig. 3B), suggesting that the ADHD group exhibits heightened posterior putamen activity as a function of training length. In the right posterior putamen, we did not find a significant main effect of Group, $F(1,48) = .25$, $p = .618$, $\eta^2_p < .01$, no main effect of Time, $F(2,96) = .11$, $p = .897$, $\eta^2_p < .01$, and no significant Group $\times$ Time interaction, $F(2,96) = 1.38$, $p = .257$, $\eta^2_p = .03$ (Fig. 3C). Please see Supplemental Fig. 3 for a more detailed depiction of these results (e.g., task and rest signal change displayed separately).

We performed a multiple regression using the late versus early contrast percent signal change derived from the parametrically weighed S–R training parameters (−1, 0, 1, as early, mid, late). We used this left posterior putamen ROI signal change as DV, and individual difference measures of medication history, symptom severity, impulsivity, and WM capacity as regressors. In the ADHD group, we found no associations between any of these regressors and the percent signal change extracted from our left posterior putamen ROI (all $p$-values > .452). Similarly in the NT group, we found no associations between these regressors and left posterior putamen activity following moderate S–R training (all $p$-values > .207). These results suggest that posterior putamen activation over the course of S–R training was not affected by individual variability in our sample’s diagnostic profile.

3.2.2. Psychophysiological interaction: posterior putamen functional connectivity

Considering the reward circuitry irregularities in ADHD (Castellanos & Tannock, 2002), we hypothesized that corticostriatal communication may be impaired during associative learning in the ADHD group. We performed a PPI analysis using our left posterior putamen ROI as a seed and searched for areas that exhibited significant task-related coupling. We found that over the course of moderate S–R training, the posterior putamen fostered diminishing functional connectivity with the prefrontal cortex in the ADHD group when compared to the NT; namely in the dorsal anterior cingulate cortex (dACC) and in the medial prefrontal cortex (mPFC; see Fig. 4). For the specific coordinates of clusters and local maxima associated with the PPI, see Supplementary Table 1.

3.2.3. Whole-brain GLM

We performed a whole-brain analysis using the GLM approach to identify regions that drive stimulus-sensitivity following moderate S–R learning in ADHD. Specifically, we calculated a linear contrast of task versus rest onset to extract stimulus-sensitivity-related activity, then parametrically weighed the early, mid, and late stages of training (as −1, 0, 1, respectively) to examine stimulus-sensitivity over the course of moderate S–R learning. Lastly, we performed a group-level contrast of ADHD versus NT group to distinguish ADHD-specific stimulus-sensitivity-related brain activity following learning (see Fig. 5). We found significant clusters in the posterior putamen, opercular/insular cortex, and the hippocampus that selectively activated in the ADHD group. The posterior putamen region that survived our thresholding parameters overlaps with our a priori ROI, which was based on Tricomi et al. (2009). For the specific coordinates of clusters and local maxima associated with the whole-brain analysis, see Supplementary Table 1. Our exploration of reward receipt produced no group differences, in that the ADHD > NT contrast did not yield significant clusters at reward delivery; however, when the groups were examined separately, they showed striatal and orbitofrontal cortex activity in response to the reward indicator images, suggesting that our task elicited reliable reward responses in both groups (please see Supplementary Fig. 4 and Supplementary Table 2).

4. Discussion

We investigated the neural signature of motivational control in ADHD by moderately training S–R associations during fMRI. This approach allowed us to identify corticostrial...
abnormalities associated with the stimulus- and outcome-driven control of action in ADHD, interrogating the neural mechanisms underlying motivation-related processes. Namely, despite the intact goal-directed control following moderate S–R training in ADHD (i.e., the behavioral similarities across groups in response rate), we found an early recruitment of a striatal sub-region that has been associated with tracking stimulus-sensitivity and the dACC/mPFC (in warm colors) over the course of S–R learning. These prefrontal areas are known to be involved in error detection, reward value tracking, and goal-directed control. Findings also revealed the posterior putamen’s deficient connectivity with the prefrontal cortex in our analysis. Contrast values are derived from a 3 mm mask of peak activation (MNI coordinates: 8, 50, 16).

Fig. 4 – PPI analysis reveals corticostrial connectivity differences in ADHD. A: We found diminished task-onset-related functional connectivity between the posterior putamen seed (in blue)—a striatal region that’s been associated with tracking stimulus-sensitivity—and the dACC/mPFC (in warm colors) over the course of S–R learning. These prefrontal areas are known to be involved in error detection, reward value tracking, and goal-directed control. B: Peak voxels from this PPI analysis show decreased strength in corticostrial connectivity in the ADHD group compared to NTs. Contrast depicted: task versus rest onset, late versus early phase; early, mid, and late training phases weighed as parametric regressors [-1 0 1]. Contrast values are derived from a 3 mm mask of peak activation (MNI coordinates: 8, 50, 16).

Fig. 5 – Whole brain analysis of cue-sensitivity over the course of moderate S–R learning in ADHD. Significant clusters in the posterior putamen, opercular/insular cortex, and the hippocampus survived our group-level comparisons of training-related cue-sensitivity activity. Clusters were defined using a Z-threshold > 2.58 (p < .005), corrected to the cluster extent threshold of p < .05. Numbers above brain slices indicate MNI coordinates. Post. Put: posterior putamen, Operc: operculum, Hipp: hippocampus.

abnormalities associated with the stimulus- and outcome-driven control of action in ADHD, interrogating the neural mechanisms underlying motivation-related processes. Namely, despite the intact goal-directed control following moderate S–R training in ADHD (i.e., the behavioral similarities across groups in response rate), we found an early recruitment of a striatal sub-region that has been associated with the execution of stimulus-sensitive behaviors (i.e., posterior putamen). Findings also revealed the posterior putamen’s deficient connectivity with the prefrontal cortex in our analysis.
ADHD sample. Additionally, we report hippocampal recruitment over the course of training in ADHD compared to NTs, and reliable reward receipt-related signaling in both groups, albeit no group differences in response to this reward delivery.

In the general population, the posterior putamen has been reported to show increased activation following over-training in a similar reward-learning paradigm (Tricomi et al., 2009). Here, we show that an early recruitment of this posterior putamen region is evident in ADHD. The neural signature found in the ADHD group following a single-day's exposure to the S–R–O associations is similar to the over-trained participants in the report by Tricomi et al. (2009). It should be noted that the NT group in our cohort does not show a significant increase in posterior putamen activity, whereas the sample in Tricomi et al. (2009) displayed heightened putamen recruitment following extended training. This discrepancy between our data and those reported in Tricomi et al. (2009) could be due to the shorter training duration (our cohort underwent 48 min of training over the course of a single day, as opposed to 96 min over the course of 3 days), or because participants recruited from the general population in Tricomi et al. (2009) were not screened for medication use or the presence of any psychiatric disorders, while our NT sample was thoroughly screened and matched to the ADHD group in demographic and cognitive variables. Heightened recruitment of the left posterior putamen in the ADHD group may be due to ADHD being associated with an early onset of stimulus-sensitivity-related neural signaling, whereas this process may come online only with more S–R training in the general population. As expected, our ROI analysis results indicated greater variability in the posterior putamen BOLD response in NTs. This may also be attributed to abbreviated training length and the sample profile. Whereas with overtraining in Tricomi et al. (2009), participants displayed heightened posterior putamen recruitment, moderate training in our study may have evoked posterior putamen activity in a more variable manner in NTs (e.g., some participants display this neural signature of stimulus-sensitivity earlier or later than others).

Our devaluation procedure resulted in comparable sensitivity to the value of the outcome in both groups, suggesting the maintenance of goal-directed control across the board. Although moderately training novel S–R–O associations was effective in identifying atypical brain function during reward learning, these behavioral similarities suggest that a direct investigation of habitual control in ADHD may require prolonged S–R training, or tasks that capture well-learned habits that do not rely on the traditional measures of devaluation sensitivity (Ceceli, Myers, & Tricomi, 2019, preprint). For example, an investigation well-learned habit expression has found a modest link between ADHD symptomology and degree of habitual control; however, this study examined symptom severity from the general population (Ceceli, Esposito, et al., 2019). Alternatively, due to the delayed maturation of cortical regions associated with cognitive control in ADHD (Shaw et al., 2007), and the gradual emergence of goal-directed control over the course of development in the general population (Decker, Otto, Daw, & Hartley, 2016), a developmental perspective on motivational control in ADHD may reveal a habit-dominated system. Nonetheless, the neural findings reported in this study do not depend on devaluation or the extinction test, as we focused on the neural signature of moderate S–R learning during the training phase. Any heterogeneity in participants' behavioral sensitivity to devaluation is independent from the late stage training—the period of interest for neural calculations of associative learning strength. The corticostriatal abnormalities reported here are evident when the S–R–O associations in both groups should have moderately strengthened in late training.

Although our study is the first to probe the brain systems underling motivational control in ADHD, there exists investigations of ADHD in rodents and humans that examine processes that may be related to behavioral rigidity. For instance, the SHR strain, often used as a rat model of ADHD, has been reported to express higher rates of lever pressing during training and extinction under operant reinforcement schedules (Sagvolden, Pettersen, & Larsen, 1993). The same rat model has also been shown to express outcome-insensitive lever press responses (Natsheh & Shiflett, 2015). These response rate differences throughout training and extinction are not clearly evident in human studies of ADHD. In the current study, we did not find response rate differences during training or extinction in adults with ADHD compared to NTs. Laboni and colleagues have reported similar response rates in children with ADHD compared to typically developing children despite children with ADHD exhibiting deficient psychophysiological markers of extinction (e.g., lack of electrodermal response during extinction of rewards) (Laboni, Douglas, & Ditto, 1997). In another study examining children, those with ADHD exerted more physical force to obtain a reward during extinction (Douglas & Parry, 1994), but interestingly, this effect was more pronounced during partial reinforcement (30% reward rate). A methodological overlap among these rodent and human studies is the focus on behavioral measures that are often borrowed from the rodent literature (e.g., response rate). Overall, these findings allude to the need for studying inflexible behaviors in ADHD using methods more apt for the nuances of human cognition, which may be especially important for better understanding habitual control as it relates to the human experience and its potential manifestation in this disorder.

The prefrontal cortex—namely the dACC and vmPFC—are regarded as playing major roles in goal-directed control. These fronto-cingular areas have been identified as components of the brain's cognitive control network (Cole & Schneider, 2007; MacDonald, Cohen, Stenger, & Carter, 2000). An aberrance in this system may relinquish control in motivated behaviors to render them automatic and habitual (Otto et al., 2015; Poldrack et al., 2005; Verbruggen & Logan, 2009). Our PPI results reveal a gradually diminishing functional connectivity between the posterior putamen sub-region of the striatum and the dACC/mPFC in the ADHD group over the course of training. In contrast, the NT group shows no significant change in corticostriatal communication throughout training. Given the dACC’s role in cognitive control (MacDonald et al., 2000), error detection (Caravan, Ross, Murphy, Roche, & Stein, 2002; Polli et al., 2005), and reward-based decision making (Bush et al., 2002), its altered connectivity with the striatum following moderate S–R training may be indicative of sub-optimal neural processing that underlies value-driven action execution in ADHD. Along
with the vmPFC—a prefrontal sub-region that is associated with value-tracking and inhibition/reversal learning (Smith et al., 2010; Zhang, Mendelsohn, Manson, Schiller, & Levy, 2016), the dACC’s abnormal connectivity with the posterior putamen in ADHD may be an important biomarker for potential aberrances in value-based decision making and goal-directed control.

ADHD has been previously linked to ACC dysfunctions. Dampered inhibitory control-related ACC activity has been reported in adults with ADHD (Schneider et al., 2010). Structural abnormalities have also been documented, as ADHD is associated with volumetric reductions in the anterior cingulate region (Carmona et al., 2005; Frodl & Skokauskas, 2012; Makris et al., 2007; Seidman et al., 2006, 2011). Healthy individuals foster an antiphasic connectivity between task-positive (e.g., the cognitive control network including the dACC) and task-negative (e.g., the default mode network—a set of brain regions that coactivate in task-negative contexts) areas (Cole, Bassett, Power, Braver, & Petersen, 2014). However, adults with ADHD have been documented to display an impairment in this functional connectivity between cognitive control and default mode regions, possibly driving the attentional lapses associated with the disorder (Castellanos et al., 2008). Children with ADHD, on the other hand, display heightened fronto-cingular connectivity patterns, in that the orbitofrontal cortex—a region associated with salience attribution and reward representations (Schultz, Tremblay, & Hollerman, 2000; Sescousse, Redouté, & Dreher, 2010)—fosters increased connectivity with the dACC (Tomasi & Volkow, 2012). This reward-related irregular connectivity may manifest as motivational deficits in ADHD, such as unfavorable value-based decision making. Our finding of a diminished corticostriatal connectivity—specifically, the communication between the posterior putamen and the dACC, may similarly allude to motivational impairments. The dACC is an important node for attentional processes such as response monitoring and selection (Bush et al., 1999; Camille, Tsuchida, & Fellows, 2011). Motivational control may also be closely intertwined with such attention-based cognitive operations, as associations between stimuli and their outcomes have been shown to influence subsequent attentional biases towards these stimuli (Le Pelley, Mitchell, & Johnson, 2013). Taken in context with ADHD’s cardinal symptom of inattention, a compromised connection between regions driving stimulus-sensitivity, such as the posterior putamen, and response selection, such as the dACC, may produce action execution that is biased towards salient, triggering stimuli rather than towards outcome value.

Our whole brain analysis yielded stimulus-related activations in the opercular/insular region following moderate S–R learning. Our exploration of reward delivery displayed no group differences, yet we found both groups to recruit orbitofrontal cortex and striatal regions—key components of the reward circuitry—at the receipt of the reward indicator. The insular recruitment in the late stage of S–R learning may be related to its role in the maintenance of rigid behaviors. The insula plays a critical role in addiction maintenance, in that damage to the insula predicts addiction disruption (Naqvi & Bechara, 2010; Naqvi, Rudrauf, Damasio, & Bechara, 2007). Thus, the insula may be an important player in developing rigid actions that eventually become outcome-insensitive habits. Future investigations of the insula and associative learning in ADHD can further elucidate the necessity of this region in executing stimulus-dependent actions. We intended to confirm whether the visual indicator of a food reward (i.e., the M&M or Goldfish image appearing below the fractal) would be sufficient in driving reward-related signaling in the striatum and the vmPFC. We also explored this idea further by performing a group comparison to determine whether ADHD is associated with heightened reward receipt signaling. We found that these visual indicators of reward indeed evoked reward-related activation, namely in the striatum and orbitofrontal cortex, yet the ADHD group did not evoke this pattern significantly more than NTs. These findings suggest that our task was successful in engaging the brain’s reward circuitry, but we did not find corroborating evidence for heightened reward receipt activity in ADHD that is reported in the literature (Furukawa et al., 2014; Tegelbeckers et al., 2018; von Rhein et al., 2015). The lack of group effects here may be attributed to the wide variability in ADHD manifestation. We did not have strong hypotheses regarding subtypes, and our sample size did not permit rigorous testing of subtype-specific patterns. However, the enhanced reward delivery signaling in the reward circuitry may be subtype-dependent, with, for instance, the combined subtype showing hyperresponsiveness to reward compared to the inattentive subtype and controls (Edel et al., 2013). Finer-tuned examinations of subtype-specific effects in future research may offer a more thorough understanding of the brain bases of ADHD, particularly in the context of reward processing.

Interestingly, we also see evidence for a hyper-recruitment of the hippocampus at task-onset following moderate S–R training in ADHD. The hippocampus is regarded as integral for declarative learning, and especially critical for contextual memory (Chun & Phelps, 1999; Greene, Gross, Elsinger, & Rao, 2007). Possibly, the fractals in each trial may also provide contextual information, in that the indicators above the fractal that signal the active button may take on the properties of a stimulus, and the fractal may serve as a context in which the stimulus signals a response-contingent reward. The ADHD-specific hippocampal activation may therefore relate to the contextual information provided by the fractals, which may be aiding in the maintenance of an outcome-driven behavioral profile despite the corticostriatal abnormalities. An interesting avenue for future research may be to further dissociate the potential hippocampal compensatory mechanisms that underlie aberrant prefrontal and striatal control systems in ADHD.

Certain limitations of our study should be considered in future investigations. Participants in this study were matched on relevant variables to effectively compare ADHD and NT groups as closely as possible. However, although we controlled for differences in WM across groups, we did not account specifically for visual WM. The Digit Span measure taps into auditory WM, yet the free-operant task is a visuomotor paradigm. Although we had no specific hypotheses regarding visual or auditory WM, considering WM deficits in ADHD that are distinct across visual and auditory domains (Alderson et al., 2015; but see also; Liebel & Nelson, 2017), it may be
interesting to explore how different domains of WM contribute to habits in future work. Additionally, we excluded individuals who displayed patterns of substance abuse or dependence. This exclusion criterion attempted to minimize the effects of psychoactive substances that alter corticostriatal neurochemistry. However, we did not control for sub-clinical or recent recreational drug use (e.g., marijuana), which may potentially influence our findings due to shared corticostriatal systems associated with drug mechanisms and brain function underlying motivational control (Mason et al., 2019). Similarly, although participants who were prescribed stimulants to manage ADHD symptoms discontinued their medication 36 h prior to the scan, long term stimulant use has been reported to alter striatal dopamine transporter levels (Fusar-Poli, Rubia, Rossi, Sartori, & Balottin, 2012), and thus may potentially influence our results. Medication discontinuation may also engender confounds driven by short-term stimulant withdrawal that can impact participants’ neural and behavioral outcomes. An interesting avenue of research in this domain may be to study motivational control in medication-naïve individuals with ADHD. Furthermore, we may have been underpowered to detect bilateral striatal effects, especially considering the largely left-lateralized findings in whole brain and ROI results. Further interrogations of striatal signaling in ADHD may benefit from a larger sample size, or the adoption of more sophisticated MRI acquisition methods to improve fMRI signal-to-noise ratio (e.g., multi-echo fMRI) (Kundu et al., 2017). 

ADHD is a highly prevalent disorder, and the wide range of reward-related irregularities warrants a closer examination of neurobehavioral mechanisms. We contribute to the growing neurobiological evidence for reward- and motivation-related dysfunctions in ADHD by highlighting key corticostriatal abnormalities affecting the posterior putamen, dACC, and mPFC during motivational control. Importantly, the atypical neural signaling related to motivational processes may indicate a potential biomarker in ADHD. Research on habits and goals in ADHD may benefit from a larger sample size, or the adoption of more sophisticated MRI acquisition methods to improve fMRI signal-to-noise ratio (e.g., multi-echo fMRI) (Kundu et al., 2017).

Declaration of Competing Interest

None.

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Supplementary data

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