Chapter

Biological Determinants of Hostility

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Abstract

Our aim was to study the association of hostility with the DRD4, DAT, MAOA genes in an open male population of 25–64 years old. A representative sample of men aged 25–64 years (n = 657 men, average age 44.3 ± 0.4 years) was examined in 1994–1995 and 45–64 years old (n = 781 men, average age - 56.48 ± 0.2 years) in 2003–2005 using the methods proposed by the WHO international program "MONICA-psychosocial" and "HAPIEE". All respondents completed the hostility questionnaire on their own. Genotyping of the DRD4, DAT and MAOA gene polymorphisms was carried out. It was established that the level of hostility in the male population was 76.9% in the group of 25–64 years old and 60.3% in the group of 45–64 years old. Genotypes 4/6, 4/7 of the DRD4 gene are reliably associated with a high level of hostility; the genotype 4/4 of the DRD4 gene is associated with an average and lower level of hostility. There was no association of individual genotypes and VNTR alleles of DAT gene polymorphism with different levels of hostility. It was found that among individuals with low-active alleles of the MAOA-L gene (alleles 2 and 3), a high level of hostility was more common - 50.9%. The results of constructing a logistic regression model showed that the presence of low-active alleles (2; 3) of the MAOA gene increases the likelihood of hostility OR = 2.103 (95% CI 1.137–3.889, p = 0.018). Based on the received data we can assume that the long alleles of the DRD4 gene and the low-level allele of the MAOA-L gene are associated with hostility.

Keywords: DRD4 gene, DAT gene, MAOA gene, hostility, open population, men

1. Introduction

Hostility is a personality trait that includes cynicism /distrusting others, anger, overt or repressed aggression [1]. From an evolutionary point of view, hostility contributes to a large number of vital functions, including: achievement of resources, deterrence of rivals, and organization of social hierarchies [2]. It is not surprising that hostile human traits are deeply rooted in its genetic basis considering the relevance of these tasks for offspring survival and development [3]. Under the assumption, numerous studies have confirmed the high heritability of pathological hostility, defined as a set of maladaptive and exaggerated hostile manifestations, such as antisocial and violent behavior [2].

From the standpoint of the psychobiological model of personality Cloninger C.R. antisocial behavior (hostility) is determined by a high 'novelty seeking' [4] and

is due to the genes function of the dopaminergic brain system [5, 6]. The dopamine receptor gene DRD4 is mapped on chromosome 11, in the 11p 15.5 region [7]. The most important role and significance is played by the widespread polymorphism of various numbers of tandem repeats of 48 bp. (VNTR) in exon 3 of the D4 gene. The human dopamine D_4 receptor contains polymorphism within the third cytoplasmic loop of the protein. The polymorphism is characterized by a varying number of direct imperfect 48-bp repeats in the gene. The alleles vary not only in the number of repeats (2–8 or 10 repeat units) but also in the sequence of the repeats [8]. One hypothesis to account for this would be that different size cytoplasmic loops affect the conformation of one or more transmembrane domains, thus altering the ligand binding site. Another possible hypothesis argues that the polymorphism affects signal transduction by altering interactions with G-proteins or other intracellular effectors [8]. It is believed that individuals with longer DRD4 (R7) alleles have higher scores for 'novelty seeking,' however, the attempts to confirm this relationship have yielded conflicting results [9].

The dopamine transporter (DAT), which is encoded by the SLC6A3 gene, mediates the active reuptake of dopamine from the synapse and is a principal regulator of dopaminergic neurotransmission. The SLC6A3 gene contains 15 exons spanning approximately 60 kb, mapped gene to chromosome 5p15.3. Vandenbergh et al. identified a 40-bp variable-number tandem repeat (VNTR) polymorphism in the 3-prime untranslated region of the DAT1 gene with repeat copy numbers ranging from 3 to 11. [10]. As in the case of the DRD4 gene, the DAT gene polymorphism may be associated with some pathological conditions in pathogenesis, which play the main role in dopamine metabolism disorders. However, the results of the study of the association between DAT and 'novelty seeking' are still contradictory [11].

The MAOA gene is located on the short arm of the X chromosome (Xp11.4-p11.23) [12], it encodes the enzyme monoamine oxidase A, this enzyme catalyzes the degradation of key brain neurotransmitters involved in pathological hostility, such as serotonin (5-hydroxytryptamine; 5 -NT) and two catecholamines - norepinephrine and dopamine [13]. In 1998, Sabol and colleagues identified a functional variable number of 30-bp. tandem repeats (MAOA-uVNTR) in the promoter region of human MAOA [14]. This repeat is present in repeats 2, 3, 3.5, 4, 5, or 6 (R), which are associated with different effects on the transcriptional and enzymatic activity of the gene [14]. The most common alleles are 4R and 3R. Alleles with 3.5R or 4R are transcribed more efficiently than alleles with 2R or 3R, and classified as alleles with high activity (MAOA-H) and alleles with low activity (MAOA -L), respectively [15].

The transcriptional efficiency of the 5R allele is controversial in the literature, because it has been classified as a low activity allele [12] and a high activity allele [16]. In a more recent study, it has been shown that the transcriptional activity of MAOA-uVNTR in carriers of alleles 2R and 3R will be lower, and in individuals with alleles 3.5R, 4R, and 5R - higher [17]. There is no functional classification of the 6R allele. Since MAOA is on the X chromosome, males only have one copy, whereas females have two copies; therefore, females can be homozygous or heterozygous. Caspi and colleagues reported on the first study G × E (gene x environment) of aggressive human behavior that showed that exposure to childhood maltreatment predicts later antisocial behavior (ASP) in males with the MAOA –L allele [18]. This innovative finding prompted numerous replication attempts in the following years, with varying results. However, two meta-analyzes, one in 2006 [19] and the other in 2014 [20], have confirmed the initial findings of Caspi et al. [18]. Thus, the aim of our study was to study the association of hostility with the DRD4, DAT, and MAOA genes in an open population of men aged 25–64 years.

2. Materials and methods

A representative sample of men living in the Oktyabrsky district, Novosibirsk city, Russian Federation was examined. The sample of men 25–64 years old (n = 657 men, average age 44.3 ± 0.4 years) in 1994–1995 was examined under the WHO MONICA program (Multinational Monitoring of Trends and Determinants of Cardiovascular Disease) [21]. A sample of men 45–64 years old (n = 781 men, average age 56.48 ± 0.2 years), respectively, was examined within the framework of the IV screening of the international program HAPIEE" (Health, Alcohol and Psychosocial factors In Eastern Europe) [22] in 2003–2005.

All respondents independently completed the hostility questionnaire, which was proposed and tested in the WHO program 'MONICA-psychosocial.' They singled out a high level of hostility (HH), average level of hostility (AH), no hostility (NH), and the respondents also completed the Jenkins Activity Survey (JAS) [21].

Genotyping of the studied polymorphisms of the DRD4, DAT and MAOA genes [23, 24] was carried out according to the published methods in the laboratory of molecular genetic studies (Head is Prof. Maksimov V.N.) Statistical analysis was carried out using the software package SPSS version 11.5. To verify the statistical significance of the differences between the groups, Pearson's Chi-squared test $\chi 2$ was used. To estimate the OR (odds ratio) of disease development by logistic regression, genetic (genotypes and alleles) parameters were used as covariates (factors), hostility was a dependent variable [25, 26]. Reliability in all types of analysis was accepted at a significance level of $p \leq 0.05$.

3. Results

In the male population of 25–64 years of age (III screening) the prevalence of hostility was 76.9% (AH - 19.1%, HH - 32.5%). In the population of 45–64 years of age (IV screening), the prevalence of hostility was 60.3%, AH - 19.7%, and HH - 40.6%. **Table 1** shows the distribution of carriers of various VNTR genotypes of DRD4 gene polymorphism by the level of hostility.

In a comparative aspect, it turned out that carriers of the 4/4 genotype are more often found in the group with an average level of hostility (73.9%): than in the group with a high level of hostility (40.2%) as among carriers of all other genotypes of the DRD4 gene ($\chi 2 = 23.263$ $\upsilon = 1$ $p < 0.0001$), and in comparison with carriers of genotype 2/4 OR = 3 (95% CI 1,1–8); ($\chi 2 = 5.178$ $\upsilon = 1$ $p = 0.023$); than in the group where hostility is completely absent (56%), as in comparison with carriers of all other genotypes of the DRD4 gene OR = 2.2 (95% CI 1.2–4); ($\chi 2 = 6.990$ $\upsilon = 1$ $p < 0.01$), and in comparison with carriers of genotype 2/4 ($\chi 2 = 5.119$ $\upsilon = 1$ $p < 0.05$). Also, carriers of genotype 4/4 were more frequently found in the group with a low level of hostility (64.3%) ($\chi 2 = 13.044$ $\upsilon = 1$ $p < 0.0001$) or hostility was completely absent (56%) ($\chi 2 = 5.515$ $\upsilon = 1$ $p < 0.01$) than in the group with a high level of hostility (40.2%), when compared with carriers of all other genotypes.

On the contrary, carriers of longer alleles of the DRD4 gene - genotype 4/6 more often had a high level of hostility (7.1%): the lower level of hostility (2.7%) in comparison with carriers of the 4/4 genotype ($\chi 2 = 4.866$ $\upsilon = 1$ $p < 0.05$); they had the lack of hostility (1.8%) in comparison with carriers of genotype 2/2 ($\chi 2 = 3.844$ $df = 1$ $p < 0.05$); carriers of the genotype 2/4 gene ($\chi 2 = 4.014$ $\upsilon = 1$ $p = 0.045$); carriers of the 4/4 genotype ($\chi 2 = 5.192$ $\upsilon = 1$ $p < 0.05$). In the group with an average level of hostility there were more carriers of genotype 4/6 (5.4%) than in the group where there was no hostility (1.8%) ($\chi 2 = 4.401$ $\upsilon = 1$ $p = 0.05$), in contrast to carriers genotype 2/4.

Genotype	Hostility							
	No		Low		Average		High	
	n	%	n	%	n	%	n	%
2/2	10	9.2	5	4.5	4	4.3	7	6.6
2/3	0	0	0	0	0	0	1	0.9
2/4	18	16.5	14	12.5	7	7.6	14	12.5
2/5	0	0	1	0.9	0	0	1	0.9
2/6	1	09	4	3.6	1	1.1	4	3.6
2/7	0	0	0	0	0	0	1	0.9
3/3	2	1.8	2	1.8	3	3.3	1	0.9
3/4	8	7.3	6	5.4	4	4.3	6	5.4
3/6	0	0	0	0	0	0	3	2.7
3/7	0	0	0	0	0	0	2	1.8
4/4	61	56	72	64.3*	68	73.9	45	40.2*
4/5	1	0.9	1	0.9	0	0	2	1.8
4/6	2	1.8	3	2.7	5	5.4	8	7.1
4/7	1	0.9	0	0	0	0	8	7.1*
4/8	0	0	0	0	0	0	1	0.9
5/5	2	1.8	1	0.9	0	0	0	0
5/6	1	0.9	0	0	0	0	1	0.9
6/6	2	1.8	3	2.7	0	0	4	3.6
7/7	0	0	0	0	0	0	3	2.7
	$\chi^2 = 88.126$ df = 54 p = 0.002							
allele	n	%	n	%	n	%	n	%
2	39	7.9	29	12.9	16	8.7	35	15.6
3	12	5.5	10	4.5	10	5.4	14	6.3
4	152	69.7	168	75.0	152	82.6	129	57.6
5	6	2.8	4	1.8	0	0	4	1.8
6	8	3.7	13	5.8	6	3.3	24	10.7
7	1	0.5	0	0	0	0	17	7.6
8	0	0	0	0	0	0	1	0.4
	$\chi^2 = 80.293$ df = 18 p = 0.0001							

Table 1.
Frequencies of genotypes and alleles of VNTR polymorphism of the DRD4 gene in the population and the association of their hostility.

Carriers of genotype 4/7 of the DRD4 gene more often belonged to the group with a high level of hostility (7.1%) than to the group where there was no hostility (0.9%), in comparison: carriers of all other genotypes of the DRD4 gene OR = 8, 3 (95% CI 1.02–67.5); ($\chi 2 = 5.480$ $\upsilon = 1$ $p < 0.01$); carriers of genotype 2/2 ($\chi 2 = 5.488$ $\upsilon = 1$ $p < 0.01$); carriers of genotype 2/4 ($\chi 2 = 5.756$ $\upsilon = 1$ $p < 0.01$); carriers of genotype 3/3 ($\chi 2 = 3.704$ $\upsilon = 1$ $p < 0.05$); carriers of genotype 3/4 ($\chi 2 = 4.874$ $\upsilon = 1$ $p < 0.05$); carriers of the genotype 4/4 ($\chi 2 = 7.199$ $\upsilon = 1$ $p < 0.001$).

More often, there was no hostility in carriers of genotype 2/2 (9.2%), genotype 2/4 (16.5%), genotype 3/4 (7.3%). Carriers of genotype 2/6 and genotype 6/6 of the DRD4 gene had equally common a high level of hostility - 3.6% each. Carriers of genotype 3/3 of the DRD4 gene more often had an average level of hostility - 3.3%. Carriage of other genotypes of the DRD4 gene in men, differing in the level of hostility, did not exceed 3% ($\chi2 = 88.126$ $\upsilon = 54$ $p < 0.01$).

The distribution of hostility levels among carriers of alleles of the DRD4 gene ($\chi2 = 80.293$ $\upsilon = 18$ $p < 0.0001$) is presented in **Table 1**. Allele 4 of the DRD4 gene was more common in the group with an average level of hostility (82.6%): than in the group with high the level of hostility (57.6%) both among carriers of all other alleles ($\chi2 = 29.496$ $\upsilon = 1$ $p < 0.0001$), and in comparison with carriers of allele 2 OR = 2.5 (95% CI 1.3–4,8); ($\chi2 = 8.914$ $\upsilon = 1$ $p < 0.01$); in the group with a complete absence of hostility (69.7%) as among carriers of all other alleles of the DRD4 gene OR = 2 (95% CI 1.2–3.3); ($\chi2 = 8.985$ $\upsilon = 1$ $p < 0.01$), and among carriers of allele 2 ($\chi2 = 8.178$ $\upsilon = 1$ $p < 0.01$).

Carriers of allele 4 also were more often in the group either with a low level of hostility (75%) ($\chi2 = 15{,}194$ $\upsilon = 1$ $p < 0.0001$) or in the group where there was no hostility at all (69.7%) ($\chi2 = 7.026$ $\upsilon = 1$ $p < 0.01$) than in the group with a high level of hostility (57.6%) in comparison with carriers of all other alleles. Carriers of the "short" allele 2 were more common in the group where there was no hostility (17.6%) than in the group with an average level of hostility (8.7%) in comparison

Genotype	**Hostility**							
	No		**Low**		**Average**		**High**	
	n	**%**	**n**	**%**	**n**	**%**	**n**	**%**
8/8	1	1	2	1.9	0	0	1	0.9
9/9	4	4	4	3.8	3	3.5	4	3.4
6/10	1	1	1	1.0	1	1.2	0	0
8/10	1	1	0	0	0	0	0	0
9/10	31	31	37	35.6	37	43	44	37.6
10/10	60	60	55	52.9	45	52.3	63	53.8
10/11	0	0	3	2.9	0	0	1	0.9
10/12	0	0	0	0	0	0	1	0.9
11/11	2	2	2	1.9	0	0	3	2.6
	$\chi^2 = 18.930$ $\upsilon = 24$ $p = 0.756$							
allele	n	%	n	%	n	%	n	%
6	1	0.5	1	0.5	1	0.6	0	0
8	3	1.5	4	1.9	0	0	2	0.9
9	39	19.5	45	21.6	43	25	52	22.2
10	153	76.5	151	72.6	128	74.4	172	73.5
11	4	2	7	3.4	0	0	7	3
12	4	2	7	3.4	0	0	7	3
	$\chi^2 = 14.553$ $\upsilon = 15$ $p = 0.484$							

Table 2.
Frequencies of genotypes and alleles VNTR of DAT gene polymorphism in the population and their association with psychosocial factors.

with carriers of all alleles ($\chi 2 = 7.142$ υ = 1 p < 0, 01). Carriers of the "long" allele 6 were more common in the group with a high level of hostility (10.7%): than in the group with an average level of hostility (3.3%) as compared with carriers of all other alleles OR = 3.5 (95% CI 1.4–8.9); ($\chi 2 = 8.238$ υ = 1 p < 0.01), and in comparison with carriers of allele 4 ($\chi 2 = 12.605$ υ = 1 p < 0.0001); than in the group where there was no hostility among the carriers of all alleles ($\chi 2 = 8{,}164$ υ = 1 p < 0.01); and compared with the group with a low level of hostility (3.7%) ($\chi^2 = 6.087$ υ = 1 p < 0.01) in comparison with carriers of allele 4. Carriers of allele 7 more often fell into the group with a high level of hostility (7.6%) than in the group where there was no hostility (0.5%) OR = 17 (95% CI 2.3–135); ($\chi^2 = 14.379$ υ = 1 p < 0.0001), in a comparative aspect with carriers of all other alleles of the DRD4 gene.

No associative relationship was found during the comparative analysis of individual genotypes and alleles of the DAT gene with different levels of hostility (**Table 2**).

The results of molecular genetic analysis of the various alleles distribution of the MAOA gene in the male population of 45–64 years old are presented in **Table 3**. Highly active alleles (3.5 and 4) were found in 4.5% and 57.1% of men, respectively; alleles with low activity were distributed as follows: allele 3 - in 37.2%, alleles 2 and 5 - in 0.6%.

We found out that in the frequency distribution of the MAOA gene alleles in men differing in the level of hostility individuals with highly active alleles of the MAOA-H gene did not have hostility - 72.1%, and in men with low-active alleles of the MAOA-L gene, a high level of hostility was more common - 50.9% ($\chi 2 = 7.026$ df = 2, p = 0.03) (**Table 4**).

gene MAOA		
allele	**n**	%
2	1	0.6
3	58	37.2
3.5	7	4.5
4	89	57.1
5	1	0.6
Total	156	100.0

Table 3.
MAOA gene allele frequencies in a 45–64-year-old male population.

	Hostility					
gene MAOA	**NO**		**Average**		**High**	
	n	**%**	**n**	**%**	**n**	**%**
MAOA-H (allele 3.5; 4; 5)	49	72.1	20	64.5	28	49.1
MAOA-L (allele 2; 3)	19	27.9	11	35.5	29	50.9
total	68	100	31	100	57	100
	$\chi^2 = 7.026$ df = 2. p = 0.03					

Table 4.
MAOA gene allele frequencies in an open population of males 46–64 years of age compared to hostility levels.

Question relation	gene MAOA	Agree		Disagree	
		n	%	n	%
people often disappoint me	MAOA-H (allele 3.5; 4; 5)	47	54.7	50	71.4
	MAOA-L (allele 2; 3)	39	45.3	20	28.6
	χ^2 = 3.933 df = 1. p = 0.047				
I think most people have to lie to "*going to be just fine*."	MAOA-H (allele 3.5; 4; 5)	23	41.8	74	73.3
	MAOA-L (allele 2; 3)	32	58.2	27	26.7
	χ^2 = 13.669 df = 1. p = 0.0001				
I often felt that strangers look at me critically	MAOA-H (allele 3.5; 4; 5)	14	41.2	83	68
	MAOA-L (аллель 2; 3)	20	58.8	39	32
	χ^2 = 7.053 df = 1. p = 0.008				
I often find that people are jealous of my good thoughts because they did not think about it first	MAOA-H (allele 3.5; 4; 5)	35	48.6	62	73.8
	MAOA-L (allele 2; 3)	37	51.4	22	26.2
	χ^2 = 9.424 df = 1. p = 0.002				

Table 5.
MAOA gene allele frequencies in an open population of men 25–64 years old compared to a different pattern of hostile behavior.

The analysis of the pattern of hostile behavior showed that individuals with low MAOA-L alleles were more likely to agree with the statement that 'people often disappoint them', as well as with the maxim 'I think most people have to lie to '*going to be just fine*' and' I often felt that strangers look at me critically', and 'people are jealous of my good thoughts because they did not think about it first' than carriers of the highly active MAOA-H gene (**Table 5**).

The results of a comparative analysis of the behavioral activity of men differing in the presence of low- or high-active alleles of the MAOA gene in the genotype are shown in **Table 6**. Most people with low MAOA-L alleles in their youth were considered 'definitely assertive and competitive' (53.3%) than men with MAOA-H alleles (46.7%) (χ2 = 10.080 df = 3, p = 0.023).

The results of building a logistic regression model showed that the presence of low-active alleles (2; 3) increases the chance of hostility OR = 2.103 (95% CI 1.137–3.889, p = 0.018) (**Table 7**).

When you were younger. Did most people consider:	Definitely assertive and competitive		Possibly assertive and competitive		Perhaps more relaxed and carefree		Definitely more relaxed and carefree	
gene MAOA	n	%	n	%	n	%	n	%
MAOA-H (allele 3.5; 4; 5)	21	46.7	31	72.1	30	75	15	53.6
MAOA-L (allele 2; 3)	24	53.3	12	27.9	10	25	13	46.4
χ^2 = 10.080 df = 3. p = 0.023								

Table 6.
MAOA gene allele frequencies in an open population of men 46–64 years old compared with the type of behavioral activity Jenkins Activity Survey (JAS).

Variable	B	SE	Wald (χ^2)	df	p	OR	95% CI for OR	
							lower	upper
MAOA-L (allele 2; 3)	0.743	0.314	5.618	1	0.018	2.103	1.137	3.889

Table 7.
Likelihood of hostility in men with MAOA-L (logistic regression model).

4. Discussion

The studied population of men aged 25–64 can be characterized as highly hostile - almost two-thirds of individuals experienced hostility of varying degrees, which served as a prerequisite for the search for its primary source. One of the most interesting lines of research on human behavior is genetic research. According to the work of various authors, it has been established that some mental and emotional characteristics of a person are associated with polymorphism of exon 3 of the gene for the neurotransmitter system of the dopamine receptor 4-subtype (DRD4) [5, 6]. The studies show that genotypes with different tandem repeat number (VNTR) polymorphism in the DRD4 gene cause differences in the biological function of the dopamine receptor encoded by this gene. The most common alleles for this VNTR are alleles with 2, 4, or 7 copies of the repetitive DNA. Today, the 7-repeat allele (long allele) is known to function differently from the other two shorter alleles. Three functional domains seem to be altered by the status of the VNTR genotype: (1) the ability of the receptor to transmit signaling information [27]; (2) the level of mRNA transcribed from this gene [28]; and (3) protein–protein interactions with the DRD2 receptor [29]. The role of these functional differences in explaining the association of the DRD4 gene with behavioral traits, including the pursuit of novelty [30] and ADHD (hyperactivity syndrome) [31], is not yet clear. It is possible that one or all of these biological differences affect the brain's ability to respond to dopamine, which plays a significant role in 'reward' and motivated actions [32]. Thus, one of the possible reasons for the higher frequency of 'long' allelic variants of the DRD4 gene in our population among men with high levels of hostility is that the system of neurons using dopamine as a neurotransmitter is associated with the provision of reinforcement or 'reward'. It is with the 'long allelic variant' of the DRD4 gene that the lower sensitivity of the receptor to dopamine is associated. Those with both chromosomes containing 'long' alleles (encoding a less sensitive receptor) need stronger external signals in order to feel comfortable. These people need large doses of dopamine for the receptors to respond to it [33]. Probably hostility in men with a 'long' allelic variant of the DRD4 gene is one of the manifestations of the 'novelty seeking'.

On the other hand, the results of many studies GxE (gene x environment) are often interpreted as evidence of biologically based differences in environmental sensitivities. The theoretical works by Belsky 2009, Ellis 2008, 2011 and others [34–37] claim that these results reflect evolutionarily selected adaptive individual differences in environmental susceptibility (ie, differential susceptibility theory) [35, 37]. Differential susceptibility theory states that people who are more sensitive to adverse environmental conditions and who are at a higher risk of negative outcomes in these conditions may also benefit more from exposure to a favorable environment. Differential susceptibility theory is often contrasted with stress and later models of beneficial sensitivity [38], which postulate vulnerability exclusively to negative and positive environments, respectively. It is possible that DRD4 7

repeat genotypes will be associated with differences in environmental sensitivity based on this prior literature.

The process of dopamine uptake by neurons plays an important role in dopamine metabolism which is an active transmembrane transport using a dopamine transporter. At the same time, the reuptake of the mediator is important not only for the rapid completion of the action on the target organ; it also prevents the depletion of presynaptic dopamine stores during rhythmic activity. Therefore, the study of the dopamine transporter gene (DAT), localized on chromosome 5 (5p15.3), is of greater interest to researchers in connection with pathological changes in mental activity [39]. In our work, we did not obtain an associative relationship between individual genotypes and alleles of the DAT gene with different levels of hostility, which does not exclude the possibility of searching for possible associations in a larger sample in the future.

While other genes involved in the pathways of neurotransmission of monoamines are associated with antisocial behavior [40], the unique reputation of the MAOA gene lies in a large number of independent studies confirming its role in aggressive behavior [41], which served as the premise of our study. Most of the clinical data on the relationship between MAOA and hostile behavior patterns comes from genetic studies of numerous polymorphic variants of this gene [12]. The richest source of data on the functional role of MAOA in hostility is the original variable number tandem repeat polymorphism (uVNTR), which contains alleles with different repeats (2, 3, 3.5, 4, 5, and 6) [14]. According to the researchers, the two most common alleles of uVNTR, containing 3 and 4 repeats, are present in 35–39% and 59–63% of Caucasians, respectively; conversely, variants with 3 repeats are more often present in most African (52–59%), Asian (53–61%), and Latin American (70%) populations [42]. In our population the allele with 4 repeats - in 57.1% of men and with 3 repeats - in 37.2% appeared to be the most represented which is consistent with the world data covering Caucasoid samples [42]. The 2R and 3R alleles produce non-significantly different levels of transcription, but both demonstrate significantly less transcription that the 3.5R, 4R, and 5R alleles [17].

Some studies have shown the association between repeat 2 and 3 alleles with multiple aspects of aggression, including hostility and antisocial behavior [2]. The first meta-analysis of interactions between MAOA-uVNTR and childhood maltreatment and future antisocial behavior was published by Kim-Cohen et al. [19]. This meta-analysis showed that the association between child abuse and mental health problems, including antisocial behavior (ASD), symptoms of attention deficit hyperactivity disorder (ADHD), and emotional problems, was stronger in males with MAOA-L [19]. A second meta-analysis was published by Byrd and Manuck in 2014 and included 27 original papers that investigated the interaction between MAOA-uVNTR and childhood maltreatment of ASD (2014). This meta-analysis confirmed the association between MAOA and a higher likelihood of ASD among MAOA-L male carriers who were abused during childhood [20]. Lavigne JV et al. emphasized the importance of expanding the spectrum of psychosocial risk factors included in the G × E studies to provide more specific models of various phenotypes, including those with impulsive and hostile behavior [41].

In our population, men with low-active alleles of the MAOA-L gene more often had a high level of hostility - 48.2%, which is consistent with the world data. The results of building a logistic regression model showed that the presence of low-active alleles (2; 3) increases the risk of hostility by 2.103 times. In addition, a hostile pattern of behavior manifested itself in interpersonal relationships with other people, so people with low-level MAOA-L alleles more often believed that 'people disappoint them more often,' suspected people of lying, especially if it was associated with career growth, more often felt critical views of other people on

themselves, believed that others were jealous of them. Also, individuals with low MAOA-L alleles were more often considered by people to be 'definitely assertive and competitive.'

Our results highlight another interesting aspect of the study of psychological phenotypes associated with various MAOA uVNTR alleles, including specific aggression subtypes. Numerous studies have shown that low-activity options are associated with active rather than latent aggression. For example, carriers of alleles with 3 repeats are more inclined to a greater propensity to participate in hostile responses against provocations of alleged opponents and competitors [43]. Our data on the relationship of some polymorphic variants of the DRD4 and MAOA genes with hostility may determine future directions of research on the molecular basis of hostility and help in determining diagnostic markers and therapeutic goals of this condition.

5. Conclusion

The prevalence of hostility among men was 25–64 (76.9% of them had a high level of 32.5%), 45–64 years old was 60.3% (40.6% had a high level). Among men aged 25–64 years of the megalopolis of Western Siberia,the Russian Federation, the most common polymorphism of the DRD4 gene is: genotype 4/4 (57.9%); DAT gene: genotype 10/10 (54.8%). Genotypes 4/6, 4/7 of the DRD4 gene, alleles 6 and 7, respectively, were significantly associated with a high level of hostility. There was no association of individual genotypes and alleles of the DAT gene with different levels of hostility. Highly active alleles of the MAOA gene (3.5 and 4) were found among men 45–64 years old in 4.5% and 57.1%, respectively; alleles with low activity were distributed as follows: allele 3 - in 37.2%, alleles 2 and 5 - in 0.6%. Among men 45–64 years old with highly active alleles of the MAOA-H gene, hostility was more often absent (72.1%), and with low-active alleles of the MAOA-L gene, a high level of hostility was more common (50.9%). The presence of low-active alleles of the MAOA-L gene (2; 3) statistically increases the likelihood of hostility, OR = 2.103.

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