

Gender-specific expression of the DRD4 gene on adolescent delinquency, anger and thrill seeking

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The present study investigated gender differences in the associations between the DRD4 variable number tandem repeat (VNTR) polymorphism and adolescent delinquency, short temper and thrill seeking. We also explored whether the gender-specific expression of the DRD4 can be explained by gender differences in the exposure to psychosocial risks, such as poor parent-child relationship. Participants were 263 14- to 17-year olds (50% males) living in Russia. DNA was extracted from saliva samples and the VNTR DRD4 polymorphisms were genotyped using polymerase chain reaction. Participants reported on the extent of their delinquent behaviour, short temper, thrill seeking and exposure to psychosocial risk (i.e. poor parental monitoring of adolescent behaviour, exposure to violence and peer delinquency). Compared to individuals with the 4/4 genotype, males, but not females, with the 7-repeat allele (7R) had significantly higher delinquency, short temper and thrill seeking. This interaction effect, however, was completely explained by males' higher exposure to psychosocial risk factors. When parental monitoring of youths' activities and youth exposure to violence were included in the model, the 7R × gender interaction was no longer significant. Thus, social context plays an important role in explaining gender-specific phenotypic expression of the DRD4 gene.

Keywords: Dopamine; DRD4; sex differences; delinquency; impulsivity; anger

INTRODUCTION

Although biological aspects of delinquency, anger and impulsivity are not fully understood, we know that dopaminergic system plays an important role in these behaviours and psychological traits (Coccaro *et al.*, 1997; Zuckerman and Kuhlman, 2000). In particular, midbrain dopamine neurons are activated in response to novel rewards, contributing to learning of cues that predict reward occurrence and modulating novelty seeking and impulse control (Miller and Cohen, 2001). Low levels of dopamine are associated with attention deficit hyperactivity disorder (ADHD; Volkow *et al.*, 2007), while psychostimulant drugs that enhance dopamine release (e.g. methylphenidate) improve symptoms of ADHD (Konrad *et al.*, 2004; Tucha *et al.*, 2006).

Dopaminergic system also contributes to anger and delinquency (both aggressive and non-aggressive). For example, methylphenidate reduces anger outbursts (Mooney and Haas, 1993), covert antisocial behaviour (e.g. stealing; Hinshaw, *et al.*, 1992) and aggression (Pappadopulos *et al.*, 2006). Aripiprazole, an atypical antipsychotic that is a partial dopamine agonist, is linked to a reduction of anger among patients with borderline personality disorder (Nickel *et al.*, 2006), and Risperidone and Clozapine (also the atypical

antipsychotics with an affinity for dopamine receptors) are effective in reducing aggression and other behavioural problems (Glazer and Dickson, 1998; Pappadopulos *et al.*, 2006; Barzman and Findling, 2008).

Delinquency, anger and impulsivity have strong genetic components (Tellegen *et al.*, 1988; Cates *et al.*, 1993; Koopmans, 1995; Krueger *et al.*, 2002) and a number of studies have searched for specific associated genes (Rujescu *et al.*, 2002; Ebstein, 2006). Among them, the dopamine receptor D4 gene (*DRD4*) has received considerable attention for its potential impact on reward motivation, attention and approach behaviour. It is located on chromosome 11, at 11p15.5 (Van Tol *et al.*, 1991) and its most variable polymorphism encodes for a variable number of repeated sequences of 48 bp (2–11 repeats). The 4-repeat allele (4R) has the highest frequency (65%), followed by the 7-repeat allele (7R) (19%) and the 2-repeat allele (2R) (9%) (Ding *et al.*, 2002). Alleles with many repeats (long alleles), in general, and the 7R allele, in particular, have been associated with blunted dopamine response (Asghari *et al.*, 1995), sensation seeking (Benjamin *et al.*, 1996; Ebstein *et al.*, 1996), impulsivity (Congdon *et al.*, 2008), anger (Kang *et al.*, 2008), aggressive behaviour (Fresan *et al.*, 2007) and ADHD (Brookes *et al.*, 2006; Li *et al.*, 2006).

Functional differences among the *DRD4* variable number tandem repeat (VNTR) polymorphisms are associated with changes in the *DRD4* receptor protein in the region that couples to G proteins and mediates intracellular cyclic adenosine monophosphate levels. The DRD4.7 allele is associated with reduced postsynaptic inhibition, as compared

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to the *DRD4.2*, *DRD4.4* and *DRD4.9* alleles (Asghari *et al.*, 1995; Jovanovic *et al.*, 1999). There are also differences observed in the ability of misfolded (i.e. improperly synthesized) *DRD4.2*, *DRD4.4* and *DRD4.7* proteins to be restored to proper folding (Van Craenenbroeck *et al.*, 2005). The *DRD4.2* allele shows the lowest up-regulation, the *DRD4.7* allele is the most up-regulated and the *DRD4.4* allele exhibits up-regulation that is between that for *DRD4.2* and *DRD4.7*. Finally, the *DRD4.7* allele has been shown to be associated with higher reward-related ventral striatum reactivity (Forbes *et al.*, 2007).

Although the mechanisms through which the *DRD4* gene is linked to the psychological traits discussed in this study are not entirely clear, our knowledge of dopaminergic system may help explain these associations. Mid-brain dopamine neurons are activated in response to novel rewards and are responsible for successful learning of cues that predict reward occurrence (Miller and Cohen, 2001). Specifically, signals of reward initiate a phasic burst of mid-brain dopamine neurons, which, in turn, elicits positive emotional states (Schultz, 1998). Recent studies indicate that dopamine is not only released in response to activities such as food, sex and stimulant drugs, but also in response to aggression (Couppis and Kennedy, 2008). By extension, individuals who experience blunted dopamine response may be motivated to seek experiences that activate mid-brain dopamine release. Indeed, low levels of dopamine are associated with ADHD (Volkow *et al.*, 2007).

The findings for the *DRD4* gene, however, have been mixed. Although many studies find the *DRD4*–novelty seeking link, a nearly equal number of studies do not find this association (Paterson *et al.*, 1999; Kluger *et al.*, 2002; Schinka *et al.*, 2002; Munafò *et al.*, 2003). It follows that behavioural expression of the *DRD4* gene could be moderated by other factors. Indeed, several studies find that exposure to negative social environment exacerbates the risks associated with the *DRD4* gene (Keltikangas-Jarvinen *et al.*, 2004; Lahti *et al.*, 2005; Bakermans-Kranenburg and van Ijzendoorn, 2006; Van Ijzendoorn and Bakermans-Kranenburg, 2006). Another potential moderator, gender, has been largely unexplored. This is surprising, in light of the long-standing evidence that males show more pronounced impulsivity and sensation seeking (Zuckerman *et al.*, 1993; Constantino *et al.*, 2002), have higher rates of ADHD (Arnold, 1996) and exhibit more externalizing (Hyde, 1984; Eagly and Steffen, 1986).

Among the few studies that have included gender, a study of Chinese children and adolescents has found an association between the ADHD and *DRD4* for males but not for females (Qian *et al.*, 2004). In other populations, *DRD4* has been linked to novelty seeking (Becker *et al.*, 2005), smoking (Laucht *et al.*, 2005) and ADHD (El-Faddagh *et al.*, 2004) for adolescent males but not females. Finally, the link between the *DRD4* and anger has been demonstrated for males, but not females, in a recent study of Korean college

students (Kang *et al.*, 2008). With the exception of the novelty-seeking study (Becker *et al.*, 2005), none of the studies known to us has formally tested the gene–gender interaction, failing to investigate whether the *DRD4* 7R is indeed associated with higher risk for males *vs* females, or whether the amount of risk is the same for males and females, but the association failed to attain significance for females (due to other factors, such as the lower prevalence of problem behaviours for females).

The present study

The present study set out to replicate the gender-specific expression of the *DRD4* by testing the gene–gender interaction, and explored the social mechanisms that might help explain it. Specifically, we tested gender differences in the associations between the *DRD4* alleles and adolescent delinquency, short temper (an aspect of trait anger) and thrill seeking (an aspect of impulsivity) among Russian youths. Both biological and social mechanisms could be responsible for these gender differences. For example, females have higher dopamine release (Riccardi *et al.*, 2006) and dopamine receptor levels (Kaasinen, 2001). There are also differences in gender socialization that might disparately activate the behavioural expression of the *DRD4*. Specifically, there gender socialization contributes to gender differences in the amounts and types of social risks males and females are exposed to.

Given previous observations that individuals exposed to high psychosocial risk have a stronger *DRD4*–behaviour link (Keltikangas-Jarvinen *et al.*, 2004; Lahti *et al.*, 2005; Bakermans-Kranenburg and van Ijzendoorn, 2006; Van Ijzendoorn and Bakermans-Kranenburg, 2006), we hypothesize that gender differences in risk exposure can help explain gender differences in the behavioural expression of the *DRD4* gene. There are well-documented gender differences in socialization practices—outlining differences in the degree to which parents and other adults discourage antisocial behaviour for girls *vs* boys, as well as differences in the social norms for behaviour (Underwood, 2003). Thus, we propose that boys' higher exposure to psychosocial risk factors can, at least partially, explain gender differences in the behavioural expression of the *DRD4* gene. Specifically, we tested whether males, as compared to females, report lower parental monitoring of their behaviour, higher peer delinquency and higher exposure to violence and whether these gender differences, in turn, help explain gender differences in the behavioural expression of the *DRD4*.

METHODS

Participants

A total of 263 14- to 17-year-old adolescents from two large metropolitan areas in Russia were genotyped, as part of a larger study. Sample recruitment was aimed at including individuals with a wide range of exposure to negative

social and physical contexts. Consequently, we recruited participants from different types of schools—regular public schools located in working through middle class neighbourhoods and schools for youths at risk for delinquency. The determination of adolescents' at-risk status and their placement into specialized schools for at-risk youths had been made by local juvenile justice agencies. It was based on youths' previous behaviour such as criminal offending and severe school misconduct, as well as social contextual risks such as parental criminal behaviour or incarceration. Based on classroom enrolment numbers, 88% of regular public school students and 94% of youths enrolled in specialized schools for at-risk adolescents participated in the study. This sample was relatively ethnically homogenous (92% of participants reported being of Slav ancestry). Participants were on average 14.6-year old (median = 15, s.d. = 0.96) and evenly distributed by gender (50% males). Once appropriate youth assents and parental or legal guardian consents were obtained, youths participated in a survey that took place at school during two regular class sessions. A trained, native Russian-speaking research assistant was present at all times during survey administration. At the end of the first class session, participants were instructed to provide a saliva sample in a collection tube that was distributed to them with the survey. The study was conducted in accordance with the declaration of Helsinki, the protocol was approved by the UC Irvine IRB, and participants and their parents provided written consent to the study.

Measures

Delinquency was assessed with two scales. The 22-item problem behaviour scale (Chen *et al.*, 1998) that assesses frequency of engaging in a variety of problems behaviours over the past 6 months. Response categories included 0 = never, 1 = once or twice, 2 = three to four times, 4 = more often. Actual responses ranged from 0 to 2.77. The scale had high internal consistency, $\alpha = 0.89$. In addition, we employed the 23-item self-reported offending checklist (Huizinga *et al.*, 1991) that assesses engagement in the more serious/criminal activities over the past 6 months. The two scores were standardized and combined into a single measure of delinquency.

Short Temper was assessed with 15 items adapted from the Novaco Anger Scale (Novaco and Chemtob, 1998), such as 'my temper is quick and hot'. The response categories ranged from 1 (*never true*) to 3 (*always true*). The actual response ranged from 1.06 to 2.77. The scale had high internal consistency, $\alpha = 0.83$.

Thrill Seeking was measured with nine items adapted from the impulsive sensation seeking subscale of the Zuckerman–Kuhlman personality questionnaire (Zuckerman *et al.*, 1993) and the thrill and adventure seeking for children scale (Russo *et al.*, 1993). Participants endorsed items, such as 'I like to have new and exciting experiences and sensations even if they are a little

frightening'. The combined nine-item scale had adequate internal consistency, $\alpha = 0.67$. Individual items were standardized and combined into a single measure of thrill seeking.

Psychosocial risk variables included *parental monitoring*, *peer delinquency* and *exposure to violence*. *Parental Monitoring* of adolescent activities assessed parental involvement in their adolescents' lives with the 10-item parental knowledge scale (Chen *et al.*, 1998). Participants indicated the extent of parental knowledge (as perceived by youths) of various aspects of the adolescent's life, such as 'where you go, when you go out at night' and 'whom you spend your free time with'. The scale values ranged from 1 = *never know* to 4 = *always know*. The actual responses ranged from 1 to 4. The scale had adequate internal consistency, $\alpha = 0.78$. *Peer Delinquency* included 13 items from the peer delinquent behaviour scale (Thornberry *et al.*, 1994) that assessed the proportion of youths' friends who are involved in various delinquent behaviours. Response categories ranged from 0 (*none of them*) to 4 (*all of them*). The actual responses ranged from 0.77 to 3.17. The scale had good internal consistency, $\alpha = 0.79$. *Exposure to Violence* was measured with the 16-item exposure to violence and victimization scale (Schwab-Stone *et al.*, 1999). Participants responded to how often, in the past year, they had seen another person being victimized (e.g. being chased, robbed and injured) and how often they themselves had been a victim. Response categories ranged from 0 (*never*) to 3 (*often*). The actual responses ranged from 0 to 1.69. The scale had good internal consistency, $\alpha = 0.84$.

Genomic DNA was extracted from saliva samples, using DNA Genotek Oragene saliva collection kits. The following oligodeoxynucleotide primers were used: 5'-ATGCTGCTGCTCTACTGGG-3' and 5'-GGAACCTCGGCGTTGAAGACA-3'. Polymerase chain reaction (PCR) was conducted with Qiagen Core kit in 30 μ l volumes containing 30 ng genomic DNA, 3 μ l 10 \times buffer, 6 μ l Q solution, 0.6 μ l Deoxynucleotide Triphosphate (dNTP), 1.5 μ l of each primers and 0.20 μ l Taq DNA polymerase. Amplification was performed using Perkin Elmer thermal cycler with the following steps: initial denaturing at 95°C for 2 min; 15 cycles: 95°C for 30 s, 65°C for 30 s, 72°C for 1 min; 25 cycles: 95°C for 30 s, 55°C for 30 s, 72°C for 1 min and final extension at 72°C for 10 min. PCR products were visualized in a 2% agarose gel stained with ethidium bromide. The process was completed successfully for 100% of the available DNA samples.

Table 1 presents observed genotype frequencies for the whole sample and by gender. The 4/4 was the most frequently observed genotype (56%), followed by the 4/7 (13%) and 4/2 (12%) genotypes. The observed genotype groups were in Hardy–Weinberg equilibrium, $\chi^2(21) = 29.89$, $P = 0.09$, and the genotype frequencies did not differ by gender, $\chi^2(14) = 13.47$, $P = 0.49$.

Statistical analyses

Based on the observed genotypes, we constructed three comparison groups: the 4/4 group ($N=146$), the 7R group ($N=48$) and the 2R group ($N=41$). Because the 7R and 2R groups are not mutually exclusive (five participants had a 2/7 genotype), analyses made comparison of the 4/4 group with either 7R or 2R group, but not of the 7R group with the 2R group. *T*-tests were used to compare means across the groups (4/4 vs 7R and 4/4 vs 2R) for all participants (males and females). Next, a multivariate analysis of variance (MANOVA) model was used to estimate the gene–gender interaction for the three outcome measures. This model included delinquency, short temper and thrill seeking as the outcome measures. Effects of gender, the *DRD4* gene and their interaction were evaluated with the *F*-value of the Willks' Lambda multivariate test. In addition, partial eta squared values were used to evaluate estimated effect size. Significant multivariate interaction effects were examined further with the univariate *F*-tests (one test for each outcome variable). Upon establishing a significant interaction effect for all three outcomes combined (multivariate Willks' Lambda *F*) and for each of the outcomes separately

(univariate *F*), mean differences across the genotypes were estimated within each gender, while adjusting *P*-values for multiple comparisons with Bonferroni corrections. The Bonferroni corrections were estimated within the MANOVA facility.

Finally, the mediational hypotheses were tested. Because, we hypothesized that social risk factors (i.e. parental monitoring, peer delinquency and exposure to violence) mediate the gender-specific expression of the *DRD4* gene, we first established that males are exposed to higher social risk (using *t*-tests). Next, we tested whether adding the social risk variables into the MANOVA gene–gender interaction model rendered the gene–gender interaction non-significant. This model tested effects of the *DRD4*, gender, *DRD4*–gender interaction, parental monitoring, peer delinquency and exposure to violence. A change from significant to non-significant *DRD4*–gender interaction was interpreted as a significant mediation effect (Baron and Kenny, 1986). A final set of MANOVA models added the social risk variables one at a time, in order to establish which of the three social risk variables served as a mediator.

Follow-up analyses addressed the problem of the non-independence of results due to overlap between the 2R and 7R groups. We removed the five participants with the 2/7 genotype and replicated our results in a single model. Once again a MANOVA was used with three outcome variables. In contrast to the main analyses, the three-level *DRD4* variable (contrasting the 4/4, 2R and 7R groups) was used to evaluate the *DRD4*–gender interaction.

Table 1 *DRD4* genotype frequencies for the whole sample and by gender

<i>DRD4</i> Genotypes	Complete Sample ($N = 263$) <i>n</i> (%)	Females ($N = 132$) <i>n</i> (%)	Males ($N = 131$) <i>n</i> (%)
4/4	146 (56)	69 (52)	77 (59)
4/7	34 (13)	14 (11)	20 (15)
4/2	31 (12)	18 (14)	13 (10)
4/3	18 (7)	9 (7)	9 (7)
4/5	8 (3)	3 (2)	5 (4)
7/7	6 (2)	5 (4)	1 (1)
2/2	5 (2)	4 (3)	1 (1)
2/7	5 (2)	2 (2)	3 (2)
3/3	2 (1)	1 (1)	1 (1)
3/7	2 (1)	1 (1)	1 (1)
4/6	2 (1)	2 (2)	0 (0)
3/5	1 (0.4)	1 (1)	0 (0)
3/8	1 (0.4)	1 (1)	0 (0)
4/8	1 (0.4)	1 (1)	0 (0)
7/8	1 (0.4)	1 (1)	0 (0)

RESULTS

Youths in the 7R group reported higher thrill seeking, but not delinquency or short temper (Table 2). Results of a MANOVA model for delinquency, short temper and thrill seeking showed a significant 7R–gender interaction, $F(3,173) = 2.84$, $P < 0.05$ (partial $\eta^2 = 0.05$). Specifically, the magnitudes of the interaction for each outcome variable were: $F(1,175) = 6.3$, $P < 0.05$ (partial $\eta^2 = 0.03$) for delinquency; $F(1,175) = 4.18$, $P < 0.05$ (partial $\eta^2 = 0.02$) for short temper and $F(1,175) = 3.82$, $P < 0.05$ (partial $\eta^2 = 0.02$) for thrill seeking. The 7R allele was associated

Table 2 Means and standard deviations of self-reported delinquency, short temper and thrill seeking for the 4/4 genotype and the 7R allele group

	All		<i>P</i>	Females		<i>P</i> ^a	Males		<i>P</i> ^a
	4/4 ($N = 146$)	7R ($N = 47$)		4/4 ($N = 69$)	7R ($N = 23$)		4/4 ($N = 77$)	7R ($N = 24$)	
Delinquency	−0.05 0.95	0.14 1.14	0.257	−0.25 0.56	−0.39 0.43	0.411	0.13 1.18	0.62 1.37	0.009**
Short temper	1.63 0.35	1.73 0.42	0.091	1.67 0.32	1.65 0.35	0.826	1.59 0.36	1.83 0.47	0.009**
Thrill seeking	−0.02 0.16	0.16 0.48	0.025*	−0.03 0.50	−0.01 0.47	0.901	0.00 0.46	0.33 0.44	0.005**

^a*P*-values for the analyses of *DRD4* × gender were adjusted for multiple comparisons with Bonferroni corrections. * $P < .05$, ** $P < .01$.

Table 3 Means and standard deviations of self-reported delinquency, short temper and thrill seeking for the 4/4 genotype and the 2R allele group

	All		<i>P</i>	Females		<i>P</i> ^a	Males		<i>P</i> ^a
	4/4 (<i>N</i> = 146)	2R (<i>N</i> = 47)		4/4 (<i>N</i> = 69)	2R (<i>N</i> = 23)		4/4 (<i>N</i> = 77)	2R (<i>N</i> = 24)	
Delinquency	−0.05 0.95	−0.05 0.91	0.982	−0.25 0.56	−0.21 0.49	0.847	0.13 1.18	0.18 1.28	0.835
Short temper	1.63 0.35	1.76 0.46	0.044*	1.67 0.32	1.83 0.39	0.074	1.59 0.36	1.67 0.53	0.415
Thrill seeking	−0.02 0.48	0.01 0.61	0.734	−0.03 0.50	0.12 0.58	0.225	0.00 0.46	−0.13 0.63	0.357

^a*P*-values for the analyses of *DRD4* × gender were adjusted for multiple comparisons with Bonferroni corrections. **P* < .05.

with higher delinquency, short temper and thrill seeking for males, but not for females (Table 2).

Youths in the 2R group reported more problems with short temper, but not delinquency or thrill seeking (Table 3). Results of a MANOVA model for delinquency, short temper and thrill seeking did not find a significant 2R–gender interaction, $F(3,169) = 0.86$, NS.

We next tested whether gender differences in youths' exposure to social risk mediate gender differences in the association between the 7R allele and the three outcome measures. First, we established significant gender differences in risk exposure—i.e. our putative mediator variables (Table 4). Males received less parental monitoring while also had more delinquent peers and higher exposure to violence. Second, parental monitoring, peer delinquency and exposure to violence were added into the multivariate model that tested the 7R–gender interaction for the three outcome measures. After controlling for risk exposure, the 7R–gender interaction was no longer significant, $F(3,151) = 2.05$, $P = 0.11$ indicating that gender differences in the association between the 7R allele and the three outcomes were mediated by gender differences in risk exposure. A separate inspection of each of the risk-exposure variables revealed that two of these three variables mediated gender differences. Parental monitoring and exposure to violence mediated gender differences in the expression of the *DRD4* 7 [$F(3,155) = 2.26$, $P = 0.08$ and $F(3,171) = 1.33$, $P = 0.266$ after adding parental monitoring and exposure to violence, respectively, into the multivariate model]. Peer delinquency, however, did not appear to serve as a mediator [$F(3,169) = 4.12$, $P < 0.01$, $\eta^2 = 0.07$].

Follow-up analyses evaluated the *DRD4*–gender interaction in a single model and demonstrated results that are virtually identical to those for the main analyses. For this MANOVA model for delinquency, short temper and thrill seeking, there was a significant *DRD4*–gender interaction, $F(6,400) = 2.08$, $P < 0.05$ (partial $\eta^2 = 0.03$). The magnitudes of the interaction for each outcome variable were: $F(2,202) = 3.23$, $P < 0.05$ (partial $\eta^2 = 0.03$) for delinquency; $F(2,202) = 2.45$, NS for short temper and $F(2,202) = 4.44$, $P < 0.05$ (partial $\eta^2 = 0.04$) for thrill seeking. Univariate analyses confirmed that, compared to the 4/4 genotype, the 7R

Table 4 Means and standard deviations of the social risk measures

	Females	Males	<i>t</i> (227)	<i>P</i>
Parental monitoring	2.78 0.64	2.59 0.60	2.14*	0.034
Peer delinquency	1.32 0.33	1.45 0.50	2.30*	0.023
Exposure to violence	0.13 0.22	0.24 0.31	3.00**	0.003

P* < .05, *P* < .01.

allele is associated with higher delinquency and thrill seeking for males, but not for females. Similar to the main analyses, the interaction effect became not significant when the social risk variables were added to the model.

DISCUSSION

The present study tested whether gender differences in the effects of *DRD4* 7R and 2R alleles can be demonstrated in a sample of Russian youths. As expected, the 7R allele was significantly associated with delinquency, short temper and thrill seeking for males, but not for females. There were no gender differences in the link between the 2R allele and any of the three outcomes.

This gender-specific vulnerability to *DRD4* could be attributed to gender differences in biological factors, such as differences in estrogen and progesterone, which modulate the dopaminergic activity (Becker, 1999), differences in sex chromosome genes, differences in DNA methylation and differences in autosomal genes (Harrison and Tunbridge, 2008) However, we proposed that gender differences in the exposure to contextual risk factors may also explain gender differences in the behavioural expression of the *DRD4* gene.

We, therefore, examined whether the observed gender differences can be explained by males' greater exposure to risk factors such as low parental monitoring, high peer delinquency and high exposure to violence. Indeed, in our sample, girls were monitored more closely, had fewer delinquent peers and had lower exposure to violence. Furthermore, differences in parental monitoring and exposure to violence

helped explain gender differences in the association between the 7R allele and delinquency, short temper and thrill seeking.

Our findings do not completely rule out the importance of biological sex differences in behaviour. In fact, differences in social context might be evoked by early gender differences in temperament. For example, females tend to have a stronger affiliative response to stress that is related to their greater oxytocin release in response to stress and the modulation of oxytocin by estrogen (Taylor *et al.*, 2000; Taylor, 2006). Thus, biological sex differences may contribute to the construction of gender-specific social environments, which, in turn, contribute to gender-specific expression of the *DRD4* gene. Our findings reveal one aspect of the complexity of the *DRD4*-behaviour associations, underlining the need for careful examinations of both the biological and social differences in studies of gender-specific genetic expression.

Several limitations should be mentioned. First, results would be strengthened if replicated in a study that corroborates youth self-report with either parent or teacher report of adolescent behaviour. In particular, the observed gender difference in parental monitoring may mean that boys receive less monitoring than girls, as well as reflect gender differences in the perceived meaning of the parent-adolescent relationship—where boys perceive and report (but not experience) less monitoring than girls. Although an investigation of perceived *vs* experienced gender differences in the parent-adolescent relationship is beyond the scope of this study, previous research adds confidence in favour of the ‘experience’ interpretation. Stattin and Kerr (2000), for example, report that child disclosure of daily activities is significantly higher among girls than boys, regardless of whether a child or parent report is used to evaluate parental behaviour. Similarly, Crouter and colleagues (Crouter *et al.*, 1999) find that parental knowledge of adolescent activities is more accurate among girls’ than boys’ parents. Second, these findings are based on cross-sectional data and limit our ability to test the role of gender in predicting how changes in social environment might help mitigate or intensify the association between the *DRD4* and behavioural outcomes. Along the same lines, a study of younger children might reveal somewhat different results, as gender differences in parental monitoring, for example, might not be as pronounced for younger children as they are for adolescents. Finally, our study focused on a limited set of social risk factors. Further investigations are needed to test gender-specific expression of the *DRD4* in the context of other risk factors (e.g. chronic illness, trauma, maltreatment).

In summary, our results suggest that the association between the *DRD4* VNTR polymorphism and adolescent delinquency, short temper and thrill seeking is stronger for males than females, and this gender-specific expression of the *DRD4* can be explained by gender differences in exposure to violence and parental monitoring of youth activities. Further longitudinal investigations are needed to explore

the development and maintenance of these gender differences.

Conflict of Interest

None declared.

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