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Monoamine oxidase A genotype is associated with gang membership and weapon use

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Abstract

Context: A functional polymorphism in the promoter region of the monoamine oxidase A (MAOA) gene has been found to be associated with a broad range of antisocial phenotypes, including physical violence. At the same time, it is well known that gang members represent some of the most serious violent offenders. Even so, no research has ever examined the association between MAOA and gang membership.
Objectives: The aim of this study is to examine the association between MAOA and gang membership and between MAOA and weapon use.
Design: We examined the effects of MAOA by using a molecular genetic association research design.
Setting: A nonclinical sample was used in this study.
Participants: Participants were drawn from the National Longitudinal Study of Adolescent Health (1155 females, 1041 males).
Main Outcome Measures: The outcome measures of this study are gang membership and weapon use.
Results: The low MAOA activity alleles conferred an increased risk of joining a gang and using a weapon in a fight for males but not for females. Moreover, among male gang members, those who used weapons in a fight were more likely to have a low MAOA activity allele when compared with male gang members who do not use weapons in a fight.
Conclusions: Male carriers of low MAOA activity alleles are at risk for becoming a gang member and, once a gang member, are at risk for using weapons in a fight.

1. Introduction

The low-activity alleles of a functional polymorphism in the promoter region of the monoamine oxidase A (MAOA) gene confer an increased risk to developing a range of antisocial phenotypes [1,2]. To date, research has linked the low-activity MAOA alleles to various psychopathologies, maladaptive behaviors, cognitive dysfunctions, and criminal behaviors. Brunner et al [3] identified Brunner syndrome, which is an X-linked disorder characterized by impulsivity, heightened aggressiveness, mild mental retardation, and serious criminal behaviors including arson and sexual assault caused by MAOA deficiency. Samochowiec et al [4] tested whether length variation of the 30-bp repeat of the MAOA polymorphism was associated with variation in antisocial behavior and alcohol dependence using a clinical sample of 488 German males including 59 alcoholics with antisocial personality disorder. Prevalence of the low-activity 3-repeat allele was significantly higher among the 59 antisocial alcoholics compared with 185 controls (51% vs 35%, $P = .031$) and compared with 244 alcoholics without antisocial personality disorder (51% vs 32%, $P = .0008$). The authors concluded that the low-activity 3-repeat allele conferred increased susceptibility to antisocial behavior. Based on data from a sample of 41 autistic males, Cohen et al [5] found that males with the low-activity MAOA genotype demonstrated more severe autistic behaviors and had lower IQ than peers with the high-activity MAOA gene.

Caspi et al [1] used data from a New Zealand birth cohort to study gene-environment interplay involved in the relationship between childhood maltreatment and adult antisocial behavior. They found that males who possessed low-activity MAOA alleles and who had been maltreated were significantly likely to evince conduct disorder,

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antisocial personality, and violent, antisocial behavior. Subsequent validation studies affirmed the gene-environment interaction (maltreatment × MAOA) among white but not African American youths [6], whereas others reported null effects based on a community sample [7]. Recently, Kim-Cohen et al [2] reported confirmatory evidence of a link between MAOA-maltreatment and psychiatric symptoms and conducted a meta-analysis that further implicated MAOA as a candidate gene for antisocial phenotypes.

One hypothesis for the pleiotropic effects of MAOA is that it affects the regulation of emotion and cognition in the limbic system. For instance, Meyer-Lindenberg et al [8] found that carriers of the low-activity MAOA polymorphism (2, 3, or 5 repeats) showed 8% reductions in gray matter volumes in the amygdala, cingulated gyrus, insula, and hypothalamus compared with carriers of the high-activity MAOA (3.5 or 4 repeats). Functional magnetic resonance imaging analyses showed that carriers of the low-activity MAOA had increased amygdala arousal and diminished reactivity of the regulatory prefrontal cortex particularly among males. Although MAOA has been associated with a range of antisocial phenotypes, no prior study has linked it to gang membership. This study assessed the role of MAOA in predicting gang membership—and the use of weapons for violent means while involved in gangs—among a sample of youths.

2. Methods

2.1. Data

This study uses data drawn from the genetic subsample of the National Longitudinal Study of Adolescent Health (Add Health). Detailed information about the Add Health data has been published elsewhere [9,10]. Briefly, the Add Health is a prospective and nationally representative sample of American youths. Data collection efforts began in 1994 when more than 90 000 students completed self-report surveys during regular school hours. A subsample of 20 745 participants and 17 700 of their primary caregivers were reinterviewed in their homes. Approximately 1 to 2 years later, a second round of interviews was conducted with 14 738 of the respondents. The third and final wave of interviews were completed between 2001 and 2002 with 15 197 participants. Most of the respondents were young adults at the time that the wave 3 surveys were administered. All of the participants provided voluntary consent to be included in the Add Health study.

Embedded within the Add Health study is a subsample of participants who were genotyped. To be eligible to be included in the DNA subsample, respondents had to have a sibling who was also participating in the Add Health study. In total, 2574 respondents submitted buccal cells to be genotyped for a number of genetic polymorphisms that are involved in neurotransmission. Overall, the Add Health data span nearly 7 years of human development and contain phenotypic, genotypic, and environmental measures.

3. Measures

3.1. Monoamine oxidase A

The MAOA gene is a polymorphic gene that is found on the X chromosome at location Xp11.23-11.4 [11]. The polymorphism arises from a 30 base pair variable number of tandem repeats upstream in the 5′ regulatory region of the gene. The Add Health participants were genotyped for this polymorphism using a variant of the assay developed previously [12]. Primer sequences were as follows: forward, 5′ACAGCCTGACCG-TGGAGAAG-3′ (fluorescently labeled); and reverse, 5′-GAACGTGACGCTC-CATTCGGA-3′. This assay produced polymerase chain reaction (PCR) products of 291 (2-repeat allele), 321 (3-repeat allele), 336 (3.5-repeat allele), 351 (4-repeat allele), and 381 (5-repeat allele) base pairs. The genotypes were scored independently by 2 different raters.

In line with previous researchers analyzing the Add Health data [13], the MAOA gene was divided into 2 groups: a low MAOA activity group and a high MAOA activity group. The low MAOA activity group consisted of the 2-repeat allele and the 3-repeat allele, whereas the high MAOA activity group consisted of the 3.5-repeat allele, the 4-repeat allele, and the 5-repeat allele. Using this nomenclature, 42.3% of males had a low MAOA activity allele and 57.7% of males had a high MAOA activity allele. For females, 17.4% were homozygous for the low MAOA activity allele, 44.7% were heterozygous, and 37.9% were homozygous for the high MAOA activity allele. Descriptive information for MAOA and all of the variables used in the analyses are presented in Table 1.

Table 1
Descriptive statistics for the add health study variables

MAOA (males), no. (%)	
Low MAOA	440 (42.3)
High MAOA	601 (57.7)
MAOA (females), no. (%)	
Low MAOA/Low MAOA	201 (17.4)
Low MAOA/High MAOA	516 (44.7)
High MAOA/High MAOA	438 (37.9)
Gang member, no. (%)	
Yes	77 (3.5)
No	2119 (96.5)
Weapon use, no. (%)	
Yes	58 (2.6)
No	2138 (97.4)
Sex, no. (%)	
Male	1041 (47.4)
Female	1155 (52.6)
Race, no. (%)	
White	1484 (67.6)
African American	383 (17.4)
Other	329 (15.0)
Age, mean (SD)	16.47 (1.69)

3.2. Gang member

During wave 2 interviews, respondents were asked whether they had been initiated into a named gang within the past 12 months. This item was coded dichotomously, where 0 indicates not a gang member and 1 indicates a gang member. Overall, 3.5% of the sample indicated they were a gang member, with 5.2% of males and 2% of females indicating they were gang members. These prevalence estimates are similar to those garnered in other longitudinal samples of youth [14].

3.3. Weapon use

During wave 2 interviews, respondents were asked a number of questions pertaining to their involvement in serious, physical violence. One of these variables—whether the respondent had used a weapon in a fight—was identified as being indicative of gang activity. This item was coded dichotomously, where 0 indicates respondent did not use a weapon in a fight and 1 indicates respondent did use a weapon in a fight.

3.4. Control variables

Two control variables were included in the models to help prevent model misspecification. First, race was included in the analyses to help control for population stratification effects. During wave 1 interviews, respondents were asked to self-identify their racial status. In the present analyses, race was coded with a series of dummy variables measuring whether the respondent was white, African American, or other. Second, age was coded as a continuous variable measured in years.

4. Statistical analyses

The analysis for this study proceeds in a number of interlocked steps. First, logistic regression models will be calculated to determine whether MAOA is associated with gang membership and with weapon use in a fight. Second, logistic regression models will be calculated to determine whether MAOA is able to distinguish between gang members who used a weapon in a fight from those gang members who did not use a weapon in a fight. These models will be confined only to gang members. Given that MAOA is located on the X chromosome all of the analyses will be conducted separately for males and females. Last, the DNA subsample contains nested data, where more than 1 person from the same household is included in the sample. As a result, some of the observations lacked independence and thus could artificially deflate standard errors. This problem was corrected by randomly removing 1 twin from each MZ twin pair from the analyses [13] and by estimating all of the statistical models using Huber/White standard errors [15].

Table 2
Logistic regression models predicting gang membership and weapon use among females (n = 1155)

	Gang member			Weapon use		
	b	SE	Odds ratio	*b*	SE	Odds ratio
MAOA	−0.05	0.32	0.950	−0.24	0.43	0.787
White	−0.39	0.64	0.677	−0.83	1.17	0.469
African American	0.03	0.71	1.04	1.24	1.10	3.47
Age	−0.59*	0.13	0.375	−0.47*	0.16	0.627

Huber/White standard errors presented.
* $P < .05$ level, 2-tailed.

Table 3
Logistic regression models predicting gang membership and weapon use among males (n= 1041)

	Gang member			Weapon use		
	b	SE	Odds ratio	*b*	SE	Odds ratio
MAOA	0.66*	0.30	1.94	0.60*	0.30	1.82
White	−1.07*	0.35	0.342	−0.22	0.40	0.802
African American	−0.14	0.38	0.872	−0.34	0.50	0.715
Age	−0.08	0.07	0.927	−0.10	0.09	0.902

Huber/White standard errors presented.
* $P < .05$ level, 2-tailed.

5. Results

Table 2 contains the results of the binary logistic regression models predicting gang membership and weapon use for females. As can be seen, MAOA was unrelated to both gang membership and weapon use. Race was unrelated to both dependent variables, whereas age maintained an inverse relationship with gang membership and weapon use.

Table 3 contains the results of the binary logistic regression models predicting gang membership and weapon use for males. In contrast to the female models, MAOA had a statistically significant and positive effect on gang membership and on weapon use. Stated differently, males with the low MAOA genotype, compared with males with the high MAOA genotype, were 1.94 times more likely to be gang members, and they were also 1.82 times more likely to have used a weapon in a fight.

The next set of binary logistic regression models examined the association between MAOA and weapon use among gang members. The results of these models are presented in Table 4. As can be seen in the left-hand side of

Table 4
Logistic regression models predicting weapon use among gang members

	Females (n = 23)			Males (n = 54)		
	b	SE	Odds ratio	*b*	SE	Odds ratio
MAOA	−2.22	1.21	0.108	1.47*	0.71	4.37
White	−4.51*	2.26	0.011	1.19	0.78	3.28
African American	−1.35	2.54	0.257	−0.35	0.89	0.706
Age	0.61	0.51	1.85	0.47*	0.22	1.61

Huber/White standard errors presented.
* $P < .05$ level, 2-tailed.

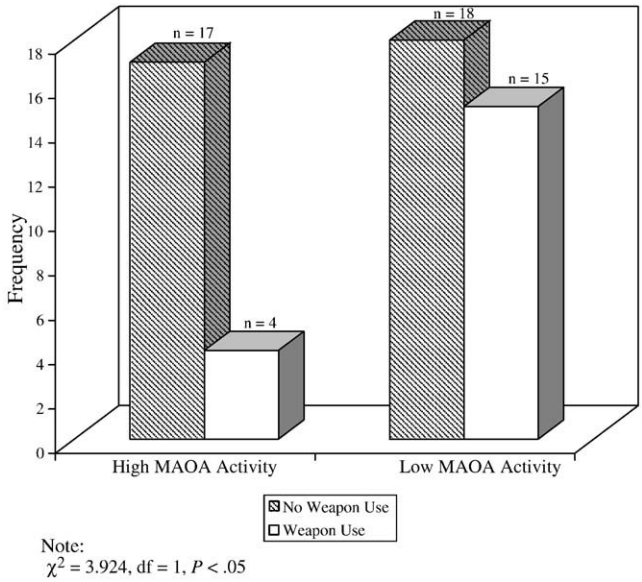

Fig. 1. The relationship between MAOA and weapon use among male gang members (n = 54). $\chi^2 = 3.924$, $df = 1$, $P < .05$.

the table, MAOA was unrelated to weapon use for female gang members. For male gang members, however, a different set of findings emerged. Male gang members who carried low MAOA activity alleles were 4.37 times more likely to use a weapon when compared with male gang members who carried high MAOA activity alleles.

The results of the binary logistic regression models revealed that MAOA was able to distinguish between male gang members who did and did not use a weapon in a fight. As a result, the next step was to examine this association in greater detail by plotting the percentage of gang members using a weapon in a fight by MAOA genotype. Fig. 1 displays the results and shows that there were 21 male gang members with the high MAOA genotype. Of these gang members, 81% had not used a weapon in a fight, whereas 19% had used a weapon in a fight. In contrast, there were 33 male gang members with the low MAOA genotype. Of these gang members, 55% had not used a weapon in a fight, whereas 45% had used a weapon in a fight. A χ^2 statistic ($\chi^2 = 3.924$, $df = 1$, $P < .05$) was calculated and confirmed that the association between MAOA and weapon use among male gang members was statistically significant.

6. Comment

An impressive amount of empirical research has demonstrated that the low MAOA activity alleles are associated with a range of antisocial phenotypes, including serious physical violence and criminal behavior. This study extended this line of research and examined the relationship between MAOA and gang membership and between MAOA and weapon use. The results of the analyses revealed that male carriers of the low MAOA activity alleles were more likely to join gangs than were males who possessed the high MAOA activity alleles. In addition, the low MAOA activity alleles also increased the odds of using a weapon in a fight for males. Also of interest was that MAOA was able to distinguish between male gang members who used weapons in a fight and male gang members who did not use weapons in a fight. This finding is of particular interest because it indicates that variation in violence among gang members may be partially circumscribed by genotype.

Also of importance was that there was no association between MAOA and gang membership and MAOA and weapon use for females. This finding was not unexpected because MAOA is X-linked, and thus, the criminogenic effects of the MAOA genotype are thought to be strongest for males. In addition, the low base rate of physical violence for females in the Add Health sample necessarily reduced substantially the statistical power needed to detect a statistically significant effect for MAOA. Future research would benefit by examining the association between MAOA and antisocial phenotypes in females as well as males.

With these findings in mind, it is important to point out that there are a number of limitations that need to be addressed before any definitive conclusions can be drawn. First, the measure of gang membership was based on self-reports, thereby bringing into question the validity and reliability of this measure. It should be noted, however, that prior researchers have used self-reports as a way to gauge gang membership, and this measurement strategy is considered acceptable [16-18]. Second, the measure of weapon use was based on a single, self-report measure. Whether MAOA would be related to other forms of extreme violence remains an open empirical question that should be addressed. Third, the DNA subsample of the Add Health data is not nationally representative, which necessarily calls into question whether the findings reported in this study would be generalizable to the general population. It should be pointed out, however, that the genotype frequencies in the Add Health are comparable to those found in other samples [13]. Still, this does not rule out the possibility that the DNA sample analyzed in this study differs in significant ways from the larger, nationally representative sample of the Add Health study. As a result, replication studies addressing these limitations are needed to test the robustness and generalizability of the findings from this study.

Despite these limitations, it should be noted that this is the first study to demonstrate a link between MAOA and gang membership. Although the precise mechanisms leading from MAOA to gang membership are unknown, it is likely the result of a gene-environment correlation [19]. It is possible, for instance, that male carriers of low MAOA activity alleles are attracted to violence and thus seek out gangs to join. Likewise, it is also possible that the most violent adolescents are recruited to join certain gangs. Although the study of gangs has largely proceeded as a sociological phenomenon, this investigation shows that gang formation and activity, like most antisocial behaviors, involves gene-environment interplay.

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