

**Profiles of Patients with Cocaine and Alcohol use Disorder Based on Cognitive
Domains and Their Relationship with Relapse**

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Abstract

Background: Relapse in drug use constitutes a research topic on addiction that is relevant for understanding both the addictive process and its clinical implications. The objective of this study was to explore if it is possible to identify patient profiles according to their performance on cognitive tasks whilst examining the relationship between such profiles and relapse. **Methods:** The sample consisted of 222 patients with dependence on cocaine and / or alcohol, of which 86% were men. Cognitive domains related to salience, decision- making, and emotional processing were measured.

Results: Latent class analysis revealed three patient profiles that differ in terms of performance on cognitive tasks. Two of these profiles are clearly differentiated in terms of their execution of the impulsive decision-making task. The third patient profile, unlike the latter two, is composed of patients with severe alterations in the three domains evaluated. Analysis revealed that patients in Profile 3 are those with the highest rates of relapse in cocaine (Profile 1 = 40.3%; Profile 2 = 35.6%; Profile 3 = 69.2%; $\text{Chi}^2 = 9.169$; $p < .05$) and cocaine and alcohol use (Profile 1 = 55.1%; Profile 2 = 54.1%; Profile 3 = 80%; $\text{Chi}^2 = 6.698$; $p < .05$). **Conclusions:** The results support the postulates of the I-RISA model. From a clinical perspective, these findings highlight the need for a comprehensive evaluation of the cognitive domains involved in addiction.

Keywords: cocaine and alcohol relapse, decision-making, emotional processing, incentive salience, latent profile

1. Introduction

Relapse in drug use is a commonly studied issue in the field of addiction. In therapeutic contexts it is widely accepted that addiction is a chronic disorder that involves relapses. These relapses should not be interpreted in terms of therapeutic failure but rather as another phase of the addictive process (Blanco and Volkow, 2019; George and Koob, 2017; McKay and Hiller-Sturmhöfel, 2011; Volkow et al., 2016). In spite of this, understanding why there is a relapse in consumption after periods of withdrawal is still of interest for advancing our understanding of addiction (Andersson et al., 2019; Blanco and Volkow, 2019).

Addiction entails brain alterations involved in the motivational bias towards consumption-related stimuli, the formation of motor habits that 'bridge' cognitive control, and the processing of stress and negative affect (Hanlon and Canterberry, 2012; Noël et al., 2013). These alterations are modelled in various theoretical frameworks such as the Reinstatement Model (de Wit and Stewart, 1981; Shaham et al., 2003), the Somatic Marker Model (Bechara and Damasio, 2005; Damasio, 1996) and the Impaired Response inhibition and Salience Attribution model (I-RISA; Goldstein and Volkow, 2002, 2011). The latter model largely integrates existing evidence to date and is complementary to other models with respect to the importance of salience attributed to drug stimuli and impaired control over decision-making. According to the I-RISA model, addiction involves brain alterations that lead to the assignment of excessive salience to drugs and drug-related stimuli, while at the same time decreasing sensitivity to non-drug-related stimuli. In addition, there is a deterioration of the circuits responsible for inhibiting maladaptive behavior, which could have negative consequences for people (Goldstein, Barrot, Everitt & Foxe, 2019). Relapse could be explained by those craving situations in which these systems acquire a greater

relevance, thereby decreasing the inhibitory control required to avoid drug use (Goldstein and Volkow, 2011).

In terms of clinical evaluation, the transdiagnostic dimensional approach (Yücel et al., 2018) proposes that the deterioration of these systems and brain circuits in addiction have a shared pathophysiological mechanism. That is why a comprehensive evaluation of different cognitive domains is necessary, including constructs such as decision making (Athamneh et al., 2019; Bickel et al., 2019), attribution of salience (Das et al., 2015; Metrik et al., 2016; Strickland et al., 2018; Zhang et al., 2018) and emotional processing (Flora and Stalikas, 2015; Verdejo-García et al., 2006), among others.

Among the decision-making tasks, the Iowa Gambling Task (IGT; Bechara et al., 1994), which assesses affective decision-making, and the Delay Discounting Test (DDT; Kirby et al., 1999), involved in balancing cognitive information (the real value of a reward) and affective information (the subjective value of the reward) are probably the most widely used. The salience of drug-associated stimuli is assessed through the Stroop and dot probe tasks fundamentally involved in selective attention and habit-directed behavior (Otto et al., 2015). However, implicit association tasks have also been used (Rooke, et al., 2008), in which drug-related signals precipitate cognitive mechanisms that generate automatic drug-related responses. Moreover, alterations in emotional processing have been evaluated through tasks such as the Ekman Face Test (Young et al., 2002) or the International Affective Picture System (IAPS; Lang et al., 1997), which are sensitive to the motivational/attentive circuit, and have proven useful for predicting relapse in patients with opiate dependence (Lubman et al., 2009) and alcohol dependence (Heinz et al., 2007; Carmona-Perera et al., 2019).

Most of the studies that analyze the relationship between these cognitive variables and relapse compare performance on these constructs between patients who relapse and

those who do not, finding mixed evidence for the importance of these domains (Díaz-Batanero et al., 2018; Domínguez-Salas et al., 2016; Lynch, 2018; Moraleda et al., 2019; Zilverstand et al., 2018). Whilst this analytical strategy is indeed allowing progress to be made in the understanding of relapse, this may not represent a comprehensive approach that reflects the combined impact of the various cognitive alterations that are presented by these patients. A complementary analytical strategy could be to identify patient profiles according to the performance they show on these cognitive domains. That is, rather than analyzing the deterioration in the execution of each of these domains, an alternative approach would be to identify groups of patients that share common alterations in these cognitive domains. This analytical approach would complement the findings of previous studies whilst offering a more comprehensive framework for the planning of therapeutic interventions. In this regard, the objectives of the present work were: i) to identify patient profiles according to their performance on decision making, attribution of salience and emotional processing; and, ii) analyze whether there is a relationship between patient profiles and relapse in consumption. In the case of the first objective, the study hypothesis is that, as described by the models, it will be possible to identify patients that show a specific combination of alterations in tasks that assess the salience of drug-related stimuli, emotional processing, and decision-making. For the second objective, it is hypothesized that the identified patient profiles will show different probabilities of relapse in consumption.

2. Materials and Method

2.1. Design

This study employed a cross-sectional design with a baseline evaluation using tasks that assess cognitive variables and a follow-up to assess consumption at one year.

2.2 Participants

The sample consisted of 227 patients treated on an outpatient basis (52.4%) in the Provincial Service of Drug Dependencies of Huelva (PSDH), and in residential treatment (47.6%) in the therapeutic communities (TCs) of Cartaya, Almonte (Huelva) and Los Palacios (Seville), in Spain. To participate in the study, patients had to meet the following inclusion criteria: i) present a diagnosis of alcohol or cocaine use disorder according to DSM-IV criteria (*American Psychiatric Association*, 1994); ii) have used any of these substances on at least 3 occasions in the last three months; iii) not present disability or other diagnoses that will make it impossible to perform the tasks; and, iv) sign the informed consent form.

Of the 227 participants, five patients presented missing values in at least one of the cognitive variables used for the creation of the latent classes. These 5 patients were discarded from the study. Of the sample, 86% were men. The average age of the sample was 38.37 (SD = 10.32). The majority of these patients were unemployed (59.5%). Regarding educational level, 55.4% had primary education, 19.8% secondary, and 24.8% had completed higher or university studies. The majority of the participants were single (65.8%) and 11.3% were married.

In terms of substance use, 51.8% of the patients presented diagnostic criteria compatible with cocaine abuse or dependence; 18.5% to alcohol, and 29.7% to both substances.

2.3. Instruments

Word Association Task for Drug Use Disorder (WAT-DUD; Gómez-Bujedo et al., 2019). This task has been developed according to the paradigm of word association tasks (Stacy, 1995; Reich and Goldman, 2005). These tasks include among their theoretical foundations the notion that repeated exposure to drugs and their consequences, along with contextual cues, increases the likelihood that users will emit a drug-related response in the presence of these contextual cues (Stacy and Wiers, 2010).

WAT-DUD has been developed under the paradigm of simultaneous conditional discrimination tasks (Lattal and Perone, 2013). For this task, participants are presented with images (neutral and ambiguous in relation to drug use) accompanied by two words (one related to the drug and the other not). Participants are required to indicate the word that evokes the image presented. In this respect, this task allows for identifying the degree of incentive salience of drugs when presented with ambiguous stimuli.

The final version of this task was composed of 73 images (35 neutral and 38 ambiguous drug-related). In terms of reliability, adequate test-retest reliability and internal consistency was found. In terms of evidence of validity, the WAT-DUD scores have shown relationships with craving and withdrawal symptoms (Gómez-Bujedo et al., 2019).

As an indicator of the salience of the patients, the proportion of drug-related words that participants point to when presented with ambiguous stimuli was used, with a higher proportion taken to indicate a greater salience attribution.

Delay Discounting Test (DDT; Kirby et al., 1999). The Spanish adaptation of this test was used (Perales et al., 2009). This test evaluates, through 27 items, impulsive decision making, exposing participants to contexts that recreate the possibility of obtaining a higher long-term gain or a lower short-term gain. A greater number of short-term benefit selections implies a lower capacity to delay reinforcement and is interpreted in terms of lower planning capacity and greater impulsiveness in decision making. In this study the area under the curve (AUC; Kirby et al., 1999) was estimated as an indicator of impulsivity. This value ranges from 0 to 1, with a higher AUC value indicative of lower impulsivity. However, in the present study the value of AUC was reversed so that a higher score is indicative of more impulsive decision making.

International Affective Picture System (IAPS; Lang et al., 1997). The IAPS is a bank of standardized images that are scored and classified in terms of their valency and arousal. Various studies have shown relationships between the presentation of these images and alterations in physiological measurements (Choi et al., 2017) as well as changes in the activation of brain circuits (i.e. Britton et al., 2006), which support the validity of these images.

In this study, forty images of the IAPS were selected according to their valence and normative arousal ratings (Moltó et al., 1999; Vila et al., 2001). The 40 images were presented in pairs on 20 trials, so that on each trial two images appeared at the same time. The 40 selected images had been checked with respect to the normative values of arousal (Range arousal: 0.14 - 0.93; mean difference = 0.48; SD = 0.31) although they varied in valence (Range valence: 1.16 - 3.83; mean difference = 2.53; SD = 0.72).

Therefore, in each pair of images there were two images with similar arousal values and with different valence. Each pair of images was presented on a computer in a randomized manner, and the participants had to point out the image that they considered to be the most pleasant.

The proportion of times that patients correctly selected the most pleasant image according to normative values was used as an indicator (Moltó et al., 1999; Vila et al., 2001). Thus, lower proportions are taken to indicate greater deterioration in relation to the normative population.

Substance Dependence Severity Scale (SDSS; Miele et al., 2000). The Spanish version adapted to the DSM-5 (González-Saiz et al., 2014) was administered, which has shown adequate psychometric properties (Dacosta et al., 2019). This instrument evaluates the severity of the dependence of patients during the month prior to the application of the test, including an evaluation for each substance. In this sample, internal consistency

values, evaluated through Cronbach's alpha, were equal to or greater than .77 in the evaluation of alcohol and cocaine dependence.

Cocaine Craving Questionnaire-Now -CCQ-N-10. The Spanish version of the CCQ-N was used to evaluate craving for cocaine (Iraurgi et al., 2009). A Cronbach's alpha value of .89 was obtained in the outpatient sample, and for patients undergoing residential treatment this was .85.

Multi-dimensional alcohol craving scale -MACS. The Spanish version of this 12-item instrument was used (Guardia-Serecigni et al., 2004). A Cronbach's alpha value of .90 was found in outpatients and .91 in residential patients.

Relapse. During the study period, participants were required to undergo toxicological screening to check if they had used cocaine or alcohol during treatment. Outpatients received the toxicological tests following the indications of the therapeutic team, whilst residential patients underwent these tests following each exit from the TC. Of the 222 participants, relapse information could not be collected for 8 patients.

Cocaine use was detected through urine analysis using the immunoenzyme analysis technique, and alcohol consumption was detected through blood tests. Carbohydrate deficient transferrin (CDT) levels were evaluated, with values greater than 1.7% considered positive.

These analyzes were conducted on patients diagnosed with abuse or dependence on these substances. Results considered to be positive in these analyses were interpreted as “relapses” and patients could show relapse for alcohol, cocaine, and both substances.

2.4.Procedure

A psychologist trained in the evaluation of patients administered the tests in individual sessions in the different centers.

Before starting the evaluations, the professionals of the centers where the study was carried out informed the patients that they fulfilled the criteria for carrying out the study, as well as the voluntary nature of their participation. It was made explicit that participation in the research was voluntary and external to their therapeutic process, and that their data would be treated solely for statistical purposes. If they agreed to participate, the patients were taken to the room where the interviewer was located, upon which the inclusion criteria were checked again, and the patients were informed of the study objectives, the voluntary nature of their participation, and the fact that this was external to their therapeutic process. They were also told that they could withdraw from the investigation whenever they wished. If the patients wished to participate in the study, they had to sign the informed consent form, and then the administration of the tests began.

After one year, the evaluator consulted with the professionals of the centers regarding the results of the toxicology tests, as well as other consumption data included in the medical records. Also, if they attended the appointment, they were asked to report their consumption during that period.

In total, results were obtained from 97.2% of patients with cocaine abuse / dependence, and 96.2% of patients with alcohol abuse / dependence. No information on cocaine relapse is available for 5 patients with cocaine abuse/dependence, and for 4 patients with alcohol abuse/dependence.

This study has been approved by the ethics committee of the University of Huelva.

2.5.Data analysis

Latent class analysis (LCA) was applied to identify profiles or groups of patients according to their performance on the WAT-DUD, DDT and IAPS. Along with these

variables, sex, age, treatment center (PSDH or CTs) and severity of cocaine and alcohol dependence were included as covariates.

The LCA is based on the premise that covariation between manifest indicators takes place due to the association they present. In this way, people are grouped according to the characteristics shared in the indicators. This assumption leads us to consider that people belonging to the same cluster are homogeneous with respect to each other and different from those of other clusters (Reboussin et al., 2006). In addition, this allows for identifying the probability of each person belonging to a particular group or profile, which is an indicator that helps to understand the heterogeneity of the sample (Monroy et al., 2010).

Determining the number of latent classes is a complex process, which must be guided by statistical fit indices and substantive interpretability (Nylund-Gibson and Choi, 2018). In this study, the profiles were identified by using as criteria the suitability of the statistical indicators, parsimony in the explanation of data, and the replicability of the latent profiles. To establish the appropriate number of latent class clusters, various models were tested by gradually increasing the number of clusters, adding one more cluster in each model. The Bayesian information criterion (BIC), the Akaike information criterion (AIC) and the Akaike variant (CAIC) were used to assess the goodness-of-fit of the models, based on log-likelihood (LL) values. Since BIC is less sensitive to sample size (Ondé and Alvarado, 2019) and CAIC is stricter than AIC when selecting more parsimonious models, both were used as main fit indices. In all of these, the lower the value of these parameters, the better the fit and the more parsimonious the model. Other indicators used were the number of parameters (Npar), which reports the most parsimonious model, and the misclassification or proportion of misclassified cases (Monroy et al., 2010). In addition, bootstrap-2LL difference was included to estimate

the p-value corresponding to the degree of fit that improves the model by including new latent classes. Regarding the stability or replicability of the profiles, a cross-validation procedure was applied, randomly selecting 75% of the sample. These analyzes were conducted using the Latent Gold v.4.5 software.

To analyze the bivariate relationship between profiles and sociodemographic and consumption variables, we used Pearson's Chi² statistics and ANOVAs according to the level of measurement of the analyzed variables. In addition, hierarchical logistic regression analysis was applied to the relapse data in order to determine the probability of relapse according to latent profiles, controlling for age, sex, and consumption-related variables. These statistical analyzes were conducted with STATA v. 14.0.

3. Results

3.1. Latent profile analysis

Solutions of between 2 and 4 latent profiles were explored. All three models showed similar BIC, AIC and CAIC values. Model 3 has the best BIC and CAIC value, and Model 4 has the best AIC value and the lowest classification error, whilst Model 2 was the most parsimonious. The inclusion of new classes was associated with less parsimonious models (Table 1). The bootstrap analysis revealed that Model 3 improved the fit with respect to Model 2, although Model 4 did not produce a statistically significant improvement with respect to Model 3. The percentage of agreement following cross-validation produced a more stable result when considering the 2 and 3-profile solution (Model 2). Taken together, these results suggest that the 3 latent class model is the most appropriate alternative.

The average conditional probability of the sample belonging to each of the three profiles is 0.97 for Profile 1, 0.89 for Profile 2, and 0.89 for Profile 3.

INSERT TABLE 1 HERE

In the 3-profile model, latent profile 1 is composed of 105 participants that are characterized by low activation in response to ambiguous images, low impulsiveness in decision making, and shows relatively few errors in identifying images of unpleasant valence (Figure 1). Profile 2 resembles the first in terms of performance on the WAT-DUD and the IAPS but differs in that this is the profile of patients that presents greater impulsiveness in decision making. Finally, the third profile identified shows moderate activation in response to ambiguous images and a relatively high level of impulsiveness in decision making. This group of patients showed the poorest discrimination between images of varying valence. Thus, Profile 1 appears to represent the group of patients with the most "normalized" values, while Profile 2 is characterized by high impulsivity, and Profile 3 by high impulsivity (although to a lesser extent than the patients of Profile 2) and high activation in response to drug-related stimuli.

According to the Wald test, the groups differed significantly on all three indicators (WAT-DUD: Wald-test: 52.40; $p < .001$; $R^2 = .33$; DDT: Wald-test: 309.74; $p < .001$; $R^2 = .66$; IAPS: Wald-test: 14.59; $p < .001$; $R^2 = .14$).

INSERT FIGURE 1 HERE

3.2. Characterization of the profiles

Table 2 shows the results of the bivariate analyzes between the profiles and the sociodemographic and consumption variables. In sociodemographic terms it is observed that the three profiles are similar, with no statistically significant differences between them. Moreover, no statistically differences were observed between inpatients and

outpatients. Regarding consumption patterns, significant differences were observed in terms of the severity of cocaine dependence. In particular, the group of patients in Profile 2 was found to have a higher severity of cocaine dependence.

With respect to the three cognitive variables, statistically significant differences were found between the three patient profiles. Bonferroni's post-hoc tests revealed that in the AUC the differences are significant between the three profiles. In contrast, in WAT-DUD and IAPS, Classes 1 and 2 differ with respect to Class 3, although there are no statistically significant differences between Classes 1 and 2 (WAT-DUD: $p = .994$; IAPS: $p = .177$).

INSERT TABLE 2 HERE

3.3. Relationship between latent profiles and relapse

The study of the relationship of each cognitive variable with relapse revealed that none of the variables showed statistically significant relationships for either the CT or PSDH patients.

Table 3 shows the percentages of patients who relapse in each profile. The analysis with all patients revealed that patients in Profile 3 are those with the highest relapse rates, with this difference being statistically significant in the case of cocaine ($\text{Chi}^2 = 9.169$; $p < .05$), and when cocaine and alcohol are analyzed together ($\text{Chi}^2 = 6.698$; $p < .05$).

Among the outpatients, patients in Profile 3 have the highest relapse rates. Statistically significant differences were found for relapse in cocaine use ($\text{Chi}^2 = 8.311$; $p < .05$) and for the use of cocaine and alcohol ($\text{Chi}^2 = 6.624$; $p < .05$). Among the inpatients, no statistically significant differences were found between the three patient profiles.

INSERT TABLE 3 HERE

Logistic regression analysis (Table 4) revealed that, for relapse in cocaine use patients in Profile 3 have a higher probability of relapse when patients in Profile 1 are taken as a reference. When cocaine and alcohol consumption are analyzed together, it was found that Profile 3 patients also present a higher probability of relapse, although in statistical terms this should be considered only as a trend ($p = .050$). This multivariate analysis also revealed that the type of treatment center is related to relapse (lower probability among inpatients). It was also observed that a higher level of craving is associated with a lower probability of relapse.

INSERT TABLE 4 HERE

4. Discussion

The identification of patient profiles with homogeneous characteristics is frequent in the study of addictions. This procedure attempts to identify groups of patients who could benefit from common psychological and pharmacological interventions (George and Koob, 2017). With this aim, various studies have analyzed patient profiles according to the pattern of drug use (Fernández-Calderón et al., 2015; Bobashev et al., 2018), combining them with cognitive measures (Harrel et al., 2014) and impulsivity (Albein-Urios et al., 2013). In this study, as in previous studies, the objective was to search for homogeneous groups of patients. However, unlike other studies, the analysis was carried out to include only those cognitive domains that are relevant to the addiction process. As stipulated by various theoretical models (Damasio, 1996; de Wit and Stewart, 1981; Goldstein and Volkow, 2002, 2011) and neuroimaging studies (Moeller et al., 2018), incentive salience, emotionality, and decision-making measures were used. In addition, some authors have pointed out the clinical utility of these cognitive domains

because of their connection with the various phases that addiction patients go through, including their recovery (Kwako et al., 2016; Verdejo-García, 2017). For this reason, the hypotheses of the present work were linked to: i) the identification of different profiles according to the cognitive measures mentioned; and, ii) the possibility that different profiles present different outcomes in terms of relapse.

With respect to the first hypothesis, our results have revealed three patterns of cognitive functioning in the domains evaluated. This indicates that it is possible to identify groups of patients that show similar performance patterns on these three tasks, whilst such patterns also serve to differentiate them from other patient groups. These cognitive patterns do not appear to be related to alcohol. However, it was observed that patients in Profile 2 (patients with a greater impairment in impulsive decision making) are those who present a greater severity of cocaine dependence. In this regard, these results are consistent with studies that have not found a relationship between performance on DDT tasks and the choice of drug (Amlung et al., 2017; Gowin et al., 2018), but with the severity of cocaine dependence (Amlung et al., 2017; Hulka et al., 2015). Other authors have also found that in inpatients, impaired performance on both attention and working memory tasks is associated with the number of days of cocaine use, showing that recent cocaine use is a predictor of cognitive decline in these domains (Ruiz-Lima et al., 2019).

The presence of these three profiles is of interest for continuing to advance our understanding of addiction. The conformation of a specific profile that differs fundamentally in terms of decision-making (Profile 1 vs. Profile 2), reinforces the discriminant nature of this domain for addictive disorders, which has been pointed out by different authors (Verdejo-García, 2017; Verdejo-Garcia et al., 2018). In addition, the different patterns of performance shown by these three profiles could indicate that

patients are in different phases of their addictive process (Goldstein and Volkow, 2002, 2011). In this sense, and converging with the I-RISA model, when considering Hypothesis 2 it was observed that those who relapse most are those who have a high level of impairment in impulsive decision making and have the greatest salience attribution. But they are also those who show a greater deterioration in the allocation of affective load to the images of the IAPS. Thus, our findings are also in line with the postulates of the somatic marker model (Verdejo and Bechara, 2009).

The fact that there is a patient profile that presents a higher probability of relapse compared with other profiles also contributes towards accounting for discrepant results found in the literature to date (Domínguez-Salas et al., 2016). Thus, in the specialized literature there are studies indicating that impulsive decision making predicts relapse (i.e. Stevens et al., 2014) while other studies do not find such a relationship (i.e. De Wilde et al. 2013). An explanation of these seemingly contradictory results emerges from the results found in this study. As we have observed, patients in Profiles 2 and 3 make impulsive decisions. But it is the patients of Profile 3 — also characterized by showing enhanced salience when presented with ambiguous stimuli and a lower capacity for emotional processing — who have the highest probability of relapse. This shows that, in order to predict relapse, studying each cognitive domain in isolation may be insufficient. These results are in line with the Research Domain Criteria (RDoc) initiative on the need to explore and comprehensively understand the cognitive mechanisms underlying addiction (Yücel et al., 2019).

Finally, it should be noted that our results should be considered within the context of some possible limitations. One limitation concerns the sample size of the study. Some authors set a minimum threshold of 300 participants (i.e. Lo et al., 2001), while other authors set this at 500 (i.e. Henson et al., 2007). However, there is no unanimous

agreement on the required sample size when using this technique, and there are a number of factors that could determine the appropriate sample size (Park and Yu, 2017). In the case of this study, the use of continuous variables entails a smaller sample size (McNeish and Harring, 2015), whilst the fact that we found three clusters with a sufficient number of participants in each of them allows us to consider the result to be reliable (Park and Yu, 2017). In addition to considerations regarding our sample size, we believe that cross-validation with 75% of the sample has demonstrated the stability of the clusters. This certainly supports the replicability of the groups of patients found. Another limitation that must be taken into account is that the study was conducted with inpatients and outpatients. Whilst this combination of patient groups does not affect the latent class analysis, it should be considered when studying relapse. In particular, outpatient centers and TCs are very different therapeutic contexts, and our findings have revealed greater relapse among outpatients than inpatients. However, our results have shown a consistent trend, with patients in Profile 3 presenting the highest probability of relapse in both contexts. Therefore, these findings indicate that this possible flaw in the study design has had no impact on the outcomes observed here. Finally, it should also be noted that some authors have demonstrated that chronicity, patterns in recent use and severity of cocaine dependence are associated with the deterioration of certain cognitive domains, along with relapse (Ruiz-Lima et al., 2019). In this study we were unable to analyze the impact of these variables on patient profiles, and future work should therefore aim to determine the effect of these variables on the deterioration of the studied cognitive domains and relapse. In view of these considerations, the conclusions of this study should be considered specific to our particular research context.

On balance, we consider that the results of this study have opened up new paths for understanding addiction and relapse, and point towards the need for a comprehensive cognitive evaluation of patients in order to predict therapeutic successes and failures.

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