

Genetic predictors of interpersonal dependence

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Abstract. For several decades, numerous scientific discussions about the definition and essence of the codependency phenomenon have been ongoing. At the same time, some researchers note a close relationship between this phenomenon and the concept of interpersonal dependence, considering its destructive and positive impact on personality. The relevance and value of the conducted research lies in the fact that despite numerous studies, including interdisciplinary ones, the question about the nature of interpersonal dependence remains open. The aim is to study the differences in levels of interpersonal dependence in different polymorphic variants of catechol-O-methyltransferase (COMT) and dopamine D2 receptor (DRD2) genes. An interdisciplinary molecular genetic and psychological study of 132 women with drug addiction in remission for more than two years was conducted. As a psychological tool was used, “The Interpersonal Dependency Inventory” developed by R. Hirschfeld and adapted by O.P. Makushina was used. For determining the polymorphic variants of candidate genes, a method of isolating genomic DNA from buccal epithelial cells was used. The candidate genes considered were genotypes and alleles of the neurotransmitter pathways COMT and DRD2. For statistical processing of the obtained data, the nonparametric Mann-Whitney U-test was used. Substantial differences were found between the levels of interpersonal dependence in the genotypes VV and VM of the catechol-O-methyltransferase (COMT) enzyme; a trend of statistically significant differences was detected between the levels of interpersonal dependence in the genotypes CT and TT of the DRD2 gene. The features identified during the study should be taken into account in the process of carrying out psychological and preventive measures for people with addictive behaviour.

1 Introduction

In today's reality, characterized by various societal crises where socio-political and economic instability greatly complicates reality, the problem of fear of reality, generating a desire to escape from reality, is sharply actualized. In search of means of protection from permanent frustration people often resort to strategies of addictive behavior, primarily the use of alcohol and drugs.

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According to several researchers (Korolenko C.P., Dmitrieva N.V., 2001; Lebedeva V.F., 2004; Andreeva M.V., 2005; Moskalenko V.D., 2009), chemical dependence has a destructive effect not only on individuals but also on social and family contexts. As a result of cohabitation with a drug or alcohol addict for close relatives become characterized by emotional, behavioral, mental reactions similar to the reactions of the addict himself, denoted by the term co-dependence.

The concept of co-dependence is an important element of the individual's internal structure and has been a subject of recent study in psychological science. Special interest specialists began to cause the problem of co-dependence in the 70s of the XX century. This concept was used to describe individuals whose lives have undergone destructive changes as a result of being involved in a relationship with a chemically dependent subject. Nevertheless, the analysis of studies on the phenomenon of co-dependence showed that the first references are found at the beginning of the XX century in the works of the German psychiatrist Emil Kraepelin, who viewed co-dependence as the desire to be "seduced" by another person, while abandoning their own free will [1]. Subsequent references to the problem of co-dependence can be found in the works of psychoanalytic theory followers. Thus, the German psychoanalyst Abraham K. noted the peculiarities of addicts, connected with their confidence that there is always someone nearby who will take responsibility for them, will anticipate their desires and provide help in any situation of life. E. Fromm paid attention to a psychological peculiarity of some people - "receptive orientation" characterized by overtrust as well as in striving to support some other person who is helpless and cannot cope with the circumstances of life [2]. Horney K. noted a certain kind of dependent relationship in which there is a particularly strong need for support and care from loved ones, which can lead to "self-destruction" [3]. The term "co-dependence" was finally coined by Robert Sabby and Ernie Larsen in 1979.

Co-dependence is a complex and multifaceted phenomenon that continues to be the subject of numerous scientific discussions, with no single definition agreed upon. To date, in psychological science, there are several approaches to understanding co-dependence, in which co-dependence is seen as: a certain emotional, psychological state; feature or violation of behavior; consequence of the influence of the "problematic loved one", disharmony of existing relationships, poor communication.

Referring to the works of domestic scientists, within the framework of the above approaches, quite fully gives the definition of Ananyeva G.A., who considers co-dependence as a specific state. It is qualified as a strong preoccupation and concern, as well as extreme dependence (social, emotional and physical) on a person or object [4]. In her opinion, "...a co-dependent is a person who has allowed another person's behavior to affect him, and who is totally absorbed in controlling that person's actions (the other person may be a child, spouse, parent, sibling, client, best friend, he may be an alcoholic or drug addict, mentally or physically ill). It is an attempt to gain self-confidence, a sense of self-importance, and an attempt to define oneself as a person." [5].

Ananyeva G.A., believes that: "... co-dependence is characterized by: self-deception, low self-esteem, bordering on self-hatred, excessive concern about someone or something while neglecting oneself, compulsive need to perform certain actions in relation to other people (patronizing, suppress, resentment, etc.), habit of experiencing the same feelings (self-pity, anger, irritation, etc.) etc.), compulsive actions, difficulties in manifestation of feelings and related problems in communication, inability to distinguish responsibility for oneself and for another, loss of psychological boundaries (co-dependent allows himself to invade another's life, as well as allows others to invade theirs, decide for himself "what is good for him, what is bad")" [5].

According to a number of experts, co-dependence is a relationship addiction [6]. Scientists consider this phenomenon as a situation of existing emotional dependence of one person from the significant, for him, another [7, 8].

According to other specialists, co-dependence is a mirror reflection of addiction, which manifests itself with the same symptoms [9]. Common intrapsychic symptoms in co-dependents are: control, pressure, guilt, low self-esteem, obsessive states and thoughts, compulsive help, self-hatred, repressed anger, uncontrollable aggression, focus on others, ignoring one's needs, withdrawal, whining, apathy, intimacy problems, depressed behavior, suicidal thoughts. Co-dependents get sick from trying to control someone else's life, something that cannot be controlled [7].

Therefore, upon analyzing both classical and more modern works, we can draw the conclusion that the definitions of co-dependence are highly diverse. Co-dependence can be defined as a painful state, a fixed reaction to stress, a concentration of thoughts on the object of dependence, a violation of adaptation, a pattern of behavior, the subordination of oneself to the state of the dependent person, the need for constant situation control, the provocation of dependence problems within the family, and an emotional, psychological, and behavioral state caused by a set of overwhelming rules.

In the narrow sense, co-dependence is a painful condition that manifests itself in a feeling of psychological discomfort, which is a consequence of adaptation to the problem of chemical dependency in the family, a reaction to stressful conditions, eventually turning into a way of life.

In a broad sense, co-dependence acts as a dependence on people, on a certain type of behavior or on specific things: money, food, shopping, work, sex.

According to some researchers, a close connection with co-dependence has such a concept as interpersonal dependence. Relying on a broad understanding of co-dependence, interpersonal dependence appears as a particular type of co-dependence, the subject of which is a person, it is dependence on a significant other [10]. Interpersonal dependence can occur in friendly, industrial, child-parent relationships. And in each type of relationship the phenomenon of interpersonal dependence will have unique specifics [10].

Currently, there are several approaches in the scientific literature to comprehend the nature of interpersonal dependence.

In psychoanalysis, interpersonal dependence is viewed exclusively as a destructive phenomenon that distorts and traumatizes the personality. Such representatives of psychoanalytic tradition as C. Horney, M. Klein, P. Mellody W. Satir described interpersonal dependence by symptom complexes of dependent love: neurotic need for love, toxic love, love-dependence, love-attachment, and love-mania [11].

From the position of the Gestalt approach, the confluence is seen as the inability to separate oneself (one's desires, needs, values, experiences) from the partner (from his desires, needs, values, experiences) as the basis of interpersonal dependence. On the one hand, a certain confluence is necessary for empathy, for understanding the inner world of the other person, for experiencing intimacy. However, on the other hand, confluence threatens with dependence on the partner, impossibility to develop, loss of freedom [12]. That is, this approach considers the phenomenon of interpersonal dependence not only from the position of destructive influence on the personality, but also designates its positive function.

On the contrary, such scientists as Zhidko M.E., Korolenko C.B., Kocharyan A.S., Kotlyarov A.V. emphasize the negative aspect of this phenomenon, considering it a primary disorder and express the idea of possibility of transformation of interpersonal dependence in secondary forms of dependence: chemical, game, sexual, etc. [13, 14].

A number of Western researchers (Hirschfield and colleagues, 1977) view interpersonal dependence from the perspective of a model describing it as a polyparametric disorder that

includes three attributes: emotional reliance on others; insecurity; and a desire for autonomy. Interpersonal dependence is defined as the sum of the first two parameters in the absence of the person's desire for personal autonomy. What is important in this model is that a categorical sign of dependence is indicated - violation of personal boundaries, which are closely connected with a person's identity [15, 16].

Four components are distinguished in the structure of interpersonal dependence: cognitive, behavioral, emotional and motivational. Cognitive includes the beliefs of the individual, speaking about his own helplessness and weakness against the background of the power of the surrounding subjects. Behavioral consists of seeking help and the need for approval from a significant person in the process of interpersonal interaction, preferring the satisfaction of others' needs and ignoring one's own. Emotional is associated with a constant sense of anxiety, especially in situations requiring taking responsibility and involving assessment by others, fear of loneliness. The motivational component includes a pronounced need for the support and guidance of significant others [11].

Generalizing various views in a stream of the given problem both domestic and foreign researchers, it is possible to draw a conclusion that interpersonal dependence affects important characteristics of the person, forming its internal structure and defining features of building of interpersonal relations. People with a high level of interpersonal dependence constantly need positive evaluation and approval from others, demonstrate less resistance to frustration, are not aware of their true needs, showing a readiness to maintain dependence relationships at all costs, even in case of mistreatment.

And despite the fact that in modern psychology both the co-dependent state of the individual and interpersonal dependence are subjected to careful and comprehensive study, there are still many unexplored questions in this field. In particular, the question of the ambiguity of the nature of these phenomena is still open.

There is an opinion that both co-dependent patterns of behavior and interpersonal dependence are influenced by social and psychological factors. Such as: presence of problems in the parental family where one of the parents was absent or parents suffered from chemical addiction; unmet emotional needs (in love, affection, close relationships); various forms of violence (physical, psychological) to which the personality was exposed [7, 9, 17-19]. And as a consequence, deformed relations with the people around, which in turn strengthen the manifestations of co-dependence [20, 21].

Besides socio-psychological factors some researchers single out psycho-physiological and individual-typological features, and there is also an opinion that co-dependent behavior and interpersonal dependence can have their genetic preconditions [18, 22].

T.M. Rozhnova and her colleagues revealed in their research that women with severe co-dependent behavior are characterized by auto-aggression and hereditary alcohol addiction [22].

Current studies suggest the existence of genes whose different variations indicate a predisposition to certain psychological traits associated with co-dependent behavior and interpersonal addiction [18, 23-26].

However, in spite of the research results, many questions on this problem are still open. That determines our interest in this problem and the possibility of further empirical study.

The aim of our study was to examine the differences in the expression levels of interpersonal dependency in different polymorphic variants of the COMT and DRD2 genes.

2 Methods and materials

The study involved 132 female drug addicts in remission for more than two years aged 25-50 years from Rostov-on-Don.

As the technique directed on revealing of the level of interpersonal dependence the questionnaire of interpersonal dependence (Interpersonal Dependency Inventory) developed by R. Girshfield in adaptation of O.P. Makushina was used. The questionnaire includes three scales: emotional reliance on others, insecurity, and desire for autonomy. The final value of interpersonal dependence is the sum of the scores on the first two scales and the scores on the third scale are subtracted.

In order to determine the polymorphic variants of candidate genes, we used the method of genomic DNA isolation from buccal epithelial cells. The candidate genotypes and alleles of the catechol-o-methyltransferase (COMT) and dopamine D2-receptor (DRD2) neurotransmitter pathway genes were considered as candidate genes.

The COMT gene encodes the enzyme catechol-O-methyltransferase, which regulates the level of the neurotransmitter dopamine in the human prefrontal cortex. Currently, there are three polymorphic variants of this gene, depending on which nitrogenous base (guanine or adenine) is part of COMT: homozygous - GG (Val158Val), heterozygous - GA (Val158Met), homozygous with mutant allele AA (Met158Met), people with this genotype have the lowest activity of COMT gene and, respectively, the highest level of dopamine mediator in the brain.

The results of numerous interdisciplinary studies show the relationship of polymorphisms of the COMT gene with such psychological traits as anxiety, nervousness (research scientists at the University of Bonn, led by Christian Montag); altruism and greed (research scientists at the University of Pennsylvania); stress resistance, impulsivity, propensity for various forms of violence, aggressiveness and hostility, as well as autoaggressive behavior. AA (Met158Met) and GG (Val158Val) genotypes are often associated by researchers with various medical pathologies. For example, the homozygous genotype is associated with an increased risk of psychosis in schizophrenia [27], Alzheimer's disease, and brain trauma [28], while the homozygous genotype with the mutant allele is associated with a predisposition to panic attacks and obsessive-compulsive disorder. Since COMT is involved in dopamine metabolism, there is speculation that the gene polymorphism may influence the development of various addictions (including addiction to computer games). Ethanol-induced euphoria is associated with rapid dopamine release. The holders of the A allele have relatively lower levels of dopamine inactivation, and they are more susceptible to the development of alcohol dependence [21].

The DRD2 gene encodes the dopamine receptor, a protein located on the surface of neurons that is conjugated to G-proteins and inhibits adenylate cyclase under the influence of dopamine. Several polymorphic variants have been studied in the DRD2 gene: CC (A2A2); ST (A2A1); TT (A1A1).

Studies by different authors have revealed the specificity of the risk of schizophrenia and alcohol, drug and gambling addiction in different combinations of the DRD2 gene alleles. Thus, allele A1 (variant T) is associated with addiction, and allele A2 (variant C) is associated with schizophrenia [29, 30].

In general, the results of studies on the relationship between the DRD2 and COMT genes and the propensity for addictive behavior are contradictory. Nevertheless, the polymorphisms of these genes may indicate the possible existence of a genetic component of interpersonal addiction as a type of addictive behavior.

Nonparametric Mann-Whitney U-criterion in Statistica 23.0 program was used for statistical processing of the obtained data.

3 Results of the study and their analysis

The results of molecular genetic analysis of V158M polymorphism of COMT gene, as well as the results of molecular genetic analysis of DRD2 gene are presented in Table 1:

Table 1. Results of molecular-genetic analysis of the DRD2 gene and COMT

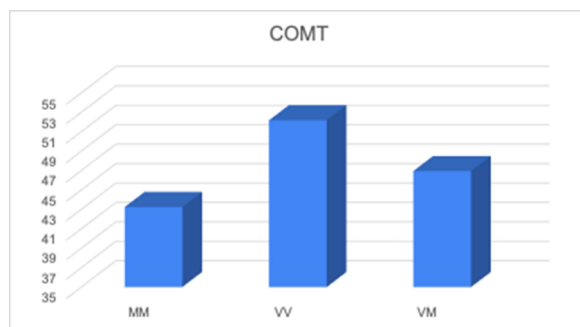
Numerical indicators	DRD2			COMT		
	CC (A2A2)	CT (A2A1)	TT (A1A1)	Homozygotes (VV)	Heterozygotes (VM)	Heterozygotes by mutation
Number of people	80	38	14	34	64	34
Percentage undocator	60	29	11	26	48	26

The heterozygous genotype of the COMT gene is found in 48% of the respondents, homozygous and homozygous with the mutant allele in 26% each. The CC genotype of the DRD2 gene is found in 60% of the study participants, the CT genotype in 29%, and the TT genotype in 11%.

The obtained data correspond to the statistical data on the distribution of the studied polymorphisms in the populations. It is known that in the European population, the occurrence of the T allele of the DRD2 gene is 18%. The heterozygous variant of the COMT gene is found in 50% of the European population, 25% are carriers of two copies of Val158, and the remaining 25% carry two copies of Met158. People who have two copies of the Met158 variant in their genome have the lowest activity of the COMT gene, which indicates the highest level of the mediator dopamine in the brain.

The results concerning the severity of interpersonal dependence, obtained with the help of R. Hirschfield's technique, showed that a high average integral index of interpersonal dependence was observed in 30% and 52% of the total sample. This indicates a strong need for emotional closeness, acceptance from significant others, a constant feeling of helplessness and fear of being alone, which indicates a high need for support even in stable remission in female drug addicts.

Next, we analyzed the distribution of genetic polymorphisms by the levels of interpersonal dependence among the respondents. The results are presented in Figures 1 and 2.

**Fig. 1.** distribution of polymorphic variants of the COMT gene by levels of interpersonal dependence severity (in mean values).

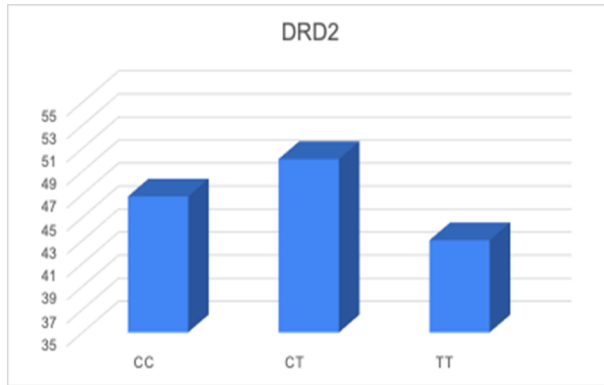


Fig. 2. Distribution of polymorphic variants of the DRD2 gene by levels of severity of interpersonal dependence (in mean values).

The analysis of the evaluation of the differences between the levels of interpersonal dependence in the polymorphic variants of MM and VV of the COMT gene using the Mann-Whitney test revealed statistically significant differences ($p \leq 0.01$). The obtained empirical value of $U_{mp}(68)$ is in the zone of significance (Figure 3).

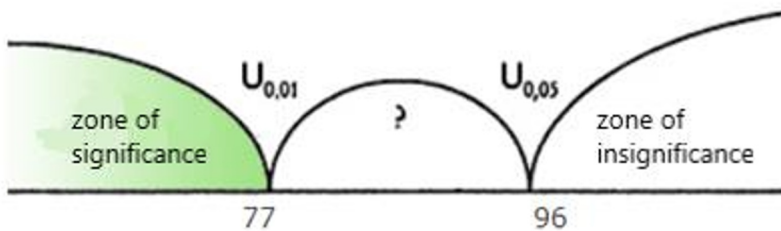


Fig. 3. Significance axis for the differences between the levels of interpersonal dependence in the COMT gene polymorphisms.

As a result of the analysis of differences between the levels of interpersonal dependence expression in the CT and TT genotypes of the DRD2 gene using the Mann-Whitney test, the trend of statistically significant differences ($p \leq 0.05$) was found. The obtained empirical value of $U_{mp}(37)$ is in the zone of uncertainty (Figure 4).

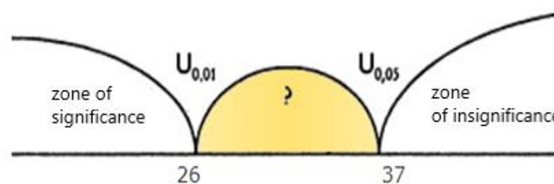


Fig. 4. Significance axis for the differences between the levels of interpersonal dependence in the DRD2 gene polymorphisms.

4 Conclusion

Therefore, the study of a group of drug-dependent women in stable remission led to the following conclusions:

- significant differences were revealed between the expression levels of interpersonal dependence in the VV and VM genotypes of the catechol-O-methyltransferase enzyme (COMT);
- a trend of statistically significant differences between the expression levels of interpersonal dependence was found in the CT and TT genotypes of the DRD2 gene;

The results obtained undoubtedly require further empirical study. In general, referring to the findings of various scientists, the Val/Val genotype of the COMT gene is associated with impaired prefrontal function in the absence of stress. The carriers of this polymorphism show a higher level of verbal aggression, which indirectly, has an overlap with the features characteristic of interpersonal dependence.

In the future, we plan to expand the study with an increase in the number of the sample, as well as adding the contingent of subjects in different stages of remission and their co-dependent relatives. Conducting a comparative analysis of both psychological and psychogenetic features of the respondents.

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