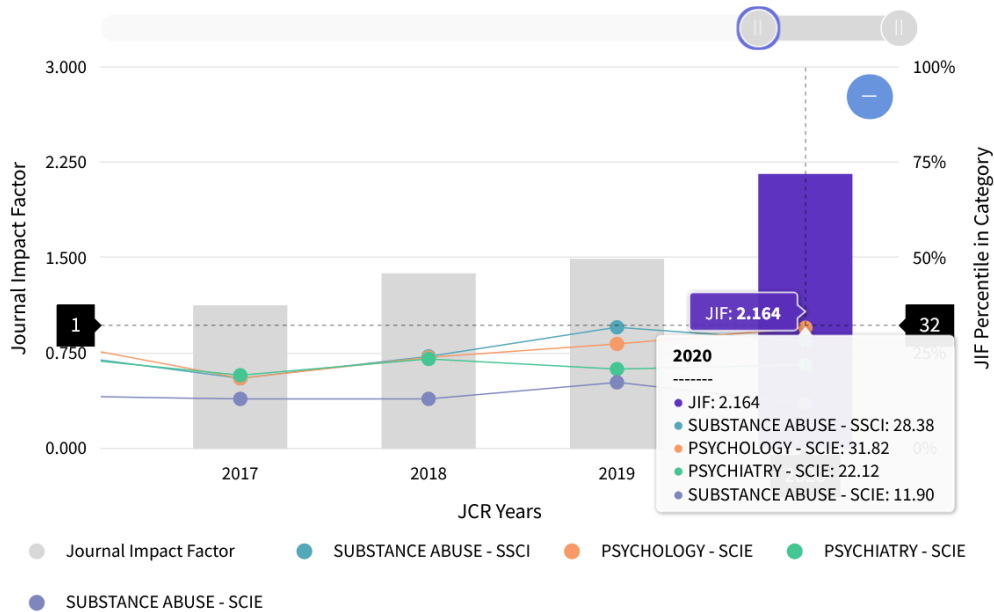1) <u>Gómez-Bujedo, J.,</u> Lorca-Marín, J. A., Pérez-Moreno, P. J., Díaz Batanero, C., Fernández-Calderón, F., & Moraleda-Barreno, E. (2022). Changes in Drug-Related Implicit Associations during Substance Use Disorder Treatment: The Role of the Therapeutic Context. *Substance Use & Misuse*, *57*(2), 185-192. https://doi.org/10.1080/10826084.2021.1995755. **(Posición: 53/77; Q3)**.

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2017	64/78	Q4	18.59	
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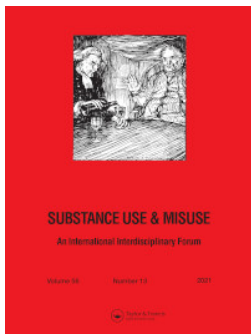
Changes in Drug-Related Implicit Associations during Substance Use Disorder Treatment: The Role of the Therapeutic Context

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Changes in Drug-Related Implicit Associations during Substance Use Disorder Treatment: The Role of the Therapeutic Context

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ABSTRACT

Background: Implicit cognition has been linked to relapse in substance use disorder (SUD). Studies on attentional bias have found different outcomes related to the therapeutic context, finding an association with relapse in inpatients but not in outpatients. There are no similar studies that use associations in semantic memory as a measure of implicit cognition. *Objectives:* (i) to analyze the relationship between a measure of associations in semantic memory and relapse in inpatients and outpatients; (ii) to compare the evolution of these associations between inpatients and outpatients after 3 months of treatment. *Methods:* Eighty nine outpatients and 94 inpatients with SUD for cocaine and alcohol participated in this study. We employed a longitudinal design with a baseline evaluation and follow-up after three months, using the Word Association Task for Drug Use Disorder (WAT-DUD). *Results:* The choice of drug-related words predicted relapse in cocaine (odds ratio = 1.97, $z = 2.01$, $p = .045$) and alcohol-cocaine (odds ratio = 2.39, $z = 2.55$, $p = .011$) use. Follow-up at 3 months revealed a reduction in the choice of drug-related words in inpatients ($Z = 2.031$, $p = .042$). *Conclusions:* A greater choice of drug-associated words in the presence of ambiguous images was related to relapse in inpatients but not in outpatients. The inpatients group showed a reduction in the semantic association with drugs during the first three months of treatment.

1. Introduction

Reports within the field of addiction research have described various neuropsychological domains thought to be involved in the relapse process. Among these, it is possible to distinguish domains that could be considered rational — such as decision-making — from others that are automatic and fall under the category of implicit cognition. According to Stacy and Wiers (2010), implicit memories are classically conditioned associations. These memories may be elicited by triggers, or stimuli, that remind an individual of certain aspects of their drug use. Although the terminology and classifications are not without controversy (De Houwer, 2006; De Houwer et al., 2009), authors such as Rooke et al. (2008) point out that implicit cognition can be evaluated using measures of implicit attitudes, attentional bias, implicit arousal, and associations in semantic memory. Theoretical approaches such as the Reinstatement Model of Drug Relapse illustrate the importance of these mechanisms in drug-seeking behavior (Bossert et al., 2013). Various factors such as the frequency of drug use (Wiers & Stacy, 2006) or the search for treatment (Vadhan et al., 2007) may contribute to the differences in cognitive bias toward the drug shown by people with SUD.

Within these neuropsychological domains, most of the studies on relapse have been conducted with the aim of evaluating attentional bias, with many showing that the latter is related to an increase in the probability of relapse in patients diagnosed with substance use disorder (SUD) (Field & Cox, 2008; MacLean et al., 2018; Díaz-Batanero et al., 2018). However, not all studies have found such relationships (Field et al., Field et al., 2014). These mixed results can be explained in terms of the addictive phase in which the patients find themselves, as well as the deterioration in other neuropsychological processes, which is at the core of the addiction (Goldstein & Volkow, 2002). Further, methodological differences between the studies could provide an explanation for the discrepancies in the findings (Christiansen et al., 2015; Domínguez-Salas et al., 2016).

In this regard, the therapeutic scope of the studies that have been carried out can help in understanding these discrepant results. Research with inpatients has generally shown a link between attentional bias measures and relapse (Marhe et al., 2013a; Waters, Shiffman, Bradley, et al., 2003, Waters, Shiffman, Sayette, et al., 2013), although there are also exceptions (Cox et al., 2002). However, the literature with outpatients has yielded mixed results, showing that some studies report this association (Carpenter et al., 2006; Charles et al.,

2015) whilst others do not (Kennedy et al., 2014; Snelleman et al., 2015). When thinking in terms of exposure to contextual cues that induce drug seeking and relapse, it appears that whilst inpatients are in controlled environments with low exposure to drug-related cues, outpatients usually find themselves in contexts in which they are surrounded by more drug-related stimuli, which can trigger cravings and increase the likelihood of relapse (Drummond, 2000; Monti et al., 2000). Thus, although the therapeutic context may contribute to understanding the relationship between implicit cognitions and relapse, no studies have yet been conducted to comparatively analyze their impact. Thus, the objectives of this work are: i) to analyze the relationship between a measure of associations in semantic memory and relapse in patients who began treatment in outpatient centers and therapeutic communities; and, ii) compare the development of these associations between inpatients and outpatients after a period of 3 months. In terms of the first objective, and according to theoretical models, it is expected that in inpatients there is a clear relationship between implicit cognition and relapse. In the case of outpatients, however, the results of previous studies do not allow us to propose a clear relational hypothesis. For the second objective, it is hypothesized that the 3-month treatment period will produce a reduction in the associations in semantic memory.

2. Method

2.1. Design

A longitudinal observational design was employed, with a baseline evaluation at the start of treatment and a follow-up evaluation after three months.

2.2. Participants

The sample consisted of 89 outpatients and 94 inpatients that began treatment in the public network of addiction centers in Andalusia (Spain). To participate in the study, patients had to meet the following inclusion criteria: 1) consumption of alcohol and/or cocaine in the last three months; 2) having a diagnosed substance use disorder for at least one of these two substances according to the diagnostic criteria of the DSM-IV; 3) being at least 18 years of age; and, 4) giving signed informed consent. The exclusion criteria applied were: 1) suffering vision problems that prevented the correct performance of the tasks; 2) suffering from any other mental disorder that could affect the execution of the tasks; and, 3) being in receipt of pharmacological treatment that could hinder cognitive abilities. Of the 89 outpatients, 69.7% ($n = 62$) had problems of abuse or dependence related to cocaine, and 49.4% ($n = 44$) had problems with alcohol. Among the inpatients, 88.3% ($n = 83$) of the patients had problems due to cocaine use, and 57.4% ($n = 54$) had problems related to alcohol use.

The fieldwork was carried out during the period of October 2016 to April 2018.

2.3. Instruments

2.3.1. Word association task for drug use disorder (WAT-DUD)

The WAT-DUD is a task that evaluates implicit associations in the semantic memory of drug users. This task adopts a simultaneous conditional discrimination paradigm, in which an image is presented (which can be neutral, ambiguous in relation to drug consumption, or explicitly related to drugs) accompanied by two words (one drug-related and the other not). The task of the participant is to point to the word that evokes the presented image. The proportion of drug-related words chosen by the participants is used as a dependent variable.

This task has been shown to have an adequate test-retest reliability as well as internal consistency. In terms of evidence of validity, it has been found that the scores correlate with constructs such as dependence severity or craving (Gómez-Bujedo et al., 2019).

2.3.2. Cocaine craving Questionnaire-Now – CCQ-N-

The Spanish version of the CCQ-N- was used to evalu-a8570te cocaine craving (Castillo et al., 2009). In the present study, internal consistency was evidenced by an alpha value of .89 in the sample of outpatients and .85 for the sample of inpatients.

2.3.3. Multidimensional alcohol craving scale – MACS

The Spanish version of this 12-item instrument was used (Serecigni et al., 2004). For the sample of outpatients, an alpha value of 0.90 was obtained, and for the inpatients this value was .91.

2.3.4. Substance dependence severity scale

SDSS (Miele et al., 2000a; 2000b). This instrument was used to evaluate the severity of patient dependence during the month prior to the interview. The Spanish version adapted to the DSM-5 was administered (Dacosta et al., 2019). In the present sample, alpha values equal to or greater than .77 were found in the evaluation of alcohol and cocaine dependence, and in both samples.

2.3.5. Treatment retention

After three months, the patients were classified according to those who either continued or abandoned treatment. Patients were considered to have abandoned their treatment when they explicitly informed the therapeutic team that they were leaving the treatment, or when they did not attend their therapeutic appointments on the date indicated or afterwards.

2.3.6. Relapse

During the study period the participants were required to undergo toxicology tests to check if they had used cocaine or alcohol during the treatment period. The outpatients underwent this screening following the indications of the therapeutic team, whilst the inpatients received these tests after each therapeutic exit from the TC.

Urinalysis using the immunoenzymoanalysis technique was used to detect cocaine, whilst alcohol was detected *via* blood samples, measuring carbohydrate-deficient transferrin (CDT). Values were considered positive when the CDT result was > 1.7%. Participants for whom the drug results were positive in the analytics were considered as 'relapses'.

2.4. Procedure

The instruments were administered in individual patient interviews by a trained psychologist with experience in patient evaluation. All the interviews took place in the treatment centers. The therapists informed the patients that the research was external to their therapeutic process and that participation was voluntary. If the patients agreed to participate, they were required to sign an informed consent form before the instruments could be administered.

This research received the approval of the ethics committee of the University of Huelva (code: Q7150008F – 2016/034).

2.5. Analysis

Univariate and bivariate descriptive statistics were applied to characterize the sample in terms of socio-demographic variables, drug consumption, task execution, and retention in treatment and relapse. Pearson chi-square and student t tests were applied to verify if there was an association between the therapeutic modality and the previously mentioned variables. In the analyses in which some of the groups had a sample size of less than 30 subjects, nonparametric statistical techniques (Mann-Whitney U tests) were applied. Logistic regression analyses were conducted to predict whether the study variables were related to relapse in alcohol use, cocaine use, or both of these drugs. ANOVA mixed models were used to analyze the evolution of the semantic association measures.

3. Results

3.1. Characterization of the sample according to treatment type

Table 1 shows the socio-demographic characteristics according to the center in which they received treatment. As observed, for the socio-demographic variables statistically significant differences were found according to the gender of the patients, with a higher percentage of men in the inpatients group. It is also observed that among outpatients there were more participants who had completed university studies and a lower percentage who had completed primary education only.

For the consumption-related variables, statistically significant differences were observed in the severity of cocaine dependence, which was higher among the inpatients.

With regard to the execution of the task, the choice of drug-related words when presented with ambiguous images did not differ between the two groups of patients. However, statistically significant differences were observed when the explicit images were presented, with inpatients selecting a greater proportion of drug-related words.

Finally, it is observed that after three months the outpatients presented a greater rate of relapse in the consumption of alcohol, whilst a greater percentage of inpatients remained in treatment.

3.2. Relationship between performance on the baseline task and relapse during the 3-month period

Initially, we analyzed the relationship between relapse in alcohol, cocaine, and alcohol and cocaine consumption and the study variables for the whole sample (inpatients and outpatients). In the case of alcohol relapse, being female (odds ratio = 0.06; $z = 2.02$, $p = .043$) and receiving treatment in the TC (odds ratio = 0.06; $z = 4.47$, $p = .000$) were associated with a lower probability of relapse. Cocaine relapse was predicted by craving (odds ratio = 1.70, $z = 1.99$, $p = .046$) and by the choice of drug-related words in the presence of ambiguous images (odds ratio = 54.76, $z = 2.51$, $p = .012$). The model for predicting alcohol or cocaine use revealed that receiving treatment in the TC was associated with a lower probability of relapse (odds ratio = 0.26, $z = 3.08$, $p = .002$) and the choice of drug-related words in the presence of ambiguous images was associated with a higher probability of relapse (odds ratio = 21.32, $z = 2.23$, $p = .025$). No interaction was observed between task execution and the type of treatment received by the patients.

Of the 44 outpatients with problems of alcohol abuse or dependence at follow-up, toxicology tests were administered to 38 patients. The remaining 6 patients abandoned the treatment before their first toxicology tests. Of the patients that underwent these tests, 47.3% tested positive for alcohol. These positive results were related to both higher alcohol consumption during the month prior to the baseline assessment and the age of the patients (Table 2). However, a multivariate analysis controlling for age and gender showed that gender was the only statistically significant variable. More specifically, being female served as a protective factor against alcohol relapse (odds ratio = 0.025, $z = 2.27$, $p = .023$).

Of the 62 outpatients with cocaine addiction, all but one underwent the toxicology tests, with 26.2% testing positive for cocaine use. When compared with those who did not relapse (Table 2), these patients were younger, showed a higher percentage of cocaine use during the previous month, greater severity of dependence, and a greater craving for cocaine. The multivariate analysis revealed that none of the variables had predictive capacity for relapse during follow-up.

Table 1. Characterization of the sample.

	Outpatients (n = 89)	Inpatients (n = 94)	Test	p
Age [mean; (SD)]	39.39 (10.51)	37.86 (10.63)	t(182) = 0.939	.329
Gender (male)	83.1	91.5	Chi2 = 2.896	.089
Education level				
Primary	51.7	63.8	Chi2 = 7.099	.029
Secondary	16.9	21.3		
University	31.5	14.9		
Employment status				
Employed	31.5	20.2	5.376	.146
Unemployed	60.2	62.8		
Retired	4.5	9.6		
Penitentiary institutions	3.4	7.4		
Marital status				
Single	56.8	62.8	1.130	.770
Married	15.9	11.7		
Separated/divorced	23.9	23.4		
Widowed	3.4	2.1		
Consumption & previous treatments				
Years of cocaine consumption	15.28 (6.74)	16.04 (10.90)	t(94)= 0.513	.609
Years of alcohol consumption	23.71 (11.30)	24.15 (10.59)	t(104) = 0.204	.839
Alcohol last 30 days	46.8	52.1	Chi2 = 0.481	.448
Cocaine last 30 days	45.6	54.3	Chi2 = 1.295	.255
Previous treatments	61.4	70.2	Chi2 = 1.585	.208
Sev Alcohol dependence	7.13 (10.48)	10.27 (15.11)	t(166.18)=1.621	.107
Sev Cocaine dependence	11.43 (13.91)	18.55 (17.28)	t(176.52)=3.080	.002
Cocaine craving (CCQ)	1.607 (1.12)	1.14 (0.84)	t(162.3)= 0.438	.662
Alcohol craving (MACS)	0.98 (1.25)	0.84 (1.04)	t(171.7) = 0.828	.409
Performance on the tasks				
Mean ambiguous drug words	0.26 (0.16)	0.29 (0.16)	t(176)=1.182	.239
Mean explicit drug words	0.92 (0.19)	0.99 (0.05)	t(95.9)=3.352	.001
Alcohol relapse	47.4	7.2	Chi2 = 26.412	.000
Cocaine relapse	26.2	16.3	Chi2 = 2.175	.140
Cocaine/Alcohol relapse	42.2	19.5	Chi2 = 9.159	.002
Retention at 3 months	32.6	64.9	Chi2 = 19.094	.000

Table 2. Relationship between performance on the baseline evaluation task, relapse, and retention at 3 months in outpatients.

	Alcohol				Cocaine				Alcohol/Cocaine			
	No relapse (n = 20)	Relapse (n = 18)	Test	p	No relapse (n = 45)	Relapse (n = 16)	Test	p	No relapse (n = 37)	Relapse (n = 27)	Test	p
Age [mean; (SD)]	43.95 (10.43)	37.0 (12.15)	109.0	.038	40.16 (9.94)	33.75 (6.88)	210.5	.014	41.97 (9.2)	35.74 (10.5)	315.5	.012
Sex (male)	70.0	94.4	3.767	.052	77.8	93.8	2.037	.153	75.7	92.6	3.138	.076
Consumption & previous treatment												
Alcohol last 30 days	30.0	76.5	7.943	.005	47.4	46.7	0.002	.963	32.3	64.0	5.606	.018
Cocaine last 30 days	35.0	43.8	0.286	.593	42.1	75.0	4.880	.027	43.8	56.0	0.843	.359
Previous treatments	60.0	61.1	0.005	.944	64.4	60.0	0.096	.757	67.6	57.7	0.642	.423
Sev Alcohol Dependence	9.5 (12.43)	8.5 (8.89)	179.5	.988	6.89 (10.2)	2.68 (4.78)	274.0	.127	6.05 (10.16)	6.07 (8.11)	467.5	.640
Sev Cocaine Dependence	11.55 (14.68)	8.94 (15.57)	166.0	.696	9.69 (12.3)	18.75 (15.46)	215.0	.016	10.46 (12.24)	12.92 (15.37)	467.5	.657
Cocaine craving (CCQ)	0.84 (0.96)	1.01 (1.5)	178.5	.963	0.98 (0.85)	1.91 (1.63)	215.5	.015	1.06 (0.87)	1.30 (1.49)	486.0	.850
Alcohol Craving (MACS)	1.25 (1.30)	1.11 (1.12)	173.5	.845	0.89 (1.23)	0.59 (1.06)	315.5	.413	0.92 (1.29)	0.79 (1.04)	492.0	.910
Mean ambiguous drug words	0.28 (0.15)	0.26 (0.13)	154.5	.615	0.25 (0.14)	0.30 (0.19)	291.5	.430	0.26 (0.15)	0.27 (0.16)	463.5	.949
Mean explicit drug words	0.93 (0.15)	0.92 (0.16)	161.5	.720	0.94 (0.18)	0.90 (0.17)	285.5	.262	0.93 (0.19)	0.94 (0.14)	447.5	.709

Of the 64 outpatients who underwent toxicology screening for alcohol or cocaine, 42.19% were found to have consumed either of these two substances. Of the variables studied, it was found that the patients who relapsed consumed a greater amount of alcohol during the previous month and were younger. From the multivariate analysis, only age was found to be a predictor variable (odds ratio = 0.93, z = 2.25, p = .024).

Among the inpatients, 83 patients underwent toxicology tests for alcohol, with 8.4% testing positive for this substance. No statistically significant relationship was found with any variable analyzed, and the logistic regression model also showed no association with any variable (Table 3).

A total of 86 inpatients underwent toxicology tests for cocaine, and of these, 16.3% tested positive for this substance. These patients who relapsed presented a greater severity of dependence and a greater craving in the baseline evaluation. In the logistic regression model, the choice of drug-related words when presented with ambiguous images was the variable that showed the capacity to predict relapse (odds ratio = 1.97, z = 2.01, p = .045).

Among the 87 patients that had been tested for alcohol or cocaine, 19.5% tested positively for one of these two substances. These patients chose more drug-related words in the presence of ambiguous images than patients who did not relapse. The logistic regression model showed that this

Table 3. Relationship between performance on the baseline evaluation task, relapse, & retention at 3 months in inpatients.

	Alcohol				Cocaine				Alcohol/Cocaine			
	No relapse (n = 77)	Relapse (n = 6)	Test	p	No relapse (n = 72)	Relapse (n = 14)	Test	p	No relapse (n = 70)	Relapse (n = 17)	Test	p
Age [mean; (SD)]	37.96 (10.87)	38.17 (9.15)	226.0	.930	37.88 (11.09)	36.86 (6.41)	484.0	.815	37.94 (11.40)	38.0 (6.94)	579.5	.868
Sex (male)	94.8	100	0.327	.567	93.1	92.9	0.001	.979	92.9	94.1	0.034	.854
Consumption & previous treatments												
Alcohol last 30 days	42.99	66.7	1.277	.258	44.4	50.0	0.146	.702	57.1	47.1	0.562	.453
Cocaine last 30 days	55.8	33.3	1.136	.286	50.0	71.4	2.163	.141	52.9	58.8	0.196	.658
Previous treatments	70.1	83.3	0.472	.492	68.1	78.6	0.615	.433	67.1	82.4	1.510	.219
Sev Alcohol Dependence	10.89 (15.6)	9.67 (13.89)	228.0	.955	11.57 (15.79)	6.57 (12.76)	389.5	.148	11.57 (15.84)	7.11 (12.61)	487.0	.213
Sev cocaine dependence	18.49 (16.67)	9.17 (13.22)	162.5	.225	16.40 (16.3)	25.38 (16.3)	333.5	.045	17.07 (16.27)	21.06 (17.55)	506.5	.340
Cocaine Craving (CCQ)	1.19 (0.86)	0.73 (0.59)	163.0	.189	1.06 (0.69)	1.62 (1.33)	347.0	.044	1.09 (0.68)	1.39 (1.31)	517.0	.359
Alcohol craving (MACS)	0.93 (1.1)	0.54 (0.6)	197.5	.535	0.95 (1.08)	0.47 (0.96)	350.0	.056	0.97 (1.09)	0.51 (0.90)	588.5	.071
Mean ambiguous drug words	0.28 (0.15)	0.32 (0.19)	205.0	.681	0.27 (0.14)	0.36 (0.19)	352.5	.086	0.26 (0.13)	0.37 (0.19)	369.5	.018
Mean explicit drug words	0.99 (0.04)	0.94 (0.14)	205.0	.391	0.99 (0.05)	0.99 (0.03)	489.5	.852	0.99 (0.04)	0.97 (0.08)	566.0	.659

variable predicted the relapse in consumption (odds ratio = 2.39, $z = 2.55$, $p = .011$).

Analysis of all patients (inpatients and outpatients) revealed statistically significant differences in cocaine relapse according to age.

3.3. Relationship between relapse and changes in interpretation bias from baseline assessment to 3-month follow-up

ANOVA models were used to test for differences in the evolution of semantic association measures as a function of patient type and relapse. The results obtained for the inpatients revealed a difference between relapse and non-relapse inpatients in the baseline evaluation of ambiguous stimuli (Bonferroni test with $p = .002$), as well as a lower score in this group of participants ($p = .004$). Likewise, for the non-relapse participants there was a statistically significant difference between inpatients and outpatients regarding the results in response to explicit images at both baseline evaluation ($p = .000$) and at follow up ($p = .022$). For the relapse patients there were statistically significant differences between inpatients and outpatients at baseline ($p = .014$), with a significant change in scores ($p = .008$) observed only in inpatients (Figure 1).

4. Discussion

The objective of this work was to analyze the relationship between implicit cognition — assessed through associations based on ambiguous cues — with relapse and retention at three months in inpatients and outpatients. Although a number of studies have been reported with inpatients and outpatients in the specialized literature, to the best of our knowledge, this is one of the first attempts to compare these two groups within a single study, and the first to do so using a measure of semantic associations.

In general, this study has shown that a greater tendency to choose drug-associated words when faced with ambiguous images is linked to a greater incidence of relapse in inpatients, but not in outpatients. Likewise, it has been observed that treatment produces a reduction in these semantic associations (as assessed by this measure) during the first three months in inpatients, but not in outpatients. However, this

reduction occurs among the inpatients that had relapsed during this period.

The specialized literature has yielded mixed results regarding the relationship between relapse and implicit cognition, and in the present study we have shown how the therapeutic context could help to explain these discrepant results. This study supports the existence of this relationship in inpatients, particularly in the relapse of cocaine use. This finding has also been reported in other studies of patients with cocaine addiction using attentional bias tasks (Marhe et al., 2013a; 2013b; Marissen et al., 2006) and alcohol addiction (Garland et al., 2012). It is possible that, in comparison with cocaine-related stimuli, the ubiquity of socially-acceptable alcohol-related stimuli means that these cues have a rather different impact on the relevant implicit associations. The effect observed in our study shows that those patients who relapse are those who have the greatest tendency to associate ambiguous images with the drug. These results suggest that implicit cognitive processes — particularly associations in semantic memory — reflect a tendency to consume substances and can be used as a predictor of relapse, as proposed by Stacy et al. (2004). In contrast, in this study we did not find such a relationship in outpatients, which is in line with the results of other studies that have evaluated attentional bias (Carpenter et al., 2012; Field et al., 2013; Kennedy et al., 2014; Snelleman et al., 2015).

In relation to the impact of treatment, at three months a statistically significant reduction was found in these implicit semantic associations in inpatients, but not in outpatients. Previous studies on inpatients and outpatients have shown that treatment produces a reduction in attentional bias (Wiers et al., 2013). However, most of these studies have included training in the reduction of attentional bias (Marissen et al., 2006, Fadardi & Cox, 2009, Schoenmakers et al., 2010, Wiers et al., 2011, Snelleman et al., 2015). In therapeutic interventions that do not include this specific training, the evidence is contradictory Snelleman et al., 2015, Ziaee et al., 2016). In this study, the reduction only occurred in the inpatients with high baseline scores.

It is therefore necessary to raise the question of whether the treatment only reduces implicit drug-related cognitions in those patients for whom these processes already occurred with intensity from the outset. In this regard, it must be borne in mind that measures of implicit cognition have
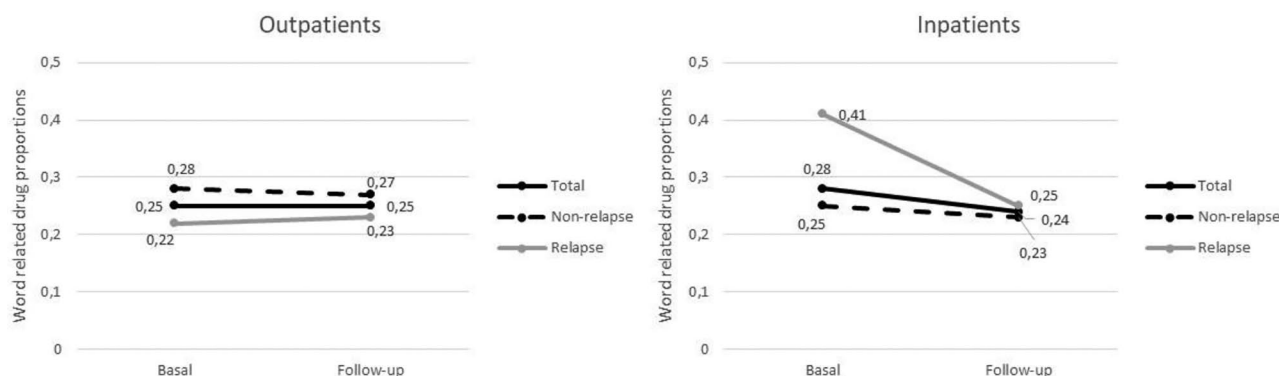
Figure 1. Changes in the proportion of drug-related words chosen by inpatients & outpatients.

been shown to be related to the severity of consumption (Field & Cox, 2008; Wiers et al., 2013; MacLean et al., 2018) and craving (Field & Cox, 2008; Field et al., 2009), which are also related to relapse.

However, it is also possible that other factors could be of importance, such as the anxiety that is often observed in situations of addiction. The literature has shown that there is an anxious memory bias toward stimuli that are perceived as threatening (Herrera et al., 2017). Further, some authors propose that the attentional bias toward drugs is influenced by factors such as anxiety and stress that are related to abuse (Vahdhan et al., Vadhan et al., 2007). It would thus be appropriate to explore the possibility that patients with a greater decrease in memory bias are those who perceive the situation to be more threatening during the baseline assessment, and whether this perception is reduced throughout treatment. This would allow us to make better treatment decisions, particularly when deciding whether to modify cognitive biases toward the drug (Zhang et al., 2018), reduce anxiety, or both (Kaplan et al., 2011). Finally, the decrease in implicit drug-related cognitions is most likely to have occurred in inpatients because these patients showed the highest baseline scores. In a meta-analysis conducted by Heitmann et al. (2018), it was found that ABM interventions are more likely to reduce AB when the latter is high before the intervention, while no such reduction occurs when the bias is low. This is consistent with our results since only those inpatients who relapsed presented high baseline scores.

Although some elements of this study are of interest for identifying the impact of implicit cognition on treatment outcomes, it is necessary to acknowledge certain limitations. These include the fact that there were participants who abandoned their therapeutic process before they underwent the toxicology tests. The opinion of the clinical professionals who treated these patients is that they probably relapsed in the use of drugs. However, we were unable to confirm this possibility, and these patients were therefore excluded from these analyzes, a fact that must be considered when interpreting the results. Moreover, the inpatient group showed the highest implicit drug-related cognitions at baseline and is the only group that showed a decline in these cognitions at follow-up. This is possibly due to differences between the two groups before the start of treatment. The patients were

assigned to one of the treatment modalities based on clinical criteria, so in future studies it would be advisable to systematize the variables related to such assignment and to include these in the model.

Further, although this study has been carried out using two samples that were similar in terms of socio-demographic variables and consumption patterns, evaluations have shown that the inpatients had significantly higher dependence severity scores. As seen in both inpatients and outpatients, severity is positively associated with relapse. In contrast, relapse rates were lower among the inpatients. Therefore, we consider that this greater severity of dependence had no impact when comparing patients using the two types of healthcare resources. However, this variable did appear to have an impact when comparing patients within the same group. Moreover, the lack of preregistration must be mentioned as a limitation of this study. Finally, it should be noted that from a therapeutic perspective it would have been desirable to compare the therapeutic process of these patients beyond the first 3 months. Some authors have pointed out that patients with high attentional bias who remain in treatment for a sufficiently long period show an eventual decrease in this bias for attentional biases measured by the Addiction Stroop Task (Snelleman et al., 2015), and for the automated biases measured by approach responses to drugs (Wiers et al., 2011). Therefore, this cognitive bias ceases to have an impact on treatment outcomes. During this later stage, it may instead be of interest to focus on other areas such as cognitive deficits, comorbid personality disorders, and the therapeutic alliance (see review by Brorson et al., 2013).

5. Conclusions

To our knowledge, this is the first study conducted with both inpatients and outpatients in treatment for SUD that used a measure of semantic association to examine the association between implicit cognition and relapse. This study shows the relationship between implicit cognition and treatment, and the different way in which this interaction occurs in inpatients and outpatients. The proportion of drug-related words chosen in the presence of ambiguous images appeared to be a predictor of the probability of

relapse in impatients. In addition, this group showed a reduction in the semantic association toward drugs during the first three months of treatment. It should be noted that these phenomena were not observed in outpatients, so more information is needed to clarify the factors related to treatment that reduce the risk of relapse in patients with SUD. Our results highlight the importance of implicit cognitions in the therapeutic process. The main clinical implication of our findings is that the WAT-DUD is a research tool that could be useful for improving clinical outcomes in inpatients by helping to predict relapse and thus develop preventive treatments. For this reason, we consider that this task could be a useful addition to the evaluation protocol employed in addiction treatment services.

Declaration of interest

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