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MAOA and Aggression: A Gene–Environment Interaction in Two Populations

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Abstract

Political scientists tend to focus on environmental triggers as the primary precipitating cause for political violence. However, little has been done to explain why certain individuals faced with certain pressures resort to violence, while others confronting the same situation seek out diplomatic and peaceful resolutions to conflict. Here, using two independent samples, we explore the interaction between genetic disposition and violent early life events and their influence on engaging in physical violence. We find that individuals with the low-activity form of monoamine oxidase-A, who are exposed to violence in youth have a greater likelihood of engaging in physical aggression later in adulthood. Our findings hold important implications for the value of environmental intervention in communities besieged by political violence in order to reduce the likelihood of the intergenerational transfer of its propensity.

Keywords

MAOA, gene–environment interaction, physical aggression, traumatic early life events, political violence

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Much of political science in general, and international relations in particular, remain preoccupied with questions of power and dominance, and how states utilize coercive means to their advantage. This literature has largely focused on the causes of aggression between states (Waltz 1979) or between states and nonstate actors. Far less work in political science has examined the basis for individual differences in the propensity to engage in violence. That is, why do some individuals engage in political violence while others, often confronting the same situations, strive to seek out more peaceful means of conflict resolution?

Part of the reason that the individual level of analysis has been less common in international relations is due to, at least in part, the predilection to analyze behavior at the level of state action. This makes sense in many cases because individuals are assumed to act embedded in institutions that may constrain their behavior in particular ways. However, both leaders and the public's individual actions exert profound influence on foreign policy decision making (Byman and Pollack 2001; McDermott 2007). Even in democratic structures, choices related to war, particularly under conditions of threat, are often made, at least initially, by individuals and remarkably small groups of people and then later vetted and validated in larger legislative and public settings. Thus, individual variance in the propensity to respond to provocation with aggression holds tremendous import for the study of many critical topics in international relations, including the study of conflict resolution. Understanding the nature and bases for such individual differences in aggressive motivation and capacity can offer meaningful insight into strategies that might prove more effective for ameliorating violence and aggression.

We do not argue that individual propensity to engage in aggression can be equated with interstate war. However, logically, individual decisions to engage in conflict must occur prior to larger institutional implementations that conduct such action. And we acknowledge that intracoalitional impulsive aggression may differ in form and motivation from the kind of intercoalitional premeditated violence which is often required in war (Boehm 1999). Nonetheless, we suggest that developing a more complete understanding of the conditions that influence individuals to engage in conflict can help illuminate the process by which states, which comprise constellations of individual actors, conduct such action. After all, if institutions alone proved sufficient to preclude conflict, interstate aggression would not exist, and yet it clearly does. If there are some types of people more disposed to engage in violence when faced with specific environment triggers which can potentiate this behavior, it is useful to examine those factors. Such examination would prove especially important if leaders actually emerge differentially from those groups more susceptible to impulsive action in the face of provocation. Of course, we cannot know this without testing of such individuals, but we can explore, using publicly available data, the incidence of particular genotypes and environmental triggers in the population at large.

Political scientists tend to focus on environmental triggers, such as territorial invasion of one state by another, as the primary precipitating cause for political

violence. Such factors no doubt often precipitate violent conflict. We do not suggest otherwise. The immediate triggers for political violence appear environmental in nature, and of course remain subject to unique cultural, historical, and religious pressures. However, here we seek to further explicate this process by examining why certain individuals faced with the same pressures engage in aggression, while others seek out diplomatic and peaceful resolution to conflict. Indeed, it is likely that environmental, structural, and institutional pressures combine with more intrinsic dispositions to potentiate individual differences in tendencies toward violence when confronting similar degrees of provocation.

Given that many mental and physical health disorders are known to emerge from an interaction between environment and genotype, we inquire into whether violence and aggressive behavior can similarly emerge from such interactions and what such implications hold for understanding political violence. In doing so, we seek to present a model which can then extrapolate to contexts specific to international security and political conflict and thus advance the paradigm of using biological markers to inform our understanding of topics of political interest.

The general notion that observable effects exist in the interactive and reciprocal relationship between an individual's genetic makeup and a person's social environment enjoys strong support in existing psychiatric genetic models of domestic violence, aggression, and other behavioral disorders. Aggressive behavior, the propensity to act violently, and conduct disorder (CD) have been explored at length from this perspective. The serotonergic, dopaminergic, and adrenergic systems have been implicated (Virkkunen et al. 1994; Nielsen et al. 1994; Strous et al. 1997; Lachman et al. 1998; Manuck et al. 1999; Retz et al. 2004;Olivier and van Oorschot 2005; Chen et al. 2005; de Boer et al. 2009). In particular, the serotongenic and dopaminergic systems have been identified for their potential contribution to impulsivity and manifest violent behavior in animals and humans (Lesch and Merschdorf 2000). They do so by playing an important role in the regulation of mood and affective stimulation, cognition, and various autonomic functions which become activated when an individual responds to stress (Thapar, Harrington, and McGuffin, 2001; Young et al. 2002).

Monoamine oxidase-A (MAOA) is a key enzyme in the catabolism of serotonin and in the regulation of adrenergic activity such as neuroephinerphrine. The low-activity allele of the *MAOA* gene has been associated with antisocial personality disorder and CD among males in adverse environments (Caspi et al. 2002; Foley et al. 2004; Nilsson et al. 2005; Kim-Cohen et al. 2006). Subsequently, the gene responsible for MAOA production has demonstrated the clearest link between a specific genetic variant and violent or aggressive behavior (Caspi et al. 2002; Meyer-Lindenberg et al. 2006; Reif et al. 2007).

We build upon previous psychiatric genetic research to provide a map for the exploration of the etiology of political violence. Specifically, we seek to approach the study of an important behavior, in this case aggression, as it develops across the life span. We examine how genetic variation in MAOA interacts with environmental

factors such as events that happen in childhood or adolescence, and how these forces might influence the expression of adult behavior later in life. Based on the earlier work in other fields, we hypothesize that individuals who carry the MAOA genetic variant, and are subject to high levels of trauma in childhood and adolescence, will prove more likely to engage in physical violence as adults. We conduct an exploratory analysis using original empirical results to examine some of the individual factors which may increase the likelihood that a person resorts to aggressive forms of violence. In doing so, we suggest that all the subtleties that a person encounters in life can interact with inherent dispositions to produce different thresholds for the propensity to respond to provocation aggressively.

This type of individual level of analysis is relevant and important for scholars of international relations because the study of war and conflict is challenging when capturing the dynamics underlying aggression, conflict initiation, and escalation. While states usually comprise the unit of analysis in the international relations literature, the actors within the state are individuals and critical decisions are often made by individual actors, from political leaders and terrorists to combat soldiers and international political activists; as a result, using an individual unit of analysis can prove informative for understanding the mechanisms that can precipitate actual violence in the wake of crisis or provocation. While many of those factors clearly derive from environmental forces, individual differences can also influence outcomes in decisive ways.

This study holds implications for intervening in those early environments which might pose particular risk for vulnerable individuals. For example, famine, floods, and conditions of endemic political violence, in and of themselves, because of the trauma they instill, increase the likelihood of spawning political violence in adolescent males who remain at particular genetic risk for such propensity. As a result, such findings suggest possible strategies for ameliorating the conditions that can potentiate violent political outcomes. Significantly, these results also hold tremendous import for our theorizing about cycles of violence in particular environments and how such patterns may signal the intergenerational transfer of such propensities. Moreover, this work suggests implications for a more widespread examination of the nature and influence of individual differences in response to provocation or threat.

This article begins with an overview of the genetic factors we explore. We then describe the sample population we examine, the methods we use to test our hypothesis about the relationship between *MAOA*, exposure to violence, and propensity toward aggression. We then offer our analysis and interpretations of our findings. We conclude with a discussion of the potential meaning and import of these results for our understanding of the factors that contribute to individual differences in predilection to engage in violence.

Background

Previous research has demonstrated that the interaction of genetic liability and environmental triggers can influence the likelihood for individuals to engage in physical

aggression (McDermott et al. 2009). In particular, males with the low-activity version of *MAOA* gene, who had also experienced traumatic events in their youth, were significantly more likely to engage in physical aggression than those who had a high-activity allele, or those with a more stable childhood. Thus, the interaction of genetic markers and environmental circumstances appears to increase the likelihood that a man will engage in physical aggression under provocation.

MAOA is an enzyme located in the presynaptic terminal responsible for the degradation of biogenic amines including the neurotransmitters epinephrine, norepinephrine, dopamine, and serotonin.[1] At the most extreme, complete MAOA deficiency has been associated with a behavioral phenotype that includes disturbed regulation of impulsive aggression. Males with this rare mutation have engaged in impulsive/aggressive behaviors including rape, arson, and assault (Brunner et al. 1993). Complementary evidence from *MAOA* knockout mouse studies, where the mouse is engineered to carry genes that have been made inoperative (*knocked out*) showed that altered mice display similar patterns of increased aggression (Cases 1995; Shih 2004).

In normal human populations, specific *MAOA* genotypes have been associated with physical aggression as well as a greater incidence of violent acts, including psychiatric diagnosis of conditions such as adolescent CD, adult antisocial personality disorder (ASPD), and other conditions associated with violence including attention-deficit hyperactivity disorder (ADHD).[2] Numerous studies have found that the low-activity allele has been associated with a greater frequency of these traits among males, especially when faced with adverse environments (Caspi et al. 2002; Foley et al. 2004; Nilsson et al., 2005; Kim-Cohen et al. 2006). However, nonreplications of the aforementioned gene–environment interaction have also been reported (Haberstick et al. 2005; Young et al. 2006). Other work demonstrated that physical forms of aggression in particular were higher among low-*MAOA* men who had experienced traumatic early life events (Frazzetto et al. 2007). McDermott et al. (2009) similarly found that individual differences in *MAOA*, in interaction with traumatic early life events, predicted behavioral manifestations of aggression under conditions of provocation.

Samochowiec et al. (1999) found a significantly greater frequency of low-activity *MAOA* alleles among antisocial alcoholics compared with control participants, and no significant differences among nonantisocial alcoholics and controls. On the other hand, Manuck et al. (2000) found a decrease in aggression and impulsivity for males with the low-activity allele, although the interaction with traumatic life events was not explored in that study. It may be that violent effects only emerge among those who carry the low-activity form of the allele once they have been subjected to difficult environmental circumstances. This would not be surprising if the existence of such traumatic life events served as the trigger for activating a defensive mechanism intended to serve a function of protecting the individual in the face of threat. In summary, differences in *MAOA* genotypes repeatedly appear associated with aggression, impulsivity, and violence.

The study of specific genetic and environmental effects may provide one avenue by which to explore some potentially influential sources of underlying liability for a wide array of politically relevant behaviors, such as violent response to political losses. In addition, such factors may increase susceptibility to the onset and recovery of posttraumatic stress disorder, which is typically characterized by powerful emotional learning, intrusive memories, and heightened aggression in the face of such flashbacks. The mechanism underlying this relationship appears to also be linked to catecholamine metabolism. MAOA and catechol-*O*-methyltransferase are both responsible for catecholamine metabolism in the brain and have also been previously implicated in power seeking and dominance behavior.

Further, the use of aggression as one of the diagnostic symptoms underlying CD and ADHD allows for the use of such disorders as effective proxies for the examination of the conditions and circumstances that influence rates of political violence. In typical laboratory studies, small provocations can result in significant shifts in behavioral outcomes among those who have the low-activity form of *MAOA*. However, if we consider the 50 percent or greater portion of the population exposed to murder and mayhem over the course of a lifetime on the West Bank or Gaza Strip, the enormous relevance of the application of this research for helping to explain individual differences in violent political activity in response to provocation becomes immediately evident. If individuals with a history of traumatic life events demonstrate increases in violence at the micro level of a laboratory experiment, imagine what the much wider scale exposure to violence might potentiate among those most affected. The work done in psychology on *MAOA* and CD or ADHD provides a methodological, theoretical, and empirical framework to examine these relationships, and an avenue by which to apply these findings to the context of political violence (Hatemi and McDermott 2012). These psychological studies offer an ideal design for the extension of this work on *MAOA* to explore its potential influence on real-life manifestations of political violence and aggression.

Methods and Measures

As noted, we propose that the application of a Gene by Environment model similar to that used in psychiatric genetics to explore the phenomena of CD will prove beneficial in this exploration of individual differences in the propensity toward aggression and violence. This Gene by Environment interaction (G $\times$ E) model is particularly important for explicating the experiences which can potentiate aggression among those subjected to extreme violence in childhood and adolescence, as typically occurs among those who grow up in war zones, for example.

We rely on standard practice in the genetic literature when exploring the relationship between genetic markers and behavior, and we employ two separate samples to ensure that any findings are replicable. The two separate data sets used to examine association between *MAOA*, exposure to traumatic early life events in childhood, and risk for engaging in aggression violence are the National Longitudinal Study

of Adolescent Health (Add Health) survey and the Virginia Twin Study of Adolescent and Behavioral Development (VTSABD). The main effects of genotypic (*MAOA*) and environmental risk factors (traumatic life events) as well as the interaction between these effects were tested to determine whether these variables posed a significant risk for expressions of physical aggression and violence. This kind of analysis represents standard practice in genetic research.

We seek to extend the findings from our normal populations to topics of political interest such as leaders. However, it is important to make clear that we do not claim that the adolescents in this sample will become national leaders. Rather we have no reason to suspect that genetic and environmental variance among leaders would differ in any systematic way in *MAOA* between leaders and the larger population from which they emerge.

Add Health Sample

Our first sample comes from the National Longitudinal Study of Adolescent Health (Add Health), which is a large publicly available study, started in 1994–95, that explores the causes of health-related behavior in adolescents between Grades 7 and 12 (ages 10–19 years); it also reports on their outcomes in young adulthood. In addition to health-related information, a large amount of information has been collected about the personality, attitudes, relationships, religious beliefs, civic activities, and political beliefs, and behaviors of the respondents. The initial wave of the study utilized a sampling design that resulted in a nationally representative study. Women comprise 49 percent of the study's participants. Racially, the sample's distribution included 12.2 percent Hispanics, 16 percent blacks, 3.3 percent Asians, and 2.2 percent Native Americans. Participants in Add Health also represent all regions of the country: the Northeast makes up 17 percent of the sample, the South 27 percent, the Midwest 19 percent, and the West 17 percent. Wave I (1994–95) included participation from 145 middle, junior high, and high schools; from those schools, 90,118 students completed a forty-five-minute questionnaire. This process generated descriptive information about each student, the educational setting, and the environment of the school.

From these respondents, a core random sample of 12,105 adolescents in Grades 7–12 were drawn plus several oversamples, totaling more than 27,000 adolescents. These students and their parents were administered in-home surveys in the first wave. Wave II (1996) was comprised of another set of in-home interviews of more than 15,000 students from the wave I sample. Finally, wave III (2001–2002) consisted of an in-home interview of 15,170 wave I participants.

In wave I of the Add Health study, researchers created a genetically informative sample of sibling pairs based on a screening of the in-school sample of 90,118 adolescents. These pairs include all adolescents who were identified as twin pairs, half siblings, or unrelated siblings raised together. Twins and half biological siblings were sampled with certainty. The wave I sibling pairs sample has been found to be

similar in demographic composition to the full Add Health sample (Jacobson and Rowe 1998). Genetic markers are available for a sample of 2,574 individuals, including markers that identify alleles of *MAOA*. Nearly 80 percent of the sibling–pair sample participants in wave I also participated in Wave III. Subjects were young adults (aged 18–26) by the time of the third wave and were asked several questions about acts of delinquency and violence they participated in during the course of the previous twelve months. Details on access to the study, DNA collection, and genotyping process are available at the Add Health website (Add Health Biomarker Team 2007).

Classification of transcriptional activity related to *MAOA* alleles was assigned to each allele, to divide them into the low- and high-activity forms.[3] Males are homozygous for *MAOA* activity forms; however, females may be heterozygous. Since it is difficult to determine the effect of each allele in heterozygous females, we follow Weder et al. (2009) and exclude these cases from the analysis. The low genotype frequency is 29 percent and 71 percent for the high genotype in the Add Health sample.

VTSABD Sample

This second data set is based on 1,299 individuals (540 twin pairs) from the Virginia Twin Study of Adolescent and Behavioral Development (VTSABD). The sample comprises twin subjects for whom data on *MAOA* genotype, CD questions, and exposure to childhood adversity were available. Informed consent was obtained in writing from parents and assent was obtained from the juvenile twin subject. Sample ascertainment and data collection have been described in detail elsewhere (Meyer-Lindenberg et al. 2006). Briefly, a sequential cohort of twin families were interviewed and followed prospectively at approximately fifteen-month intervals over four waves of data collection (Maes et al. 2007). Twins and their parents were ascertained through the Virginia public and private school systems in 1987 and 1988. The first wave of data collection took place between March 1990 and March 1992, and twins in this cohort ranged in age from eight to seventeen years. As the study progressed, twins over the age of seventeen were considered too old for inclusion and aged out of the sample. As in the Add Health sample, 2-, 3-, and 5-repeat *MAOA* alleles were classified as the low-activity alleles and the 3.5- and 4-repeat alleles as high activity (Sabol, Hu, and Hamer 1998). The distributions of low and high alleles were comparable to the Add Health sample at 34 percent and 66 percent, respectively.

Assessments of Environmental Exposure and Measures of Aggression

In order to model our outcomes of interest, we take these measures of *MAOA* and life events, and then map the process by which various relationships between genotype and experience might correspond to increased risk for aggression. In doing so, we illuminate the processes by which similar combinations of genetic predisposition

and environmental circumstance might help precipitate incidence of political violence. Data on these factors in the context of previous or existing political violence do not exist as far as we know. However, by showing the link between genetic markers, environmental effects, and violent outcomes in general, we can begin to examine these relationships more specifically.

Several measures of traumatic early life events (independent variable) and aggression (dependent variable) were used to explore the range of exposures and outcomes with relation to *MAOA*. We detail the measure for each sample in the following.

Add Health. We created a single measure of exposure to violence (ranging from 0 to 7) based on the answers to seven yes/no questions: whether respondents saw someone shoot or stab another person; someone pulled a gun or knife on them; someone shot or stabbed them; and/or they were beaten up with or without having something stolen from them. Use of aggression was indexed as *whether subjects used a weapon in a fight*. All three of these measures come from the Add Health Delinquency and Violence battery.

VTSABD. We created a single measure of exposure to a violent family environment based on the answers to three yes/no questions: whether their *parents ever shoved each other*, *hit each other*, or if the *police were ever called about parents fighting*. This measure ranges from 0 to 3. Use of aggression was measured as *whether subjects got into a fight in a public place.*

All samples consisted of data on individual twins registered in the VTSABD assessed with the Child and Adolescent Psychiatric Assessment (CAPA)—Child and Parent Version (Angold and Costello 2000), which is based on the *Diagnostic and Statistical Manual of Mental Disorders*, third edition, revised criteria.

Combining the Samples

Subjects were slightly younger in the Add Health sample than in the third wave of the VTSABD study (ages 12–17). Both studies also asked several questions about acts of delinquency and violence which subjects had participated in during the course of the previous twelve months. Table 1 presents all the means and standard errors for all variables in each data set.

Analysis

Genetic association studies test whether an allele or genotype occurs more frequently within a group exhibiting a particular trait than among those with absent trait. Simply regressing the phenotype of interest on an allele or genotype provides a formal test of association. In our case, we are interested in understanding whether having the ''low'' *MAOA* genotype moderates traumatic experiences to produce violent behavior more frequently; therefore, we focus on testing the significance of the parameter on the interaction between *MAOA* and each of our independent variables.

Table 1. Means and Standard Errors

	VTSABD ($N = 954$)		Add Health ($N = 1,711$)	
Variable	Mean	*SE*	Mean	*SE*
MAOA low-activity allele	0.29	0.02	0.34	0.01
MAOA high-activity allele	0.71	0.02	0.66	0.01
Fight	0.13	0.01		
Used weapon in fight			0.01	0.00
Parental Violence Index	0.10	0.02		
Violence Index			0.16	0.02
Male	0.62	0.02	0.62	0.01
Age	14.93	0.05	21.93	0.05

Note: DV= dependent variable; VTSABD = Virginia Twin Study of Adolescent and Behavioral Development. Low is the frequency of subjects that are homozygous for the *MAOA* low allele and high is the frequency of subjects that are homozygous for the *MAOA* high allele (one high allele for men and two high alleles for women). Male is an indicator variable taking the value of 0 for males, Age is self-reported age in the third wave of the study. For the VTSABD sample, Fight is whether respondents got into a fight in a public place. Parental Violence is an additive index (0–3) made up of answers to the yes/no questions whether their parents ever shoved each other, hit each other, or if the police were ever called about parents fighting. For the Add Health sample, Weapon (DV) is whether respondents used a weapon in a fight. Violence is an additive index (0–7) made up of answers to yes/no questions whether they saw someone shoot or stab another person, someone pulled a gun or knife on them, someone shot or stabbed them, and/or they were beaten up with or without having something stolen from them.

A significant parameter estimate may give a false positive signal due to population stratification, occurring because groups may have different allele frequencies due to their genetic ancestry, rather than a true signal of association. Population differences in the *MAOA* have been demonstrated to exist. For instance, the *MAOA* 3-repeat allele has a much higher incidence in the Maori population in New Zealand (Gilad et al. 2002). Among this population, the frequency of the polymorphism exists in about 60 percent of the population. Caucasian populations in comparison have a prevalence of approximately 30 to 35 percent. To guard against this possibility, we only study subjects who self-report as Caucasian.

We also include individuals from the same family in the analysis, and thus the observations are not independent. Therefore, we use a generalized estimating equations approach (Liang and Zeger 1986), with an independent working correlation structure for the clustered errors, to estimate the model. We also adjusted for the effects of both age and gender, as there are numerous instances of age and sex effects in gene–environment interactions.

Results

Table Table 2 demonstrates a significant interaction between the low-activity genotype of *MAOA* and the additive index of exposure to violent events in the Add Heath

Table 2. Coefficients and *p* Values (in Parenthesis)

DV/IV	VTSABD Fight/Parental violence	Add Health Used weapon in a fight/violence
Low	0.01. (.96)	0.01. (.99)
IV	0.13 (.67)	0.26 (.31)
Male	1.50 (<.001)	2.15 (.04)
Age	−0.05 (.55)	−0.27 (.12)
Low × IV	**1.08 (.01)**	**0.87 (.02)**
N	719	1,298

Note. MAOA = monoamine oxidase-A; VTSABD = Virginia Twin Study of Adolescent and Behavioral Development. All results are based on a Logit General Estimating Equations model. Analysis is restricted to Caucasian subjects. *Low* is an indicator of whether or not the subject is homozygous for the *MAOA* low allele (one low allele for men and two low alleles for women), *Male* is an indicator variable taking the value of 0 for males, *Age* is self-reported age in the third wave of the study. The dependent (DV) and independent variables (IV) are listed in the second row of the table.
Bold interactions shows they are significant at convention levels *(0.05)*. *p*-values in the parenthesis is the exact level of significance (1% and 2%)

sample, or experienced exposure to the violence in the form of *exposure to interparental violence* in the Virginia sample. However, possessing the low-activity form of the allele alone did not prove sufficient to generate aggressive outcomes in our dependent variables, such as *using a weapon in a fight* in the Add health sample or *getting into a fight in a public place* in the Virginia sample. That is, a low-activity form of *MAOA* alone does not predict violent behavior. Equally important, the environmental independent variables alone proved equally insufficient in potentiating violent outcomes. Only when the two factors existed in tandem did subjects engage in violent outcomes to a significantly greater degree. To further test whether the interaction term improves model fit, we compared the deviances for models with and without the interaction term. In both cases, the interaction term improves model fit ($p = .01$ for both samples).

Since interaction terms are difficult to evaluate in a logit model, we present simulated first differences in Table 3, comparing each level of our environmental variable among subjects with the low- versus high-activity genotype. The first difference is defined as the difference in the predicted probability of the dependent variable, given the differences in independent variables of interest. In our case, we were interested in comparing individuals with low- and high-activity genotypes at different levels of exposure to violence. Therefore, based on our regression results, we estimated the predicted probability of a typical individual in our sample with a low- and high-activity genotype, as well as the first difference, for chosen levels of the environmental variable. In the VTSABD sample, the parental violence variable takes on values from 0 to 3 and for the Add Health sample, the values of violence range from 0 to 7. The predicted probability of getting in a fight is significantly higher for individuals with low *MAOA* activity genotype than for those with a high genotype

Table 3. Simulated First Differences and 95% Confidence Intervals (in parenthesis)

First difference	IV value	0	1	2	3	4	5	6	7
Fight (VTSABD)	Parental violence	.00 (−.04, .06)	.16 (.03, .33)	.41(.09, .70)	.60 (.19, .88)				
Use weapon in a fight (Add Health)	Violence	.00 (−.01, .01)	.01 (.00, .04)	.05 (.003, .15)	.17 (.02, .47)	.37 (.04, .78)	.57 (.10, .93)	.70 (.14, .97)	.76 (.12, .99)

Note: VTSABD = Virginia Twin Study of Adolescent and Behavioral Development. Parental violence (0–3) and violence (0–7) are additive indexes.

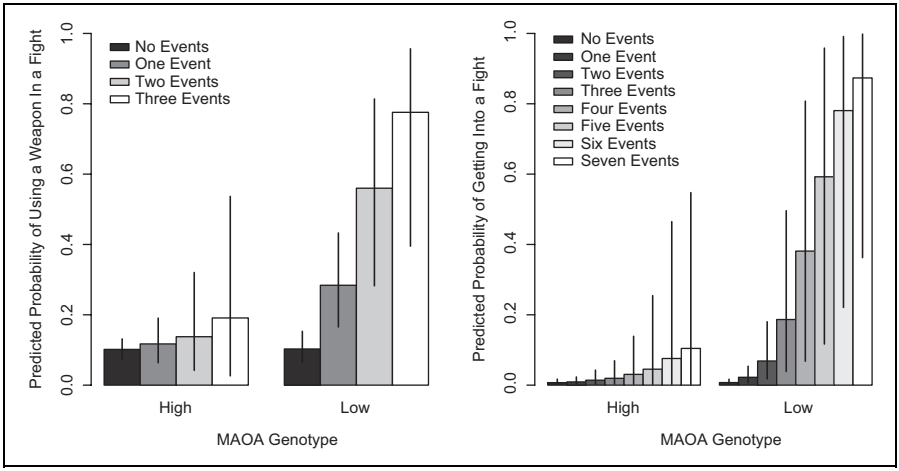

Figure 1. Predicted probabilities, based on simulations of Table 2 parameters, are presented along with 95% confidence intervals. All other variables are held at their means.

at all three nonzero values of the Parental Violence Index in the VTSABD sample. Among subjects experiencing more than one violent act in the Add Health sample, the predicted probability of using a weapon in a fight is significantly higher for low-*MAOA* activity genotype subjects than for those with a high-activity genotype.[4] The predicted probabilities for each sample are illustrated in Figure 1.

Limitations

In this study, we have offered just one approach among numerous possibilities to study the origins of political violence. Like other approaches, it is grounded on assumptions and limitations, both theoretical and statistical. Because this approach is somewhat new to the political science community, we offer an extensive description of the known limitations and assumptions here.

First, an important limitation relates to the low prevalence of many of our variables in the population sampled. Engaging in or being a victim of violence is not common. As such, the magnitude of G × E, particularly in the absence of significant main effects of *MAOA* on violence exposure may be overestimated. While other studies have found main effects for *MAOA* and aggressive or violent behavior, the lack of any main effect of *MAOA* on violence in our sample requires caution in interpreting the results. We can say this no more clearly than to state *MAOA* is *not* a warrior gene, it does not represent a gene for violence, and under no circumstances can behavior in a normal population be attributed solely to single genetic marker. Nor should individuals be absolved of responsibility for their behaviors simply because they have a specific genotype. Humans are complex, we have the ability

to choose and realize our actions. We are not ruled by genotype anymore than we are ruled by environment. However, just as environmental stimulus plays a role in behavior, so too does genetic disposition.

In addition, the detection and estimation of G × E is dependent on measurement. It is possible that extremely low sample sizes of individuals participating in a violent outcome for a specific genotype at the extreme levels of environmental exposure may result in the spurious detection of significant G × E. Previous studies in different domains reported similar results (e.g., Caspi et al. 2002), reducing this concern. However, additional studies are needed to extend the investigation of these relationships into other populations, using different variables to measure exposure to difficult early life events as well as various manifestations of aggression in adolescence and adulthood.

A second limitation is the use of data from Caucasian adolescents only. These results may not generalize to populations of differing ethnicities and cultural norms. We focused on a single ancestry to reduce the chance of population stratification and false positives. However, our confidence in these results is increased by the fact that similar results related to physical aggression have been found in other populations (Brunner et al. 1993; Caspi et al. 2002; Domschke et al. 2005). Frequency of *MAOA* differs greatly by population and different populations may express liability in divergent ways. For example, analyses have shown that the Maori population in New Zealand displays about a 60 to 65 percent incidence of the *MAOA-L* polymorphism whereas Western European populations typically report about a 30 to 35 percent rate of appearance (Gilad et al. 2002). Not everyone may react with aggression at the intersection of *MAOA* and traumatic early life events, but some might, and the implications of this interaction for the study of leadership, and mass political violence may well warrant further investigation. This work highlights the need for future study into the role of environmental risk factors related to violence across development in conjunction with the investigation of additional genetic markers which might relate to aggression. Further, these results encourage the need to study this interaction in a variety of samples to determine replicability of these results.

The *MAOA* polymorphisms, in combination with environmental triggers, are clearly limited in the overall population, typically affecting about a third of the men in white, western populations. Further, the activation of these behavioral tendencies is likely potentiated hormonally as well as spurred by other triggers. This effect may manifest behaviorally as a particular kind of charismatic leadership, characterized by lack of fear, physical strength, high levels of confidence, courage, and perhaps even a dose of narcissism. However, it may prove supremely difficult to pull these particular behaviors apart from other people who display some but not all of these features. Developmental features, such as exposure to traumatic early life events, can prove critical in delineating the creation and elicitation of these aggressive behaviors; under certain conditions, these tendencies can emerge as effective leadership, under others, it might appear as overly aggressive activities that can land someone in jail; in a third, it might lead to political rebellion in the form of terrorist

activity. The ability to separate and determine the origin and consequences of such genetic polymorphisms in combination with environmental triggers not only encourages more finely honed research programs but also helps delineate the specific environmental conditions under which particular genetic proclivities erupt and serve protective or destructive purposes.

Third, we find no main effects. Although there was a main effect for *MAOA* in the original research into the sources of CD using a similar method derived from work in psychiatric behavior genetics, we did not find one for *MAOA* and our measures of physical aggression here. In one sense, if the results are to be believed, the implication is hopeful for humanity; people are not inclined toward violence in general based solely on genotype. Rather, it appears with meaningful intervention it is possible to reduce the risk factors which might otherwise potentiate violence in at risk populations. The other critical factor to highlight relates to the nature of the interaction effect we do find. Such interaction effects work in two directions. First, those who have the genotype and are exposed to traumatic early life events are more prone to engage in physical violence later in life; however, such an interaction effect also suggests that those possessing the genotype who do *not* experience traumatic early life events are actually *less* prone to engage in violence as adults, just as those who do not have the genotype seem to be less prone to aggression.

Fourth, the nature of the variables differs somewhat between samples. This is both a limitation and a benefit. In one sense, the analyses do not represent exact replication. Even a one word difference in measurement precludes exact replication. However, measuring a complex behavior like aggression is not as simple as measuring height or weight, or number of moles, or finger ridge count. We used measures to represent an underlying trait. In our two samples, the nature of the activities are quite similar and remain comparable, especially since both sets are designed to tap into underlying dimensions related to exposure to, and experience with, violence and aggression. And we argue that the replication across two large data sets with essentially identical outcomes, but small deviations in the measures adds confidence and credibility to the results. This illustrates the robust nature of the interactive and reciprocal dynamic that exists between genotype and environment in encouraging at least some aspects of aggression.

Finally, we also note that the potential for gene–environment interaction ($G \times E$) covariation exists. Specifically, individuals receive their genes from their parents, but most children also grow up with their parents, so they likely receive two different forms of exposure to factors which may elicit violence. Thus, children remain passive recipients of the environments their parents create as they grow up. If such environments are prone to violence because of parental genotypic or phenotypic factors, children raised in such an environment may experience additional risk for engaging in violence as adults. In addition, an individual's genetic predilection may incline them to select into environments that expose them to increased rates of violence and aggression from an early age. People self-select into the environments in which they operate. For example, tendencies toward narcissism or altruism may

affect the proclivity toward selfish or helping behavior toward others. Sometimes behavior is constrained by situational and institutional forces. But sometimes room for greater freedom of action exists. Under these circumstances, the environments in which people invest themselves inform observers of their intrinsic preferences. When all avenues are open, it is easy to capture instances of aggression among those who find this outlet amenable. This tendency remains important because it helps enlighten the mechanisms and motivations by which individuals seeks political power. Moreover, these variables can help illuminate how and why individuals might gravitate toward administrative versus executive sources of power as well as resort to violent or peaceful forms of political protest.

Discussion and Conclusion

The findings from two independent samples provide support for the hypothesis that males with a specific low-activity variant of *MAOA*, in interaction with traumatic early life events, have a higher probability of engaging in aggressive behavior as adults. However, it is important to clarify what this statistical finding represents. The effect of *MAOA* only reflects one gene product within the serotoneric and dopamineric pathways as well as other related systems. These systems are composed of thousands of gene products. Any single genetic marker in these systems will not affect any complex social behaviors, aggression, or any other, to a great degree. Rather, finding that a specific *MAOA* genotype emerges significant in interaction with early life events, helping predict aggression, most likely reflects that this pathway is significant in the emergence of this behavior. Thus, this specific genotype is only the tip of the iceberg. We cannot yet identify additional remaining pathways which also may be indicted in the production and maintenance of this behavior.

Indeed, the effect of our single marker on violence is quite small. We were encouraged to examine the effect of this specific genetic marker because so much prior literature had implicated *MAOA*, in interaction with environmental precipitants in heightening the risk for physical aggression later in life. Therefore, no other gene will account for the majority of variance in any complex social behavior. We hope that studies such as this which examine the effect of a genetic marker related to neurotransmitter function can begin to help illuminate those genetic and developmental pathways which play a key role in susceptibility to violence. Identifying individual markers, like determining particular environmental precipitants, is only a first step in understanding the greater mechanisms which, in turn, might offer the possibility for future intervention and prevention.

Nevertheless, our findings do indicate that the *interaction* between environmental triggers and genotypic vulnerabilities can help explain some of the individual differences in the propensity to engage in aggression. As a result, the findings in this study hold several important political implications. First, this demonstration of the interactive nature of genes and environment in potentiating aggression illustrates the subtle and nuanced interplay between intrinsic propensities and environmental

circumstances. It should not be surprising that genotype cannot explain such complex outcomes alone; nor, alternatively, should it prove surprising that environment alone cannot produce such effects either. *MAOA* may serve carriers best when it expresses its influence only under particular circumstances, as might be required when the individual has been provoked. Those who carry the polymorphism may on average operate similar to everyone else in normal environments, but when confronted with a history of hostile or challenging circumstances, may prove more able to act to defend and protect the best interests of those who possess it against those who might challenge them. In this way, the environment serves an important input function, informing the person directly that such activity is needed because the environment that the individual confronts demands quick and strong reaction, or indicating that such behavior is not necessary in a safer environment, and might indeed prove counterproductive for purposes of cooperation and mating. Those individuals who possessed this flexible capacity in the face of challenge may have proved more likely to reproduce over long periods, but only if they were able to dial their aggressive tendencies back sufficiently to find mates during peaceful times.

Second, this study points to the critical influence of environment in triggering liable individuals who might otherwise remain peaceful to engage in aggression and violence under provocative circumstances. Such individuals may encounter traumatic early life events in a variety of ways, not all of which manifest individually, such as parental illness or neglect. Some of these forces, such as growing up in violent conditions, famine, or war, take place on widespread societal levels and can affect large swaths of the population. Even when high degrees of intrinsic liability may exist, these individuals may not manifest antisocial outcomes unless they first encounter the environmental triggers which cue its activity. Even then, they may not turn violent except in the face of provocation. This provides a profoundly hopeful note to those who argue that environmental interventions can operate to break the cycle of violence in certain areas or communities. It simultaneously offers a deeply note of caution to those who work to break endemic cycles of violence within particular societies.

Indeed, this study highlights the value of extending these investigations into field studies of political violence. For example, it would be ideal to study the interaction between exposure to violence and the *MAOA* genotype in populations with a common culture and ancestry with the exception of exposure to political violence such as individuals who live on the West Bank or the Gaza strip and those who live in Jordan. Comparisons between those exposed to similar situations who react differently can help elucidate the relative influence of history and heritage on the perpetuation of political violence. Further, such an analysis can also be used to potentially inform many other places plagued by endemic violence, such as Northern Ireland and many parts of Africa.

Our model indicates that childhood adversity in the context of a particular genotype leads to increased prevalence of violence in adulthood. Our results speak to the effect of genetic liability in interaction with environmental effects on

outcomes that matter in real-life behavior. The outcomes which examine the long-term patterns resulting from the influence of genetic polymorphism in combination with challenging early life events, on behavioral manifestations of aggression, is precisely what has been missing from much traditional political science analysis of violence. Genetic proclivity does not exist in a vacuum; rather, environmental, situational, and socialized experiences affect both who a person is, what that actor is exposed to in life, and how those forces combine to influence the subtleties of subsequent behavior. This gene–environment interaction analysis may provide a suitable model for more widespread investigation of other populations at large-scale risk for political violence due to either genotypic prevalence or environmental circumstance. Designing effective intervention of such environmental precipitants in targeted at risk populations may help ameliorate the activation of such violence in some situations. Since both genetic propensity and environmental circumstances collide to provide greater liability to reacting aggressively, actions which can ameliorate the influence of environment on genetic expression can change the manifestation of individual action just as surely as any other intervention, by working to prevent its activation in inappropriate circumstances.

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Notes

1. Monoamine oxidase-A (*MAOA*) is localized to Xp11.4-Xp11.3. A mutation in exon 8 (Gln296Stop) causes the truncation of the protein at codon 296, resulting in the loss of MAOA activity (Brunner et al. 1993). The promoter region contains a variable number tandem repeat (VNTR) polymorphism with suggested effects on transcription level. This VNTR has been reported to alter messenger RNA (mRNA) transcription efficiency which in turn is expected to affect the efficiency by which MAOA metabolizes neurotransmitters.
2. The *MAOA* promoter polymorphism has been associated with increased risk for attention-deficit/hyperactivity disorder (ADHD). Individuals with ADHD are more likely to be disciplined in school, suspended or expelled, have learning difficulties, be rejected by peers, and sustain physical injuries (Hinshaw 2002). In one study, the 4-repeat allele was reported to have increased maternal transmission (Manor et al. 2002). However, two other studies identified an association between the three-repeat allele and ADHD (Lawson et al., 2003; Domschke et al. 2005). Unfortunately, the pathway from genotype to behavioral phenotypes remains unclear.
3. These alleles consisted of 2-, 3-, 3.5-, 4-, and 5-repeating sequences consisting of 291, 321, 336, 351, and 381 base pair fragment sizes, respectively. This classification results from

prior studies of transcriptional efficiency of the MAOA gene promoter as low activity for the 3- and 5-repeat alleles, and high activity for the 3.5- and 4-repeat alleles (Sabol, Hu, and Hamer 1998). Further, recent work has reported low transcriptional efficiency for the rare 2-repeat allele (Guo et al., 2008). We treat the 2-, 3-, and 5-repeat alleles as having low transcriptional activity, and the 3.5- and 4-repeat alleles as having high transcriptional activity.

4. It is important to point out that these predicted probabilities and first differences are computed based on values the independent and dependent variable may take on in our sample. Therefore, they should not be interpreted beyond our sample. Their purpose is to more clearly illustrate our regression results.

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