Catechol-O-Methyltransferase Activity in Individuals with Substance Use Disorders: A Case Control Study

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Abstract

Background

Impulsivity and substance use disorders (SUD) can be related to the same environmental factors. In this study, we intended to evaluate the dopaminergic function in imprisoned SUD offenders through the determination of s-COMT activity.

Methods

The study included 46 male individuals from a Portuguese penal institution. The participants were assessed through a battery of standardised instruments: Psychopathy Checklist-Revised (PCL-R), Barratt Impulsivity Scale Version 11 (BIS-11), and the European version of the Addiction Severity Index (EuropASI). s-COMT erythrocyte activity was evaluated.

Results

Overall, 73.9% (n=34) of the individuals had Antisocial Personality Disorder (ASPD) and 58.7% (n=27) presented SUDs. We evidenced, for the first time, that, in SUD individuals, s-COMT activity is correlated with the severity of drug dependence (EuropASI) ($p<0.05$), and with BIS-11 factors self-control ($p<0.0001$) and non-planning ($p=0.002$).

Conclusions

This study opens new perspectives regarding the pharmacological intervention on drug dependence through the interference on dopamine pathways.

Introduction

Impulsivity has been recognized as a multi-dimensional construct associated with an array of psychiatric disorders [1]. It results in a tendency to engage in inappropriate, maladaptive or poorly conceived behaviors characterized by absence of forethought or consideration of outcomes, delayed gratification, novelty-seeking, impatience, short attention span, difficulty to persist at a particular activity [2].

Behavioral, neurobiological, and imaging techniques have evidenced the association of impulsive behaviors with alcohol and drug abuse, both as a vulnerability markers and as a consequences [2, 3]. In fact, substance users are known to be highly impulsive and present a variety of well identified symptoms: impaired control, social impairment, risky use, and pharmacological tolerance and withdrawal [2]. On the other hand, impulsivity may be understood as an imbalance of bottom-up and top-down neural systems suppressed by automatic or reward-driven responses with diminished cognitive control to demands [3].

Clinical evidence shows that impulsivity and substance use disorders (SUD) can coexist and can be related to the same environmental factors [3]. This complex relationship shall be analyzed considering three main factors: i) impulsivity as a trait with focus on decreased cognitive and response inhibition; ii) the effect of acute or chronic substance use on brain structure and function; and iii) genetic and environmental factors [3, 4].

From a neurobiological perspective, both impulsivity and drug abuse have been associated with changes in dopaminergic processes [3]. It has been evidenced that, in individuals with SUD, increased brain dopamine concentrations, in limbic brain regions, are responsible for reinforcing effects [5]. However, the mechanisms involved in drug dependence are far more complex and rely also on structural changes of the prefrontal cortex (PFC) with reduction of the activity of this region, through a mechanism of downregulation of dopamine receptors type 2 (DRD2), in the striatum, resulting in impaired self-control and impulsive behaviours [6]. On the other hand, research indicates that impulsivity is also modulated by the levels of dopamine in the PFC [7].

Dopamine metabolism in the PFC and limbic brain depends mostly on catechol-O-methyltransferase (COMT) [8]. In fact, COMT is the primary mechanism for dopaminergic inactivation in the PFC [9] and is widely distributed in human brain. Still, research evidenced that, COMT is directly involved in the regulation of synaptic dopamine concentration in prefrontal neurons [9]. In the striatum, this mechanism is regulated through neuronal uptake of dopamine by abundant specific transporters. In this context, low COMT activity would result in increased concentration of dopamine at the synapse and, therefore, in higher action at the dopamine receptors of the receiving neuron. However, several studies evidenced an inverted-U-shaped relationship between extracellular dopamine concentration and global PFC network activity [10, 11], so that both excessive and insufficient levels may impair cognitive performance. This could suggest the existence of a COMT mediated mechanism through which optimal levels of dopamine can modulate signal gain to support cognitive functioning.

Soluble COMT (s-COMT) activity has been assessed in the setting of impulsivity and SUDs with the objective of clarifying the physiological mechanisms underlying these disorders [3, 12]. We postulate that, considering all the aspects of dopamine brain metabolism, it is possible that individuals with excessively high but also those with low COMT activity could display high impulsivity and, perhaps, more severe dependence due to impaired self-control.

Despite all this and considering that addictive behaviors may also have a genetic component, the presence of one or more variant genes might act as risk factor for drug addiction. Since dopamine is the main neurotransmitter involved in the reward pathway, genes related with dopamine synthesis, degradation, receptors, and transporters are possible research topics [13]. In this context, the COMT Val¹⁵⁸Met (rs4680) polymorphism has been studied in the scope of drug addiction with evidence of a significant correlation in drug addicted patients [14, 15]. The COMT Val¹⁵⁸Met polymorphism determines the dopamine concentration in the prefrontal cortex (PFC), but not in the striatum [16]. In fact, we can find only a few DRD2 receptors in the PFC [17]. However, they are abundant in the striatum, meaning that, to

evaluate the dopaminergic component of addiction, dopamine receptors shall also be investigated. In this setting, several studies have shown that Taq I A1 allele of the DRD2 gene is associated with alcoholism, drug abuse, and other impulsive behaviors and personality traits so that it became a topic of research during the characterization of individuals with SUD [13, 18].

In incarcerated populations, drug abuse and psychiatric and psychological disorders, like impulsivity, are expressive and, as such, prisons are an adequate environment to collect data that can clarify the neurobiology of this association and improve the search for novel therapeutic approaches [19]. Even though the dopaminergic pathways of SUD have already been studied, as far as we know, this kind of evaluation has never been performed in combination with impulsivity assessment in incarcerated individuals.

In this study, we intended to evaluate the dopaminergic function in imprisoned SUD offenders through of the correlation between s-COMT activity, impulsivity and dependence severity.

Materials And Methods

Study Population

This study was conducted in a medium/high security penal institution for male offenders, in the North of Portugal. At the time of the protocol application, the penitentiary institution had a total number of 710 inmates, which had received sentences longer than 10 years.

Our sample included 46 male inmates, recruited by a convenience sampling strategy, between January and March 2015. Participants were referred to the Psychiatry clinical services due to SUD and as a part of a methadone treatment plan. Participants should also be over 18 years old. The ability to read and provide written informed consent was also taken into consideration. Participation was voluntary and no reward was offered in exchange for participation. The participants were able to leave the research at any time without any consequences, and the individuals who decided not to participate received the same treatment offered to participants. In accordance with the Declaration of Helsinki, written, informed consent was obtained after explaining the procedures to each participant. The study followed a case-control design.

The research protocol was formally approved by an Ethics Committee from Centro Hospitalar e Universitário de São João (Document number 48.14) and by the hosting institution, the General Directorate for Probation and Prison Services.

Procedures and instruments

The participants that agreed to participate were interviewed and went through a blood sample collection, in the clinical department of the penitentiary institution.

Individuals were diagnosed by a forensic psychiatrist (JA) using a standardised interview – the Mini-International Neuropsychiatric Interview (MINI) [20]. SUD diagnosis was achieved with this tool. Participants were assessed by means of the Portuguese version [21]. The psychometric assessment of participants included a battery of standardised instruments: the Psychopathy Checklist-Revised (PCL-R) [22], the Barratt Impulsivity Scale Version 11 (BIS-11) [23], and the European version of the Addiction Severity Index (EuropASI) [24]. Participants and scorers were blinded to the results of the s-COMT assay.

The only biological variable was S-COMT erythrocyte activity.

Psychopathy Checklist-Revised (PCL-R)

The PCL-R measures psychopathic traits by collecting information from clinical records and applying a semi-structured interview. The 20 items that compose the PCL-R are scored as absent (0), present to some degree (1), or fully present (2), providing a maximum total score of 40 points. The PCL-R is a four-factor model comprising interpersonal, affective, lifestyle, and antisocial facets. The structural properties of PCL-R were previously validated in Portuguese samples [25].

Barratt Impulsiveness Scale Version 11 (BIS-11)

The BIS-11 is a self-report questionnaire used for assessing general impulsivity [23]. The current scale version contains 30 items that are rated from 1 (rarely/never) to 4 (almost always/always). Factor analyses reveal six first-order factors (Attention, Cognitive Instability, Motor, Perseverance, Self-Control–reverse scoring–, and Cognitive Complexity), and three second-order factors (Attentional, Motor, and Non-planning). The structural properties of BIS-11 were replicated in Portuguese-speaking subjects [26].

European version of the Addiction Severity Index (EuropASI)

The EuropASI was applied to assess the SUDs' severity. This semi-structured interview offers an inventory of problems that occurred over the previous month in six areas: physical health, work income, drug use, legal status, family and social relationships, and psycho-emotional status. The EuropASI also assesses history of suicide attempts and criminality type. This multidimensional clinical and research instrument is an adapted version of the Addiction Severity Index (fifth version) [24].

The composite scores of each dimension ranged from 0 to 1, while higher scores indicated greater severity. The reliability measures indicated moderate to good internal consistency in the European samples (Cronbach's alpha: 0.69–0.92) [27].

Erythrocyte soluble catechol-O-methyltransferase (S-COMT) assay

Erythrocyte S-COMT was obtained from washed erythrocytes submitted to haemolysis as described elsewhere [28]. Venous blood samples were collected between 08.00 and 09.00 a.m., after an overnight fast, and kept on ice in K₃EDTA tubes until processing. Blood samples were centrifuged at 1500 g for 10 minutes at 4 °C, the plasma was removed, and the uppermost cell layer was separated for genetic

analysis. Afterwards, a volume of cold 0.9% NaCl solution was added to the erythrocytes and gently vortexed. Thereafter, the tubes were centrifuged (at 1500 g, 10 minutes, 4 °C), and the supernatant discarded. This process was repeated twice. Washed erythrocytes were stored at -70°C, until the enzyme assay was carried out. On the day of the experiment, the frozen erythrocytes were thawed on ice.

Haemolysis was conducted at a ratio of 4:1 (water:erythrocytes; V:V). Following vigorous mixing, the tubes stood on ice for 10 minutes. Then, the tubes were centrifuged at 20,000 g for 20 minutes at 4°C, and the supernatant was collected for the assay of erythrocyte S-COMT. The protein content was determined using human serum albumin as standard [29].

COMT activity was determined by the ability of enzyme preparations to methylate adrenaline to metanephrine. The reaction was stopped with perchloric acid. The samples were kept at 4°C for two hours, and then centrifuged (5400 g, 10 minutes, 4°C). 500 µl aliquots of the supernatant, filtered on 0.22 µm pore size Spin-X filter tubes (Costar), were used for the assay of metanephrine.

Assay of catechol derivatives

Metanephrine was determined HPLC with electrochemical detection, in aliquots of samples from the COMT assay, as previously described by Vieira-Coelho [30]. In each assay, aliquots of 20 or 50 µl were injected into the chromatographic system by means of an automatic sample injector (Gilson 231) connected to a Gilson dilutor (Gilson 401). The chromatographic system included a pump (Gilson 307) and a stainless steel 5 mm ODS2 column (Biophase; Bioanalytical Systems, West Lafayette, IN, USA) of 25 cm length and 4.6 mm diameter. The degassed mobile phase was pumped at a rate of 1.0 ml/min; it was composed of citric acid 0.1 mM, sodium octylsulphate 0.5 mM, sodium acetate 0.1 M, Na₂EDTA 0.17 mM, dibutylamine 1 mM, and methanol (10% v/v); pH was adjusted to 3.5 with PCA 2 M. Detection was performed electrochemically by means of a glassy carbon electrode, an Ag/AgCl reference electrode, and an amperometric detector (Gilson 142); the detector operated at 0.75 V. Gilson Unipoint HPLC software was used to monitor the produced current. The detection limit of metanephrine ranged from 350 to 1000 fmol.

Drugs

S-adenosyl-L-methionine, DL-metanephrine and adrenaline (bitartrate salt) were purchased from Sigma Chemical Co. (St Louis, MO).

DNA extraction

Genomic DNA extraction from leukocytes was performed following the manufacturer's instructions of the Quick-DNA Plus Kits (Zymoresearch, CA, USA). A 100 ng/µL DNA aliquot was stored at -80°C until use.

Genotyping

Allelic discrimination for the COMT Val¹⁵⁸Met (rs4680) and DRD2/ANKK1 TaqIA (rs1800497) polymorphisms were determined through real-time polymerase chain reaction (PCR) technique, using a TaqMan SNP genotyping assay with fluorogenic probes (Applied Biosystems, Foster City, CA). Briefly, 15

ng of DNA was amplified in a total volume of 8 µL containing 0.2 µL of a minor groove binder (MGB) probe solution (Applied Biosystems) and 4 µL of TaqMan universal polymerase chain reaction master mix (Applied Biosystems). PCR conditions were provided by the manufacturer: 40 cycles of 95°C denaturation (15 sec), 60°C anneal/extension (1 min).

Thermal cycling and fluorescence signal genotyping were performed through the StepOnePlus Real-Time PCR system (Applied Biosystems, Foster City, CA). A positive control for each possible genotype and a negative control were included in each 96-well plate.

Statistical analysis

Data were summarised using descriptive statistics: continuous variables are presented as mean (standard deviation) or median (interquartile range [Q1, Q3]), while categorical variables are presented as absolute or relative frequencies. Continuous variables were subjected to normality testing (Kolmogorov–Smirnov test). In data with normal distribution t-Student Test was used to compare medians. Multiple comparisons were performed via Bonferroni post-hoc method. When data did not meet the requirements of parametric tests, non-parametric Mann–Whitney was used. A *p* value <0.05 was considered to be statistically significant.

The degree of association between variables without normal distribution was measured by the Spearman correlation coefficient.

Analyses were carried out using IBM SPSS Statistics for Mac, Version 26.0 (Armonk, NY, USA: IBM Corp.)

Results

Study population

Our sample comprised 46 individuals with a median age of 36.0 (33.0, 42.0). The median education level was 6.0 (6.0, 9.0), while the median length of imprisonment, at the time of the assessment, was 102.0 (60.0, 166.0) months. A total of 54.3% (n=25) of the inmates had been convicted for violent crimes (physical assault, murder, or attempted murder. The sociodemographic, clinical, and criminal characteristics of the overall population are summarized in Table 1. Overall, 73.9% (n=34) of the individuals had Antisocial Personality Disorder (ASPD), 58.7% (n=27) of the individuals presented SUDs, 21.7% (n=10) had depressive disorders, 30.4% (n=14) had anxiety disorders, 43.5% (n=20) exhibited psychopathy, 32.7% (n=15) had personal histories of suicide attempts.

Table 1
Sociodemographic, criminal, and clinical characteristics of the study population.

	Overall population (n=46)
Age (years)	36.0 (33.0, 42.0)
Education level (years)	6.0 (6.0, 9.0)
Length of imprisonment (months)	102.0 (60.0, 166.0)
Violent crimes	25 (54.3%)
ASPD	34 (73.9%)
Depressive disorders	10 (21.7%)
Psychopathy	20 (43.5%)
Anxiety disorders	14 (30.4%)
Suicide attempts	15 (32.7%)
Substance use disorders	27 (58.7%)
Results are presented as median (Q1, Q3) for continuous variables and n (%) for categorical variables.	
ASPD: Antisocial Personality Disorder.	

The sample was divided in two groups according to the presence or absence of SUDs (Table 2). The two groups were comparable on age, education, time spent in prison, frequency of violent crimes, presence of depressive and anxiety disorders, and history of suicide attempts (Table 2). Individuals with SUD had a higher frequency of ASPD, and a higher score in first order factor self-control ($p=0.0036$), and in the PCL-R F3-lifestyle parameter ($p=0.020$), than individuals without SUD (Table 2). S-COMT activity and COMT polymorphisms were similar in both groups (Table 2).

Table 2
Sociodemographic, criminal, and clinical characteristics of participants with and without SUD.

	No SUDs (n=19)	SUDs (n=27)	p value
Age (years)	35.0 (28.0, 39.0)	35.0 (31.0, 43.0)	0.070
Education (years)	6.0 (6.0, 10.0)	8.0 (6.0, 9.0)	0.446
Length of imprisonment (months)	120.0 (60.0, 174.0)	96.0 (60.0, 180.0)	0.797
Violent crimes	12 (63.2%)	13 (48.1%)	0.310
ASPD	11 (57.9%)	23 (85.2%)	0.038
Depressive disorders	6 (31.6%)	14 (51.8%)	0.170
Psychopathy	6 (31.6%)	4 (14.8%)	0.180
Anxiety disorders	5 (26.3%)	9 (33.35)	0.610
Suicide attempts	4 (21.1%)	11 (40.7%)	0.160
BIS-11 Total	53.0 (43.0, 70.0)	62.0 (51.0, 69.0)	0.146
<i>First order factors</i>			
Attentional	9.0 (5.0, 11.0)	9.0 (7.0, 11.0)	0.586
Cognitive instability	5.0 (3.0, 7.0)	6.0 (4.0, 8.8)	0.065
Motor	10.0 (7.0, 14.0)	13.0 (10.0, 15.0)	0.213
Self-control	8.0 (6.0, 13.0)	11.0 (8.0, 16.0)	0.036
Cognitive complexity	11.0 (8.0, 14.0)	11.0 (8.0, 13.0)	0.371
<i>Second order factors</i>			
Attentional	15.0 (9.0, 17.0)	15 (12.0, 20.0)	0.320
Motor	16.0 (13.0, 21.0)	20.0 (17.0, 24.0)	0.080
Non-planning	20.0 (14.0, 26.0)	23.0 (19.0, 29.0)	0.090
PCL-R total	25.0 (18.0, 32.0)	28.0 (25.0, 33.0)	0.290
F1-Interpersonal	4.0 (4.0, 8.0)	8.0 (4.0, 8.0)	0.130

Results are presented as median (Q1, Q3) for continuous variables and n (%) for categorical variables or mean±SD for categorical variables.

ASPD: Antisocial Personality Disorder; BIS-11: Barratt Impulsiveness scale version 11; PCL-R: Psychopathy Checklist-Revised; S-COMT: catechol-O-methyltransferase; SUD: Substance Use Disorder.

	No SUDs (n=19)	SUDs (n=27)	p value
F2-affective	5.0 (2.0, 8.0)	6.0 (2.0, 8.0)	0.950
F3-Lifestyle	8.0 (5.0, 10.0)	10.0 (8.0, 10.0)	0.020
F4-Antisocial	6.0 (5.0, 10.0)	8.0 (4.0, 10.0)	0.700
S-COMT activity (pmol/mg prot/h)	19.14±0.95	18.17±0.76	0.455
COMT Val ¹⁵⁸ Met (met/met and met/val)	12 (63.2%)	18 (66.7%)	0.330
Frequency of A1 allele of DRD2 receptors CTTT	4 (21.1%)	9 (33.3%)	0.430
Results are presented as median (Q1, Q3) for continuous variables and n (%) for categorical variables or mean±SD for categorical variables.			
ASPD: Antisocial Personality Disorder; BIS-11: Barratt Impulsiveness scale version 11; PCL-R: Psychopathy Checklist-Revised; S-COMT: catechol-O-methyltransferase; SUD: Substance Use Disorder.			

Among the individuals with SUD (n=27), the median age of first consumption was 14 (10, 16) years (Table 3). Most individuals (56%) were not consuming any kind of drug, at the time of the study. The participants that were still in active drug consumption reported to have consumed cannabis and heroin, in 20 and 27 days of the previous month, respectively. In this group, SUD were mostly associated with heroin and the individuals were reported to the psychiatry consultation as part of the protocol of methadone treatment. S- COMT activity and all the parameters regarding SUD characterization (EuropASI factors and methadone dosage) are similar in both groups (Table 3).

Table 3
Characteristics of the dependence in SUD participants with and without current drug consumption.

	SUD No consumption (n=19)	SUD Consumption (n=27)	<i>p</i> value
Age (years)	37 (34, 45)	33 (28, 39)	0.063
Age at first consumption (years)	15 (12, 17)	10 (9, 16)	0.093
EuropASI Total	1.1 (0.0, 2.0)	2.3 (1.4, 3.1)	0.053
Medical	0.0 (0.0, 0.7)	0.0 (0.0, 0.7)	0.755
Job satisfaction	0.5 (0.0, 0.8)	0.5 (0.2, 1.0)	0.480
Alcohol use	0.0 (0.0, 0.0)	0.0 (0.0, 0.0)	0.710
Drug use	0.0 (0.0, 0.1)	0.3 (0.1, 0.4)	0.001
Legal status	0.2 (0.0, 0.4)	0.4 (0.3, 0.6)	0.041
Family	0.0 (0.0, 0.4)	0.0 (0.0, 0.2)	0.940
Social relations	0.0 (0.0, 0.5)	0.0 (0.0, 0.4)	1.000
Psychiatric status	0.0 (0.0, 0.4)	0.4 (0.1, 0.5)	0.093
Heroin use (days of the previous month)	-	27 (0, 30)	-
Cannabis use (days of the previous month)	-	20 (1, 30)	-
Methadone dosage (mg)	25.0 (18.0, 32.0)	28.0 (25.0, 33.0)	0.290
S-COMT activity (pmol/mg prot/h)	17.98±3.87	18.42±4.19	0.990
Results are presented as median (Q1, Q3) or mean±SD.			

Correlation between S-COMT erythrocyte activity and BIS-11

In the whole cohort and in SUD individuals (Figure 1), S-COMT erythrocyte activity was correlated with the first order factor self-control (SUD $r=0.63$, $p<0.0001$; whole cohort $r=0.36$, $p=0.015$) and with the second order factor non-planning of BIS-11 (SUD $r=0.53$, $p=0.002$; whole cohort $r=0.29$, $p=0.047$). In the group of individuals without SUD no correlation between BIS-11 scores and the S-COMT erythrocyte activity was observed.

Correlation between S-COMT erythrocyte activity and EuropASI

In the group of individuals with SUD, S-COMT erythrocyte activity was correlated with the total score of EuropASI ($r=0.38$, $p<0.01$), (Figure 2).

Discussion

This study is part of a broad project that was implemented in a medium/high security penal institution for male offenders, in the North of Portugal with the objective of identifying aggression predictive factors among incarcerated individuals. On previous studies we evaluated the prevalence of premeditated and impulsive aggression in male offenders with antisocial personality disorder (and determined the impact of impulsivity, SUD, psychopathy on aggression type) [31], and studied the association between COMT activity and premeditated aggression (submitted article).

In this study we studied S-COMT activity and impulsivity in male offenders with SUD and found that, in these individuals, S-COMT activity is correlated with self-control (BIS-11 first order factor) and non-planning (BIS-11 second order factor).

The profile of our overall population is similar to those described in recent reports of male prisons in developed countries: most individuals are below 40 years old, with low education level and moderate imprisonment length [19]. In terms of psychiatric disorders, most individuals were incarcerated due to violent crimes, presented ASPD and SUD, in close agreement with other evaluations performed in European prisons [32]. Anxiety disorders and suicide attempts rates were higher than those described before in similar populations [33]. We believe that these aspects can be related not only to specificities of the individuals, such as the mechanisms of dealing with the committed crime and with imprisonment, but also to the conditions of the prison in terms of facilities, medical and psychological care, and social dynamics. Regarding the prevalence of SUD, our results evidence the dimension of this problem in Portuguese prisons with values up to 45% similar to those reported in other penal institutions worldwide [34].

The registered significant differences between the individuals with and without SUD regarding ASPD (Table 2, $p=0.038$) are in good agreement with literature regarding the prevalence of this disorder among drug addicts [35]. This trend has been extensively explored in the last decades and research has shown that ASPD is one of the most common psychiatric diagnoses among individuals with SUD [36].

The evidenced significant difference between the two groups regarding Factor 3 of the PCL-R illustrates the impact of this aspect of psychopathy on externalizing behaviors as showed before by Patrick and co-workers [37].

Our results showed also a significant difference, between the two groups, in the BIS first order factor self-control (Table 2, $p=0.036$), which is not surprising considering the extensive evidence on this subject [38]. Imaging studies showed that continuous drug consumption is associated with a downregulation of DRD2 in the striatum, which consequently reduces the activity in the PFC resulting in impaired capacity to exert self-control leading to impulsive and compulsive behaviors, common in individuals with SUD [38]. This

trend is further reinforced by the calculated significant correlation between BIS-11 self-control factor and COMT activity in individuals with SUD (Figure 1). In fact, COMT is a key factor in dopaminergic processes and, as such, this correlation is not surprising. Impulsive behaviours and self-control have been extensively studied through the measurement of COMT activity and the results evidence that enzyme levels correlate with levels of impulsivity [7, 8, 12]. This correlation has been confirmed by studies in which COMT inhibitors have proved to reduce impulsive addictive behaviors [39].

Our study showed also that COMT activity is correlated with the severity of the addiction measured by the EuropASI scale (Figure 2). Even though this association has never been reported before, it confirms the dopaminergic pathways of drug addiction [6, 12]. However, we could also find differences in COMT activity or COMT polymorphisms in SUD and non-SUD patients (Table 2). In addition, active drug consumption did not show to affect COMT activity nor the severity of dependence (Table 3). These results seem to direct the attention to impulsivity as major determinant for SUD, as evidenced by the already mentioned differences in the BIS-11 self-control and non-planning factors (Table 2).

This study presents some limitations. First, this is a monocentric study including participants from only one penal institution. This kind of study tends to carry a higher probability of not finding differences between groups and can have type 2 errors. Second, our sample is small and thus our results shall be confirmed in a more expressive number of subjects. However, sample size shall be evaluated considering the particularities of this specific population and the limitations regarding the contact with participants, consultations, and research approval. These facts alerted us for the need to create adequate conditions to perform research inside prisons.

In conclusion, our study evidenced, for the first time, a correlation between the severity of drug dependence and COMT activity and highlighted the correlation between non-self-control and COMT activity, in individuals with SUD. This further opens new perspectives regarding the pharmacological intervention on drug dependence through the interference on the dopamine pathways catalysed by COMT.

Abbreviations

ASPD: Antisocial personality disorder

BIS-11: Barratt Impulsiveness scale version 11

COMT: catechol-O-methyltransferase

EuropASI: European version of the Addiction Severity Index

MINI: mini-International Neuropsychiatric Interview

PCL-R: Psychopathy Checklist-Revised

PFC: prefrontal cortex

SUD: substance use disorders

Declarations

Ethics approval and consent to participate

The research protocol was formally approved by an Ethics Committee from Centro Hospitalar e Universitário de São João (Document number 48.14) and by the hosting institution, the General Directorate for Probation and Prison Services.

In accordance with the Declaration of Helsinki, written, informed consent was obtained after explaining the procedures to each participant.

Consent for publication

Not applicable

Availability of data and materials

Original datasets are available in a publicly accessible repository:

The original contributions presented in the study are publicly available. This data can be found here: [https://datadryad.org/stash/share/YNn2Rt_VawfkndMH3NPkYc-YLytKZ3zDrF33S345RHg].

Competing interests

The authors declare that they have no conflict of interest.

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Authors' contributions

All authors contributed to the study conception and design.

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Figures

Figure 1

Correlation between S-COMT erythrocyte activity and the first order factor self-control ($r=0.63$. $p<0.0001$), in the SUD group.

Figure 2

Correlation between the S-COMT erythrocyte activity the total score of EuropASI, in the SUD group.