GSC Advanced Research and Reviews

eISSN: 2582-4597 CODEN (USA): GARRC2

Cross Ref DOI: 10.30574/gscarr

Journal homepage: https://gsconlinepress.com/journals/gscarr/

(REVIEW ARTICLE)

Check for updates

Genetics behind violent behavior

Regina Hernandez [1,*], Aleli Y Félix [1], Esaú N Fernández [1], Yara C Quiñonez [1], Manuel A Bautista [1] and Brissia Lazalde [2]

[1] *Faculty of Medicine and Nutrition, Universidad Juarez del Estado de Durango, Durango, Dgo Mexico.*
[2] *Center for Research in Precision Genomics and Rare Diseases, Faculty of Medicine and Nutrition, Universidad Juarez del Estado de Durango, Durango, Dgo Mexico.*

GSC Advanced Research and Reviews, 2025, 23(03), 181-186

Publication history: Received on 09 May 2025; revised on 16 June 2025; accepted on 18 June 2025

Article DOI: https://doi.org/10.30574/gscarr.2025.23.3.0170

Abstract

The aim of this article is to provide a review of the influence of genetic factors on aggressive behaviour. A variety of factors, including impulsivity, aggression, and rule-breaking, are complex traits influenced by both genetic predispositions and environmental exposures. Recent research has focused on gene-gene interactions, particularly between the serotonin transporter-linked polymorphic region (5-HTTLPR) and the dopamine D4 receptor (DRD4) gene variants, as key modulators of such behaviors. The extant literature suggests that the presence of the DRD4 7-repeat (7r) allele alters the effect of 5-HTTLPR on externalizing behavior, indicating an epistatic interaction that may contribute to individual differences in behavioral responses. These findings support the notion that genetic variants do not act in isolation but interact to influence the risk of developing violent and impulsive behaviors. Comprehension of these intricate genetic relationships is imperative for the identification of individuals with elevated risk. This understanding offers potential avenues for the development of personalized prevention and treatment approaches for behavioral disorders. Further studies are needed to explore the mechanisms underlying these interactions and their interplay with environmental factors.

Keywords: Serotonin; 5-HTTLPR; DRD4; Externalizing behavior; Gene-gene interaction; Impulsivity; Aggression

1. Introduction

Violence can be classified as a behavioral disorder, in which many of the symptoms may result from poor control of emotions such as anger. The definition of this behavioral disorder is as follows: "A repetitive and persistent pattern of behavior in which the basic rights of others or major age-appropriate societal norms or rules are violated, as manifested by the presence of at least three of fifteen criteria in the past twelve months, with at least one criterion present in the past six months." The classification of an individual within this category is contingent upon the consideration of the criteria outlined in the following aspects: aggression toward people and animals, destruction of property, deceitfulness or theft, and serious violations of rules. This particular disorder manifests at a higher frequency in males compared to females and typically emerges during childhood or adolescence. A multitude of risk factors have been identified, including temperamental, environmental, genetic, and physiological factors, as well as factors that may influence the course of the condition.[1]

2. Historical Background

In the mid-nineteenth century, Francis Galton was a pioneering figure in the field of human behavior and heredity studies. The integration of disparate fields such as genetics, psychology, neurobiology, and biology is a viable approach to elucidating human behavior. This multifaceted endeavor entails the examination of the interplay between genetics

* Corresponding author: Regina Hernandez

and the environment, with the environment emerging as the predominant determining factor. A substantial body of research has demonstrated that a minimum of 50% of violent behaviors are attributable to genetic predisposition. The remaining 50% are considered to be a result of environmental influences (GxE).[2]

It is noteworthy that environmental risks may exert a more substantial influence on the emergence of aggressive and antisocial behaviors in comparison to genetic predispositions. Moreover, a considerable number of nascent theories regarding the etiology of crime and criminality were predicated on the notion that individuals who perpetrate criminal acts frequently hail from socioeconomically disadvantaged backgrounds.[3]

Reactive aggression is typically associated with diminished activity in the prefrontal cortex (PFC) and heightened activity in limbic regions, such as the amygdala and striatum, particularly in response to negative social stimuli, including provocation, social exclusion, and angry facial expressions.[4]

Prolonged exposure to childhood trauma, defined as physical, sexual, emotional abuse, or neglect, has been demonstrated to exert a detrimental impact on the neural structure and function of the brain.[5]. Epigenetics comprises a variety of processes, including DNA methylation, modifications in histone proteins, and gene silencing mediated by small RNAs. The influence of both isolated violent events and prolonged exposure to situations on genome regulation and epigenetic expression has been demonstrated. The interplay between genetic predispositions and environmental influences during childhood has been identified as a contributing factor to an increased likelihood of violent behaviors manifesting in later life.[6]

3. Neuronatomic approach

From a neuroanatomical perspective, researchers have endorsed a correlation between aggression and dysfunction in specific areas of the human brain. Furthermore, they have suggested that violent attitudes and the inability to control them appear to be influenced by both genetic and environmental factors. A plethora of studies on adoption have demonstrated that genetic factors play a significant role in the manifestation of aggressive behaviour, which is influenced by a multitude of environmental variables. These include, but are not limited to, familial discord, antisocial tendencies, and exposure to violent environments.

The amygdala, a part of the human brain involved in the detection of threats by means of emotional regulation, primarily of fear and anxiety, has been linked to reactive aggressive responses. Concurrently, the prefrontal cortex, which is implicated in the regulation of inhibitory control and decision-making processes, exhibits diminished functionality in individuals grappling with challenges in modulating aggressive impulses. Neuroimaging studies have demonstrated that these regions, in conjunction with the basal ganglia, constitute components of dysregulated neuronal networks in individuals exhibiting chronic aggressive tendencies (7).

The development of brain neurochemistry plays a crucial role in this process, with the serotonergic and dopaminergic systems in particular having been identified as key modulators of aggressive behaviour. The role of serotonin, through its receptors and transporters, is linked to the inhibition of impulsive responses, while dopamine is involved in motivation and reward feelings. A malfunction in these systems has the potential to engender a diminished tolerance for frustration, diminished emotional control, and heightened emotional reactivity to stimuli perceived as a threat by the individual (7,10).

A number of studies have enforced a genetic approach to identify allelic variations inherent in aggressive behaviours. These studies were conducted with the objective of identifying the different genetic variants implicated in violent behaviours. Furthermore, they sought to ascertain how the majority of the genes investigated code for multiple proteins involved in the neurotransmission of both dopamine and serotonin, as well as various enzymes and hormones (7).

4. Genes involved in aggressive behavior

It is an established fact that aggression is the result of the interplay of multiple genes. Genes including *MAOA* (monoamine oxidase A), *SLC6A4* (serotonin transporter), *NR3C1* (glucocorticoid receptor) and OXTR (oxytocin receptor) are of particular significance in the mediation of aggression and have the capacity to affect individuals in a variety of ways. The most extensively studied of these is the *MAOA gene*, which encodes the enzyme monoamine oxidase A. This enzyme is responsible for the catabolism of amines. Genome-wide association studies (GWAS) in adults and children have identified *MAOA* as the most prominent gene in terms of frequency and relevance to violence [4]. The A form has been demonstrated to exhibit an affinity for serotonin (5HT), norepinephrine (NE), and dopamine (DA). In

humans, a mutation has been identified in the *MAO-A gene* (located on the X chromosome, region Xp11.23–11.4) which introduces a premature stop codon. This mutation has been found in a family with a tendency toward impulsive violent behaviour. In addition to this mutation, another variation has been identified: an upstream variable number of tandem repeats (uVNTR) polymorphism located in the promoter region and with a repeat unit length of 30 bp, which has been one of the most studied variants in aggressive behaviour (12, 13, 14). The Dunedin Multidisciplinary Study of Health and Development was initiated in 1972 in New Zealand. The present study revealed that children who had been subjected to severe abuse were more likely to exhibit antisocial behaviour compared to those who suffered little or no abuse. Furthermore, researchers observed that this type of behaviour was even more prevalent in children who, in addition to being subjected to abuse, exhibited an underactive version of the *MAO gene.* According to Grey Carey, a geneticist at the University of Colorado, the strongest genetic indicator associated with violence continues to be the presence of the Y chromosome, a characteristic of the male sex (14).

COMT gene is another key gene. It has been demonstrated that the encoded catechol-O-methyltransferase is involved in the metabolism of dopamine, epinephrine, and norepinephrine. The Met158 allele of the catechol-O-methyltransferase (COMT) gene has substantiated to be associated with increased levels of catecholamines in the prefrontal cortex, which may in turn increase the likelihood of aggression. (15)

Research has identified a correlation enclosed by specific variants of the 10-repeat (10R) variable number of tandem repeats (VNTR) of the serotonin transporter gene *(SLC6A3)* and variations in synaptic dopamine levels. These variations have been associated with impaired impulse control and violent behavior, particularly when they occur in conjunction with a detrimental social environment or adverse early experiences. The dopamine transporter DAT1, which is encoded by the *SLC6A3 gene*, has been the focus of extensive research in the context of a number of impulsive and behavioral problems, including violence and aggression. VNTR polymorphisms in the 3' untranslated region of the gene can be utilized to investigate this association, since they may have an impact on the expression of dopamine transporters in key brain areas that regulate emotion, such as the prefrontal cortex and striatum. (24)

The *DRD4 gene* has been the focus of numerous studies, particularly in relation to behavioral traits including novelty seeking. The extant scientific literature suggests an association between this personality trait and a propensity for impulsive behavior, sensation seeking, and lower risk aversion. These characteristics may, in turn, be associated with violent behavior, particularly within specific social or psychological contexts.

Furthermore, a relationship has been identified between the *DRD4 gene* and the following disorders:

- The condition known as schizophrenia.
- Attention-deficit/hyperactivity disorder (ADHD)
- The condition is known as obsessive-compulsive disorder with tics.
- Bipolar disorder

A significant proportion of these conditions, particularly when not adequately addressed, may manifest as symptoms of impulsivity, irritability, or aggression. This, in turn, can heighten the probability of violent behavior in certain individuals. (22,23)

The *HTR1B gene* has been proven as a potential contributor to behaviors associated with violence and impulsivity. A study was conducted to evaluate the associations between serotonin 1B receptor (5-HT1BR) levels and brain reactivity to provocations. The study established a correlation between the levels of 5-HT1BR and amygdala reactivity to provocations in male subjects exhibiting a wide spectrum of aggressive behavior. Consequently, 5-HT1BR has been identified as a promising target for the reduction of heightened neural responses to provocations and the potential mitigation of violent behavior.(15)

Epigenetic provides a significant framework for comprehending how environmental factors interact with the genome to regulate gene expression without altering the DNA sequence. As previously mentioned, a variety of specific epigenetic gene patterns have been identified as a response to stress and emotional autoregulation, including *NR3C1*. These epigenetic modifications have the potential to persist throughout the lifespan, thereby increasing the likelihood of aggressive behavior manifesting in subsequent life events. The role of epigenetics in emotional development and impulse control is a field of research that has gained significant attention in recent years. This field has identified that epigenetic factors, such as DNA methylation and histone modification, can regulate gene activity implicated in emotional development and impulse control. A substantial body of research has demonstrated a robust correlation between adverse experiences, particularly those occurring during the early stages of life—such as child abuse or child abandonment—and genetic alterations. (8,9,11)

The field of animal studies has made significant contributions to the understanding of molecular mechanisms and the assessment of aggression. Through experiments on genetically modified mice, researchers have gained insight into the underlying mechanisms of aggressive behavior. Specifically, they have identified that the deletion of the *TPH2 gene*, which is involved in serotonin synthesis, results in aggressive behavior. Conversely, the study has revealed that the expression or inhibition of 5-HT1A receptors can modulate the intensity and frequency of aggressive responses(10) this substantiates the argument posited in the present article, which demonstrates the manner in which genetic elements exert a direct influence on behavioral expression and the manner in which individuals respond to given circumstances. Two distinct forms of aggression have been distinguished based on their conceptual and neurobiological characteristics: reactive aggression and proactive aggression. It is imperative to comprehend the distinction between these phenomena when conducting an analysis of studies or undertaking research on the subject, as each form of aggression is associated with distinct neurogenic and epigenetic configurations. Reactive aggression is typified by intense and impulsive emotional responses to provocations, and it is associated with diminished prefrontal activity and heightened amygdala reactivity. Conversely, proactive aggression is meticulously orchestrated and provoked by extrinsic objectives, exhibiting a correlation with modifications in the dopaminergic reward system.(7,11)

By considering the interplay between genetic predispositions and environmental influences through epigenetic and neurobiological mechanisms, we can develop a comprehensive understanding of the underlying causes of aggression. This understanding facilitates the identification of potential biomarkers and therapeutic targets for the prevention and treatment of aggression.

The serotonin transporter (5HTT) is pivotal in regulating synaptic serotonin levels, thus ensuring the maintenance of serotonergic balance. Individuals exhibiting impulsive and aggressive behaviour have been shown to have a marked decrease in 5HTT availability in the anterior cingulate cortex. This suggests that 5HTT may be involved in violent behaviour (16). It is intriguing to note that mice deficient in the 5HTT gene exhibit reduced levels of aggression, thereby further substantiating this hypothesis (17).

A study was conducted that appeared to demonstrate an interaction effect between childhood environment and 5HTT genotype on violent behaviour. The findings of the study demonstrated that exposure to elevated levels of adversity during early childhood exerted a significant impact on the propensity for violence in later life, particularly in instances where the short promoter alleles were present. This finding suggests the presence of intricate interactions between genetic variation and environmental factors (18).

A study conducted on 298 adolescents revealed that individuals carrying two copies of the 5-HTTLPR short allele and the DRD4 7r variant exhibited the highest levels of aggressive and/or delinquent behaviour in comparison to other genotypes. However, these findings indicate that 5-HTTLPR influences externalising behaviour only when the DRD4 7r variant is present, with no observable effect when it is absent (19)

5. Conclusion

Violence is a multifaceted phenomenon that emerges as a result of the interplay among genetic, epigenetic, neurobiological, and environmental factors. Genes like *MAOA*, *SLC6A4, DRD4, COMT*, and *HTR1B* have been demonstrated to play a significant role in the regulation of key neurotransmitters associated with aggressivity. Furthermore, a multitude of environmental factors during early life can influence gene expression through epigenetic mechanisms. Aggression can be classified as reactive or proactive, with each type exhibiting a distinct biological basis. Comprehension of these interactions is essential for the identification of risks and the design of more efficient prevention strategies and treatment. However, further research is necessary to apply this knowledge in a clinical and social context.

Compliance with ethical standards

Disclosure of conflict of interest

In accordance with the submission guidelines of *GSC Advanced Research and Reviews*, all authors are required to disclose any actual or potential conflicts of interest or competing interests that might influence the publication of this manuscript. Specifically, this includes:

- Any financial, personal, or professional relationship with institutions or products mentioned in the manuscript or that may affect the study outcomes.

- Any affiliations or ties to competing products relative to those discussed in the manuscript
    - **Regina Hernandez:** No competing interests to declare.
    - **Aleli Y. Félix:** No competing interests to declare.
    - **Esaú N. Fernández:** No competing interests to declare.
    - **Yara C. Quiñonez:** No competing interests to declare.
    - **Manuel A. Bautista:** No competing interests to declare.
    - **Brissia Lazalde:** No competing interests to declare

References

[1] American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders. 5.ª ed., revisión del texto (DSM-5-TR). Arlington, VA: American Psychiatric Publishing; 2022.

[2] Lagoa A, Santos A, Pinheiro MF, Magalhães T. Genetics and criminal behaviour: recent accomplishments. Medicine, Science and the Law. 2009;49(4):274-282. doi:10.1258/rsmmsl.49.4.274.

[3] Tuvblad C, Baker LA. Human aggression across the lifespan: genetic propensities and environmental moderators. Adv Genet. 2011;75:171-214. doi: 10.1016/B978-0-12-380858-5.00007-1.

[4] Kolla NJ, Bortolato M. The role of monoamine oxidase A in the neurobiology of aggressive, antisocial, and violent behavior: A tale of mice and men. Prog Neurobiol. 2020 Nov;194:101875. doi: 10.1016/j.pneurobio.2020.101875. Epub 2020 Jun 20.

[5] Fachim VA, Corsi-Zuelli F, Loureiro CM, Iamjan S, Shuhama R, Joca S, et al. Early-life stress effects on BDNF DNA methylation in first-episode psychosis and in rats reared in isolation. Prog Neuropsychopharmacol Biol Psychiatry. 2021;108:110188. doi:10.1016/j.pnpbp.2020.110188.

[6] Li Piani L, Somigliana E, Micci LG, Spinelli G, Barbara G. Going Beyond Childhood and Gender-Based Violence: Epigenetic Modifications and Inheritance. Womens Health Rep (New Rochelle). 2024 May 28;5(1):473-484. doi: 10.1089/whr.2024.0010.

[7] Cupaioli FA, Zucca FA, Caporale C, Lesch KP, Passamonti L, Zecca L. The neurobiology of human aggressive behavior: Neuroimaging, genetic, and neurochemical aspects. Prog Neuropsychopharmacol Biol Psychiatry. 2021 Mar 2;106:110059. doi: 10.1016/j.pnpbp.2020.110059.

[8] Palumbo S, Mariotti V, Iofrida C, Pellegrini S. Genes and Aggressive Behavior: Epigenetic Mechanisms Underlying Individual Susceptibility to Aversive Environments. Front Behav Neurosci. 2018 Jun 13;12:117. doi: 10.3389/fnbeh.2018.00117.

[9] Provençal N, Binder EB. The effects of early life stress on the epigenome: From the womb to adulthood and even before. Exp Neurol. 2015 Jun;268:10-20. doi: 10.1016

[10] Popova NK. From genes to aggressive behavior: the role of serotonergic system. Bioessays. 2006 May;28(5):495-503. doi: 10.1002/bies.20412.

[11] McGowan PO, Sasaki A, D'Alessio AC, Dymov S, Labonté B, Szyf M, Turecki G, Meaney MJ. Epigenetic regulation of the glucocorticoid receptor in human brain associates with childhood abuse. Nat Neurosci. 2009 Mar;12(3):342-8. doi: 10.1038/nn.2270.

[12] Fernàndez-Castillo N, Cormand B. Aggressive behavior in humans: Genes and pathways identified through association studies. Am J Med Genet B Neuropsychiatr Genet. 2016 Jul;171(5):676-96. doi: 10.1002/ajmg.b.32419.

[13] Sabol, S., Hu, S. and Hamer, D. A functional polymorphism in the monoamine oxidase A gene promoter. Hum Genet 103, 273–279 (1998). https://doi.org/10.1007/s004390050816

[14] Brunner HG, Nelen M, Breakefield XO, Ropers HH, van Oost BA. Abnormal behavior associated with a point mutation in the structural gene for monoamine oxidase A. Science. 1993 Oct 22;262(5133):578-80. doi: 10.1126/science.8211186.

[15] Stokstad E. PSYCHOLOGY: Violent Effects of Abuse Tied to Gene. Science [Internet]. 2 de agosto de 2002 [cited on may 28th, 2025];297(5582):752a—752.

[16] Bhakta SG, Zhang JP, Malhotra AK. The COMT Met158 allele and violence in schizophrenia: a meta-analysis. Schizophr Res. 2012;140(1–3):192–7. doi:10.1016/j.schres.2012.06.026.

[17] da Cunha-Bang S, Fisher PM, Hjordt LV, Perfalk E, Beliveau V, Holst K, Knudsen GM. Men with high serotonin 1B receptor binding respond to provocations with heightened amygdala reactivity. Neuroimage. 2018;166:79–85. doi:10.1016/j.neuroimage.2017.10.032

[18] Frankle WG, Lombardo I, New AS, Goodman M, Talbot PS, Huang Y, et al. Brain serotonin transporter distribution in subjects with impulsive aggressivity: A positron emission study with [11C]McN 5652. Am J Psychiatry [Internet]. 2005 May 1 [cited 2025 May 28];162(5):915–23.

[19] Holmes A, Murphy DL, Crawley JN. Reduced aggression in mice lacking the serotonin transporter. Psychopharmacology (Berl). 2002;161(2):160–7.

[20] Reif A, Rösler M, Freitag CM, Schneider M, Eujen A, Kissling C, et al. Nature and nurture predispose to violent behavior: serotonergic genes and adverse childhood environment. Neuropsychopharmacology. 2007;32(11):2375–83. doi:10.1038/sj.npp.1301359

[21] Hohmann S, Becker K, Fellinger J, Banaschewski T, Schmidt MH, Esser G, Laucht M. Evidence for epistasis between the 5-HTTLPR and the dopamine D4 receptor polymorphisms in externalizing behavior among 15-year-olds. J Neural Transm (Vienna). 2009;116(12):1621–9. doi:10.1007/s00702-009-0290-1

[22] Aguirre-Samudio AJ, Nicolini H. The dopamine D4 receptor gene and its association with mental disorders [DRD4 polymorphism and the association with mental disorders]. Rev Invest Clin. 2005 Jan-Feb;57(1):65-75. Spanish.

[23] Kramer MS, Last B, Getson A, Reines SA. The effects of a selective D4 dopamine receptor antagonist (L-745,870) in acutely psychotic inpatients with schizophrenia. D4 Dopamine Antagonist Group. Arch Gen Psychiatry. 1997 Jun;54(6):567-72. doi: 10.1001/archpsyc.1997.01830180085011. Erratum in: Arch Gen Psychiatry 1997 Dec;54(12):1080.

[24] Silva MA, Grevet EH, Salgado CA, Bau CHD, Belmonte-de-Abreu P, Hutz MH. Allele distribution of the VNTR polymorphism in the 3' untranslated region of the DAT1 gene (SLC6A3) in São Paulo/Brazil and its importance for genetic studies of neuropsychiatric disorders in ethnically mixed populations. Rev Med Chil. 2005 Nov;133(11):1392-3.