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

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**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/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:** ADHD, Attention-deficit/hyperactivity disorder, 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.

Here, we test this association by using fMRI to compare neural activity in ADHD and healthy controls during a reward anticipation task previously shown to produce reliable increases in ventral striatum (VS) activity in both healthy adults (Knutson et al 2001) and healthy adolescents (Björk et al 2004). We hypothesized that children with ADHD would differ in the extent of striatal activation during reward anticipation. In addition, considering symptoms of ADHD dimensionally (Levy et al 1997), we investigated the association between ADHD symptom clusters and striatal activation during reward anticipation. On the basis of findings that ventral striatum-lesioned rats demonstrate symptoms of hyperactivity/impulsivity but not inattention (Cardinal et al 2001), we hypothesized that ventral striatal activation would be specifically negatively associated with symptoms of hyperactivity/impulsivity, but not with symptoms of inattention.

## 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 left-hander 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

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Received November 14, 2005; revised April 13, 2006; accepted April 18, 2006.

0006-3223/07/$32.00
doi:10.1016/j.biopsych.2006.04.042

**Table 1.** Group Characteristics

| | ADHD $n = 11$ (9)[a] | | Controls $n = 11$ (8)[a] | | |
|---|---|---|---|---|---|
| | M | SD | M | SD | *p* |
| Age | 14.3 | 1.6 | 13.9 | 1.4 | ns |
| Wechsler Abbreviated Scale of Intelligence | | | | | |
| Verbal IQ | 100.9 | 11.4 | 105.3 | 19.3 | ns |
| Performance IQ | 102.6 | 10.9 | 99.9 | 13.1 | ns |
| Estimated full-scale IQ | 102.3 | 12.0 | 102.9 | 17.4 | ns |
| Wechsler Individual Achievement Test: average T score | 104.2 | 10.5 | 100.2 | 20.5 | ns |
| Conners' Parent Rating Scale | | | | | |
| Oppositional | 68.5 | 13.0 | 53.7 | 12.3 | <.05 |
| Inattention | 67.6 | 9.7 | 53.1 | 9.3 | <.01 |
| Hyperactive | 74.5 | 11.6 | 50.5 | 5.2 | <.01 |
| Anxious | 54.7 | 13.7 | 52.0 | 5.8 | ns |
| Perfectionism | 56.1 | 10.5 | 46.0 | 6.5 | <.05 |
| Social problems | 55.9 | 10.3 | 48.0 | 5.9 | <.05 |
| Psychosomatic | 60.6 | 14.5 | 49.9 | 8.5 | <.05 |
| ADHD index | 69.6 | 12.3 | 51.6 | 8.3 | <.01 |
| Global index restless–impulsive | 70.6 | 12.5 | 49.6 | 7.2 | <.01 |
| Global index emotional | 63.9 | 14.4 | 50.0 | 10.3 | <.05 |
| Global index total | 70.2 | 12.6 | 49.5 | 8.5 | <.01 |
| DSM-IV inattentive | 70.9 | 11.6 | 52.1 | 7.7 | <.01 |
| DSM-IV hyperactive | 68.6 | 13.9 | 52.9 | 7.1 | <.01 |
| DSM-IV total | 73.7 | 11.8 | 52.6 | 6.9 | <.01 |
| Child Behavior Checklist | | | | | |
| Anxious/depressed | 62.4 | 12.9 | 51.7 | 3.2 | <.05 |
| Withdrawn | 56.3 | 6.2 | 56.1 | 5.2 | ns |
| Somatic complaints | 58.5 | 8.5 | 55.9 | 6.3 | ns |
| Social problems | 60.7 | 10.7 | 54.9 | 5.2 | ns |
| Thought problems | 61.7 | 10.9 | 54.6 | 6.3 | ns |
| Attention problems | 65.5 | 10.6 | 54.0 | 3.6 | <.01 |
| Rule breaking | 59.9 | 7.5 | 54.0 | 4.1 | <.05 |
| Aggressive | 64.9 | 15.3 | 53.5 | 4.5 | <.05 |

ADHD, attention-deficit/hyperactivity disorder; IQ, intelligence quotient.
[a]Number of males.

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

## Discussion

We found decreased ventral striatal activation in adolescents with ADHD during reward anticipation, which correlated with symptoms of hyperactivity/impulsivity. These results provide neural evidence to support the hypothesis that the salience of

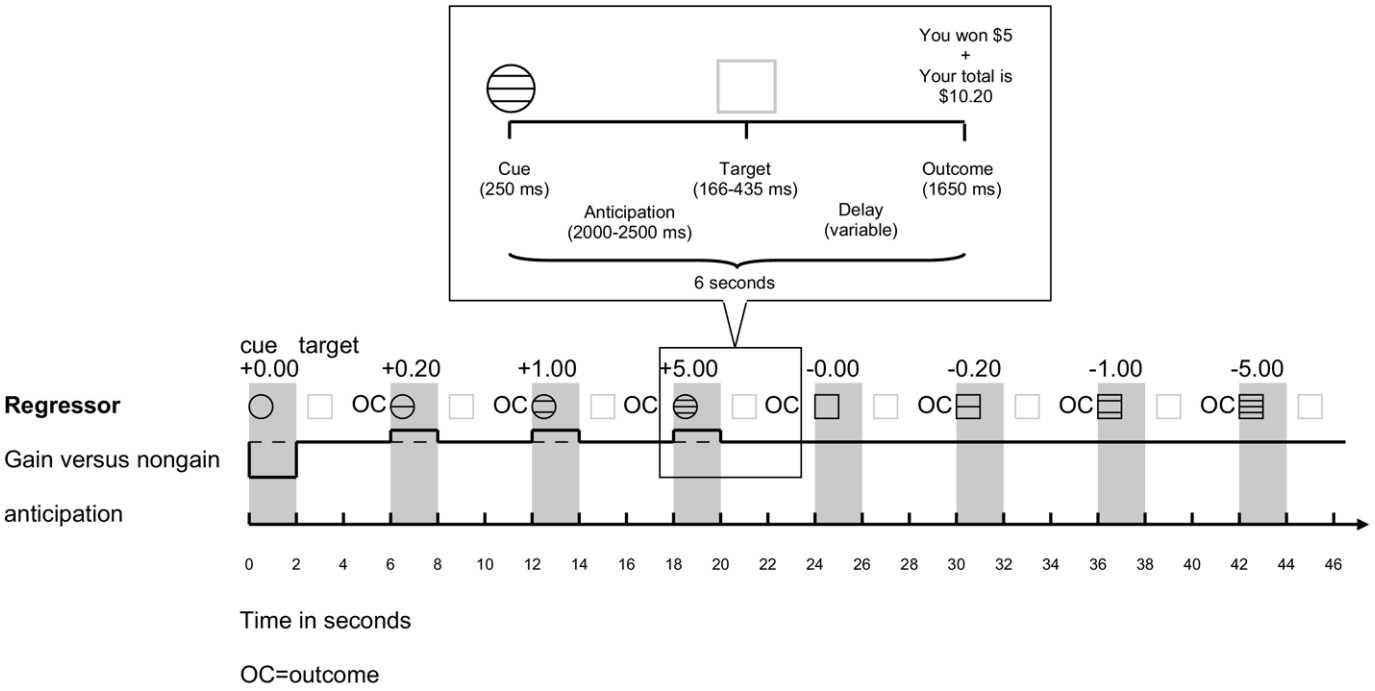


**Figure 1.** Task design and regressors of interest.

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 behavior, 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

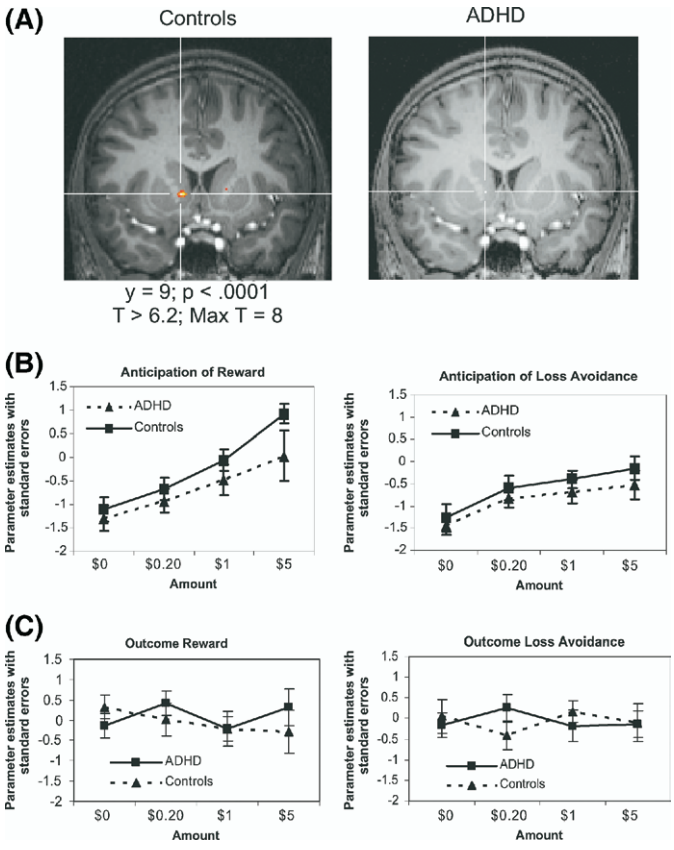


**Figure 2.** Impact of reward anticipation and outcome on ventral striatum (VS) activity.

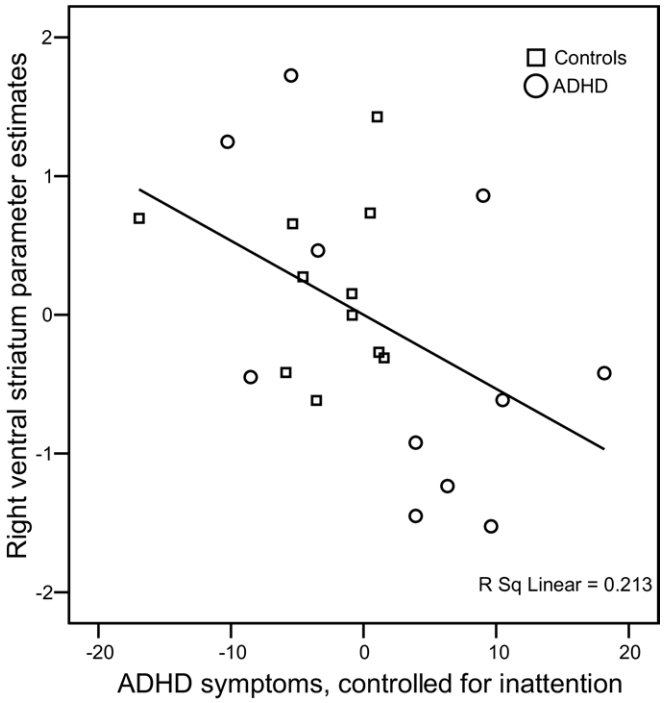


**Figure 3.** Correlation between hyperactivity/impulsivity and right ventral striatum (VS) activation.

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 track VS activation as participants learn the association between cues and outcomes (Galvan et al 2005).

The principal limitation of this study is related to the modest sample size, which may have minimized the ability to detect subtle group differences during anticipation of loss avoidance and which did not allow separate analysis of the potential effects of recent discontinuation of stimulant medications. However, visual inspection of the time course data suggests that discontinuation cannot account for our observed group differences. Still, replication of this study in larger, completely medication-naïve samples will be important and will provide opportunity to further explore this potential index of ADHD.

This study was designed to provide an initial glimpse into the relevance of mesolimbic circuitry to ADHD. If replicated, these results may complement findings suggesting inefficient recruitment of frontostriatal networks during executive functioning in ADHD (Bush et al 2005), and reduced activation in lateral PFC during gambling in ADHD (Ernst et al 2003). The present findings underscore the need to neurally disentangle executive function from reward processing. They further suggest that ADHD may involve abnormalities not only in executive neural pathways but also in motivational neural pathways (Sonuga-Barke 2002).

*This work was supported by National Institute of Mental Health Grant No. MH0660393. FXC received research support from McNeil Consumer and Specialty Pharmaceuticals.*

*We gratefully acknowledge Marianne Dijkstra, Eleanor Ainslie, Jaclyn Balkan, Adriana Di Martino, and Amy Krain for their help in data collection; Keith Sanzenbach for technical support; Armin Heinecke and Catharyn Crane for assistance with data analyses; Lori Evans, Vilma Gabbay, Glenn Hirsch, Mark Krusbelnycky, Steven Kurtz, Melvin Oatis, and Maurizio Zambenedetti for assistance in recruiting participants; Alan Sanfey for helpful comments; and most of all, the participants and their parents.*

*Supplementary material cited in this article is available online.*

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