Psychiatry Research: Neuroimaging 327 (2022) 111561

Contents lists available at ScienceDirect

Psychiatry Research: Neuroimaging

journal homepage: www.elsevier.com/locate/psychresns

Reward modality modulates striatal responses to reward anticipation in ADHD: Effects of affiliative and food stimuli

Emi Furukawa [a,*], Patricia Bado [b], Raquel Quimas Molina da Costa [b], Bruno Melo [b], Pilar Erthal [b], Iara Peixoto de Oliveira [b], Jeff R Wickens [a], Jorge Moll [b], Gail Tripp [a], Paulo Mattos [b]

[a] Okinawa Institute of Science and Technology Graduate University (OIST), Okinawa, Japan
[b] D'Or Institute for Research and Education (IDOR), Rio de Janeiro, Brazil

ARTICLE INFO

Keywords:
Affiliative reward
Reinforcement sensitivity
Anticipatory responses
Motivation
fMRI
Classical conditioning

ABSTRACT

Altered reward sensitivity has been proposed to underlie symptoms of attention deficit hyperactivity disorder (ADHD). Functional magnetic resonance imaging (fMRI) studies have reported hypoactivation to reward-predicting cues in the ventral striatum among individuals with ADHD, using experimental designs with and without behavioral response requirements. These studies have typically used monetary incentives as rewards; however, it is unclear if these findings extend to other reward types. The current study examined striatal responses to anticipation and delivery of both affiliative and food reward images using a classical conditioning paradigm. Data from 20 typically developing young adults, and 20 individuals diagnosed with ADHD were included in a region-of-interest analysis for *a priori* striatal regions. Consistent with findings from studies using monetary rewards, individuals with ADHD showed decreased activation to cues predicting affiliative rewards in the bilateral ventral and dorsal striatum and increased activation to the delivery of affiliative rewards in the ventral striatum. No group differences were found in striatal responses to food reward cues or images. These results suggest hyposensitivity to reward-predicting cues in ADHD extends to affiliative rewards, with important implications for understanding and managing the learning and social functioning of those with ADHD.

1. Introduction

Attention deficit hyperactivity disorder (ADHD) is characterized by elevated levels of inattention and/or overactivity/impulsivity that impair daily, academic, occupational and social functioning. Symptoms emerge in childhood, often persisting into adulthood (American Psychiatric Association, 2013). Altered reward sensitivity has been hypothesized as one pathway to symptoms of the disorder (Luman et al., 2010; Tripp and Wickens, 2008). Experimental studies have identified differences in the behavioral responses of individuals with and without ADHD to reward (Luman et al., 2005). Those with ADHD demonstrate a stronger preference for immediate rewards (see Marx et al., 2021; Patros et al., 2016 for a review) and their performance is differentially affected by reward contingencies (Alsop et al., 2016; Luman et al., 2009; Marx et al., 2013; Meyer et al., 2019), compared with their typically developing peers.

The neural circuitry of reward is well defined in humans and other animals, with dopamine neurons projecting to striatal regions (Haber and Knutson, 2010). Animal studies show that midbrain dopamine cells fire in response to unexpected rewards. When a cue reliably precedes a reward, the dopamine cells come to fire in response to the cue, with responses to the reward itself declining (Pan et al., 2005; Schultz, 1998). Tripp and Wickens (2008) proposed that this process may be impaired in ADHD; i.e., the transfer of the dopamine response from the reward to the reward predicting cue is disrupted, leading to altered reward sensitivity and symptoms of ADHD. Functional magnetic resonance imaging (fMRI) studies consistently show reduced striatal responsiveness to reward-predicting cues (see Baroni and Castellanos, 2015; Plichta and Scheres, 2014 for reviews). Some studies also report increased responsiveness to subsequent reward delivery in those with ADHD (Furukawa et al., 2014; Paloyelis et al., 2012; Ströhle et al., 2008).

These fMRI studies typically use monetary rewards. However, in everyday life a variety of outcomes can serve as rewards, shaping and maintaining behavior. Social affiliation and food are basic human needs

* Corresponding author at: Okinawa Institute of Science and Technology Graduate University, Human Developmental Neurobiology Unit, 1919-1 Tancha, 904-0495 Onna, Okinawa, Japan.
E-mail address: furukawa@oist.jp (E. Furukawa).

https://doi.org/10.1016/j.pscychresns.2022.111561
Received 6 May 2022; Received in revised form 12 October 2022; Accepted 23 October 2022
Available online 25 October 2022

and universal motivators (Feldman, 2017; Sescousse et al., 2013). In typically developing adults, striatal activation to affiliative (Feldman, 2017; Moll and de Oliveira-Souza, 2009) and food stimuli (Beaver et al., 2006; Cornier et al., 2007; Pursey et al., 2014; Rothemund et al., 2007; Tang et al., 2012) have been reported. There is also some evidence that striatal responses to the *anticipation* of affiliative and food rewards are similar to anticipatory responses to monetary rewards (Bortolini et al., 2021; Goerlich et al., 2017; Rademacher et al., 2010; Simon et al., 2015; Spreckelmeyer et al., 2009). Increased activation has been reported in response to cues that reliably precede images of happy faces (Goerlich et al., 2017; Rademacher et al., 2010; Spreckelmeyer et al., 2009), babies (Bortolini et al., 2021), snacks (Simon et al., 2015) and high-calorie foods (Bortolini et al., 2021). These findings suggest similar neural responses in anticipation of monetary, affiliative and food rewards in typically developing individuals (Báez-Mendoza and Schultz, 2013; Gu et al., 2019; Sescousse et al., 2010).

We identified only two previous studies examining neural responsiveness to affiliative or food reward in those with elevated symptoms of ADHD (Kohls et al., 2014; Martin et al., 2020). Kohls and colleagues (2014) assessed the effects of cues signaling both social reward (images of positive facial expressions) and monetary reward (images of coins) for correct performance in a go/no-go task. Children with ADHD showed increased activation in the ventral striatum during both social and monetary reward trials during the go blocks. Typically developing children demonstrated increased striatal responses to monetary rewards only. More recently, Martin (2020) identified a positive correlation between striatal responses to high-calorie food and ADHD symptoms in a community sample of young adults. Neither of these studies distinguished between anticipation and delivery of affiliative or food rewards, precluding direct comparison with monetary reward responses distinguishing anticipation and delivery in individuals with ADHD.

In the current fMRI study, we examined BOLD responses to both the anticipation and delivery of affiliative (images of two people interacting/connecting) and food rewards (images of high caloric food), in young adults with and without ADHD. Reward delivery was preceded by previously neutral visual cues in a classical conditioning paradigm (Furukawa et al., 2020, 2014). As in our previous studies with monetary reward, we examined ventral and dorsal striatum bilaterally in a region-of-interest (ROI) analysis. Given their strong motivational properties, social affiliation and food are expected to serve as rewards for both typically developing controls and those with ADHD. Based on the available research, we expect the control group to show increased BOLD activation to cues predicting both reward types. For the ADHD group, we expect reduced striatal responses to cues predicting food and affiliative rewards, together with increased responses to reward delivery as with monetary incentives. Similar BOLD response patterns across reward types would support altered reward sensitivity as a potential biomarker of ADHD. Alternatively, differences across reward types might indicate reward specific neural mechanisms.

2. Methods

The study was approved by the ethics committee of the D'Or Institute for Research and Education (IDOR) in Rio de Janeiro, Brazil. All volunteer participants provided written informed consent.

2.1. Participants

Ninety-two right-handed adults aged 18 – 35 years were recruited (67 for the ADHD and 25 for the control group) among students attending the Federal University of Rio de Janeiro, Brazil, and through referrals by area physicians. All underwent a comprehensive assessment of past and current symptoms of ADHD, and other comorbid conditions, by a team of qualified psychiatrists at IDOR, trained and supervised by a senior psychiatrist (PM). Semi-structured interviews confirmed the presence and severity of past and current ADHD symptoms (Disruptive Behavior section of the Kiddie-Schedule for Affective Disorder and Schizophrenia-PL (KSADS-PL) (Grevet et al., 2005)) and the current symptoms of other psychiatric conditions (Structured Clinical Interview (SCID) (Del-Ben et al., 2001). Participants were also administered an abbreviated measure of IQ (WAIS Vocabulary and Block Design (Nascimento, 2004)).

Twenty-four ADHD group and 21 control group participants met the study inclusion criteria. The ADHD group participants demonstrated five or more current symptoms of inattention and/or hyperactivity/impulsivity and six or more symptoms before age 12. Control participants were required to demonstrate four or less current and five or less previous symptoms of inattention and hyperactivity/impulsivity. Exclusion criteria for both groups were: MRI contraindications; current non-prescription drug use, psychotic symptoms, major depressive disorder, bipolar disorder or eating disorder; and a history of any neurological disorder.

Four additional participants in the ADHD group and one participant in the control group were subsequently excluded from data analysis due to signal dropout or excessive movement-related artifacts[1]. The final sample included 20 participants in each group (Table 1). Three participants in the ADHD group were treated with stimulant medication (two with methylphenidate and one with lisdexamfetamine); they withheld their medication for 48 h prior to study participation. One ADHD group participant was taking vortioxetine and one control participant was taking vortioxetine and bupropion, however neither met the criteria for major depressive disorder at the time of participation (they were not asked to withhold their non-stimulant medication). Descriptive statistics were summarized using IBM SPSS Statistics, Version 26 (https://www.ibm.com/products/spss-statistics).

Participants arrived between 8 and 9 am on a Saturday. They were asked not to eat before arrival. A consent procedure was followed by a light breakfast (a glass of juice or yogurt, a slice of white bread or two crackers with a slice of cheese and ham [approx. 255 kcal total]); participants were not required to eat all the food during the 30 min period allocated for breakfast. After the breakfast, clinical interviews were administered and then the fMRI task. Following fMRI scanning, participants were administered the IQ test.

2.2. fMRI experimental design

To examine the effects of reward-predicting cues and reward stimuli, a classical conditioning task was implemented in an event-related design (Fig. 1). Three initially neutral stimuli were used as cues (three Japanese

Table 1
Participant characteristics.

	ADHD (n = 20)			Control (n = 20)		
	Mean	sd	Range	Mean	sd	Range
Age (years)	25.30	3.51	21–35	25.25	3.25	20–33
Estimated IQ	123.06	9.22	103–134	122.90	10.95	109–137
Education (years)	17.65	3.05	12–24	17.35	2.78	11–22
males n (%)	8 (40%)			9 (45%)		
# Inattention Symptoms (KSADS)	6.90	1.41	5–9	0.80	1.24	0–4
# Hyperactivity/ Impulsivity Symptoms (KSADS)	3.70	2.41	0–8	0.75	1.21	0–4

[1] Movements were inspected using ART Toolbox (https://www.nitrc.org/projects/artifact_detect), and participants with movements exceeding one voxel size (3mm) were excluded.

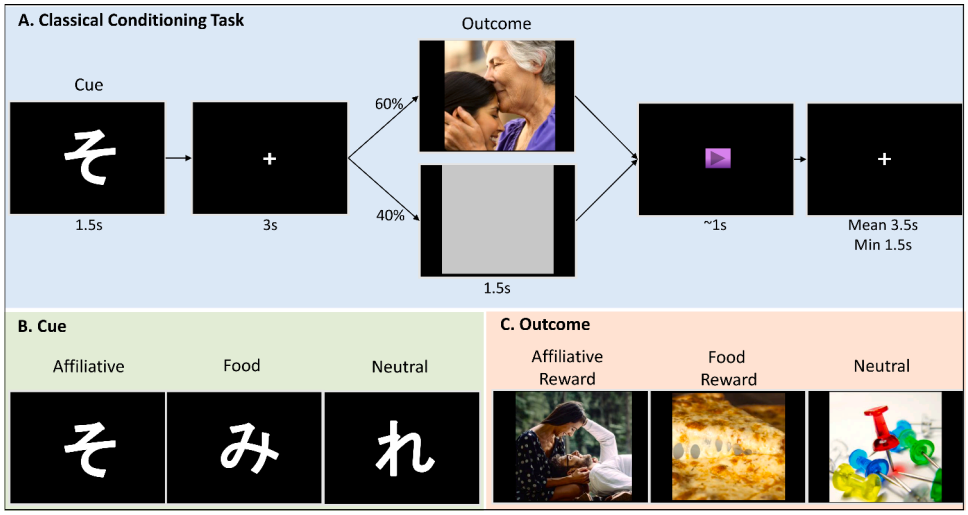

Fig. 1. Experimental design. (A) The classical conditioning paradigm in which a cue is predictive of an outcome 60% of the time. (B) Three cue types. (C) Three outcome types.

characters deemed abstract by Brazilian participants; Cue A [み], Cue B [そ], Cue C [れ]). Each cue was repeatedly paired with one of three outcome types (food reward, affiliative reward, or neutral outcome). Food reward outcomes were pictures of high-calorie food (e.g., pizza, brownies). Affiliative reward outcomes were pictures of two people connecting (e.g., a parent kissing the forehead of the child, two friends hugging). Neutral outcomes were pictures of everyday objects (e.g., colored pins, an umbrella) (see Supplemental Methods).

Each trial began with one of the cues displayed for 1.5 s, followed by a 3 s delay. The time between a cue and outcome was kept constant to establish the predictive properties of the cue (Furukawa et al., 2014; Metereau and Dreher, 2013). The use of a constant time interval between the cue and reward facilitates the transfer of striatal responses from the predicted reward to the reward-predicting cue (Bermudez and Schultz, 2014; Fiorillo et al., 2008). Following the delay, an outcome (food reward, affiliative reward, or neutral outcome) was displayed 60% of the time, a gray square 40% of the time. These displays were 1.5 s in duration. After the display, participants were encouraged to press a 'play' button during a 1 s window. Participants were told that pressing the button would start the next trial. The next trial began after a short delay regardless of the button press. This was followed by a variable inter-trial interval (Poisson distribution: minimum 1.5 s, median 3.5 s). The button press was included to maintain participants' engagement during the passive classical-conditioning task. The experimenter monitored button pressing during scanning. All participants included in the final sample were observed to press the button consistently throughout the fMRI session.

One run of the task was administered on a computer outside the MRI scanner as a practice. Three runs were administered in the scanner. Each run consisted of 45 trials: 9 trials of Cue A followed by an affiliative reward, and 6 trials of Cue A followed by a gray square; 9 trials of Cue B followed by a food reward and 6 trials of Cue B followed by a gray square; 9 trials of Cue C followed by a neutral outcome and 6 trials of Cue C followed by a gray square. There were nine different pictures for each outcome. The pictures were repeated across, but not within, each run. Picture order presentation within a run was random.

In the middle of and after completion of the training run, participants were asked which type of pictures came after each cue, to check if they had made the cue-outcome association. After the fMRI experiment, participants rated the likability of the three cues and each outcome picture on a 4-point Likert scale. These ratings were analyzed using SPSS.

2.3. fMRI data acquisition parameters

Functional images were acquired with a 3T Siemens scanner, using an 8-channel SENSE head coil, LCD display with a mirror, single shot T2*-weighted fast-field echo, echo-planar imaging sequence (TR = 2000 ms, TE = 30 ms, Matrix = 80 × 80, FOV = 240 mm, flip angle = 90º, isotropic voxel size 3 mm, 36 slices interleaved with no gap, slice thickness = 3 mm, 240 volumes per run, 3 runs). Total functional scanning time was 28.5 min. Reference anatomical images were acquired using a T1-weighted SD magnetization-prepared, rapidly acquired gradient echo sequence (TR = 1800 ms, TE = 2,26 ms, Matrix/FOV = 256 mm, isotropic voxel size 1 mm, 176 sagittal slices). The trial number, sequence and time were uniform across all the participants.

2.4. fMRI data analysis

Functional images were analyzed using Statistical Parametric Mapping software (SPM12; http://www.fil.ion.ucl.ac.uk/spm/software/spm12/). Preprocessing was conducted using CONN 18b preprocessing pipeline (https://web.conn-toolbox.org/), which included realignment, slice-time correction, outlier detection, segmentation and normalization, and smoothing (8 mm Gaussian kernel) resulting in the reconstructed functional images with voxel dimensions of 2 mm. Stimulus onset for specified events were convolved with the hemodynamic response function with autocorrelation correction (AR(1)) and high-pass filtering (128 s) for each participant.

There were 9 condition-specific regressors: Cue A, Cue B, Cue C, Affiliative reward, Food reward, Neutral outcome (pictures of everyday objects), Gray square preceded by Cue A, Cue B and Cue C. The fixation period was modeled together with the cues (4.5 s). The contrasts of the interest were: Cue A vs. Cue C, Cue B vs. Cue C, Affiliative reward vs. Neutral outcome, and Food reward vs. Neutral outcome. Gray squares were not used in the contrasts. The variance inflation factors of the full design matrix and of regressors of interest were under 2.5 (https://github.com/canlab/CanlabCore/tree/master/CanlabCore/diagnostics; scn_spm_design_check.m).

2.5. Region-of-interest (ROI) analysis[2]

The MNI coordinates (12/−12, 10, −6 for bilateral ventral striatum [VS]; 20/−20, 4,18 for bilateral dorsal striatum [DS]) were the same meta-analytical coordinates (Liu et al., 2011) used in our previous study (Furukawa et al., 2020) examining striatal responses to the reward cue and monetary reward outcome in ADHD. Control vs. ADHD group random-effects on the contrasts of interest were examined for the ventral and dorsal striatum regions using GLM in SPM 12. Small volume correction (SVC) was applied for the 5 mm spheres around the *a priori* MNI coordinates with an initial uncorrected threshold of $p < 0.005$.

3. Results

3.1. Rating results

All participants in the final sample correctly reported the cue-outcome associations at the end of the training run, prior to the MRI scanning. Following the MRI scanning, participants rated affiliative and food reward cues higher than the cue associated with the neutral outcome (Mixed ANOVA, within-subject effect of the cue, $F(2, 76) = 28.977$, $p < 0.001$). The mean likability ratings were similar for the affiliative and food reward pictures, while they were higher than the mean rating for the neutral outcome pictures (Mixed ANOVA, within-subject effect of the cue, $F(2, 76) = 181.614$, $p < 0.001$). No significant difference was observed for the control vs. ADHD groups on the likability ratings of the cues and pictures.

3.2. Sensitivity to affiliative cues and affiliative image rewards

The ROI analyses indicated greater differences in bilateral ventral and dorsal striatal responses to Cue A (affiliative reward cue) vs. Cue C (neutral outcome cue) in the control group, compared to the ADHD group (Fig. 2, Table 2, Supplemental Results Fig. 1). The exploratory whole-brain analysis showed effects consistent with the ROI analysis (Supplemental Results Table 1). Compared to the control group, reduced activation to the affiliative reward cues was observed in the ADHD group.

A significant effect was also observed in the right ventral striatum for the affiliative reward vs. neutral outcomes in the ROI, indicating greater responses in the ADHD group, compared to the control group (Table 2).

3.3. Sensitivity to food cues and food image rewards

No group difference was observed in striatal responses to Cue B (food reward cue) vs. Cue C (neutral outcome cue). In addition, the ADHD and control groups did not differ in their responses to food reward and neutral outcome delivery.

3.4. Post-hoc analysis to examine reward modality by group interaction effects

To check the reward modality (affiliation vs. food) by group interaction effects, Mixed ANOVAs were conducted using the contrast beta values extracted for the ROI 5mm spheres (Supplemental Table 3).

Significant interaction effects for the cues were observed in rVS $F(1, 38) = 5.813$, $p = 0.021$) and lDS ($F(1, 38) = 5.168$, $p = 0.029$). The control vs. ADHD group difference was greater for responses to the affiliative cues than to the food cues. Main effects of group were observed in rVS ($F(1, 38) = 9.563$, $p = 0.004$) and lVS ($F(1, 38) = 7.488$, $p = 0.009$). In these regions, responses to the cues across the two reward modalities were greater for the control than the ADHD group. No significant main effects of the cues were observed.

For responses to reward outcomes, no significant interaction or main effects were observed (Supplemental Table 3).

4. Discussion

The current study provides evidence that the neural activation associated with affiliative rewards is altered in ADHD, in a manner similar to that previously reported with monetary rewards. Young adults with ADHD showed reduced activation to affiliative reward cues in bilateral ventral and dorsal striatum compared with their typically developing peers. They also showed increased activation to delivery of affiliative images in the right ventral striatum. These effects, in the regions selected *a priori,* were not seen for food reward cues or delivery of food images.

The differential striatal activation patterns to affiliative reward cues among individuals with and without ADHD are consistent with those reported in previous studies using monetary rewards (see Baroni and Castellanos, 2015; Plichta and Scheres, 2014 for reviews). The increased BOLD activation to the delivery of affiliative rewards in those with ADHD is consistent with the results of our earlier study using monetary rewards in a similar classical conditioning paradigm (Furukawa et al., 2014). Neither of these paradigms requires a behavioral response, unlike the more widely used Monetary Incentive Delay task, but did produce neural activation. The present study provides new empirical evidence of altered striatal activation to non-monetary reward cues and reward delivery in those with ADHD, indicating an impaired processing of reward cues across modalities in ADHD. The current study provides further support for the hypothesized disruption in the transfer of dopamine responses from rewards to reward-predicting cues in ADHD (Tripp and Wickens, 2008).

The absence of significant group differences in striatal responses to food cues contrasts with the current findings of group differences in responses to affiliative reward cues and previous reports of hypo-sensitivity to monetary reward cues (Baroni and Castellanos, 2015; Plichta and Scheres, 2014). This was not due to a lack of responses; the two groups were similar in their striatal responses to food cues and to food reward pictures. Responses to the cues across the two reward modalities were generally greater for the control group, relative to the ADHD group. However, the group difference was more pronounced and only significant for responses to the affiliative reward cues. Levels of satiation and/or the lack of opportunity to consume the food rewards may have impacted the development of cue-reward associations across groups. Alternatively, processing of food reward may involve unique neural pathways (Kringelbach and Rolls, 2004), providing distinct afferent modulations of dopamine neurons in the striatum (Beier et al., 2015; Watabe-Uchida et al., 2012). For example, sensory rewards such as palatable food or drink activate posterior regions of the orbitofrontal cortex (de Araujo et al., 2003), while monetary rewards more anterior orbitofrontal regions (O'Doherty et al., 2001). Responses in these regions may be altered in ADHD and could in turn differentially modulate striatal responses. Differential cortical activation in these regions was not evident in the whole brain analysis in the current study and these were not our *a-priori* regions. Future studies should investigate possible interaction effects of ADHD and reward modalities on these and other brain regions involved in the processing of different types of rewards.

Altered sensitivity to affiliative reward cues and their delivery has important implications for the everyday functioning of individuals with ADHD. Praise, acknowledgement, and acceptance by others are commonly used reinforcers that help shape and maintain human behavior and learning (van der Oord and Tripp, 2020). Reduced sensitivity to affiliative reward cues, together with increased sensitivity to reward delivery, may contribute to suboptimal learning in those with ADHD. Although based on pictures of affiliative behavior rather than actual experience, the current findings provide support for the use of

[2] A whole brain analysis was also conducted as an exploratory analysis for the Cue A (affiliative reward cue) vs Cue C (neutral outcome cue) contrast due to the significant effects observed in the ROI analysis (Supplemental Results 1).

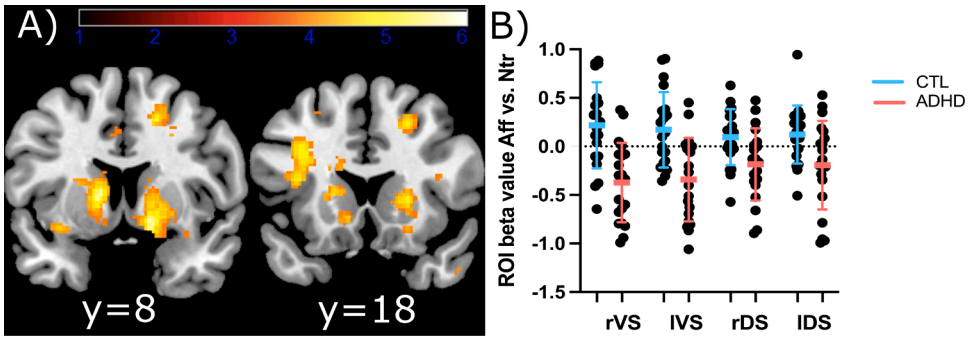

Fig. 2. Striatal responses to the affiliative versus neutral cues for the control versus ADHD groups. (A) Brain maps represent whole brain activation displayed at $p < 0.001$, showing increased activation in bilateral ventral striatum and left dorsal striatum during affiliative reward anticipation in the control group compared with the ADHD group. Y indicates the posterior-anterior positions of the coronal slices. (B) Mean parameter estimates of the affiliative versus neutral cue contrast beta values, extracted for the *a priori*-defined ROIs (GraphPad prism 9, https://www.graphpad.com).

Table 2
BOLD responses to anticipation of affiliative reward (affiliative cue versus neutral cue); *a priori* ROI analysis.

Anatomical region	SVC cluster size	*FWE corr p-value*	MNI coordinates x	y	z	*Z-score*
Anticipation						
Control > ADHD						
rVS	81	<0.001	14	8	−8	4.74
lVS	78	0.001	−12	12	−6	4.05
rDS	22	0.002	18	0	16	3.81
lDS	25	0.002	−22	6	14	3.79
ADHD > Control	No FWE-corrected significant *a priori* ROI					
Outcome						
Control > ADHD	No FWE-corrected significant *a priori* ROI					
ADHD > Control						
rVS	5	0.017	12	6	−8	3.00

Resels: 214.77 voxels. FWHM = 11.9 12.0 12.0 mm mm mm.

frequent and immediate praise to facilitate learning and maintain appropriate behavior, recommended for the behavioral management of ADHD (van der Oord and Tripp, 2020). These findings also offer a possible explanation for the social difficulties of those with ADHD (Vacher et al., 2020). The pattern of striatal responses seen in individuals with ADHD could contribute to an increase in the intensity of social behaviors to elicit affiliative rewards, which may be experienced as inappropriate or annoying by others. Those with ADHD might also engage in other actions to elicit the attention of others, e.g., nagging, clowning about. It would be helpful to test these suggestions using these specific affiliative rewards in future studies.

As one of the few fMRI studies to assess sensitivity to the anticipation and delivery of non-monetary rewards in ADHD, it is important to consider any study limitations. The sample size is relatively small, however participants were carefully selected, with all those in the ADHD group meeting DSM-5 criteria for the disorder. The young adults in our sample were high functioning; while this may limit generalizability of the findings to other samples, it increases our confidence that identified differences are due to the presence of ADHD. Extending the study to include individuals with subthreshold ADHD symptoms, and those with other disorders, will allow dimensional examination to evaluate whether the identified alteration in affiliative reward anticipation is specific to ADHD. We did not test the effects of gender given the sample size; gender could differentially influence responses to affiliative and food rewards. The provision of a light breakfast may have impacted the food reward results. Extending the number of trials would potentially allow the examination of changes in striatal responses to cues and rewards over time during classical conditioning. Considering these limitations, together with the importance of the findings, we encourage other researchers to extend their investigations to include non-monetary rewards in ADHD populations. Given reported alterations in striatal responses to monetary rewards in other disorders, such as addictions (Luijten et al., 2017), we also encourage studies using non-monetary rewards in other population groups.

The current study demonstrates striatal hypoactivation to reward-predicting cues extends beyond monetary rewards in ADHD. Adults with ADHD showed reduced sensitivity in anticipation of affiliative rewards together with increased sensitivity to their delivery. These results are consistent with the hypothesis that the transfer of dopamine cell firing from unexpected rewards to reward predicting cues is impaired in those with ADHD. The evidence for altered neural responsiveness to affiliative reward in those with ADHD has important implications for understanding and managing the social difficulties commonly reported in those with this disorder. Additional research with affiliative and food rewards is needed to confirm the current findings.

CRediT authorship contribution statement

Emi Furukawa: Conceptualization, Formal analysis. **Patricia Bado:** Data curation, Formal analysis. **Raquel Quimas Molina da Costa:** Data curation. **Bruno Melo:** Formal analysis. **Pilar Erthal:** Data curation. **Iara Peixoto de Oliveira:** Formal analysis. **Jeff R Wickens:** Conceptualization. **Jorge Moll:** Conceptualization. **Gail Tripp:** Conceptualization. **Paulo Mattos:** Conceptualization, Data curation.

Declaration of Competing Interest

PM received research grant and speaker honoraria from Takeda in the last three years.

Data availability

Data will be made available on request and will be deposited to NeuroVault (https://neurovault.org/).

Acknowledgements

This study was supported by a joint research agreement between OIST and IDOR. We would like to thank all individuals who took part in the study and IDOR staff who assisted with data collection and processing, especially Ivanei E Bramati, Rodrigo Basilio, Tiago Bortolini, Débora Lima, and Bruno Palazzo Nazar.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.pscychresns.2022.111561.

References

Alsop, B., Furukawa, E., Sowerby, P., Jensen, S., Moffat, C., Tripp, G., 2016. Behavioral sensitivity to changing reinforcement contingencies in attention-deficit hyperactivity disorder. J. Child Psychol. Psychiatry 57, 947–956.
American Psychiatric Association, 2013. Diagnostic and Statistical Manual of Mental Disorders, 5th ed. Author, Arlington, VA.
Báez-Mendoza, R., Schultz, W., 2013. The role of the striatum in social behavior. Front. Neurosci. 7, 233.

Baroni, A., Castellanos, F.X., 2015. Neuroanatomic and cognitive abnormalities in attention-deficit/hyperactivity disorder in the era of "high definition" neuroimaging. Curr. Opin. Neurobiol. 30, 1–8.
Beaver, J.D., Lawrence, A.D., van Ditzhuijzen, J., Davis, M.H., Woods, A., Calder, A.J., 2006. Individual differences in reward drive predict neural responses to images of food. J. Neurosci. 26, 5160–5166.
Beier, K.T., Steinberg, E.E., DeLoach, K.E., Xie, S., Miyamichi, K., Schwarz, L., Gao, X.J., Kremer, E.J., Malenka, R.C., Luo, L., 2015. Circuit architecture of VTA dopamine neurons revealed by systematic input-output mapping. Cell 162, 622–634.
Bermudez, M.A., Schultz, W., 2014. Timing in reward and decision processes. Philos. Trans. R. Soc. Lond. B Biol. Sci. 369, 20120468.
Bortolini, T., Melo, B., Basilio, R., Fischer, R., Zahn, R., de Oliveira-Souza, R., Knutson, B., Moll, J., 2021. Striatal and septo-hypothalamic responses to anticipation and outcome of affiliative rewards. Neuroimage 243, 118474.
Cornier, M.A., Von Kaenel, S.S., Bessesen, D.H., Tregellas, J.R., 2007. Effects of overfeeding on the neuronal response to visual food cues1. Am. J. Clin. Nutr. 86, 965–971.
de Araujo, I.E.T., Rolls, E.T., Kringelbach, M.L., McGlone, F., Phillips, N., 2003. Taste-olfactory convergence, and the representation of the pleasantness of flavour, in the human brain. Eur. J. Neurosci. 18, 2059–2068.
Del-Ben, C.M., Vilela, J.A.A., Crippa, J.A., de, S., Hallak, J.E.C., Labate, C.M., Zuardi, A. W., 2001. Confiabilidade da "Entrevista clínica estruturada para o DSM-IV - versão clínica" traduzida para o português. Rev. Bras. Psiquiatr. 23, 156–159.
Feldman, R., 2017. The neurobiology of human attachments. Trends Cogn. Sci. 21, 80–99.
Fiorillo, C.D., Newsome, W.T., Schultz, W., 2008. The temporal precision of reward prediction in dopamine neurons. Nat. Neurosci. 11, 966–973.
Furukawa, E., Bado, P., Tripp, G., Mattos, P., Wickens, J.R., Bramati, I.E., Alsop, B., Ferreira, F.M., Lima, D., Tovar-Moll, F., Sergeant, J.A., Moll, J., 2014. Abnormal striatal BOLD responses to reward anticipation and reward delivery in ADHD. PLoS One 9, e89129.
Furukawa, E, da Costa, RQM, Bado, P, Hoefle, S, Vigne, P, Monteiro, M, Wickens, JR, Moll, J, Tripp, G, Mattos, P., 2020. Methylphenidate modifies reward cue responses in adults with ADHD: An fMRI study. Neuropharmacology 162, 107833.
Goerlich, K.S., Votinov, M., Lammertz, S.E., Winkler, L., Spreckelmeyer, K.N., Habel, U., Gründer, G., Gossen, A., 2017. Effects of alexithymia and empathy on the neural processing of social and monetary rewards. Brain Struct. Funct. 222, 2235–2250.
Grevet, E.H., Bau, C.H.D., Salgado, C.A.I., Ficher, A., Victor, M.M., Garcia, C., Sousa, N. O., Nerung, L., Belmonte-de-Abreu, P., 2005. Interrater reliability for diagnosis in adults of attention deficit hyperactivity disorder and oppositional defiant disorder using K-SADS-E. Arq. Neuropsiquiatr. 63, 307–310.
Gu, R., Huang, W., Camilleri, J., Xu, P., Wei, P., Eickhoff, S.B., Feng, C., 2019. Love is analogous to money in human brain: coordinate-based and functional connectivity meta-analyses of social and monetary reward anticipation. Neurosci. Biobehav. Rev. 100, 108–128.
Haber, S.N., Knutson, B., 2010. The reward circuit: linking primate anatomy and human imaging. Neuropsychopharmacology 35, 4–26.
Kohls, G., Thönessen, H., Bartley, G.K., Grossheinrich, N., Fink, G.R., Herpertz-Dahlmann, B., Konrad, K., 2014. Differentiating neural reward responsiveness in autism versus ADHD. Dev. Cogn. Neurosci. 10, 104–116.
Kringelbach, M.L., Rolls, E.T., 2004. The functional neuroanatomy of the human orbitofrontal cortex: evidence from neuroimaging and neuropsychology. Prog. Neurobiol. 72, 341–372.
Liu, X., Hairston, J., Schrier, M., Fan, J., 2011. Common and distinct networks underlying reward valence and processing stages: a meta-analysis of functional neuroimaging studies. Neurosci. Biobehav. Rev. 35, 1219–1236.
Luijten, M., Schellekens, A.F., Kühn, S., Machielse, M.W.J., Sescousse, G., 2017. Disruption of reward processing in addiction: an image-based meta-analysis of functional magnetic resonance imaging studies. JAMA Psychiatry 74, 387–398.
Luman, M., Oosterlaan, J., Sergeant, J.A., 2005. The impact of reinforcement contingencies on AD/HD: a review and theoretical appraisal. Clin. Psychol. Rev. 25, 183–213.
Luman, M., Tripp, G., Scheres, A., 2010. Identifying the neurobiology of altered reinforcement sensitivity in ADHD: a review and research agenda. Neurosci. Biobehav. Rev. 34, 744–754.
Luman, M., Van Meel, C.S., Oosterlaan, J., Sergeant, J.A., Geurts, H.M., 2009. Does reward frequency or magnitude drive reinforcement-learning in attention-deficit/hyperactivity disorder? Psychiatry Res 168, 222–229.
Martin, E., Kaisari, P., Dourish, C., Rotshtein, P., Higgs, S., Spetter, M., 2020. ADHD symptoms are associated with binge eating and enhanced reward-related neural activation to food stimuli. Eur. Neuropsychopharm. 29, S58.
Marx, I., Hacker, T., Yu, X., Cortese, S., Sonuga-Barke, E., 2021. ADHD and the choice of small immediate over larger delayed rewards: a comparative meta-analysis of performance on simple choice-delay and temporal discounting paradigms. J. Atten. Disord. 25, 171–187.
Marx, I., Höpcke, C., Berger, C., Wandschneider, R., Herpertz, S.C., 2013. The impact of financial reward contingencies on cognitive function profiles in adult ADHD. PLoS One 8, e67002.
Metereau, E., Dreher, J.C., 2013. Cerebral correlates of salient prediction error for different rewards and punishments. Cereb. Cortex 23, 477–487.
Meyer, Meyer, Beckers, Tripp, Oord, V.der, 2019. Deficits in conditional discrimination learning in children with ADHD are independent of delay aversion and working memory. J. Clin. Med. 8, 1381.
Moll, J., de Oliveira-Souza, R., 2009. Extended attachment" and the human brain: internalized cultural values and evolutionary implications. In: Verplaetse, J., Schrijver, J., Vanneste, S., Braeckman, J. (Eds.), The Moral Brain: Essays on the Evolutionary and Neuroscientific Aspects of Morality. Springer Netherlands, Dordrecht, pp. 69–85.
Nascimento, E. do, 2004. Adaptação, validação e normatização do WAIS-III para uma amostra brasileira. WAIS-III: manual para administração e avaliação 1, 161–192.
O'Doherty, J., Kringelbach, M.L., Rolls, E.T., Hornak, J., Andrews, C., 2001. Abstract reward and punishment representations in the human orbitofrontal cortex. Nat. Neurosci. 4, 95–102.
Paloyelis, Y., Mehta, M.A., Faraone, S.V., Asherson, P., Kuntsi, J., 2012. Striatal sensitivity during reward processing in attention-deficit/hyperactivity disorder. J. Am. Acad. Child Adolesc. Psychiatry 51, 722–732.
Pan, W.X., Schmidt, R., Wickens, J.R., Hyland, B.I., 2005. Dopamine cells respond to predicted events during classical conditioning: evidence for eligibility traces in the reward-learning network. J. Neurosci. 25, 6235–6242.
Patros, C.H.G., Matt Alderson, R., Kasper, L.J., Tarle, S.J., Lea, S.E., Hudec, K.L., 2016. Choice-impulsivity in children and adolescents with attention-deficit/hyperactivity disorder (ADHD): a meta-analytic review. Clin. Psychol. Rev. 43, 162–174.
Plichta, M.M., Scheres, A., 2014. Ventral-striatal responsiveness during reward anticipation in ADHD and its relation to trait impulsivity in the healthy population: a meta-analytic review of the fMRI literature. Neurosci. Biobehav. Rev. 38, 125–134.
Pursey, K.M., Stanwell, P., Callister, R.J., Brain, K., Collins, C.E., Burrows, T.L., 2014. Neural responses to visual food cues according to weight status: a systematic review of functional magnetic resonance imaging studies. Front. Nutr. 1, 7.
Rademacher, L., Krach, S., Kohls, G., Irmak, A., Gründer, G., Spreckelmeyer, K.N., 2010. Dissociation of neural networks for anticipation and consumption of monetary and social rewards. Neuroimage 49, 3276–3285.
Rothemund, Y., Preuschhof, C., Bohner, G., Bauknecht, H.C., Klingebiel, R., Flor, H., Klapp, B.F., 2007. Differential activation of the dorsal striatum by high-calorie visual food stimuli in obese individuals. Neuroimage 37, 410–421.
Schultz, W., 1998. Predictive reward signal of dopamine neurons. J. Neurophysiol. 80, 1–27.
Sescousse, G., Caldú, X., Segura, B., Dreher, J.C., 2013. Processing of primary and secondary rewards: a quantitative meta-analysis and review of human functional neuroimaging studies. Neurosci. Biobehav. Rev. 37, 681–696.
Sescousse, G., Redouté, J., Dreher, J.C., 2010. The architecture of reward value coding in the human orbitofrontal cortex. J. Neurosci. 30, 13095–13104.
Simon, J.J., Skunde, M., Wu, M., Schnell, K., Herpertz, S.C., Bendszus, M., Herzog, W., Friederich, H.C., 2015. Neural dissociation of food- and money-related reward processing using an abstract incentive delay task. Soc. Cogn. Affect. Neurosci. 10, 1113–1120.
Spreckelmeyer, K.N., Krach, S., Kohls, G., Rademacher, L., Irmak, A., Konrad, K., Kircher, T., Gründer, G., 2009. Anticipation of monetary and social reward differently activates mesolimbic brain structures in men and women. Soc. Cogn. Affect. Neurosci. 4, 158–165.
Ströhle, A., Stoy, M., Wrase, J., Schwarzer, S., Schlagenhauf, F., Huss, M., Hein, J., Nedderhut, A., Neumann, B., Gregor, A., 2008. Reward anticipation and outcomes in adult males with attention-deficit/hyperactivity disorder. Neuroimage 39, 966–972.
Tang, D.W., Fellows, L.K., Small, D.M., Dagher, A., 2012. Food and drug cues activate similar brain regions: a meta-analysis of functional MRI studies. Physiol. Behav. 106, 317–324.
Tripp, G., Wickens, J.R., 2008. Research review: dopamine transfer deficit: a neurobiological theory of altered reinforcement mechanisms in ADHD. J. Child Psychol. Psychiatry 49, 691–704.
Vacher, C., Goujon, A., Romo, L., Purper-Ouakil, D., 2020. Efficacy of psychosocial interventions for children with ADHD and emotion dysregulation: a systematic review. Psychiatry Res 291, 113151.
van der Oord, S., Tripp, G., 2020. How to improve behavioral parent and teacher training for children with ADHD: integrating empirical research on learning and motivation into treatment. Clin. Child Fam. Psychol. Rev. 23, 577–604.
Watabe-Uchida, M., Zhu, L., Ogawa, S.K., Vamanrao, A., Uchida, N., 2012. Whole-brain mapping of direct inputs to midbrain dopamine neurons. Neuron 74, 858–873.