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Monoamine oxidase A regulates antisocial personality in whites with no history of physical abuse

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Abstract

Objective: Preclinical and human family studies clearly link monoamine oxidase A (MAOA) to aggression and antisocial personality (ASP). The 30–base pair variable number tandem repeat in the MAOA promoter regulates MAOA levels, but its effects on ASP in humans are unclear.
Methods: We evaluated the association of the variable number tandem repeat of the MAOA promoter with *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition*, ASP disorder (ASPD) traits in a community sample of 435 participants from the Hopkins Epidemiology of Personality Disorders Study.
Results: We did not find an association between the activity of the MAOA allele and ASPD traits; however, among whites, when subjects with a history of childhood physical abuse were excluded, the remaining subjects with low-activity alleles had ASPD trait counts that were 41% greater than those with high-activity alleles ($P < .05$).
Conclusion: The high-activity MAOA allele is protective against ASP among whites with no history of physical abuse, lending support to a link between MAOA expression and antisocial behavior.

1. Introduction

The etiology of many psychiatric conditions is multifactorial with genetic and environmental influences interacting to produce psychopathology. Because antisocial personality (ASP) traits are so pervasive and have such deleterious effects on society, there has been intense interest in identifying genetic and environmental etiologic factors that could be treated, ameliorated, or prevented [1,2]. However, gene-environment interactions contributing to ASP are complex and poorly understood. For example, although maltreatment as a child increases the risk of developing ASP disorder (ASPD) by approximately 50%, most maltreated children do not develop ASPD [3,4], suggesting that other factors such as genetic vulnerability play a role in susceptibility to the adverse consequences of child abuse.

The monoamine oxidase A (MAOA) enzyme metabolizes norepinephrine, serotonin, and dopamine at the synapse. As early as the 1960s, a link was made between decreased MAO activity and aggressive behavior in rodents administered MAOA inhibitors [5]. Pintar et al [6] assigned the MAOA gene to the human X chromosome, and some years later, deficient MAOA activity was linked to antisocial behavior in males with an X chromosome deletion [7] and a point

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mutation at the MAOA gene [8]. Confirming the association between decreased MAOA activity and antisocial behavior, Cases et al [9] reported that mice lacking the MAOA gene manifested increased levels of brain norepinephrine, serotonin, and dopamine and increased aggression.

Sabol et al [10] first reported a variable number tandem repeat (VNTR) polymorphism, 30 base pairs (bp) in length, located in the promoter of the MAOA gene, which they demonstrated affects transcriptional activity in gene reporter assays. "High activity" alleles (which mostly have 4 repeats of the 30-bp sequence) transcribe at 2 to 10 times the rate at which "low activity" alleles transcribe (which mostly have 3 repeats of the 30-bp sequence). Denney et al [11] reported MAOA activity in human fibroblast cultures obtained from 11 donors correlated with whether subjects had high or low-activity VNTR alleles. However, ASPD traits and/or substance abuse have inconsistently demonstrated an association between the low-activity MAOA alleles and antisocial or conduct disordered behavior in human behavioral studies enriched for subjects with histories of being abused [12-17]. Two recent community samples have also failed to find an association between MAOA alleles alone and conduct disordered behaviors [18] and ASP traits [19]; however, both these studies suggest that low-activity MAOA alleles increase the risk of conduct disorder and ASP traits in the presence of an adverse childhood environment. Other studies, however, have failed to find such a gene-environment interaction [17,20].

In this study, we used a community sample, from the Hopkins Epidemiology of Personality Disorders Study [1] (HEPS), to evaluate the association between the MAOA promoter VNTR alleles and ASPD traits. We studied whites and African Americans separately because they have different rates of high- and low-activity alleles [10,15] and because race may differentially affect how MAOA and abuse history predict ASP [15]. We first examined whether whites and African Americans in our sample with low-activity MAOA alleles have significantly higher rates of ASP traits than those with high-activity alleles. We then evaluated the association after excluding subjects with an environmental factor known to regulate ASP, namely, childhood physical abuse [19,21-23], which could obscure or mask any genetic mediation of ASP by MAOA. Finally, we also made parallel assessments of the association of MAOA alleles with childhood conduct disorder and adult NEO-PI-R (Revised NEO Personality Inventory) personality traits [24].

2. Materials and methods

2.1. Sample

The sample used for evaluating population genetic substructure is a subset of the Baltimore Epidemiologic Catchment Area (ECA) Program and includes all subjects in the HEPS. In 1981, 175 211 adult residents of East Baltimore were sampled probabilistically for participation in the Baltimore site of the ECA Program [25,26]. From 1993 through June 1996, 1920 of those interviewed in 1981 were interviewed again as part of the Baltimore ECA follow-up survey [27]. In 2004 and the first half of 2005, 1071 of those interviewed in 1993 to 1996 were interviewed again ("wave 4"), and DNA samples were obtained from subjects who consented. Genetic analyses for population substructure were conducted on this sample as well as on any HEPS subjects who were not evaluated in 2004.

The 742 subjects who participated in the HEPS were selected from the 1920 subjects reinterviewed between 1993 and 1996. From these 1920 subjects, we selected all those who were examined by psychiatrists in 1981 as well as all subjects who were identified by the Diagnostic Interview Schedule as having a lifetime diagnosis of any of 6 Axis I diagnoses (mania, depression, panic disorder, obsessive-compulsive disorder, alcohol use disorder, or drug use disorder) at follow-up in 1993. In addition, a 25% (222/884) random sample was selected from the remaining subjects.

Informed consent was obtained from each subject for participation in the study including for the collection of DNA samples as described below. The research reported in this study was approved by the Johns Hopkins University Institutional Review Board.

2.2. DNA isolation

Subjects from wave 4 who agreed to provide DNA in 2004/2005 were sampled by venous blood or cheek swab if they did not want to provide a venous sample. Hopkins Epidemiology of Personality Disorders Study subjects who agreed to provide DNA were sampled by finger-stick onto a specially formulated "Isocode" Card. DNA was isolated from peripheral blood leukocytes using Puregene Blood Kit chemistry on an Autopure LS automated DNA purification instrument (Qiagen, Valencia, Calif). Buccal swabs were isolated manually using a Puregene DNA isolation kit (Qiagen) following manufacturer's protocol. Blood collected on Isocode Cards was isolated according to the manufacturer's instructions by heating hole punches (made by the American Red Cross) in distilled water at 95°C for 30 minutes. DNA concentrations were determined by spectrophotometry using a DU 530 Life Science UV/Vis Spectrophotometer (Beckman Coulter, Brea, California).

For both the population substructure and MAOA analyses presented here, only DNA collected by venous sample or finger-stick was used. Genotyping for population substructure was successfully conducted on 906 subjects, with 81.7% of samples being from venous collection and 19.3% from finger-stick. For the MAOA analysis, 618 individuals were successfully genotyped, with 71.7% of samples being from venous collection and 28.3% from finger-stick.

2.3. Population substructure

Because this is the first of a series of association studies we are conducting, we initially looked for population genetic

substructure in our sample using 23 markers with high efficiency at clustering individuals into population subgroups [28]. Short tandem repeat markers D1S252, D2S319, D12S352, D17S799, D8S272, D1S196, D7S640, D8S1827, D7S657, D22S274, D5S407, D2S162, D10S197, D11S935, D9S175, and D5S410 were selected from Applied Biosystems (Foster City, Calif) Linkage Mapping Set v2.5 and amplified following manufacturer's protocol. Markers D7S2469, D16S3017, D10S1786, D15S1002, D6S1610, and D1S2628 were synthesized by Applied Biosystems with fluorophore positron emission tomography to allow genotyping in the same lane with the other markers. Amelogenin was included to determine sex. Polymerase chain reaction products were pooled before electrophoresis on a 3730 DNA Analyzer (Applied Biosystems). Data were collected and analyzed with GeneMapper software (Applied Biosystems) that calculates fragment length in reference to an internal lane standard (Genescan-500 labeled with LIZ). The last of the 23 markers genotyped was the Duffy SNP rs#2814778 performed using predesigned TaqMan SNP Genotyping Assays C__15769614 (Applied Biosystems) following manufacturers' supplied protocols. Polymerase chain reaction and end point detection of fluorescence were carried out in an ABI Prism7900HT Sequence Detection System (Applied Biosystems) using default settings. Fluorescence data were analyzed with ABI Prism 7900 allelic discrimination software. All genotypes were manually checked.

We used population analysis software Structure 2.2 to identify population substructure within the sample and found 2 genetically distinct clusters that largely correspond to self-reported race, namely, white and African American (see Supplementary Data). Accordingly, we therefore assigned subjects their self-reported race.

2.4. Monoamine oxidase A genotyping

Primer sequences were MAO APT1 (5′-ACAGCCTGACCGTGGAGAAG-3′) and MAO APB1 (5′-GAACGGACGCTCCATTCGGA-3′) described by Sabol et al [10]. The MAO APT1 was 5′-labeled with 6FAM fluorophore. Polymerase chain reaction was carried out in 10 μL containing 0.1 μmol primers, 0.16 mmol each dNTP (Amersham, Piscataway, NJ), 10 mmol Tris (pH 8.3), 50 mmol KCl, 1.5 mmol MgCl, 0.6 U of Ampli Taq Gold DNA polymerase (Applied Biosystems), 0.1% bovine serum albumin, 10% dimethyl sulfoxide, and 40 ng DNA. Amplification was carried out in a Thermo Hybaid MBS 0.2S (Needham Heights, Mass) using the following cycling conditions: initial 8-minute denaturing step at 94°C, followed by 35 cycles of 94°C for 30 seconds, 58°C for 30 seconds, and 72°C for 30 seconds followed by a final extension of 72°C for 10 minutes. Polymerase chain reaction products were assayed on a 3730 DNA Analyzer (Applied Biosystems). Data were collected and analyzed with GeneMapper software (Applied Biosystems) that calculates fragment length in reference to an internal lane standard (Genescan-500 labeled with LIZ) and quantifies the amount of fluorescence in each fragment.

Based on self-reported race, our sample consisted of the following: white, 59.1%; African American, 37.5%; Hispanic, 1%; Asian, 0.6%; Native American, 0.2%; and other, 1.6%. Because individuals self-identified as Asian, Native American, Hispanic, and "Other" are genetically similar to whites according to our population substructure analysis, we included MAOA data from these subjects with data from white subjects, and henceforth, the term *white* in this study includes these minorities in our sample. African American subjects were considered separately. The allele frequencies for white and African American are shown in Table 1. As has been reported previously, allele frequency rates differ between the 2 populations [10,15]. We used the classification of Sabol et al [10] and Caspi et al [19] to designate rare alleles as either low or high activity. Accordingly, 2 and 5 repeats were grouped with those with 3 repeats (ie, "low activity"). Those with 3.5 repeats were grouped with those with 4 repeats (ie, "high activity"). Because the MAOA gene is X-linked, females who are heterozygous (46% of our female sample) cannot be characterized with certainty, as it is not possible to tell which of the 2 alleles is inactivated. Therefore, the subsequent analyses included 224 males and 211 females.

2.5. Childhood physical abuse

As part of a battery of questions focused on parenting behavior and childhood experiences, subjects in the HEPS sample were asked, "Did a parent or other care provider discipline you excessively?" If a positive response was elicited, the subject was asked to provide details and the rater was instructed to code based on judgment of presence or absence of childhood physical abuse. This is a dichotomous variable, with the presence or absence of physical abuse based on the answer to those questions. In earlier work, we found strong correlations between our measure of physical abuse and other measures we obtained of parenting behavior including punishment and restrictive rules [22].

2.6. Adult ASP traits

As described in Reti et al [22], the assessment of ASPD traits was conducted using the International Personality Disorder Examination [29], a semistructured instrument designed for administration by clinicians that detects all relevant criteria for *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition*, personality disorders.

Table 1
MAOA VNTR allele frequencies

	2	3	3.5	4	5
Whites	0.50%	34.10%	1.20%	62.80%	1.40%
African American	4.70%	48.70%	0.20%	45.50%	0.90%

MAOA VNTR repeats.

There are 7 items pertaining to adult ASPD traits. The psychologists were directed to evaluate abnormal traits manifest over the subject's entire adult life. Each criterion was rated 0 (absent), 1 (accentuated or exaggerated), 2 (criterion level or pathological), or 9 (missing or unknown), based on the responses of both the subject and at least one knowledgeable informant who had known the individual for most of his/her adult life. In reliability exercises, the intraclass correlation coefficient for number of ASPD traits rated present was 0.8 [1].

A scale for adult ASPD traits was constructed by assigning a score of 0 to ratings of 0 and a score of 1 point to ratings of either 1 or 2 for the 7 relevant items. In this way, the metric for the scale was the number of antisocial traits present. If 4 or more items were recorded, the diagnostic algorithm was operated by assigning the value of 0 to data items that were missing or unknown. If fewer than 4 items were recorded, an adult ASPD trait scale score was not calculated for that individual; this was the case for 6 individuals.

2.7. Childhood conduct disorder traits

Conduct disorder traits were also assessed using the International Personality Disorder Examination. There are 15 items pertaining to childhood conduct disorder traits, and each criterion was rated in a similar manner to ASPD traits. In reliability exercises, the intraclass correlation coefficient for number of conduct disorder traits rated present was 0.92. Two conduct disorder trait scales were constructed, with a score of 0 being assigned to a rating of 0 for both scales. One scale was constructed like the ASPD trait scale with a score of 1 point to ratings of either 1 or 2. The second scale was constructed by assigning a score of 0 to rating of 1, thereby creating a scale that only reflected severe childhood conduct pathology.

2.8. Assessment of personality traits

The NEO-PI-R is a 240-item, self-report questionnaire designed to measure the 5-factor model of personality. The NEO-PI-R measures 6 specific traits, or facets, that define each of the 5 broad factors, and uses a 5-point Likert response scale ranging from "strongly disagree" to "strongly agree." Details regarding the instrument's reliability, validity, and longitudinal stability can be found in Costa and McCrae [23]. Most subjects in the HEPS (89.5%) completed the NEO-PI-R.

3. Results

We first checked, in each population, whether there was a difference in ASPD trait scores between high- and low-activity subjects (Table 2). Among whites, the mean ASPD trait score for low-activity subjects was 2.14, whereas it was 1.9 for high-activity subjects, which was not significantly different. Among African Americans, the mean ASPD trait score for low-activity subjects was 2.2, whereas it was 2.15 for high-activity subjects, which was also not significantly different.

Table 2
Mean number of adult ASPD items scored 1 or 2 by MAOA allele

	Whites		African Americans	
	Low activity	High activity	Low activity	High activity
Total population	2.14 (88)	1.9 (195)	2.2 (86)	2.15 (66)
Physical abuse history	3 (16)	3.33 (51)	3 (18)	3 (12)
No physical abuse history	1.94 (72)	1.38 (144)*	1.99 (68)	1.96 (54)

Mann-Whitney *U* test for comparing samples by MAOA allele. The number in brackets is the sample size.
* $P \leq .05$.

We had previously observed both high reports of childhood physical abuse in the HEPS sample and a strong correlation between it and later ASP [22]. To determine whether MAOA alleles modified the risk of ASP after childhood physical abuse, we analyzed this relationship separately in subjects who reported abuse and those that did not (Table 2). We did not find that MAOA activity modified the number of ASPD traits in subjects who had been physically abused. In fact, ASPD trait scores were nonsignificantly lower among whites with a history of abuse and low-activity MAOA activity. However, in white subjects with no history of childhood physical abuse, mean ASPD trait score was 1.38 in high-activity subjects and 1.94 in low-activity subjects ($P < .05$), an increase of 41%. When Native Americans, Hispanics, Asians, and "Other" were excluded from the analysis, the results were very similar with the ASPD trait score among "true" whites at 1.37 for high-activity allele subjects and at 1.97 ($P < .05$) for low-activity allele subjects, an increase of 44%. Similar trends were also obtained when white males and females were analyzed separately, although the results did not reach statistical significance. ASPD trait scores among African Americans with no history of abuse were virtually identical in low and high MAOA activity subjects. Also, the chances of experiencing childhood physical abuse were not significantly affected by MAOA allele length in either whites or African Americans.

To further evaluate the relative roles of physical abuse and the MAOA allele in ASPD trait scores among whites, we performed a multiple linear regression analysis with ASPD trait score as the dependent variable and physical abuse, the MAOA allele, and a physical abuse × MAOA allele interaction term as independent variables. The results shown in Table 3 support the stratification analysis, although the effect of the interaction term did not reach statistical significance. The data suggest that reporting a history of childhood physical abuse is associated with an approximately 1-point higher ASPD trait score on average than not reporting physical abuse regardless of MAOA allele type, consistent with the stratification analysis. Among those not

Table 3
Multiple linear regression analysis of effects of physical abuse, MAOA allele, and the interaction term physical abuse × MAOA allele on number of adult ASP traits among whites

Variables influencing ASP	Regression coefficient	t	Significance	95% confidence interval	
Physical abuse	1.057	1.97	.05	0.002	2.112
MAOA allele	0.558	−1.98	.049	−1.114	−0.003
Physical abuse × MAOA allele	0.892	1.43	.153	−0.333	2.117

$r^2 = 0.135$.

reporting a history of childhood physical abuse, the high-activity allele is associated with approximately a half-point lower ASPD trait score than that of the low-activity allele, also consistent with the stratification analysis. The data also suggest that the effect of physical abuse is stronger for those with the high-activity MAOA allele compared with those with the low-activity allele. Because the ASPD trait score is a right-skewed score running from 0 to 7 and thus not normally distributed, we also performed ordinal logistic regression to assess sensitivity to failure of normality, and findings were qualitatively and quantitatively similar.

We also evaluated how MAOA allele activity influences the likelihood of each ASPD trait in whites and African Americans who had not experienced physical abuse (Table 4). Among whites, the proportion of subjects positive on each trait was higher in those with the low-activity allele compared with those with the high-activity allele. The difference was statistically significant at the 0.05 level for "Impulsivity to plan ahead" and for "Lack of remorse" and significant at the 0.1 level for "Reckless disregard for safety of self and others." Among African Americans, there was no pattern or trend regarding likelihood of being positive on a trait among individuals with low- vs high-allele activity genotypes.

Table 4
Proportion of subjects without a history of physical abuse scoring 1 or 2 on each ASP disorder trait by MAOA allele

	Whites		African Americans	
	Low activity	High activity	Low activity	High activity
1. Failure to conform to social norms—arrests	0.39	0.33	0.38	0.41
2. Deceitfulness	0.13	0.09	0.15	0.22
3. Impulsivity or failure to plan ahead	0.1	0.03*	0.05	0.09
4. Irritability and aggressiveness—fights	0.37	0.27	0.4	0.29
5. Reckless disregard for safety of self and others	0.5	0.36**	0.27	0.3
6. Consistent irresponsibility	0.24	0.2	0.53	0.44
7. Lack of remorse	0.29	0.14*	0.31	0.31

Pearson χ^2 test to compare rates between MAOA alleles. Fisher exact test when any cell contains less than 5 subjects.

* $P \leq .05$.

** $P \leq .1$.

We also used an alternate methodology to confirm our finding that MAOA genotype influences ASPD trait score in whites who have not experienced physical abuse. We checked NEO trait scores by MAOA allele activity in whites who had not experienced childhood physical abuse (using a 2-tailed unpaired t test). We found that individuals with low-activity alleles had higher neuroticism factor scores than those with high-activity alleles ($P < .1$). Several neuroticism facet scores, namely, vulnerability ($P < .1$), angry hostility ($P < .05$), and anxiety ($P < .05$), were higher in individuals with low-activity compared with high-activity alleles. Individuals with low-activity alleles also had lower scores on the agreeableness factor ($P < .05$) and lower agreeableness facet scores on trust ($P < .05$), altruism ($P < .05$), and compliance ($P < .1$). We also evaluated whether an expert-generated prototypic ASPD profile generated by Lynam and colleagues varied by MAOA allele. Prototypes formed by experts have been used to verify the facets that capture pure antisocial traits [30,31]. Miller et al [32] developed a NEO-PI-R index that captures *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition*, ASPD criteria, comprising the sum of 17 individual facets (see Supplementary Data). We found that individuals with low-activity alleles had higher scores on the scale than those with high-activity alleles ($P < .1$).

We also checked whether the MAOA polymorphism influenced childhood conduct disorder scores in whites with no history of childhood physical abuse. We did not find that MAOA genotype influenced conduct disorder scores when scores of 1 and 2 were assigned a value of 1. However, when scores of 1 were assigned a value of zero and scores of 2 were assigned a value of 1, creating a scale that reflected severe childhood conduct pathology, those with low-activity MAOA alleles had significantly higher scores than those with high-activity alleles ($P < .01$, Mann-Whitney U test). Among childhood conduct disorder traits, those that were significantly more likely to score 2 compared with 0 or 1 among low-activity individuals were "Lied/conned" ($P < .01$), "Destroy property" ($P < .1$), "Burglary" ($P < .05$), and "Truant" ($P < .05$). (For these calculations, we used a Pearson χ^2 test to compare rates between MAOA alleles, except when a cell contained less than 5 subjects; in which case, we used a Fisher exact test.)

4. Discussion

Preclinical studies of MAOA function as well as studies of human families with deficient MAOA activity strongly suggest the gene plays a key role in mediating aggression and ASP. Because the 30-bp VNTR promoter polymorphism of MAOA regulates the expression of MAOA in vitro [10,33] and probably in vivo [11], researchers have predicted that it would also regulate human ASP. However, studies evaluating an association between this VNTR and ASP have yielded mixed results. In this study, we found that this

MAOA polymorphism did not significantly regulate ASPD trait scores in either whites or African Americans when each population as a whole was analyzed. However, because environmental factors known to regulate ASP, including a history of childhood physical abuse [19,21-23], could obscure or mask any genetic mediation of ASP by MAOA, we also analyzed our sample excluding subjects with a history of physical abuse. In subjects without a history of childhood physical abuse, we found that the VNTR MAOA promoter polymorphism did predict ASP in whites, but not African Americans. Whites with low-activity alleles had ASP scores that were, on average, 41% higher than subjects with high-activity alleles. As far as we are aware, this is the first study to find that the high-activity MAOA allele is protective in subjects without a history of childhood physical abuse.

Unlike some other recent studies [15,19], we failed to find that the MAOA VNTR promoter polymorphism is associated with ASPD traits in those who experienced childhood physical abuse. In fact, among whites, those with high-activity MAOA alleles had (nonsignificantly) higher levels of ASPD traits than those with low-activity alleles. Other studies have also failed to find such a gene-environment interaction [17,20]; however, Weder et al [34] recently showed that MAOA was only protective if the abuse was moderate. Unfortunately, we do not have data about the severity of physical abuse experienced by each subject in our study. As we have reported previously [22], we also found in these new analyses that HEPS subjects who experienced childhood physical abuse have significantly higher levels of ASP than those who did not.

We found an effect of the MAOA polymorphism on ASPD trait scores in whites with no history of childhood physical abuse, but not in African Americans. The explanation for the racial difference we observed may lie in a combination of genetic and environmental factors. Like us, other studies have also reported racial differences in both MAOA allele distribution [10,21] and in the effect of MAOA on ASP traits. For example, Widom and Brzustowicz [21] found that high levels of MAOA activity were protective only in whites but not in non–white populations. In addition, there may be other genetic factors modulating MAOA expression and other genes that differ by race influencing antisocial behavior. Environmental factors that differ by race may also play a role in generating the racial difference we observed including economic and other disparities in the childhood of African Americans and whites [35]; racial disparities have been noted as early as birth, with African American infants being at higher risk for low birth weight [36]. In addition, deciding whether to record an ASP trait (especially trait number 1) as present or absent may have been influenced by the subject's report of legal problems including arrests, which may be more likely among African American adults than white adults for an identical crime [37].

Our study is strengthened by 2 independent measures in the same subject that are related to the ASPD trait measure, confirming our finding that MAOA genotype influences ASP trait score in whites who have not experienced physical abuse. We found that the low-activity MAOA allele was associated with significantly higher neuroticism and lower agreeableness facet scores in this population. Elevated neuroticism and lower agreeableness scores have been previously associated with higher ASPD trait scores [38,39]. We also found that the low-activity MAOA allele was associated with higher scores on the childhood conduct disorder scale among whites with no history of childhood physical abuse. However, the result was only significant for a childhood conduct disorders scale in which only severe or pathologic behaviors were counted.

Our study is limited by childhood physical abuse being a retrospective measure. Nonetheless, we have previously shown that it correlates strongly with other retrospective measures of parental behavior obtained in the HEPS survey including being beaten or receiving other harsh punishment [22]. On the other hand, a significant strength of the study is that ratings were made by psychiatrists and outside informants to corroborate information from subjects.

In summary, we have shown that when we exclude subjects with an adverse environmental exposure clearly associated with later ASP, there is a significant association between the allele activity of the MAOA promoter VNTR polymorphism and ASP in whites. These findings lend support to preclinical and human family studies showing a clear link between MAOA expression and antisocial behavior.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.comppsych.2010.05.005.

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