Проблемы здоровья и экологии/Health and Ecology Issues 2021;18(3):23–32

УДК 616.89-008.441.44:616.89-008.444.9]-056.7-078.088.7
DOI: https://doi.org/10.51523/2708-6011.2021-18-3-3

Genetic control of the predisposition to suicide and aggressive behavior

S. A. Kostiuk[1], S. V. Davidouskij[1], D. D. Kostiuk[2], O. S. Poluyan[1]
[1]*Belarusian Medical Academy of Postgraduate Education, Minsk, Belarus*
[2] *Wrocław State University, Institute of Psychology, Wrocław, Poland*

ABSTRACT

It has been established recently that both genes and the environment contribute to the risk of suicide. In this case, a combination of genes predisposing to certain qualities is of paramount importance. In the article, the authors provide an analytical review of literature devoted to the study of the genetic aspects of suicidality.

Keywords: *suicide, gene polymorphism, dopamine, serotonin.*
Author contributions. Kostiuk S.A., Davidouskij S.V., Kostiuk D.D., Poluyan O.S.: reviewing publications on the topic of the article, checking critical content, editing, discussing data, approving the manuscript for publication.
Conflict of interests. The authors declare no conflict of interest.
Funding. The study was conducted without sponsorship.
For citation: Kostiuk SA, Davidouskij SV, Kostiuk DD, Poluyan OS. Genetic control of the predisposition to suicide and aggressive behavior. *Health and Ecology Issues*. 2021;18(3):23–32. (In Russ.). DOI: https://doi.org/10.51523/2708-6011.2021-18-3-00

Генетический контроль предрасположенности к суициду и агрессивному поведению

С. А. Костюк[1], С. В. Давидовский[1], Д. Д. Костюк[2], О. С. Полуян[1]
[1]*Белорусская медицинская академия последипломного образования, г. Минск, Беларусь*
[2]*Вроцлавский государственный университет, Институт психологии, г. Вроцлав, Польша*

РЕЗЮМЕ

В настоящее время установлено, что в риск совершения самоубийства вносят свой вклад как гены, так и общая среда. При этом носительство сочетания генов, предрасполагающего к определенным качествам, имеет первостепенное значение. В статье авторами приведен аналитический обзор литературы, посвященный изучению генетических аспектов суицидальности.

Ключевые слова*: суицид, полиморфизм генов, дофамин, серотонин.*
Вклад авторов. Костюк С.А., Давидовский С.В., Костюк Д.Д., Полуян О.С.: обзор публикаций по теме статьи, проверка критически важного содержания, редактирование, обсуждение данных, утверждение рукописи для публикации.
Конфликт интересов. Авторы заявляют об отсутствии конфликта интересов.
Источники финансирования. Исследование проведено без спонсорской поддержки.
Для цитирования: Костюк СА, Давидовский СВ, Костюк ДД, Полуян ОС. Генетический контроль предрасположенности к суициду и агрессивному поведению. *Проблемы здоровья и экологии*. 2021;18(3):23–32. DOI: https://doi.org/10.51523/2708-6011.2021-18-3-00

Suicide is an extreme form of aggressive behavior individuals direct at themselves. According to the World Health Organization (WHO), up to one million people commit suicides every year, and their number steadily increases every year.

According to literary data, the overwhelming majority of suicide attempts are committed by people in a state of severe depression caused by various sorts of stressful situations. At the same time, judging by the results of twin anal-

2021;18(3):23–32 Проблемы здоровья и экологии/Health and Ecology Issues

ysis, the probability of a suicide depends on the genotype at a rate of 30-60%. These data attest to the fact that the cause of suicides is most likely the combination of two factors: firstly, the genetically controlled predisposition to suicide; secondly, the conditions contributing to the manifestation of the genetic predisposition to suicide, i.e. stressful situations, severe experiences, etc. [1, 2, 3, 4].

Traditionally, the research is carried out according to the following scheme: either suicides (more precisely – their posthumous DNA samples) or people who have attempted a suicide are used as the subjects. At the same time, when selecting specific subjects, researchers try to ensure that they are as homogeneous as possible with respect to other factors that can provoke a suicide. For example, only schizophrenics or people suffering from severe forms of depression are selected. Patients with the same diagnoses who have never attempted suicide or otherwise mentally sane individuals are selected as control ones [2, 3, 4, 5].

At present, it is the understanding that the human serotonin regulatory system in humans is involved in the control of aggression. The results of clinical studies indicate that low levels of 5-hydroxyindoleacetic acid (the main serotonin derivative in the cerebrospinal fluid) correlate with the propensity for aggression and, in particular, suicide [2, 3, 4, 6].

Therefore, the genes that ensure the functioning of the serotonin system are among the most likely candidates as genetic controls of the predisposition to suicide. Undoubtedly, the number of these genes is quite large, but the main focus is on the seven of them — TPH*1,* TPH*2, SLC6*A*4,* HT*R1*A, HT*R1*B, HT*R2*A and MAOA, which control the key serotonin biosynthesis phases, serotonin re-importation into the cell, its reception and degradation [1, 2, 3, 4, 6, 7].

Serotonin is known to be synthesized in all mammals from tryptophan, one of 20 amino acid variants. This process consists of two consecutive stages (Figure 1). The former is provided by hydroxylase, a highly substrate-specific enzyme involved exclusively in serotonin biosynthesis. The latter is served by aromatic amino acid decarboxylase. This enzyme has a wide substrate specificity and is included in many molecular processes involving tryptophan, phenylalanine, and tyrosine derivatives. It has been shown that the former stage is the limiting one: it determines the amount of serotonin synthesized in an individual. Therefore, in genetic studies of the predisposition to suicide, the focus is on tryptophan hydroxylase.

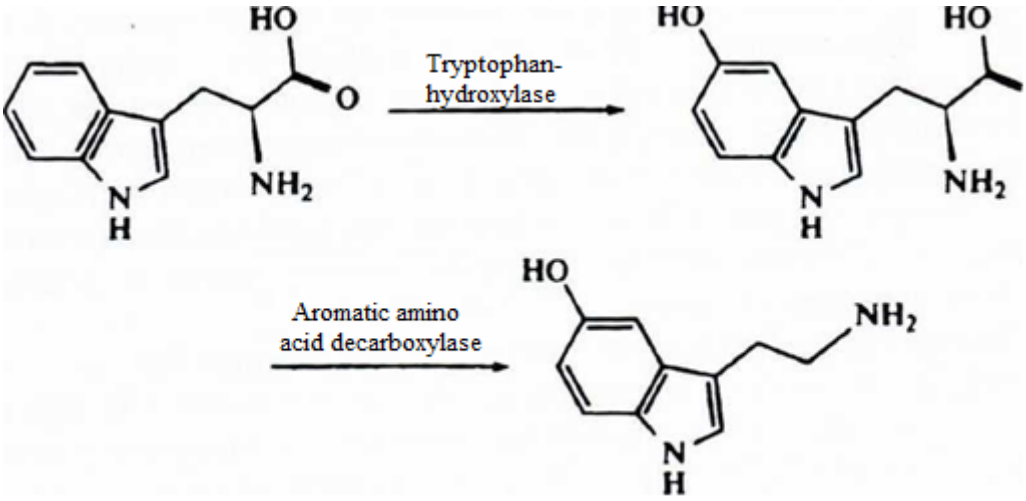

Figure 1 – Serotonin biosynthesis

This enzyme is represented in humans by two isoforms that differ significantly in their tissue specificity. One isoform encoded by the TRH1 gene functions primarily in the walls of the duodenum, as well as in the liver, heart, lungs, kidneys and adrenal glands. It can also be found in some parts of the brain, but in much lower concentrations. Meanwhile, the second isoform of tryptophan hydroxylase, which is encoded by the TRH2 gene, is unique only to brain neurons [6, 8].

The *TRH1* gene exists as a set of alleles that differ from each other by substitutions of individual nucleotides. Such substitutions

Проблемы здоровья и экологии/Health and Ecology Issues **2021;18(3):23–32**

have been found in about 200 positions, mainly in the promoter region or introns. The studies of the genetics of suicidal behavior have so far used 11 of these positions.

The first obtained results indicate that the 218A and 779C substitutions, which are localized within the seventh intron, are closely associated with the propensity for suicidal behavior. This conclusion was also corroborated in some subsequent studies. However, the vast majority of the conducted research studies have failed to detect the sought-for association [9].

The meta-analysis does not provide definitive clarity, either. For example, the analysis of 17 independent studies found no association with any of the listed substitutions. Meanwhile, three other, more rigorous, analyses showed a weak statistically significant association between the predisposition to suicide and the 218A substitution. This nucleotide substitution occurs slightly more frequently in suicidal individuals than in control groups. However, the detected difference is relatively small and is statistically confirmed only for very large samples. Therefore, none of the studied nucleotide substitutions has a pronounced influence on the predisposition to suicide [2, 3, 4].

The *TRH2* gene has been discovered in humans comparatively recently. It is characterized by a high degree of polymorphism: to date, more than 900 positions with substitutions of single nucleotides are known. Approximately 30 sites are involved in the genetic analysis of the human predisposition to suicide. Judging by available scientific data, suicidal behavior is associated with the 519T, 2058G, 40237G, and 59665C substitutions [3]. However, there is still no independent scientific evidence, so this conclusion should be regarded only as tentative.

Serotonin is one of the most important neurotransmitters. Corresponding synapses are found in the central nervous system: mainly in the amygdala, raphe nuclei, hippocampus, hypothalamus, striatum and frontal lobes of the cerebral cortex, as well as in the digestive tract and some other peripheral organs. Depending on their specific localization, they regulate various aspects of the vital bodily functions: sleep, hunger, thirst, body temperature, sexual behavior, general mood and anxiety. The last two aspects are closely connected with suicidal tendencies. However, unfortunately, it is not yet known which synapses are directly involved in suicidal behavior control [3, 4].

The molecules of serotonin entering the synaptic cleft are rapidly re-imported to the presynaptic terminal. This process is ensured by a special membrane protein called "serotonin transporter", which is a product of the *SLC6A4* gene. More than 500 nucleotide substitutions have been found in this gene, as well as two sites varying in their lengths:

• A 44-nucleotide sequence in the promoter, approximately 1,000 nucleotide pairs before the start of transcription. This sequence can be either present or absent, leading to the existence of two promoter variants: long and short (L and S, respectively);

•17-nucleotide repeats in intron 2; there may be 9, 10, or 12 of them.

• As of today, the following polymorphism is used in the molecular genetic analysis of the predisposition to suicidal behavior:

• L- and S-promoter variants. It has been shown that the S-promoter is less efficient: it causes a reduced level of gene transcription. As a result, due to the lack of serotonin transporter, the corresponding synapses must be cleared insufficiently. In turn, it would seem that this should lead to a significant increase in the activity of the serotonin system, but in reality the opposite is observed: the S-promoter reduces the activity of the serotonin system. The reason for this phenomenon currently remains unknown;

• nucleotide polymorphism at position -179. It is interesting because the -179G substitution disrupts an important part of the promoter region and also leads to weakened gene transcription;

• the number of repeats in intron 2. It has been shown that alleles containing 12 repeats are transcribed more efficiently than others [3, 4, 6, 7, 8].

The most studies is the polymorphism of the promoter region size. The following regularity is clearly observed: S-promoter increases the probability of "hard" suicides — those involving the use of various weapons, self-immolation, hanging, jumps from height, etc. Meanwhile, for relatively "soft" forms of suicide — slashing wrists or taking lethal doses of sleeping pills — none of the studies have found a reliable relationship.

Therefore, the propensity for "hard" or "soft" suicide scenarios should be considered as two independent behavioral characteristics, which is convincingly confirmed by meta-analysis [2, 3, 4, 6] (see Table 1). At the same time, if all types of suicide are considered together, it is usually impossible to detect the influence of S-promoter. The results of meta-analysis for summarized data of 18 independent studies testify to the same. This association may really exist, but it is extremely weak and is only significant in samples of many thousands.

2021;18(3):23–32 Проблемы здоровья и экологии/Health and Ecology Issues

Table 1. Meta-analysis of the association between the S-promoter of the SLC6A4 gene and various forms of suicidal behavior (SB)

Analyzed samples		Result of analysis
Suicidal behavior	Control	
Frequency of the S-promoter variant in the analyzed samples		
Patients with "hard" forms of SB	Mentally sane people	Weak association (p = 0.0396)
Patients with "soft" forms of SB	Mentally sane people	No association (p = 0.7558)
Patients with "hard" forms of SB	Patients with no suicidal experience	Strong association (p = 0.0009)
Patients with "soft" forms of SB	Patients with no suicidal experience	No association (p = 0.4901)
Frequency of SS+SL detection in the analyzed samples		
Patients with "hard" forms of SB	Mentally sane people + Patients with no suicidal experience	Strong association (p < 0.0001). Predisposition to "hard" forms of suicide in an individual is closely associated with the presence of at least one copy of the SLC6A4 gene with a short form of the promoter in their genotype. This promoter variant manifests itself as dominant.
Patients with "soft" forms of SB	Mentally sane people + Patients with no suicidal experience	No association (p=0.7897)

What is the difference between "hard" and "soft" forms of suicide? In the former case, an individual wishes to die immediately, whereas in the latter, an individual plans to die in the near future and knows that their death can be prevented as a result of timely medical intervention. Therefore, people who opt for "soft" suicide are less determined to die as compared to people who go for "hard" suicide forms. The S-promoter is closely associated not only with the "hard" form, but also with some other forms of suicidal behavior. In particular, it has been shown to be associated with repeated attempts, as well as with attempts resulting in severe consequences. Suicidal behavior associated with the S-promoter is thus realized much more intensively than that associated with the full-size variant.

Judging by the results of four independent studies, nucleotide polymorphism at position -179 has no significant influence on the predisposition to suicide. The situation with repeats in intron 2 is not so unambiguous. According to some data, alleles with 10 repeats are rather closely associated with the tendency to suicide. However, no such association has been found by most studies. Nor is it detected as a result of meta-analysis. Therefore, it is currently accepted that this polymorphism is not associated with the predisposition to suicide [2, 3, 4].

The role of the *MAOA* gene controlling serotonin degradation is of a scientific interest. It is common knowledge that a significant portion of serotonin re-imported from the synapse undergoes rapid degradation at the presynaptic terminal. This process is jointly provided by several enzymes, the most important of which is monoamine oxidase. This enzyme is involved in the degradation not only of serotonin, but also of a number of other biological amines, including dopamine, adrenaline and noradrenaline. Therefore, it can play a very important role in the regulation of the activity of many synaptic contacts and thereby influence various forms of behavior [2].

In humans, monoamine oxidase is represented by two highly homologous isoforms (A and B), which are products of the *MAOA* and MAOB genes. Both function in the neurons of the brain, mainly in the frontal lobes of the cerebral cortex, hippocampus, amygdala, hypothalamus, and some others. However, despite the similarity of both the isoforms, so far only one of them, namely monoamine oxidase A, has received the main attention [10].

More than 800 nucleotide substitutions have been found in the corresponding gene, as well as three sites varying in their lengths:

- 30-nucleotide repeats in the promoter, approximately 1,200 base pairs before the start of transcription. They occur in three, three-and-a-half, four, or five copies;
- 23-nucleotide repeats in intron 1;
- $(CA)_n$ repeats in intron 2.

Four polymorphic sites in the *MAOA* gene are currently involved in the molecular genetic analysis of the predisposition to suicide:

- 30-nucleotide repeats in the promoter region. It is known that alleles with three and

Проблемы здоровья и экологии/Health and Ecology Issues **2021;18(3):23–32**

a half or four repeats are transcribed several times more intensively than the others and precondition increased levels of monoamine oxidase A, hence more efficient degradation of serotonin, which should lead to increased aggression;

• $(CA)_n$ repeats in intron 2;

• T/G nucleotide substitutions at position 941 (exon 8). It has been shown that the presence of guanine at this position contribute to a significant increase in enzyme strength;

• C/T nucleotide substitutions at position 1460 (exon 14). These substitutions also affect enzyme strength: in the presence of thymine, it increases several times.

Judging by the results of most of the studies, polymorphism at these sites is not associated with the propensity for suicide. However, an association has been found in two studies. In one, with the predisposition to "hard" forms of suicide (three and a half and four copies of repeats in the promoter are associated); in the other, with the propensity for suicide only in men (nucleotide substitution 1460T association). Therefore, it is quite likely that the other studies could not detect the effect of the *MAOA* gene because of insufficiently fractional analysis of the feature.

In humans, 14 types of serotonin receptors have been described, each of which is encoded by a different gene (see Table 2). Some of them are located on postsynaptic membranes and ensure the perception of transmitted nerve impulses, and some, on the contrary, have presynaptic localization and regulate the amount of released neurotransmitter. Depending on a specific type of receptors, their activation can either excite or, on the contrary, inhibit the next cell.

Table 2. Basic characteristics of serotonin receptors in humans

<table>
<tr><th>Receptor type</th><th>Principle</th><th>Activation result</th><th>Main localization</th><th>Controlled processes</th><th>Gene</th></tr>
<tr><td>1A</td><td rowspan="6">G-protein-coupled receptors. The secondary messenger is cAMP. Its content is reduced by phosphodiesterase stimulation.</td><td>Postsynaptic inhibition</td><td rowspan="8">CNS</td><td>Sleep, satiation, thermoregulation, anxiety</td><td>HTR1A</td></tr>
<tr><td>1B</td><td rowspan="2">Presynaptic inhibition</td><td>Blood pressure</td><td>HTR1B</td></tr>
<tr><td>1D-α</td><td rowspan="2">Motor activity, blood pressure</td><td>HTRDaA</td></tr>
<tr><td>1D-β</td><td>HTR1Db</td></tr>
<tr><td>1E</td><td rowspan="2">Unknown</td><td rowspan="2">Unknown</td><td>HTR1E</td></tr>
<tr><td>1F</td><td>HTR1F</td></tr>
<tr><td>2A</td><td rowspan="3">G-protein-coupled receptors. Secondary messengers are inositol-3-phosphate and diacylglycerol. Their content is increased by phospholipase stimulation.</td><td>Postsynaptic excitation</td><td>Training, blood pressure, smooth muscle contractions</td><td>HTR2A</td></tr>
<tr><td>2B</td><td rowspan="3">Unknown</td><td>Stomach</td><td>Stomach contractions</td><td>HTR2B</td></tr>
<tr><td>2C</td><td>CNS</td><td>Excretion of cerebrospinal fluid</td><td>HTR2C</td></tr>
<tr><td>3</td><td>Serotonin-dependent Na+ and K+ channels. Receptor activation depolarizes the membrane</td><td>CNS, PNS</td><td>Anxiety, vomiting</td><td>HTR3</td></tr>
<tr><td>4</td><td>G-protein-coupled receptor. The secondary messenger is cAMP. Its content increases by adenylate cyclase stimulation.</td><td>Postsynaptic excitation</td><td>CNS, heart, digestive tract</td><td>Digestive tract contractions</td><td>HTR4</td></tr>
<tr><td>5A</td><td>G-protein-coupled receptor. The secondary messenger is cAMP. Its content is reduced by phosphodiesterase stimulation.</td><td rowspan="3">Unknown</td><td>CNS</td><td rowspan="3">Unknown</td><td>HTR5A</td></tr>
<tr><td>6</td><td rowspan="2">G-protein-coupled receptor. The secondary messenger is cAMP. Its content is increased by adenylate cyclase stimulation</td><td>CNS</td><td>HTR6</td></tr>
<tr><td>7</td><td>CNS, digestive tract</td><td>HTR7</td></tr>
</table>

Studies focusing on the predisposition to suicidal behavior have shown the involvement of nine genes: HT*R1*A, HT*R1*B, HT*R1Da,* HT*R1*E, HT*R1F,* HT*R2*A, HT*R2*C, HT*R5*A and HT*R6* [7, 11, 12, 13]. For most of them, sporadic studies using only one or two nucleotide substitutions are available. This is the case for the genes HT*R1Da,* HT*R1F,* HT*R1E,* HT*R2*C, HT*R5*A and HT*R6*. No association with the predisposition to suicide was detected for them.

The *HTR1A, HTR1B,* HT*R2*A genes were studied in somewhat more detail. Three nucleotide substitutions were analyzed in the first one, one of which (-1019G) is quite closely associated with the propensity for suicide. However, as long as there is no independent corroboration, these data should be viewed as preliminary. Three substitutions in the HTR1B gene were also investigated, but none of them has any effect on suicidal behavior. The most attention is given to the HTR2A gene: seven nucleotide substitutions were analyzed, with two of them, located in the promoter (-1420T and rs6311), showing a weak association with the propensity for suicide, but these data have not yet been conclusively confirmed by repeated scientific studies. A more distinct association was initially demonstrated for the 102C substitution in exon 1, but it was not confirmed in further studies, nor was it detected by meta-analysis.

At present, there are no clear data on the influence of genes that encode the serotonin receptors on a person's predisposition to suicidal behavior. Naturally, serotonin performs many functions in the human body, one of the most important being the enhancement of dopamine system activity, so the corresponding genes should obviously be involved in the genetic analysis of the propensity for suicide as well [4, 14, 15, 16]. But, unfortunately, for the time being, these genes have not been adequately studied. The situation with the *TH* gene is a vivid example. Its product is the enzyme tyrosine hydroxylase, the key participant in dopamine and norepinephrine biosynthesis. However, only two experimental works analyzing the effect of this gene on suicidal behavior are known. One showed that the K3 allele is closely associated with suicide attempts in Swedes suffering from psychiatric disorders. The other demonstrated that carriers of the same allele had significantly reduced levels of 3-methoxy-4-hydroxyphenylglycol, the main derivative of noradrenaline. However, these data are still insufficient to draw a clear scientific conclusion.

The genes encoding various dopamine receptors have also been the subject of sporadic studies. The study of the polymorphism of the DRD4 gene showed no association between the number of repeats in exon 3 and the probability of suicide attempts. A negative result was also obtained for the DRD2 gene when cytosine dropout at position -141 was analyzed. At the same time, the nucleotide substitution in intron 8 is associated with multiple suicide attempts in alcoholics [3].

Catechol-O-methyltransferase, the key enzyme that ensures the degradation of dopamine, as well as that of adrenaline and noradrenaline, plays an important role in the regulation of dopamine system activity. This enzyme is a product of the COMT gene, in which about 300 polymorphism sites are known. But the focus is on only one, Val158Met in exon 4. It has been shown that the substitution of 158Met leads to a significant decrease in the activity of the enzyme. At the same time, about half of the studies have demonstrated its association with a suicidal tendency — not with any, but predominantly with the "hard" manifestations [13].

The dopamine system is closely related to the adrenaline system. In this connection, the *ADRA2A* gene that encodes the α2A adrenaline receptor was also involved in the genetic analysis of the predisposition to suicide. For three polymorphic sites in the promoter region (G-1800T, C-1291G, and G-261A), no association with propensity for suicide could be found. At the same time, a rare nucleotide substitution characteristic of only a few suicides has been described [11, 12]. Whether this is a coincidence remains unclear.

The analysis of aggressive behavior unrelated to suicide is a very difficult task from the methodological perspective. Firstly, it is connected with the fact that in comparison with suicides such aggression is much more difficult to account for; secondly, its manifestations are much more diverse; thirdly, there are no unified approaches to classify these manifestations clearly. Not surprisingly, the results obtained in this field are extremely fragmentary and still largely contradictory.

Men are commonly believed to be more aggressive than women. This opinion, which is firmly rooted in the public consciousness, is mainly based on criminal statistics. Indeed, about 90% of all grave crimes are committed by men. According to twin analysis, this difference is largely controlled by genotype and is caused

Проблемы здоровья и экологии/Health and Ecology Issues **2021;18(3):23–32**

by different sets of sex chromosomes (XX for women, XY for men): the presence of the Y chromosome significantly increases a person's predisposition to violence and murder.

Many chromosomal anomalies have been described in humans. In particular, some men (approximately one in 1,000) have two copies of the Y chromosome, rather than one. It would seem quite logical that such individuals should differ from normal men by excessive aggression and should be considered as potential rapists and murderers. Studies carried out in several U.S. prisons have shown that an extra copy of the Y chromosome is found in convicts approximately 10 times more often than in the general male population. A similar conclusion was made for psychiatric patients. As a result, the hypothesis of high aggressiveness in men with an extra copy of the Y chromosome was widely accepted in scientific circles and even entered a number of psychology textbooks. Meanwhile, there was a significant flaw in the conducted research. The authors neither used relevant questionnaires in their work, nor directly observed their subjects. All the conclusions relied exclusively on indirect assessments of aggression. When this blunder was eliminated, it became clear that the presence of an additional Y chromosome had virtually no effect on the degree of a person's aggression. In addition, most inmates with the XYY chromosome set were serving sentences for fraud and theft, rather than for murder.

Further research found that men with two copies of the Y chromosome were significantly more impulsive than the norm, and were therefore easily involved in various scams. The second characteristic feature of these men is a somewhat reduced level of intelligence. Apparently, it is the combination of these two factors that leads to an increased likelihood of imprisonment or ending up in a psychiatric clinic: a man commits some shady acts without really thinking about responsibility and possible consequences. Moreover, men with an extra Y chromosome are normally very tall, which draws increased attention of others [14, 15].

In recent years, experimental work has been conducted seeking a connection between the propensity for violence and specific genes. It has been shown that the 5-promoter of the *SLC6A4* gene is associated with especially grave crimes, with repeated violent crimes in alcoholics, as well as with manifestations of violence in psychiatric patients.

The situation with the COMT gene is less clear. Several independent studies suggest that the 158Me: nucleotide substitution is associated with the propensity for violence, especially in men, but other studies do not detect this regularity.

Contradictory results have been also obtained for the *MAOA* gene [10]. A mutation leading to a complete defect of the corresponding enzyme was found in a Dutch family. Men carrying this mutation are distinguished from the norm by bouts of aggressive behavior, especially in the presence of external provoking factors, but these data are hardly consistent with the following fact: a small chromosomal abnormality is known in humans, in which both monoamine oxidase genes are missing. Such people suffer from a number of severe abnormalities (e. g., rapidly progressive loss of sight), but their level of aggression is quite normal. Several independent studies have shown that weakly transcribed alleles of the *MAOA* gene are associated with a tendency to reproduce the "cycle of violence": a person who was abused in early childhood later becomes a source of violence [4, 13, 16].

Do genes and mutations in people determine their emotional, mental and intellectual features within the norm [1, 2, 17, 18]? The first evidence for this was obtained in numerous studies of the cognitive and psychological characteristics of monozygotic (genetically identical) and dizygotic (genetically different) twins when they were separated and grew up in different environmental conditions. At the level of comparison of the intellectual and psychological characteristics of such twins it was shown that in almost all cognitive, mental, psychological and behavioral characteristics monozygotic twins are similar to each other and to their biological rather than adoptive parents – regardless of whether twins grew up together or apart, with biological parents or with adoptive parents.

It is believed that even such seemingly distant from purely biological characteristics as the level of intellect, independence and dependence, activity and passivity, suspicion and anxiety, extroversion and introversion, sensitivity or tolerance to stress, altruism and egoism, aggressiveness and sexuality are genetically determined [2, 3, 11, 14, 17, 19, 20]. Such seemingly socially determined human characteristics as political preferences (conservatism, liberalism, radicalism), attitudes toward the death penalty (for or against), musi-

cal tastes (classical, light or electronic music), pathological gambling, alcoholism, preferable type of vacations, manic depressive psychosis, schizophrenia, criminal behavior are also considered genetically determined to a great extent [5, 14]. Recently, "social behavior" genes have been discovered in the seventh chromosome, in which some mutations lead to "open behavior", increased sociability (extroversion) and friendliness, increased linguistic abilities, and high levels of general cognitive abilities [18].

Anxiety, susceptibility or tolerance to stress are genetically determined characteristics underlying many psychiatric disorders [2, 3]. It has been found that anxiety and susceptibility to stress are caused by mutations in the *5-HTT* (serotonin transporter) and *COMT* (Catechol-O-methyltransferase) genes [9, 13].

At present, the list of genes directly involved in programming human cognitive characteristics includes more than 150 units. It is believed that mutations in genes involved in the encoding of metabolism of such neurotransmitters as serotonin, dopamine, glutamine, and others have a significant influence on personality characteristics [4, 6, 11, 12, 16]. The discovery of genes in which special mutations characterize what is commonly referred to as the national character, or ethnopsychological features, is quite illustrative. The first "molecular" breakthrough in the study of the genomics of ethnopsychological traits was the discovery of mutations that program "belligerence or peacefulness". Anthropologists consider South American Indians, in particular the Yanomamö tribe, to be the so-called "archetype of ferocity", whose members are regularly on the warpath. This is caused by the special 7R mutation in the gene encoding the dopamine neurotransmitter receptor (DRD4), which is very frequently encountered in these Indians, making them very aggressive, excitable, impulsive and uncooperative. In Bushmen and East Asian farmers ("peaceful archetypes"), this mutation is extremely rare. Psychiatric genomics has shown that other types of mutations in this gene lead to hyperactivity, increased proneness to conflict, constant search for thrills. Emotional restraint and interpersonal sensitivity characteristic of the Japanese are encoded by the so-called "short" mutant forms of the *5HTTLPR* serotonin neurotransmitter transporter gene. It is believed that the high frequency of this mutation in the Japanese population is the result of selection aimed at avoiding individual exclusion from the society [9].

The near-term outlook in the genetics of human aggressive behavior is associated with progress in the following areas:

• isolation of elementary manifestations of human aggression;

• search for the genes controlling these elementary manifestations;

• study of genetic controls of "trigger mechanisms" which regulate the level of aggression in various situations;

• study of molecular mechanisms by means of which aggressive behavior is controlled by social factors.

In the foreseeable future, fast sequencing of the genomes of specific individuals will be possible. The strategic goal — to decipher the human genome for $ 1,000 within a few days — is expected to be achieved in the coming years. Personality genomics methods are believed to have capacity to dramatically change the face of not only medicine, but the society as a whole, making it possible to predict not only the development of many diseases, but also intellectual, mental and behavioral traits of individuals.

References

1. Baranov VS, Baranova YeV, Ivashchenko TE, Aseyev MV. The human genome and predisposition genes (introduction to predictive medicine. SPb.: «Intermedika»; 2000. (In Russ.).

2. Tihodeev ON. Fundamentals of psychogenetics: a textbook for students of institutions of higher specialized education. M. : Publishing center «Akademiya»; 2011. (In Russ.).

3. Bondy B, Buettner A, Zill P. Genetics of suicide. *Molecular Psychiatry*. 2006;11:336-351.
DOI: https://doi.org/10.1038/sj.mp.4001803

4. Dierick HA, Greenspan RJ. Molecular Analysis of Flies Selected for Aggressive Behavior. 2006 Sep;38(9):1023-1031.
DOI: https://doi.org/10.1038/ng1864

5. Vitaro F, Brendgen M, Barker ED. Subtypes of aggressive behaviors: a developmental perspective. *Int J Behav Dev*. 2006;30(1):12-19.
DOI: https://doi.org/10.1177/0165025406059968

6. Popova NK. From genes to aggressive behavior: the role of serotonergic system. *BioEssays*. 2006 May;28(5):495-503.
DOI: https://doi.org/10.1002/bies.20412

7. Filipenko ML, Beilina AG, Alekseyenko OV, Dolgov VV, Kudryavtseva NN. Repeated experience of social defeats increases serotonin transporter and monoamine oxidase A mRNA levels in raphe nuclei of male mice. *Biochemistry*. 2002 Apr;67(4):451-455.

8. Rujescu D, Thalmeier A, Moller HJ, Bronisch T, Giegling I. Molecular genetic findings in suicidal behavior: what is beyond the serotonergic system? *Arch Suicide Res*. 2007;11(1):17-40.
DOI: https://doi.org/10.1080/13811110600897317

9. Li D, He L. Meta-analysis supports association between serotonin transporter (5-HTT) and suicidal behavior. *Mol Psychiatry*. 2007 Jan;12(1):47-54.
DOI: https://doi.org/10.1038/sj.mp.4001890

10. Young SE, Smolen A, Haberstick BC, Hewitt JK. Clinical validation of possible links between MAO-A genotype and maltreatment in the risk for adolescent conduct disorder. *American J. Psichiatry*. 2006; Jun;163(6):1019-1025.

11. Faraone SV, Khan SA. Cardidate gene studies of attention-deficit/hyperactivity disorder. *The Journal of Clinical Psychiatry*. 2006;67 Suppl 8:13-20

12. Gizer IR, Ficks C, Waldmaan ID. Candidate gene studies of ADHD: a meta-analytic review. *Hum. Genet*. 2009; Jul;126(1):51-90.
DOI: https://doi.org/10.1007/s00439-009-0694-x

13. Kia-Keating BM, Glatt SJ, Tsuang MT. Meta-analyses suggest association between COMT, but not HTR1B, alleles, and suicidal behavior. American journal of medical genetics. *Part B Neuropsychiatr Genet*. 2007; Dec 5;144B(8):1048-1053.
DOI: https://doi.org/10.1002/ajmg.b.30551

14. Theilgaard A. A psychological study of the personalities of XYY – and XXY-men. *Acta Psychuatrica Scandinavica. Supplements*. 1984;69(315):1-133.

15. Bressan RA, Crippa JA. The role of dopamine in reward and pleasure behavior-review of data from preclinical research. *Acta Psychiatrica Scandinavica*. 2005;427(111):14-21.
DOI: https://doi.org/10.1111/j.1600-0447.2005.00540.x.

16. Girault J, Greengard P. The Neurobiology of Dopamine Signaling. *Arch Neurol*. 2004 May;61(5):641-644.
DOI: https://doi.org/10.1001/archneur.61.5.641

17. Kostyuk SA. Genes of predisposition to multifactorial diseases and genetic polymorphism: what is it? *Medical news*. 2020;7. (In Russ.).

18. Ertekin-Taner N. Genetics of Alzheimer's disease: a centennial review. *Neurologic clinics*. 2007; Aug;25(3):611-667, v.
DOI: https://doi.org/10.1016/j.ncl.2007.03.009

19. Willemsen R, Oostra BA, Bassell GJ, Dictenberg J. The fragile X syndrome: from molecular genetics to neurobiology. *Mental Retardation Developmental Disabilities Research Review*. 2004; 10(1):60-67.
DOI: https://doi.org/10.1002/mrdd.20010

20. Wang E, Ding YC, Flodman P. The genetic architecture of selection at the human dopamine receptor D4 (DRD4) gene locus. *Am J Hum Genet*. 2004; May;74(5):931-944.
DOI: https://doi.org/10.1086/420854

Список литературы

1. Баранов ВС, Баранова ЕВ, Иващенко ТЭ, Асеев МВ. Геном человека и гены «предрасположенности» (введение в предиктивную медицину). СПб.: «Интермедика», 2000.

2. Тиходеев ОН. Основы психогенетики: учебное пособие для студентов высших специальных учебных заведений. М.: Издательский центр «Академия»; 2011.

3. Bondy B, Buettner A, Zill P. Genetics of suicide. *Molecular Psychiatry*. 2006;11:336-351.
DOI: https://doi.org/10.1038/sj.mp.4001803

4. Dierick HA, Greenspan RJ. Molecular Analysis of Flies Selected for Aggressive Behavior. 2006 Sep;38(9):1023-1031.
DOI: https://doi.org/10.1038/ng1864

5. Vitaro F, Brendgen M, Barker ED. Subtypes of aggressive behaviors: a developmental perspective. *Int J Behav Dev*. 2006;30(1):12-19.
DOI: https://doi.org/10.1177/0165025406059968

6. Popova NK. From genes to aggressive behavior: the role of serotonergic system. *BioEssays*. 2006 May;28(5):495-503.
DOI: https://doi.org/10.1002/bies.20412

7. Filipenko ML, Beilina AG, Alekseyenko OV, Dolgov VV, Kudryavtseva NN. Repeated experience of social defeats increases serotonin transporter and monoamine oxidase A mRNA levels in raphe nuclei of male mice. *Biochemistry*. 2002 Apr;67(4):451-455.

8. Rujescu D, Thalmeier A, Moller HJ, Bronisch T, Giegling I. Molecular genetic findings in suicidal behavior: what is beyond the serotonergic system? *Arch Suicide Res*. 2007;11(1):17-40.
DOI: https://doi.org/10.1080/13811110600897317

9. Li D, He L. Meta-analysis supports association between serotonin transporter (5-HTT) and suicidal behavior. *Mol Psychiatry*. 2007 Jan;12(1):47-54.
DOI: https://doi.org/10.1038/sj.mp.4001890

10. Young SE, Smolen A, Haberstick BC, Hewitt JK. Clinical validation of possible links between MAO-A genotype and maltreatment in the risk for adolescent conduct disorder. *American J. Psichiatry*. 2006; Jun;163(6):1019-1025.

11. Faraone SV, Khan SA. Cardidate gene studies of attention-deficit/hyperactivity disorder. *The Journal of Clinical Psychiatry*. 2006;67 Suppl 8:13-20

12. Gizer IR, Ficks C, Waldmaan ID. Candidate gene studies of ADHD: a meta-analytic review. *Hum. Genet*. 2009; Jul;126(1):51-90.
DOI: https://doi.org/10.1007/s00439-009-0694-x

13. Kia-Keating BM, Glatt SJ, Tsuang MT. Meta-analyses suggest association between COMT, but not HTR1B, alleles, and suicidal behavior. American journal of medical genetics. *Part B Neuropsychiatr Genet*. 2007; Dec 5;144B(8):1048-1053.
DOI: https://doi.org/10.1002/ajmg.b.30551

14. Theilgaard A. A psychological study of the personalities of XYY – and XXY-men. *Acta Psychuatrica Scandinavica. Supplements*. 1984;69(315):1-133.

15. Bressan RA, Crippa JA. The role of dopamine in reward and pleasure behavior-review of data from preclinical research. *Acta Psychiatrica Scandinavica*. 2005;427(111):14-21.
DOI: https://doi.org/10.1111/j.1600-0447.2005.00540.x.

16. Girault J, Greengard P. The Neurobiology of Dopamine Signaling. *Arch Neurol*. 2004 May;61(5):641-644.
DOI: https://doi.org/10.1001/archneur.61.5.641

17. Костюк СА. Гены предрасположенности к мультифакторным заболеваниям и генетический полиморфизм: что это такое? Медицинские новости. 2020;7.

18. Ertekin-Taner N. Genetics of Alzheimer's disease: a centennial review. *Neurologic clinics*. 2007; Aug;25(3):611-667, v.
DOI: https://doi.org/10.1016/j.ncl.2007.03.009

19. Willemsen R, Oostra BA, Bassell GJ, Dictenberg J. The fragile X syndrome: from molecular genetics to neurobiology. *Mental Retardation Developmental Disabilities Research Review*. 2004; 10(1):60-67.
DOI: https://doi.org/10.1002/mrdd.20010

20. Wang E, Ding YC, Flodman P. The genetic architecture of selection at the human dopamine receptor D4 (DRD4) gene locus. *Am J Hum Genet*. 2004; May;74(5):931-944.
DOI: https://doi.org/10.1086/420854

Information about the authors / Информация об авторах

Svetlana A. Kostiuk, DMedSc, Professor, Chief Researcher at the Science-Research Laboratory of Belarusian Medical Academy of Postgraduate Education
ORCID: https://orcid.org/0000-0002-3252-2626
e-mail: s.kostiuk@mail.ru

Sergej V. Davidouskij, PhD (Med), Associate Professor, Associate Professor at Psychotherapy and Medical Psychology Department of Belarusian Medical Academy of Postgraduate Education
ORCID: https://orcid.org/0000-0003-3955-8936
e-mail: davidouski@yandex.ru

Darya D. Kostiuk, student, Institute of Psychology of Wrocław State University
ORCID: https://orcid.org/0000-0002-8816-7280
e-mail: kostyuk20001402@mail.ru

Olga S. Poluyan, PhD (Med), Leading Researcher at the Science-Research Laboratory of Belarusian Medical Academy of Postgraduate Education
ORCID: https://orcid.org/0000-0001-7130-2776
e-mail: olga.poluyan@mail.ru

Костюк Светлана Андреевна, д.м.н., профессор, главный научный сотрудник Научно-исследовательской лаборатории, ГУО «Белорусская медицинская академия последипломного образования»
ORCID: https://orcid.org/0000-0002-3252-2626
e-mail: s.kostiuk@mail.ru

Давидовский Сергей Владимирович, к.м.н. доцент, доцент кафедры психотерапии и медицинской психологии, ГУО «Белорусская медицинская академия последипломного образования»
ORCID: https://orcid.org/0000-0003-3955-8936
e-mail: davidouski@yandex.ru

Костюк Дарья Дмитриевна, студент, Институт психологии Вроцлавского государственного университета
ORCID: https://orcid.org/0000-0002-8816-7280
e-mail: kostyuk20001402@mail.ru

Полуян Ольга Сергеевна, к.б.н., ведущий научный сотрудник Научно-исследовательской лаборатории, ГУО «Белорусская медицинская академия последипломного образования»
ORCID: https://orcid.org/0000-0001-7130-2776
e-mail: olga.poluyan@mail.ru

Corresponding author / Автор, ответственный за переписку

Svetlana A. Kostiuk
e-mail: s.kostiuk@mail.ru

Костюк Светлана Андреевна
e-mail: s.kostiuk@mail.ru

Received / Поступила в редакцию 25.08.2021
Revised / Поступила после рецензирования 01.09.2021
Accepted / Принята к публикации 20.09.2021