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Genetic Correlates of Behavioral Self-Control: COMT and DRD2 Associations With Self-Regulation, Reflection and Meaningfulness of Life in Women

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Abstract: The objective of our study was to investigate the genetic predictors of self-regulation and related characteristics indicative of a higher level of rational behavior control. The study 107 female participants aged between 22 and 52 years, with an average age of 33.5 years (Russian Federation). In order to measure level of self-regulation and other characteristics corresponding to a higher level of rational behavioral control the following psychological tests were employed: the "Differential Type of Reflection" questionnaire (Leontyev D.A.), the "Style of Self-Regulation of Behavior" questionnaire (Morosanova, Kholopova, 1995), and the Test of Life-Meaning Orientations (D.A. Leontyeva, 1988). Genotyping was use to examine polymorphisms of the COMT, DRD2 genes. Our findings demonstrate significant differences in the level of systemic reflection among carriers of different genotypes of the DRD2 and COMT genes. The highest level of systemic reflection in carriers of the CC genotype for the DRD2 gene and a heterozygous variant of the COMT gene suggests a balance between the elevated dopaminergic activity characteristic of the CC DRD2 genotype and moderate COMT activity, fostering optimal dopamine metabolism.

Keywords: *behavioral self-control, rational behavior, self-regulation, reflection, gene polymorphism, COMT, DRD2, psychogenetics*

Introduction

In today's dynamic world, understanding the genetic factors influencing human self-regulation is essential. Exploring the interplay between personal choices, habits, and the pursuit of rationality has become a focal point of modern society. Codependent behavior, characterized by irrational attitudes, impulsiveness, and reactivity in decision-making (Artemtseva, Malkina, 2022; Faizova, 2020; Stebakova, 2023), can be considered a model behavior for studying rationality and behavioral control. Furthermore, the ability to construct and sustain healthy long-term interpersonal relationships is integral to sustainable behavior (Pardee, 1990).

The semantic content of the term "codependency" has evolved over years of addiction research. Presently, codependency is not only perceived as cohabitation with a dependent person but more broadly as "behavior motivated by dependence on other people" (Barone, Leedom, 2017; Askian, Krauss, Baba et al., 2021; Vederhus, Kristensen, Timko, 2019). Current research, including our own, indicates that women in relationships with or connected to addicts exhibit high levels of anxiety, decreased self-esteem, and a propensity for using pseudo-compensations and psychological defense mechanisms. These factors can impact their adaptive capabilities in conditions of health impairment (Kolenova, Denisova, Kukulyar, Ermakov, 2023; Ismailova, 2020; Tulebaeva, 2020).

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Literature presents some controversy concerning the relationship between self-regulation and codependency. Medvedeva O.L.'s (2020) research discovered a negative relationship between self-regulation and mental health participants with low emotional intelligence, lacking experience as mental health professionals. This negative correlation extended to emotional intelligence. Krasnyatova Yu.A. and Stoyanova I.Ya. (2018) identified a negative relationship between self-regulation and codependency in women. Kupchenko V.E. (2020) demonstrated that mothers of chemical addicts with moderate codependency exhibit higher self-control compared to those with severe codependency. The level of codependency in individuals associated with substance users hinges on their ability to effectively regulate emotions (Berdichevsky, Padun, Gagarina, Arkhipova, 2021).

The field of behavioral genetics recognizes that genetic factors may underlie individual differences in self-regulation, including stress responses and the ability to regulate emotions, maintain internal balance, and make rational choices effectively. In psychogenetic research, significant attention is directed towards genes within neurotransmitter systems, particularly the dopaminergic system responsible for endogenous reinforcement of behavior. Studies have demonstrated that the DRD4 gene, regulating dopamine receptors, is associated with interest in social stimuli, impacting attention to social events and sensitivity to social rewards (Golimbet et al., 2005). Associations of the DRD2 gene have been identified with various aspects of cognitive abilities, such as long-term memory, attention, and information processing (Li, Bäckman, Persson, 2019). Variations in genes linked to the serotonin system, like 5-HTTLPR, may influence social sensitivity and responses to stressful situations (Alfimova et al., 2017; Kosonogov et al., 2018). Genes regulating monoamine catabolism, such as MAOA and COMT, are linked to the level of cognitive decline. Variants of these genes influence individual sensitivity to neurotransmitters and impact a range of cognitive processes, including emotional and executive functions (Mueller et al., 2014; Cha et al., 2022).

In summary, despite increasing interest, a comprehensive theory on the psychological and genetic factors shaping sustainable behavior remains elusive. Our study aims to explore the genetic predictors of self-regulation and related characteristics indicative of a higher level of rational behavior control.

Materials and Methods

Participants

The study involved 107 female participants aged between 22 and 52 years, with an average age of 33.5 years. Among them, 60 women aged 22 to 52 years (average age 35.3 years) were included, all of whom were either in a relationship or had a connection with an individual struggling with addiction, including alcoholism, drug addiction, or non-chemical addictions.

Research methods

In order to study the self-regulation, reflection, and the meaningfulness of life, the following psychological tests were employed: the "Differential Type of Reflection" questionnaire (Leontyev D.A.), the "Style of Self-Regulation of Behavior" questionnaire (Morosanova, Kholopova, 1995), and the Test of Life-Meaning Orientations (D.A. Leontyev, 1988).

Genetic predictors were examined using the method of molecular genetic analysis, considering the genotypes of the dopamine receptor DRD2 (rs1800497) and the COMT enzyme gene (Val158Met) as candidate genes. Genetic material (buccal epithelium) was collected from participants immediately after the completion of psychological diagnostics, primarily in the first half of the day. DNA analysis employed allele-specific polymerase chain reaction (PCR) with real-time detection.

Procedure

The study was conducted in person in online format from September 13, 2022, to March 20, 2023. The participation of respondents was voluntary. Prior to the study, goals of the study was explained to the respondents. Personal data has been anonymized.

Statistical data analysis

Statistical analysis involved the use of the Shapiro-Wilk test to assess normal distribution. Differences among subgroups were examined through ANOVA analysis of variance, with pairwise comparisons conducted using Dunn’s method as a post hoc analysis. The JASP 0.16 software package was utilized for statistical processing.

Results

At the initial stage of data analysis, the percentage distribution of various genotypes in the sample was computed (Table 1).

Table 1. Quantitative distribution of the representation of various genotypes of the COMT and DRD2 genes

Genotypes N		Entire sample (N=107)		Codependents (N = 60)		Control group (N=47)	
		Percent	N	Percent	N	Percent	
COMT	MM	31	29%	15	25%	16	34%
	VM	50	47%	31	52%	19	40%
	VV	26	24%	14	23%	12	26%
DRD2	CC	63	59%	31	52%	32	68%
	CT	40	37%	26	43%	14	30%
	TT	4	3,5%	3	5%	1	2%

For the COMT gene, the sample revealed the smallest number of carriers of the homozygous variant MM (29%) and the largest number of carriers of the heterozygous variant VM (47%). No deviations from the Hardy-Weinberg equilibrium were detected. Concerning the DRD2 gene, the majority of the sample consisted of CC homozygotes (59%), CT heterozygotes accounted for 37%, and TT homozygotes represented only 4 people (3.5%). Analyzing genotype distribution between the control and experimental groups, it was observed that the number of MM homozygotes for the COMT gene was higher in the control group, while VM heterozygotes were more prevalent in the group of women in a relationship or related to an addict. For the DRD2 gene, a slightly higher percentage of CC homozygotes was noted in the control group, and CT heterozygotes were more prominent in the codependent group. However, no significant differences in the representation of different genotypes between the groups were detected.

Table 2. ANOVA Results

Depended variable	Factors	Sum of Squares	Mean Square	**F**	**p**	**η²**
General level of self-regulation	DRD2	5.733	5.733	0.046	0.831	4.501e-4
	COMT	376.119	188.059	1.505	0.227	0.030
	DRD2 ✻ COMT	239.255	119.628	0.958	0.387	0.019
	Residuals	12116.796	124.915			
Systemic reflection	DRD2	6.019	6.019	0.279	0.598	0.003
	COMT	23.422	11.711	0.543	0.583	0.010
	DRD2 ✻ COMT	213.429	106.715	4.949	0.009	0.091
	Residuals	2091.467	21.562			
Meaningfulness of Life	DRD2	1140.345	1140.345	3.462	0.066	0.035
	COMT	825.431	412.715	1.253	0.291	0.025
	DRD2 ✻ COMT	1155.676	577.838	1.754	0.179	0.036
	Residuals	29314.376	329.375			

To examine the significance of the effect of the genotypes of the studied genes and their interactions on the level of self-regulation and other characteristics corresponding to a higher level of rational behavioral control, an ANOVA analysis of variance was conducted (Table 2). Since no significant differences in genotype representation were found in the control and experimental groups, ANOVA was carried out on the entire sample, without dividing into subgroups. Additionally, carriers of the TT genotype for the DRD2 gene were excluded from further analysis due to their small number.

The obtained effects can be visually represented as shown in Figure 1.

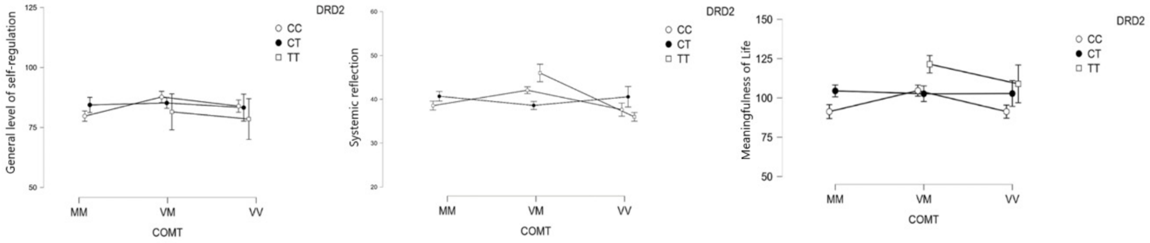

Figure 1. Graphic display of the levels of the studied variables in subgroups of carriers of different COMT and DRD2 genotypes

The obtained results reveal a significant average effect in the interaction between DRD2 ✻ COMT genes and the level of systemic reflection (f = 4.9, p = 0.009, $\eta^2 = 0.091$). Specifically, carriers of the CC genotype for the DRD2 gene and the VM genotype for the COMT gene exhibit the highest level of systemic reflection (average score of 87.72 points), while the lowest level (average score of 79 points) was observed in carriers of the COMT MM and DRD2 CC genotypes. Additionally, small effects, as indicated by eta-square values, were observed between the level of meaningfulness of life and the genotypes of the DRD2 gene ($\eta^2 = 0.035$), genotypes of the COMT gene ($\eta^2 = 0.025$), and the interaction DRD2 ✻ COMT ($\boldsymbol{\eta^2} = 0.036$). Concerning the general level of self-regulation, a small effect was noted for COMT gene genotypes ($\boldsymbol{\eta^2} = 0.030$).

Discussions

The described results of the study revealed significant differences in the level of systemic reflection among carriers of different genotypes of the DRD2 and COMT genes. Consistent with existing literature, these genes are associated with various aspects of behavior and cognitive function. Individuals with the CC genotype may exhibit more pronounced dopamine receptor activity, linked to characteristics such as increased speed of information processing and behavioral reactivity (Li, Bäckman, Persson, 2019). The COMT gene, responsible for catecholamine metabolism, including dopamine, displays different variants (VV, VM, and MM genotypes) reflecting enzyme activity levels. Carriers of the VM genotype, with intermediate enzyme activity, may demonstrate greater variability in regulation, including enhanced emotional and executive functions, contributing to more efficient neurotransmitter pathways (Mueller et al., 2014; Cha et al., 2022). The highest level of systemic reflection in carriers of the CC genotype for the DRD2 gene and a heterozygous variant of the COMT gene suggests a balance between the elevated dopaminergic activity characteristic of the CC DRD2 genotype and moderate COMT activity, fostering optimal dopamine metabolism. This reveals potential interpretations for the functioning of the brain's reinforcement system in consolidating dysfunctional behavioral patterns. The heightened dopaminergic activity associated with the CC genotype of the DRD2 gene may contribute to reinforcing specific behavioral responses, potentially amplifying reactivity and influencing information processing. This increased reinforcement could perpetuate and solidify certain dysfunctional patterns in behavior. Moreover, the interplay with the COMT gene, particularly in individuals with the VM genotype, introduces an intriguing dimension. The intermediate enzyme activity associated with the VM genotype might contribute to a nuanced balance in dopamine metabolism. This equilibrium could affect the reinforcement dynamics, potentially influencing the persistence of specific behavioral patterns. Further investigation into these potential interpretations is warranted to unravel the complex relationship between genetic factors, brain function, and behavioral outcomes.

Conclusions

The objective of this study was to explore the genetic predictors of self-regulation and related characteristics indicative of a higher level of rational behavior control.

This study aimed to identify genetic predictors of self-regulation and related characteristics indicative of a higher level of rational behavior control. The selected candidate genes were from the dopaminergic system, specifically the dopamine receptor type 2 gene DRD2 (polymorphic locus rs1800497) and the COMT enzyme gene (polymorphic locus Val158Met). The findings indicate significant differences in the level of systemic reflection among carriers of different genotypes of the DRD2 and COMT genes. Notably, carriers of the CC genotype for the DRD2 gene and a heterozygous variant of the COMT gene exhibited the highest level of systemic reflection.

While these findings contribute valuable insights into the genetic correlates of self-regulation, reflection, and meaningfulness of life, several limitations should be acknowledged. Firstly, the sample size of 107 participants, though providing meaningful data, might limit the generalizability of the findings. Secondly, the choice of candidate genes was based on the dopaminergic system, excluding potential influences from other genetic factors. Future research incorporating a broader range of genes could offer a more comprehensive understanding of the genetic underpinnings of behavioral self-control.

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Conflict of interests

The authors declare no conflict of interest.

Author Contributions

Conceptualization – P.N.E. and A.S.K.; Data curation – E.G.D.; Formal Analysis – E.G.D. and A.S.K.; Investigation – E.G.D., A.S.K. and A.M.K.; Methodology – E.G.D. and A.S.K.; Project administration – P.N.E.; Software – E.G.D.; Supervision – A.S.K.; Validation – E.G.D. and A.S.K.; Visualization – E.G.D. and A.M.K.; Writing – original draft – E.G.D., A.S.K. and A.M.K.; Writing – review & editing – P.N.E., E.G.D., A.S.K. and A.M.K. All authors have read and agreed to the published version of the manuscript.

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