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SEARCH FOR GENETIC AND PHENOTYPICAL BASES OF HUMAN PREDISPOSITION TO RISK BEHAVIOR

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As a result of the study, the systemic organization of the genetic and phenotypic mechanisms of the individual formation of a person's propensity for risky behavior is substantiated. Predisposition to risky behavior in men is due to the minor A/A genotype within the SNP rs1851048 (CACNA2D3), while in women it is due to the major genotype G/G rs1851048 (CACNA2D3) and the major genotype A/Ars2562456 (ZNF). Both in men and women, the phenotypic factors of risky behavior are: an increased level of irritability, neuroticism, reactive aggressiveness, emotional lability, touchiness, and the severity of psychotype A.
Keywords: risky behavior; genetic status; phenotype; psychological status.

INTRODUCTION

The propensity to take risks is a natural element of the individual specifics of goal-directed behavior. Depending on the type of activity, risky behavior can lead to the achievement of both positive and negative results. From a medical point of view, risky behavior is clearly assessed as negative, which threatens human life and health. The scientific study of risky behavior is initially based on its negative assessment, where the propensity for risk is defined as self-destructive behavior, due, among other things, to the low adaptive capabilities of the individual [1].

In psychology, when studying risky behavior, there are two main approaches: situational, aimed at identifying external factors that determine the specifics of an individual's actions in each specific situation, and a personal approach that ensures the determination of stable individual characteristics and qualities of a person that characterize his ability to risky behavior. External factors that predetermine risky behavior include the specific socio-cultural context, the rules and norms of social life, and the possibility of violating the laws adopted in society with impunity. Internal factors predetermining risky behavior are gender, age and behavioral characteristics, the specifics of the course of individual biological, emotional and cognitive processes, attitudes and beliefs of a person [2].At the same time, despite the certain significance of exogenous factors that potentially provoke an individual to risky actions, nevertheless, the likelihood of implementing risky behavior under any circumstances primarily depends on the individual psychophysiological and psychological characteristics of a person [3].

Questions of biological determination of risky behavior remain less studied in science. The widely known anthropological theory of C. Lombroso, which tried to substantiate the connection between criminal behavior and somatotypic characteristics of a person, found its continuation in the constitutional theories of E. Kretschmer and W. Sheldon [4], but did not receive further wide development. Currently, this direction is developing in the direction of research into the genetic determinism of various forms of deviant behaviour [5]. The basis of modern psychogenetics is the discovery by W. Pearson of the connection of an extra Y-chromosome in men with a predisposition to criminal violence. The most popular genetic studies of a person's predisposition to the consumption of psychoactive substances, to the development of aggression, to depression and suicidal behavior. In addition, neuromorphological and neurophysiological correlates of deviant behavior are being actively studied. However, the biological concepts of deviant behavior, in particular risky behavior, do not have a systematic, comprehensive development in modern science. There are no genetically determined integrative indicators of a person's propensity for specific forms of risky behavior. As a rule, the role of gender is ignored when looking for factors initiating risk behavior.

As a result of our own studies, we have substantiated the property of integrativity of the level of general nonspecific reactivity of the organism (LGNRO), which comprehensively reflects the genetic, functional, psychophysiological and psychological status of a person. The possibility of instrumental express-assessment of LGNRO by taking into account the threshold of pain sensitivity (TPS) was substantiated [6]. The genetic determinism of LGNRO has been proven, a number of single-nucleotide polymorphisms associated with TPS and the psychological status of a person have been identified [7, 8].

The purpose of the study – to identify factors of genetic and phenotypic conditionality of a person's propensity for risky behavior

MATERIALS AND METHODS

The study involved 300 clinically healthy men and women aged 18–25, selected by random sampling from 1800 students, representatives of the Caucasian race, indigenous people of 6 main territories of Russia: 1 – North-West (Karelia, Arkhangelsk, Leningrad, Vologda regions), 2 – Center (Samara, Voronezh, Saratov regions), 3 – South (Stavropol Territory, Volgograd Region), 4 – Crimea, 5 – Ural-Siberia (Chelyabinsk Region, Gorny Altai), 6 – Far East (Primorsky Territory). All work was carried out in accordance with the principles of the Universal Declaration of Bioethics and Human Rights (Articles 4 (good and harm), 5 (independence and individual responsibility), 6 (consent) and 9 (privacy and confidentiality) [9].

The psychological status of the study participants was determined by assessing the indicators of the Freiburg multifactorial personality questionnaire – FPI (I. Farenberg, H. Zarg, R. Gampel), temperament and character accentuations (K. Leonhard) [10], behavioral, social, professional, economic, political activity and social destructiveness (Yu. A. Shatyr and others) [11].

The height and body weight of the study participants were determined. The assessment of LGNRO was performed by identifying the time of exposure to infrared

radiation, which has a threshold nociceptive effect on the skin of the dorsal surface of the distal phalanx of the middle finger, using a laboratory algesimeter of the UgoBasile type (Italy). At the moment of reflex removal of the hand from the thermal stimulus, the time in seconds corresponding to the TPS was automatically recorded. High LGNRO corresponds to the minimum values of TPS, low LGNRO corresponds to the maximum values, and average LGNRO corresponds to intermediate values of the TPS [6].

Laboratory genetic study of biological material was carried out by real-time PCR using kits produced by Synthol (Russia) and real-time amplifier RotorGene 6000 (Corbett Research, Australia). Genomic DNA was isolated from buccal epithelium by adsorption on magnetic particles. Polymorphisms that are promising in terms of association with LGNRO and propensity to risky behaviors were studied: rs6923492 in the GRM1 gene, rs6280 in the DRD3 gene, rs1851048 in the CACNA2D3 gene, and rs2562456 in the ZNF gene [12].

For the primary statistical analysis of the total data array, the Python programming languages of the pandas, matplotlib.pyplot, phik, numpy, seaborn, scipy packages were used. The correlation methods Phi_K Correlation and Global Correlations were applied with the calculation of the corresponding coefficients ϕk and gk [13]. This provided a screening of relationships, including non-linear ones, from 0.0 to 1.0, without taking into account their direction, between all the studied indicators. The methodological apparatus used provided automatic calculation of relationships between categorical, ordinal and interval variables. The severity of phenotypic traits in the studied SNP genotypes was assessed using the nonparametric Kruskal-Wallis test.

RESULTS AND DISCUSSION

To identify the main, most pronounced systemic relationships of the analyzed indicators, the global correlation coefficients were calculated for the sample populations of men (Fig. 1) and women (Fig. 2).

The presented data made it possible to identify potential factors initiating or blocking various vectors of risky behavior.At the same time, based on the results of previously performed own studies (3) and known literature data (10), the most promising phenotypic signs of risk behavior were identified from the list of analyzed indicators.The list of indicators provoking risky behavior included: high LGNRO, asociality, depression, dysthymia, cardiotype (psychotype) A, masculinity, neuroticism, touchiness, political activity, irritability, reactive aggressiveness, social destructiveness.Phenotypic indicators that prevent risky behavior were identified: low LGNRO, body weight, shyness, sociability, anxiety, poise, emotional lability.

Then, the potential impact of the analyzed single nucleotide polymorphisms on the phenotypic indicators of a person's propensity to risky behavior was assessed. To do this, for each genotype of the studied SNPs (rs6280 in the DRD3 gene, rs6923492 in the GRM1 gene, rs1851048 in the CACNA2D3 gene, rs2562456 in the ZNF gene), the medians of the selected phenotype indicators were distributed taking into account the sex of the subjects.The data obtained indicate single associations of SNPs with phenotypic signs of a person's propensity to risk behavior. In doing so, two points should be highlighted. First, the associations of rs6280 in the DRD3 gene and rs6923492 in the

GRM1 gene with individual indicators of the psychological status of the subjects do not have a systemic, pronounced character, which makes it possible to further interpret them. Secondly, for both rs1851048 in the CACNA2D3 gene and rs2562456 in the ZNF gene, statistically significant associations with individual phenotypic indicators of risky behavior appear only in relation to men (Table 1) or only in relation to women (Table 2). These tables present only phenotype scores with statistically significant associations or trends towards statistically significant associations ($p < 0.1$) with the analyzed SNPs.

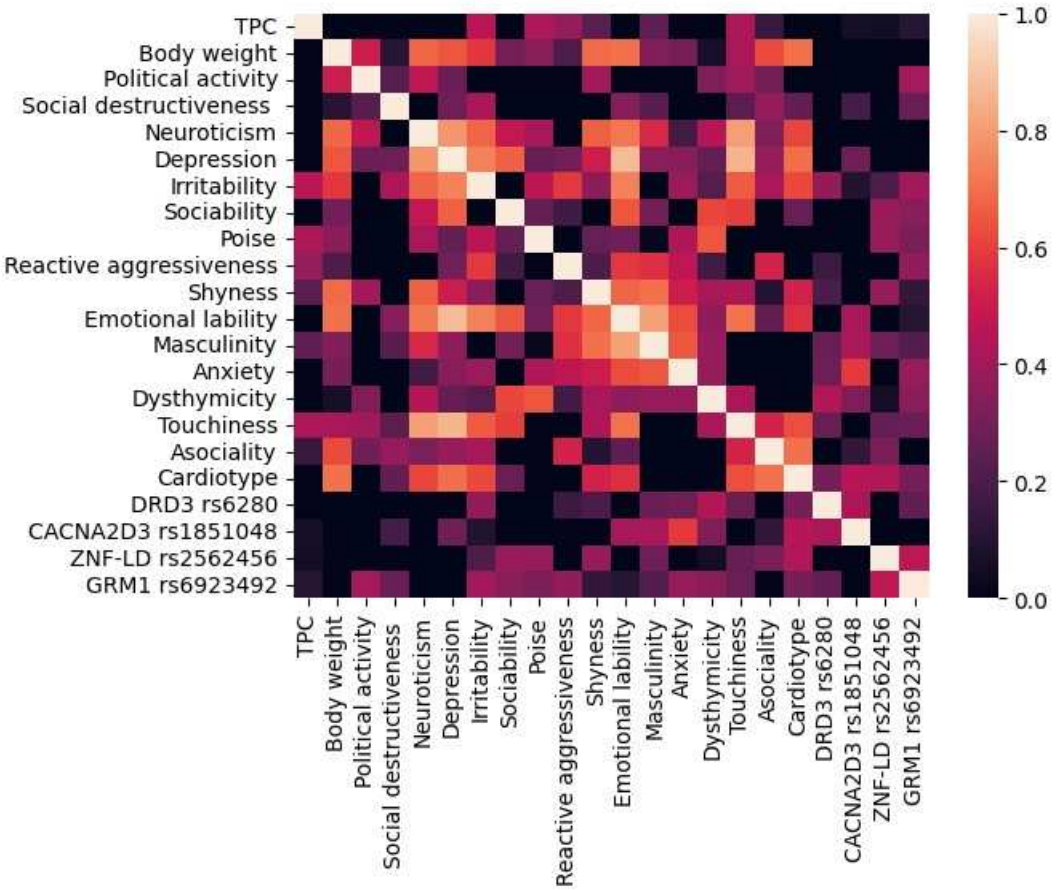

Fig. 1. Relationship between genotypic and phenotypic indicators of potential propensity for risky behavior in men.

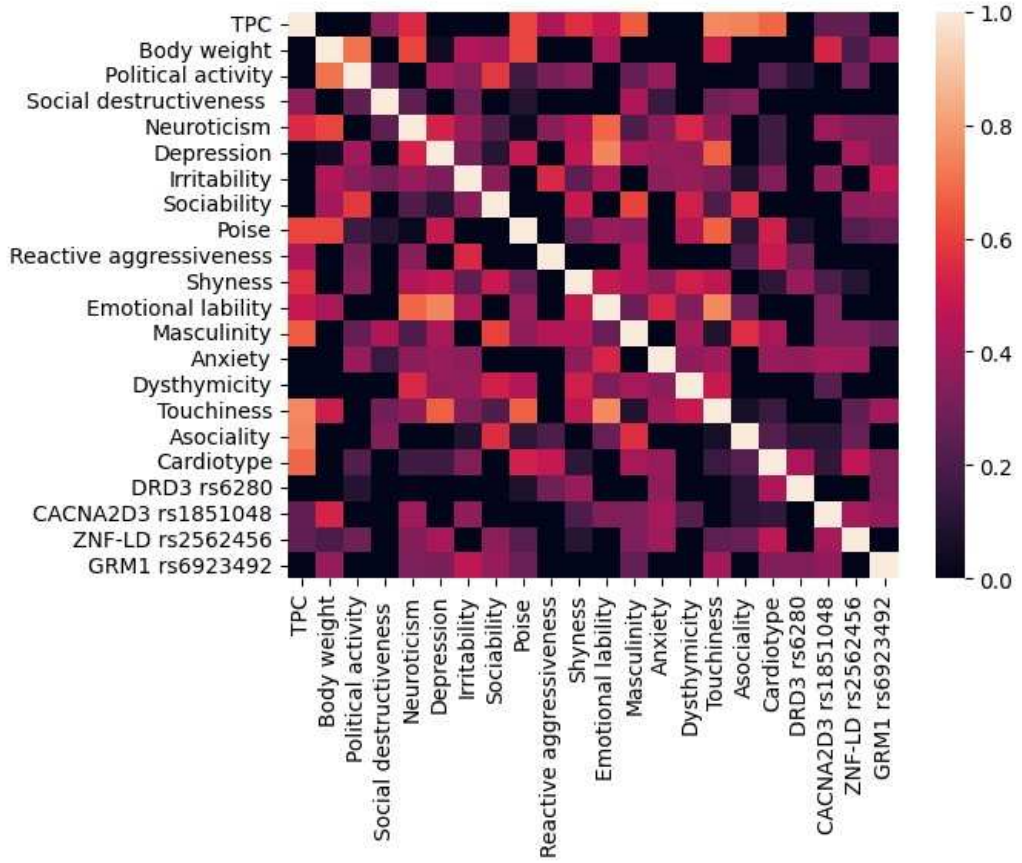

Fig. 2. Relationship between genotypic and phenotypic indicators of potential propensity for risky behavior in women.

Table 1

Relationship of genotypic and phenotypic indicators of potential propensity to risky behavior in men

Indicators	SNP							
	CACNA2D3 rs1851048 G/A				ZNF-LD rs2562456 A/G			
	G/G	G/A	A/A	p	A/A	A/G	G/G	p
Cardiotype	9	10	12,5	0,071	9,5	10	11	0,7
Masculinity	8	8	6,5	0,245	8	8	6	0,017
Touchiness	5	4	6,5	0,058	4,5	4	5	0,661
Irritability	3	4	6	0,041	4	4	4	0,942
Poise	6	5	4,5	0,457	5	6	4	0,039

Table 2

Relationship of genotypic and phenotypic indicators of potential propensity to risky behavior in women

Indicators	SNP							
	CACNA2D3 rs1851048 G/A				ZNF-LD rs2562456 A/G			
	G/G	G/A	A/A	p	A/A	A/G	G/G	p
TPC	8,5	8	13	0,073	7	9	15	0,04
Body weight	55,5	61	52,25	0,011	58,5	58	51,5	0,025
Asociality	2	3	2	0,432	2	3	3	0,072
Depression	7	4	6	0,001	6	5	5	0,455
Dysthymicity	9	6	6	0,093	9	6	9	0,581
Neuroticism	9	5	7	0,001	7	6	8	0,552
Emotional lability	7	4	6	0,005	6	6	6	0,948
Anxiety	12	9	15	0,057	12	9	13,5	0,554

Based on the results of assessing the potential impact of the analyzed single nucleotide polymorphisms on the phenotypic indicators of a person's propensity to risky behavior, taking into account gender, isolated associations of SNPs with phenotypic signs of a person's propensity to risky behavior were established.

In men, the association of the minor A/A genotype rs1851048 (CACNA2D3) with irritability, resentment, and cardiotype A can be interpreted as an element of propensity for risky behavior. The major genotype A/Ars2562456 (ZNF) in men is associated with masculinity against the background of a minimal, statistically insignificant, severity of the cardiotype. Such a combination of indicators of the psychological status in men indicates the absence of a tendency to risky, in particular, auto-aggressive behavior.

In women, the major genotype G/Grs1851048 (CACNA2D3) is statistically significantly associated with depression, neuroticism, emotional lability, and body weight, which in this aggregate confirms its possible role in provoking risky behavior. The major genotype A/ASNPrs2562456 (ZNF) in women is statistically significantly associated with body weight and low TPC, which is associated with risk behavior.

When analyzing the possible phenotypic prerequisites for risky behavior, the main vectors of the phenomenon under study were identified: the risk of social pressure (social destructiveness), the risk of criminal pressure (reactive aggressiveness), the risk of autoaggression (depression) and the risk to life and health associated with diseases of the cardiovascular system (cardiotype A) (Table 3).

Table 3

Correlations of phenotypic signs of potential propensity to risky behavior in men and women

Indicator	sex	Psychological markers of the main vectors of risky behavior			
		Social destructiveness	Reactive aggressiveness	Depression	Cardiotype
Destructiveness	m	1	0.449*	-0.033	0.144
	w	1	0.416*	0.016	0.181*
Neuroticism	m	0.02	0.061	0.743*	0.369*
	w	0.093	0.109	0.769*	0.334*
Depression	m	-0.033	0.193*	1	0.383*
	w	0.016	0.121	1	0.305*
Irritability	m	0.219*	0.488*	0.642*	0.462*
	w	0.312*	0.536*	0.484*	0.476*
Sociability	m	0.180*	0.094	-0.552*	-0.004
	w	0.106	0.229*	-0.482*	0.071
Poise	m	0.132	-0.016	-0.466*	-0.325*
	w	0.167	0.164	-0.367*	-0.057
Reactive aggressiveness	m	0.449*	1	0.193*	0.323*
	w	0.416*	1	0.121	0.326*
Shyness	m	-0.185*	-0.115	0.692*	0.190*
	w	-0.127	-0.269*	0.630*	0.075
Emotional lability	m	0.017	0.124	0.915*	0.372*
	w	0.07	0.076	0.877*	0.255*
Masculinity	m	0.383*	0.435*	-0.452*	0.07
	w	0.303*	0.483*	-0.416*	0.160
Anxiety	m	-0.067	-0.033	0.478*	0.197*
	w	0.064	-0.083	0.370*	0.177
Dysthymicity	m	-0.194*	-0.138	0.467*	0.056
	w	-0.063	-0.182*	0.474*	0.01
Touchiness	m	0.031	0.158	0.720*	0.317*
	w	0.062	0.128	0.634*	0.378*
Asociality	m	0.373*	0.293*	0.174*	0.149
	w	0.313*	0.237*	-0.002	0.187*
Cardiotype	m	0.144	0.323*	0.383*	1
	w	0.181*	0.326*	0.305	1
Bodyweight	m	0.171	0.171	-0.206*	-0.030
	w	0.107	-0.006	-0.103	0.016
TPC	m	-0.07	-0.039	-0.182*	-0.016
	w	-0.005	-0.013	-0.021	0.033

Note: * is a statistically significant level of correlation.

The presented data made it possible to determine the phenotypic prerequisites for various vectors of risky behavior. Social destructiveness in men and women is positively associated with irritability, reactive aggressiveness, masculinity and asociality. Reactive aggressiveness in groups of men and women is positively associated with destructiveness, irritability, masculinity, asociality, and cardiotype A. Depression in groups of men and women is positively associated with irritability, shyness, emotional lability, anxiety, dysthymia and touchiness, and negatively with sociability, poise and masculinity. Both in men and women, cardiotype A is statistically significantly positively associated with neuroticism, depression, irritability, reactive aggressiveness, emotional lability, and touchiness. Among the analyzed phenotype indicators, irritability should be singled out, showing a positive statistically significant relationship with the severity of all vectors of risky behavior. In addition, neuroticism, reactive aggressiveness, emotional lability, resentment, and cardiotype A are characterized by a unidirectional positive association with identified signs of risky behavior in men and women.

CONCLUSIONS

As a result of the study, the systemic organization of the genetic and phenotypic mechanisms of the individual formation of a person's propensity for risky behavior is substantiated. Predisposition to risky behavior in men is due to the minor A/A genotype within the SNP rs1851048 (CACNA2D3), while in women it is due to the major genotype G/G rs1851048 (CACNA2D3) and the major genotype A/Ars2562456 (ZNF). Both in men and women, the phenotypic factors of risky behavior are: an increased level of irritability, neuroticism, reactive aggressiveness, emotional lability, resentment, and the severity of psychotype A.

The lack of a person's inclination to risky behavior, regardless of gender, is primarily due to the psychological properties of the individual: sociability, poise and masculinity. The major A/A genotype in males and the minor G/G genotype in females within the rs2562456 (ZNF) SNP are also likely to be associated with a low risk behavior propensity.

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Шатыр Ю. А. Поиск генетических и фенотипических основ предрасположенности человека к рискованному поведению / Шатыр Ю. А., Назаров Н. О., Глушаков Р. И., Улесикова И. В., Кухталёв В. В., Мулик А. Б. // Ученые записки Крымского федерального университета им. В. И. Вернадского. Биология, химия. – 2023. – Т. 9 (75), №3. – С. 291–299.

Обоснована системная организация генетических и фенотипических механизмов индивидуального формирования склонности человека к рискованному поведению. Предрасположенность к рискованному поведению у мужчин обусловлена минорным генотипом A/A в SNP rs1851048 (CACNA2D3), а у женщин – мажорным генотипом G/G rs1851048 (CACNA2D3) и основным генотипом A/Ars2562456 (ZNF). Как у мужчин, так и у женщин фенотипическими факторами рискованного поведения являются: повышенный уровень раздражительности, нейротизм, реактивная агрессивность, эмоциональная лабильность, обидчивость, выраженность психотипа А.

Ключевые слова: рискованное поведение; генетический статус; фенотип; психологический статус.