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Association of Dopamine Gene Variants, Emotion Dysregulation and ADHD in Autism Spectrum Disorder

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Abstract

The aim of the present study was to evaluate the association of dopaminergic gene variants with emotion dysregulation (EMD) and attention-deficit/hyperactivity disorder (ADHD) symptoms in children with autism spectrum disorder (ASD). Three dopamine transporter gene (*SLC6A3/DAT1*) polymorphisms (intron8 5/6 VNTR, 3'-UTR 9/10 VNTR, rs27072 in the 3'-UTR) and one dopamine D2 receptor gene (*DRD2*) variant (rs2283265) were selected for genotyping based on *a priori* evidence of regulatory activity or, in the case of *DAT1* 9/10 VNTR, commonly reported associations with ADHD. A sample of 110 children with ASD was assessed with a rigorously validated *DSM-IV*-referenced rating scale. Global EMD severity (parents' ratings) was associated with *DAT1* intron8 ($\eta^2=0.063$) and rs2283265 ($\eta^2=0.044$). Findings for *DAT1* intron8 were also significant for two EMD subscales, generalized anxiety ($\eta^2=0.065$) and depression ($\eta^2=0.059$), and for *DRD2* rs2283265, depression ($\eta^2=0.053$). *DRD2* rs2283265 was associated with teachers' global ratings of ADHD ($\eta^2=0.052$). *DAT1* intron8 was associated with parent-rated

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Conflicts of Interest

Dr. Gadow is shareholder in Checkmate Plus, publisher of the Child Symptom Inventory-4. For the remaining authors, none were declared.

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hyperactivity ($\eta^2=0.045$) and both *DAT1* 9/10 VNTR ($\eta^2=0.105$) and *DRD2* rs2283265 ($\eta^2=0.069$) were associated with teacher-rated inattention. These findings suggest that dopaminergic gene polymorphisms may modulate EMD and ADHD symptoms in children with ASD but require replication with larger independent samples.

Keywords

autism; autism spectrum disorder; depression; emotion dysregulation; ADHD; DAT1; DRD2

1. Introduction

Children with autism spectrum disorder (ASD) experience a wide range of psychiatric symptoms consistent with emotion dysregulation (EMD), such as depression, anxiety, anger, and irritability, as well as attention-deficit hyperactivity disorder (ADHD; Gadow, DeVincent, Pomeroy, & Azizian, 2005, 2006). These symptoms are associated with high rates of social and academic impairment (Kaat, Gadow, & Lecavalier, 2013), but little is known about pathogenic variables that may contribute to their co-occurrence with ASD. EMD and ADHD in children with ASD are phenomenologically similar in many ways to comparable symptoms and disorders in non-ASD youth (Gadow, DeVincent, & Drabick, 2008; Gadow, DeVincent, & Pomeroy, 2006; Gadow, Guttman-Steinmetz, Rieffe, & DeVincent, 2012; Guttman-Steinmetz, Gadow, DeVincent, & Crowell, 2010), and this suggests that research about the latter may inform the former (e.g., Cohen et al., 2011; Gadow et al., 2013; Guerini et al., 2011).

Dopamine, brain regions rich in dopamine receptors, and genes involved in dopamine metabolism and signaling are all shown to be involved in emotion regulation and dysregulation (Alcaro, Huber, & Panksepp, 2007; Badgaiyan, Fischman, & Alpert, 2009; Beiderbeck et al., 2012; Garcia-Garcia, Clemente, Domínguez-Borràs, & Escera, 2010; Levita, Dalley, & Robbins, 2002; Opmeer, Kortekaas, & Aleman, 2010; Salgado-Pineda, Delaveau, Blin, & Nieoullon, 2005), including depression (Klimek, Schenck, Han, Stockmeier, & Ordway, 2002; Meyer et al., 2001; Roy, Karoum, & Pollack, 1992), as well as ADHD (Levy, 1991; Wender, 1971). For example, the 9/10 variable number tandem repeat (VNTR) in the 3'-untranslated region (UTR) of the dopamine transporter (DAT) gene (*DAT1/SLC6A3*) was found to be associated with depression (Felten, Montag, Markett, Walter, & Reuter, 2011), anxiety (Gadow, Roohi, DeVincent, & Hatchwell, 2008), and processing negative emotional stimuli (Garcia-Garcia et al., 2010). It also evidences modest association with ADHD (Gizer, Ficks, & Waldman, 2009) as do other *DAT1* variants including a VNTR on intron8 and the single nucleotide polymorphism (SNP) rs27072, but effect sizes across studies are generally heterogeneous. Researchers have recently established regulatory functions for the *DAT1* intron8 5/6 repeat VNTR and rs27072 variants (Pinsonneault et al., 2011) as well as SNP (rs2283265) in the dopamine D2 receptor gene (*DRD2*) (Zhang et al., 2007), which enables a focused approach to gene-behavior associations founded on strong evidence for genetic influence in dopaminergic signaling.

Although research findings suggest that (a) dysregulation of dopamine metabolism or signaling is likely implicated in the etiology of EMD and ADHD, and (b) specific functional

dopaminergic gene variants may modulate symptom severity, little is known of their relation with comparable symptoms in children with ASD. The primary objective of the present study was to explore potential relations of the aforementioned dopamine gene variants with severity of EMD and ADHD symptoms in children with ASD. This seemed reasonable because both spectra are common in children with ASD and often co-occur in ASD samples (suggesting shared pathogenic mechanisms). We also considered whether *DAT1* intron8 and *DRD2* rs2283265 jointly led to a non-additive association with symptom severity because prior work has documented a functional epistatic interaction (Sullivan et al., 2013).

2. Material and Methods

2.1 Participants

Participants were recruited from referrals to a university hospital developmental disabilities specialty clinic located on Long Island, New York. All youth ($N=110$) between 4 and 14 years old with the prerequisite measures and a diagnosis of ASD were included in the present study. Demographic characteristics were as follows: age ($M=7.5\pm2.6$), gender (86% male), ethnicity (91% Caucasian), socioeconomic status assessed with Hollingshead's (1975) index of occupational and educational social status ($M=42.0\pm11.2$), single-parent household (10%), and current psychotropic medication use (25%). Most children (73%) had IQs ≥ 70 based primarily on WISC or Stanford-Binet test scores obtained from the school. A subsample of youth ($n=67$) participated in prior studies of other gene variants (e.g., Gadow et al., 2008; Roohi, DeVincent, Hatchwell, & Gadow, 2009) as did the entire (Gadow et al., 2013; Gadow, Smith, & Pinsonneault, in press). Both referred (Gadow et al., 2005) and epidemiologic (Simonoff et al., 2008) samples of children with ASD indicate high levels of co-occurring psychopathology. In the present study, the percentage of youth with T scores >65 for parent/teacher ratings (Gadow & Sprafkin, 1997, 2002, 2008) were as follows: ADHD (63%/46%), oppositional defiant disorder (22%/29%), generalized anxiety disorder (21%/25%), major depressive episode (36%/39%) and separation anxiety disorder (7%, parents' ratings only). This study was approved by a university Institutional Review Board; informed consent was obtained; and appropriate measures were taken to protect patient (and rater) confidentiality.

2.2 Procedure

Prior to scheduling their initial clinic evaluation, the parents of potential participants were mailed a packet of materials including behavior rating scales, background information questionnaire, and permission for release of school evaluation records. Ratings of child behavior were obtained from parents (primarily the mother) and teachers for 105 and 97 children, respectively. Diagnoses of ASD were confirmed by an expert diagnostician and based on five sources of information about ASD symptoms to verify *DSM-IV* criteria: (a) comprehensive developmental history, (b) clinician interview with child and caregiver(s), (c) prior evaluations, (d) informal observations of the child in the clinic setting, and (e) review of validated ASD rating scales including the Child Symptom Inventory-4 (CSI-4) (Gadow & Sprafkin, 2002), which evidenced high sensitivity and specificity in identifying 5-12-year-old children with ASD in two independent studies (DeVincent & Gadow, 2009; Gadow, Schwartz, DeVincent, Strong, & Cuva, 2008). Most youth (81%) were also

evaluated with the Autism Diagnostic Observation Schedule (Lord et al, 2000) and/or Autism Diagnostic Interview-Revised (Rutter, LeCouteur, & Lord, 2003). Exceptions were children who had previously received an ASD diagnosis from a qualified clinician.

2.3 Genotyping

Standard methods were employed to determine genotypes, and these have been described elsewhere for the *DAT1* variants (Pinsonneault et al., 2011) and for *DRD2* rs2283265 (Moyer et al., 2011).

2.4 Child Genotypes

The distribution (frequencies/percents) of genotypes were as follows: *DAT1* intron8 VNTR 5-5 (7/6), 5-6 (38/35), 5-11 (1/1), 6-6 (63/57), and 6-12 (1/1); *DAT1* 3'-UTR VNTR were 9-6 (1/1), 9-9 (11/10), 9-10 (38/34), 10-10 (54/49), 10-11 (1/1); *DAT1* rs27072 were C-C (76/69), T-C (32/29), and T-T (1/1); and *DRD2* rs2283265 were G-G (73/66), T-G (29/26), and T-T (1/1). None of the variants deviated from Hardy-Weinberg equilibrium ($p > .05$). Genotype groups were not significantly different in terms of age, gender IQ, ethnicity, SES, maternal education, single parent household, current special education or current psychotropic medication. Owing to infrequency and uncertainties about the functionality of the rare variants and consistent with prior research, genotype groups were constructed as follows: *DAT1* intron8 VNTR (5-6 versus 6-6 repeats), *DAT1* 3'-UTR VNTR (9-9, 9-10, 10-10 repeats), *DAT1* rs27072 (C-C vs. T-C), and *DRD2* rs2283265 (G-G vs. T-G).

2.5 Measures

The CSI-4 (Gadow & Sprafkin, 2002) is a behavior rating scale that assesses the behavioral symptoms of a broad range of psychiatric syndromes and has both parent and teacher versions. The number of items in the parent and teacher versions is 97 and 78 items, respectively. The teacher version excludes symptoms from the parent version (e.g., separation anxiety) that teachers are unlikely to have direct knowledge. Individual items bear one-to-one correspondence with *DSM-IV* symptoms (i.e., high content validity). To assess symptom severity, items are scored (never=0, sometimes=1, often=2, and very often=3) and summed separately for each symptom dimension. Confirmatory factor analysis of parents' and teachers' ratings of children with diagnosed ASD supports the internal construct validity of *DSM-IV* syndromes in this clinical population (Lecavalier, Gadow, DeVincent, & Edwards, 2009). Numerous studies indicate that both parent and teacher CSI-4 symptom subscales demonstrate satisfactory psychometric properties in community-based normative, clinic-referred non-ASD, and ASD samples (Gadow & Sprafkin, 2011). CSI-4 scores show little relation to age, IQ, or SES. For the present study, symptom severity scores for oppositional defiant disorder (ODD) (anger, irritability), generalized anxiety disorder (GAD), separation anxiety disorder (SAD), and major depressive episode (MDE) were examined separately but were also transformed into *z* scores and then summed to create a global Emotion Dysregulation (EMD) score. The internal consistency (Cronbach's alpha) of the EMD subscale based on untransformed scores was high ($\alpha = .89$). Prior research has demonstrated that each of the ADHD subscales (inattention, hyperactivity, impulsivity) is associated with different clinical features in children with ASD (Gadow et al., 2006).

2.6 Statistical Analyses

Chi-square tests and ANOVAs were used to examine potential differences in demographic characteristics between genotype groups, and correlation analyses were conducted to determine associations between these characteristics and dependent variables. Both sets of analyses were used to identify potential covariates. Primary analyses pertained to two dependent variables: severity of EMD (transformed scores) and ADHD (all symptoms). One-way ANOVAs (and in some cases ANCOVAs) were conducted to examine main effects of genotype groups. Severity of ADHD and ASD were considered potential covariates in EMD and ADHD analyses, respectively, if they were not related to genotype (Miller & Chapman, 2001). Secondary analyses examined severity of component phenotypes. In the case of EMD, these were ODD, GAD, SAD, and MDE. For ADHD, these were inattention, hyperactivity, and impulsivity. We report partial eta-squared (η^2) to gauge the magnitude of group differences (i.e., proportion of variance in dependent variables accounted for by independent variables). A rule of thumb for determining the magnitude of η^2 suggests the following: 0.01-0.06=small, 0.06-0.14=moderate, and >0.14=large (Cohen, 1988).

3. Results

3.1 Emotion Dysregulation

DAT1 intron8 polymorphism was associated with parents' ratings of EMD, with youth homozygous for the 6-repeat allele exhibiting more severe symptoms than 5/6 heterozygotes (Table 1). The association was somewhat stronger co-varying severity of ADHD symptoms, $F=7.81$, $p=0.006$, $\eta^2=0.077$. Secondary analyses indicated that intron8 genotype was significant for subdomains of EMD (untransformed scores): depression ($F=5.81$, $p=.018$; $\eta^2=0.059$) and generalized anxiety ($F=6.47$, $p=.013$; $\eta^2=0.065$). Anger/irritability was marginally significant ($F=3.74$, $p=.056$; $\eta^2=0.038$), but when co-varying severity of ADHD, was significant ($p=0.032$). In all cases, the 6/6 group obtained more severe ratings than the 5/6 group (Figure 1).

Because the *DAT1* intron8 variant was also associated with severity of parent-rated ASD (6/6 > 5/6), co-varying severity of ADHD ($F=4.75$, $p=0.032$; $\eta^2=0.049$), we constructed a composite phenotype comprised of a summary of z-scores for EMD and total ASD symptoms. Children homozygous for the 6-repeat allele had more severe EMD+ASD symptoms than the 5/6 group ($F=8.08$; $p=.005$; $\eta^2=0.080$), which was also the case when co-varying ADHD symptom severity ($F=11.41$, $p=.001$, $\eta^2=0.110$).

DRD2 rs2283265 was associated with parents' ratings of EMD, and youth homozygous for the main G allele had more severe symptoms than the T-G group (Table 1). Secondary analyses indicated that the G/G group ($M=5.9\pm3.7$) compared with heterozygotes ($M=4.1\pm2.7$) had more severe depression symptoms ($F=5.21$, $p=0.025$, $\eta^2=0.053$). Teachers' ratings were marginally significant ($p=.054$) for EMD, and consistent with parents' ratings, the G-G group received higher symptom scores than the T-G group (Table 1).

3.2 Attention-Deficit Hyperactivity Disorder

There was one significant (*DRD2* rs2283265) and one marginally significant (*DAT1* 3'-UTR VNTR) effect of genotype for global severity of ADHD, and both pertained to teachers' ratings (Table 1). There was a marginally significant ($p=0.048$) effect of *DAT1* rs27072 for parents' global ratings of ADHD co-varying ASD severity.

Secondary analyses examining the three subdomains of ADHD revealed that the *DAT1* intron8 5-6 repeat genotype was associated with more severe parent-rated hyperactivity symptoms than 6-6 repeat genotype co-varying ASD severity (Table 2). There was a significant effect of *DAT1* 3'-UTR VNTR for teachers' ADHD inattention symptoms (Table 2), and post hoc analyses indicated significant differences between 9-9 and 9-10 ($p=0.010$) and 9-9 and 10-10 ($p=0.007$). The *DRD2* rs2283265 G-G group had more severe teacher-rated inattention symptoms than the T-G group.

3.3 Gene-Gene Interaction

A 2×2 ANOVA examining a statistical interaction between *DAT1* intron8 5/6 repeat VNTR and *DRD2* rs2283265 found that the interaction term was not significant for EMD ($p>0.10$); however, consistent with our prior analyses for individual variants, the 6-6 repeat/G-G group did evidence the most severe EMD whereas the 5-6/TG group had the least severe symptoms (Figure 2).

4. Discussion

Findings of this study suggest that dopaminergic gene variants *may* be modulators of EMD and ADHD symptoms in children with ASD. Specifically, there was a moderate-strength ($\eta^2=.063$) association of the *DAT1* intron8 VNTR with parent-rated EMD. Children with lower activity 6-6 repeat genotype had more severe symptoms than 5-6 heterozygotes. Of particular interest is the breadth of associations to include generalized anxiety, depression, and anger/irritability, and a moderate-strength ($\eta^2=0.110$) association with a composite EMD+ASD phenotype. The *DRD2* rs2283265 variant was also associated with parent-rated EMD ($\eta^2=0.041$) where children homozygous for the G allele had more severe symptoms than heterozygotes (T-G), and follow-up analyses indicated a significant association for depression ($\eta^2=0.053$).

Children homozygous for the *DAT1* intron8 6-repeat allele were rated by their parents as having more severe ADHD hyperactivity than 5/6 heterozygotes (co-varying ASD severity), but the effect size was modest ($\eta^2=0.045$). A meta-analysis of five studies of the *DAT1* intron8 variant and ADHD indicated a modest association with the 6-repeat being the risk allele, but there was significant heterogeneity in effect sizes across studies (Gizer et al., 2009). In the present study, there was a significant effect of *DAT1* 3'-UTR VNTR genotype for teachers' ratings of ADHD inattention ($\eta^2=0.105$) where children homozygous for the 9-repeat allele had less severe symptoms than the 9-10 and 10-10 groups. A meta-analysis of 34 studies of children with ADHD found the 10-repeat allele to be a risk variant, but the magnitude of the association was modest and effect sizes across studies were heterogeneous (Gizer et al., 2009). Research indicates the *DAT1* 3'-UTR VNTR does not appear to be a functional variant (Pinsonneault et al., 2011), but may be a marker for other causative *DAT1*

haplotypes. There was a significant association for *DRD2* rs2283265 and teacher-rated inattention ($\eta^2=0.069$), but there is little prior research about this SNP and ADHD.

Some differences were observed in genotype-phenotype associations between teacher and parent report, and this is consistent with an extensive literature that supports contextual variation in child behavior (behavioral plasticity), which appears to vary as a function of genotype (Belsky, et al., 2009; Gadow & Drabick, 2012; Gadow et al., 2013; Kuepper et al., 2012). In other words, children may behave differently in a classroom compared with the home because different types of demands are placed on them in each setting, and this likely contributes to discrepancies between informant reports of symptoms. Importantly, it is only by examining both parent and teacher evaluations that we can begin to understand the implications of contextual variation for gene-behavior relations.

5. Study Strengths, Limitations, and Future Directions

The strengths of this study include limiting the sample to children within a relatively restricted age range, assessment of symptom phenotypes with a psychometrically sound and validated measure, and focus on a small number of gene variants previously shown to (a) regulate expression of *DAT1* and *DRD2* (Pinsonneault et al., 2011; Zhang et al., 2007), key players in dopaminergic signaling, and (b) be associated with EMD or ADHD in prior research with non-ASD individuals. However, generalization of results is bounded by several qualifications. The size of the study sample is relatively small, and this may increase the probability of Type 1 (false positives) and Type 2 (false negatives) errors. With regard to the former, our results are strengthened by the facts that risk genotypes were relatively common, and targeted variants and symptoms were informed by *à priori* research findings. Conversely, some marginally significant results (e.g., *DRD2* rs2283265 and teachers' ratings of EMD) warrant consideration in future studies of youth with ASD as does the potential epistatic effect in *DAT1* intron8 5/6 repeat VNTR and *DRD2* rs2283265. Results were unchanged when analyses were limited to Caucasians, but findings may not generalize to other ethnicities. It is widely acknowledged that a range of biopsychosocial variables impact psychiatric symptom expression, and the present study did not examine other aspects of the child's genetic environment or their interactions with environmental variables. Although some of our results are consistent with the extant literature involving non-ASD samples, they are presented here primarily as guides for future research and should not be considered as hypothesis confirming.

6. Conclusion

Research conducted in several different countries indicates that most children with ASD have EMD or ADHD symptoms that are severe enough to impair social or academic functioning. Our results suggest that at least some regulatory dopaminergic gene variants *may* modulate the severity of these co-occurring symptoms, but they are tentative pending replication in larger, independent samples.

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Highlights

Most children with ASD experience impairing emotion dysregulation (EMD) or ADHD symptoms.

Evidence suggests that dysregulation of dopamine metabolism or signaling is likely implicated in the etiology of EMD and ADHD

Results suggest some regulatory dopaminergic gene variants *may* modulate the severity of these co-occurring symptoms

Findings should be considered tentative pending replication in larger, independent samples.

Figure 1.

Association of *DAT1* intron8 VNTR 5-6 and 6-6 repeat genotypes and severity of oppositional defiant disorder (ODD), generalized anxiety disorder (GAD), separation anxiety disorder (SAD), and major depressive episode (MDE) symptoms controlling for severity of ADHD symptoms. Group differences were significant ($p < 0.05$) for GAD and MDE and marginally significant ($p = 0.056$) for ODD.

Figure 2.

Mean severity of parent-rated emotion dysregulation symptoms (EMD) for *DAT1* intron8 5/6 repeat VNTR (5-6, 6-6) and *DRD2* rs2283265 (G-G, G-T) genotype groups. The interaction was not significant ($p=0.41$).

Table 1

Informants' Global Severity Ratings of Emotion Dysregulation and Attention-Deficit Hyperactivity Disorder

Genotypes	Emotion Dysregulation ^a				ADHD Combined			
	Mean (SD)	F	p=	η^2	Mean (SD)	F	p=	η^2
PARENTS' RATINGS								
<i>DAT1</i> intron8 VNTR		6.28	.014	.063		0.33	.856	.000
5-6 repeat (<i>n</i> =36/36)	14.2 (8.2)				29.7 (10.8)			
6-6 repeat (<i>n</i> =60/59)	18.4 (10.4)				29.3 (10.6)			
<i>DAT1</i> 3' UTR VNTR		0.85	.430	.018		1.40	.252	.028
10-10 (<i>n</i> =50/50)	17.3 (10.6)				28.8 (10.4)			
9-10 (<i>n</i> =37/36)	17.0 (9.1)				30.6 (11.2)			
9-9 (<i>n</i> =11/11)	13.4 (8.6)				24.2 (14.0)			
<i>DAT1</i> rs27072		0.27	.603	.003		1.13	.290	.011
C-C (<i>n</i> =72/72)	15.1 (10.6)				28.5 (11.4)			
T-C (<i>n</i> =30/29)	15.4 (9.1)				30.9 (9.7)			
<i>DRD2</i> rs2283265		4.37	.039	.044		0.39	.534	.004
G-G (<i>n</i> =68/67)	17.6 (10.7)				29.9 (10.3)			
T-G (<i>n</i> =28/28)	14.0 (7.70)				28.4 (11.8)			
TEACHERS' RATINGS								
<i>DAT1</i> intron8 VNTR		0.64	.425	.007		0.38	.537	.004
5-6 repeat (<i>n</i> =33/33)	14.9 (11.9)				28.8 (14.6)			
6-6 repeat (<i>n</i> =56/56)	16.6 (9.4)				27.0 (12.0)			
<i>DAT1</i> 3' UTR VNTR		1.28	.283	.028		2.93	.058	.061
10-10 (<i>n</i> =46/46)	14.7 (8.9)				27.2 (11.9)			
9-10 (<i>n</i> =35/35)	16.9 (11.1)				28.2 (13.3)			
9-9 (<i>n</i> =12/12)	11.3 (10.6)				18.0 (16.0)			
<i>DAT1</i> rs27072		0.07	.798	.001		0.15	.703	.002
C-C (<i>n</i> =66/66)	15.1 (10.6)				26.5 (14.1)			
T-C (<i>n</i> =31/30)	15.4 (9.1)				27.6 (11.3)			
<i>DRD2</i> rs2283265		3.81	.054	.041		4.81	.031	.052
G-G (<i>n</i> =64/63)	15.8 (9.6)				28.2 (12.6)			

Genotypes	Emotion Dysregulation ^a			ADHD Combined		
	Mean (SD)	F	p=	Mean (SD)	F	p=
T-G (n=26/26)	11.4 (9.6)			21.6 (13.6)		

^aUntransformed scores

Table 2
Informants' Severity Ratings of Attention-Deficit Hyperactivity Disorder Subdomain Symptoms

Genotypes	Inattention			Hyperactivity			Impulsivity		
	<i>M (SD)</i>	<i>F</i>	<i>p</i> =	η^2	<i>M (SD)</i>	<i>F</i>	<i>p</i> =	η^2	<i>F</i>
PARENTS' RATINGS									
<i>DAT1</i> intron8 VNTR ^a		0.31	.577	.003		4.34	.045	.045	0.18
5-6 repeat (<i>n</i> =36)	16.0 (6.2)				8.9 (4.3)				4.9 (2.9)
6-6 repeat (<i>n</i> =59)	16.5 (5.8)				8.1 (4.5)				4.8 (3.1)
<i>DAT1</i> 3' UTR VNTR ^a		2.15	.122	.044		0.16	.851	.003	0.14
10-10 (<i>n</i> =50)	15.7 (5.8)				8.1 (4.2)				4.9 (3.2)
9-10 (<i>n</i> =36)	17.5 (6.3)				8.6 (4.5)				4.9 (2.8)
9-9 (<i>n</i> =11)	12.9 (6.9)				7.1 (5.2)				4.2 (3.8)
<i>DAT1</i> rs27072 ^a		2.67	.105	.027		0.90	.344	.009	0.43
C-C (<i>n</i> =72)	15.5 (6.4)				8.2 (4.6)				4.7 (3.1)
T-C (<i>n</i> =29)	17.5 (5.1)				9.0 (3.7)				5.1 (3.1)
<i>DRD2</i> rs2283265 ^a		0.00	.982	.000		0.22	.642	.002	0.06
G-G (<i>n</i> =67)	16.5 (6.1)				8.5 (4.2)				5.0 (3.0)
T-G (<i>n</i> =28)	16.0 (6.1)				7.9 (4.7)				4.7 (3.4)
TEACHERS' RATINGS									
<i>DAT1</i> intron8 VNTR		0.10	.752	.001		2.26	.137	.026	0.35
5-6 repeat (<i>n</i> =33)	16.3 (8.1)				8.3 (5.0)				4.1 (3.7)
6-6 repeat (<i>n</i> =56)	15.8 (6.6)				6.6 (5.2)				4.6 (3.6)
<i>DAT1</i> 3' UTR VNTR		5.30	.007	.105		0.95	.391	.021	0.37
10-10 (<i>n</i> =46)	16.3 (7.1)				6.6 (4.8)				4.3 (3.8)
9-10 (<i>n</i> =35)	16.3 (6.4)				7.3 (5.4)				4.6 (3.6)
9-9 (<i>n</i> =12)	9.1 (9.1)				4.9 (5.2)				3.5 (3.1)
<i>DAT1</i> rs27072		0.65	.423	.007		0.77	.782	.001	0.57
C-C (<i>n</i> =66)	15.2 (7.9)				6.9 (5.4)				4.5 (3.8)
T-C (<i>n</i> =30)	16.5 (6.0)				7.2 (4.7)				3.9 (3.2)
<i>DRD2</i> rs2283265		6.53	.012	.069		0.61	.437	.007	3.30

Genotypes	Inattention			Hyperactivity			Impulsivity		
	<i>M (SD)</i>	<i>F</i>	<i>p</i> =	η^2	<i>M (SD)</i>	<i>F</i>	<i>p</i> =	η^2	<i>F</i>
G-G (<i>n</i> =64)	16.8 (7.2)			6.9 (5.1)				4.5 (3.5)	
T-G (<i>n</i> =26)	12.4 (7.6)			6.0 (4.9)				3.0 (3.2)	

^aControlling for severity of autism spectrum disorder symptoms.