Reward Processing Deficits During a Spatial Attention Task in Patients With ADHD: An fMRI Study

Baris Metin[1], Zeynep C. Tas[2], Merve Çebi[1], Ayşe Büyükaslan[3], Aysegül Soysal[4], Deniz Hatıloglu[1,4], and Nevzat Tarhan[1]

Abstract

Objective: In this study, we aimed to explore how cues signaling rewards and feedbacks about rewards are processed in ADHD. **Method:** Inside the scanner, 16 healthy children and 19 children with ADHD completed a spatial attention paradigm where cues informed about the availability of reward and feedbacks were provided about the earned reward. **Results:** In ventral anterior thalamus (VA), the controls exhibited greater activation in response to reward-predicting cues, as compared with no-reward cues, whereby in the ADHD group, the reverse pattern was observed (nonreward > reward). For feedbacks; absence of rewards produced greater activation than presence in the left caudate and frontal eye field for the control group, whereas for the ADHD group, the reverse pattern was again observed (reward > nonreward). **Discussion:** The present findings indicate that ADHD is associated with difficulty integrating reward contingency information with the orienting and regulatory phases of attention. *(J. of Att. Dis. XXXX; XX(X) XX-XX)*

Keywords

ADHD, reward processing, spatial attention, fMRI, motivation

Introduction

ADHD is characterized by persistent inattention, and/or hyperactivity and impulsivity. Although the neuropsychological cause of these symptoms is not fully known, motivational theory suggests that deficient reward processing may explain the typical symptoms of ADHD. Accordingly, individuals with ADHD do not properly perceive environmental cues heralding upcoming rewards, especially when such rewards are delayed and behavior is adjusted depending on to the presence or absence of immediate rewards (Sonuga-Barke, Wiersema, van Der Meere, & Roeyers, 2010).

Evidence supporting motivational theory in ADHD comes from a number of studies. Children with ADHD are well known to be easily distracted under low motivation and boring conditions, whereas they can engage in stimulating activities for a long period of time (American Psychiatric Association, 2013; Carlson, Booth, Shin, & Canu, 2002; Imhof, 2004). Such children also cannot tolerate or have an aversion to delayed rewards, which results in the selection of immediately available small rewards over larger delayed reward options (Sonuga-Barke, Taylor, Sembi, & Smith, 1992). For example, when given a choice-delay task in which participants choose between small immediate and large delayed rewards (e.g. 5 cents now vs. 10 cents 30 s later), children with ADHD typically choose the small immediate reward (Metin et al., 2016). Clinically, this "delay aversion" might result in seeking immediate rewards and the inability to tolerate delaying rewards which could contribute to the clinical symptoms such as hyperactivity and impulsivity in ADHD. Moreover, reward processing in ADHD could also have an effect on neuropsychological performance in individuals with ADHD. For instance, individuals with ADHD typically have moderately impaired executive functions, which can be measured via inhibition or working memory tasks (Willcutt, Doyle, Nigg, Faraone, & Pennington, 2005). However, patients with ADHD correct their errors in the classical Go/No-Go task (Kuntsi, Wood, van Der Meere, & Asherson, 2009) and stop-signal reaction time task (Marx, Höpcke, Berger, Wandschneider, & Herpertz, 2013) when reward is available.

[1]Uskudar University, Turkey
[2]Marmara University, Turkey
[3]Istanbul Medeniyet University, Turkey
[4]NPIstanbul Brain Hospital, Turkey

Corresponding Author:
Baris Metin, School of Humanities and Social Sciences, Psychology Department, Uskudar University, Haluk Turksoy Sok., No. 14, 34662, Altunizade, Uskudar, Istanbul, Turkey.
Email: baris.metin@uskudar.edu.tr

Neural responses to the rewarding stimuli in ADHD have been investigated in electrophysiological and fMRI studies. Event-related potential studies reported that children with ADHD have an altered neural response to reward contingencies as compared with healthy controls (Ibanez et al., 2012; van Meel, Heslenfeld, Oosterlaan, Luman, & Sergeant, 2011). In addition, fMRI studies have used a monetary incentive delay (MID) task to explore the neural response associated with reward expectation. Cues during an MID task provide information about a potential reward. Following these cues, targets appear and participants are expected to press a button as quick as they decide, and then feedback on the outcome is provided. The findings from several studies confirm ventral striatal hyporesponsiveness in ADHD patients during the reward anticipation phase following the cues, although a meta-analysis showed that the summary effect size was only moderate (Plichta & Scheres, 2014). Interestingly, a recent study showed that while individuals with ADHD show hyporesponsiveness to reward-predicting stimuli, they show hyperresponsiveness to reward delivery (Furukawa et al., 2014). This result is important in that it lends support to dopamine transfer deficit (DTD) hypothesis (Tripp & Wickens, 2008). According to this hypothesis, individuals with ADHD fail to transfer the phasic dopaminergic response from actual rewards to reward-predicting cues. This deficit results in failure to regulate behavior according to the future reward contingencies and thus leads to a preference for immediate rewards. Despite these studies, direct effect of rewards on task-related networks has not been extensively studied. Liddle et al. (2011) examined the effect of incentives (points earned) on default-mode network (DMN) activity and reported that incentives caused an increase in the DMN suppression in children with ADHD. Rubia et al. (1999) also showed that the presence of rewards caused an increase in orbitofrontal activation in children with ADHD.

In summary, evidence suggests that ADHD is associated with an altered neural response to rewards. Earlier fMRI studies focused primarily on reward anticipation; however, the effect of rewards on individual stages of attention has not been adequately demonstrated. Reward-perception deficit in ADHD might be due to impaired perception of rewards during the early stages of attention such as orienting, or during the regulatory phases. The former deficit is associated with impaired preparatory activity in response to environmental cues, whereas the latter produces abnormal reward-related learning. Taken together, the present study aimed to determine the effect of rewards on different stages of attention based on a spatial attention task and fMRI. The effect of rewards on attention control was evaluated using a spatial attention task in which cues inform about availability of rewards and feedbacks are provided on the amount of reward earned. This task was chosen because it allows to test neural responses to rewards during the orienting (cues) and regulatory control phases of attention, according to feedback. We predicted that children with ADHD would fail to respond reward-predicting cues as much as controls especially in striatum where reward cues are perceived. On the contrary, we also predicted that, in consistency with DTD model, they would show hyperresponsiveness to reward delivery (i.e., feedbacks).

Material and Method

Participants

The study was approved by the local ethics committee, and all parents gave written informed consent. For this study, 19 drug-naïve children with ADHD (combined presentation) were recruited from a university hospital (ADHD group). The diagnosis of ADHD was confirmed using the Schedule for Affective Disorders and Schizophrenia for School-Age Children (Kiddie-Sads-Present and Lifetime Version [K-SADS-PL]) (Kaufmann et al., 1997) by child psychiatrists (Z.C.T. and A.B.). The control group included 21 healthy children who were recruited via word of mouth. The parents of each participant completed the Turgay ADHD questionnaire, which measures 18 ADHD questions found in *DSM* in addition to symptoms of oppositional defiant disorder (ODD) (Ercan, Amado, Somer, & Cikoglu, 2001) in addition to Conners' Parent Rating Scale (Dereboy, Senol, Sener, & Dereboy, 2007). Based on Turgay ADHD scores, three children in the control group were excluded because they had >5 hyperactivity/impulsivity symptoms or >3 ODD symptoms. In addition, two other children in the control group were excluded due to excessive movement (see "Motion Analysis" section). Following these exclusions, final sample consisted of 19 children in the ADHD group and 16 in the control group (see Table 1 for demographic information).
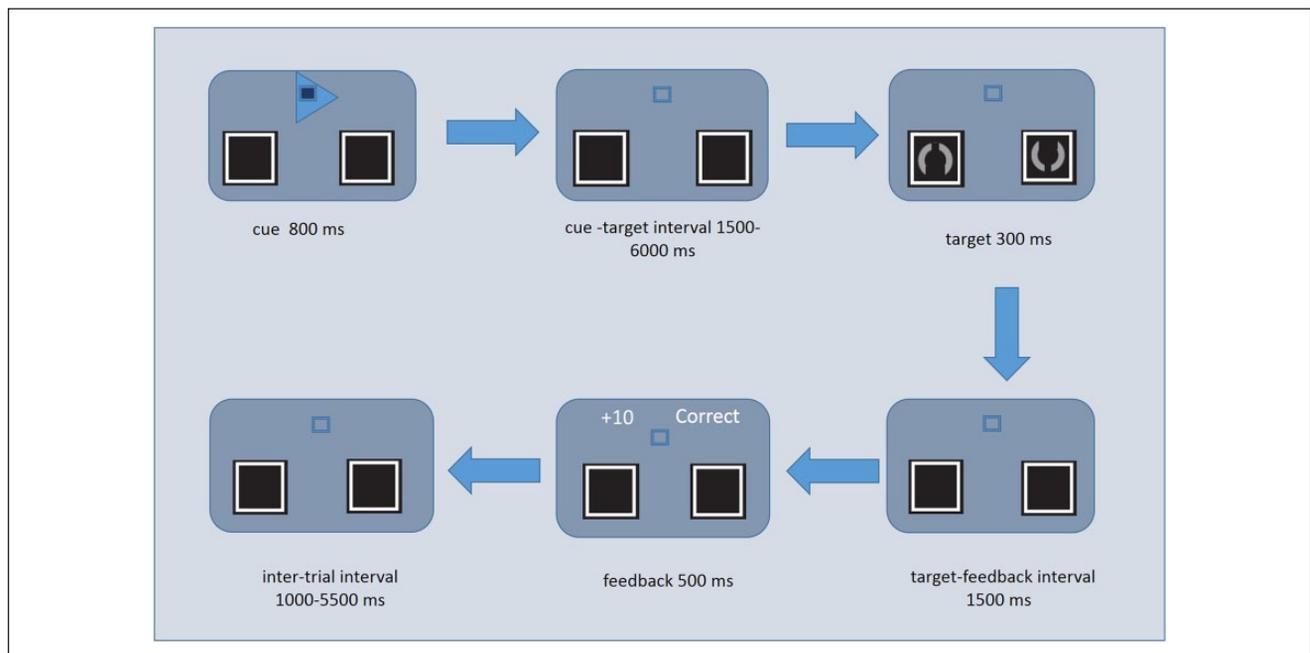
The Spatial Attention Task

Task details and stimulus durations are given in Figure 1. The cued spatial attention task consisted of 96 trials; 50% of the trials yielded a reward if the participant earned a hypothetical 10 points for a correct answer. The order of the trials was the same for all participants. During each trial, the participants had to decide whether the upper or lower gap in a circle (target) was larger. Two circles appeared on a computer screen—one on the left side and one on the right side—and the participants' covert attention was directed to one side (50% of the time to the left and 50% to the right) by a cue (triangle) that appeared before the target. The cues also signaled the presence (triangle with a black square) or absence (triangle with a white square) of rewards. After the target appeared, the participants received feedback informing whether their answer was correct or incorrect, and the reward earned for that trial. During nonrewarded trials, the

Table 1. Demographic Data and Symptom Scale Scores, According to Group.

	ADHD group	Control group	Group difference (*p*)
Age (years)	10.32 (1.95)	10.50 (1.83)	.8
Gender ratio (male:female)	14:5	10:6	.7
IQ	113.53 (20.76)	117.38 (14.01)	.5
Conners inattention score	7.00 (2.60)	1.88 (1.59)	<.001
Conners hyperactivity score	6.32 (2.56)	3.38 (2.6)	.002
Conners' ODD score	9.58 (6.90)	2.44 (2.78)	<.001
Turgay inattention score	17.74 (6.12)	2.44 (3.37)	<.001
Turgay hyperactivity score	13.05 (6.39)	3.44 (2.80)	<.001
Turgay ODD score	7.95 (6.01)	3.69 (2.82)	<.001

Note. ODD = oppositional defiant disorder.

Figure 1. Cued spatial attention paradigm.

participants received feedback informing them only that they earned 0 points for that trial. Incorrect answers did not cause any loss of points both for rewarded or nonrewarded trials. The participants were instructed to earn as many points as possible, as the total points earned would affect the final reward earned. However, regardless of performance, all participants received the same toy as reward at the end. The cue-target interval and inter-trial interval were jittered for effective identification of BOLD signal responses to cues and feedbacks (see Figure 1). The stimuli were presented using an MR compatible LCD monitor located behind the head, and the participants observed the screen via a mirror. Responses were collected using MR compatible pads and conveyed to the computer located outside the scanner room. When the spatial attention task was completed, each participant received the same toy as a reward.

fMRI Acquisition

fMRI was performed using a 1.5 Tesla Philips Achieva scanner (Philips, Best, The Netherlands). First, a high-resolution MPRAGE T1 image (~3.5 min) was acquired (Repetition Time (TR): 8.6 s; Echo Time (TE): 4 ms; Field of View (FoV): 256 × 256; voxel size: 0.94 × 0.94, slice thickness: 1.2 mm; number of slices: 140). During task performance, 315 Echo Planar Imaging (EPI) volumes (~15 min) were acquired (TR: 2.8 s; TE: 50 ms; FoV: 64 × 64; voxel size: 3.6 × 3.6; slice thickness: 3 mm: slice spacing: 3 mm; number of slices: 30).

Table 2. Summary Statistics for Behavioral Performance.

	Reward M (SD)	No-reward M (SD)
ADHD		
% accuracy	78 (20)	78 (18)
MRT	755.61 (179.30)	798.13 (189.46)
Control		
% accuracy	88 (17)	86 (18)
MRT	848.52 (173.86)	867.42 (183.48)

Note. MRT = mean reaction time (ms).

Motion Analysis

All fMRI volumes were analyzed for movement and outliers (https://www.nitrc.org/projects/artifact_detect/). Outliers were defined as any signal >3 standard deviations of the mean or any movement >3 mm. Only two participants from the control group were excluded for having >10% outlier volumes.

fMRI Analysis

fMRI analysis was completed using SPM8 (Wellcome Trust Centre for Neuroimaging, University College, London, UK). SPM segmentation procedure was used for spatial normalization of anatomical scans, and the images were resliced to a voxel size of $1 \times 1 \times 1$ mm. All functional EPIs were slice-time corrected, realigned to the first acquired EPI and normalized based on anatomical scan segmentation parameters, resliced to a final voxel size of $3 \times 3 \times 3$ mm, and preprocessing was finalized with smoothing with an isotropic full-width half-maximum Gaussian kernel of 8 mm. For first-level, analysis a general linear model was constructed with delta functions at stimulus onsets (rewarded cue, nonrewarded cue, rewarded feedback, and nonrewarded feedback), which were subsequently convolved with hemodynamic response functions (HRFs). For second-level analysis, a full-factorial model implemented in SPM8 was used with group as between-subject, and stimulus type (cue and feedback) and reward as within-subject variables. To prevent type I errors that may arise due to multiple comparisons, we used a cluster-extent–based threshold method as recommended by Woo, Krishnan, and Wager (2014). In this procedure, first a primary voxel-based ($p < .001$) threshold is applied. Then, to correct for errors that may arise due to multiple comparisons, a cluster-extent ($N = 9$ voxels) threshold was applied. This threshold is calculated by SPM based on random field theory and the sampling distribution of the largest null cluster size under the null hypotheses of no signal (Woo et al., 2014). On the second step, beta values for clusters showing significant interaction were extracted using MarsBar software (http://marsbar.sourceforge.net/) and were used to compare with behavioral measures using correlation analyses. Significant p value was set to <.05 in this step.

Statistical Analysis

All analyses were completed in SPSS software (Version 24). Reaction time data were analyzed using repeated measures ANOVA with group as reward subject and group as between-subject variables. Accuracy data were analyzed using Mann–Whitney U test due to ceiling effects. Partial correlation analysis was performed with all participants to explore the relationship between BOLD activations and symptom scores. In this analysis, hyperactivity scores were used as a control variable when calculating the correlation coefficient for inattention symptoms and vice versa.

Results

Behavioral Analysis

Accuracy data were analyzed using nonparametric tests (Mann–Whitney U) due to ceiling effects. The ADHD group had fewer correct answers than the control group under both rewarded ($U = 87.5$, $z = 2.14$, $r = .36$, and $p = .03$) and nonrewarded ($U = 95.5$, $z = 1.88$, $r = .32$, and $p = .06$) conditions; however, the reward effect and group by reward interactions were not significant ($p > 0.5$) (see Table 2 for summary statistics). Reaction time data were analyzed using a repeated measures ANOVA with group as a between-subject and reward as a within-subject variable. The two groups did not differ in terms of reaction times, $F(1, 33) = 1.76$, $p = .195$, $= 0.05$. The reward condition yielded significantly faster reaction times than the nonreward condition, $F(1, 33) = 22.89$, $p < .001$, $= 0.41$. The difference between rewarded and nonrewarded reaction times for the patients appeared to be larger, although this difference was not statistically significant, $F = 3.38$; $p = .08$, $= .09$.

fMRI Analysis

The reward main effect was significant in one cluster. Reward cues elicited greater activation in the right caudate nucleus. Reward by group interaction for cues was significant in one cluster in the ventral anterior thalamus (VA; Figure 2). The ADHD group exhibited greater activation in this cluster in response to nonreward cues as compared with reward cues; however, in the control group, there was greater activation in the same cluster in response to reward cues (Figure 3a). Reward by group interaction for feedback was significant (also significant after false discovery rate correction) in a large cluster corresponding to the bilateral frontal eye fields (FEF; Figure 2). The ADHD group had greater activation in response to reward feedback as compared with nonreward feedback, whereas the control group had greater activation in response to nonreward feedback (Figure 3b). Another cluster that exhibited a similar and
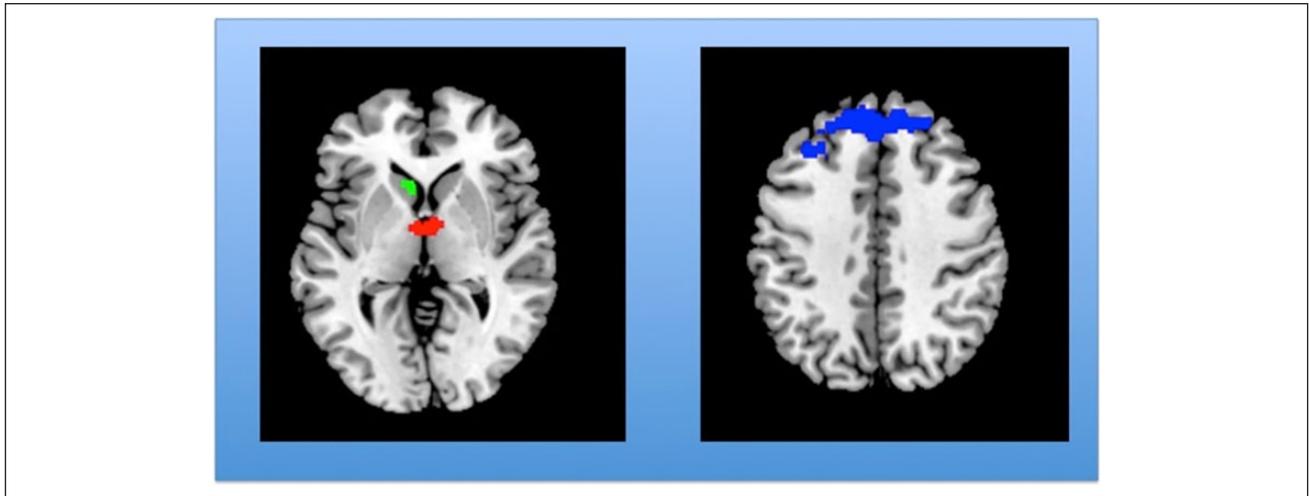
Figure 2. Clusters showing significant interaction effects.
Note. Blue = frontal eye field; red = ventral anterior thalamus; green = caudate nucleus.
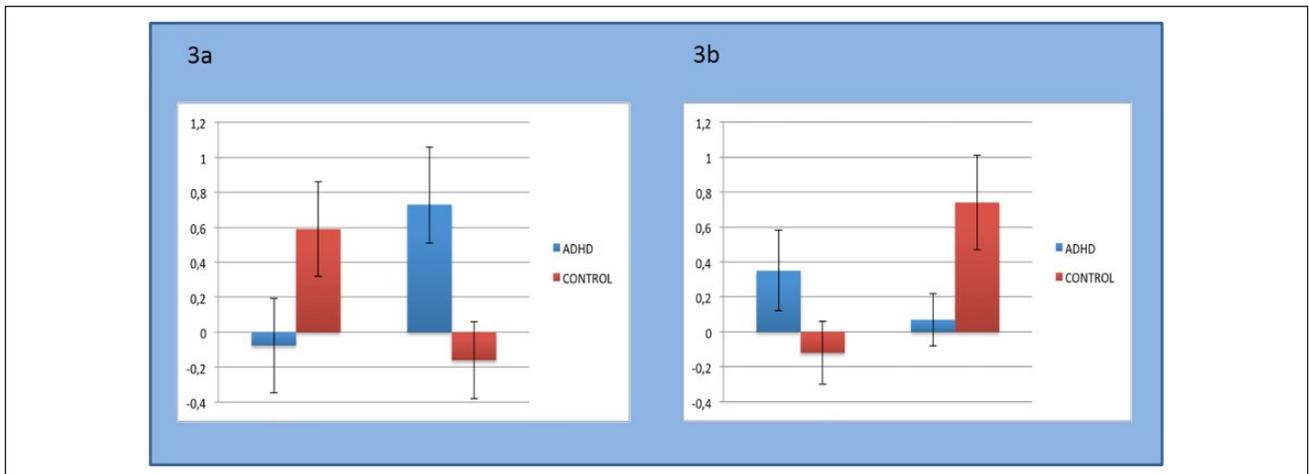

Figure 3. Beta weights in both groups for the (3a) ventral anterior thalamus and (3b) FEF clusters during reward and no-reward conditions.

significant interaction was in the left caudate nucleus. Details of the significant clusters are presented in Table 3.

The difference in activation in the VA between the rewarded and nonrewarded conditions was associated with the Turgay inattention score ($r = -.35$, $p = .04$) (see Figure 4 for scatterplot), and the differences in activations in the FEFs and left caudate nucleus were correlated to the Conners' inattention score ($r = .35$, $p = .04$; $r = .34$, $p = .049$, respectively). However, activation differences and hyperactivity scores were not significantly correlated (Table 4).

Discussion

The present study examined in detail reward-processing deficits in children with ADHD using neuroimaging techniques. In particular, the aim was to determine whether children with ADHD have difficulty perceiving rewards during the orienting and feedback phases of attention. To accomplish this, a cued spatial attention task was used, in which different cues signaled the presence or absence of a reward, and feedback about the reward was provided.

fMRI results showed that, for both groups, the presence of a reward resulted in activation in the right caudate nucleus; in particular, the right caudate nucleus was more active in response to the reward-predicting cues than in response to cues predicting a nonreward trial. Studies have shown that the caudate nucleus is involved in reward processing (Ding & Hikosaka, 2006; Kobayashi et al., 2007; Platt, 2002). These studies reported that information about rewards associated with cues was coded by neurons in the

Table 3. Reward Main Effect and Group by Reward Interaction Effect, Based on Voxel-Wise Whole Brain Analysis.

Main effect: Reward cue > no-reward cue

Region	Brodmann Area (BA)	MNI			T value	Size (voxels)
Right caudate	9	17	1		3.94	11
Interaction effect: Reward cue > no-reward cue, ADHD > control						
VA	6	−4	1		3.88	27
		−3	−7	1		3.51
Interaction effect: Reward FB > no-reward FB, ADHD < control						
FEF	BA8	−6	41	43	4.23	175
	BA8	24	41	43	4.06	
	BA9	6	44	40	3.96	
FEF	BA8	−33	26	43	3.68	12
Left caudate		−6	17	1	3.35	16

Note. Expected voxels per cluster = 9. VA = ventral anterior thalamic nucleus; FB = feedback; FEF = frontal eye field; MNI = Montreal Neurological Institute Coordinates.
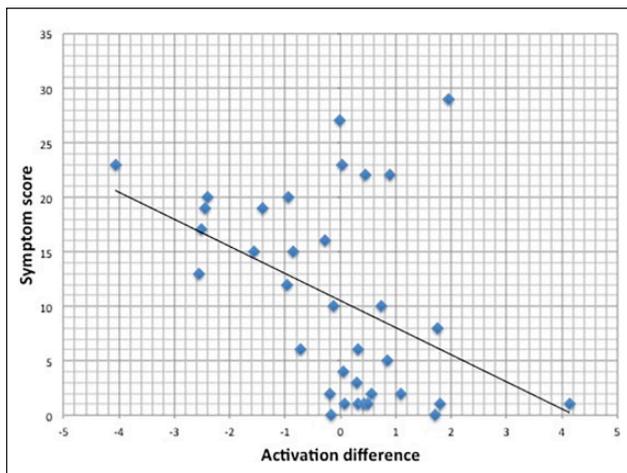

Figure 4. The scatterplot for the correlation between VA activation difference between rewarded and nonrewarded cues and the inattention symptoms.
Note. VA = ventral anterior thalamic nucleus.

caudate nucleus. In addition, an earlier fMRI study that used a task identical to that used in the present study reported similar caudate nucleus findings in healthy adults (Krebs, Boehler, Roberts, Song, & Woldorff, 2012). The present findings, therefore, confirm that the caudate nucleus plays a role in the perception of reward associated with cues during the orienting phase of attention.

For cues, there was also a significant interaction effect for the VA. The interaction indicated that the reward effect was in different directions for two groups. Specifically, activity in the VA was greater in the controls in response to rewarded cues than to nonrewarded cues; however, in the ADHD group, the reverse was observed. The present findings show that children with ADHD might have an altered

preparatory response to rewards during the orienting phase of attention, which might be associated with a deficit in guiding attentional resources according to reward contingencies and may lead to impaired information processing. VA is typically not considered a part of the reward network; however, in an fMRI study, Metzger et al. (2010) showed that this region is specifically involved in motor preparation after cues. Interestingly, according to the state regulation deficit model, the core deficit in ADHD is at the motor preparation phase (see Sonuga-Barke et al., 2010). This motor preparation deficit is particularly evident in event rate tasks, where individuals with ADHD respond slower or less accurately when stimulus presentation speed is suboptimal (Metin, Roeyers, Wiersema, van der Meere, & Sonuga-Barke, 2012). The role of striato-thalamic circuits in motor preparation should be investigated in future studies.

For feedback, there was a group by reward interaction noted in two brain regions. FEF activity was greater in the control group in response to nonreward feedback, whereas in the ADHD group, FEF activity was greater in response to reward-feedback. The FEF is typically responsible for mediating saccades; however, animal studies show that it also responds to reward magnitude during saccade tasks. More importantly, research has shown that the FEF sends modulatory feedback to visual areas, so as to enhance their activity during shifts in covert attention (Gutteling, van Ettinger-Veenstra, Kenemans, & Neggers, 2010; Hamker & Zirnsak, 2006). A similar interaction for feedback was also observed in the left caudate nucleus, an area primarily involved in the perception of rewards. These findings indicate that the children with ADHD had difficulty perceiving reward-associated feedback and integrating this reward information with corticocortical feedback loops that modulate activity in primary sensory areas.

Table 4. Coefficients for Correlations Between Activity Differences and Symptom Scores.

Region	Conners inattention	Conners hyperactivity	Turgay inattention	Turgay hyperactivity
Ventral anterior thalamus	−.30	.03	−.35**	.04
Frontal eye field	.35**	−.29	.27	−.02
Left caudate	.34**	.10	.27	.23

**p < .05.

Moreover, our findings also give important information on neural activity when reward in unavailable. For instance, as can be seen Figure 2, controls showed larger activity than ADHD group in response to nonreward feedback. Interestingly, van Meel et al. (2011) reported absent feedback-related electrophysiological potentials in response to omitted gains and omitted losses in ADHD. Reinforcement learning deficits are frequently reported by both behavioral and electrophysiological studies (Luman, van Meel, Oosterlaan, Sergeant, & Geurts, 2009). Our results suggest that such deficits may occur due to impaired neural responsiveness to environmental feedback signaling the absence of reward.

It is also important to note that differences in activation in the VA, FEF, and caudate nucleus between the rewarded and nonrewarded conditions were significantly correlated with inattention scores, but not hyperactivity scores. According to these findings, it could be concluded that reward-processing deficit during orienting and control phases of attention may be involved in the development of attentional dysfunction. The findings also support motivational accounts of ADHD, according to which motivational deficit resulting from impaired reward processing produces suboptimal regulation of behavior due to insufficient mental effort allocation (van der Meere, Börger, & Wiersema, 2010).

The present study has two limitations. The first is the small study population; however, it should be noted that scanning children is a difficult and time-consuming process. Nevertheless, the present study's population was greater than the average sample size in earlier fMRI studies on ADHD (see Cortese et al., 2014; Plichta & Scheres, 2014). The other limitation is that only the effect of feedback associated with correct trials was evaluated and the error rate was low. This was because the focus was on correct trials in an effort to increase the number of analyzable trials per participant; however, use of a different task with an adjusted and higher error rate might yield different findings regarding responses to rewards associated with feedback. On the contrary, a notable strength of the study is the inclusion of drug-naïve children with ADHD. Recent studies indicate that stimulant use has normalizing effects on brain activations and, therefore, inclusion of children receiving methylphenidate treatment might have reduced the study's statistical power (Schweren, de Zeeuw, & Durston, 2013).

In conclusion, the present findings show that the children with ADHD exhibited deficient integration of reward information during the orienting and feedback phases of attention. Future studies should investigate the role of the striatum, VA, and FEF further in the pathogenesis of ADHD.

References

American Psychiatric Association. (2013). *Diagnostic and statistical manual of mental disorders* (5th ed.). Arlington, VA: American Psychiatric Publishing.

Carlson, C. L., Booth, J. E., Shin, M., & Canu, W. H. (2002). Parent-, teacher-, and self-rated motivational styles in ADHD subtypes. *Journal of Learning Disabilities*, 35, 104-113.

Cortese, S., Kelly, C., Chabernaud, C., Martino, A. D., Milham, M. P., Proal, E., . . . Xavier, F. (2014). Towards systems neuroscience of ADHD: A meta-analysis of 55 fMRI studies. *The American Journal of Psychiatry*, 169, 1038-1055.

Dereboy, C., Senol, S., Sener, S., & Dereboy, F. (2007). Validation of the Turkish versions of the short-form Conners' Teacher and Parent Rating Scales. *Turkish Journal of Psychiatry*, 18, 48-58.

Ding, L., & Hikosaka, O. (2006). Comparison of reward modulation in the frontal eye field and caudate of the macaque. *The Journal of Neuroscience*, 26, 6695-6703.

Ercan, E. S., Amado, S., Somer, O., & Cikoglu, S. (2001). Development of a test battery for the assessment of attention deficit hyperactivity disorder. *Turkish Journal of Child and Adolescent Mental Health*, 8, 132-144.

Furukawa, E., Bado, P., Tripp, G., Mattos, P., Wickens, J. R., Bramati, I. E., … Moll, J. (2014). Abnormal striatal BOLD responses to reward anticipation and reward delivery in ADHD. *PLoS ONE*, 9(2), Article e89129.

Gutteling, T. P., van Ettinger-Veenstra, H. M., Kenemans, J. L., & Neggers, S. F. W. (2010). Lateralized frontal eye field activity precedes occipital activity shortly before saccades: Evidence for cortico-cortical feedback as a mechanism underlying covert attention shifts. *Journal of Cognitive Neuroscience*, *22*, 1931-1943.

Hamker, F. H., & Zirnsak, M. (2006). V4 receptive field dynamics as predicted by a systems-level model of visual attention using feedback from the frontal eye field. *Neural Networks*, *19*, 1371-1382.

Ibanez, A., Cetkovich, M., Petroni, A., Urquina, H., Baez, S., Gonzalez-Gadea, M. L., . . . Manes, F. (2012). The neural basis of decision-making and reward processing in adults with euthymic bipolar disorder or attention-deficit/hyperactivity disorder (ADHD). *PLoS ONE*, *7*(5), Article e37306.

Imhof, M. (2004). Effects of color stimulation on handwriting performance of children with ADHD without and with additional learning disabilities. *European Child & Adolescent Psychiatry*, *13*, 191-198.

Kaufman, J., Birmaher, B., Brent, D., Rao, U., Flynn, C., Moreci, P., . . . Ryan, N. (1997). Schedule for affective disorders and schizophrenia for school-age children-present and lifetime version (K-SADS-PL): Initial reliability and validity data. *Journal of the American Academy of Child & Adolescent Psychiatry*, *36*, 980-988.

Kobayashi, S., Kawagoe, R., Takikawa, Y., Koizumi, M., Sakagami, M., & Hikosaka, O. (2007). Functional differences between macaque prefrontal cortex and caudate nucleus during eye movements with and without reward. *Experimental Brain Research*, *176*, 341-355.

Krebs, R. M., Boehler, C. N., Roberts, K. C., Song, A. W., & Woldorff, M. G. (2012). The involvement of the dopaminergic midbrain and cortico-striatal-thalamic circuits in the integration of reward prospect and attentional task demands. *Cerebral Cortex*, *22*, 607-615.

Kuntsi, J., Wood, A. C., van Der Meere, J., & Asherson, P. (2009). Why cognitive performance in ADHD may not reveal true potential: Findings from a large population-based sample. *Journal of the International Neuropsychological Society*, *15*, 570-579.

Liddle, E. B., Hollis, C., Batty, M. J., Groom, M. J., Totman, J. J., Liotti, M., . . . Liddle, P. F. (2011). Task-related default mode network modulation and inhibitory control in ADHD: Effects of motivation and methylphenidate. *Journal of Child Psychology and Psychiatry*, *52*, 761-771.

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 Research*, *168*, 222-229.

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*(6), Article e67002.

Metin, B., Roeyers, H., Wiersema, J. R., van der Meere, J. J., Gasthuys, R., & Sonuga-Barke, E. J. S. (2016). Environmental stimulation does not reduce impulsive choice in ADHD: A "pink noise" study. *Journal of Attention Disorders*, *20*, 63-70.

Metin, B., Roeyers, H., Wiersema, J. R., van der Meere, J., & Sonuga-Barke, E. (2012). A meta-analytic study of event rate effects on go/no-go performance in attention-deficit/hyperactivity disorder. *Biological Psychiatry*, *72*, 990-996.

Metzger, C. D., Eckert, U., Steiner, J., Sartorius, A., Buchmann, J. E., Stadler, J., . . . Walter, M. (2010). High field FMRI reveals thalamocortical integration of segregated cognitive and emotional processing in mediodorsal and intralaminar thalamic nuclei. *Frontiers in Neuroanatomy*, *4*, Article 138. doi:10.3389/fnana.2010.00138

Platt, M. L. (2002). Caudate clues to rewarding cues. *Neuron*, *33*, 316-318.

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. *Neuroscience & Biobehavioral Reviews*, *38*, 125-134.

Rubia, K., Overmeyer, S., Taylor, E., Brammer, M., Williams, S. C., Simmons, A., & Bullmore, E. T. (1999). Hypofrontality in attention deficit hyperactivity disorder during higher-order motor control: A study with functional MRI. *The American Journal of Psychiatry*, *156*, 891-896.

Schweren, L. J. S., de Zeeuw, P., & Durston, S. (2013). MR imaging of the effects of methylphenidate on brain structure and function in attention-deficit/hyperactivity disorder. *European Neuropsychopharmacology*, *23*, 1151-1164.

Sonuga-Barke, E. J. S., Taylor, E., Sembi, S., & Smith, J. (1992). Hyperactivity and delay aversion—I. The effect of delay on choice. *Journal of Child Psychology and Psychiatry*, *33*, 387-398.

Sonuga-Barke, E. J. S., Wiersema, J. R., van Der Meere, J. J., & Roeyers, H. (2010). Context-dependent dynamic processes in attention deficit/hyperactivity disorder: Differentiating common and unique effects of state regulation deficits and delay aversion. *Neuropsychology Review*, *20*, 103-120.

Tripp, G., & Wickens, JR. (2008). Research review: dopamine transfer deficit: a neurobiological theory of altered reinforcement mechanisms in ADHD. *Journal of Child Psychology and Psychiatry, 49*(7),691-704

van der Meere, J. J., Börger, N. A., & Wiersema, J. R. (2010). ADHD: State regulation and motivation. *CML: Psychiatry*, *21*, 14-20.

van Meel, C. S., Heslenfeld, D. J., Oosterlaan, J., Luman, M., & Sergeant, J. A. (2011). ERPs associated with monitoring and evaluation of monetary reward and punishment in children with ADHD. *Journal of Child Psychology and Psychiatry*, *52*, 942-953.

Willcutt, E. G., Doyle, A. E., Nigg, J. T., Faraone, S. V., & Pennington, B. F. (2005). Validity of the executive function theory of attention-deficit/hyperactivity disorder: A meta-analytic review. *Biological Psychiatry*, *57*, 1336-1346.

Woo, C. W., Krishnan, A., & Wager, T. D. (2014). Cluster-extent based thresholding in fMRI analyses: Pitfalls and recommendations. *NeuroImage*, *91*, 412-419.

Author Biographies

Baris Metin is an associate professor of neurology and has a PhD in psychology. He is conducting research on ADHD and neuroimaging of neuropsychiatric disorders.

Zeynep C. Tas is a Child and Adolescent psychiatrist. She completed her residency training in Germany, LVR Clinics-Bedburg-Hau. As a clinician her special area of interest is the neuropsychology of autism and ADHD.

Merve Çebi received a BA degree in psychology and MSc degree in neuroscience. She has been a PhD student in advanced neurological sciences since 2013. Her research interests include neuroimaging of neurodegenerative and neuropsychiatric disorders, neuropsychology, and aging.

Ayşe Büyükaslan is a Child and Adolescent psychiatrist working at Medeniyet University in Istanbul, Turkey. She conducted research on emotional and social intelligence in children with ADHD.

Aysegül Soysal, MSc, is a clinical psychologist working mainly with children and adolescents with ADHD. Her research interests are in the following areas: neuroimaging, ADHD and neuropsychology.

Deniz Hatiloglu is the head of radiology department at NPIstanbul Brain Hospital and is an assistant professor teaching in Imaging Techniques and Radiotherapy programs at Uskudar University. Her research interest is neuroradiology.

Nevzat Tarhan is a professor of psychiatry. He is also the founder and the president of Uskudar University. His research interests include neuroimaging of psychiatric disorders, applying brain mapping techniques for developing biomarkers, precision medicine and transcranial magnetic stimulation.