ORIGINAL ARTICLE

Moderating effect of gender and MAOA genotype on aggression and violence

G. Castillo-López a, F. Ostrosky-Shejet b,*, B. Camarena-Medellín c, A.E. Vélez-García a

a Laboratorio de Neuropsicología y Psicofisiología, Facultad de Psicología, Universidad Nacional Autónoma de México (UNAM), México, D.F., Mexico
b Directora del Laboratorio de Neuropsicología y Psicofisiología, Facultad de Psicología, Universidad Nacional Autónoma de México (UNAM), México, D.F., Mexico
c Instituto Nacional de Psiquiatría, Ramón de la Fuente Muñiz, México, D.F., Mexico

Received 16 December 2014; accepted 19 March 2015
Available online 7 April 2015

KEYWORDS
Biological sex; Gender; Monoamine oxidase A; Aggression; Violence

Abstract

Introduction: Biological sex contributes to aggression, but there are other factors, like gender and genes, which have also proven to contribute to this behavior. Gender is defined as the stereotyped characteristics of each sex, but currently four gender identities have been stated: androgynous, instrumental, expressive and undifferentiated. MAOA gene has been more often related to aggression, particularly the low variant (MAOAL) of the MAOA-uVNTR polymorphism.

Objective: This study investigated whether there was an interaction between gender and MAOA genotype on aggression.

Method: 292 healthy undergraduates were assessed using an aggression questionnaire (AQ) and an inventory of gender traits (EDAIE). The genotyping technique was employed to obtain the students’ MAOA genotype. Main and interaction effects split by sex were analyzed by two-way MANOVAs.

Results: Androgynous traits had an effect on verbal aggression, anger, hostility and total aggression in males and females; while instrumental traits had an effect on physical aggression in males. MAOAH genotype had an effect on hostility in males; and MAOALH genotype on verbal aggression in females. Finally, a gender by MAOA-uVNTR interaction was observed on anger and total aggression in males.

Conclusions: Males are more likely to show anger and aggression when the predisposing genetic and environmental factors interact. Androgynous identity seems to lead to general aggression in both sexes; while instrumental identity to physical aggression just in males. On the other
Moderating effect of gender and MAOA genotype on aggression and violence

Introduction

Aggression and violence

Aggression is a multifactorial phenomenon that could be specified as an adaptive, natural behavior regulated by reinforcements, whose immediate goal is to provoke physical or psychological damage to another individual or object, in order to survive and maintain the species.\(^1\)\(^-\)\(^11\) Anger and hostility may predispose to aggression,\(^12\)\(^-\)\(^16\) as they have been claimed to be its emotional and cognitive components, respectively.\(^3\) Regarding its expression, two different types of aggression have been proposed: direct and indirect one.\(^8\)

The first one includes physical and verbal aggression; while the second one refers to aggression by social means.\(^17\)

When it is extreme, destructive, unjustified and not socially approved, aggression has been better considered as violence, which is more commonly related to human beings than animals.\(^2\)\(^,\)\(^18\) This behavior has always been present in the human history and is currently increasing as a rising problem of mortality in Latin America\(^10\) and insecurity in Mexico.\(^19\)

Gender and aggression

Biological sex contributes significantly to aggression, being males more generally aggressive than females, particularly in a physical manner.\(^16\),\(^20\)\(^-\)\(^24\) However, there are other factors that also contribute to explain aggression, such as gender, which is the identity men and women have shaped through what their society has set as typical for each sex: masculinity and femininity. Hence, people are supposed to behave according to their internalized gender. Masculinity highlights acting, strength, control, independence, selfishness and domain; while femininity is more related to emotions, nursing, tenderness, passivity and obedience.\(^25\)\(^-\)\(^27\) However, as typical traits could coexist in the same person, regardless its biological sex, four gender identities have

PALABRAS CLAVE
Sexo Biológico; Género; Monoamino Oxidasa A; Agresión; Violencia

Efecto moderador del género y el genotipo MAOA sobre la agresión y la violencia

Resumen

Introducción: El sexo biológico contribuye a la agresión, pero existen otros factores, como el género y los genes, que también contribuyen a la misma. El género corresponde a las características estereotípicas de cada sexo, pero recientemente se han propuesto cuatro tipos: andróginos, instrumental, expresivo e indiferenciado. El gen de la MAOA es el que más se ha asociado a la agresión, particularmente la variante de baja actividad (MAOALH) del polimorfismo MAOA-uVNTR.

Objetivo: Investigar si existía una interacción entre el género y el genotipo MAOA sobre la agresión.

Método: Se evaluaron 292 universitarios sanos mediante un cuestionario de agresión (AQ) y un inventario de rasgos de género (EDAIE). Se usó la técnica de genotipificación para obtener el genotipo MAOA de los participantes y se analizaron los efectos principales y de interacción para cada sexo, mediante MANOVAs factoriales.

Resultados: Se observó un efecto de los rasgos andróginos sobre la agresión verbal, el enojo, la hostilidad y el total de agresión en hombres y mujeres; y de los rasgos instrumentales sobre la agresión física en hombres. Se identificó un efecto del genotipo MAOAH sobre la hostilidad en hombres; y del genotipo MAOALH sobre la agresión verbal en mujeres. También se apreció un efecto de la interacción entre el género y el genotipo MAOA sobre el total de agresión y el enojo en hombres.

Conclusiones: Los hombres parecen ser más susceptibles al enojo y a la agresión cuando hay una interacción de factores genéticos y ambientales predisponentes. Los rasgos andróginos parecen predisponer a la agresión en ambos sexos; y los rasgos instrumentales sólo a la agresión física en hombres. En cambio, los rasgos indiferenciados aparentemente conducen a menor agresión. Tales hallazgos apuntan hacia factores que podrían ser indicadores de un comportamiento violento posterior.

© 2014 Sociedad Médica del Hospital General de México. Publicado por Masson Doyma México S.A. Todos los derechos reservados.
been proposed: instrumental, expressive, androgynous and undifferentiated.\textsuperscript{25,28,29} Instrumental people have a narrowly defined masculine or executive identity; expressive persons hold a tightly feminine or expressive identity; androgynous grasp a mixed identity (masculine and feminine); and undifferentiated individuals are those with a non-defined identity.\textsuperscript{25}

Previous research has claimed masculine/instrumental people are more directly aggressive,\textsuperscript{22,30–36} as well as androgynous;\textsuperscript{30} while holding a feminine/expressive identity has been negative related to aggressive traits.\textsuperscript{22,32,33,38} It has also been suggested that feminine/expressive and undifferentiated persons could have more aggressive cognitive and affective traits, such as hostility and anger.\textsuperscript{13} Thus, people aggressive behavior could correspond to their internalized gender identity.

**MAOA genotype and aggression**

Another factor that contributes to explain aggression is genetics.\textsuperscript{37–42} However, its contribution could be modified by some other factors, so it is better to explain aggression as a result of a gene–environment interaction.

A particular x-linked polymorphism has been well identified in the research of genetic predisposition to aggression: the MAOA-uVNTR polymorphism.\textsuperscript{47} It is a functional variable-number tandem repeat (VNTR) polymorphism in the upstream region of the gene that codifies for the enzyme monoamine oxidase A (MAOA). It consists in a sequence of 30 base-pairs repeats with high-activity (MAOA: 3.5 and 4 repeats) and low-activity (MAOA: 2, 3 and 5 repeats) variants. These participate in regulating serotonin concentration in the brain, especially before birth because its enzyme is present at adult levels at this stage. High-activity variants have been associated with a lower concentration of serotonin and low-activity ones with a higher concentration.

Pioneering studies found an association between MAOA deficiency and aggression in males when the MAOA gene had suffered an experimental or natural modification.\textsuperscript{51,52} As a result, several studies have focused in the MAOA-uVNTR environment interaction on aggression. Findings remain unclear regarding whether MAOH or MAOA should be considered as the variant that increases susceptibility to aggression. Although many studies claim for the MAOL variant,\textsuperscript{47,53–61} a few ones, including a meta-analysis, claim for the MAOH variant.\textsuperscript{64,65}

### The current study

Aggression is an important feature of violent behavior, which is an increasing serious socioeconomic and public health problem, since it leads to high social, economic and human costs. Therefore, it is relevant to have a deep understanding of factors that increase susceptibility to violent behavior in order to improve its prevention and the existing methods for its regulation. As aforementioned, aggression is better explained as a gene–environment interaction result; and it has been demonstrated that gender identity, which is shaped through experience, and MAOA-uVNTR polymorphism, both contribute significantly to explain individual differences in aggressive traits. Thus, the present study investigated whether there was a gender by MAOA-uVNTR interaction on aggression, in a sample split by sex. It was hypothesized that there would be differences among gender identities and that these would be enhanced in males who carry the MAOA variant.

### Method

**Participants**

A non-probabilistic and incidental sampling was performed. 292 healthy undergraduates (with a mean age of 23.06 ± 4.76 years) from several careers formed the final sample, which was classified by gender identity (see EDAIE at instruments section) and MAOA genotype (see MAOA genotyping section). Table 1 shows the sample distribution by biological sex, gender and MAOA genotype. Table 2 presents the descriptive characteristics of the participants.

Healthy undergraduates were included in the sample. Participants with psychiatric and/or neurological disorders, substance abuse, police records or a missing MAOA genotype were excluded from the sample.

<table>
<thead>
<tr>
<th>Table 1 Sample distribution.</th>
<th>Males n = 115</th>
<th>Females n = 177</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>MAOAL</td>
<td>MAOAH</td>
</tr>
<tr>
<td>Androgynous</td>
<td>12 (10.43%)</td>
<td>14 (12.17%)</td>
</tr>
<tr>
<td>Instrumental</td>
<td>17 (14.78%)</td>
<td>21 (18.26%)</td>
</tr>
<tr>
<td>Expressive</td>
<td>5 (4.35%)</td>
<td>11 (9.56%)</td>
</tr>
<tr>
<td>Undifferentiated</td>
<td>7 (6.09%)</td>
<td>28 (24.35%)</td>
</tr>
</tbody>
</table>

*Note: Percentages are referred from male and female total sample size.*

<table>
<thead>
<tr>
<th>Table 2 Descriptive characteristics of the sample.</th>
</tr>
</thead>
<tbody>
<tr>
<td>n = 292</td>
</tr>
<tr>
<td>Age (years) = 23.06 (4.76) Range 18–46</td>
</tr>
<tr>
<td>Scholarship (years) = 13.57 (1.59) Range 12–19</td>
</tr>
<tr>
<td>Semester = 3.71 (2.98) Range 1–9</td>
</tr>
</tbody>
</table>

*Mean; SD = standard deviation.*
**Instruments**

*Buss-Perry Aggression Questionnaire (AQ).* It is the most frequently self-reported instrument used to assess prone to aggression, and is based on the hostility inventory. It is formed by four subscales: physical aggression (e.g. If someone provoked me, I could hit him), verbal aggression (e.g. When people bother me, I argue them), anger (e.g. I get angry very quickly, but it passes fast) and hostility (e.g. Sometimes I am quite envious), that sum up for a total aggression scale. It consists of 29 items answered in a 5-point scale, from 1 = completely wrong for me to 5 = completely genuine for me. In its Spanish version, which was used in this study, the Cronbach α values were: physical aggression (α = 0.86), verbal aggression (α = 0.77), anger (α = 0.68) and total aggression (α = 0.88).

*Inventory for assessing the attributional dimensions of instrumentality and expressiveness (EDAIE).* It is a self-reported instrument that assesses the representative cultural traits that respond to an instrumental/masculine identity (e.g. responsible, qualified, risky, violent, dominant, heedless, etc.) or an expressive/feminine identity (e.g. tenderness, sensitive, complaining, maternal, obedient, etc.), each composed of positive and negative traits. The short version used in this study consists of 65 items answered in a 5-point scale, from 1 = it does not describe me at all to 5 = it completely describes me. Internal consistency for the global instrument was 0.93 and Cronbach alphas for its dimensions ranged from 0.63 to 0.90. It was used to classify the sample by gender identity, according to the median scores in its principal dimensions: instrumentality and expressiveness. High on the first one and low on the second one correspond to an instrumental/masculine identity; high on the second one and low on the first one correspond to an expressive/feminine identity; high on both dimensions correspond to an androgynous identity; and low on both ones correspond to an undifferentiated identity.

**MAOA genotyping**

DNA was extracted from buccal cells using the Buccal Cell Kit Gentra Puregen (QiaGen). Polymorphism analysis of MAOA-uVNTR was performed by the polymerase chain reaction (PCR) method. The sequences of the oligonucleotides used in this study were sense orientation: 5′-ACA GCC TGA CGG TGG AGA AG-3′, antisense orientation: 5′-GAA CGG ACG CTC CAT TCG GA-3′. The PCR reaction was performed in a final volume of 12.5 µl containing 1.5 µM MgCl₂, 200 µM of each primer, 0.2 µM of dNTPs (dATP, dCTP, dGTP, dTTP), 0.25 U of Taq Flexi Promega Go and 50 ng genomic DNA. After 4 min of denaturing at 95 °C, 35 cycles were performed with the following conditions: 1 min at 95 °C, 1 min at 62 °C and 1 min at 72 °C. It ended with a step of 4 min at 72 °C. The PCR products were analyzed by agarose gel electrophoresis/ Metaphor 2.5% and visualized under UV light after staining with ethidium bromide.

MAOA genotypes were classified according to the variants already identified.28,30 Thus, hemizygous males with high-activity variants were assigned to MAOAH group and those with low-activity variants to MAOAL group. For females, however, as MAOA gene is an X-linked gene, the variants distribution was different because they could be homozygous or heterozygous. Therefore, they were classified in three groups: MAOAL, MAOAH and MAOALH. The first one was assigned when they carried two low-activity variants; the second one when they carried two high-activity variants; and the third one when they carried an intermediate-activity variant, which is a mixture of both, high and low variants.

**Procedure**

Data were collected in a private University of Mexico City by means of self-reported instruments. Upon approval of University authorities, students were voluntarily asked to take part in the study. Their written consent was required to collaborate in the research project and their data confidentiality was assured. Four sessions were necessary to administer the instruments. Students were supervised while responding to clarify questions when necessary. They were recruited in small groups during the application in order to obtain the genetic samples, which were further analyzed.

**Statistical analysis**

Statistical analysis was performed using SPSS 17.0 software for Windows (SPSS, Chicago, IL) and epidemiological analysis for tabulating data (EPIDAT) software 3.1. First, descriptive analyses were carried for identifying if sample characteristics and chi-squares were run for comparing the allele frequency distribution of Mexican samples. Then, two-way MANOVAs, split by sex, were performed. For males, a 2 (MAOAL vs MAOAH) × 4 (androgynous vs instrumental vs expressive vs undifferentiated) design was used for each aggression scale; while for females, a 3 (MAOAL vs MAOALH vs MAOAH) × 4 (androgynous vs instrumental vs expressive vs undifferentiated) design was used for each aggression scale. Gender, MAOA genotype and their interaction termwere entered as fixed factors. Total aggression, physical aggression, verbal aggression, anger and hostility scores were entered as dependent variables. A significance level of P ≤ 0.05 adjusted for multiple comparisons through Bonferroni method was chosen.

**Results**

For the design used in this study, participants were divided by MAOA genotype, but as the allelic distribution was different for males and females, therefore, the results were split by sex and thus, as well, are reported in this section. First, allelic distribution is described and then, significantly main and interaction effects for males and females are explained.

**Allelic distribution**

A frequency analysis revealed that, among males, the allelic frequency was: 4 repeats (64.3%), 3 repeats (34.8%), and 5 repeats (0.9%); while among females, the allelic frequency was: 3,4 repeats (48%), 4,4 repeats (39.5%), 3,3 repeats (10.2%), 2,4 repeats (1.1%), 4,5 repeats (0.6%), and 2,3 repeats (0.6%). Infrequent alleles (2 and 5 repeats) for Mexicans were found, which indicates the presence of
individuals with a different genetic background. However, allelic frequency distribution among this sample did not significantly deviate from those reported from other Mexican samples (males: \( \chi^2 = 0.06, P = 0.969 \); females: \( \chi^2 = 0.14, P = 0.711 \)).

### Males

Main effects of gender identity were observed for all aggression scales (see Table 3). A main effect of MAOA genotype was found for hostility (\( F_{3,115} = 4.63, P = 0.034 \)), in which MAOAH carriers (mean = 15.86, SD = 5.81) scored higher than MAOAL carriers (mean = 14.17, SD = 5.13). A genotype by gender interaction was also observed for total aggression (\( F_{3,115} = 2.81, P = 0.043 \)) and anger (\( F_{3,115} = 2.88, P = 0.039 \)). MAOAL androgynous scored higher than other MAOAL gender identities in total aggression (see Fig. 1). They also scored higher than MAOAL instrumental and undifferentiated identities in anger (see Fig. 2).

### Females

Main effects of gender identity were found for almost all aggression scales (see Table 4). A main effect of MAOA genotype was observed for verbal aggression (\( F_{2,177} = 3.63, P = 0.029 \)), in which MAOALH carriers (mean = 13.31, SD = 4.26) scored higher than MAOAL carriers (mean = 10.47, SD = 4.10). No main effect was found for genotype by gender interaction.

### Discussion

This study investigated whether there was a gender by MAOA-uVNTR interaction on aggression. It was hypothesized that there would be differences among gender identities and that these would be enhanced in males who carry MAOAL variant, which was verified in our results. Main and interaction term effects are discussed by sex and then, some limitations, future research and conclusions are presented.

### Males

Main effects of gender identity were observed for total aggression, physical aggression, verbal aggression, anger and hostility in males. It seems that internalizing an androgynous identity predispose males to show more anger, hostility and verbal aggression than internalizing any other gender identity. Another study had already found this prone to anger for androgynous identity, but not for hostility and verbal aggression. Regarding physical aggression in males, internalizing an instrumental/masculine identity seems to be more risky than internalizing an expressive/feminine identity. These findings are consistent with those claiming instrumental identity as a predisposing factor for direct aggression. Thus, having a mixture of instrumental and expressive traits (androgynous identity) could lead males to a non-physical aggression; while having prevalent instrumental traits to physical aggression. Hence, expressive traits could be partly negatively related.

![Diagram](image1.png)

**Figure 1** Genotype by gender interaction effect on total aggression in males.

![Diagram](image2.png)

**Figure 2** Genotype by gender interaction effect on anger in males.
Moderating effect of gender and MAOA genotype on aggression and violence

<table>
<thead>
<tr>
<th>Scale</th>
<th>A (n = 51)</th>
<th>I (n = 34)</th>
<th>E (n = 58)</th>
<th>U (n = 34)</th>
<th>F</th>
<th>P</th>
<th>Post hoc Bonferroni</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>65.75 (16.27)</td>
<td>61.32 (16.08)</td>
<td>56.36 (14.49)</td>
<td>50.50 (14.41)</td>
<td>4.45</td>
<td>0.005</td>
<td>A vs U</td>
</tr>
<tr>
<td>Verbal aggression</td>
<td>14.10 (3.99)</td>
<td>13.94 (4.13)</td>
<td>12.09 (4.14)</td>
<td>11.26 (3.81)</td>
<td>3.45</td>
<td>0.018</td>
<td>A vs U</td>
</tr>
<tr>
<td>Anger</td>
<td>18.04 (4.81)</td>
<td>17.09 (4.94)</td>
<td>15.22 (4.63)</td>
<td>13.44 (4.82)</td>
<td>3.62</td>
<td>0.014</td>
<td>A vs U</td>
</tr>
<tr>
<td>Hostility</td>
<td>16.53 (5.79)</td>
<td>13.59 (5.00)</td>
<td>15.45 (5.10)</td>
<td>12.41 (4.90)</td>
<td>3.83</td>
<td>0.011</td>
<td>A vs U</td>
</tr>
</tbody>
</table>

A, androgynous; I, instrumental; E, expressive; U, undifferentiated; M, mean; SD, standard deviation.

to aggression, but only in reference to physical damage and not in experiencing it verbally or as negative thoughts (hostility) or emotions (anger).

Contrary to these findings, previous research had suggested that androgynous and instrumental/masculine identities were more adaptable and mentally healthier than expressive/feminine and undifferentiated identities. However, the present study claims to the opposite. Not internalizing a prevalent instrumental or expressive identity (undifferentiated identity) could yield less aggression than any other gender identity. Therefore, it is possible that not having to meet any social expectation could lead to a flexible perception of social norms and so, to a healthier behavior; while internalizing a prevalent instrumental or expressive identity could force to an expected behavior, or to a struggle among different expectations in androgynous identity. Namely, instrumental/masculine people are more likely to perceive the social norms as privileging aggression than expressive/feminine people. Thus, differences in male aggression could partly emerge from how rearing and sociocultural experiences shape traditional stereotypes regarding aggressive traits.

Concerning MAOA genotype, a main effect was found for male hostility. MAOAH carriers seem to be more hostile than MAOAL carriers. A broader literature on MAOAL variant as the one that increases susceptibility for aggression differs from this study; while some other, including a meta-analysis, has supported MAOAH variant. Nevertheless, these findings should be taken cautiously, since MAOAH group included more participants (n = 74/115) than MAOAL group (n = 41/115) in males; and likewise because a single variant effect is quite little. So, it remains unclear which variant has a greater contribution to differences in aggression. Indeed, some research has demonstrated MAOA activity deficiency and brain serotonin concentration are critical during development and not later in life, since compensatory mechanisms could exist, such as monoamine oxidase B action and other catecholaminergic transporters. There is a study that found no differences in brain MAO activity between high and low MAOA genotypes in healthy human adult males. Thus, although a main effect suggested that MAOA variant could lead to more negative thoughts (hostility) in males, it is better to explain this genetically complex behavior through the interaction of epistatic and epigenetic mechanisms. More research is needed in order to enrich these results.

Finally, a gender by MAOA genotype interaction was also observed for total aggression and anger in males. Androgynous who carry MAOAL variant seem to be more aggressive than any other gender identities with the same variant. They also seem to be more prone to anger than instrumental and undifferentiated identities that carry this variant. Therefore, differences among male gender identities become greater when MAOAL variant is present. As aforementioned, androgynous identity is a predisposing factor for aggressive traits, as well as MAOAL variant, while interacting with other genetic and environmental factors. Thus, these findings have verified their joint effect, which supports a gene–environment contribution to susceptibility for aggression in males. It is noteworthy that genetic factors have a lesser contribution to explain aggression than environmental factors. However, they may weight for modifying how males experience aggression, since its emotional component (anger) was evident in MAOAL male androgynous. Therefore, males having the genetic predisposing variant (MAOAL) and a personality type (androgynous) that perceive more permissive social norms regarding aggression, could be more prone to anger and aggression. Nevertheless, these findings need to be cautiously interpreted due to an unbalanced allelic frequency among groups. Even more, further research is needed to determine the hormonal and neural circuitry influencing this effect, as it has been suggested that hormones regulate MAOA gene expression and that there is a disruptive socioaffective corticolimbic circuitry (amygdala, rostral cingulate and medial prefrontal cortex) underlying MAOA’s role in genetic susceptibility for aggression.

Females

Main effects of gender identity were found for total aggression, verbal aggression, anger and hostility in females. Again, internalizing an androgynous identity seems to be the predisposing factor for aggressive traits, compared to internalizing an undifferentiated identity. Namely, having a mixture of instrumental/masculine and expressive/feminine traits (androgynous identity) could lead females to verbal aggression, negative thoughts (hostility) and emotions (anger). This latter component had been already found in previous androgynous female research. Contrary to males, internalizing an instrumental/masculine identity does not seem to prone females to aggress physically, which has been more related to men; while verbal aggression and anger have been more related to women. Indeed, some authors have claimed that women develop alternative indirect methods for aggression, in order to cover society expectations. Hence, being female and internalizing expressive/feminine traits seem to be protective factors for physical aggression; while internalizing an undifferentiated identity could yield to less aggression in general. Therefore,
rearing and sociocultural experiences shaping traditional stereotypes of women could contribute significantly to explain their differences in experiencing aggression.

Regarding MAOA genotype, a main effect was observed for verbal female aggression. MAOALH carriers seem to be more verbally aggressive than MAOAL ones. Again, these findings are consistent with previous research regarding verbal aggression in women. Nevertheless, they are inconsistent with findings supporting an association between MAOAL variant and aggressive female behaviors. The present results should be taken with caution, since MAOALH effect may be biased due to a major number of participants included in that group (n=88/177). Furthermore, it is important to consider that a single variant effect has a minor contribution in a complex behavior and that women have a more complex allelic distribution, which could lead to female differences in MAOA expression and aggression due to X-inactivation mechanisms underlying X-linked genes. More research is needed in order to determine a clear gene–environment interaction on female aggression. Here, no gender by MAOA genotype interaction effect was found in females as it was in males, who had been demonstrated to be more vulnerable to genetic effects on aggression.

**Limitations and future research**

The present study leads to a deeper understanding of predisposing genetic and environmental factors for aggression and, therefore, contributes to a broader literature on gene–environment interaction. Further research is needed in order to enrich these findings, as this is a novel study integrating gender identity and MAOA variants. It is also important to clear MAOA variants contribution to aggression because the unbalanced allelic frequency in this study limits the analysis and the interpretation of the results, especially in women, whose allelic distribution is more complex than men and minor research has been done in this sample. Furthermore, as a single gene variant has little effect on complex behaviors, it would be better to focus on epistatic and more complex epigenetic mechanisms of aggression, or on growing the sample to enhance the genetic effect. Finally, this study lacks the inclusion of variables, such as neural circuitry and sexual hormones, modifying the gene–environment interaction on aggression. Thus, a finer and more complete model is missing.

**Conclusions**

In conclusion, a gender by MAOA-uVNTR interaction on aggression was found in men, but not in women. Thus, men seem to be more prone to anger and aggression than women when they have an androgenous identity and a MAOAL genotype. In other words, males are more likely to show anger and aggression when the predisposing genetic and environmental factors interact. Sociocultural experiences leading to an androgenous identity could importantly contribute to general aggression in both sexes; while those leading to an instrumental/masculine identity could only contribute to physical aggression in males. Undifferentiated traits seem to be protective factors that could yield to less aggression in both sexes. Single MAOA variants contribution remains unclear. These findings may shed light on predisposing factors to aggression in healthy people, which could be initial indicators of what could later lead to violent behavior.

**Funding**

This work was partially supported by PAPIIT IN305313: “Conducta violenta y sus bases biológicas: neuroimagen, neuropsicología y electrofisiología”.

**Conflict of interest**

The authors declare that they have no conflict of interests.

**Acknowledgements**

Genotyping analyses were done at Instituto Nacional de Psiquiatría Ramón de la Fuente. The authors are very grateful to all the authorities and undergraduates from the University that collaborated in this study and to the Neuropsychology and Psychophysiology Laboratory team for all their support.

**References**

3. Ramírez JM, Andreu JM. Aggression and some related psychological constructs (anger, hostility, and impulsivity); some comments from a research project. Neuroci Biobehav Rev. 2005;30:1–16.
11. http://lema.rae.es/drae/val=agres%C3%B3n [accessed May 2014].


