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The role of monoamine oxidase A in neurobiology of aggressive and violent behavior in men

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ABSTRACT

Over the past two decades, converging evidence has underscored the substantial contribution of genetic determinants to the predisposition toward aggressive, antisocial, and violent behaviors. Among the genetic factors investigated, the monoamine oxidase A (MAOA) gene has emerged as the most extensively characterized locus. MAOA encodes a critical enzyme involved in the catabolism of catecholamines and serotonin, neurotransmitters that play central roles in modulating affective and behavioral regulation. Polymorphic variants associated with reduced enzymatic activity—particularly those transmitted maternally—have been consistently implicated in heightened vulnerability to aggression and antisocial behavior (ASB), with the effect most pronounced among males exposed to childhood maltreatment.

The interaction between low-activity MAOA alleles and adverse early-life environments constitutes one of the most robustly documented gene–environment (G×E) associations in the psychopathology of aggression and ASB. Neurobiological investigations further demonstrate that reduced central MAOA activity correlates with an elevated propensity toward violent behavior. Moreover, prenatal exposure to tobacco smoke has been postulated to exacerbate this vulnerability, potentially through the suppression of MAOA expression, thereby representing an additional mechanistic pathway linking environmental insults with behavioral outcomes.

In parallel, preclinical studies employing murine models of MAOA deficiency and G×E interactions have yielded critical insights into the molecular, neurochemical, and behavioral phenotypes associated with impaired MAOA function. These models not only corroborate clinical findings but also provide an experimental framework for disentangling the neurobiological mechanisms underlying antisocial and aggressive behaviors.

The objective of this article is to deliver a comprehensive and critical appraisal of the current state of evidence regarding the role of MAOA in the emergence of aggression, integrating findings from both preclinical and clinical domains to advance understanding of this complex gene–behavior relationship.

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FREE CONTENT

1. Introduction

Aggression constitutes a heterogeneous construct encompassing a wide spectrum of behaviors unified by the intent to inflict harm on other organisms, either for offensive or defensive purposes. In the majority of animal species, the primary adaptive function of aggression is to enhance survival and reproductive success (Kong et al., 2011). Analogously, human aggression has been conceptualized as an adaptive response that serves several evolutionary purposes, including the maintenance or enhancement of social status within hierarchical structures, increased access to sexual partners and resources, and the facilitation of defensive responses to external threats (Bull, 2011; Lane et al., 2009). Nevertheless, in human societies, the expression of aggression is constrained by cultural norms and social conventions.

The classification of aggression into subtypes is particularly valuable, as it facilitates the delineation of biological and evolutionary mechanisms underlying distinct behavioral manifestations and supports the operationalization of diverse aggressive profiles in adults. Among the most widely accepted heuristic models, aggression is commonly categorized into reactive and proactive forms (Carré et al., 2002; Wrangham, 2018). Reactive aggression refers to impulsive, affectively driven responses elicited by perceived provocation or threat, whereas proactive aggression reflects instrumental, goal-directed behavior aimed at securing personal gain. Although these forms differ in developmental antecedents and neurobiological substrates (Vitaro et al., 2006), they frequently co-occur within individuals (Polman et al., 2007). Both subtypes may be adaptive under certain contexts; however, they become pathological when disproportionate to the eliciting stimuli or when they contravene prevailing sociocultural standards. Such pathological aggression is strongly associated with criminality, interpersonal dysfunction, and adverse psychosocial outcomes for both perpetrators and victims.

In recent years, advances in neuroimaging—particularly functional magnetic resonance imaging (fMRI)—have contributed significantly to elucidating the neural correlates of aggression. Reactive aggression has been consistently associated with hypoactivity in prefrontal cortical regions and hyperactivity in limbic structures, including the amygdala and striatum. These patterns align with the view of reactive aggression as a maladaptive response to negative social cues such as provocation, social exclusion, or threatening facial expressions (Marsh et al., 2011; Fanning et al., 2017; Coccaro et al., 2018a). Structural studies further indicate alterations such as increased gray matter density in the dorsomedial prefrontal cortex, abnormal connectivity between the precuneus and prefrontal cortex, and volumetric changes in posterior cingulate regions. In contrast, proactive aggression has received comparatively less empirical attention, although emerging evidence suggests distinct neural underpinnings (Zhu et al., 2019). Importantly, reactive and proactive features often coexist within the same behavioral episodes, prompting calls for more nuanced taxonomies that incorporate dimensions such as modality, timing, and qualitative features of aggression (Konar et al., 2019).

The Research Domain Criteria (RDoC) initiative has further advanced the conceptualization of aggression by emphasizing transdiagnostic frameworks and biologically informed models of risk (Cuthbert & Insel,

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FREE CONTENT

2013). Within the RDoC matrix, aggression was initially classified under the Negative Valence Systems (NVS) domain. The NVS workgroup subsequently proposed a finer distinction, suggesting that reactive aggression encompasses two subtypes: (i) frustrative aggression, characterized by hostility arising from reward omission despite sustained effort, and (ii) defensive aggression, conceptualized under the "Acute Threat" construct and oriented toward eliminating perceived danger. Even these refinements, however, may fall short in capturing the full phenomenological complexity of reactive aggression. For example, some accounts posit that pathological aggression arises from dysfunctional interactions between the cognitive control system and the NVS domain, resulting in impaired inhibitory regulation in response to perceived threats (Cuthbert & Insel, 2013).

Furthermore, the RDoC framework distinguishes offensive aggression, characterized by instrumental behaviors aimed at securing resources, dominance, and social rank, from reactive subtypes. Offensive aggression is therefore more appropriately situated within the Social Processes domain of the RDoC matrix (Golden & Shaham, 2018). This multidimensional conceptualization underscores the necessity of integrating biological, cognitive, and social perspectives in advancing our understanding of the mechanisms underlying aggression.

2. MAOA's molecular features and brain distribution.

2.1. The MAOA enzyme's structure as well as function.

Using a transmembrane region consisting of 22 amino acids (aa) through its C-terminus, the enzyme MAOA (EC:1.4.3.4) is shown to be bound towards the outer mitochondrial membrane (Son et al.,2008) The structure consists of a flavin adenine dinucleotide (FAD) that is covalently attached to a cysteine residue through an 8α-(S cysteinyl)-riboflavin linking relationship. As was indicated before, MAOA is responsible for catalyzing the oxidative deamination of a number of monoamine neurotransmitters, such as 5-HT as well as the catecholamines norepinephrine as well as dopamine (Bortolato et al., 2008) – into aldehydes (Figure 1), via the side products of ammonia as well as hydrogen peroxide being produced as a result of the reaction

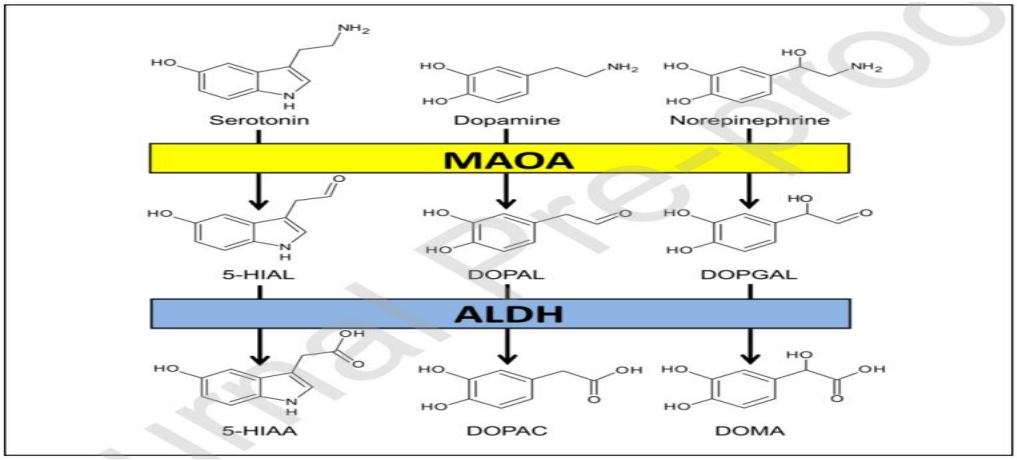

Figure 1. Degradation of serotonin, dopamine, as well as norepinephrine is facilitated by MAOA and ALDH, respectively.For example, 5-HIAL stands for 5-hydroxy indole aldehyde; DOPAL stands for 3,4-

dihydroxy phenyl acetaldehyde; DOPGAL stands for 3,4-dihydroxy phenyl glycol aldehyde; 5-HIAA stands for 5-hydroxy indole acetic acid; DOPAC stands for 3,4-dihydroxy phenylacetic acid; DOMA stands for 3,4-dihydroxymandelic acid.

contains a significant amount of similarities including its isoenzyme, which is called monoamine oxidase B. (MAOB). Although the length of these enzymes is comparable (human MAOA is 527 aa as well as human MAOB is 520 aa) and their weight is approximately 60 kilodaltons, the substrate affinity profiles of these enzymes are somewhat distinct from one another. The affinity of MAOA for 5-HT as well as norepinephrine is significantly higher than that of MAOB, which is especially selective for trace amine substrates like β-phenylethylamine or other similar substances (PEA).In human beings, the two isoenzymes exhibit comparable affinity for the neurotransmitters dopamine as well as tyramine (Bortolato et al., 2008). This same catabolism of histamine has indeed been demonstrated to involve MAOB, but not MAOA. This is accomplished by MAOB catalyzing that oxidative destruction of it's own metabolite, N-methylhistamine (Maintz and Novak, 2007). Last but not least, MAOB has been previously linked to the metabolism of the diamine putrescine, which ultimately leads to the production of γ-aminobutyric acid (GABA).In spite of these distinctions, research conducted on mice with knockout (KO) mutations has revealed that the catalytic activities of the two isoenzymes share considerable similarities. To be more specific, the deletion of both Maoa as well as Maob results in a significantly higher buildup of 5-HT and other substrates than the loss of the functional activity of each isoenzyme on its own (Yoon et al., 2014). Nevertheless, it is important to highlight that now the catalytic activity of MAOA as well as MAOB in rodents could not completely represent the pathways that are reported in primates (Gaweska and Fitzpatrick, 2011; Gaweska and Fitzpatrick, 2011; Gallardo-Pujol et al., 2013).

2.2 The MAOA is regulated both genetically and epigenetically

A location on the X chromosome (Xp11.23) that is next to the MAOB gene is where the MAOA gene can be found in humans. The two genes exhibit a somewhat similar exon-intron arrangement, consisting of 15 exons as well as around 70 percent sequence identity. Additionally, the FAD-binding site is found on exon 12 of both genes, that is highly endangered and accounts for 93.9 percent of the total identity. The two MAO paralogues are thought to have been produced by a tandem duplication of the very same parent gene due to the high degree of similarity that exists between them. To be more specific, there is just one MAO that has been described in protochordates. (Yamamoto and Vernier, 2011) fish that are teleosts (Anichtchik et al., 2006), having physiological characteristics that overlap with those of MAOA as well as MAOB in mammals for example (Arslan and Edmondson, 2010). In contrast, it has been established that anuran amphibians contain two MAO enzymes, which leads one to believe that the duplication of both the MAO progenitor gene took place during the transition between fish to amphibians for these organisms.Particularly noteworthy is the fact that the MAOA gene is X-linked in eutherian mammals, but not for other subdivisions of tetrapods, according to the genome data that is currently available from the more than 200 animal types that are published there in Gene NCBI database (consisting of animals such as monotremes, birds, reptiles, as well as marsupials).

2.3 Neuroanatomical localization of MAOA.

Multiple analytical approaches have been utilized in order to investigate the brain-regional distribution of MAOA in both human as well as animal subjects. With the use of neuroimaging approaches like positron

emission tomography (PET) as well as single-photon emission computation tomography (SPECT), which make use of radio-ligated MAOA particular inhibitors, the data that is now obtainable on the density of MAOA inside this brain in vivo have been gathered. There are three primary PET radiotracers that are accessible for the treatment of MAOA. These include the irreversible inhibitor [11C]clorgyline (Fowler et al., 2007), [11C]harmine as well as [11C]befloxatone are the 2 reversible blockers that are being discussed (Bottlaender et al., 2010). Due to the fact that they are reversible, extremely selective for the MAOA isoenzyme, as well as bind via such a high intensity to the substrates cavity of MAOA, the two radiotracers that are now available are very well-suited for the purpose of quantifying the quantities of MAOA with in brain (Son et al., 2008). [11C]harmine, on the other hand, is the only one of the two reversible radioligands that has been employed in human investigations up. SPECT investigations of brain MAOA were only present carried out in rodents, as well as the radiopharmaceutical [125I]iodoclorgyline was an essential component. Due to the fact that the density of MAOA and its metabolic activity are substantially associated, the binding of MAOA is employed as a surrogate for its expression in these neuroimaging investigations. Through the use of radio-ligated clorgyline (R=0.82) as well as harmine (R=0.86), research conducted on post-mortem brain specimens shown that the levels of MAOA protein, which were determined through immunoblotting, have a good correlation with the results obtained from PE (Tong et al., 2013). According to the findings of these research, the cerebral cortex of adults has a significant amount of MAOA, notably in the regions of the medial frontal and cingulate areas for adults. Within the subcortical regions, the hippocampal uncus, the medial pulvinar of the thalamus, as well as the hypothalamus are the regions that contain the highest amounts of the substance ;Furthermore, the striatum and the globus pallidus also have extremely low quantities of the substance.The cerebellar cortex as well as white matter appeared to have the lowest levels of expression (Tong et al., 2013).

3. Polymorphisms of human MAOA gene

3.1 Tandem repeats.

Numerous minisatellite polymorphisms have been linked to a wide variety of behavioral effects, and the MAOA gene is one of the genes that demonstrates these polymorphisms. At the position -1142 to -1262 in relation to the ATG translation initiation codon of the gene, It is a functional upstream variable-number tandem repeat (uVNTR) that is thirty base pairs long and is situated in the promoter region. This particular MAOA tandem repeat polymorphism is the most well-known of all the varieties. Numerous alleles have been identified, each of which has 2, 3, 3.5, 4, 5, or 6 copies of a sequence that is thirty base pairs long. Additionally, a rare variety with a single repetition (1R) has been described in the Iraqi population in current times (Al-Tayie and Ali, 2018). A total of five repetitions of the 6-nucleotide motif ACCVGY may be found in the 30 base pair sequence (ACCGGCACCG GCACCAGTAC CCGCACCAGT).Every one of these sequences is always preceded by a motif that is 15 base pairs long (ACCGGCACCG GCACC), which corresponds to the first half of the repeating; This particular sequence was not previously incorporated into the initial name of the alleles. For the sake of this modification, a number of authors have argued for the utilization of a categorization factoring that is more stringent; On the basis of this alternate practice, for instance, the 4-repeat (4R) variation has been referred to as 4.5R on occasion, as well as so on (Im et al., 2019). There are three (3R) and four repeats in the two alleles that are most commonly found (4R). According to the information obtained from the most comprehensive research on MAOA, the prevalence of the 3R variant is expected to be between 51 and 59 percent in African Americans as well as between 33 and 37 percent in Caucasians (Haberstick et al., 2014). On the

JOMBC Journal of Medical Pest Control
Immunology and Microbiology
ISSN : 10036245
FREE CONTENT

other hand, the 4R allele is expressed in between 36 and 43 percent of African Americans as well as among 60 and 65 percent of Caucasians. While the majority of estimations of these populations have already been relied on little cohorts up to this point, the frequency data on other nationalities, including Asians, non-white Hispanics, as well as Pacific Islanders, are still unknown. With regard to the frequency of MAOA 3R as well as 4R variants in Han Chinese in Taiwan, for instance, a number of studies have demonstrated that the 3R variant is more prevalent than the 4R allele, with the 3R variant accounting for 54-62 percent of the total. These studies were conducted on analyses that included up to approximately 200 control subject areas for each research (37-44 percent).Other findings from Taiwan as well as the People's Republic of China, on the other hand, have not corroborated this predominance, which suggests that additional thorough research are required to validate the dispersion of MAOA genotypes in this ethnic grouping. For instance, the 2-repeat (2R) variant has been observed in approximately five percent of African Americans. All other variants, on the other hand, are uncommon in the total population (and in 0.1 percent of Caucasians)(Beaver et al., 2013; Haberstick et al., 2014). On the other hand, the 3.5-repeat (3.5R) allele is discovered in about approximately 1.5 percent of Caucasians and 0.01 percent of African Americans (Haberstick et al., 2014).

3.2 Single nucleotide polymorphisms (SNPs).

Twenty single nucleotide polymorphisms (SNPs) of the MAOA gene have indeed been found as well as investigated for their functional features. To this day, the data from the dbSNP repository on MAOA reveal a total of 14,922 distinct polymorphisms (when different nomenclatures from same polymorphism are not taken into account). Intronic polymorphisms account for around 92.7 percent of all, while coding regions are home to 7.3 percent of all SNPs. Out of the 37 single nucleotide polymorphisms (SNPs) that have been the focus of published research, only a small number of them have been linked to a functional involvement in the regulation of MAOA expression. On the basis of the activity of the FnuHI and EcoRV restriction endonucleases, accordingly, the two most important functional SNPs that have been defined to this point, rs6323 as well as rs1137070, were initially recognized as two synonymous polymorphisms which can be extracted (McSwiggan et al., 2014). Every guanine (G) allele of rs6323 produces an enzyme which has a higher activity than that of the thymine (T) variant; likewise, the thymine (T) variant with rs1137070 is linked greater activity than that of the cytosine (C) allele. This evidence was demonstrated by the approach described above (Udogadi et al., 2022).

4. The part that MAOA plays in aggressive behavior and ASB: the proof of human genetics

4.1 Brunner syndrome.

Following the diagnosis of Brunner syndrome, which is an X-linked recessive disease that is defined by a nonsense mutation of something like the MAOA gene, the first discovery that established the involvement of MAOA in antisocial as well as aggressive behavior was made (rs72554632).All males in a Dutch pedigree who were afflicted exhibited disruptive and violent outbursts, which manifested themselves in the form of attempted murder, rape, and burning of the victim. While these behavioural abnormalities were occurring, there was a significant decrease in the amount of 5-HT and catecholamine metabolites found in the urine. On the other hand, more recent research has demonstrated that Brunner syndrome is characterized by a group of symptoms that are significantly more complicated than what was widely viewed. As an illustration, the few instances of newborns who have been diagnosed with this condition have the behavioral transformations and developmental cognitive impairments that are characteristic of the autism spectrum (Bortolato et al., 2018). Neurons produced from proband pluripotent stem cells have

been used in recent research to investigate the neurobiological pathways that are responsible for Brunner syndrome. According to the findings of these studies, there was a significant rise in the levels of N-methyl-D-aspartate (NMDA) glutamate subunits NR2A as well as NR2B, which is strikingly similar to the modifications that were found in Maoa control mice (Shi et al., 2019).

4.2 MAOA polymorphisms have direct consequences on aggressive behavior, violent behavior, psychopathy, and antisocial behavior.

These MAOA-L alleles of the uVNTR polymorphism have been shown to be fundamentally related with a larger predisposition for antisocial behavior (ASB), psychopathy, as well as, in specific, criminal violence in male adolescents as well as adults, according to several research that have been conducted. There have been a number of these research that have concentrated on the uncommon 2R variation, which has been found to be strongly related with a high propensity to engage in violent offenses (Guo et al., 2008). A more comprehensive research of 2574 participants from the National Longitudinal Investigation of Adolescent Health provided further evidence that these findings are accurate (NLSAH)(Shi et al., 2019). Particularly noteworthy is the possibility that the incredibly low rates of enzyme activity that are linked with this variant might be the cause of the higher risk of violent behavior in 2R carriers (approximately equivalent to one-half of the 3R).In conjunction with the fact that Brunner syndrome individuals exhibit highly aggressive behavior, these findings imply that the propensity for aggression in adulthood may be negatively related to the levels of MAOA activity that were present throughout the early phases of growth. It would be necessary to conduct additional research, potentially by analyzing the levels of DOPEG and MHPG in the plasma of young people, in order to verify this possibility (Udogadi et al., 2022).

4.3 Influence of environmental factors as well as MAOA polymorphisms on aggressiveness and ASB in combination.

It is becoming increasingly clear that behavioural phenotypes are the result of a complicated interaction among the expression of genes as well as the impacts of the environment. The MAOA-L genotype as well as childhood maltreatment are the subjects of the most extensive research on the G × E connection related with aggressive and antisocial behavior (ASB).In 2015, Poulton as well as his colleagues made history by conducting the first research to evaluate the G × E interaction in a group of 442 males who were part of the Dunedin Multidisciplinary Health as well as Research on Growth. This investigation was conducted on a population cohort consisting of 1037 subjects who were born in New Zealand among April 1972 as well as March 1973 (Poulton et al., 2015). Most of these people had backgrounds of environmental adverse situations that were really well categorized, and all these histories had been evaluated longitudinally to periodic analyses beginning at the age of three years. Antisocial findings as well as criminal backgrounds were also present in some of these persons, acquired through the use of police documents as well as conversations the with subjects and persons who are familiar with them. The most important finding of the research was those male carriers of the MAOA-L genotype who had been subjected to maltreatment had a higher possibility of engaging in antisocial behavior (ASB) compared to their peers who had also been subjected to maltreatment and owned the MAOA-H variation (Tong et al., 2013).

JOMBC Journal of Medical Pest Control
Immunology and Microbiology
ISSN : 10036245
FREE CONTENT

5. The function of MAOA in aggressive behavior: studies involving human neuroimaging

A limited number of investigations have been investigated to study the function that MAOA plays in aggressive behavior and ASB. Presented here is the most recent evidence that has been acquired through PET and MRI investigations pertaining to this matter.

5.1 Analysis of the MAOA's aggressiveness and activity using PET

This non-invasive neuroimaging technology known as positron emission tomography (PET) offers a glimpse into the neurotransmitter systems of the living human brain, includes the brains of people who have attention-deficit/hyperactivity disorder (ASPD) (Kolla and Houle, 2019). The initial PET investigations of MAOA concentrated on the association among trait anger as well as aggression in subjects who were healthy during the study (Alia-Klein et al., 2008; Soliman et al., 2011). An inverse connection among trait anger as well asaggression and decreased MAOA binding was shown to exist, according to the findings of these investigations, which were consistent with one another. To put it another way, persons who scored higher on personality tests measuring aggressiveness as well as angry/hostility had lower levels of MAOA binding in both cortical as well as subcortical areas. Remarkably, it was shown that the levels of MAOA in the brain explained more than thirty percent of the variation in behaviors associated with aggression. In accordance with the research on animals and the PET experiments conducted on healthy participants that were described before,When we contrasted the control group to the ASPD patients with high psychopathic features and violence, we discovered that the MAOA density determined with [11C]harmine PET substantially lower in the orbitofrontal cortex (OFC) as well as ventral striatum (VS) of the ASPD patients (Kolla et al., 2015). Furthermore, there was a negative correlation between the binding of MAOA in the VS and levels of impulsivity. Not only do these findings highlight the significance of the MAOA KO as an essential component in comprehending the pathophysiology of aggressive-depressive disorder (ASPD) as well as aggression, but they also imply that MAOA might be a viable target for treatments or preventative methods.

5.2 Structural MRI (sMRI).

This is one of the earliest examinations of a population that is antisocial (RomeroRebollar et al., 2015) VBM, which stands for voxel-based morphometry, was utilized in order to investigate the relationship between MAOA gene-environment interactions and regional alterations in brain structure. In the experimental group, which consisted of twenty-five individuals, diagnostic interviews were not conducted; rather, the participants were chosen on the basis of high psychopathic traits and other indicators of aggression. A comparative group consisting of twenty-eight individuals who scored poorly on all instruments was included. Each and every participant had their genotypes analyzed for the uVNTR polymorphism. Despite the absence of any discernible variations in grey matter volumes among high as well as low psychopathic groups or between different MAOA uVNTR genotypes, a G × E interaction was observed. This interaction revealed that MAOA-L carriers who exhibited higher levels of aggression exhibited a reduction in grey matter in the right better temporal pole. According to the publishers, their findings were in line with those of other neuroimaging analyses that reported abnormal connections among this area and other regions of the brain that are commonly linked via attention-deficit/hyperactivity disorder (ASPD), like the amygdala or the frontal cortex (OFC). There have been other VBM

JOMBC Journal of Medical Pest Control
Immunology and Microbiology
ISSN : 10036245
FREE CONTENT

investigations that have indicated a comparable decline in the amount of grey matter inside the temporal pole in ASPD (Kolla and Bortolato, 2020).

6. Discussion

There is a growing body of evidence that demonstrates that the MAOA uVNTR polymorphism is linked to structural and functional alterations in the brain of individuals with ASPD. The field of imaging genetics shows great potential for the elucidation of neural endophenotypes that highlight aggressive and violent behavior in individuals with ASPD and psychopathy. The experimental and clinical evidence that was presented in the preceding sections collectively demonstrates that a rise in susceptibility to ASPD is associated with a decrease in the activity of MAOA in vitro, which is combined with stress experienced during the early years of life. The findings obtained from animal models of G × E interactions shed light on the significant role that 5-HT2A receptors play in the mechanism that gives rise to this biosocial interaction. These findings bring to light the possibility that HT2RA polymorphisms may act as a moderator in the relationship between MAOA and autonomic nervous system disorders or psychopathy. It is necessary to do further research in order to assess the impact of epistatic MAOA × HT2RA interactions on the development of ASPD and psychopathy. In order to have a better understanding of the connection between MAOA and both reactive and proactive aggression, it is possible that these and other epistatic interactions are fundamental players. It is possible that 5-HT2A receptor antagonists could be a viable treatment strategy for premorbid and prodromal manifestations of ASB. This could be extremely beneficial in reducing the susceptibility for ASPD, psychopathy, and violent behavior. This is yet another intriguing corollary of this discovered phenomenon. For the purpose of determining whether or whether selective 5-HT2A receptor antagonists are effective as a potential new therapeutic and preventative tool, it may be essential to develop newer animal models that are more specific and mirror the role of MAOA in ASPD and psychopathy. From this point of view, it is important to point out that pimavanserin, a novel 5-HT2A receptor inverse agonist, was granted approval in 2014 for clinical usage as a novel antipsychotic medication for individuals suffering from Parkinson's disease (Kolla and Bortolato, 2020).

7. Conclusion

The data in the preceding sections show how the investigation of MAOA uVNTR polymorphism in connection to ASPD, psychopathy, The basic landscape for the research of MAOA uVNTR genetic variations in bigger and more fully defined sample of antisocial results was supplied by the presence of aggression as well as antisocial outcomes among small specimens. The finding that MAOA-L genetic variations, when combined with unfavorable environmental consequences, enhanced the chance for aggressive and antisocial symptoms was a significant step forward for the discipline. Nevertheless, the

remarkable heterogeneity of the findings demonstrates that a wide variety of complex processes are responsible for this variation. It is possible, for instance, that inconsistencies in findings among groups that are otherwise comparable can be explained by variations in the definition, duration, as well as nature of early traumatic experiences.

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