Salud Mental 2014;37:83-91
ISSN: 0185-3325
DOI: 10.17711/SM.0185-3325.2014.010

Genetics of antisocial personality disorder: literature review

Tomás Efrén Holguín Mendoza,[1] Juan Jorge Palacios Casados[2]

Update bye topics

SUMMARY

Antisocial Personality Disorder (ASPD) is characterized by an incapacity of an individual to adapt themselves to social norms. These social norms are extremely important because they govern many aspects of behavior during adolescence and adulthood. Patients with ASPD typically have irritability problems and aggressive feelings toward other people. These aggressive feelings are expressed in a context of threat and intimidation. ASPD is less common in clinical settings comparing the total population, in which the prevalence is 1.1. The familial aggregation for ASPD has been recorded, in which some 40%-50% of the variance can be explained by genetic influences. Most of the studies of ASPD in molecular genetics have been applying the hypothesis of association of candidate genes, focusing on genes associated with neurotransmission pathways. This has been extremely relevant to the monoamine oxidase gene (MAO). Genes that promote specific behavior between individuals must have been selected through the process of natural selection. Aggressive behaviors and other types of behavior that have an evolutionary origin are similar in the fact that they have to be codified in the genes and will later be transmitted to their descendants.

Key words: Antisocial Personality Disorder, quantitative genetics, molecular genetics.

RESUMEN

El trastorno antisocial de la personalidad (TAP) consiste en una incapacidad para adaptarse a las normas sociales que habitualmente rigen numerosos aspectos de la conducta de las personas en la adolescencia y la edad adulta. Los pacientes con TAP característicamente tienen problemas de irritabilidad y sentimientos agresivos hacia los demás, los cuales se expresan en el contexto de la amenaza o la intimidación. El TAP es menos común en la clínica comparándolo con la población general en la que se reporta una prevalencia media del 1.1. Se ha registrado una agregación familiar para el TAP en la que el 40-50% de la varianza puede ser explicada por influencias genéticas. La mayoría de los estudios de genética molecular en el TAP se han realizado utilizando la hipótesis basada en los estudios de asociación con genes candidatos, enfocándose en los genes relacionados a vías de neurotransmisión, siendo uno de los más relevantes, hasta el momento, el gen para la monoamino oxidasa (MAOA). Aquellos genes que promueven que cierta conducta exista entre los individuos debieron haberse elegido a través del proceso de la selección natural. De manera similar a otros comportamientos que tienen orígenes evolutivos, los comportamientos agresivos también deben ser codificados en los genes, que a la postre serán transmitidos a la descendencia.

Palabras clave: Trastorno antisocial de la personalidad, genética cuantitativa, genética molecular.

DEFINITIONS

Personality disorders (PDs) are defined by the DSM-IV-TR (Diagnostic and Statistical Manual of Mental Disorders) as a rigid pattern of internal experience and behavior that markedly differs from the cultural expectations of the individual; it is persistent and inflexible, starts in adolescence or early adulthood, is stable over time, and brings with it discomfort or deterioration.[1]

One of the oldest and most controversial aspects in the field of classifying PDs has been whether they should be conceptualized dimensionally or categorically. It seems that there is general agreement that PDs are better classified dimensionally,[2-4] and various alternative systems are discussed in the DSM-5.[5]

Among all of the other personality disorders, only criteria for Antisocial Personality Disorder (ASPD) have historically produced acceptable levels of reliability, and these criteria have emphasized openly criminal activities.

ASPD consists of an incapacity to adapt oneself to the social norms that govern many aspects of behavior in adolescence and adult life. Characteristically, patients with

[1] Specialty Hospital Dr. Bernardo Sepúlveda. 21st Century National Medical Center of the Mexican Social Security Institute.
[2] Genetic Psychiatry Clinic. National Institute of Psychiatry Ramón de la Fuente Muñiz.

Correspondence: Dr. Tomás Efrén Holguín Mendoza. Calle Dr. Velasco 14 int. 511B, Doctores, Cuauhtémoc, 06720. Mexico City. Telephone: (55) 5588-9369. Cellphone: (55) 4487-2812. E-mail: praximeo@me.com

Received: February 27, 2013. Accepted: October 30, 2013.

ASPD easily show irritability and aggressive feelings towards others, which are expressed in a context of threat or intimidation.

The DSM-IV-TR describes it as a disorder characterized by a general pattern of contempt for, and violation of, the rights of others which begins after the age of 15.

Longitudinal research has documented that children and adolescents with behavioral disorders have a greater risk of presenting antisocial disorders as adults.[6]

Although not all antisocial behaviors in adulthood have a background in childhood,[7] disorders with genetic contributing factors tend to manifest themselves early in life. Up to half of those who present an early behavioral disorder can still experience it in adulthood, while individuals with a later start in their symptoms can experience transitory symptoms and achieve remission.[8-11]

EPIDEMIOLOGY

In 12 studies on the general population which looked at the prevalence of various personality disorders, prevalence for ASPD was reported from 0.2 to 4.5, with a median of 1.1. The first study was from 1989, and the last was from 2007. They were carried out in the USA, the United Kingdom, and Norway, with structured interviews from the DSM-III, DSM-III-R, and the DSM-IV as measuring instruments from each era.[12]

ASPD is less common in clinics, compared to the general population. This is due to patients with antisocial thought and behavior patterns rarely seeking treatment.[13]

It is more frequently present in men than in women.[14-16] Within the B *cluster* of personality disorders in the DSM-IV-TR, people with features of, or marked ASPD are usually younger,[17] and have a higher frequency of divorces, separations, or have never been married; when they are interviewed they are frequently single and live alone.

Some studies document that ASPD – or people with those traits – are related with a low education. One study in 2006 found that all disorders in the B cluster were associated with a low social class;[18] and a 2004 study documented an association with low income.[19] However, a study in 2002 did not find any association with income.[20]

Data from Mexico

In statistics on minor offenders, an increase can be observed in the number of subjects referred to the Council for Minors; that is, those submitted to criminal proceedings. The figure rose from 2,623 records in 1999 to 3,506 in 2003.[19,21] It has been observed that males make up the greater proportion of those who commit offences, and furthermore, that adolescents are referred to the Council for Minors at an earlier age. Robberies constitute the main offence, but in more recent years there have been offences documented that, although committed by a small proportion of adolescents, can be considered more serious, such as homicide, carrying weapons, rape, and sexual abuse.[22]

The most important results from a revision of antisocial behavior in Mexican adolescent students also show that males make up the greater proportion of those who are involved in this type of behavior, and in particular, involvement in fights, hitting or damaging things, hitting or injuring other people, and stealing money all stand out. Behaviors considered more serious have been documented in a lower proportion of students, such as dealing drugs or attacking others.[23-26]

A set of measurements were carried out in 1997, 2000, and 2003, on adolescent students of a middle and upper-middle level of education in public and private schools in Mexico City. In one study of the tendency towards antisocial behavior, an increase of 1.9% of any antisocial behavior was found between 1997 and 2000, and from 2000 to 2003, the increase was 6.7%. In general terms, the study concludes that there was an increase in antisocial behavior that is not serious related to violence and robbery, such as taking part in fights, hitting or damaging objects, hitting or injuring other people, shoplifting, and stealing amounts of 50 pesos or less, as well as more serious antisocial behavior; specifically theft of amount of 500 pesos or more, and attacking someone using an object or weapon, this last behavior with minor increases.[27]

These situations were similarly present in men and women, although women still represent a smaller proportion, with a ratio of almost two men for every woman.

The present text will focus on the genetic factors of ASPD, making reference to the interaction that seems to occur between genes and environment for the disorder or trait to develop, while considering the evolutionary perspective of these behaviors.

GENETIC ASPECTS

Psychiatric genetics is a multidisciplinary field a little more than 100 years old, with roots in human genetics, psychiatry, statistics, and epidemiology. The earliest work in this field involved methods of clinical and behavioral genetics (or quantitative genetics), such as studies on families, twins, and adoption, which are effective in establishing whether genetic factors influence a certain trait, and to what extent. The field was subsequently diversified to include methods of molecular genetics such as analysis of linkage and association, which, it was supposed, would allow the isolation of regions of chromosomes (*locus* candidates) and the identification of specific genes that were measuring the family transmission of a behavioral trait.

Quantitative genetics

Normal personality traits have repeatedly been shown to be influenced by genetic factors, with estimations that range between 30% and 60% of inheritability, approximately.[28,29] Similar estimations of inheritability have been found in dimensional classifications of PDs based on self-reporting.[30]

Studies on genetic epidemiology indicate that the ten personality disorders classified in the second axis of the DSM-IV-TR are mildly to moderately hereditary.

Family studies

Family aggregation has been recorded for ASPD.[31] There is a family pattern that manifests itself in a frequency five times higher among families with immediate male relations affected than among families with control individuals.[32]

ASPD seems to have as many genetic roots as environmental ones. An adopted adult who has a biological father with a history of having been in prison due to antisocial behavior has four times' greater likelihood of having an aggressive behavior problem than a person without that biological vulnerability. At the same time, a person with an adoptive father who has ASPD has three times' greater likelihood of developing the disorder compared with the general population without that background, despite their biological history.[33]

Studies on twins and adoption

In a study on a population of twins using dimensional representation for the PDs in cluster B of the DSM-IV, hereditariness for ASPD was found at 38%[34] The added genetic factors account for 49% of the variance and are more important than the shared environment for psychopathology.[35]

In his work, *Psychiatric Genetics*: *A Primer* (*2008*), Tsuang estimates inheritability (h2) for ASPD at 69%, equivalent to Borderline Personality Disorder, lower than stuttering, and higher than Obsessive Compulsive Disorder.[36]

A meta-analytical revision of ASPD in 1997 suggests that 40%-50% of the variance can be explained by genetic influences.[37] In another meta-analysis conducted by Rhee et al. in 2002 with 51 studies on twins, adoption and antisocial behavior based on records, self-reporting, and family reporting, it was found that the variance could be explained by additive genetic factors (32%), non-additive genetic factors (9%), shared environmental factors (16%), and specific individual environmental factors (43%),[35] without there being significant differences in the magnitude of genetic and environmental influences for males and females. In a more recent meta-analysis in 2010, Ferguson found that genetic influence represented the most important component in the variance of ASPD at 56%, the shared environmental factors at 11%, and the specific individual environmental factors at 31%. At the same time, he found that genetic influences had a greater predictive power for ASPD in young individuals than in adults. These results indicate that the genetic component is an important contributor for ASPD, but that non-genetic influences, particularly unique life experiences, are also important.[38]

In any case, in accordance with the information on ASPD and other personality disorders, it is important to recognize that all estimations of inheritability are dependent on the sample.

A study by Torgersen at al. (2008) on a population of twins which included the *cluster* B PDs indicated that ASPD seemed to contain many more genetic risk factors that those contents in common with other *cluster* B PDs, with the exception of Borderline Personality Disorder.

Numerous studies of families, twins, and adoption have demonstrated that ASPD, behavioral disorders, and disorders of substance abuse (frequently called externalized disorders) carry with them a common genetic risk.[39,40] In a study of families with twins carried out by Hicks et al. (2004), a high general inheritable vulnerability was found (80%) for all externalized disorders, which represented the majority of the family relationships.[41]

A study on twins carried out by Lyons et al. (1995) demonstrated that the genetic influence in the symptoms of ASPD of the DSM-III-R was more prominent in adults than in adolescents.[42]

All these results suggest that genetic influences have a significant contribution to ASPD.

In 1974, Crowe[43] found that early institutional care was a risk factor for subsequent antisocial behavior only when a genetic risk factor was present. In another study on adoption, Cadoret et al. (1983)[44] found a significant gene-environment interaction when they showed that there existed a negligible risk for antisocial behavior if the genetic risk factor was the only one (antisocial behavior in the biological father) and no effect if there was only an adverse environment in the adopted family, but that there was a substantial effect when both risk factors were present. This finding was later replicated in a study with a larger number of adopted people.[45] Using a twins design, Jaffe at al. (2005)[46] found a significant gene-environment interaction with respect to child abuse and the development of antisocial behavior, and a study of twins by Tuvblad et al. (2006)[47] demonstrated significant gene-environmental interaction, demonstrating that inheritability for antisocial behavior in adolescents is greater in disadvantaged socioeconomic environments. Using an advanced family study, Feinberg at al. (2007)[48] found an interaction of the genotype with parental negligence and scarce affection, predicting antisocial behavior. In a study on a population of twins, Hicks et al. (2009) demonstrated a significant gene-environment reaction with distinct environmental risk factors, showing that a greater environmental adversity was associated with an increasing genetic risk for ASPD and disorders due to substance consumption.[49]

Translation of the original version published in spanish in:
Salud Mental 2014, Vol. 37 Issue No. 1.

Molecular genetics

The majority of studies on molecular genetics in PDs have been carried out using the hypothesis based on studies associated with candidate genes, focusing on genes related to neurotransmission pathways, especially in the serotoninergic and dopaminergic systems. Examples of genes related to metabolism include Catechol-O-methyltransferase (COMT), monoamine oxidase (MAOA), and dopamine beta-hydroxilase (DBH); those related to the morphology of the receptor include dopamine receptor D2 (DRD2), dopamine receptor D4 (DRD4), serotonin receptor 1B (5HTR1B), and serotonin receptor 2A (5HTR2A); and those related to transporter activities include the serotonin transporter (in particular a polymorphism in the promoter region of the gene referred to as the "serotonin-transporter-linked polymorphic region" or 5HTTLPR) and the dopamine transporter (DAT).

Analysis of linkage and association

Multiple lines of evidence suggest that a dysfunction in the serotonin system (5-HT) is associated with impulsivity, aggression, emotional lability, and suicide. Genes linked to the function of these neurotransmitters can be considered candidate genes for ASPD.

Located in chromosome 17 (17q11.2), the serotonin transporter (5HTT or SLC6A4) codifies a protein transporter that removes the serotonin from the synaptic space and introduces it to the pre-synaptic neurons. This site is a target for the action of antidepressant medication. A variable number tandem repeat (VNTR) in the promoter of this gene (5HTTLPR) has shown that it affects the proportion of serotonin reuptake and can play a role in illness behavior, with the short alleles in this polymorphism essentially diallelic (whether short or long), being related to low levels of transcription of this gene.[44]

Cadoret et al. (2003) found a relationship between the low activity of the short variant of 5HHTLPR and the spectrum of externalized disorders when facing environmental adversity after controlling other variables, such as sex and age.[50]

A study by Lyons-Ruth et al. (2007) found a significant relationship between the short allele of 5HHTLPR and AD,[51] but other studied have failed to find an association between this polymorphism and any *cluster* B personality disorder.[52]

In a study by Retz et al. (2004) a relationship was found between the serotonin transporter promoter gene (5-HTT) and impulsive violence in a forensic sample of 153 men. Specifically, a deletion/insertion type polymorphism in this gene predicted impulsive violent behavior in this population.[53] Other researchers have also examined the antisocial/unsocial behavior phenotype, finding correlations with the form of low activity of 5HTTLPR in women with bulimia,[54] and in men and women in a variety of scenarios,[55-58] but Monuteaux et al. (2009) did not find an association between 5HTTLPR and behavior disorders in a sample of individuals with ADHD.[59]

Once again, Retz et al. (2008) confirmed that the carriers of two long alleles had more symptoms of ADHD in infancy and adulthood, but that the subjects with at least one short allele were more sensitive to adversity in infancy than those who carried two long alleles.[60] Subsequently, Retz and Rosler (2009) presented an interesting selective revision of ADHD, aggression, and 5HTTLPR, noting that the scientific literature generally upheld the idea that common polymorphisms could produce different effects under difficult circumstances; they concluded that those individuals carrying two long alleles were at greater risk of ADHD, but those with short alleles had a greater risk for ADHD and violent behavior under scenarios of environmental stress.[61]

Recent studies have implicated the receptor gene for serotonin 5HTR2A in impulsivity, aggression, and antisocial behaviour.[62-64]

A study by Dick et al. (2006) found that individuals who had a polymorphism in the gene GRBRA2 associated with alcohol dependence were less likely to be married, partly because they had a raised risk of ASPD and were less motivated by the desire to please others.[65]

Polymorphisms in the MAOA gene have been associated with B *cluster*[66] personality disorders and with antisocial traits.[67] The MAOA gene is localized in the X chromosome (Xp11.4-p11.3) and codes for monoamine oxidase A, an enzyme that degrades amine neurotransmitters, such as dopamine, noradrenaline, and serotonin. The mutation in this gene results in a deficiency in monoamine oxidase, or Brunner's syndrome, which is characterized, in part, by serious impulsive behaviour.[44]

Based on the results of quantitative studies of genetics that showed a gene-environment interaction in antisocial behavior, Caspi et al. (2002)[68] studied the association between child abuse and a functional polymorphism in the promoter region of the MAOA gene on antisocial behavior, assessed by means of a range of categorical and dimensional measures using questionnaires, interviews, and official records. The results did not show an exclusive important effect of the gene, just a mild effect for abuse, but it did show a substantial and significant interaction between the gene and adversity. Mistreated children that were carriers for low levels of expression of the MAOA gene developed behavior disorders and an antisocial personality with greater frequency than those children with a genotype of high activity for MAOA. Foley at al. (2004)[69] repeated these findings and extended the initial analysis when showing that the gene-environmental reaction could not be explained by a gene-environmental correlation; other studies have replicated these findings of low activity genotype of the MAOA.[70-81]

Other studies suggest that the effects of these genes do not contribute to the prediction of disruptive behavior in

those with a history of abuse or other stressors during the developmental period.[82,83]

Weder et al. (2009) found that vulnerability was induced by MAOA in moderate levels of environmental trauma, but that the genotype did not contribute to the prediction of aggression in extreme levels of environmental trauma.[84] Sjoberg at al. (2008) suggest that the MAOA genotype could interact with testosterone in predicting the antisocial behavior spectrum, although they did not find a direct association between low activity of the variant and aggressive behaviors,[85] while Beaver at al. (2010) did not find direct effects of the MAOA genotype with scales of delinquency in a sample of adolescents. In contrast, they did report that the MAOA genotype seemed to interact with neuropsychological deficits in predicting delinquency.[86] Buckholtz and Meyer-Lindenberg (2008) revised the bibliography available on MAOA in impulsive aggression, and proposed a mechanism by which the variant of low activity of MAOA could sensitize neuronal circuits pertinent to stress in early life, while they concluded that the variation of MAOA VNTR gave rise to only a small amount of variance in the risk.[87]

In a meta-analysis by Kim-Cohen et al. (2006), Caspi's original findings were replicated. Furthermore, the findings were extended to include children (close to the time of mistreatment), and the possibility of a spurious finding was discarded, taking account of the gene-environment correlation.[88] Not all studies have replicated the findings previously discussed.[89-91]

In terms of COMT, different studies have implicated valine/methionine (val/meth) polymorphism in aggression among individuals with schizophrenia,[92,93] and more recent studies suggest that homozygote subjects for the val/meth allele had greater aggression.[94-97]

In a study of 240 children with Attention Deficit Hyperactivity Disorder (ADHD), those with the valine/methionine variant in the Catechol-O-methyltransferase (COMT) gene showed more antisocial behaviors than those without that variant.[98]

Wagner et al. (2010) reported that women with the val/val polymorphism, a history of sexual abuse in childhood, and current Borderline Personality Disorder showed less impulsive aggression than those who carried the val/meth or meth/meth polymorphisms.[99]

It is important to note that these genes do not seem, in themselves, to determinedly cause ASPD in the same sense that the mutant HD gene determinedly causes Huntington's Disease. Rather, these genes probably interact with one another in such a way as to be difficult to understand. Furthermore, there are probably many other existing genes that are involved, whether directly or indirectly (eg. through interactions), and which have yet to be identified. But ultimately, these studies demonstrate that genetic vulnerability and exposure to family violence interact among themselves to produce ASPD.

AN EVOLUTIONARY PERSPECTIVE

Those genes that cause certain behavior to exist among individuals must have been chosen by the process of natural selection. In a similar way to other behaviors that have evolutionary origins, aggressive behaviors must also be coded in the genes, which are ultimately transmitted through descendants of sexual reproduction.[41]

ASPD can be understood as a byproduct of normal human aggression. Specifically, aggression can be defined as the production of an intentional behavior to cause physical damage or humiliation to another person who wishes to avoid such damage. However, as well as all the above, violent antisocial behavior is carried out without caring for the wellbeing or rights of others. For example, acting in self-defense in response to a threatening individual could be considered aggressive behavior, but not antisocial behaviour.[41,100]

Taking into consideration the existence of apparent qualitative subtypes of aggression, it is possible to develop a sensible construct that hypothesizes a dichotomy between an impulsive-reactive-hostile-affective (defensive aggression) subtype and a controlled-proactive-instrumental-predatory (offensive aggression) subtype.[101] Although the majority of neurobiological studies on aggression and violence unfortunately do not differentiate between defensive and offensive aggression, this distinction could be relevant in understanding the neurobiological bases of aggressive behavior, especially if they are influenced by anatomical neuronal and functionally distinct circuits.[102] It is believed that the propensity for impulsive aggression, which is relatively unplanned and spontaneous, but which culminates in physical violence, is found to be associated with a low threshold for activation of negative emotions and a failure to respond appropriately to the potential legal consequences predicted by such behavior. Socio-psychological research underlines the relationship between cognition, emotion, and aggression; negative emotions such as fear and anxiety frequently spark, accentuate, and modulate aggressive behavior. As such, it seems reasonable that the neuronal circuits that affect emotional states, such as the central serotonergic system, would also affect the predisposition for aggressive behaviour.[103]

Aggression can be considered as an adaptive response that can provide certain benefits, such as the co-option or defense of resources, greater pairing options, and partner fidelity, as well as a better status.

Our understanding of antisocial conduct can be structured on different suppositions that derive from the models of evolutionary psychology, which are: 1) Human aggression is a normative and adaptive response that provides a selective advantage to individuals (it should be noted that this does not imply that it is morally desirable); 2) Limitation of aggression (eg. impulse control) is also a normative

Translation of the original version published in spanish in: Salud Mental 2014, Vol. 37 Issue No. 1.

and adaptive response that provides a selected advantage to individuals; 3) Instincts of aggression and aggressive impulse control respond to environmental stimuli, or catalysts, which are cognitively processed with the object of selecting the more adaptive response to a certain environmental stressor. 4) The human brain has developed systems or independent "mechanisms" to separately manage the units responsible for aggression and control/reduction of aggressive impulses. These mechanisms can sometimes end up competing among themselves, particularly when the environmental catalysts are ambiguous.[104]

From an evolutionary perspective, a behavior as ubiquitous as aggression can be better understood as an adaptation to the pressures of the environment and something that provides selective advantage to members of the species.[105]

Although aggression in moderate amounts and in proportion to environmental threats can be beneficial, high levels of aggression can clearly be "too much of a good thing", phenoptically speaking. High levels of aggression can place an individual at extreme risk of harm, or could lead to social rejection and deprivation of the benefits of social groups, which also contribute to survival of the individual hominid organisms. As such, an individual does not benefit from being aggressive, but rather, by knowing when to be aggressive and when to control these impulses. Just as an aggressive instinct can provide a selective advantage in certain circumstances, an instinct of reducing aggression can provide a selective advantage in others.[52] The instinct of reducing aggression can be synonymous with what is frequently referred to as "impulse control" or "executive functions". Deficits in parts of the brain (eg. the frontal lobe cortex) related to executive functions have shown to predict excessively aggressive behaviors (eg. antisocial behaviors).[106-108] Neuroimaging studies document that injuries to the frontal cortex are associated with impulsive aggression, or at least with aggressive traits.[109] Individuals with ASPD have 11% more grey matter in the prefrontal cortex in comparison with individuals who do not have this disorder. This was even the case for individuals without a history of brain injury. One study found similar results in violent individuals, in comparison with non-violent controls, in the prefrontal cortex, amygdala, and hippocampus.[110] Studies on the prefrontal cortex and violence are numerous, and there are excellent revisions on the subject.[111,112]

It is important to emphasize gene-environmental interaction, given that from an antisocial genotype existing, as with any other genotype, the probability of producing a static behavior pattern in environmental situations is low. Rather, the genotype produces a range of behaviors with the object of allowing the individual to adjust themselves to different environmental threats. Environments with few threats or little tension are less likely to produce responses of antisocial behavior, contrary to environments with high threats or tension. Understanding which environmental situations are most likely to produce antisocial behaviors in individuals with a high-risk genotype for antisocial personality could provide promising methods for prevention and intervention directed towards increasing the behavioral range of antisocial individuals, providing them with non-aggressive behavior options. From an evolutionary perspective, the way in which genes and the environment interact makes the individual more flexible to facing a series of possible environmental threats. A behaviorally-flexible organism is inherently more adaptive than one whose behavior is rigid.[41]

As has been indicated throughout this text, the presence of a significant genetic component in ASPD suggests the evolutionary nature of these behaviors. Understanding genetic influences on behavior and identifying the genetic risk factors in individuals may result in treatments that could theoretically be directed early on and preventatively towards those individuals who have similar genetic risk factors. Understandably, the discussion of these possibilities includes ethical concerns.[113] This does not presume that such techniques cannot be proven useful in future; rather, that great care should be taken to ensure that any behavioral intervention or medication directed to preventing violence is only carried out under strict guidelines and ethical parameters.[41]

REFERENCES

1. Trastornos de la personalidad. En: López J, Valdés M (eds). DSM-IV-TR. Breviario. Criterios Diagnósticos. Barcelona: Masson; 2002.
2. Oldham JM, Skodol AE. Charting the future of axis II. J Personal Disord 2000;14:17-29.
3. Widiger TA, Samuel DB. Diagnostic categories or dimensions? A question for the Diagnostic and Statistical Manual of Mental Disorders-Fifth Edition. J Abnorm Psychol 2005;114:494-504.
4. Widiger TA, Trull TJ. Plate tectonics in the classification of personality disorder-shifting to a dimensional model. Am Psychologist 2007;62:71-83.
5. Krueger RF, Skodol AE, Livesley WJ et al. Synthesizing dimensional and categorical approaches to personality disorders: refining the reseacrh agenda for DSM-V Axis II. Int J Methods Psych Res 2007;16:S65-S73.
6. Robins LN. Deviant children grown up: A sociological and psyhiatric Study of Sociopathic Personality. Baltimore: Williams & Wilkins; 1966.
7. Langbehn, DR, Cadoret RJ. The adult antisocial syndrome with and without antecedent conduct disorder: Comparisons from an adoption study. Comprehensive Psychiatry 2001;42(4):272-282.
8. Barker ED, Maughan B. Differentiating early-onset persistent versus childhood-limited conduct problem youth. American J Psychiatry 2009;166(8):900-908.
9. Diamantopoulou S, Verhulst FC, Van der Ende J. Testing developmental pathways to antisocial personality problems. J Abnormal Child Psychology 2010;38(1):91-103.
10. Earls F, Mezzacappa E. Conduct and oppositional disorders. En: Rutter M, Taylor E (eds). Child and adolescent psychiatry. Cuarta edición. Oxford: Blackwell; 2003; pp. 419-436.
11. Weinberg W, Harper C, Brumback R. Substance use and abuse: Epidemiology, pharmaco- logical considerations, identification and suggestions towards management. En: Rutter M, Taylor E (eds.). Child and adolescent psychiatry. Oxford: Wiley; 2003; pp. 438-454.
12. Torgersen S. Prevalence, sociodemographics, and functional impairment. En: Oldham J, Skodol A, Bender D (eds.). Essentials of personality disorders. Arlington: American Psychiatric Publishing, Inc.; 2009.

13. Oldham J. Personality disorders. Recent history and the DSM System. En: Oldham J, Skodol A, Bender D (eds.). Essentials of personality disorders. Arlington: American Psychiatric Publishing, Inc.; 2009.
14. Torgersen S, Kringlen E, Cramer V. The prevalence of personality disorders in a community simple. Arch Gen Psychiatry 2001;58:590-596.
15. Zimmerman M, Coryell W. DSM-III personality disorder diagnoses in a nonpatient simple: demographic correlates and comorbidity. Arch Gen Psychiatry 1989;46:682-689.
16. Zimmerman M, Coryell WH. Diagnosing personality disorders in the community: a comparison of self-report and interview measures. Arch Gen Psychiatry 1990;47:527-531.
17. Grant BF, Hasin DS, Stinson FR et al. Prevalences, correlates, and disability of personality disorders in the United States: Results from the National Epidemiologic Survey on Alcohol and Related Conditions. J Clin Psychiatry 2004;65:948-958.
18. Coid J, Yang M, Tyrer P et al. Prevalences and correlates of personality disorder. Br J Psychiatry 2006;423-431.
19. Secretaría de Seguridad Pública [SSP]. Consejo de Menores. Sitio Internet http://www.ssp.gob.mx/application?pageid=cmenores_sub_2&docId=838.
20. Samuels J, Eaton WW, Bienvenu OJ III et al. Prevalences and correlates of personality disorders in a community simple. Br J Psychiatry 2002;180:536-542.
21. Consejo de Menores [CM]: Memoria 1996-1999. México: Secretaría de Gobernación; 2000.
22. Consejo de Menores [CM]: Memoria 1996-mayo 1997. México: Secretaría de Gobernación; 1997.
23. Castro ME, García G, Rojas E et al. Conducta antisocial y uso de drogas en una muestra nacional de estudiantes mexicanos. Salud Pública Mex 1988;30(2):216-226.
24. Catro ME, Rojas E, De La Serna J. Estudio epidemiológico sobre el uso de drogas y problemas asociados entre la población estudiantil que asiste a los planteles de Bachilleres. Salud Mental 1988;11(1):35-47.
25. Juarez F, Medina-Mora ME, Berenzon S et al. Antisocial behavior: its relation to selected sociodemographic variables and alcohol and drug use among mexican students. Subst Use Misuse 1998;33(7):1437-1459.
26. Juarez F, Villatoro J, Fleiz C et al. Conducta antisocial, ambiente familiar e interpersonal en estudiantes adolescentes del Distrito Federal. En: AMEPSO. La psicología social en México. México: AMEPS; 2002.
27. Juárez F, Villatoro J, Gutiérrez M et al. Tendencias de la conducta antisocial en estudiantes del Distrito Federal: mediciones 19997-2003. Salud Mental 2005;28(3):60-68.
28. Bouchard TJ, Loehlin JC. Genes, evolution, and personality. Behav Genet 2001;18:379-393.
29. Ando J, Suzuki A, Yamagata S et al. Genetic and enviromental structure of Cloninger´s temperament and carácter dimensions. J Personal Disord 2004;18:379-393.
30. Livesley WJ, Jang KL, Vernon PA. Phenotypic and genetic structure of traits delineating personality disorder. Arch Gen Psychiatry 1998;55:941-948.
31. White CN, Gunderson JG, Zanarini MC et al. Family studies of borderline personality disorder: A review. Harv Rev Psychiatry 2003;11:8-19.
32. Trastornos de la personalidad. En: Sadock B, Sadock V (eds). Kaplan & Sadock. Sinopsis de psiquiatría. Barcelona: Lippincont Williams & Wilkins; 2009.
33. Cadoret RJ, Yates WR, Troughton E et al. Genetic-environmental interaction in the génesis of agressivity and conduct disorders. Arch Gen Psychiatry 1995;52:916-924.
34. Torgersen S, Czajkowski N, Jacobson K et al. Dimensional representations of DSM-IV cluster B personality disorders in a population-based simple of Norwegian twins: a multi variate study. Psychol Med 2008;38:1617-1625.
35. Rhee SH, Waldman ID. Genetic and environmental influences on antisocial behavior: a meta-analysis of twin and adoption studies. Psychol Bull 2002;128:490-529.
36. Glatt S, Faraone S, Tsuang M. Psychiatric genetics: A primer. En: Smoller J, Sheidley B, Tsuang M(eds.). Psychiatric genetics. Applications in clinical practices. Arlington: American Psychiatric Publishing, Inc.; 2008.
37. Miles D, Carey G. Genetic and environmental architecture on human aggression. J Pers Soc Psychol 1997;72:207-217.
38. Ferguson C. Genetic contributions to antisocial personality and behavior: A meta-analytic review from an evolutionary perspective. J Soc Psychol 2010;150(2):160-180.
39. Kendler KS, Prescott CA, Myers J et al. The structure of genetic and environmental risk factores for common psychiatric and substance use disorders in men and women. Arch Gen Psychiatry 2003;60:929-937.
40. Krueger RF, hICKS bm, Patrick CJ et al. Etiologic connections among substance dependence, antisocial behavior, and personality: modeling the externalizing spectrum. J Abnorm Psychol 2002;111:411-424.
41. Hicks BM, Krueger RF, Iacono WG et al. Family transmission and heritability of externalizing disorders : a twin-family study. Arch Gen Psychiatry 2004;61:922-928.
42. Lyons MJ, True WR, Eisen SA et al. Differential heritability of adult and juvenile antisocial traits. Arch Gen Psychiatry 1995;52:906-915.
43. Crowe RR. An adoption study of antisocial personality. Arch Gen Psychiatry 1974;31:785-791.
44. Cadoret RJ, Cain CA, Crowe RR. Evidence for gene-environment interaction in the development of adolescent antisocial behavior. Behav Genet 1983;13:301-310.
45. Cadoret RJ, Yates WR, Troughton E et al. Genetic-environmental interaction in the génesis of aggressivity and conduct disorders. Arch Gen Psychiatry 19995;52:916-924.
46. Jaffe SR, Caspi A, Moffitt TE et al. Nature X nurture: genetic vulnerabilities interact with physical maltreatment to promote conduct problems. Dev Psychopathol 2005;17:67-84.
47. Tuvblad C, Grann M, Lichtenstein P. Heritability for adolescent antisocial behavior differs with socioeconomic status: gen-environment interaction. J Child Psychol Psychiatry 2006;47:734-743.
48. Feinberg ME, Button TMM, Neiderhiser JM et al. Parenting and adolescent antisocial behavior and depression -evidence of genotype x parenting environment interaction. Arch Gen Psichiatry 2007;64:457-465.
49. Hicks BM, South SC, Dirango AC et al. Environmental adversity and increasing genetic risk for externalizing disorders. Arch Gen Psychiatry 2009;66:640-648.
50. Cadoret RJ, Langbehn D, Caspers K et al. Associations of the serotonin transporter promoter polymorphism with aggressivity, attention deficit, and conduct disorder in an adoptee population. Compr Psychiatry 2003;44(2):88-101.
51. Lyons-Ruth K, Holmes BM, Sasvari-Szekely M et al. Serotonin transporter polymorphism and borderline or antisocial traits among low-income Young adults. Psychiatr Neurosci 2007;17:339-343.
52. Jacob CP, Strobel A, Hohenberger K et al. Association between allelic variation of serotonin transporter function and neuroticism in anxious cluster C personality disorders. Am J Psychiatry 2004;161:569-572.
53. Retz W, Retz-Junginger P, Supprian T et al. Association of serotonin transporter promoter gene polymorphism with violence: Relation with personality disorders, impulsivity and childhood ADHD psychopathology. Behav Sci Law 2004;22:415-425.
54. Steiger H, Richardson J, Joober R et al. Dissocial behavior, the 5HTTLPR polymorphism, and maltreatment in women with bulimic syndromes. American J Medical Genetics Part B: Neuropsychiatric Genetics 2008;147(1):128-130.
55. Gerra G, Garofano L, Santoro G et al. Association between low-activity serotonin transporter genotype and heroin dependence: Behavioral and personality correlates. American J Medical Genetics Part B: Neuropsychiatric Genetics 2004;126(1):37-42.
56. Liao DL, Hong CJ, Shih HL et al. Possible association between serotonin transporter promoter region polymorphism and extremely violent crime in Chinese males. Neuropsychobiology 2004;50(4):284-287.
57. Reif A, Rosler M, Freitag CM et al. Nature and nurture predispose to

violent behavior: Serotonergic genes and adverse childhood environment. Neuropsychopharmacology 2007;32(11):2375-2383.
58. Sakai JT, Young SE, Stallings MC et al. Case-control and within-family tests for an association between conduct disorder and 5HTTLPR. American J Medical Genetics Part B: Neuropsychiatric Genetics 2006;141(8):825-832.
59. Caspi A, McClay J, Moffitt TE et al. Role of genotype in the cycle of violence in maltreated children. Science 2002;297:851-854.
60. Monuteaux MC, Biederman J, Doyle AE et al. Genetic risk for conduct disorder symptom subtypes in an ADHD sample: Specificity to aggressive symptoms. J Am Acad Child Adolesc Psychiatry 2009;48(7):757-764.
61. Retz W, Freitag CM, Retz-Junginger P et al. A functional serotonin transporter promoter gene polymorphism increases ADHD symptoms in delinquents: Interaction with adverse childhood environment. Psychiatry Res 2008;158(2):123-131.
62. Retz W, Rosler M. The relation of ADHD and violent aggression: What can we learn from epidemiological and genetic studies? International J Law Psychiatry 2009;32(4):235-243.
63. Burt SA, Mikolajewski AJ. Preliminary evidence that specific candidate genes are associated with adolescent-onset antisocial behavior. Aggressive Behavior 2008;34(4):437-445.
64. Mik HM, Ehtesham S, Baldassarra L et al. Serotonin system genes and childhood-onset aggression. Psychiatr Genet 2007;17(1):11.
65. Preuss UW, Koller G, Bondy B et al. Impulsive traits and 5-HT2A receptor promoter polymorphism in alcohol dependents: Possible association but no influence of person- ality disorders. Neuropsychobiology 2001;43(3):186-191.
66. Dick DM, Agrawal A, Shuckit MA et al. Marital status, alcohol dependence, and GRBRA2: evidence for gene-environment correlation and interaction. J Stud Alcohol 2006;67:185-194.
67. Jacob CP, Muller J, Schmidt M et al. Cluster B personality disorders are associated with allelic variation of monoamine oxidase a activity. Neuropsychopharmacology 2005;30:1711-1718.
68. Williams LM, Gatt JM, Kuan SA et al. A polumorphism of the MAOA gene is associated with emotional brain markers and personality traits on an antisocial index. Neuropsychopharmacology 2009;34:1797-1809.
69. Foley DL, Eaves LJ, Wormley B et al. Childhood adversity, monoamine A genetype, and risk for conduct disorder. Arch Gen Psychiatry 2004;61:738-744.
70. Nilsson K, Sjoberg R, Wargelius H et al. The monoamine oxidase A (MAO-A) gene, family function and maltreatment as predictors of destructive behaviour during male adolescent alcohol consumption. Addiction 2007;102:389-398.
71. Kim-Cohen J, Caspi A, Taylor et al. MAOA, maltreatment, and gene-environment interaction preceding children´s mental health: new evidence and a meta-analysis. Mol Psychiatry 2006;11:903-913.
72. Contini V, Marques FZ, Garcia CE et al. MAOA-uVNTR polymorphism in a Brazilian sample: Further support for the association with impulsive behaviors and alcohol dependence. American J Medical Genetics Part B: Neuropsychiatric Genetics 2006;141(3):305-308.
73. Ducci F, Enoch MA, Hodgkinson C et al. Interaction between a functional MAOA locus and childhood sexual abuse predicts alcoholism and personality disorder in adult women. Mol Psychiatry 2008;13:334-347.
74. Enoch MA, Steer CD, Newman TK et al. Early life stress, MAOA, and gene-environment interactions predict behavioral disinhibition in children. Genes, Brain, Behavior 2009;9(1):65-74.
75. Huang YY, Cate SP, Battistuzzi C et al. An association between a functional polymorphism in the monoamine oxidase a gene promoter, impulsive traits and early abuse experiences. Neuropsychopharmacology 2004;29(8):1498-1505.
76. Kinnally EL, Huang YY, Haverly R et al. Parental care moderates the influence of MAOA-uVNTR genotype and childhood stressors on trait impulsivity and aggression in adult women. Psychiatr Genet 2009;19(3):126-133.
77. Nilsson KW, Sjoberg RL, Damberg M et al. Role of monoamine oxidase A genotype and psychosocial factors in male adolescent criminal activity. Biol Psychiatry 2006;59(2):121-127.
78. Prom-Wormley EC, Eaves LJ, Foley DL et al. Monoamine oxidase A and childhood adversity as risk factors for conduct disorder in females. Psychol Med 2009;39(4):579-590.
79. Reif A, Rosler M, Freitag CM, et al. Nature and nurture predispose to violent behavior: Serotonergic genes and adverse childhood environment. Neuropsychopharmacology 2007;32(11):2375-2383.
80. Wakschlag LS, Kistner EO, Pine DS et al. Interaction of prenatal exposure to cigarettes and MAOA genotype in pathways to youth antisocial behavior. Mol Psychiatry 2010;15(9):928-937.
81. Williams LM, Gatt JM, Kuan SA, et al. Polymorphism of the MAOA gene is associated with emotional brain markers and personality traits on an antisocial index. Neuropsychopharmacology 2009;34:1797-1809.
82. Haberstick BC, Lessem JM, Hopfer CJ et al. Monoamine oxidase A (MAOA) and antisocial behaviors in the presence of childhood and adolescent maltreatment. Am J Med Genet Part B: Neuropsychiatric Genetics 2005;135(1):59-64.
83. Young SE, Smolen A, Hewitt JK et al. Interaction between MAO-A genotype and maltreatment in the risk for conduct disorder: Failure to confirm in adolescent patients. Am J of Psychiatry 2006;163(6):1019-1025.
84. Weder N, Yang BZ, Douglas-Palumberi H et al. MAOA genotype, maltreatment, and aggressive behavior: The changing impact of genotype at varying levels of trauma. Biol Psychiatry 2009;65(5):417-424.
85. Sjoberg RL, Ducci F, Barr CS et al. A non-additive interaction of a functional MAO-A VNTR and testosterone predicts antisocial behavior. Neuropsychopharmacology 2008;33(2):425-430.
86. Beaver KM, DeLisi M, Vaughn M et al. Intersection of genes and neuropsychological deficits in the prediction of adolescent delinquency and low self control. International J Offender Comparative Criminology 2010;54(1):22-42.
87. Buckholtz JW, Meyer-Lindenberg A. MAOA and the neurogenetic architecture of human aggression. Trends Neurosci 2008;31(3):120-129.
88. Kim-Cohen J, Caspi A, Taylor A et al. MAOA, maltreatment, and gene-environment interaction predicting children´s mental health: new evidence and a meta-analysis. Mol Psyquiatry 2006;11:903-913.
89. Koller G, Bondy B, Preuss UW et al. No association between a polymorphism in the promoter region of the MAOA gene with antisocial personality traits in alcoholics. Alcohol Alcohol 2003;38(1):31-34.
90. Prichard ZM, Jorm AF, Mackinnon A et al. Association analysis of 15 polymorphisms within 10 candidate genes for antisocial behavioural traits. Psychiatr Genet 2007;17(5):299-303.
91. Huizinga D, Haberstick BC, Smolen A et al. Childhood maltreatment, subsequent antisocial behavior, and the role of monoamine oxidase A genotype. Biol Psychiatry 2006;60:677-683.
92. Rujescu D, Giegling I, Gietl A et al. A functional single nucleotide polymorphism (V158M) in the COMT gene is associated with aggressive personality traits. Biol Psychiatry 2003;54(1):34-39.
93. Volavka J, Bilder R, Nolan K. Catecholamines and aggression: The role of COMT and MAO polymorphisms. Ann N Y Acad Sci 2004;1036:393-398.
94. Caspi A, Langley K, Milne B et al. A replicated molecular genetic basis for subtyping antisocial behavior in children with attention-deficit/hyperactivity disorder. Arch Gen Psychiatry 2008;65(2):203-210.
95. DeYoung CG, Getchell M, Koposov RA et al. Variation in the catechol-O-methyltransferase Val/Met polymorphism associated with conduct disorder and ADHD symptoms, among adolescent male delinquents. Psychiatr Genet 2010;20:20-24.
96. Kulikova MA, Maluchenko NV, Timofeeva MA et al. Effect of functional catechol-O-methyltransferase Val/Met polymorphism on physical aggression. Bulletin Experimental Biology Medicine 2008;145(1):62-64.
97. Monuteaux MC, Biederman J, Doyle AE et al. Genetic risk for conduct disorder symptom subtypes in an ADHD sample: Specificity to aggressive symptoms. J Am Acad Child Adolesc Psychiatry 2009;48(7):757-764.
98. Thapar A, Langley K, Fowler T et al. Catechol O-Methyltransferase gene variant and birth weight predict early-onset antisocial behavior

in children with attention-deficit/hyperactivity disorder. Arch Gen Psychiatry 2005;62:1275-1278.
99. Wagner S, Baskaya O, Anicker NJ et al. The catechol o-methyltransferase (COMT) val/met polymorphism modulates the association of serious life events (SLE) and impulsive aggression in female patients with borderline personality disorder (BPD). Acta Psychiatr Scan 2010;122(2):110-117.
100. Baron R, Richardson D. Human aggression. New York: Plenum Press; 1994.
101. Vitiello B, Stoff DM. Subtypes of aggression and their relevance to child psychiatry. J Am Acad Child Adolesc Psychiatry 1997;36:307-315.
102. Lesch K-P, Merschdorf U. Impulsivity, aggression, and serotonin: a molecular psychobiological perspective. Behav Sci Law 2000;18:581-604.
103. Reif A, Rösler M, Freitag C et al. Nature and nurture predisponse to violent behavior: Serotonergic genes and adverse childhood environment. Neuropsychopharmacology 2007;32:2375-2383.
104. Buss D, Shackelford T. Human aggression in evolutionary psychological perspective. Clin Psychol Rev 1997;17:605-619.
105. Sagan C, Druyan A. Shadows of forgotten ancestors: A search for who we are. New York, NY: Random House; 1992.
106. Mercer K, Selby M. The effects of psychopathy, violence and drug use on neuropsychological functioning. American J Forensic Psychology 2005;23:65-86.
107. Donovan W, Ferraro R. Frontal lobe deficits in domestic violence offenders. Genet Soc Gen Psychol Monogr 1999;125:71-102.
108. Soderstrom H, Hultin L, Tullberg M et al. Reduced frontotemporal perfusion in psychopathic personality. Psychiatry research: Neuroimaging 2002;114:81-94.
109. Leon-Carrion J, Chacartegui-Ramos F. Brain injuries and violent crime. En: Ferguson C (ed.). Violent crime: Clinical and social implications. Thousand Oaks: Sage;
110. Critchley HD, Simmons A, Daly EM et al. Prefrontal and medial temporal correlates of repetitive violence to self and others. Biol Psychiatry 2000;47(10):928-34.
111. Davidson R, Putnam K, Larson C. Dysfunction in the neural circuitry of emotion regulation —a possible prelude to violence. Science 2000;289:591-594.
112. Hare R. Without conscience. New York, NY: Guilford Press; 1993.
113. Williams J. Violence, genes and prejudice. Discover Magazine 1994. Retrieved January 14, 2007, from http://discovermagazine.com/1994/nov/violencegenesand446.

Declaration of conflict interest: None

Translation of the original version published in spanish in: Salud Mental 2014, Vol. 37 Issue No. 1.