

# Contributions of the *DAT1* and *DRD2* genes to serious and violent delinquency among adolescents and young adults

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**Abstract** As far as we know, this is the first national study that reports compelling evidence for the main effects of genetic variants on serious and violent delinquency among adolescents and young adults. This study investigated the association between the self-reported serious and violent delinquency and the *TaqI* polymorphism in the *DRD2* gene and the 40-bp VNTR in the *DAT1* gene. The study was based on a cohort of more than 2,500 adolescents and young adults in the National Longitudinal Study of Adolescent Health in the United States. The trajectories of serious delinquency for the *DAT1*\*10R/10R and *DAT1*\*10R/9R genotypes are about twice as high as that for the *DAT1*\*9R/9R genotype (LR test,  $P = 0.018$ , 2 *df*). For *DRD2*, the trajectory of serious delinquency for the heterozygotes (A1/A2) is about 20% higher than the A2/A2 genotype and about twice as high as the A1/A1 genotype, a phenomenon sometimes described as heterosis (LR test,  $P = 0.005$ , 2 *df*). The findings on violent delinquency closely resemble those on serious delinquency. The trajectories of violent delinquency for the *DAT1*\*10R/9R and *DAT1*\*10R/10R genotype are again about twice as high as that for *DAT1*\*9R/9R (LR test,  $P = 0.021$ , 2 *df*). The two homozygotes of *DRD2*\*A1/A1 and *DRD2*\*A2/A2 scored lower (LR

test,  $P = 0.0016$ , 2 *df*) than the heterozygotes. The findings in the models that consider *DAT1* and *DRD2* jointly (serious delinquency  $P = 0.0016$ , 4 *df*; violent delinquency  $P = 0.0006$ , 4 *df*) are essentially the same as those in the single-gene models, suggesting the absence of a significant correlation between the two genetic variants. These results only apply to males. Neither variant is associated with delinquency among females.

## Introduction

Social origin has been linked to adolescent delinquency and criminal behavior (Paternoster and Brame 1997; Sampson et al. 2005; Sampson and Laub 2005). One general principle guiding empirical research is that an individual is more likely to engage in delinquency or crime when social control is weakened (Hirschi 1969; Gottfredson and Hirschi 1990; Sampson and Laub 1993). Parenting styles, parent–child emotional bond, school attachment, peer influence in adolescence, marital stability, military service, and employment are examples of social control. In spite of the wide recognition that individuals may differ in the propensity to commit serious delinquent and criminal acts (e.g., Moffitt 1993; Gottfredson and Hirschi 1990; Caspi et al. 1994; Paternoster and Brame 1997), few studies have investigated the potential connections between genetic variants and serious and violent delinquency in humans. A notable exception is recent work by Caspi et al. (2002) who showed that maltreated children in New Zealand with a genotype associated with low levels of *MAOA* activity were more likely to engage in violent behavior than maltreated children with a normal level of *MAOA* activity.

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The objective of this study is to investigate the association between the self-reported serious and violent delinquency and the 40-bp variable number of tandem repeats (VNTR) in the *DATI* gene and the *TaqI* polymorphism in the *DRD2* gene. The study was based on a cohort of more than 2,500 adolescents and young adults in the United States in the National Longitudinal Study of Adolescent Health (Add Health).

A genetic contribution to delinquency has been reported by a number of twin and sibling studies (Rodgers et al. 2001; Christiansen 1977; Gottesman et al. 1983; Malone et al. 2004). A number of biometrical studies also identified shared environmental influences as important contributors to delinquency (Lyons et al. 1995; Cloninger and Gottesman 1987; Rowe 1992). Many of the studies on genetic variants and aggression have focused on the role of dopamine and its receptors and transport sites (de Almeida et al. 2005; Miczek et al. 2002). The most common pharmacotherapeutic interventions of human aggression use dopaminergic antagonists (de Almeida et al. 2005). For instance, the dopamine D2 receptor (*DRD2*) antagonist haloperidol has long been used to treat aggressive behavior in psychotic patients.

Civelli and colleagues were the first to clone and sequence a dopamine D2 receptor (Bunzow et al. 1988) and the first to describe the 3' *TaqI* polymorphism in this gene (Grandy et al. 1989). The *TaqI* polymorphism is a T to C transition in the 3' non-coding region of the gene, 10.5 kb downstream of the stop codon and 9.4 kb downstream of the polyA signal. There have been mixed findings regarding the functional significance of this polymorphism. Noble and colleagues reported an association between the *DRD2*\*A1 allele and a lower  $B_{max}$  for dopamine receptors in the brain (Noble et al. 1991) and the activity differences between *DRD2*\*A1 respondents and those homozygous for the *DRD2*\*A2 genotype (Noble et al. 1997). The *DRD2*\*A1 allele was shown to be associated with decreased receptor density in one study (Pohjalainen et al. 1998), but not in others (e.g., Laurelle et al. 1998).

The soluble carrier family 6 dopamine transporter member three gene (*DAT*, locus symbol: *SLC6A3*) codes for a dopamine transporter protein (DAT), which limits the level and duration of dopamine receptor activation (Bannon et al. 1995). A study using mice with the dopamine-transporter gene knocked out established not only the central importance of dopamine transporter in controlling synaptic dopamine levels, but also its role as an obligatory target for the behavioral and biochemical action of amphetamine and cocaine (Giros et al. 1996). Vandenbergh et al.

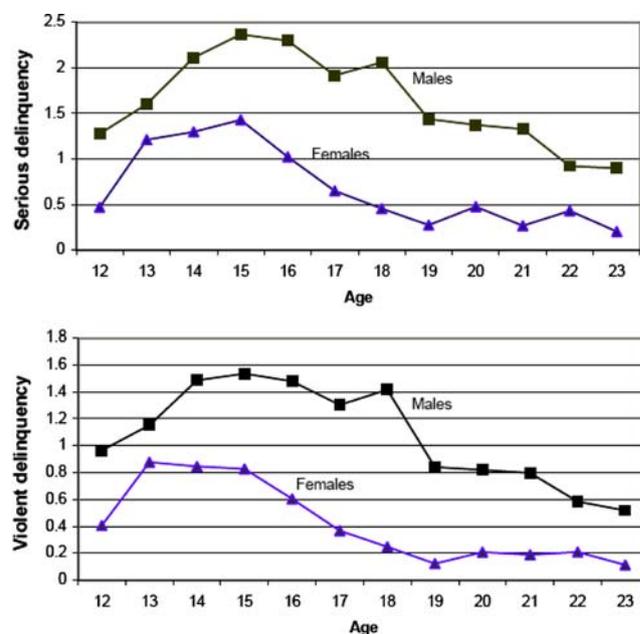
(1992) identified several polymorphisms in *DATI*, including a polymorphic 40 bp repeat in the transcribed portion of the gene which is most commonly repeat 9 (*DATI*\*9R) to 10 times (*DATI*\*10R).

One study found that human subjects homozygous for the 10R allele exhibited significantly lower dopamine transporter binding than carriers of the 9R allele (Jacobson et al. 2000) although the findings from another study are inconsistent (Heiz et al. 2000). A number of studies have demonstrated an association between the 10R allele in the *DATI* gene and attention deficit hyperactivity disorder (ADHD) (Cook et al. 1995; Daly et al. 1999; Gill et al. 1997; Waldman et al. 1998; Cornish et al. 2005). The *DATI*\*9R allele was reported to be associated with both a lower score in novelty seeking and a greater success in smoking cessation (Sabol et al. 1999). A study of a community sample of 790 children reported an association between the VNTR polymorphism in the *DATI* gene and parent-reported externalizing behavior assessed at ages 4 and 7, but not at age 9 years (Young et al. 2002).

## Results

### Contingency table analysis

Figure 1 plots the empirical trajectory or mean score of serious delinquency (Panel 1) and violent delinquency (Panel 2) by age and gender. Table 1 compares the



**Fig. 1** Serious and Violent delinquency scale score by age and gender

mean score of serious delinquency and violent delinquency across genotypes within each gender and each of the three Add Health Waves. The declining trend of both serious delinquency and violent delinquency over the Waves is a reflection of the age pattern described in Fig. 1. For the *DATI* gene, the most interesting result is the sharply reduced serious delinquency scores and violent delinquency scores at each of the three Waves among the males with the *DATI*\*9R/9R genotype as compared with the *DATI*\*10R/10R genotype and the *DATI*\*10R/9R genotype. For example, the males with the *DATI*\*9R/9R genotype on average scored 1.5 on the delinquency scale at Add Health Wave I much lower than 2.38 and 2.34 scored by those with the *DATI*\*10R/10R genotype or the *DATI*\*10R/9R genotype, respectively. The females with the 9R/9R genotype, however, do not seem to score differently from the 10R/10R or 10R/9R genotype.

The results with regards to the *DRD2* gene are more complicated, but equally interesting. The male respondents heterozygous for the A1 and A2 alleles seem to consistently score higher on both the serious delinquency and the violent delinquency scale across all three Add Health Waves than the *DRD2*\*A1/A1 or the *DRD2*\*A2/A2 genotype. This pattern of much higher or lower value for the heterozygotes relative to both types of homozygotes is sometimes described as heterosis and reviewed recently by Comings and MacMurray (2000). These results apply again only to

males. The initial findings of the association concerning both *DATI* and *DRD2* do not seem to vary by Add Health Waves or age, suggesting that the genotype effects may be relatively constant or the trajectories of delinquency across genotypes are likely to be parallel over adolescence and young adulthood. Because of the sibling clustering in the data, standard significance tests are not valid for these comparisons. The next section presents significance tests for the genotype effects obtained from the mixed regression-models that take the correlations into consideration.

### Regression analysis

The findings from the regression analysis (Table 2) are highly consistent with those from the contingency table analysis (Table 1). Table 2 presents the estimated associations of the genetic variants in *DATI* and *DRD2* with serious delinquency and violent delinquency among male adolescents and young adults. We have estimated models based only on the female sample; the models run parallel to those in Table 2. Neither *DATI* nor *DRD2* variants are associated with number of partners in these models (data not shown). Table 2 reports six models with three for serious delinquency and three for violent delinquency. After considering one polymorphism at a time in the first two of the three models, the third model considers the two polymorphisms simultaneously. Each of the six models

**Table 1** Mean score of serious delinquency and violent delinquency by genotype, gender, and Add Health Waves

	Genotype	Genotype frequency (Wave I)	Serious delinquency			Violent delinquency		
			Wave I	Wave II	Wave III	Wave I	Wave II	Wave III
Age range			12–18	13–19	19–25	12–18	13–19	19–25
<b>Males</b>								
<i>DATI</i> gene	10R/10R	703	2.41	1.58	1.25	1.62	0.98	0.76
	10R/9R	406	2.53	1.87	1.16	1.82	1.23	0.65
	9R/9R	60	1.47	1.00	0.52	1.00	0.67	0.23
	Other/Other	45	1.96	1.43	1.77	1.27	1.07	1.11
	Sample size	1,214	1,214	1,119	927	1,214	1,119	927
<i>DRD2</i> gene	A2/A2	659	2.15	1.78	1.05	1.27	1.12	0.64
	A1/A2	453	2.62	2.25	1.05	1.71	1.46	0.72
	A1/A1	95	2.06	1.18	1.02	1.31	0.73	0.64
	Sample size	1,207	1,207	1,113	927	1,207	1,113	927
	<b>Females</b>							
<i>DATI</i> gene	10R/10R	801	1.09	0.92	0.26	0.67	0.53	0.31
	10R/9R	422	1.13	0.96	0.25	0.55	0.55	0.15
	9R/9R	60	1.19	1.01	0.54	0.62	0.66	0.30
	Other/Other	33	1.27	1.03	0.32	1.12	0.72	0.15
	Sample size	1,316	1,316	1,228	1,059	1,316	1,228	1,059
<i>DRD2</i> gene	A2/A2	723	1.00	0.92	0.29	0.53	0.51	0.15
	A1/A2	491	1.15	0.93	0.27	0.67	0.53	0.15
	A1/A1	104	1.55	1.03	0.27	1.06	0.74	0.16
	Sample size	1,318	1,318	1,228	1,059	1,318	1,228	1,059

**Table 2** Estimated association of the genetic variants with serious and violent delinquency among male adolescents and young adults

	Serious delinquency						Violent delinquency					
	<i>DATI</i>		<i>DRD2</i>		Two combined		<i>DATI</i>		<i>DRD2</i>		Two combined	
	$\beta$	<i>P</i>	$\beta$	<i>P</i>	$\beta$	<i>P</i>	$\beta$	<i>P</i>	$\beta$	<i>P</i>	$\beta$	<i>P</i>
Intercept	-4.14	0.060	-3.01	0.16	-3.76	0.08	-1.74	0.26	-0.934	0.54	-1.42	0.36
Age	0.70	0.004	0.70	0.004	0.69	0.004	0.36	0.036	0.36	0.037	0.35	0.039
Age <sup>2</sup>	-0.023	0.0005	-0.023	.0005	-0.023	0.0005	-0.01	0.005	-0.013	0.006	-0.012	0.006
White	-	-	-	-	-	-	-	-	-	-	-	-
Black	0.46	0.048	0.45	0.054	0.46	0.047	0.41	0.010	0.39	0.01	0.40	0.013
Hispanic	0.51	0.037	0.58	0.021	0.58	0.020	0.40	0.018	0.43	0.01	0.43	0.012
Asian	0.32	0.311	0.31	0.32	0.31	0.32	0.14	0.517	0.11	0.60	0.12	0.58
9R/9R	-	-	-	-	-	-	-	-	-	-	-	-
10R/9R	1.03	0.005	-	-	0.96	0.009	0.70	0.006	-	-	0.64	0.012
10R/10R	0.84	0.020	-	-	0.76	0.035	0.54	0.032	-	-	0.49	0.053
A1/A2	-	-	-	-	-	-	-	-	-	-	-	-
A1/A1	-	-	-0.96	0.002	-0.91	0.004	-	-	-0.68	0.002	-0.65	0.003
A2/A2	-	-	-0.34	0.050	-0.33	0.060	-	-	-0.32	0.008	-0.31	0.010
LR test against no-gene model	<i>P</i> = 0.018, 2 <i>df</i>		<i>P</i> = 0.005, 2 <i>df</i>		<i>P</i> = 0.0016, 4 <i>df</i>		<i>P</i> = 0.021, 2 <i>df</i>		<i>P</i> = 0.0016, 2 <i>df</i>		<i>P</i> = 0.0006, 4 <i>df</i>	
-2 Log L	16,387.9		16,385.5		16,378.6		14,241.0		14,235.9		14,229.2	
No of persons	1,163		1,163		1,163		1,163		1,163		1,163	
No of measures	3,121		3,121		3,121		3,121		3,121		3,121	

Random parameters are not presented in this table

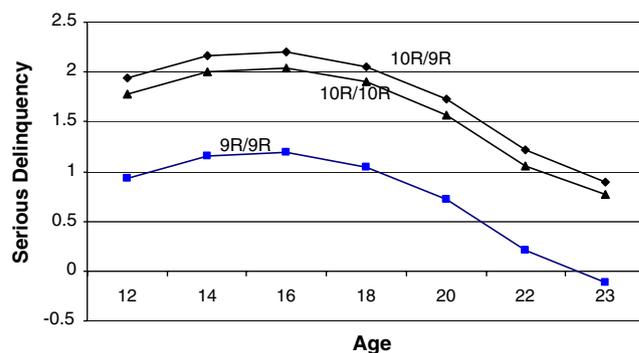
also reports the number of respondents as well as the number of observations used in the model. A respondent does not have to contribute an observation at all three Waves to be included in the analysis. The random parameters in the mixed model described by Eq. 1 are not shown in Table 2.

In order to facilitate likelihood ratio tests across different models to test the overall genotype effects, we used exactly the same number of observations (3,121) in the models on serious delinquency and violent delinquency. Using samples with the maximum number of observations (about 3,243) yielded almost identical results.

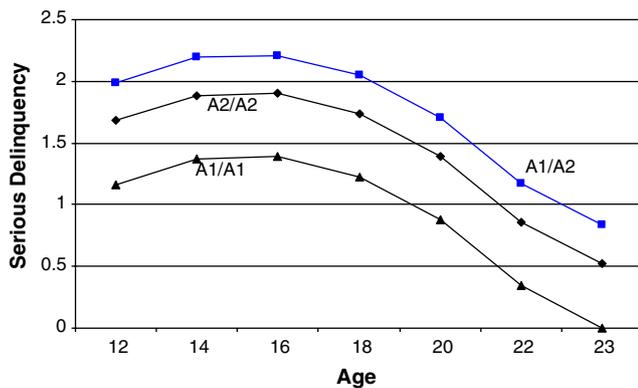
The models of *DATI* included only respondents with the *DATI*\*10R/10R, *DATI*\*10R/9R, and *DATI*\*9R/9R genotypes. The three genotypes amount to about 98% of the sample. The *DATI* model shows that the male respondents with the *DATI*\*10R/10R and *DATI*\*10R/9R genotypes scored 1.03 and 0.84 points higher on the delinquency scale, respectively, than those with the *DATI*\*9R/9R genotype; the corresponding *P* values are 0.005 and 0.026, respectively, each with 1 *df*. A likelihood ratio test for the two categories of *DATI*\*10R/10R and *DATI*\*10R/9R against *DATI*\*9R/9R yielded a *P* value of 0.018 with 2 *df*. Consistent with the findings in the contingency-table analysis (Table 1), the A1/A1 or the A2/A2 genotype in the *DRD2* model of serious delinquency scored lower than the heterozygotes (A1/A2) (-0.96 and -0.34 lower with *p* values of 0.002 and 0.05, respectively). A

likelihood ratio test of the two categories of the homozygotes against the heterozygotes yielded a *P* value of 0.005 with 2 *df*.

Figures 2 and 3 graph the effects of genotype (based on results in Table 2) for serious delinquency for the White males. The relative differences across genotypes within each of the other ethnicities are the same though the absolute levels of delinquency need to be adjusted for the effects of ethnicity. In Fig. 2, the trajectory of serious delinquency for the *DATI*\*10R/10R genotype or the *DATI*\*10R/9R genotype is about twice as high as the trajectory for the *DATI*\*9R/9R genotype at most ages in adolescence and young adulthood. In Fig. 3, the trajectory of serious delinquency for the heterozygotes (*DRD2*\*A1/A2) is the



**Fig. 2** Genotype effects of *DATI* on trajectory of serious delinquency



**Fig. 3** Genotype effects of *DRD2* on trajectory of serious delinquency

highest, with the trajectory for the *DRD2*\*A1/A1 genotype located about half as high as the heterozygotes and the *DRD2*\*A2/A2 genotype about 20% lower than the heterozygotes. The graphs for violent delinquency are similar and not shown.

The findings in the model of serious delinquency that considers *DATI* and *DRD2* jointly are very similar to those from the two models that consider one gene at a time. The parameter estimates in the joint model are slightly lower and the *P* values are slightly larger than those in the single-gene models, suggesting the absence of major correlations among the two polymorphisms. The likelihood ratio test of the joint model against the model (not shown here) without the two genetic polymorphisms produced a *P* value of 0.0016 with 4 *df*.

The three models of violent delinquency closely resemble the three models of serious delinquency. *DATI*\*10R/9R and *DATI*\*10R/10R on average scored 0.70 (*P* = 0.006) and 0.54 (*P* = 0.032) points higher than *DATI*\*9R/9R, respectively; the likelihood ratio test between the model with the two genotype parameters against the model without the parameters produced a *P* value of 0.021 with 2 *df*. The two homozygotes of *DRD2*\*A1/A1 and *DRD2*\*A2/A2 scored lower (−0.68 and −0.32 with *P* values of 0.002 and 0.008, respectively) than *DRD2*\*A1/A2, the likelihood ratio test with 2 *df* yielding a *P* value of 0.0016. The findings in the two-gene model for violent delinquency are essentially the same as those in the single-gene models. The likelihood ratio test of the model with four parameters for the two polymorphisms against the model without the genetic variants gives a *P* value of 0.0006.

To address potential bias from population stratification, we controlled for self-reported race/ethnicity in all regression models estimated in Table 2. In addition, we performed Allison's procedure (1999, Eq. 2) for all

four single-gene models. The model includes one random effect ( $\beta_j$ ) at the sibling-cluster level, a second random effect at the individual level ( $e_{ijk}$ ), and the key interaction term  $[(\alpha\beta)_{ij}]$  between genotype and the random effect at the sibling-cluster level. In all four models, the random interaction term is highly significant with a *P* value smaller than 0.0001. More importantly, the genotype effects in these Allison models have remained statistically significant at a similar level as those in the models in Table 2. For example, in the model of serious delinquency, the *P* value for the effect of *DATI*\*Any10R in the Allison model is estimated to be 0.023 as compared with 0.005 and 0.020, respectively for the effects of *DATI*\*10R/9R and *DATI*\*10R/10R in Table 2. Similarly, in the model of violent delinquency, the *P* value for *DATI*\*Any10R is 0.030 in the Allison model as compared with 0.006 and 0.032, respectively for *DATI*\*10R/9R and *DATI*\*10R/10R in Table 2. The results from these additional testing suggests that our findings may not be sensitive to population stratification.

## Discussion

Evidence that links dopamine to aggressive behavior primarily comes from two sources: (1) neurobiological studies of animals, mostly rodents and cats, and (2) mechanistic studies of pharmacotherapeutic interventions in the aggressive acts of patients (Miczek and Fish 2005). Animal models have clearly implicated the dopaminergic system in aggressive behavior even though it is less clear how dopamine and its receptor families in neural circuits specifically mediate aggressive behavior (Miczek and Fish 2005). Neuroleptic drugs that target the D2 receptor family have proved effective reducing violent behavior in both humans and laboratory rodents pointing to the D2 receptor as a critical cite of action (Brizer 1988; Krsiak et al. 1981).

Related human studies are mostly on ADHD, externalizing behavior, and hyperactivity among young children. The 10R allele in the *DATI* gene has been repeatedly shown to be associated with attention deficit hyperactivity disorder (ADHD) (Cook et al. 1995; Daly et al. 1999; Gill et al. 1997; Waldman et al. 1998; Cornish et al. 2005). The VNTR polymorphism in the *DATI* gene has been linked to externalizing behavior at ages 4 and 7 (Young et al. 2002). However, a similar study examining the links between the same VNTR in the *DATI* gene and hyperactivity, other externalizing behavior problems, and related temperament traits in a general population sample did not find the associations (Jorm et al. 2001).

Although measures such as ADHD, externalizing behavior, and hyperactivity are related to our measures of serious delinquency and violent delinquency, at least two important differences exist between the two. First, externalizing behavior is typically used to measure behavior among young children. Second, externalizing behavior represents a less severe and more inclusive disruptive and destructive behavior in childhood (Shaw and Winslow 1997, p. 148, 149). Externalizing disorders consist of disruptive, hyperactive, and aggressive behaviors (Hinshaw 1987), but some hyperactive children are not antisocial. The construct of externalizing behavior also includes the DSM-IV oppositional defiant disorder (American Psychiatric Association; APA 1994), which involves oppositional behavior (negative, hostile, and defiant behavior) especially shown by young children to their parents and teachers. These early behavior problems are generally less severe than and may be viewed as the forerunner of the serious and violent delinquency among adolescents and young adults measured in our study.

Genetic studies of serious delinquent behavior and criminal behavior in non-patients or general human populations seem rare. Caspi et al. (2002) reported an interaction between maltreatment in childhood and level of *MAOA* activity for violent behavioral problems; they failed to find a main effect of the *MAOA* gene. Chen et al. (2005) hypothesized the association of aggressive behavior in adolescents with both the dopamine D2 receptor gene and the dopamine transporter gene. They provided suggestive evidence from a small study of 11 adolescents diagnosed to have impulsive-aggressive violent behavior.

The findings regarding the *DRD2* gene are somewhat unusual in the sense that the heterozygotes scored higher on the serious and violent delinquency scales than both the homozygotes for *DRD2*\*A1 and the aggressive violent behavior. As far as we know, ours is the first national study that reported significant main effects homozygotes for *DRD2*\*A2. This type of results are sometimes described as *heterosis* defined more generally for cases in which individuals heterozygous for a genetic variant exhibit a greater or lesser effect for a trait than homozygotes (Comings and MacMurray 1997a, b, 2000). Heterosis is systematically studied and taken advantage of in agriculture. For example, hybrid corn consistently demonstrates higher yields than either parental strain (Strickberger 1968; Gardner and Snustad 1981). In human genetics, the sickle cell anemia represents one of the most well-known examples of heterozygote advantage. Individuals with the heterozygous state possess a resistance to malarial infection—a resistance absent in the homozygous

normal or the wild type, while the homozygous carriers will typically die from the genetic disorder. A particularly relevant study of  $\alpha$ -*CaMKII* knockout mice demonstrated a strong effect of heterosis for aggressive behavior using three types of mice: mice in which the gene was heterozygously disrupted, mice in which the gene was homozygously disrupted, and the wild type (Chen et al. 1994). Those with a heterozygous deletion of the  $\alpha$ -*CaMKII* gene scored 80 on the defensive aggression scale while the homozygous wild type and those with a homozygous deletion scored 22 and 0, respectively.

From the evolutionary point of view, aggressive behavior is likely to be adaptive. Aggression could aid securing food and safe resting places, protecting the young, and obtaining advantage in a reproductive context. However, not all levels of aggression are adaptive or equally adaptive. As Edward O. Wilson (1975, p. 254) pointed out, “in order to be adaptive it is enough that aggressive patterns be evoked only under certain conditions of stress such as those that might arise during food shortages and periodic high population densities.” A level of aggression adaptive to a certain set of conditions may not be adaptive to another. Aggressive behavior adaptive to circumstances one million years ago, 200 years ago in an agrarian society, and contemporarily in a digital society is likely to differ considerably. It is thus possible that some genetic variants associated with serious and violent delinquency today could have once had a selective advantage.

Investigating one polymorphism in each of the two well-studied genes has limitations. Although it is plausible that these variants are causally related to serious and violent delinquency, an alternative explanation is that other functional variants within the *DAT1* gene and the *DRD2* gene or in an adjacent region are in linkage disequilibrium with the variants. These other variants could be the real delinquency-predisposing polymorphisms. Additional work is needed to replicate our findings that uses additional genetic variants within and near the *DRD4* and *DRD2* genes.

We examined both serious and violent delinquency in adolescence and young adulthood measured at ages from 12 to 23. The age range is available because of considerable age range within the Add Health sample (12–18 at Wave I) and also because of repeated measures obtained at Waves I–III. The wide age range has advantages and disadvantages. It allows for an examination of the age patterns of delinquency (Fig. 1); but, because the same set of questions were asked of the Add Health respondents at all Waves, the serious and

violent delinquency scales may not be equally valid at all ages. Petty crimes such as stealing something worth less than \$50 may be committed more commonly by adolescents than young adults.

We are planning on a major replication of the reported results, which are based on about 2,500 respondents out of the entire Add Health cohort of about 20,000. Add Health Wave IV is funded and scheduled to collect DNA samples from the entire cohort. When the DNA samples become available, a replication study will be performed using the Add Health respondents whose DNA is not available for the current study.

## Materials and methods

### Subject

The data source for our analysis is the sibling subsample of more than 2,500 participants in the National Longitudinal Study of Adolescent Health (Add Health), which started as a nationally representative sample of more than 20,000 adolescents in grades 7–12 in 1994–1995 (Wave I) in the USA (Harris et al. 2003). Add Health is longitudinal; the respondents have been followed by two additional in-home interviews in 1995–1996 (Wave II) and 2001–2002 (Wave III). Add Health is school-based and the adolescents were from 134 schools. The school sample was stratified by region, ethnic mix, size, urbanicity (urban/suburban/rural), and school type (public/private/parochial). Our analysis uses the sibling sample of Add Health because DNA measures collected at Wave III in 2002 are available only for this subset of the Add Health respondents. The subset consists of about 2,500 MZ twins (16.5%), DZ twins (23.6%), and full biological siblings (59.8%). We estimated the heritability of serious delinquency (0.51) and violent delinquency (0.60) using only the paired male MZ twins, DZ twins, and full biological siblings (333 pairs).

### Measures

We constructed a *serious delinquency* scale and a *violent delinquency* scale using the 12 questions asked of all the Add Health respondents at Waves I–III. The questions and scaling weights used to create the scales are given in [Appendix](#). These two scales are variations of a widely-used type of scales in contemporary research on delinquency and criminal behavior (Thornberry and Krohn 2000). Our scales are closely related to the scales used by, for example, Hagan and Foster

(2003) and Haynie (2001, 2003) in analysis of Add Health data and by Hannon (2003) in analysis of data from the National Longitudinal Study of Youth.

Following the delinquency literature (Hagan and Foster 2003; Haynie 2001, 2003), we divide the 12 questions/items into the non-violent and violent types. The non-violent delinquency includes stealing amounts larger or smaller than \$50 with or without breaking and entering, and drug selling. Violent delinquency includes serious physical fighting that resulted in injuries needing medical treatment, use of weapons to get something from someone, involvement of physical fighting between groups, shooting or stabbing someone, deliberately damaging property, and pulling a knife or gun on someone. The serious delinquency scale (non-violent and violent) is based on the entire 12 items and the violent scale is based on a subset (eight) of the 12 items. The empirical distributions of the two delinquency scales are skewed to the right ranging 0–36 and 0–24, respectively.

The Cronbach's alpha for the serious delinquency scale for Waves I, II, and III, respectively, are 0.81, 0.79, and 0.73. Our serious delinquency scale overlaps with Hagan and Foster's (2003) delinquency scale to a substantial extent. Our serious delinquency scale is designed to capture a wide range of serious delinquent behavior that could result in state sanction of arrest, conviction, and incarceration. Hagan and Foster (2003) utilized a 15-item scale that included most of the 12 items used for our scale as well as a number of items on acts more typically viewed as common adolescent deviance such as lying to parents/guardians about where had been, minor vandalism, being loud in a public place, and driving a car without its owner's permission. As the name suggests, our violent delinquency scale focuses on an array of violent delinquent behavior that could potentially be classified as violent offenses by the criminal justice system. For Waves I, II, and III, the Cronbach's alpha values for the violent delinquency scale are 0.75, 0.74, and 0.66, respectively.

Measuring delinquency and crime is challenging. Official measures based on the police reports and the prison and court system have been long known to substantially underestimate delinquency and crime (Robison 1936; Murphy et al. 1946; Thornberry and Krohn 2000; Hood and Sparks 1970) because official measures reflect not only the behavior of offenders, but also the decisions made by the justice system. For these reasons, many criminologists have turned to self reports in recent decades (Hindelang et al. 1979, 1981). Self reports are now a fundamental method of measuring criminality and seem capable of yielding reliable and valid data (Thornberry and Krohn 2000).

As with any survey of sensitive private information, reporting accuracy is a concern. To protect confidentiality, the entire Add Health questionnaire was completed anonymously without requiring names and other identifying information. Anonymous surveys on sensitive behavior have been shown to be more likely to yield accurate responses than non-anonymous surveys (Alexander and Fisher 2003). To further protect confidentiality, reduce non-responses, and increase reporting accuracy, this section of the interview in Add Health was self-administered by audio-computer assisted self interview (CASI). The sensitive question was read to respondents by means of audio headphones. Respondents were given instructions by the computer on how to complete their answers. Self-reported rates of illegal and embarrassing behavior are higher when computer-assisted techniques, particularly self-administered techniques, are used (Tourangeau and Smith 1996; Wright et al. 1998).

The percent of the US adult population that has ever been incarcerated in a state or federal prison increases sharply in the age group of 25–34 over 18–24 (Bonczar 2003), pointing to a likely heavier sample attrition among more chronic offenders because of incarceration at Wave III than at Waves I and II. Add Health Wave III recorded the specific causes of why some of the Waves I and II respondents were not interviewed at Wave III; approximately one dozen individuals from the sibling sample were not interviewed due to incarceration. Chantala et al. (2004) estimated the extent of underreporting at Wave III relative to Wave I, using the respondents and the reports at Wave I and taking advantage of the observation that some of the respondents at Wave I were non-responders at Wave III. These estimates indicate that most of the delinquent and violently delinquent activities could be underrepresented by 1–2.5% in the Wave III data relative to the Wave I population and that selling drugs, carrying a weapon, and shooting or stabbing someone could be underrepresented by about 5%. To reduce the potential impact of disproportional sample attrition at Wave III, we have removed observations of serious and violent delinquency measured at ages 24 or older. These observations account for fewer than 6% of the total number of observations obtained at Wave III. The genotypic distribution and the mean serious and violent delinquency scores by genotype among these observations (data not shown) are very similar to those in the main sample described by Table 1. We chose age 24 because, in our data, the proportion of having ever being arrested shows a marked decline among those who are 24 or older indicating a more severe disproportional attrition in this age group.

## DNA preparation and genotyping

At Wave III, in collaboration with the Institute for Behavioral Genetics in Boulder, Colorado, Add Health collected, extracted, and quantified DNA samples from the sibling sub-sample. Genomic DNA was isolated from buccal cells using a modification of published methods (Lench et al. 1988; Meulenbelt et al. 1995; Spitz et al. 1996; Freeman et al. 1997). All of the methods employed Applied Biosystems instruments and reagents. Microsatellite and VNTR polymorphisms were done using fluorescent primers that were analyzed on an ABI capillary electrophoresis instrument. Single nucleotide polymorphisms were analyzed using an ABI Sequence Detection System and 5'-nuclease (Taqman®) methodology. To reduce errors, two individuals independently scored all genotyping. The additional details on DNA collection and genotyping can be found at Add Health website (Smolen and Hewitt, <http://www.cpc.unc.edu/projects/addhealth/>).

A 40 bp Variable Number Tandem Repeat (VNTR) polymorphism in the 3' untranslated region of the *DAT1* gene has been genotyped with a modified method of Vandenberg et al. (1992). The primer sequences were: forward, 5'-TGTGGTGTAGGGAACGGCTGAG-3' (fluorescently labeled), and reverse: 5'-CTTCCTGGAGGTCACGGCTCAAGG-3'. This VNTR ranges from 3 to 11 copies with the 9-repeat (9R or 440 bp) and 10-repeat (10R or 480 bp) polymorphisms being the two most common alleles in Caucasian, Hispanic and African American populations (Doucette-Stamm et al. 1995). In our analysis sample, the 9R and 10R account for about 21 and 76% of all alleles, respectively; 35, 59, and 0.048% of the respondents possess one 10R, two 10Rs, and two 9Rs, respectively. The variation across ethnic groups appears to be moderate with the 10R allele accounts for 80, 86, 80, and 90% of all alleles in Whites, Blacks, Hispanics, Asians, respectively. The apparent outlying case of Asians could be due to its small sample size ( $n = 186$  or about 7% of the sample).

The *DRD2* gene has a polymorphic *TaqIA* restriction endonuclease site about 2,500 bp downstream (3' untranslated region) from the coding region of the gene. The A1 allele of this polymorphism has a point mutation C → T (TCGA to TTGA). The *DRD2 TaqIA* genotyping was performed using the fluorogenic 5'-nuclease (Taqman®, Applied Biosystems, Foster City, CA) method with reagents (VIC<sup>TM</sup> and 48 FAM<sup>TM</sup> labeled probes and TaqMan® Universal PCR Master Mix without AMPerase® UNG) obtained from Applied Biosystems (ABI) (Haberstick and Smolen 2004). In our analysis sample, the proportion of *DRD2*\*A1/A2

accounts for 25.9, 36.7, 39.1, and 20.0% of all genotype in Whites, African, Hispanic, and Asian Americans, respectively. A series of  $\chi^2$  tests for each polymorphism and for each self-reported ethnic group (European, African American, Hispanic, and Asian) reveals no deviation from the Hardy–Weinberg equilibrium.

### Analytical strategies

To test the associations of the polymorphisms with serious and violent delinquency, we adopted a three-step analytical strategy. The first step is a contingency-table analysis in which the mean scores of serious delinquency and violent delinquency across genotypes were compared within each Add Health Wave and gender. The second step is a mixed regression model (Searle 1971; Searle et al. 1992) that describes the trajectory of serious and violent delinquency over age. The regression also adjusts for race/ethnicity and for correlation among siblings and repeated measures in the data. The third step addresses potential bias from population stratification.

In the rest of this section, we elaborate on the second and third steps. Our sample consists of twins and siblings as well as the repeated observations of the same individual over different Add Health Waves; these observations are not independent. The mixed model has long been established in the statistical literature for analysis of data that are not independent (Searle 1971; Searle et al. 1992). The following equation describes the basic structure of the mixed models used in our analysis

$$\begin{aligned} \text{Delinquency}_{jit(s)} = & \beta_0 + \beta_1 \text{genotype}_{ji} + \beta_2 \text{age}_{jit} \\ & + \beta_3 \text{age}_{jit}^2 + \beta_4 \text{gender}_{ji} + \beta_5 \text{ethnicity}_{ji} \\ & + u_{j0(s)} + v_{ji} + e_{jit(s)}, \end{aligned} \quad (1)$$

where  $j$ ,  $i$ , and  $t$  index sibling pair or cluster, individual, and Add Health Waves, respectively;  $s = m, d$ , or  $f$  indicates whether the sibling cluster or pair are MZ twins, DZ twins, or full biological siblings. The basic trajectory of serious and violent delinquency is described by age and age<sup>2</sup> and their parameters. The model allows the random effect at the sibling cluster level and the level of observations to vary by type of sibling cluster because the strength of the correlation in these types of sibling clusters varies considerably. Conditional on the three random intercepts at the level of sibling clusters and one random intercept at the individual level, the siblings and repeated measures are assumed to be independent.

Equation 1 does not account for the potential source of clustering due to the Add Health sampling design at the school and/or neighborhood level. Incorporating school or neighborhood random effects would make Eq. 1, which is a three-level model, a four or five-level model. More importantly, school and/or neighborhood effects tend to be quite small in most cases (Guo and Zhao 2000).

We used two strategies to address the potential impact of population structure. First, we adjusted for self-reported race/ethnicity in all regression analysis so that the comparisons across genotypes are made after adjusting for the effects of race/ethnicity. Tang et al. (2005) showed a near-perfect correspondence between the four self-reported ethnic categories (European Americans, African Americans, East Asians, and Hispanics) and the categories determined by 326 micro-satellite markers.

As a second strategy, we applied Allison et al.'s (1999) procedure to test for possible population stratification. Following the idea used in the development of sibship tests of linkage and association (Curtis 1997; Boehnke and Langefeld 1998; Spielman and Ewens 1998), Allison et al. (1999) reasoned that the probabilities of genotypes of siblings depended entirely on parental genotypes and that controlling for the effects of sibship would be equivalent to controlling for parental genotypes. Indexing sibships by  $j$ , individuals by  $k$ , and genotypes by  $i$ , they proposed a procedure that can be written as a mixed model

$$Y_{ijk} = \mu + \alpha_i + \beta_j + (\alpha\beta)_{ij} + e_{ijk}, \quad (2)$$

where  $\alpha_i$ , or the effect of genotype  $i$ , is assumed to be fixed;  $\beta_j$ , or the effect of sibship  $j$ , is assumed to be random; and  $(\alpha\beta)_{ij}$  is an interaction term specifying the dependence of the random effect of sibship on genotype. The conditioning on sibship in the model eliminates the possible confounding of population stratification. This model is a special case of the mixed model (Searle 1971; Searle et al. 1992).

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### Appendix: The serious delinquency scale and the violent delinquency scale<sup>3,4</sup>

1. In the past 12 months, how often did you hurt someone badly enough to need bandages or care from a doctor or nurse?<sup>1</sup>
2. In the past 12 months, how often did someone hurt you badly enough to need bandages or care from a doctor or nurse?<sup>1</sup>
3. In the past 12 months, how often did you use or threaten to use a weapon to get something from someone?<sup>1</sup>
4. In the past 12 months, how often did you take part in a fight where a group of your friends was against another group?<sup>1</sup>
5. In the last 12 months, how often did you deliberately damage property that didn't belong to you?<sup>1</sup>
6. In the past 12 months how often did you carry a handgun to school or work?<sup>1</sup>
7. In the past 12 months, how often did you steal something worth more than \$50?<sup>1</sup>
8. In the past 12 months, how often did you steal something worth less than \$50?<sup>1</sup>
9. In the past 12 months, how often did you go into a house or building to steal something?<sup>1</sup>
10. In the past 12 months, how often did you sell marijuana or other drugs?<sup>1</sup>
11. In the past 12 months, have you shot or stabbed someone?<sup>2</sup>
12. In the past 12 months, have you pulled a knife or gun on someone?<sup>2</sup>

<sup>1</sup> For this question, the score value on the scale is determined in the following manner: The score is coded as zero if the event did not occur in the past 12 months; the score is coded as one if the event occurred once or twice in the past 12 months; the score is coded as two if the event occurred three or four times in the past 12 months; the score is coded as three if the event occurred five or more times in the past 12 months.

<sup>2</sup> For this question, the score value on the scale is determined in the following manner: the score is coded as zero if the event did not occur in the past 12 months; the score is coded as three if the event did occur once or more during the past 12 months.

<sup>3</sup> In the construction of the serious delinquency scale, individuals with more than two missing responses were excluded from analysis. In the construction of the violent delinquency scale, individuals with more than one missing response were excluded from analysis.

<sup>4</sup> The violent scale is based upon 8 of the 12 items and they are items 1–6, 11, and 12.

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