

Personality traits of Russian men of 18–30 years old with different diplotypes in polymorphic loci COMT VAL158MET and MAOA-uVNTR

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ABSTRACT

AAim and Scope: The article is devoted to the analysis of associations of genotype combinations of neurotransmitter system genes of MAOA and COMT with psychological features of young Russian men. **Material and Methods:** The study aimed finding associations of diplotypes by polymorphic loci Val158Met COMT and -uVNTR MAOA with such psychological characteristics as aggressiveness level and preferred forms of its expression, hostility level (Buss-Durkee Hostility Inventory), propensity to various kinds of addictive behavior, level of legitimized aggression, formally dynamic properties of individuality (diagnostication of personal inclination to deviant behavior), strategies of behavior in conflict, level of achievement motivation and personal traits (MMPI), were analyzed. **Result and Discussion:** It shows that carriers of a highly active diplotype have the lowest level of aggressiveness and are inclined to cooperate in the conflict; carriers of the highly active genotype MAOA in combination with the heterozygous genotype COMT have an average level of aggressiveness and high rates of emotional lability; carriers of low-level MAOA in combination with heterozygous genotype COMT have the highest rates of motivation to achieve success and verbal aggression; and carriers of low-level MAOA and highly active COMT are emotionally labile and non-aggressive. Men who are carriers of a low-active diplotype, have the highest level of aggressiveness and addiction to addictive behavior, which may indicate the association of this diplotype in a sample of young Russian men with social disadaptation. **Conclusion:** Russian men, carriers of different diplotypes at polymorphic loci Val158Met of gene COMT and -uVNTR of gene MAOA, have significant differences in the severity of such psychological characteristics as the level and forms of aggression and hostility, propensity to deviant behavior, strategies of behavior in a conflict, the level of motivation to achieve success, the formal dynamic properties of individuality, and the level of emotional lability, depressiveness, and suspicion.

KEY WORDS: Diplotypes, Genotype, Neurotransmitter system genes, Polymorphic loci, uVNTR MAOA, Val158Met COMT, Young men

INTRODUCTION

The study of the relationship of diplotypes (combinations of genotypes at different polymorphic gene loci) with psychological characteristics of people

belonging to different groups is the level of data analysis following the study of the links of individual SNPs with different personal characteristics. Today, a full analysis of the genome is available, but for a large volume of analyzed information, significant details often get lost. In view of the latter, the analysis of combinations of several genes responsible for certain neurochemical transformations and their manifestation in specific psychological characteristics is still relevant.

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Traditionally, in psychogenetic studies attention is paid to describing the personality characteristics of carriers of only some individual genotypes; In this paper, the characteristics of carriers of different combinations of genotypes of the genes of the catecholaminergic system MAOA and COMT are presented, which significantly expands the available ideas about the relationship of the studied genes with different psychological characteristics, as well as the features of their interaction.

The MAOA and COMT genes are associated with the activity of enzymes that break down neurotransmitters in synaptic space with catecholaminergic neurotransmission^[1] and therefore are indirectly related to the duration and intensity of the ongoing emotions, which in their turn may impose an imprint on stable personal characteristics and features of human behavior. Previously, we described the results obtained in the study of the relationship of individual genes with the psychological characteristics of men and women;^[2-4] this article is devoted to the analysis of the connection of a combination of genotypes at the polymorphic loci Val158Met of the COMT gene and the -uVNTR gene of MAOA with the psychological characteristics of men. This type of analysis can allow us to identify specific features of the interaction of genes, reflected in psychological signs.

As the subject of the study, we chose the genes of the neurotransmitter systems MAOA - the monoamine oxidase type A gene, minisatellite VNTR sequences in the promoter region of the gene; men may have high- (H; 3.5, 4, 4.5 repetitions) and low-activity (L; 2, 3, 5 repetitions) genotypes and COMT - catechol-O-methyltransferase gene; GenBank AY341246 sequence, mutation 23753G> A Val158Met, rs-code rs4680; and possible genotypes: Homozygous for allele G (GG; Val/Val), heterozygous (GA; Val/Met), and homozygous for allele A (AA; Met/Met).

As it is known, the MAOA gene is a candidate gene of aggressive behavior. Numerous studies support this postulate.^[5] Various polymorphisms of the MAOA gene are also associated with a propensity to suicidal behavior,^[6] which in general probably indicates the role of dysfunction of monoaminergic transmission in the formation of various non-adaptive behavioral features. In recent years, there have been reports of a link with the level of aggressiveness and other personality traits (high levels of anxiety, neuroticism, etc.) of polymorphism Val158Met of COMT gene.^[7,8]

Hypothesis about the interaction of factors of heredity and environment (the diathesis-stress hypothesis) in the predisposition to high aggressiveness has become widespread in the genetics of behavior, and it is confirmed by many researchers.^[9,10] In a number of experiments, attempts have been made to find

associations between genotypes of the MAOA and COMT genes and psychological characteristics, taking into account environmental influences. Thus, Gottschalk and Domschke^[11] show the relationship between the minor genotype of the gene COMT (AA) and “harm avoidance,” “anticipatory worry,” and “fear of uncertainty” in the sample of women, while MAOA H in the sample of adolescents is associated with higher rates of generalized anxiety.

Recently, hypothesis of differential susceptibility to different parenting conditions of carriers of different genotypes has become more relevant. In his work, Baumann *et al.*^[12] show that carriers of low-activity genotypes of MAOA and COMT, who have experience of violence, are prone to manifesting reactive aggression, the level of which is lower among carriers of these genotypes with a favorable parenting experience. Thus, the differences in the features of gene-environment (G × E) interactions and their influence on the severity of various forms of aggression are shown. The article also notes that the presence of early experience of violence in carriers of low-activity genotypes of MAOA and COMT of men is associated with a high risk of developing anxiety disorders.^[12] Data on the interaction of factors “level of aggressiveness” and “violence in childhood” are confirmed by many researchers for different ethnic groups.^[13] However, in a number of studies, it is noted that the increase in crime is more affected by distal stress (violence in childhood), the presence of proximal stress (violence in adulthood) is a factor that enhances this relationship.^[14] The hypothesis of differentiated susceptibility is also confirmed in the study by Zhang *et al.*,^[15] which shows an association of low-activity genotypes MAOA (T941G) and COMT (Val158Met) with reactive aggression of Chinese teenagers with low positive parenting.

MAOA and COMT are genes of the catecholaminergic system, and they can influence neurotransmitter metabolism in combination. The today existing results of studies on the analysis of associations of diplotypes MAOA and COMT with different psychological characteristics mainly have a clinical focus and are performed in the study of genetic correlates of various mental illnesses such as generalized anxiety disorder, depression, schizophrenia; part of the research is devoted to the study of the psychological experience of pain.^[16] Thus, in a sample of women, a relationship was shown between a low-activity MAOA L + COMT AAdiplotype and a high risk of developing a clinical,^[17] as well as postpartum depression.^[18]

However, at the present stage, there is not enough research describing associations of diplotypes of these genes with aggressiveness and other personal characteristics in the sample of men. In addition, in the scientific literature, there is no detailed description

of the psychological characteristics of carriers of different genotypes combinations, which is also of great interest. The factors listed above have determined the choice of the purpose and subject of this study.

MATERIALS AND METHODS

The purpose of this study is to study personality characteristics of men who are carriers of various diplotypes of polymorphic loci COMT Val158Met and MAOA-uVNTR.

Hypothesis of the study: Carriers of different diplotypes at polymorphic loci Val158Met of gene COMT and -uVNTR of gene MAOA have significant differences in the severity of such psychological characteristics as the level and forms of aggression (including socially approved and legitimized) and hostility, propensity to deviant behavior, strategies of behavior in a conflict, the level of motivation to achieve success, the formal dynamic properties of individuality, and the level of emotional lability, depressiveness, and suspicion.

The sample consisted of 76 Russian men, including 13 carriers of diplotype MAOA H + COMT GG, 15 carriers of MAOA H + COMT GA, 12 carriers of MAOA H + COMT AA, 12 carriers of MAOA L + COMT GG, 12 carriers of MAOA L + COMT GA, and 12 carriers of MAOA L + COMT AA.

In the course of the study, the following psychodiagnostic toolkit was used: The multidisciplinary personality methodology in the adaptation of Berezin,^[19] a questionnaire of formal-dynamic properties of individuality by Rusalov,^[20] Thomas' test,^[21] A. Mehrabian test questionnaire for measuring achievement of motivation (in adaptation of M.Sh. Magomed-Eminov),^[22] Buss-Durkee Hostility Inventory adapted by A. Osnitsky, 1998,^[23] the "LA-44" test for determining the level and types of legitimized (socially approved) aggression,^[24] and the technique of diagnosing a person's propensity for deviant behavior by Oryol.^[25]

To determine genotypes, a method was used to isolate DNA from buccal epithelium cells followed by polymerase chain reaction diagnostics (SFU center for the collective use of "High Technologies," Russia, Rostov-on-Don).

Statistical Processing

Analysis of Variances (ANOVA), *post-hoc* Fisher analysis, and least significant difference (LSD) test, $P \leq 0.05$, were used.

RESULTS

The results obtained during the study make it possible to judge the following peculiarities of the relationships

between the diplomats of the MAOA and COMT genes with psychological characteristics of men.

According to the results obtained, carriers of a highly active diplotype (MAOA H + COMT GG) have a low level of verbal aggression (average 54,7 points, $P = 0,02$), aggressive motivation (average 17,8 points, $P = 0.007$; Figures 1 and 2; $P \leq 0.05$), as well as legitimized aggression (average 78 points, $P = 0.04$), are inclined to choose cooperation strategies in the conflict (average 6.4 points, $P = 0.42$) and avoidance (compare the results of 6.1 points, $P = 0.28$). The described features characterize this group as the most non-aggressive in the sample under study.

According to the data received, the carriers of the diplotype MAOA H + COMT GA are not inclined to avoid conflicts (average 4.3 points, $P = 0.28$), have a low index of legitimized aggression (average: 76, $P = 0.04$, Figures 1 and 2; $P \leq 0.01$), high indices of general emotionality (average 86.8 points, $P = 0.01$), and emotional lability (Hy scale), and are not inclined to aggression and violence. In general, this group of men is characterized by high sensitivity, insecurity, anxiety in various spheres of activity, and communication, as well as emotional instability. In this case, the level of aggression in men of this group is in mean values; the most pronounced form of aggression is verbal.

Carriers of the diplotype MAOA L + COMT GA have a significantly higher level of achievement of motivation (average, 155.3 points), compared to MAOA H + COMT AA carriers (compare 126.2 b., Figure 3; $P = 0.04$). At the same time, they have a high level of verbal aggression (compare: 80, $P = 0.02$).

Male carriers of the combination MAOA L + COMT GG have the highest indicators on the scale of emotional lability of Hy, compared to carriers of other combinations (average: 66.7 T, $P = 0.02$), and the lowest indices of aggression (average 5.3 points, $P = 0.02$), general emotionality (mean 54.7 points, $P = 0.01$), the level of aggressive motivation (average 15.7 points, $P = 0.007$), and are not inclined to addictive (average 4 points, $P = 0.001$) and delinquent behavior (average 12 points, $P = 0.02$; Figure 4).

Let's pay attention to the fact that the carriers of the genotype COMT AA in combination with MAOA H and MAOA L have the highest rates on the scale of verbal aggression in the studied sample (average 74.8 points and 104.5 points, respectively, $P = 0.08$).

Carriers of the low-activity diplotype MAOA L + COMT AA have a number of psychological characteristics that distinguish them from other participants of the study. There are high rates on the scales of physical, verbal, and socially approved aggression, a high aggression index and the level

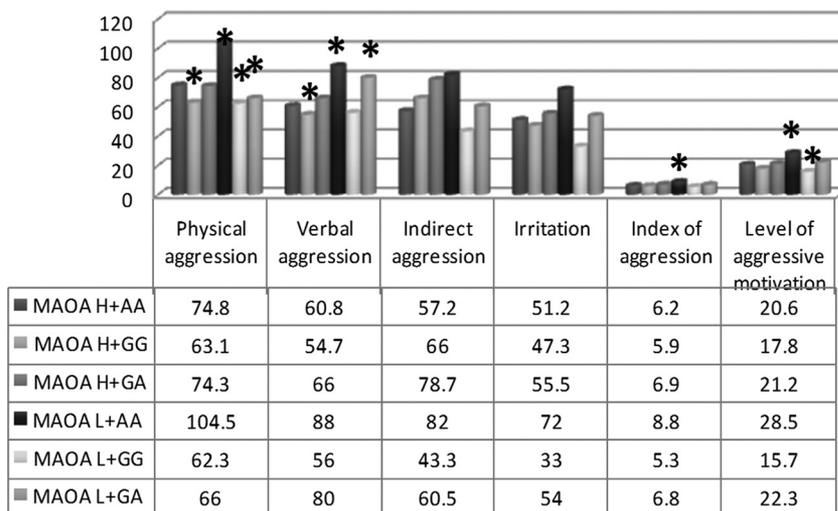


Figure 1: The level of aggressiveness in men with several diplotypes in polymorphic loci Val158Met of the COMT gene and -uVNTR of the MAOA gene (*post hoc* Fisher analysis, least significant difference test); Legend: * $P \leq 0.05$.

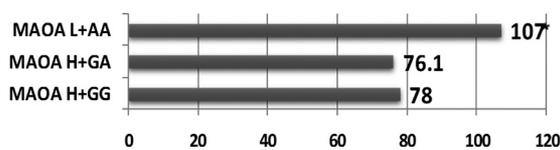


Figure 2: The integral level of the legitimized aggression in men with several diplotypes in polymorphic loci Val158Met of the COMT gene and -uVNTR of the MAOA gene (*post hoc* Fisher analysis, least significant difference test); Legend: * $P \leq 0.01$.

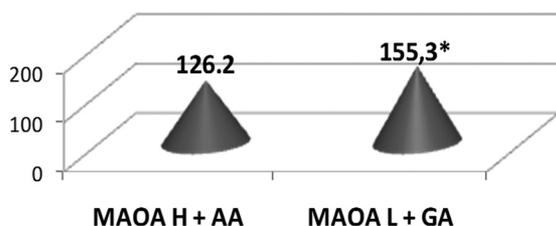


Figure 3: The level of achievement motivation in men with several diplotypes in polymorphic loci Val158Met of the COMT gene and -uVNTR of the MAOA gene (*post hoc* Fisher analysis, least significant difference test); Legend: * $P \leq 0.01$

of aggressive motivation, propensity to addictions (average 16.5 points, $P = 0.001$), and delinquent behavior (average 12 points, $P = 0.001$), compared to carriers of the combination MAOA L with COMT GG (average 3.3 points, $P = 0.02$), and also to the implementation of aggression and violence in direct behavior (Figure 4, $P \leq 0.01$). The described features characterize this group as the most aggressive one among carriers of different diplotypes at polymorphic loci VAL158MET of the COMT gene and -uVNTR of the MAOA gene.

In addition to high level of aggressiveness, carriers of the low active diplotypes have higher, compared with other men, scores on pessimism and paranoid scales

($P = 0.02$), which may manifest itself in the domination of the representatives of this group of depressed mood and excessive suspicion.

DISCUSSION

The neuronal and biochemical mechanisms underlying these associations are still unknown, but in our opinion a very reasonable is assumption of a link between the low-activity genotypes MAOA and COMT with a violation of regulation of the limbic system structures activity by the prefrontal cortex, i.e., with a disturbance in the regulation of emotions.^[26,27]

Research prospects: It is necessary to take into account the fact that behavior is a complex feature that involves various factors. Undoubtedly, it is promising to analyze genome modifications that do not affect the DNA sequence but which have an effect on gene activity - supergene (epigenetic) factors, as well as environmental factors affecting manifestation of psychological characteristics of carriers of different genotypes. In addition to external factors, there are factors of the internal environment that also influence the behavior and psychological characteristics of a person. These include the hormonal background, the level of which is also determined by genetic and environmental influences (most often there are studies in which aggressive behavior is associated with sex hormones, testosterone,^[28] and estradiol).^[29] A complex study of these parameters will create a clearer picture of the studied phenomena. Interesting is also the study of gene-by-stress and gene-by-alcohol interactions. The GWAS genome analysis method is widely used to reveal the data of role of synaptic plasticity and characteristics of neurodevelopment in the prediction of aggressiveness and other psychological characteristics.^[29]

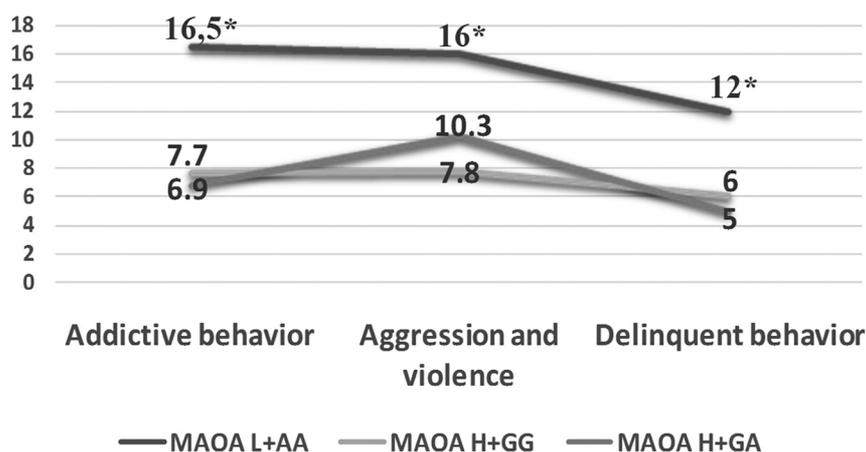


Figure 4: Manifestation of the deviant behavior types in men with several diplotypes in polymorphic loci Val158Met of the COMT gene and -uVNTR of the MAOA gene (*post hoc* Fisher analysis, least significant difference test); Legend: * $P \leq 0.01$.

CONCLUSION

Based on the obtained results, we can conclude that the genetic predictor of high aggressiveness of men is a combination of low-activity genotypes MAOA and COMT. Their presence individually increases the level of various types of aggression: MAOA L is probably more associated with an increase in aggressiveness level as a personality trait, as well as with paranoid, pessimistic, and high levels of legitimate violence. The genotype of COMT AA of men is more associated with the tendency to different forms of deviation. In combination, the described genotypes enhance each other's action.

Personal characteristics of carriers of low-active forms of MAOA and COMT genes, according to the obtained data, are manifested in the presence of destructive nature, which can contribute to the social disadaptation of the represented group of men. Low-active diplotype carriers tend to commit offenses and attempt to solve problems through escape from reality through the use of psychoactive substances or development of non-chemical addictions, as well as the approval of manifestations of aggression and violence in society. The described behavioral strategies can be called "dopamine addiction." To get new unusual impressions and to avoid collisions with a frightening reality, people who have a similar genotype resort to the use of auxiliary means that can raise the level of neurotransmitters and correct the mood background get rid of anxiety and fear.

Due to the relation of the MAOA and COMT genes in the monoamine neurotransmitters (dopamine, serotonin, and norepinephrine) in synaptic space, the reverse acquisition of neurotransmitters of carriers of different diplotypes occurs at different rates, which may affect the duration of the course of emotional reactions and their intensity, and can be associated with stable emotional reactions and state (mood). Carriers of low-active diplotypes have a slower reverse capture of neurotransmitters, which

manifest itself in more prolonged and intense emotional reactions. The described mechanism can explain the high level of aggressiveness, pessimism, and paranoid nature of members of this group.

The presence of highly active alleles of the G gene of COMT and H gene of MAOA gene of men is probably associated with an average, adaptive level of aggressiveness, which may be related to the average duration of how long monoamines are in synaptic space. The presence of H in the diplotype MAOA probably alleviates the predisposition to high aggressiveness embedded in allele A of the COMT gene; the GG genotype in combination with MAOA L probably reduces the level of propensity to aggression inherent in the latter.

Emotional reactions of men with highly active diplotype probably proceed and replace each other more quickly, which may explain the lower level of aggressiveness of members of this group (it is important to take into account that at the physiological level ability to quickly calm down may occur, i.e., replacement of aggressive state with a balanced one).

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