

ORIGINAL RESEARCH ARTICLE

Exploring the role of genetic factors in
personality disorders among women with
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Abstract

Heroin dependence is a severe psychiatric issue that often coexists with mood disorders and personality disorders, which further compound the complexity and severity of the dependence. The utilization of genetic factors in predicting psychiatric disorders has made notable advancements. We enrolled female patients diagnosed with heroin dependence ($n = 263$) and assessed individuals with paranoid personality disorder, depressive personality disorder, antisocial personality disorder, and schizoid personality disorder based on the DSM-IV criteria. Our objective was to examine the single nucleotide polymorphisms (SNPs; rs174696, rs174699, rs4680, rs4818, rs737866, rs933271, rs12953076, and rs44458044) and their association with personality. We discovered a significant association of antisocial personality disorder with rs1544325, rs4680, and rs4818 ($P < 0.05$). Additionally, hallucinogen use was associated with rs3792738 ($P < 0.05$), rs10062367 ($P < 0.05$), and rs1875999 ($P < 0.01$). However, we did not observe a relationship between the SNPs and schizoid personality disorder, paranoid personality disorder, or depressive personality disorder. Heroin dependence is linked to specific personality disorders, particularly antisocial personality disorder. The influence of genetic factors could have a significant impact on the emergence of personality alterations linked to the consumption of heroin.

Keywords: Heroin dependence; Heroin dependence treatment; Drug addiction; Psychotic disorder; Personality disorder; Hallucinogen use; Antisocial personality disorder

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1. Introduction

The abuse or dependence on heroin is a widespread and frequently encountered issue,¹ and it associated with negative mood states,² cardiovascular problems,³ poor oral health,⁴ cognitive impairment,⁵ accelerated aging,⁶ impulsivity,⁷ experimentally-induced aggressiveness,⁸ and impaired behavior.⁹ The health-related quality of life is negatively impacted in Asian individuals who use heroin and report experiencing psychopathological symptoms.¹⁰

The consumption of heroin can potentially lead to alterations in one's personality, while individuals with specific personality traits such as positive urgency¹¹ may be inclined to engage in heroin use. Individuals possessing positive urgency may have a higher likelihood

of engaging in heroin use, which could potentially result in alterations to their personality. The clinical manifestation of addiction primarily revolves around mood and impulse-control dysregulation¹² while heroin dependence has a negative effect on impulse control.¹³ People with specific personality characteristics, such as a tendency for risk-taking behaviors, may demonstrate a predisposition towards heroin use. For instance, a prior study¹⁴ indicated that antisocial personality disorder was the only domain where a cumulative risk was observed for heroin overdose. Antisocial personality disorder is frequently identified as the predominant comorbid diagnosis among individuals with substance abuse issues.^{15,16} Furthermore, it is crucial to emphasize that an individual's personality traits may influence their preference for a particular drug. A previous study¹⁷ has identified a specific externalizing dimension that distinguishes heroin users from those who use alcohol, marijuana, and cocaine. This suggests that certain personality traits may be associated with a higher likelihood of choosing heroin over other substances. Nevertheless, it remains uncertain which specific personality traits have an impact on the preference for heroin over other substances. Furthermore, the use of heroin may be linked to several personality disorders, such as schizoid, depressive, and paranoid personalities. Schizoid and depressive personality disorders have been found to be associated with feelings of loneliness, and individuals experiencing loneliness may turn to drug use as a way to cope with its impact. Drugs can temporarily alleviate negative emotions, provide a sense of euphoria, or serve as a distraction from feelings of loneliness. However, using drugs as a coping mechanism for loneliness is problematic and can lead to a vicious cycle. Drug use can exacerbate symptoms of depression and anxiety, impair social functioning, and further isolate individuals from supportive relationships. It can also lead to the development of substance use disorders, which can further worsen their overall well-being.

Moreover, previous research findings have demonstrated that combining personality traits with demographic information enables the prediction of drug consumption.¹⁸ However, the relationship between specific personality disorders and heroin abuse remains uncertain, as does the association between genetic factors and heroin abuse. While the influence of genetics on personality variations is well recognized, our understanding of the precise mechanisms involved is limited.¹⁹ Moreover, the identification of common genetic associations among co-occurring addiction disorders in this patient population has the potential to open up new avenues for treatment. This could involve pinpointing specific gene biomarkers in individuals with genetic susceptibility.²⁰ A prior investigation²¹ explored the potential links between the dopamine D2 receptor and

characteristics of individuals with heroin dependence. In comparison to control subjects, the individuals with heroin dependence exhibited elevated scores for personality traits related to novelty seeking and harm avoidance. In addition, a variation in the gene responsible for producing catechol-O-methyltransferase (*COMT*) has been demonstrated to impact human executive cognition and the functioning of the prefrontal cortex and this influence is likely due to its effect on prefrontal dopamine signaling.²² Moreover, the *COMT* gene can play a role in personality traits.²³ Certain variations (polymorphisms) of the *COMT* gene can result in different levels of enzyme activity, leading to variations in dopamine regulation.

Collectively, our goal was to investigate single nucleotide polymorphisms (SNPs) of *COMT* and those related to stress, as well as their relationship with personality disorders among women with heroin dependence.

2. Methods

The study protocol was authorized by the review boards at the Shanghai Mental Health Center (SHMC), School of Medicine, Shanghai Jiao Tong University. The research adhered to the principles outlined in the Declaration of Helsinki. All patients gave their informed consent, prior to participating in the study. Furthermore, meticulous records were kept to document the number of interviews conducted with each patient for precise record-keeping. The frequency of employment is depicted in Figure 1.

2.1. Measures

2.1.1. Demographic information and heroin use

The demographic information collected encompassed age, gender, education (categorized as completion of

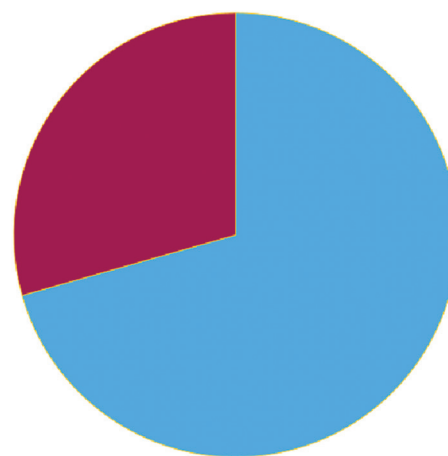


Figure 1. Distribution of employment status among study subjects. Blue part denotes unemployed ($n = 185$, 70.3%), whereas as red part represents employed ($n = 77$, 29.3%)

secondary school or not), marital status (married or not), and employment status (employed or unemployed). Participants in this study were individuals who met the definition of drug dependence, which refer to individuals who have relapsed to drug use after being initially identified as drug users by the public security system. Hence, all participants had experienced at least one relapse when they were enrolled in the compulsory rehabilitation centers at the beginning of the study. The participants were in a state of abstinence.

2.1.2. Participants

We initially enrolled approximately 564 participants from four drug rehabilitation centers in Shanghai. Subsequently, we narrowed down the inclusion criteria to exclusively include female participants ($n = 263$). Patients needed to meet criteria for heroin dependence according to the fourth edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV): Age over 18 years old, and had a heroin use history in the 30 days before the compulsory rehabilitation. Each participant in the rehabilitation program underwent a face-to-face interview within the initial month. The interviews were scheduled to take place in a comfortable environment with the intention of putting the participants at ease. Initial heroin use data was collected through self-report. Participants in the study belonged to the Han Chinese ethnic group, according to their national identity card. The study specifically focused on females, and their average age of first drug use was 21.79 years. Out of the total sample size, 28 individuals reported having used hallucinogens.

Inclusion criteria included: being 18 years or older, resident of Shanghai, meeting the criteria for heroin dependence according to the DSM-IV, having abstained from heroin for a period of 1 – 30 days prior to enrollment, being put in compulsory detoxification institutions for <1 year, and not receiving any medical treatments at the time of survey. Participants were excluded if they met the DSM-IV criteria for other axis I psychiatric disorders or if they used substances other than heroin. Urine and blood samples were collected and screened for illicit drugs. Additionally, potential subjects were informed that they had the option to decline participation or withdraw from the study at any time. Every patient underwent a mandatory, standardized rehabilitation program. This program consisted of daily exercise and educational sessions focused on preventing relapse.

2.2. SNPs genotyping

An examination was conducted to investigate the SNPs of *COMT* and those related to stress, including rs174696, rs174699, rs4680, rs4818, rs737866, rs933271, rs12953076, and rs44458044.

Genomic DNA was extracted from lymphocytes.

Based on data from the HAPMAP database for Beijing Han Chinese, it was observed that the *CRH* genes demonstrated a relatively conservative pattern without polymorphism distribution in the Chinese population. Therefore, the focus of the research shifted to the *CRH* receptor 1 (*CRHR1*) and *CRH*-binding protein (*CRHBP*). Through screening of the *CRHR1* and *CRHBP* genes, as well as the upstream region within a 10 KB range satisfying the criteria of $r^2 > 0.8$ and minor allele frequency (MAF) >10%, specific SNPs (*CRHR1*: rs12953076, rs4458044, rs242924, rs17689966; *CRHBP*: rs1715751, rs3792738, rs32897, rs10062367, rs1875999) were selected. The genotyping of these SNPs was performed using the ABI Prism 7900 sequence detection system. The TaqMan SNP genotyping assay, a well-established and dependable technique in genetic analysis, was employed to conduct the genotyping of genes.

2.3. Statistical analysis

Demographic data including age, gender, education (completed secondary school or not), marriage status (married or not), and employment (employed or unemployed) were gathered. The association between SNPs and personality traits was examined by utilizing Chi-square test (Table 1). Statistical Package for the Social Sciences (SPSS) version 24 was used to conduct statistical analysis.

Missing categorical variables such as genetic variables were replaced with mode of the value while missing non-categorical values were replaced with the mean value. Spearman correlation or Pearson correlation were applied according to normality of the parameters. The selected threshold for the *P*-value was set at 0.05. In addition, we computed the effect size by utilizing Cramer's V as a measure. The Cramer's V value is presented in Table 1.

3. Results

Overall, no significant relationship was found between personality disorders (paranoid personality disorder, depressive personality disorder, and schizotypal personality disorder) and the SNPs of *COMT* gene and those associated with stress. Only antisocial personality disorder was found to be associated with several SNPs, such as rs1544325, rs4680, rs4818, and rs242924 (all $P < 0.05$). Furthermore, hallucinogen use was associated with rs3792738 ($P < 0.05$), rs10062367 ($P < 0.05$), and rs1875999 ($P < 0.01$) (Table 1).

After conducting correlation tests, we discovered that there is only a weak correlation between certain personality disorders. No significant correlation was found between antisocial personality disorder, schizoid personality disorder, and depressive personality disorder

Table 1. Personality disorders and genetic parameters

	Paranoid personality disorder	Depressive personality disorder	Antisocial personality disorder	Schizotypal personality disorder	Hallucinogen use	Alcohol use
rs1544325	$P > 0.05$	$P > 0.05$	$P < 0.05$; χ^2 : 12.082 ϕ : 0.131	$P > 0.05$	$P > 0.05$	$P > 0.05$
rs174696	$P > 0.05$	$P > 0.05$	$P > 0.05$	$P > 0.05$	$P > 0.05$	$P > 0.05$
rs4680	$P > 0.05$	$P > 0.05$	$P < 0.05$; χ^2 : 10.460 ϕ : 0.124	$P > 0.05$	$P > 0.05$	$P > 0.05$
rs4818	$P > 0.05$	$P > 0.05$	$P < 0.05$; χ^2 : 9.601 ϕ : 0.117	$P > 0.05$	$P > 0.05$	$P > 0.05$
rs933271	$P > 0.05$	$P > 0.05$	$P > 0.05$	$P > 0.05$	$P > 0.05$	$P > 0.05$
rs737866	$P > 0.05$	$P > 0.05$	$P > 0.05$	$P > 0.05$	$P > 0.05$	$P > 0.05$
rs12953076	$P > 0.05$	$P > 0.05$	$P > 0.05$	$P > 0.05$	$P > 0.05$	$P > 0.05$
rs4458044	$P > 0.05$	$P > 0.05$	$P > 0.05$	$P > 0.05$	$P > 0.05$	$P > 0.05$
rs242924	$P > 0.05$	$P > 0.05$	$P < 0.05$; χ^2 : 9.202 ϕ : 0.112	$P > 0.05$	$P > 0.05$	$P > 0.05$
rs17689966	$P > 0.05$	$P > 0.05$	$P > 0.05$	$P > 0.05$	$P > 0.05$	$P > 0.05$
rs3792738	$P > 0.05$	$P > 0.05$	$P > 0.05$	$P > 0.05$	$P < 0.05$; χ^2 : 7.875 ϕ : 0.104	$P > 0.05$
rs1715751	$P > 0.05$	$P > 0.05$	$P > 0.05$	$P > 0.05$	$P > 0.05$	$P > 0.05$
rs32897	$P > 0.05$	$P > 0.05$	$P > 0.05$	$P > 0.05$	$P > 0.05$	$P > 0.05$
rs10062367	$P > 0.05$	$P > 0.05$	$P > 0.05$	$P > 0.05$	$P < 0.05$; χ^2 : 9.342 ϕ : 0.113	$P > 0.05$
rs1875999	$P > 0.05$	$P > 0.05$	$P > 0.05$	$P > 0.05$	$P < 0.01$; χ^2 : 13.147 ϕ : 0.135	$P > 0.05$

($P > 0.05$). However, a correlation was observed between antisocial personality disorder and schizotypal personality disorder ($P < 0.05$, $r = 0.150$) as well as between antisocial personality disorder and paranoid personality disorder ($P < 0.01$, $r = 0.187$).

After controlling for the impact of schizoid personality disorder, a weak but significant correlation ($P < 0.05$, $r = 0.124$) was found between depressive and paranoid personality disorder. However, when also considering the influence of antisocial personality disorder in addition to schizoid, the correlation between depressive and paranoid personality disorder was not found to be significant ($P > 0.05$). Figure 2 presents a visual summary or overview of this work.

4. Discussion

The main findings of the study indicated that specific personality disorders may be associated with genetic factors

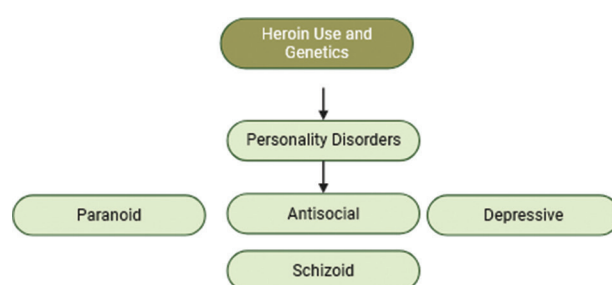


Figure 2. A summary of the main subjects overviewed in the current work

related to stress and *COMT*. Our analysis revealed a significant association between antisocial personality disorder and the following SNPs: rs1544325 (χ^2 : 12.082), rs4680 (χ^2 : 10.460), rs4818 (χ^2 : 9.601), and rs242924 (χ^2 : 9.202).

Furthermore, hallucinogen use was associated with rs3792738 ($P < 0.05$), rs10062367 ($P < 0.05$), and rs1875999

($P < 0.01$). The strongest effect size among the variables investigated was observed in the association between hallucinogen use and a specific SNP (rs1875999).

Genetic factors were not found to be linked with other investigated personality disorders (paranoid personality disorder, depressive personality disorder, and schizotypal personality disorder). Moreover, our analysis did not reveal any significant associations between alcohol use and the SNPs under investigation.

Our findings provide an explanation for the relationship between heroin use and personality changes observed in certain individuals. Genetic factors (e.g., *COMT*) are likely to play a role in explaining this relationship. Our study uncovered a significant association of certain SNPs of *COMT* and those related to stress with the presence of antisocial personality disorder and hallucinogen use. The majority of the pertinent factors were found to be associated with *COMT*. Variations in the *COMT* gene have been associated with differences in cognitive functions,²⁴ emotional processing,²⁵ and stress response. Hence, it could be associated with specific personality disorders.

Based on the literature on heroin dependence, numerous factors such as epigenetics, genetics, environmental, treatment-related factors (e.g., duration of drug use), culture, and age are potential confounding variables.

4.1. Confounding factors related to heroin dependence and personality disorders

The diagnosis of psychiatric disorders, such as heroin dependence, can be subject to variations as different clinicians may approach the diagnosis in diverse ways. In heroin dependence studies, a diverse range of variables, such as age, epigenetic factors and psychological factors, that can introduce confusion or distortion were encountered. For instance, heroin dependence could be linked to particular personality disorders, whereas the etiology of schizoid personality disorder is associated with a combination of intrapsychic, cultural, and ethnic factors.²⁶ The rate of heroin use among women is growing at a faster pace compared to men (Marsh, Park, Lin, and Bersamira, 2018). Moreover, a previous study reports how these two facets of impulsiveness could be associated with different aspects of heroin dependence.²⁷

The prevalence of antisocial personality disorder decreases with age.²⁸ Therefore, age is also one of the major confounding factors in this study. Moreover, the concurrent use of multiple substances, including alcohol and hallucinogens, represents a significant confounding factor in this context.

The inclination for novelty seeking poses a risk factor for developing drug addiction, and the presence

of immature character traits and personality disorders heightens the vulnerability to substance abuse.²⁹ Novelty seeking is influenced by certain genetic factors³⁰ and is related to certain personality characteristics.³¹ Hence, novelty seeking represents a significant influencing factor.

Based on the self-medication hypothesis, the preferences for specific substances are impacted by attachment.³² Therefore, family environment may be one of the major confounding factors, along with cultural factors related to family environment. Stimulants like heroin may give the addicted individuals, particularly teenagers, a sense of liberating themselves from parental control. Moreover, in our study, it is important to consider that Chinese culture showcases nuances compared to other cultures.

A significant portion of patients dependent on heroin reported experiencing inadequate sleep quality,³³ while a lack of sleep may be related to personality parameters.³⁴ Furthermore, sufficient sleep plays a critical role in promoting optimal emotional functioning.³⁴ Therefore, sleep quality is also one of the potential confounding factors in this study. In our study, it is important to note that sleep quality was not recorded, and this omission may represent a potential confounding factor in the study.

Taken together, the diagnosis of psychiatric disorders, including heroin dependence, can vary due to the diverse approaches taken by different clinicians. Various variables analyzed in studies on heroin dependence can introduce confusion or distortion, including age, sleep, duration of drug use, environmental factors, novelty seeking, genetic factors, epigenetic factors, cultural, and psychological factors.

4.2. Heroin and hallucinogen

There is limited literature available that explores the comorbidity between heroin use and hallucinogen use. Hallucinogen use has been associated with the development of psychotic symptoms. The use of hallucinogens has the potential to elicit positive symptoms similar to those observed in schizophrenia. A strong dependence on psychostimulants is linked to an increased risk of psychosis, whereas severe dependence on heroin exhibits a contrasting negative association with psychosis.³⁵

Moreover, genetics plays a crucial role in both personality disorders and individual responses to hallucinogen use.

Studies investigating the utilization of hallucinogens have uncovered both potential advantages and potential drawbacks linked to their use. The immediate effects of hallucinogen use can have a significant impact, causing disorientation, cognitive difficulties, and potentially inducing changes in perception.³⁶

Moreover, individuals with nonaffective psychosis are at increased risk of heroin.³⁷ As a result, the use of hallucinogens may influence the probability of heroin use. According to the Swedish system for substance use, all the studied substances are linked to increased risk of psychosis.³⁸ However, the literature on the heroin use and risk of psychosis is controversial.

Another research paper investigated the usage patterns of heroin and delved into a longitudinal study assessing the outcomes of treatment for heroin dependence. Notably, the study highlights the substantial prevalence of psychiatric comorbidities within this population, including a lifetime occurrence of 37% for post-traumatic stress disorder, 23% for major depression, 75% for anti-social personality disorder, and 51% for borderline personality disorder.³⁹

The precise mechanism by which hallucinogens influence genetic factors remains uncertain. One animal study provided the initial evidence showing that the administration of a low dose of d-LSD, which has significant behavioral implications, leads to the immediate activation of c-Fos gene in specific regions of the rat forebrain.⁴⁰

In our study, hallucinogen use was associated with rs3792738 ($P < 0.05$), rs10062367 ($P < 0.05$), and rs1875999 ($P < 0.01$). Further research is needed to expand our understanding of the complex relationship between heroin use, hallucinogen use, genetic factors, and psychiatric comorbidity.

4.3. Genetics and personality disorder

Genetic studies indicate that personality disorders classified under DSM-IV axis II exhibit a moderate level of heritability.⁴¹ The heritability of addictions falls within a moderate-to-high range, which presents a paradox since these disorders involve substance use, which is influenced by genetic and environmental factors.⁴² Another study proposes that individuals with more impulsive behavior may have an increased risk for substance use disorders due to a reduced expression of the gene responsible for encoding the 5-HTT transporter, which can be attributed to the “S” promoter polymorphism.⁴³

Numerous individuals are exposed to addictive substances during pain treatment, yet the majority do not develop addiction, despite experiencing temporary tolerance and dependence. The likelihood of initial substance use and the development of pathological usage patterns are influenced by inherent factors such as genotype, gender, preexisting addictive disorders, or other mental illnesses.⁴⁴ To mitigate the influence of gender, we incorporated exclusively female participants in this study.

Another study discovered a positive association between prior hallucinogen use and specific traits related to seeking new sensations, impulsive behavior, and challenges in regulating emotions among adolescents who were hospitalized for treatment.³⁶ It is important for clinicians to recognize the prevalence of hallucinogen use and the increased likelihood of encountering mental health problems among individuals who engage in such use.⁴⁵ The existing body of literature has outlined the current understanding of the molecular genetic responses occurring in the brain in response to psychedelics, and has explored how changes in gene expression can potentially lead to modified cellular physiology and behaviors.⁴⁶

The *COMT* enzyme is responsible for the breakdown of dopamine and other catechols.⁴⁷ Comorbid substance use in individuals with schizophrenia was found to be linked to genetic variations in genes associated with dopaminergic neurotransmitter systems.⁴⁸ Furthermore, numerous studies have shown that *COMT* gene variants are associated with personality traits.⁴⁹ Moreover, a previous study demonstrated that in individuals with substance use disorder, the activity of soluble *COMT* was found to be correlated with the severity of drug dependence. Additionally, it was associated with factors related to impulsivity (self-control and non-planning).⁵⁰

Our study uncovered a significant association between certain genetic factors related to *COMT* and stress and the presence of antisocial personality disorder. The majority of the pertinent factors were found to be associated with *COMT*.

4.3.1. Schizoid personality disorder, genetics and heroin use

Schizoid personality disorder is one of the “cluster A” personality disorders.⁵¹ Individuals with schizoid personality disorder may be at an increased risk for developing addictive behaviors as a means of coping with their emotional detachment and social isolation. The tendency to experience limited emotional range and difficulty forming meaningful connections can lead to a reliance on substances or addictive behaviors, a way to alleviate feelings of emptiness or numbness.

Overall, our study revealed no significant association between schizotypal personality disorder and investigated genetic factors (e.g., *COMT*) in female individuals with heroin dependence.

4.3.2. Paranoid personality disorder

When examining the relationship between paranoid personality disorder and heroin use, it is important to consider the potential implications and interactions. While

research specifically focusing on paranoid personality and heroin comorbidity is limited, there are several factors to consider. Paranoia can be associated with certain substance abuses, such as the use of cocaine⁵² and methamphetamine.⁵³ However, the literature on paranoid personality disorder and heroin use is limited.

Additionally, we observed no association between genetic factors and paranoid personality disorder in females with heroin dependence.

4.3.3. Antisocial personality disorder and heroin

A previous study claimed that heroin dependence is in high degree in comorbidity with antisocial personality disorder.⁵⁴ Antisocial personality disorder is a personality disorder characterized by a pervasive pattern of disregard for and violation of the rights of others. Heroin dependence, on the other hand, is a substance use disorder involving a compulsive and harmful dependence on heroin.

Antisocial personality disorder and heroin dependence are two distinct yet interconnected mental health conditions that can significantly impact an individual's quality of life.⁵⁵ Another study found that psychopathy may exacerbate decision-making deficits in heroin dependent individuals.⁵⁶ The association between 5-HTTVNTR and DATVNTR interactions may be linked to the co-occurrence of antisocial personality disorder in male patients dependent on heroin.⁵⁷

Antisocial personality disorder is associated with increased psychiatric problems⁵⁸ and criminal activities.⁵⁹ Hence, it is crucial to comprehend the interconnection between heroin use and crime, as well as the causal relationship between the two.

Overall, we found that antisocial personality disorder is associated with following SNPs: rs1544325 (χ^2 : 12.082), rs4680 (χ^2 : 10.460), rs4818 (χ^2 : 9.601), and rs242924 (χ^2 : 9.202). Additionally, rs242924 is related to corticotropin-releasing hormone, a neuropeptide that plays a crucial role in response to stress.⁶⁰

In addition, a previous study offers additional evidence supporting the involvement of the *COMT* gene as a modifier that influences the variation between individuals in their inclination towards violent behavior, specifically in subjects without significant mental disorders.⁶¹ Moreover, the role of *COMT* is to facilitate the breakdown of catecholamines-like dopamine.⁶² The chronic use of addictive drugs (e.g., heroin) can lead to a reduction in the expression of dopamine receptors in the brain.⁶³ Moreover, the hyperreactivity of the dopaminergic reward system at the neurochemical and neurophysiological levels can serve

as a neural basis for impulsive-antisocial behavior and substance abuse in individuals with psychopathy.⁶⁴ The *COMT* gene's impact on dopamine mechanism can have implications for antisocial personality traits, potentially accounting for notable differences observed among individuals with different *COMT* variants.

4.3.4. Depressive personality disorder

The literature is scarce on the relationship depressive personality disorder and genetics in individuals with heroin dependence. Patients with personality disorders had a higher frequency of previous depressive episodes.⁶⁵ Depression increases the risk of developing substance use disorders.⁶⁶ Furthermore, a previous study claimed that in heroin-dependent individuals, higher levels of depression was correlated with higher levels of psychoticism and neuroticism.⁶⁷

While there is limited research specifically examining the relationship between depressive personality disorder and heroin dependence, there are some connections between the two considering self-medication hypothesis and vulnerability to addiction. In general, our research revealed no significant genetic factors (e.g., *COMT*) associated with depressive personality disorder.

The current literature lacks sufficient evidence on the relationship between depressive personality disorder and genetics in heroin-dependent individuals. However, patients with personality disorders have been found to have a higher frequency of previous depressive episodes, and depression itself has been linked to an increased risk of developing substance use disorders.

5. Conclusion

In individuals with heroin dependence, *COMT* SNPs are associated with the development of personality changes, including antisocial personality disorder. Genetic factors, however, were not found to be linked with other personality disorders, such as paranoid personality disorder, depressive personality disorder, and schizotypal personality disorder, under investigation.

5.1. Limitations

The current study has several significant methodological limitations. Firstly, due to its cross-sectional nature, it is challenging to determine the temporal sequence between the variables. Consequently, we cannot establish whether the variables preceded or followed the symptoms.

Moreover, a substantial portion of the data relied on self-reported measures (personality scale results), which introduce a risk of biased self-presentation. It is important to acknowledge that personality is a complex construct,

whose characterization extends beyond the limitations of scales and categories.

The research findings highlighted a notable prevalence of concurrent multiple drug use among patients. Furthermore, the inclusion of smokers among the participants may have influenced the study outcomes. Moreover, it is crucial to recognize that studies focusing on substance abuse cannot be easily generalized to individuals specifically dependent on heroin. The manner in which personality disorders are conceptualized could also impact our findings.⁶⁸

Experimental validation has consistently confirmed various personality traits among individuals with heroin dependence. Nonetheless, it remains difficult to determine whether these characteristics represent an inherent “addictive personality” that predated drug use, or if they are a result of drug addiction.⁶⁹ One of the limitations of the current study is the absence of a control group.

5.2. Suggestions for further studies

Conducting prospective studies will help to further explore the relationship between drug use, genetic factors, personality disorder, and outcomes.

Furthermore, personality studies can be complemented and supported by brain imaging findings. The amalgamation of investigating genetic factors can offer valuable insights into the intricate connection between personality disorders and heroin dependence.

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Conflict of interest

The authors declare that they have no competing interests.

Author contributions

Conceptualization: Kadir Uludag

Formal analysis: Kadir Uludag

Investigation: Kadir Uludag

Methodology: Kadir Uludag

Writing – original draft: Kadir Uludag

Writing – review & editing: All authors

Ethics approval and consent to participate

The study protocol was authorized by the review boards at the Shanghai Mental Health Center (SHMC), School of Medicine, Shanghai Jiao Tong University. Informed consent was obtained from study participants.

Consent for publication

Informed consent of the study participants was obtained for publishing this work.

Availability of data

Data are available from the corresponding author upon reasonable request.

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