Ventral Striatal Hyporesponsiveness During Reward Anticipation in Attention-Deficit/Hyperactivity Disorder

Anouk Scheres, Michael P. Milham, Brian Knutson, and Francisco Xavier Castellanos

Background: Although abnormalities in reward processing have been proposed to underlie attention-deficit/hyperactivity disorder (ADHD), this link has not been tested explicitly with neural probes.

Methods: This hypothesis was tested by using fMRI to compare neural activity within the striatum in individuals with ADHD and healthy controls during a reward-anticipation task that has been shown previously to produce reliable increases in ventral striatum activity in healthy adults and healthy adolescents. Eleven adolescents with ADHD (5 off medication and 6 medication-naïve) and 11 healthy controls (ages 12–17 y) were included. Groups were matched for age, gender, and intelligence quotient.

Results: We found reduced ventral striatal activation in adolescents with ADHD during reward anticipation, relative to healthy controls. Moreover, ventral striatal activation was negatively correlated with parent-rated hyperactive or impulsive symptoms across the entire sample.

Conclusions: These findings provide neural evidence that symptoms of ADHD, and impulsivity or hyperactivity in particular, may involve diminished reward anticipation, in addition to commonly observed executive dysfunction.

Key Words: Attention-deficit/hyperactivity disorder, ADHD, fMRI, impulsivity, reward, striatum

ADHD is a common behavioral disorder characterized by excessive inattention, hyperactivity, and impulsivity (American Psychiatric Association 1994). Functional imaging studies that have focused on executive function report that children with ADHD show inefficient recruitment of frontal-striatal regions during response inhibition (e.g., Casey et al 1997; Durston et al 2003; Konrad et al 2006; Rubia et al 1999; for a review see Bush et al 2005). However, only a subgroup of children with ADHD shows poor response inhibition (see Nigg 2005). Although many children with ADHD are characterized by an unwillingness to delay gratification (Luman et al 2005), incentive processing in ADHD has received less investigation. For instance, it is not clear whether children with ADHD show hyper- or hyporesponsiveness to rewarding incentives, both behaviorally (Luman et al 2005; Scheres et al 2001; Tripp and Alsop 1999) and neurally (see Sagvolden et al 2005). Solanto et al (2001) showed that preference for sooner but smaller rewards explained more variance in ADHD symptoms than poor response inhibition, and that reward preferences and inhibitory deficits did not correlate. On the basis of these findings, Sonuga-Barke (2002) proposed that both executive–inhibitory and motivational–reward pathways can lead to ADHD (see also Castellanos and Tannock 2002). In addition, animal models of ADHD implicate abnormalities in mesolimbic reward circuits projecting from midbrain ventral tegmentum to subcortical areas including ventral striatum (Carboni et al 2003; Johansen et al 2002; Viggiano et al 2004). Suggested alterations in striatal dopamine transporter density in patients with ADHD (Spencer et al 2005) also support the potential relevance of this circuitry. However, the responsiveness of mesolimbic reward circuitry has yet to be directly examined in ADHD.

Methods and Materials

The study was approved by the institutional review boards of New York University School of Medicine and Faculty of Arts and Science, and all participants provided prior written informed assent or consent. The sample consisted of 11 adolescents with ADHD (5 off medication on the scan day and 6 medication-naïve) and 11 matched healthy controls. Groups did not differ significantly in gender, age, intelligence quotient, achievement level, or handedness (Table 1; one lefthander per group). Participants performed the event-related Monetary Incentive Delay task (Knutson et al 2001), which explicitly elicits ventral striatal activation related to the anticipation of responding for potential monetary rewards. Trials consisted of five parts: cues, variable anticipatory delays, targets, responses, and outcome. Cues signaled the opportunity to either win money (gain trials) or avoid losing money (loss-avoidance trials) by responding with a button press during subsequent target presentation (Figure 1). Control trials also required a button press, but cues signaled that no money would be won or lost, regardless of response speed. Target durations varied individually so that responses would occur within target duration and lead to gain or loss avoidance on ~66% of all trials, thus obviating potential group differences in performance (see Supplement Methods and Results). After each response, participants were informed whether they had won or not (gain trials) or lost or not (loss-avoidance trials),...
and the total cumulative amount was updated. After task completion, participants were paid their earnings in cash.

Because of our specific hypotheses, our primary analyses focused on changes in striatal blood oxygen level-dependent (BOLD) signal contrast occurring immediately after cue presentation. First, random-effect analyses were run for each group separately by time-course contrasts between gain trials and control trials with hemodynamically convolved models. Next, for striatal regions found to be active in either group (minimum cluster size 2 functional voxels of $3 \times 3 \times 4$ mm each), we performed separate analyses of variance (ANOVAs) for gain and loss-avoidance trials with group as a between-subject factor, and increase in BOLD signal (parameter estimates) across dollar amounts, following the cue as the dependent variable (see Supplement Methods). To determine specificity of striatal activation in association with reward anticipation, ANOVA with valence as within-subject factor and group as between-subject factor was conducted as well. To determine specificity of striatal activation in association with reward anticipation, we also conducted this ANOVA for outcome, controlling for anticipation (Figure 1). Full-brain analyses for each group contrasting BOLD signal immediately after cue presentation for gain trials versus control trials are reported in the Supplementary Results (Supplements 1 and 2).

In addition to the categorical group analysis, we treated ADHD dimensionally. Specifically, for striatal regions found to be active in either group, we computed two partial correlations between striatal activation and ADHD symptoms across the sample (the mean T score of all Conners’ parent rating scale [CPRS] ADHD scales): one while controlling for symptoms of inattention (the mean T-score of all CPRS inattention scales) and one while controlling for symptoms of hyperactivity and impulsivity (the mean T-score of all CPRS hyperactivity and impulsivity scales).

### Results

Groups did not differ significantly for any performance measure: overall hit rates were .60 and .58 for ADHD and control groups, respectively (see Supplement Methods and Results).

Random effects analyses revealed increases in VS activation associated with reward anticipation in healthy adolescents (reward > no reward, threshold: $p < .0001$, uncorrected; right VS: $x = 10, y = 9, z = 2$; left VS: $x = -12, y = 5, z = 3$), with larger monetary amounts producing larger increases. These activation foci are within 1–6 mm of those reported by Knutson and colleagues (Bjørk et al. 2004; Knutson et al. 2001). We report and display results for right VS (rVS) here, but note that the data for left VS yield similar results.

Consistent with models implicating VS dysfunction in ADHD, within-group analysis for the ADHD group did not reveal statistically detectable increases in VS activation when reward trials were compared with nonreward trials (Figure 2A). It is important to note that between-group analysis further supported this finding: the ADHD group showed significantly less rVS activation during reward anticipation relative to the control group [$F(1,20) = 5.6, p < .05$], but not during anticipation of loss avoidance [$F(1,20) = .72$, ns]. A significant group by valence interaction for increases in BOLD signal across dollar amounts [$F(1,20) = 5.5, p < .05$] further supported the specificity of the group difference for reward trials (Figure 2B). Although rVS activation during both reward anticipation and anticipation of loss avoidance to some extent (Figure 2B), a main effect of valence [$F(1,20) = 16.1, p < .01$] indicated that anticipatory rVS activation was related more strongly to reward anticipation than to anticipation of loss avoidance. Reductions in rVS activation related to ADHD appeared to be specifically related to anticipation of rewards rather than outcomes as well, because ANOVA revealed no group differences for rVS activation during receipt of increasing dollar amounts (Figure 2C).

As hypothesized, dimension analysis revealed that lower levels of VS activation during reward anticipation (averaged across reward amounts) were associated with higher levels of hyperactivity or impulsivity after adjusting for inattention ($r = -.45, p < .05$ [2 tailed]; Figure 3) but not with inattention after adjusting for hyperactivity or impulsivity ($r = .03$, ns).

### Discussion

We found decreased ventral striatal activation in adolescents with ADHD during reward anticipation, which correlated with symptoms of hyperactivity or impulsivity. These results provide neural evidence to support the hypothesis that the salience of anticipated rewards is diminished in ADHD (Johansen et al. 2002; Volkow et al. 2004). However, neural hyporesponsiveness to anticipated reward is not necessarily equivalent to behavioral hyporesponsiveness. In fact, neural hyporesponsiveness to anticipated reward may provoke increased reward-seeking behav-

![Image](https://example.com/image.png)

### Table 1. Group Characteristics

<table>
<thead>
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<th></th>
<th>ADHD $n = 11 (9)$</th>
<th>Controls $n = 11 (8)$</th>
<th>M</th>
<th>SD</th>
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<th>SD</th>
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<td>Age</td>
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<td>1.6</td>
<td>13.9</td>
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<td>105.3 19.3</td>
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<td>102.9 17.4</td>
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<tr>
<td>Wechsler Individual Achievement Test: average T score</td>
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<td>100.2 20.5</td>
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<td></td>
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<td></td>
</tr>
</tbody>
</table>

ADHD, attention-deficit/hyperactivity disorder; IQ, intelligence quotient.

*Number of males.

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ior, as a means of compensating for relatively low levels of VS activation (Robbins and Everitt 1999). This may provide one account for the observed association between low VS activation and symptoms of impulsivity or hyperactivity. Impulsivity has been associated previously with increased reward-seeking behavior (American Psychiatric Association 1994; Monterosso and Ainslie 1999), as has addiction (Reuter et al 2005; Robbins and Everitt 1999). Thus, diminished neural reward anticipation may contribute to ADHD’s status as a risk factor for substance abuse (Wilens 2004). Similarly, some theorists have interpreted substance abuse in ADHD as a form of self-medication and have suggested that treatment with psychostimulants may decrease the risk for substance abuse in ADHD (Wilens 2004).

Reduced VS activation in adolescents with ADHD is unlikely to reflect differences in learning about the association between cue and outcome, because all participants correctly reported what each cue signaled after practicing the task before scanning, and groups did not significantly differ in any behavioral performance parameter. Moreover, groups did not differ in terms of outcome-related activity in VS. Similarly, reduced VS activation in adolescents with ADHD was not related to performance, because no group differences or group by incentive magnitude interactions were found for any of the behavioral measures. Instead, the current findings may provide neural support for common clinical observations that children with ADHD require more consistent delivery of rewards to shape their behavior (Barkley 2002).

The lack of a group difference or a group by reward magnitude interaction for behavioral performance may appear to be inconsistent with the diminished salience interpretation of the fMRI data. However, diminished reward anticipation need not necessarily be accompanied by poorer performance—in fact, the MID task is designed to dissociate the two (Knutson et al 2001). Group differences in performance may have been present during task practice before scanning (60 trials). Future ADHD studies might administer this task in the scanner without practice and

![Figure 1. Task design and regressors of interest.](Image)

**Figure 1.** Task design and regressors of interest.

![Figure 2. Impact of reward anticipation and outcome on ventral striatum (VS) activity.](Image)

**Figure 2.** Impact of reward anticipation and outcome on ventral striatum (VS) activity.
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Supplementary material cited in this article is available online.


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**Figure 3.** Correlation between hyperactivity or impulsivity and right ventral striatum (VS) activation.


