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ORIGINAL ARTICLE

Motivation deficit in ADHD is associated with dysfunction of the dopamine reward pathway

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Attention-deficit hyperactivity disorder (ADHD) is typically characterized as a disorder of inattention and hyperactivity/impulsivity but there is increasing evidence of deficits in motivation. Using positron emission tomography (PET), we showed decreased function in the brain dopamine reward pathway in adults with ADHD, which, we hypothesized, could underlie the motivation deficits in this disorder. To evaluate this hypothesis, we performed secondary analyses to assess the correlation between the PET measures of dopamine D2/D3 receptor and dopamine transporter availability (obtained with [^{11}C]raclopride and [^{11}C]cocaine, respectively) in the dopamine reward pathway (midbrain and nucleus accumbens) and a surrogate measure of trait motivation (assessed using the Achievement scale on the Multidimensional Personality Questionnaire or MPQ) in 45 ADHD participants and 41 controls. The Achievement scale was lower in ADHD participants than in controls (11 ± 5 vs 14 ± 3, $P < 0.001$) and was significantly correlated with D2/D3 receptors (accumbens: $r = 0.39$, $P < 0.008$; midbrain: $r = 0.41$, $P < 0.005$) and transporters (accumbens: $r = 0.35$, $P < 0.02$) in ADHD participants, but not in controls. ADHD participants also had lower values in the Constraint factor and higher values in the Negative Emotionality factor of the MPQ but did not differ in the Positive Emotionality factor—and none of these were correlated with the dopamine measures. In ADHD participants, scores in the Achievement scale were also negatively correlated with symptoms of inattention (CAARS A, E and SWAN I). These findings provide evidence that disruption of the dopamine reward pathway is associated with motivation deficits in ADHD adults, which may contribute to attention deficits and supports the use of therapeutic interventions to enhance motivation in ADHD.
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Introduction

Attention-deficit hyperactivity disorder (ADHD) is the most recognized and treated psychiatric disorder of childhood[1] and it is increasingly recognized and treated in adults.[2] ADHD is characterized by symptoms of inattention and/or hyperactivity/impulsivity that produce impairment across cognitive, behavioral and interpersonal domains of function.[1] However, the hypothesis that there is a dysfunction in reward and motivation was proposed more than two decades ago[3] and there is increasing evidence that this has a role in ADHD.[3,4] For example, children with ADHD require stronger incentives to modify their behavior than those without ADHD,[5] they also show a failure to delay gratification, have impaired responses to partial schedules of reinforcement and preference for small immediate rewards over larger delayed rewards.[6,7]

The mesoaccumbens dopamine (DA) pathway, which projects from the ventral tegmental area in midbrain to the nucleus accumbens (NAcc) in the ventral striatum, is critically involved in reward and motivation,[8] and has been hypothesized to underlie the reward and motivational deficits observed in ADHD.[6,9] Indeed, using positron emission tomography (PET) we showed lower than normal availability of DA D2/D3 receptors (measured with [^{11}C]raclopride) and of DA transporters (DAT; measured with [^{11}C]cocaine) in the midbrain and in NAcc in drug-naive ADHD participants compared with non-ADHD control subjects.[10] Here we report on secondary analyses that were performed on a subset of subjects

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in whom we had collected personality measures, including trait measures of motivation, to test the hypothesis that disruption of the DA reward pathway is associated with the motivation deficit in ADHD.

For this purpose, we measured the correlations between our PET measures of D2/D3 receptors and DAT in the DA reward pathway (midbrain and NAcc) and questionnaire measures of trait motivation in drug-naive ADHD participants and group-matched controls. DA D2/D3 receptor availability was measured with [^{11}C]raclopride[11] and DAT availability was measured with [^{11}C]cocaine.[12] The Multidimensional Personality Questionnaire (MPQ),[13] obtained in 45 ADHD participants (never medicated) and 41 controls, was used to obtain scores on the Achievement scale, which was used as a surrogate trait measure of motivation. The Achievement scale of the MPQ evaluates a motivational disposition that comprises social dominance, enthusiasm, energy, assertiveness, ambitiousness and achievement striving. We hypothesized that the deficits in the DA reward pathway in ADHD participants would be associated with lower scores in the Achievement scale (surrogate trait measure of motivation), and that lower scores in this surrogate measure of motivation would predict more severe ADHD symptoms.

Materials and methods

Participants

Attention-deficit hyperactivity disorder participants were recruited from the ADHD programs at Duke University, Mount Sinai Medical Center and UC Irvine, and controls were recruited from advertisements in local newspapers at Brookhaven National Laboratory. The study included 45 never medicated ADHD participants (23 men; 32 ± 8 years of age; 16 ± 2 years of education; body mass index 26 ± 5) and 41 healthy controls (28 men, 31 ± 5 years of age; 15 ± 2 years of education; body mass index 25 ± 3) from an imaging study that measured group differences in DA D2/D3 receptor and DAT availability.[10] Details on subject inclusion and exclusion criteria have been described.[10] Briefly, inclusion criteria for ADHD participants were: *Diagnostic and Statistical Manual of Mental Disorders*, fourth edition (DSM-IV) diagnostic criteria for ADHD, presence of at least six of nine inattention symptoms (ascertained with semi-structured psychiatric interviews), evidence that some symptoms of ADHD started during childhood (before age 7) and a Clinical Global Impressions Severity scale[14] rating of 4 or greater. Exclusion criteria were history of substance abuse (other than nicotine; three ADHD participants and one control were active smokers) or a positive urine drug screen during assessment, previous or current treatment with psychotropic medications (including stimulants), psychiatric comorbidities (axis I or II diagnosis other than ADHD), neurological disease, medical conditions that may alter cerebral function (that is, cardiovascular, endocrinological, oncological or autoimmune diseases) or head trauma with loss of consciousness (>30 min). Controls met the same exclusion criteria but not the inclusion criteria for diagnosis of ADHD and were excluded if they described symptoms of inattention or hyperactivity that interfered with their everyday activities.

Clinical scales

In addition to the categorical assessment of symptom severity by interview and questionnaires, we assessed the underlying traits of the two DSM-IV domains of attention and activity/reflectivity using the Strengths and Weaknesses of ADHD-symptoms and Normal-behavior (SWAN). The SWAN uses a seven-point scale (−3 to +3) to represent the full range of these dimensions in the population, with average behavior as a reference point (zero).[15] The SWAN scores traits that are below average and represent severity of psychopathology on a positive scale (from 1 to 3), and traits above average on a negative scale (from −1 to −3). The SWAN was completed in 37 of the controls and 39 of the ADHD participants. We also obtained standard assessments of symptom severity with the Conners Adult ADHD Rating Scale (CAARS), long version.[16] The CAARS provides self-assessment of severity of ADHD symptoms on a four-point scale (Not at All = 0, Just a Little = 1, Pretty Much = 2 and Very Much = 3). Eight subscales are provided: (1) Inattention/Memory problems, (2) Hyperactivity/Restlessness, (3) Impulsivity/Emotional lability, (4) Problems with self-concept, (5) DSM-IV Inattentive symptoms, (6) DSM-IV Hyperactive-impulsive symptoms, (7) DSM-IV Total ADHD Symptoms, (8) ADHD Index. The CAARS was completed in 36 of the controls and 43 of the ADHD participants. The scores on these clinical scales are shown in Table 1.

Personality measures

The MPQ,[13,17] which has 276 true–false items that score three broad factors (Positive Emotionality, Negative Emotionality and Constraint) and 11 primary trait dimensions, was administered. The trait dimension of Achievement (hard working, driven, tenacious, perfectionistic, enthusiastic) was used as a surrogate trait measure of motivation. The Achievement scale consists of items such as 'works hard, drives self, enjoys working hard, welcomes difficult and demanding tasks, persists where others give up, is ambitious, puts work and accomplishments before many other things, sets high standards, is a perfectionist' vs 'does not like to work harder than is strictly necessary, avoids very demanding projects, sees no point in persisting when success seems unlikely, is not terribly ambitious or a perfectionist'. The MPQ Achievement scale has been shown to correlate with leadership role occupancy among a large sample (N = 238) of identical male twins,[18] consistent with previous meta-analysis studies.[19] The activation and sustainment of achievement motivation has been conceptualized to be accomplished by central representations of delayed rewards.[20]

Table 1 Scores on the clinical scales in Controls and in ADHD participants and number of subjects for whom measures were obtained for each group

	Controls (n = *36*)	*ADHD* (n = *43*)	*Motivation ADHD*
CAARS			
1. Inattention	5 ± 4	25 ± 6	−0.43, $P<0.005$
2. Hyperactivity	7 ± 4	22 ± 7	NS
3. Impulsivity	5 ± 3	20 ± 7	NS
4. Self-concept	3 ± 2	9 ± 4	NS
5. DSM Inattentive	3 ± 3	20 ± 4	−0.43, $P<0.005$
6. DSM Hyperactive	3 ± 3	15 ± 5	
7. Total symptoms	6 ± 5 ($n=37$)	35 ± 6 ($n=39$)	
SWAN			
Inattention	−1.5 ± 1	1.5 ± 1	0.44, $P<0.005$
Hyperactivity	−1.2 ± 1	0.4 ± 1	

Abbreviations: CAARS, Conners Adult ADHD Rating Scale; DSM, *Diagnostic and Statistical Manual of Mental Disorders*; NS, not significant; SWAN, Strengths and Weaknesses of ADHD-symptoms and Normal-behavior.
Measures correspond to means and standard deviations.

To assess if the correlations with the DA measures were specific for the surrogate trait measure of motivation, we also inspected correlations with the broad trait measures of Positive Emotionality (combination of scores on well-being, social potency, achievement), Negative Emotionality (combination of scores for stress reaction, alienation and aggression) and Constraint (combination of scores for self-control, harm avoidance and traditionalism).

PET scans. We used a Siemens HR+ tomograph (resolution $4.5 \times 4.5 \times 4.5$ mm full-width half-maximum). Dynamic scans were started immediately after injection of 4–10 mCi [^{11}C]raclopride (specific activity 0.5–1.5 Ci/μM at end of bombardment) and after injection of 4–8 mCi [^{11}C]cocaine (specific activity >0.53 Ci/μmol at end of bombardment) and were obtained for 60 min as described.[11,12] Arterial blood was obtained to measure the concentration of unchanged [^{11}C]raclopride and [^{11}C]cocaine in plasma.

Image analysis and statistics
We manually obtained regions of interest (ROI) in ventral striatum (in the location of the NAcc), midbrain and cerebellum.[11] The carbon-11 concentration in each ROI was used to generate time–activity curves for [^{11}C]cocaine and [^{11}C]raclopride as previously described.[11,12] The time–activity curves for tissue concentration and unchanged tracer in plasma were used to calculate the distribution volumes using a graphical analysis technique for reversible systems[21] to estimate the equilibrium ratio of tissue concentration to plasma concentration in NAcc, midbrain and cerebellar regions. The ratios of distribution volumes in the accumbens and midbrain regions to that in cerebellum correspond to (B_{max}/K_d) +1 and were used as measures of D2/D3 receptor and DAT availability.

Table 2 Scores on the Achievement Scale (surrogate trait measure of motivation) and on the Positive and Negative Emotionality and Constraint factors from the MPQ in controls and ADHD participants

	Controls (n = *41*)	*ADHD* (n = *45*)	P
Achievement Scale	15 ± 3	11 ± 5	0.0003
Positive Emotionality	52 ± 10	48 ± 14	0.13
Negative Emotionality	12 ± 9	16 ± 11	0.04
Constraint	52 ± 10	42 ± 12	0.0001

Abbreviation: ADHD, attention-deficit hyperactivity disorder.
Comparisons correspond to independent *t*-tests (two tail).
Measures correspond to mean and standard deviations.

Pearson's product moment correlations were used to assess the association between our trait measure of motivation and D2/D3 receptor and DAT availability in the midbrain and NAcc regions. These correlations were calculated first for all participants and then separately for each group of participants (that is, for the ADHD and Control group separately). We also measured the correlation between the Achievement scale (surrogate trait measure of motivation) and the symptom ratings of inattention and hyperactivity in the ADHD participants using the CAARS and the dimensions of attention and activity/reflectivity from the SWAN. Significance for the *a priori* hypothesis (that is, association of DA measures with motivation, and association of motivation with ADHD symptoms) was set at $P<0.05$. The significance level for the correlations of the DA measures and scores on the three broad traits of the MPQ (Positive Emotionality, Negative Emotionality and Constraint factors) was set at $P<0.008$ (that is, Bonferroni correction for three personality and two DA measures).

Results

Personality measures
The scores on the Achievement scale were significantly lower in ADHD participants than in controls (11 ± 5 vs 15 ± 3; $t=3.5$, $P<0.001$). Compared to control participants, the ADHD participants also showed lower scores for Constraint ($t=5.2$, $P<0.0001$) and a trend for higher scores on Negative Emotionality ($t=2.1$, $P<0.05$), but the two groups did not differ on scores of Positive Emotionality (Table 2).

Dopamine measures
Compared with controls, the ADHD participants had significantly lower measures of D2/D3 receptor and of DAT availability in NAcc and midbrain regions (averaged for left and right regions) (Table 3).

Correlation between DA and personality measures

The correlation analysis between the Achievement scale and DA measures in NAcc (averaged left and right ROI) was significant for D2/D3 receptors ($r=0.27$, $P<0.01$) but not for DAT ($r=0.20$, $P<0.07$) when all subjects were included. Separate group analyses showed the correlation was significant for ADHD participants for both D2/D3 receptors ($r=0.39$, $P<0.008$) and DAT ($r=0.35$, $P<0.02$), but not for either in the control participants (see Figure 1).

The correlation analysis between the Achievement scale and the DA measures in midbrain (averaged left and right ROI) when all subjects were included was significant for D2/D3 receptors ($r=0.36$, $P<0.0007$)

Table 3 Measures of DA D2/D3 receptor availability (B_{max}/K_d) in ADHD participants and controls in the NAcc and midbrain regions and correlations with the scores on the Achievement Scale (surrogate trait measure of motivation) for analysis performed with all subjects (ALL) and for analysis performed with only ADHD participants (ADHD)

	Controls (n = *41*)	*ADHD* (n = *45*)	*Correlations with achievement scale*
D2/D3 receptors			
NAcc region*	2.65 ± 0.27	2.53 ± 0.22	ALL: $r=0.27$, $P<0.01$; ADHD: $r=0.39$, $P<0.008$
Midbrain**	0.28 ± 0.12	0.20 ± 0.17	ALL: $r=0.36$, $P<0.0007$; ADHD: $r=0.41$, $P<0.005$
DAT			
NAcc region*	0.60 ± 0.14	0.55 ± 0.10	ALL: $r=0.20$, $P<0.07$; ADHD: $r=0.35$, $P<0.02$
Midbrain	0.14 ± 0.09	0.10 ± 0.09	ALL: $r=0.18$, NS; ADHD: $r=0.17$, NS

Abbreviations: ADHD, attention-deficit hyperactivity disorder; DAT, DA transporter; NAcc, nucleus accumbens; NS, not significant.
The correlations with controls were not significant. Measures correspond to mean and standard deviation. Comparisons between groups correspond to independent samples *t*-tests (two tail) *$P<$ 0.05; **$P<0.01$.

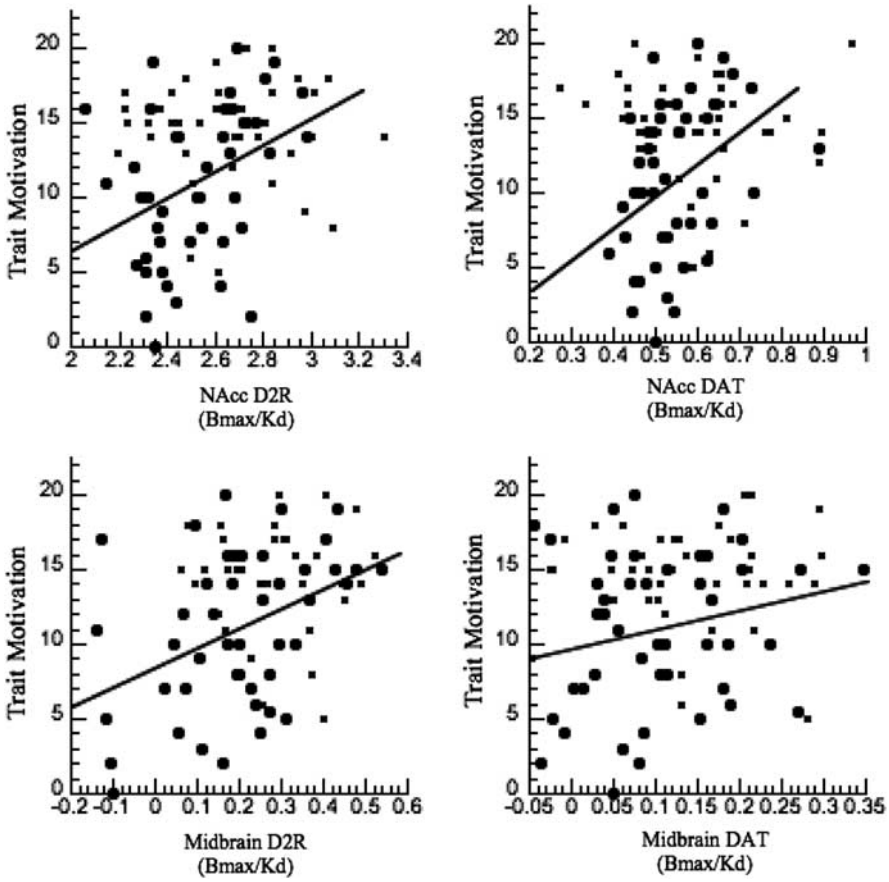

Figure 1 Scattergram showing the regression between the measures of DA D2/D3 receptor and of DAT availability in the NAcc and in the midbrain regions and Trait Motivation (MPQ Achievement scale) in ADHD participants (circles) and in controls (x).

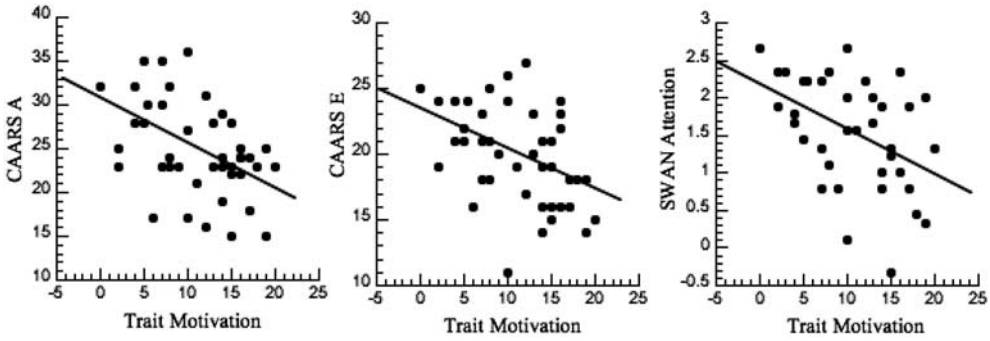

Figure 2 Scattergram for the regression between Trait Motivation (MPQ Achievement scale) and the measures of inattention (CAARS A, CAARS E and SWAN I) in the ADHD participants.

but not DAT ($r=0.18$, not significant). Separate group analyses showed the correlation was significant for ADHD participants for D2/D3 receptor ($r=0.41$, $P<0.005$) but not DAT; in controls neither correlation was significant (Figure 1).

The correlations with the other personality measures when all subjects were included revealed a significant correlations between Positive Emotionality and D2/D3 receptor in midbrain ($r=0.34$, $P<0.002$) and separate group analysis showed that this correlation was significant in ADHD participants ($r=0.41$, $P<0.005$) but not in controls. The correlations with Negative Emotionality and Constraint factors were not significant.

Correlation of achievement (surrogate trait measure of motivation) and clinical symptoms

To assess if our surrogate trait measure of motivation contributed to symptoms in ADHD participants, we also measured the correlation between the scores in the Achievement scale and ADHD symptoms, which was significant for the CAARS A ($r=-0.43$, $P<0.005$), CAARS E ($r=-0.43$, $P<0.005$) and the SWAN Attention dimension ($r=-0.44$, $P<0.005$) (Figure 2); the lower the scores in the Achievement scale the greater the inattention. In viewing the regression slopes in Figure 2, note that the positive SWAN score in attention reflects greater symptoms whereas the negative values reflect the opposite of the symptom. The correlations between scores in the Achievement scale and ratings of hyperactivity were not significant. Correlations between the other personality measures and symptoms of inattention or hyperactivity were also not significant.

Discussion

This study provides evidence of the predicted association between synaptic DA markers in regions of the mesoaccumbens DA pathway (NAcc and midbrain) and the trait of motivation in adults with ADHD. These are key brain regions for reward,[22] and the observed decreased availability of D2/D3 receptors and DAT could explain the decreased motivation in these patients.

The correlation between our surrogate measure of motivation (Achievement scale) and symptoms of inattention also suggest that impaired motivation may contribute to severity of symptoms of inattention in ADHD. These findings are consistent with the clinical recognition that attentional deficits in individuals with ADHD are most evident in tasks that are boring, repetitive and considered uninteresting (that is, tasks or assignments for which intrinsic motivation is low).[23] However, the correlational approach in our study does not allow us to assess which of these dimensions is more primary; the motivation deficit produces inattention as opposed to the attention deficit resulting in decreased motivation. Alternatively, these two dimensions could have common neurobiological substrates (DA reward pathway) as well as unique features (that is, noradrenergic prefrontal pathways for inattention).

The observation of a deficit in the DA reward pathway is further evidence that deficits in motivation may be contributing to impairment in ADHD adults.[6] This finding is also consistent with a recent fMRI study that reported decreased activation of the ventral striatum (the location of the NAcc) in adults with ADHD when compared to controls for both immediate and delayed rewards.[24]

We also showed a significant positive correlation between Positive Emotionality and D2/D3 receptor availability in midbrain in ADHD participants. Because the Achievement scale is part of the Positive Emotionality factor, this correlation is likely to reflect the association between D2/D3 receptor availability and this surrogate trait measure of motivation.

Clinical implications of findings

Our findings may have clinical relevance. They support the use of interventions to enhance the saliency of school and work tasks to improve motivation and performance. Indeed, both motivational intervention and contingency management have been shown to improve performance in ADHD patients.[25] For example, the use of intrinsically interesting activities (perhaps in areas where the individual shows talent and has successes) to reinforce mundane but necessary behaviors offers a

therapeutic strategy to overcome a motivation deficit. Also methylphenidate, which is one of the most frequent pharmacological interventions for ADHD, has been shown to increase motivation and interest in a cognitive task in proportion to the drug-induced DA increases in striatum.[26]

Decreased activity of the reward system in individuals with ADHD is likely to translate into problems in engaging in activities that are not inherently rewarding or reinforcing (and therefore may be described as less interesting or less motivating). By extrapolation to children, our observations in adults with ADHD could explain the reports of some parents that their child with ADHD can spend hours playing video games, but cannot focus attention on tasks at school, and the reports of children with ADHD that schoolwork is 'boring', which is commonly used to explain their lack of effort. The strong correlation between low scores in the surrogate trait measure of motivation and symptoms of inattention observed in this study suggests the need to consider the possibility of including 'motivation or interest deficit' as part of the core pathology of ADHD.

Personality measures and ADHD

In this study we report lower scores on the Achievement scale (surrogate trait measure of motivation) in ADHD participants than in controls, which was negatively associated with symptoms of inattention in ADHD. This is consistent with studies in children with ADHD in whom temperament measures of effortful control were linked to core symptoms of ADHD.[27] Specifically, Martel and Nigg described two overall dimensions of temperament, effort control and reactive control, and suggested that inattention symptoms might be considered as extreme of the former (effort control) and hyperactive/impulsive symptoms as the extreme of the latter (reactive control).[28] In our study hyperactivity did not correlate with any of the personality measures. The difference between our findings and those in children with ADHD could reflect either the low occurrence of symptoms of hyperactivity in our adult ADHD participants, or indicate that the association of personality measures with ADHD symptoms is different in adults than in children with ADHD.

We also found decreases in scores on the Constraint factor of the MPQ in ADHD participants. This factor is a combination of scores for self-control, harm avoidance and traditionalism, but the main difference was because of the lower scores on the self-control subscale in ADHD participants than in controls (data not shown). This is consistent with previous studies reporting poor self-control as one of the main behavioral characteristics that distinguishes adults with ADHD from controls.[29] Moreover, impaired inhibition is considered a core symptom of ADHD.[30]

Using the Achievement scale, we had previously reported in healthy controls an association with asymmetry in striatal measures of D2/D3 receptor availability such that greater scores on trait measures of motivation were associated with higher left relative to right receptor availability.[31] The current study does not corroborate this finding (data not shown), which may reflect the sensitivity of laterality measures to the position of the head in the field of view of the scanner.

Limitations

[^{11}C]Raclopride measures are influenced by extracellular DA, so decreased binding could reflect low D2/D3 receptor levels or increased DA release.[32] However, the latter is unlikely as we have previously reported that DA release in a subgroup of the ADHD participants reported in this study was lower than in the controls.[33]

The relatively low affinity of [^{11}C]raclopride and [^{11}C]cocaine for their targets and the relatively poor spatial resolution of PET decrease the signal to error in measures performed in small brain regions, such as NAcc, or in regions with lower relative concentration of D2/D2 receptors or of DAT, such as midbrain. Future studies using radiotracers with higher affinity and PET instruments with higher resolution will enable more accurate assessments.

We used the MPQ Achievement scale as a surrogate trait measure of motivation, which in and of itself is a complex construct. However, we have previously shown that the Achievement scale correlated with the dorsolateral prefrontal cortical response to monetary reward, which was in turn correlated with reinforcement-driven reaction time in cocaine-addicted individuals.[34] In this study, it would have been useful to have also collected measures of objective task motivation. Such a measure would have enabled us to assess the relationship between sustained performance on a challenging task and the self-reported measure of motivation in ADHD and in control participants. In future studies we plan to include reaction time measures in response to tasks of varying difficulty and reward expectation, which primate studies have shown reflect behavioral markers of state motivation.[35]

Our findings show a significant correlation between DA measures in NAcc and midbrain and the MPQ Achievement scale, which we interpret to suggest an association between these two measures. However, correlations do not necessarily connote causality and further studies are required to address this. Nonetheless, our previous findings in healthy controls, in whom we showed that increases in striatal DA induced by methylphenidate were also associated with increases in the motivation to perform a cognitive task, provide evidence that DA is involved in motivation.[23] Further studies are also required to assess the directionality of the association between inattention and motivation deficit (that is, poor motivation resulting in inattention vs inattention resulting in poor motivation).

In conclusion, these findings show that reductions in DA D2/D3 receptor and DAT availability in the DA reward pathway of ADHD participants are associated with low scores in the MPQ Achievement scale (trait

measures of motivation). Moreover, the correlation between scores in the MPQ Achievement scale and symptoms of inattention in the ADHD participants suggests that deficits in motivation contribute to inattention in ADHD. Our findings and those from other studies reporting motivation deficits in ADHD strongly suggest that ADHD is a disorder not only of attention deficit and hyperactivity/impulsivity but also of motivation deficit, which appears to reflect a hypofunctional DA reward pathway.

Conflict of interest

Dr Newcorn reported being a recipient of research support from Eli Lilly and Ortho-McNeil Janssen, and serves as a consultant, advisor or both for Astra Zeneca, BioBehavioral Diagnostics, Eli Lilly, Novartis, Ortho-McNeil Janssen and Shire, and as a speaker for Ortho-McNeil Janssen. Dr Kollins reported receiving research support, consulting fees or both from Addrenex Pharmaceuticals, Otsuka Pharmaceuticals and Shire Pharmaceuticals. Dr Wigal reported receiving support from Eli Lilly, McNeil, Novartis and Shire. Dr Swanson reported receiving support from Alza, Richwood, Shire, Celgene, Novartis, Celltech, Gliatech, Cephalon, Watson, CIBA, Janssen and McNeil; has been on the advisory boards of Alza, Richwood, Shire, Celgene, Novartis, Celltech, UCB, Gliatech, Cephalon, McNeil and Eli Lilly; has been on the speaker's bureaus of Alza, Shire, Novartis, Cellthech, UCB, Cephalon, CIBA, Janssen and McNeil; and has consulted to Alza, Richwood, Shire, Clegene, Novarits, Celltech, UCB, Gliatech, Cephalon, Watson, CIBA, Jansen, McNeil and Eli Lilly. The other authors declare no conflict of interest.

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References

1 National Institutes of Health Consensus Development Conference Statement: diagnosis and treatment of attention-deficit/hyperactivity disorder (ADHD). *J Am Acad Child Adolesc Psychiatry* 2000; **39**: 182–193.
2 Dopheide JA, Pliszka SR. Attention-deficit-hyperactivity disorder: an update. *Pharmacotherapy* 2009; **29**: 656–679.
3 Haenlein M, Caul WF. Attention deficit disorder with hyperactivity: a specific hypothesis of reward dysfunction. *J Am Acad Child Adolesc Psychiatry* 1987; **26**: 356–362.
4 Johansen EB, Killeen PR, Russell VA, Tripp G, Wickens JR, Tannock R *et al*. Origins of altered reinforcement effects in ADHD. *Behav Brain Funct* 2009; **5**: 7.
5 Kollins SH, Lane SD, Shapiro SK. The experimental analysis of childhood psychopathology: a matching analysis of the behavior of children diagnosed with attention deficit hyperactivity disorder. *Psychol Rec* 1997; **47**: 25–44.
6 Sonuga-Barke EJ. The dual pathway model of AD/HD: an elaboration of neuro-developmental characteristics. *Neurosci Biobehav Rev* 2003; **27**: 593–604.
7 Tripp G, Wickens JR. Research review: dopamine transfer deficit: a neurobiological theory of altered reinforcement mechanisms in ADHD. *J Child Psychol Psychiatry* 2008; **49**: 691–704.
8 Wise RA. Brain reward circuitry: insights from unsensed incentives. *Neuron* 2002; **36**: 229–240.
9 Sonuga-Barke EJ. Causal models of attention-deficit/hyperactivity disorder: from common simple deficits to multiple developmental pathways. *Biol Psychiatry* 2005; **57**: 1231–1238.
10 Volkow ND, Wang GJ, Kollins SH, Wigal TL, Newcorn JH, Telang F *et al*. Evaluating dopamine reward pathway in ADHD: clinical implications. *JAMA* 2009; **302**: 1084–1091.
11 Volkow ND, Fowler JS, Wang GJ, Dewey SL, Schlyer D, MacGregor R *et al*. Reproducibility of repeated measures of carbon-11-raclopride binding in the human brain. *J Nucl Med* 1993; **34**: 609–613.
12 Fowler JS, Volkow ND, Wolf AP, Dewey SL, Schlyer DJ, Macgregor RR *et al*. Mapping cocaine binding sites in human and baboon brain *in vivo*. *Synapse* 1989; **4**: 371–377.
13 Tellegen A, Waller NG. Exploring personality through test construction: development of the Multidimensional Personality Questionnaire. In: Boyle GJ, Matthews G, Saklofske DH (eds). *Handbook of Personality Theory and Testing: Vol. II. Personality Measurement and Assessment*. JAI Press: Greenwich, CT, 2008.
14 Guy W. Clinical Global Impression (CGI) scale. In: Rush AJ, First MB, Blacker D (eds). *Handbook of Psychiatric Measures*. American Psychiatric Publishing: Washington, DC, 2000.
15 Young DJ, Levy F, Martin NC, Hay DA. Attention deficit hyperactivity disorder: a Rasch analysis of the SWAN rating scale. *Child Psychiatry Hum Dev* 2009; **40**: 543–549.
16 Conners CK. Rating scales in attention-deficit/hyperactivity disorder: use in assessment and treatment monitoring. *J Clin Psychiatry* 1998; **59**(Suppl 7): 24–30.
17 Krueger RF, Caspi A, Moffitt TE, Silva PA, McGee R. Personality traits are differentially linked to mental disorders: a multitrait-multidiagnosis study of an adolescent birth cohort. *J Abnorm Psychol* 1996; **105**: 299–312.
18 Arvey RD, Rotundo M, Johnson W, Zhang Z, McGue M. The determinant of leadership role occupancy: genetic and personality factors. *Leadership Q* 2006; **17**: 1–20.
19 Judge TA, Bono JE, Ilies R, Gerhardt MW. Personality and leadership: a qualitative and quantitative review. *J Appl Psychol* 2002; **87**: 765–780.
20 Depue RA, Collins PF. Neurobiology of the structure of personality: dopamine, facilitation of incentive motivation, and extraversion. *Behav Brain Sci* 1999; **22**: 491–517.
21 Logan J, Fowler JS, Volkow ND, Wolf AP, Dewey SL, Schlyer DJ *et al*. Graphical analysis of reversible radioligand binding from time–activity measurements applied to [N-11C-methyl]-(−)-cocaine PET studies in human subjects. *J Cereb Blood Flow Metab* 1990; **10**: 740–747.
22 Wise RA, Rompre PP. Brain dopamine and reward. *Ann Rev Psychol* 1989; **40**: 191–225.
23 Barkley RA. *Attention Deficit Hyperactivity Disorder: A Handbook for Diagnosis and Treatment*. The Guilford Press: New York, NY, 1990.
24 Plichta MM, Vasic N, Wolf RC, Lesch KP, Brummer D, Jacob C *et al*. Neural hyporesponsiveness and hyperresponsiveness during immediate and delayed reward processing in adult attention-deficit/hyperactivity disorder. *Biol Psychiatry* 2009; **65**: 7–14.

25 Barkley RA. Adolescents with attention-deficit/hyperactivity disorder: an overview of empirically based treatments. *J Psychiatr Pract* 2004; **10**: 39–56.
26 Volkow ND, Wang GJ, Fowler JS, Telang F, Maynard L, Logan J *et al*. Evidence that methylphenidate enhances the saliency of a mathematical task by increasing dopamine in the human brain. *Am J Psychiatry* 2004; **161**: 1173–1180.
27 Martel MM, Nigg JT. Child ADHD and personality/temperament traits of reactive and effortful control, resiliency, and emotionality. *J Child Psychol Psychiatry* 2006; **47**: 1175–1183.
28 Nigg JT. Temperament and developmental psychopathology. *J Child Psychol Psychiatry* 2006; **47**: 395–422.
29 De Quiros GB, Kinsbourne M. Adult ADHD. Analysis of self-ratings on a behavior questionnaire. *Ann NY Acad Sci* 2001; **931**: 140–147.
30 Lampe K, Konrad K, Kroener S, Fast K, Kunert HJ, Herpertz SC. Neuropsychological and behavioural disinhibition in adult ADHD compared to borderline personality disorder. *Psychol Med* 2007; **37**: 1717–1729.
31 Tomer R, Goldstein RZ, Wang GJ, Wong C, Volkow ND. Incentive motivation is associated with striatal dopamine asymmetry. *Biol Psychol* 2008; **77**: 98–101.
32 Gjedde A, Wong DF, Rosa-Neto P, Cumming P. Mapping neuroreceptors at work: on the definition and interpretation of binding potentials after 20 years of progress. *Int Rev Neurobiol* 2005; **63**: 1–20.
33 Volkow ND, Wang GJ, Newcorn J, Telang F, Solanto MV, Fowler JS *et al.* Depressed dopamine activity in caudate and preliminary evidence of limbic involvement in adults with attention-deficit/hyperactivity disorder. *Arch Gen Psychiatry* 2007; **64**: 932–940.
34 Goldstein RZ, Alia-Klein N, Tomasi D, Zhang L, Cottone LA, Maloney T *et al*. Is decreased prefrontal cortical sensitivity to monetary reward associated with impaired motivation and self-control in cocaine addiction? *Am J Psychiatry* 2007; **164**: 43–51.
35 Satoh T, Nakai S, Sato T, Kimura M. Correlated coding of motivation and outcome of decision by dopamine neurons. *J Neurosci* 2003; **23**: 9913–9923.