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ORIGINAL ARTICLE

Impulsivity Predicts Relapse—but Not Dropout—in Outpatients with SUD: a Longitudinal Study

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Abstract
The objective of this study was to compare performance on a comprehensive impulsivity battery of SUD outpatients who dropout versus those who do not dropout and of abstainers versus relapsers at 3 and 12 months of treatment follow-up. Impulsivity was measured at the start of treatment and adherence and relapse at 3 and 12 months. The participants are 115 outpatients with SUD. Motor impulsivity (Affective Go/No Go), attentional impulsivity (Stroop), delay discounting (Monetary Choice Questionnaire; MCQ), and decision making (Iowa Gambling Task; IGT) were assessed. Impulsivity was not associated with dropout. There were no relationships between treatment outcomes and the MCQ and IGT. Stroop and affective Go-No Go were associated with relapse at 3 and 12 months. Affective motor disinhibition and cognitive disinhibition predict relapse in outpatients. No cognitive aspect of impulsiveness is related to dropout.

Keywords Ambulatory treatment · Dropout · Impulsivity · Relapse · Substance use disorders

Impulsivity, defined as "actions which are poorly conceived, prematurely expressed, unduly risky or inappropriate to the situation and that often result in undesirable consequences" (Daruna & Barnes, 1993, p. 23), is considered an endophenotype of numerous mental disorders (Dalley et al., 2011; Moeller et al., 2001), including addiction (Bechara, 2005; Bickel & Yi, 2008; Heatherton & Wagner, 2011). Some authors point to impulsivity as a marker associated with substance use disorders (SUD). The abnormal manifestations of impulsivity can be understood as arising from an imbalance of top-down and bottom-up regulation in the fronto-amygdalar network (Kozak et al., 2019; Zare-Sadeghi et al., 2019). Thus, the impaired response inhibition and salience attribution (iRISA) model proposes that disinhibition is involved in the relapse of patients with SUD (Goldstein & Volkow, 2011). Because different cognitive processes or personality traits underlie impulsivity, it is regarded as a multifaceted construct (Reynolds et al., 2006; Whiteside & Lynam, 2001).

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Therefore, various dimensions of impulsivity are related to the characteristics of addiction, including substance-specific addictions, comorbidities, and treatment response (Vassileva & Conrod, 2019). Moreover, impulsivity is also related to treatment outcomes through the mediation of other environmental and genetic factors (Perry & Carroll, 2008), so that the same type of impulsivity affects different patients differently.

In this paper, we will focus on measures of state impulsivity using behavioral tasks, which have received increasing attention in recent years (Nguyen et al, 2018; Sharma et al, 2014). Building on animal models of impulsivity (Winstanley et al., 2010), the construct has been divided into impulsive action (which includes cognitive disinhibition and motor disinhibition) and impulsive choice or decision-making (including delay discounting and decision-making). Some commonly employed tests for measuring impulsivity that have shown to be valid for assessing its various dimensions include the Stroop Color Word Test for cognitive disinhibition (or interference control) (Duckworth & Kern, 2011; Nguyen et al, 2018; Periañez et al., 2021), Go/No-Go test for motor disinhibition (Duckworth & Kern, 2011; Hamilton et al., 2015; Nguyen et al, 2018; Votruba & Langenecker, 2013), the Monetary Choice Questionnaire for delay discounting (Monterrosso et al., 2001; Duckworth & Kern, 2011; Myerson et al., 2014; Nguyen et al, 2018), and the Iowa Gambling Task for impulsive decision-making (Monterrosso et al., 2001; Buelow & Suhr, 2009; Duckworth & Kern, 2011). For a more complete description of neuropsychological impulsivity modalities and the tests used to measure this construct, see Stevens et al. (2014).

Deficits in impulsive action make it difficult to inhibit prepotent responses (such as those associated with routine use), which has led to the proposal that addicted individuals with impairments in motor or cognitive inhibition may have difficulty overriding the attentional bias towards drug-related stimuli and are at greater risk of prematurely dropping out of treatment or having problems maintaining abstinence (Field & Cox, 2008; Liu et al., 2011; Stevens et al., 2014; Streeter et al., 2008).

On the one hand, the preference for immediate stimuli (such as those provided by consumption) over delayed gratification may contribute to drug use relapse (Winstanley et al., 2010). On the other hand, it has been proposed that difficulty in making appropriate decisions in complex scenarios is essential for achieving long-term goals such as maintaining abstinence (Verdejo-García et al., 2022). In addition, numerous studies have reported associations between the poor performance shown by SUD patients on tests assessing these constructs and alterations detected in brain activity caused by neuroadaptation to excessive drug use (Goldstein & Volkow, 2011; Zilverstand et al., 2018).

It is widely documented that high impulsivity is associated with negative clinical outcomes when treating patients with SUD (Domínguez-Salas et al., 2016; Loree et al., 2015; Stevens et al., 2014). However, the evidence on which dimensions of impulsivity are associated with adherence and which are associated with relapse is diverse and sometimes contradictory. This discrepancy has prompted various review studies that have provided a contextualized overview of the findings. For example, Stevens et al. (2014) reviewed works that analyze the relationship between the different types of impulsivity and treatment outcomes, concluding that cognitive inhibition, delay discounting, and decision-making tasks are risk factors for relapse without being related to motor impulsivity. However, they found that impulsivity is not related to premature treatment abandonment. However, Loree et al. (2015) concluded after their review that greater impulsivity prior to treatment, regardless of the dimensions evaluated, is generally associated with poor treatment outcomes. However, due to methodological differences, these studies could not establish the relevance of each dimension for clinical outcomes. Finally, Domínguez-Salas et al. (2016), in an extensive review of the evidence linking cognitive-executive functions with addiction treatment

outcomes, found evidence of associations between general cognition and treatment adherence (but not with impulsivity) and between reward-based decision-making and relapse. Based on these findings, some authors have recently suggested that impulsive choice (but not impulsive action) should be considered when developing addiction treatment (Verdejo-García et al., 2022).

These review studies have also highlighted various methodological limitations that hinder a common interpretation of the results. Thus, it has been pointed out that there is variability between studies in operationalizing clinical outcomes, while these have a highly subjective component for their measurement. For example, relapse is usually assessed through self-reports as opposed to toxicological tests. In the case of adherence, most studies do not measure the therapeutic outcome of treatment but rather treatment attendance time during relatively short periods (3 or 6 months) (Domínguez-Salas et al., 2016).

In addition to the above, it should be noted that the available evidence is also limited by the relatively few existing studies and the small sample sizes (Domínguez-Salas et al., 2016; Loree et al., 2015; Pattij & De Vries, 2013; Stevens et al., 2014). Finally, few studies have employed a comprehensive assessment of impulsive action and impulsive choice and are limited to measuring specific dimensions of impulsivity, making it difficult to determine how different types of impulsivity influence treatment outcomes. To our knowledge, only four studies have comprehensively analyzed the various dimensions of impulsivity and its relationship with treatment outcomes. For example, Passetti et al. (2008) found that performance on decision-making tasks in a sample of outpatients being treated for opiate addiction predicted abstinence from illicit drugs at 3 months of treatment. However, there was no relationship with performance on tests of motor disinhibition, reflection-impulsivity, or delay discounting. In a similar study with inpatients and outpatients (Passetti et al., 2011), it was also observed that in a sample of outpatients, performance on decision-making tasks predicted abstinence, while no such relationship was found for patients in residential treatment. On the other hand, Moraleda-Barreno et al. (2019), in a study with inpatients, found that worse decision-making on the Iowa Gambling Task (IGT) was associated with premature treatment dropout, while commission errors on the Go/No-Go affective test were associated with higher relapse rates, which could be due to the fact that positive moods favor risk-taking behaviors and prepotent responses (Clore & Huntsinger, 2007; Galentino et al., 2017). However, cognitive inhibition was not related to treatment outcomes. Finally, with a sample of patients with SUD in a therapeutic community, Gomez-Bujedo et al. (2020) found that impulsive decision-making was associated with higher dropout rates.

Taken together, the evidence suggests a relationship between deficits in impulsive choice and the ability to maintain abstinence. However, the relationship between impulsivity dimensions and treatment adherence is inconsistent.

Although the involvement of impulsivity in substance use disorders is well documented, our knowledge of the relationship between impulsivity and treatment outcomes is much weaker and inconsistent since most studies have been based on one or a few trials and employed cross-sectional assessments with subjective outcome measures using relatively small sample sizes. For these reasons, more evidence is needed based on larger-scale studies employing objective methods to operationalize clinical outcomes, along with a comprehensive measure of impulsivity. In this paper, we set out to examine whether individual differences in various types of impulsivity at treatment initiation are related to the extent to which patients benefit from addiction treatment.

To achieve this objective, this study aims to longitudinally analyze the association between multidimensional cognitive measures of impulsivity (cognitive inhibition, motor disinhibition, delay discounting, and decision-making) and treatment outcomes (retention

and relapse) in a sample of outpatients. Regarding specific dimensions of impulsivity, and in line with the results of previous studies, we hypothesized that worse scores on affective motor disinhibition, delay discounting, and impulsive decision-making would be associated with a higher probability of relapse.

Material and Methods

Design

We conducted a follow-up study with a baseline assessment at the beginning of treatment (between 15 and 25 days after admission to outpatient treatment) and two follow-ups at 3 and 12 months following the baseline assessment.

Participants

The effect size estimation was based on results found in previous similar studies (Moraleda et al., 2019). In these, the affective Go/No-Go was shown to be the variable most predictive of patients' relapse, with a mean effect size (Cohen's $d = 0.56$). Based on this value, and considering $\alpha/2 = 0.025$ and a power (1—β) of 90%, the estimated sample size required was 44 participants. With this sample size in mind, the sample consisted of 126 outpatients diagnosed with SUD (109 patients with cocaine use disorders, 72 patients with alcohol use disorders, 72 patients with cannabis use disorders, and 46 patients with heroin use disorder) who began treatment in public centers specialized in addictions in the province of Huelva (Spain) between October 2016 and April 2018. In this period, there were a total of 364 patients who met the inclusion criteria. All patients starting treatment who met the inclusion criteria were invited to participate, and patient recruitment was finalized after the necessary sample size was achieved.

The inclusion criteria were as follows: (1) patients with moderate or severe SUD starting treatment for alcohol, cannabis, cocaine, or heroin dependence according to DSM-IV criteria; (2) not having vision problems that prevent computer-based activities; (3) patients over 18 years old; and (4) signing the informed consent form. In addition, the following patients were excluded: (1) patients with mild SUD; (2) patients whose mobility was expected to interrupt their treatment and, therefore, could not be followed up; (3) patients with severe psychiatric comorbidities that compromised task performance; (4) patients undergoing pharmacological treatment (methadone) that would affect performance of the task; and (5) patients who did not sign the informed consent form.

Of the participants, 82.6% were men with a mean age of 38.5 years ($SD = 10.32$); 47.8% had completed basic/primary education and 42.6% secondary education, and 9.6% of the patients had completed university studies. Concerning employment status, 35.7% were employed before starting treatment, 58.8% were unemployed, and 5.3% were pensioners. Of the patients, 65.8% were single, 12.3% married, 18.4% divorced, and 3.5% widowed.

Most of the patients had a diagnosis of cocaine dependence (87%); 56.5% of the patients had alcohol dependence, 55.7% had cannabis dependence, and 36.5% had heroin dependence. In addition, 86.1% of the patients had poly-drug dependence. More than half of the patients (56.5%) had previously been in treatment for drug dependence.

Instruments

Cognitive Assessment

We used an approach based on impulsivity theories by including a well-validated measure of each of the facets of impulsivity defined in cognitive models of the construct (Lee et al., 2019).

Motor Impulsivity—Affective Go/No-Go (Verdejo-García et al., 2007) This is a computerized task in which participants were required to press any button on the keyboard as soon as the Go stimulus (a letter) was presented on the screen (80% of trials) and to withhold the response when the No-Go stimulus (a different letter) was presented on the screen (20% of trials). Distinct auditory feedback was available to signal correct responses versus errors. The task consisted of two different blocks of 60 trials. In the first block, these trials were administered after presenting a series of neutral images on the screen, and in the second block, after a series of positive affective images. Each block consisted of two sets of 10 images, followed by 30 Go or No-Go trials. The images were taken from the International Affective Picture System (IAPS), which have been shown to generate a sustained affective state (Lang, 2005). We included positive affective pictures, given the well-established link between positive affective states and more disinhibited/risky behaviors (Weiss et al., 2015). The impulsivity index in this task was the percentage of commission errors (i.e., responses to No-Go stimuli) in the neutral and positive blocks.

Cognitive Disinhibition—Stroop Task (Pardo et al., 1990) This test measures response inhibition, selective attention, and cognitive flexibility (Spreen & Strauss, 1998). In this test, interference is created between the reading of words and the naming of colors (Stroop interference effect) so that the reaction time varies according to the congruence or incongruence between the word and the color. Participants must inhibit the reading of the written word and respond with the color in which it is written. The index of impulsivity in this task was the Stroop interference score (Golden and Freshwater, 1978).

Delay Discounting—Monetary Choice Questionnaire (MCQ) (Kirby et al., 1999) This questionnaire comprises a fixed set of 27 options and a monetary choice in which participants are asked about their preferences when choosing between small but immediate rewards and larger but delayed rewards. Further details on delays and monetary amounts can be found in Kirby et al. (1999). This test yields two well-validated indices of impulsivity: the area under the curve (AUC) (Myerson et al., 2001) and the K parameter (Kirby et al., 1999). In this study, we used the K parameter. Higher values are taken to indicate greater impulsivity.

Decision-making—Iowa Gambling Task (Bechara et al., 1994) This test assesses decision-making. Participants must choose from four decks of cards with different reinforcement and punishment schedules. The task is to choose cards to obtain the maximum profit. This test is sensitive to deficits in impulsive choice. The computerized version (described in Hooper et al., 2004) was used, using the total score as an index of impulsive decision-making. Higher values are taken to indicate better decision-making.

Outcome Measures

Treatment Adherence Two time points were analyzed: at 3 months and up to 1 year. At the 3-month follow-up, patients were categorized according to whether they had dropped out or remained in treatment. Adherence up to 1 year of treatment was coded as follows: (1) dropouts, which included participants who discontinued treatment without meeting the therapeutic goals established by the team; (2) program discharge, which includes patients who, according to the clinical assessment, had achieved the therapeutic objectives; and (3) participants who remained in treatment, which were those who continued their treatment in the CPD after the 12 months.

Relapse Participants underwent blood and urine tests that were used to determine relapse in substance use. Detection of cannabis, cocaine, and opiate use was performed through urinalysis using the enzyme immunoassay technique. Alcohol detection was performed through blood samples, measuring carbohydrate-deficient transferrin (CDT). Values were considered positive when the CDT result was > 1.7%. Participants who showed positive drug results in the analyses were considered "relapses."

Procedure

The data collection process began when the clinicians of the addiction service informed the patients that a research project was being conducted. The therapists explained to the patients the voluntary nature of their participation and that the information collected was not the responsibility of the clinicians and would not be considered part of their therapeutic process. If the patient wished to participate, the therapists provided the patient's contact information to the research team members. The interviewer set a date 15 to 20 days after the initial interview with the therapist. This timeframe was established to rule out the residual effects of drug use on cognitive task performance.

The tests were administered by a psychologist, who was a member of the research team and trained to administer the tasks, in a room of the addiction center. The psychologist informed the patients about the study's objectives, its voluntary nature, and the possibility of discontinuing the administration of the tests at any time during the study. They were also asked for authorization to consult their clinical history concerning the results of the toxicological tests (at least 1 at 3 months and another at 12 months) and their treatment progress. If they wished to participate, they were instructed to sign the informed consent form, and the inclusion and exclusion criteria were checked. Finally, if the patient was eligible to participate in the study, the tests described above were administered.

At 3 and 12 months, the interviewer collected information related to toxicological tests and the patient's treatment status (dropout or adherence to treatment).

The research project protocol was approved by the ethics committee of the University of Huelva (Q7150008F—2016/034).

Analysis

The analyses were conducted on 115 patients, as 11 patients did not complete all the instruments administered and were therefore eliminated from the analyses. In terms of

performance on the cognitive tasks, no statistically significant differences were observed between patients excluded from the analyses ($n=11$) and those who had completed all the tasks ($n=115$).

Contingency tables and Chi-square tests were employed to test the association between sociodemographic and previous use variables, treatment adherence, and relapse. In addition, non-parametric tests were applied to analyze the relationship between cognitive task performance and outcomes since the cognitive task scores did not follow a normal distribution (Table 1).

Moreover, logistic and multinomial regression analyses were applied (for adherence to treatment at 1 year) to determine the predictive capacity of the study variables for the outcomes.

Results

Adherence to Treatment During the First 3 Months

During the first 3 months, 47.8% of patients dropped out of treatment. As shown in Table 2, none of the sociodemographic or previous use variables showed statistically significant relationships with dropout or treatment adherence. In addition, no statistically significant differences were observed between cognitive measures and dropout/treatment adherence (Table 3).

Therapeutic Outcomes Between Treatment Initiation and 1 Year of Follow-up

The results revealed that 67% of the patients dropped out of treatment before completing 1 year. The mean time in treatment for these patients was 68.1 days (SD = 68.6). In addition, 15.7% of patients were discharged from treatment, with a mean time on treatment of 219 days (SD = 87.66). Finally, 17.4% of patients continued their treatment for more than 1 year.

None of the sociodemographic or previous use variables showed an association with treatment outcomes (Table 4). Among the cognitive variables, a weaker Stroop task interference effect is observed among those who remain in treatment, the differences being statistically significant (Table 5). However, multinomial regression analysis, controlling for gender, age, and dependence on the different drugs, revealed that none of the variables presented statistically significant regression coefficients (Table S1).

Table 1 Descriptive statistics of impulsivity measures

	Mean	Sd	Median	skewness	kurtosis	Shapiro–Wilk statistics	p
Commission errors neutral stimuli	.06	.03	.07	.63	.49	.96	.000
Commission errors affective stimuli	.07	.04	.07	.22	-.34	.96	.002
Stroop interference effect	77.52	54.77	70.24	.60	1.06	.97	.021
Delay discounting	.07	.09	.03	1.40	.37	.69	.000
IOWA gambling task	4.14	28.28	4.00	.00	2.22	.95	.00

Table 2 Association between sociodemographic and related consumption variables with adherence to treatment during the first 3 months

	Drop out ($n=55$)	Under treatment ($n=60$)	Chi-square	p	Effect size (Cramer V)
Sociodemographic variables					
Gender (male)	83.6	81.7	0.077	.781	.026
Education level					
Primary	56.4	40	3.079	.079	.164
Secondary	36.4	48.3	1.681	.195	.121
University	7.3	11.7	0.640	.424	.075
Employment status					
Employed	27.3	44.1	3.486	.062	.175
Unemployed	63.6	54.2	1.038	.308	.095
Pensioned	9.1	1.7	3.123	.077	.166
Marital status					
Single	58.2	72.9	2.733	.098	.155
Married	14.5	10.2	0.506	.477	.067
Separated/divorced	21.8	15.3	0.816	.366	.085
Widowed	5.5	1.7	1.188	.276	.102
Variables related to consumption and treatment					
Previous treatments	59.3	55	0.210	.646	.043
Alcohol dependence	54.5	58.3	0.168	.682	.038
Cannabis dependence	60	51.7	0.807	.369	.084
Cocaine dependence	85.5	88.3	0.210	.647	.043
Opiate dependence	34.5	38.3	0.178	.673	.039
Alcohol use 30 days before	44.2	46.7	0.067	.796	.024
Cannabis use 30 days before	35.3	38.3	0.109	.741	.031
Cocaine use 30 days before	51.9	43.3	0.825	.364	.086
Opiate use 30 days before	12.0	15.0	0.208	.648	.044

Table 3 Association between cognitive measures and adherence to treatment during the first 3 months

Cognitive measures (mean ranks)	Drop out ($\boldsymbol{n}=55$)	Under treatment ($\boldsymbol{n}=60$)	Mann–Whitney $\boldsymbol{U}$	$\boldsymbol{p}$	Effect size (Cohen's d)
Commission errors neutral stimuli	57.49	58.47	1622.0	.874	0.029
Commission errors affective stimuli	59.19	56.91	1584.5	.711	0.069
Stroop interference effect	55.37	59.43	1504.0	.510	0.153
Delay discounting	60.07	56.10	1536.0	.522	0.119
IOWA gambling task	57.02	58.90	1596.0	.762	0.056

Table 4 Association between sociodemographic and related consumption variables with treatment outcomes at one-year follow-up

Variable	Drop out ($n=77$)	Therapeutic discharge ($n=18$)	Under treatment ($n=20$)	Chi-square	p	Effect size (Cramer V)
Sociodemographic variables						
Gender (male)	84.4	83.3	75	0.987	.610	.093
Education level						
Primary	53.2	22.2	50	5.674	.059	.222
Secondary	37.7	61.1	45	3.337	.189	.170
University	9.1	16.7	5	1.551	.460	.116
Employment status						
Employed	32.9	50	35	1.859	.395	.128
Unemployed	60.5	50	60	0.681	.712	.077
Pensioned	6.6	0	5	0.829	.661	.085
Marital status						
Single	62.3	82.4	65	2.485	.289	.148
Married	14.3	11.8	5	1.276	.528	.106
Separated/divorced	19.5	5.9	25	2.412	.299	.145
Widowed	3.9	0	5	0.784	.676	.083
Variables related to consumption and treatment						
Previous treatments	59.2	50	55	0.544	.762	.069
Alcohol dependence	53.2	72.2	55	2.160	.340	.137
Cannabis dependence	53.2	61.1	60	0.551	.759	.069
Cocaine dependence	85.7	100	80	3.658	.161	.178
Opiate dependence	37.7	33.3	35	0.142	.931	.035
Alcohol use 30 days before	43.2	50	50	0.462	.794	.064
Cannabis use 30 days before	32.9	44.4	45	1.510	.470	.117
Cocaine use 30 days before	52.7	38.9	35	2.591	.274	.152
Opiate use 30 days before	16.7	5.6	10	1.784	.410	.127

Predictor Variables of Relapse at 3 Months

Among patients with alcohol dependence that had undergone toxicological tests ($n=43$), 18.5% relapsed into alcohol consumption. However, none of the variables analyzed showed statistically significant relationships with alcohol relapse (Table S2).

Among the patients with cannabis dependence that had undergone toxicological tests ($n=51$), 28.1% relapsed in the consumption of this substance. It was observed that patients who have completed secondary studies had a higher relapse rate than the rest (72.2% vs. 39.4%, Chi2 = 5.203, $p=0.025$). On the cognitive tasks, patients who relapsed showed a more pronounced Stroop task interference effect than those who did not relapse (mean ranks: no relapse = 21.94 vs. relapse = 33.44; Mann–Whitney $U=163$, $p=0.008$). Logistic regression analysis controlling for gender, age, educational level, and dependence on other

Table 5 Association between cognition measures and outcomes at one-year follow-up

Cognitive measures (mean ranks)	Drop out ($n=77$)	Therapeutic discharge ($n=18$)	Under treatment ($n=20$)	Kruskal–Wallis H	p	Effect size (Cohen's d)
Commission errors neutral stimuli	58.23	54.64	60.15	0.276	.871	0.25
Commission errors affective stimuli	58.95	59.08	53.38	0.475	.788	0.235
Stroop interference effect	61.01	61.94	40.15	6.695	.035	0.418
Delay discounting	58.71	50.11	62.35	1.389	.499	0.148
IOWA gambling task	58.08	58.06	57.68	0.002	.999	0.27

drugs showed that patients with a greater Stroop task interference effect were more likely to relapse into cannabis use (odds ratio = 1.27, $p = 0.007$).

Among patients with cocaine dependence who had undergone toxicological tests ($n = 81$), 26% relapsed. The analyses showed that none of the sociodemographic or previous use variables was associated with relapse into using this drug. When analyzing cognitive variables, more commission errors were observed in the Go/No-Go task with affective stimuli among those who relapsed (mean ranks: no relapse = 34.73 vs. relapse = 54.27; Mann–Whitney $U = 674.00$, $p < 0.001$). Logistic regression analysis controlling for gender, age, and dependence on other drugs showed that more commission errors on this task were associated with a higher probability of relapse after the first 3 months of treatment (odds ratio = 1.43, $p = 0.001$).

Finally, among patients with opiate dependence who had undergone toxicological tests ($n = 32$), 14.3% relapsed. None of the variables studied showed statistically significant relationships with relapse.

Predictors of Relapse After 3 Months of Treatment

Five patients with alcohol dependence dropped out of treatment after the first 3 months (none had relapsed into alcohol consumption in the first 3 months). In addition, one patient who had not consumed in the first 3 months showed evidence of consumption after the 3 months. None of the study variables was associated with relapse into use of this drug (Table S3).

Two patients with cannabis dependence dropped out of treatment after the first 3 months. In both cases, the patients had not relapsed into cannabis use during the first 3 months. There was also one patient who used cannabis after the first 3 months. In this group of patients, logistic regression analysis showed similar results to those obtained at 3 months; thus, a greater Stroop task interference effect was associated with a higher probability of relapse (odds ratio = 1.26, $p = 0.010$).

Of the patients with cocaine dependence, four patients who had not used the drug during the first 3 months dropped out of treatment. In addition, five patients did not use the drug in the first 3 months but did so after this period. When analyzing relapse during the first 3 months, logistic regression analysis revealed that patients who produced more commission errors in the Go/No-Go task with affective stimuli had a higher probability of relapse (odds ratio = 1.41, $p = 0.001$). In addition, it was also observed that those who produced fewer commission errors in the Go/No-Go task with neutral stimuli had a higher probability of relapse (odds ratio = 0.79, $p = 0.026$).

Finally, of the patients with opioid dependence, three patients who did not relapse in the first 3 months dropped out of treatment. One patient also relapsed after the first 3 months of treatment. None of the variables showed a statistically significant association with relapse during the first 3 months.

Discussion

This is one of the few studies to provide a comprehensive assessment of impulsivity to predict clinical outcomes. Our objective was to longitudinally analyze the specific components of impulsivity that are associated with relapse and low adherence to treatment in outpatients. Our results show that relapsing participants present higher impulsive behavior,

while no differences were found concerning treatment adherence. However, these findings are only partially consistent with hypotheses based on previous literature, since impulsive decision-making—but not cognitive disinhibition—was related to abstinence (Stevens et al., 2014).

One of the most interesting findings of this work is the relationship between both components of impulsive action and relapse. Emotion-driven motor disinhibition predicted relapse at 3 and 12 months. Although previous studies had not found effects of impulsive action on relapse (see, for example, the review by Domínguez-Salas et al., 2016), in their extensive review, Steven et al. (2014) already suggested that the absence of relationship between performance on motor disinhibition tasks and relapse could be due to the lack of sensitivity of the measures. To solve this problem, they proposed using tests with an affective component to capture the dynamics of the interaction between the top-down executive and bottom-up systems, which was the method applied in the present study. It is worth noting that these results are consistent with the only previous work in which an affective manipulation of the Go/No-Go task had also been employed, and the higher number of errors committed when presented with positive stimuli on this test was also associated with a higher probability of relapse (Moraleda-Barreno et al., 2019).

Thus, our results are consistent with evidence obtained using ecological momentary assessment, showing that real-time positive mood states are significant precursors of relapse (Epstein et al., 2009). Our findings can be explained in the context of affect-as-information processes, according to which affect provides compelling information about the value attributed to stimuli. Positive affective information promotes cognitive responses that are accessible or dominant in a particular situation (Clore & Huntsinger, 2007), increasing the likelihood of engaging in risk behaviors (Galentino et al., 2017). Our results suggest that factors related to motor inhibition—when an affective component is present—may facilitate relapse up to 1 year after treatment initiation. From a clinical standpoint, this information could be useful for designing patient training programs in cognitive control strategies and emotion regulation for the long-term maintenance of abstinence (Ross & Witkiewitz, 2017). Our finding that a higher relapse rate is linked to fewer errors in response to neutral stimuli in the Go-No Go test could be due to a type I error since the previous literature consistently contradicts these results (Stevens et al., 2014; Loree et al., 2015; Domínguez-Salas et al., 2016; Moraleda-Barreno et al., 2019).

Although many studies have addressed the predictive ability of the Stroop task for relapse, most of them use variations of the Stroop drug task that measure attentional biases toward drugs (see, for example, Christiansen et al., 2015). In our case, using the classic Stroop task, cognitive inhibition scores predict relapse after 3 months of treatment, a surprising finding considering that, using the same type of task, only one article has reported similar results, using a sample of smokers (Mueller et al., 2009). In contrast, two studies with polyconsumer inpatients (Moraleda-Barreno et al., 2019; Gómez Bujedo et al., 2020) and two others with cocaine-consuming outpatients (Brewer et al., 2008; Kennedy et al., 2014) found no such relationship. Our results do not support the most accepted hypothesis that difficulties in controlling interference are relatively unimportant for maintaining abstinence. Therefore, our findings suggest that the ability to inhibit prepotent drug use responses is critical for maintaining abstinence. We believe that it is necessary to revise the currently accepted hypothesis that impulsive choice tests are the only consistent and robust predictor of relapse failures and to increase the number of treatment outcome studies that include various operationalizations of impulsivity as predictors.

We should bear in mind that both modalities of impulsive action (motor inhibition and cognitive inhibition) are closely related and depend on the activation of the inhibitory

control network (mainly the dorsolateral prefrontal cortex and the ventromedial prefrontal cortex), as shown by neuroimaging studies (Zilverstand et al., 2018). Moreover, the involvement of both impulsive action modalities in relapse is consistent with the impaired response inhibition and salience attribution (iRISA) model, which proposes that impaired response inhibition plays a crucial role in the tendency toward chronic relapse observed in addiction patients (Goldstein & Volkow, 2011). An important clinical implication of these results is the need to consider including response inhibition training in the cognitive treatment of patients with SUD. For example, according to Verdejo-García et al. (2022), the most promising approaches in this field involve combined interventions that exploit bottom-up versus top-down cognitive processes while training patients to apply decision-making strategies. It would be interesting to test whether the inclusion of training in inhibition of prepotent behaviors in some of these treatment strategies results in improved abstinence rates. In this regard, preliminary evidence suggests that the use of drugs that increase response inhibition such as modafinil or aripiprazole in patients in treatment for AUD improves abstinence in participants with high impulsivity, but not in those with better inhibition skills (Tomko et al, 2016). In light of our results, it would be interesting for future research to explore the effectiveness of this type of treatment in patients with high impulsive action. However, although delay discounting and impulsive decision-making are considered relatively consistent predictors of abstinence (Domínguez-Salas et al., 2016; Stevens et al., 2014), the results of the present study do not support this relationship in the case of delay discounting and do so only marginally in the case of impulsive decision-making. Furthermore, several works have failed to find a relationship between these constructs and relapse (Passetti et al., 2011; Washio et al., 2011; Czapla et al., 2016; Moraleda-Barreno et al., 2019), which has led some to propose that its effect may be mediated by the treatment program and setting, the task used in the assessment, the group of drug users (Stevens et al., 2014), and the use of a treatment modality that is less cognitively demanding (Carroll et al., 2011).

Concerning treatment adherence, as expected, no relationship was found with any of the four measures of impulsivity. Although some studies in the literature have reported a relationship between impulsive action and dropout (Brewer et al., 2008; Streeter et al., 2008; Fagan et al., 2015; Rupp et al., 2016; Van Emmerik-van Oortmerssen et al., 2020), the vast majority of works have found no such relationship (Passetti et al., 2008, 2011; Schmitz et al., 2009; Carroll et al., 2011; Verdejo -García et al., 2012; Winhusen et al., 2013; Moraleda-Barreno et al., 2019; Gómez-Bujedo et al., 2020). The lack of relationship between impulsive choice and treatment adherence is even more robust (see reviews by Stevens et al., 2014; and Domínguez-Salas et al., 2016), and although some recent works do observe a relationship (Moraleda- Barreno et al., 2019; Gómez-Bujedo et al., 2020), these studies have been conducted exclusively with patients in residential treatment as opposed to outpatients. Failure to adhere to treatment is thus most likely related to the difficulty in benefiting from the talking therapies used in treating addictions, which is caused by general cognitive difficulties rather than impulsivity (Domínguez-Salas et al., 2016).

The discrepant results concerning the relationship between impulsivity and treatment outcomes are probably due to other factors. Contemporary neurocognitive models postulate that both impulsivity and addiction result from an imbalance between the top-down and bottom-up systems. Therefore, it would be necessary to consider how other domains such as emotional, social, and personality variables (closely related to bottom-up processing) modulate the interaction between impulsivity and poor treatment outcomes. Some studies suggest that impulsivity is related to SUD through other factors (mainly reactivity to rewards and early environmental experiences) that interact with impulsivity and

addiction during all phases of the disorder (see review by Perry & Carroll, 2008). These factors contributing to individual differences could be implicated in the variations in treatment responses between patients with similar impulsivity characteristics.

We believe that one of the reasons for the discrepant results found among the various studies in this field is that most of these have employed small samples, used subjective measures of treatment outcomes, and adopted a unidimensional approach to impulsivity. Therefore, the main strengths of the present work include the use of a multidimensional approach to the assessment of impulsivity, the use of objective measures for treatment outcomes, and the use of a long-term longitudinal design. We propose that such methodological approaches should be employed in future research on the relationship between impulsivity and treatment outcomes.

Our findings suggest that impulsive action plays an important role in outpatient relapse, which has implications for personalized clinical approaches and long-term case management. Furthermore, since impulsivity has been shown to be a relevant factor for treatment outcomes in patients with SUD, the modulatory effect of impulsivity should be considered in the therapies used.

Although the present study has generated results of great interest for both research and clinical practice, it also presents certain limitations. First, a larger sample size would have been desirable to improve statistical power. However, it should be noted that these types of studies are generally conducted with smaller sample sizes than those used in this work (Domínguez-Salas et al., 2016). Second, the outcome measures were operationalized according to clinical guidelines established by addiction treatment authorities; however, the findings obtained with these measures may not generalize to other settings. Third, the gender imbalance of our sample (lower percentage of females) means that the findings are not generalizable to women, especially given the gender differences in impulsivity and personality traits noted by some authors. This gender bias is due to the low percentage of women in treatment in this study setting (European Monitoring Centre for Drugs & Drug Addiction, 2019). Finally, the results are correlational, so causal relationships cannot be established between variables.

Conclusions

The results of this investigation show that, in an outpatient sample, affective motor disinhibition and cognitive disinhibition scores predict patient relapse in both the short and long term, whereas no facets of impulsivity are associated with treatment adherence. An important clinical implication of this work is the need to apply a comprehensive assessment of impulsivity (motor, attentional, delay discounting, and decision-making) to identify specific predictors of treatment relapse.

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Data Availability If required by the reviewers, the authors will send them the data.

Declarations

Ethics Approval The research project protocol was approved by the ethics committee of the University of Huelva (Q7150008F—2016/034).

Consent to Participate Informed consent was obtained from all individual participants included in the study.

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