Theory of Mind Impairments in Women with Cocaine Addiction

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ABSTRACT. Objective: This study investigates the theory of mind performance of female cocaine-dependent users (CDUs) and possible associations between theory of mind performance and features of cocaine use. **Method:** Sixty women controlled for age, education, individual income, and IQ participated in this study: 30 in the CDU group and 30 in the healthy control group. Participants were assessed for theory of mind with the Reading the Mind in the Eyes Test (RMET), a test of understanding of first-order and second-order false beliefs, and the Hinting task. Drug use parameters, clinical symptoms, and neuropsychological functioning were also assessed. **Results:** Analyses of covariance indicated theory of mind impairments in negative mental states within the RMET and second-order false-belief understanding of theory of mind stories. In addition, theory of mind impairment was associated with drug use characteristics, including craving and number of hospitalizations. **Conclusions:** High-demand theory of mind is suggested to be impaired in CDU women, and the deficits appear to be related to drug addiction severity. We found associations between theory of mind deficits and worse clinical and social outcomes. (*J. Stud. Alcohol Drugs, 78,* 000–000, 2017)

COCAINE USE DISORDERS ARE RELATED to inefficacy in managing social and interpersonal problems (e.g., criminal involvement, interpersonal and family conflicts) (Proctor et al., 2014). Efficacy of social interaction depends on a set of psychological processes involved in evaluation of social stimuli, collectively referred to as social cognition (Fiske & Taylor, 1991). Theory of mind (ToM) is one of the most important sociocognitive processes, and ToM impairments have been related to several symptoms of psychiatric disorders, including aggressiveness, depressive symptoms, and social isolation (Cusi et al., 2012; Sprong et al., 2007). ToM is the ability to interpret and infer the thoughts of others, as well as oneself (Premack & Woodruff, 1978). ToM is a psychological function related to other cognitive functions, particularly working memory, verbal fluency and executive functions (Ahmed & Miller, 2010; Corcoran & Frith, 2003).

Emotion recognition is one of the core components of ToM (Ahmed & Stephen Miller, 2010; McDonald et al., 2013), and this function has been shown to be impaired in substance use disorders (Kornreich et al., 2003; McDonald et al., 2013; Sanvicente-Vieira et al., 2017), leading some authors to suggest that sociocognitive impairments may underlie the social dysfunctions found in individuals with substance use disorders (Homer et al., 2008; Volkow et al., 2011a). Consistent with this hypothesis, sociocognitive performance has been suggested to be a predictor of clinical outcomes (e.g., dependence severity, number of hospitalizations), and it has been proposed that there is an association between social cognition and addiction (Fernández-Serrano et al., 2010; McDonald et al., 2013; Sanvicente-Vieira et al., 2017).

However, the nature of this relationship is complex, since we still do not know whether the ToM impairment is mostly a consequence of use or if it predisposes individuals to use, with greater use reflective of less ability to regulate emotional states. Although some ToM understanding occurs around the age of 4 years, ToM continues to develop and be refined throughout childhood and even into late adulthood (Homer et al., 2008). In this way, individuals usually grow in families characterized by high levels of negative affect, difficulties in representation, and impaired recognition of emotional expressions and could be more susceptible to socioemotional difficulties later in life (Bateman & Fonagy, 2010). As sociocognitive functioning has recently been suggested to be related to clinical (Gizewski et al., 2013; McDonald et al., 2013) and social outcomes (Fernández-Serrano et al., 2010; Preller et al., 2014b), some authors proposed that treatments for substance-related disorders should target social cognition (Homer et al., 2008; Uekermann & Daum, 2008).

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Specific brain areas, including the insula and the prefrontal cortex, have recently been shown to contribute to processing for ToM tasks (Adolphs, 2009; Cusi et al., 2012; Gizewski et al., 2013). Prefrontal cortex deterioration theory proposed that the behavioral changes observed in addiction are the result of toxin-related *prefrontal* cortex neuroadaptations that occur as a result of repeated drug use (Moselhy et al., 2001). Because changes in prefrontal cortical activation have been associated with drug dependency (Bolla et al., 2004; Hester et al., 2013; Volkow et al., 2011b), impairments in ToM from substance use disorders might be expected (Uekermann & Daum, 2008). Investigations of ToM in alcohol (Bosco et al., 2014; Kornreich et al., 2011; Onuoha et al., 2016; Uekermann et al., 2007) and methamphetamine (Henry et al., 2009) dependents showed that the performance of these populations was impaired in comparison to that of healthy controls (HCs). It has also been shown that methamphetamine abusers display deficits in ToM performance in comparison with controls (Kim et al., 2011).

Although these studies provide some evidence to support the hypothesis that impairments in the ability to depict mental states are present during the course of substance use disorders, only a few studies have investigated ToM in cocaine addiction. There is evidence for cocaine-dependent users (CDUs) showing sociocognitive deficits, including deficits in emotion recognition from voices (Hulka et al., 2013), emotional empathy, and mental perspective-taking (ToM) (Preller et al., 2014a). In addition, brain regions associated with cocaine addiction—for example, the insula (McHugh et al., 2013) and the prefrontal cortex (Ersche et al., 2011)—have been shown to contribute to ToM functioning (Adolphs, 2009). However, the few studies investigating ToM within CDUs showed mixed results—indicating that there are ToM impairments regarding prosody processing, emotional empathy, and mental perspective-taking but not for visual emotion perception from eye pairs and faces (Hulka et al., 2013; Preller et al., 2014b). Although most of the results indicate that substance use–related disorders are also related to ToM impairments, a recent systematic review found that published evidence did not support the same effect from recreational use (Sanvicente-Vieira et al., 2017). In addition, the authors of this review suggest that future studies may consider strategies to cope with some of the limitations of the published studies, including the investigation of different drugs and sex effects.

Therefore, considering that women use cocaine differently than men (Najavits & Lester, 2008) and that they can respond to cocaine (Lukas et al., 1996) and cocaine cues (Fox et al., 2014; Kennedy et al., 2013) differently, we believe that women should be investigated as an independent sample. Particularly when considering that women have different patterns of medial prefrontal brain activation during ToM tasks when compared with men (Krach et al., 2009), in this study, we choose to investigate a women-only sample. We compared ToM functioning between CDU women in early abstinence and female HCs. We also tested whether ToM was related to other cognitive functions, clinical outcomes, or drug use parameters.

Method

Study design

The study protocol was approved by the ethics committees of the involved institutions, and all the participants were provided with written informed consent prior to their enrollment. This is a case–control study designed to compare ToM performance in CDU women and HCs. Before data collection, we estimated that a sample with 30 participants in each group would be needed to detect effects with an effect size (Cohen's *d*) of .80. Estimation of required sample size was based on the means and standard deviations of ToM measures reported in other studies of social cognition, which used participants with substance use disorders in the early abstinence period (fewer than 30 days of abstinence) (Kim et al., 2011; Thoma et al., 2013).

Participants

The initial sample was comprised of 115 potential CDU participants with formal cocaine dependence diagnoses—confirmed by the Structured Clinical Interview for DSM-IV Axis I disorders (SCID-I; First, 1997). It was important that cocaine dependence was the primary diagnosis for consideration for participation, but the presence of a second substance use disorder was not an exclusion criterion due to the high frequency of such comorbidity. Eighty-five participants were excluded because of the occurrence of a psychiatric disorder other than drug dependence or because of the presence of psychotic symptoms ($n = 56$); current use of psychiatric medication ($n = 7$); presence or history of neurological diseases ($n = 6$); history of head trauma, anoxia, stroke, or encephalitis ($n = 4$); and presence of severe cognitive deficits (assessed with the Mini-Mental State Examination [MMSE], cutoff score < 18 or IQ < 70; $n = 1$). The IQ score was obtained from the Vocabulary and the Matrix Reasoning subtests of the Wechsler Abbreviated Scale of Intelligence (Psychological Corporation, 1999).

All CDU participants were inpatients at a secure detoxification facility for alcohol and drug dependence in southern Brazil. As part of their treatment, all patients remained in a controlled, abstinence environment for three weeks, during which patients do not have any access to illicit drugs, tobacco, or alcohol. The treatment program also included psychoeducation and support groups. CDU participants were invited to enroll in the study only after they had completed two weeks of treatment in order to avoid severe withdrawal symptoms affecting the study.

Once the 30 CDU participants had been assessed, HCs were recruited through advertisements. After a telephone screening, an initial group of 37 potential HC women was assessed considering exclusion criteria, and 30 HC participants were selected. Exclusion criteria for the HC group were any lifetime use of illicit drug; occurrence of any psychiatric or neurological disorders (except nicotine dependence) ($n = 4$); use of any medication within the previous 6 months ($n = 2$); history of head trauma, anoxia, stroke, or encephalitis; presence of psychotic symptoms; and severe cognitive deficits (MMSE < 18 or IQ < 70; $n = 1$).

Procedures

Assessment took place over two sessions within a maximum of seven days. Four trained clinical psychologists administered the protocol. Participants in the HC group were required to abstain from using alcohol and other psychoactive substances except nicotine for at least 48 hours prior to the assessment. Informed consent was obtained from all participants, and the research was approved by the ethics committees of all institutions involved in this study.

Instruments

ToM measures.

(A) *Reading the Mind in the Eyes Test (RMET):* The RMET (Baron-Cohen et al., 2001) is a ToM task that assesses the ability to infer mental states from the eyes region of the face. Participants are presented with 36 photographs of the eyes region of actors. Each photograph is surrounded by four (one correct, three foil words) possible single-word descriptions of the mental state of the individual in the photograph. Participants are required to choose the word that best matches the expression. The number of correct answers provides a total score. Subtotals based on the emotional valence of the expressions can also be calculated (Hysek et al., 2012), providing subscores for positive (eight items), negative (12 items), and neutral (16 items) expressions. An adapted computerized version of the RMET was used (Sanvicente-Vieira et al., 2014).

(B) *Theory of mind stories task:* ToM is assessed using questions about first-order and second-order false beliefs (Frith & Corcoran, 1996). The task comprises six stories that are read to the participant by the researcher. All stories are presented with drawings that illustrate the story. To answer first-order questions, the participants are required to infer that a particular character from the story holds a belief that is counter to reality. Second-order false belief questions require the participant to infer the beliefs that one character has about the beliefs of another character. A total ToM Stories score is computed by summing the first-order false belief understanding score and the second-order false belief understanding score.

(C) *Hinting task:* The Hinting task uses an indirect speech paradigm to test the ToM of participants (Corcoran et al., 1995). It comprises 10 short vignettes; in each, an interaction between two characters is presented. A researcher reads the vignettes out loud to the participant. At the end of each vignette, one of the characters drops a hint to the other; the participant is required to explain what the first character really meant by the hint. A correct response scores 2 points. If the participant gives an incorrect response, additional vignette information is provided in the form of a second, more obvious hint. A correct response after the second reading scores 1 point, and a second incorrect response scores 0 points.

Cognitive measures. In view of the relationship between ToM and other cognitive functions, the following functions were assessed: processing speed, set-shifting, working memory, and verbal fluency. Processing speed and set-shifting were assessed by the Trail-Making Test (TMT; Reitan & Wolfson, 1985). Processing speed was measured by subtest A of the TMT (TMT-A), and set-shifting was assessed by the TMT subtest B (TMT-B). Total completion times for TMT-A and TMT-B were used as outcomes; higher times represented worse performance (i.e., slower processing speed and lower set-shifting ability). Working memory was assessed by the Forward Digit and Backward Digit Span subtests of the Wechsler Adult Intelligence Scale–III (WAIS-III; Wechsler, 1997). Verbal fluency was assessed by the FAS Test (Spreen & Benton, 1977).

Clinical measures. Symptoms of depression and anxiety were evaluated using the Beck Depression Inventory–II (BDI-II; Beck et al., 1996) and the Beck Anxiety Inventory (BAI; Beck et al., 1988), respectively. In view of the association between ToM and psychotic symptoms, the positive and negative subscales of the PANSS (Kay et al., 1987) were applied. In addition, a clinical interview regarding the pattern of drug use was applied. The craving score of the Cocaine Selective Severity Assessment (Kampman et al., 1998) was used to assess craving, which refers to the sum of items four and five.

Statistical analyses

The two groups were compared on clinical, sociodemographic, cognitive, and ToM variables. The distribution of all variables for each group was tested for normal distribution using the Shapiro–Wilk test. Where variables were normally distributed, independent sample t tests were used, and where variables were nonnormally distributed, the Mann–Whitney U tests were used. Categorical variables were compared using chi-square tests. Group differences for individual ToM tests were tested by analyses of covariance (ANCOVAs) to statistically control the linear effect of variables that can influence ToM performance and that could not be controlled through research design: depressive and anxiety symptom se-

TABLE 1. Demographic, clinical, and drug use characteristics of participants

Variable	CDUs (n = 30)		HCs (n = 30)		Statistics	p	Effect size
	M or %	(SD) or n	M or %	(SD) or n			
Demographic							
Age, in years	28.9	(7.75)	31.16	(8.57)	t = 1.073	.288	-0.27
Education, in years	11.1	(1.9)	9.53	(1.96)	t = 1.358	.180	0.81
Income, in U.S. $/month	1,273.47	(1,306.14)	1,284.92	(690.31)	t = 0.892	.376	-0.01
Global cognition							
MMSE	25.66	(3)	26.2	(2.6)	t = 0.734	.466	-0.19
IQ	87.96	(8)	90.46	(12.63)	t = 0.916	.364	-0.23
Clinical							
BDI-II	12.93	(6.6)	6.63	(4.42)	t = 4.34	<.001	1.12
BAI	10.06	(6.36)	6.9	(4.48)	t = 2.227	.03	0.57
PANSS positive	9.3	(2.61)	8.66	(2.46)	U = 361	.176	0.25
PANSS negative	9.7	(3.41)	8.33	(2.52)	U = 346.5	.106	0.45
Drug use							
Cocaine							
Days in abstinence	16.2	(4.5)					
First use, in years	20.06	(0.85)					
Years of dependence	8.37	(1.078)					
Average dose per episode, g[a]	4.25	(0.6)					
Frequency of episodes, times per month	12.3	(0.65)					
CSSA score for craving	3.6	(3.14)					
Crack as primary way of administration	86.7%	n = 26					
Alcohol							
Regular use	100%	n = 30	86.7%	n = 26	χ^2 = 4.286	.112	0.57
Dependence disorder	23.3%	n = 7					
Days in abstinence	22.8	(1.3)	22.13	(1.86)	U = 447	.962	0.41
First use, in years	13.6	(3.33)	18.7	(4.21)	t = 5.198	<.001	-1.34
Average dose per episode, g	144.8	(112.898)	12.79	(15.32)	t = 3.293	.013	1.63
Frequency of episodes, no. of times per month	8.57	(1.5)	5.66	(1.6)	t = 4.117	<.001	1.87
Cannabis							
Regular use	96.7%	n = 29					
Dependence disorder	23.3%	n = 7					
Days in abstinence	24.3	(5.98)					
First use, in years	17	(0.79)					
Average dose per episode, no. of cigarettes	2.35	(2.88)					
Frequency of episodes, no. of times per month	5.26	(2.45)					
Tobacco							
Regular use	80%	n = 24	26.66%	n = 8	χ^2 = 17.143	<.001	2.148
Days in abstinence	19.66	(8.24)	0.375	(0.744)	t = 6.534	<.001	3.29
First use, in years	14.17	(3.17)	17.71	(7.52)	t = 2.386	.022	-0.61
Average no. of cigarettes per day	19.91	(8.89)	16.37	(5.97)	t = 1.044	.305	0.46
No. of psychiatric hospitalizations	3.37	(0.43)					

Notes: CDU = cocaine-dependent user; HC = healthy control; MMSE = Mini-Mental State Examination; BDI-II = Beck Depression Inventory–II; BAI = Beck Anxiety Inventory; PANSS positive = positive subscale of the Positive and Negative Syndrome Scale; PANSS negative = negative subscale of the Positive and Negative Syndrome Scale; CSSA = Cocaine Selective Severity Assessment; t = unpaired t test; U = Wilcoxon–Mann–Whitney test; χ^2 = chi-square test. [a]As a result of a high number of CDU participants reporting the administration of cocaine through the smoking of crack, we asked the participants to report how many rocks they used to smoke per episode; based on toxicological analyses in Brazilian samples of street origin crack rocks, we estimated its composition as containing 57.7% cocaine, with each rock weighing on average 0.24 g (Herculiani et al. 2009). For those participants who snorted cocaine, we asked them directly about the average number of grams they used to consume per episode. Effect sizes presented are Cohen's deltas.

verity (Hezel & McNally, 2014; Zobel et al., 2010), working memory (Dennis et al., 2009; Uekermann et al., 2007), and fluency performance (Woodward et al., 2009). The level of significance for all comparative reported data was assumed for $p < .05$ (two tailed).

A series of Pearson's correlations was carried out to investigate associations between ToM variables and other demographic, clinical, and cognitive characteristics. Subsequently, correlational analyses considering only the CDU group were performed due to our interest in the possible associations between ToM and drug use characteristics.

Results

Demographic and clinical characteristics

Between-group comparisons for demographic and clinical characteristics are summarized in Table 1. As predicted, there were significant group differences regarding depressive and anxiety symptoms and drug use patterns. We found that more than 25% of HC participants were smokers compared with 80% of CDU participants, but we did not find any effects of tobacco on the ToM measures (data not shown).

Table 2. Comparisons on cognitive function

Cognitive measures	CDUs *M* (*SD*)	HCs *M* (*SD*)	*t*	*df*	*p*	Effect size
Processing speed						
TMT-A, in seconds	46.64 (17.33)	45.4 (21.25)	0.250	58	.804	-0.06
Set-shifting						
TMT-B, in seconds	123.85 (79.17)	106.8 (56.55)	0.96	58	.341	-0.24
Working memory						
Forward Digit Span[a]	11.66 (3.88)	12.7 (3.74)	1.049	58	.299	0.27
Backward Digit Span[a]	5.43 (2.48)	6.83 (2.00)	2.402	58	.02	0.62
Verbal fluency						
FAS test	32.16 (9.13)	37.7 (8.61)	2.413	58	.019	0.62
Theory of mind						
Total RMET	57.93 (12.86)	69.62 (7.54)	4.575	58	<.001	1.18
Positive RMET	60.41 (19.89)	76.66 (19.89)	2.437	4,987	.18	0.62
Negative RMET	54.44 (16.77)	76.94 (12.51)	5.89	58	<.001	1.52
Neutral RMET	55 (14.98)	60.62 (11.27)	1.643	53.84	.106	0.42
Hinting task	69.5 (16.26)	78.66 (17.26	2.117	58	.039	0.54
First-order false belief	92.22 (11.35)	93.33 (10.35)	0.431	58	.738	0.05
Second-order false belief	57.7 (21.76)	73.8 (16.19)	3.253	58	.002	0.85

Notes: CDU = cocaine-dependent user; HC = healthy control; TMT-A = subtest A of the Trail-Making Test; TMT-B = subtest B of the Trail-Making Test; FAS = Verbal Fluency Test; RMET = Reading the Mind in the Eyes Test. effect size = Cohen's delta. [a]Forward and Backward Digit Span subtests of the Wechsler Adult Intelligence Scale-III.

General cognition

Table 2 summarizes comparisons on cognitive function. The HC group exhibited better performance in comparison to the CDU group on one subtest of working memory and on verbal fluency.

Theory of mind

There were significant differences in the total score and in the positive and negative subscores of the RMET. The CDU group had lower scores than the HC group for second-order false belief understanding within the ToM Stories task and the Hinting task score. Data regarding ToM measures and comparisons are summarized in Table 2.

Analyses of covariance. Group comparisons for individual ToM measures using ANCOVAs yielded significant main effects for the group on RMET-negative and on second-order false belief understanding for the ToM Stories scores. Each ANCOVA included one of the ToM measures as a dependent variable and the group as a fixed factor. ANCOVAs are presented in Table 3.

Correlations. Correlations among ToM measures as well as clinical and cognitive measures considering the overall sample are displayed in Table 4. Correlations for RMET-neutral scores and first-order false belief understanding were omitted, because no significant correlational result was found. We found associations between depressive symptoms and the ToM performance for the total RMET, RMET-positive, and RMET-negative scores. Negative psychotic symptoms were associated with the RMET-positive and Hinting task scores. Verbal fluency was associated with ToM performance in terms of the RMET-positive and RMET-negative scores, the Hinting task score, and second-order false belief understanding. Processing speed was negatively correlated with total RMET and RMET-positive scores, being the former result only true for CDU group. Set-shifting measures were negatively associated with the total RMET-positive score.

Additional correlation analyses were computed only for the CDU group considering drug use characteristics. The

Table 3. Theory of mind measures between groups

	CDU group		HC group		Main effect of group		
ANCOVA[a]	*M*[b]	*SE*	*M*[b]	*SE*	*F*(1, 54)	*p*	η^2
ToM measure							
Positive RMET	4.83	2.45	6.13	1.59	0.126	.724	.002
Negative RMET	6.53	2.01	9.23	1.5	14.608	<.001*	.213
Neutral RMET	8.8	2.3	9.7	1.8	0.307	.586	.006
First-order false belief	5.53	0.68	5.6	0.62	0.498	.484	.009
Second-order false belief	3.46	1.3	4.43	0.97	6.894	.011*	.113
Hinting task	13.9	3.25	15.73	3.45	2.281	.137	.041

Notes: CDU = cocaine-dependent user; HC = healthy control; ANCOVA = analysis of covariance; RMET = Reading the Mind in the Eyes Test. [a]Controlled by using the scores of Beck Depression Inventory–II, Beck Anxiety Inventory score, Backwards Digit Span, and the verbal fluency FAS test; [b]adjusted values; ^{2} = effect size partial eta-squared. *Significant with Bonferroni type adjustment.

TABLE 4. Correlations between theory of mind measures[a] and clinical and cognitive outcomes

Variable	Total RMET	RMET positive	RMET negative	Second order false belief	Hinting task
Depressive symptoms					
CDU group	-.391*	-.382*	-.480**	.271	.134
HC group	-.189	-.110	-.33	-.243	.206
Total	-.424**	-.285*	-.408**	-.114	.04
Anxiety symptoms					
CDU group	-.021	-.278	.046	.212	.198
HC group	-.178	.31	-.99	-.101	.094
Total	-.19	-.251	-.166	-.018	.064
Negative psychotic symptoms					
CDU group	-.23	-.455*	-.247	-.207	-.28
HC group	-.079	-.11	.106	-.061	-.282
Total	-.238	-.357*	-.231	-.228	-.282*
Positive psychotic symptoms					
CDU group	.099	-.277	-.228	-.042	-.146
HC group	-.141	-.05	.003	-.153	-.079
Total	-.024	-.216	-.18	-.129	-.132
Processing speed					
CDU group	-.38*	-.38*	-.299	-.041	-.049
HC group	-.104	-.35	.298	-.232	-.335
Total	-.21	-.426**	-.030	-.131	-.211
Set-shifting					
CDU group	-.214	-.219	-.115	-.128	-.005
HC group	-.248	-.352	.213	-.211	-.144
Total	-.249	-.285*	-.077	-.192	-.094
Working memory (forward digit span)					
CDU group	-.15	-.1	-.024	.038	.201
HC group	-.005	.086	-.219	.166	.33
Total	-.088	-.018	-.076	.089	.270
Working memory (backward digit span)					
CDU group	.228	.210	.118	-.16	-.144
HC group	-.093	-.004	.025	.145	.278
Total	-.238	.215	.246	.078	.127
Verbal fluency					
CDU group	.123	.117	.391*	.34	.583**
HC group	.029	.345	-.216	.243	.428*
Total	.207	.274*	.290*	.380**	.544**

Notes: RMET = Reading the Mind in the Eyes Test; CDU = cocaine-dependent user; HC = healthy control. [a]Excluding RMET-neutral score and first-order false belief because neither had a significant correlational result.
*$p < .05$; **$p < .001$.

average cocaine dose per episode and RMET-positive score were found to be correlated ($r = .344$, $p = .038$); in addition, second-order false belief ($r = .481$, $p = .02$) and the Hinting task ($r = .321$, $p = .045$) scores were correlated with time of cocaine dependence. The cocaine craving was negatively correlated with total RMET ($r = -.281$, $p = .45$) and the RMET-positive score ($r = -.381$, $p = .038$). Number of hospitalizations was negatively correlated with second-order false belief understanding ($r = -.506$, $p = .005$).

Discussion

We found some ToM impairments in CDU women in contrast to HC women who were independent of clinical symptoms and cognitive impairments. However, these impairments were not widespread. Poorer performance was restricted to high demand measures, such as second-order false belief understanding and interpretation of negative emotional states from pictures of the region of the eyes. ToM performance was associated with mood symptoms, some cognitive functions, and some drug use parameters

CDU women showed impaired understanding of second-order false beliefs, corroborating an earlier report of impairments in the prosodic elements, emotional empathy, and mental perspective-taking of social cognition in cocaine dependence (Preller et al., 2014b). We did not find group differences in understanding of first-order false beliefs, probably due to the ceiling effect. Similar data have been reported for people with alcohol dependence (Bosco et al., 2014). CDU women also had impairments in ToM based on visual stimuli, particularly when recognizing negative emotional states. In this sense, there is other evidence that stimulant use is related to impairments in recognizing facial expressions of fear, sadness, and anger (Fernández-Serrano et al., 2010; Kemmis et al., 2007; McDonald et al., 2013).

It should be noted that our results are partially different from some previous findings. Preller et al. (2014b) found no difference in the performance of CDU and HC participants on the RMET. They applied a study design very similar to ours, but they used a nonpatient sample of mixed sex and with a wide range of cocaine use severity, whereas we only investigated female in-patients who were all crack dependent. Our decision to limit our sample to women was based on evidence of sex-based differences in cocaine dependence (Dluzen & McDermott, 2008; Elman et al., 2001) and in social cognition (Morgan & Marshall, 2013). There were other differences between the samples, 75% of control participants in Preller et al (2014b) were smokers compared to approximately 25% in our study, and they did not exclude control participants who were regular users of cannabis. Although cannabis use was not correlated with social cognition parameters in the study of Preller et al. (2014b), long-term cannabis use may have had a negative effect on social cognition (Sánchez-Torres et al., 2013), including ToM (Platt et al., 2010).

Thus, our positive findings may be attributed to the use of a control group limited to drug-naive women. Additionally, duration of exposure to the drug has been cited as a possible predictor of impairments in social cognition (Gizewski et al., 2013); our sample had longer drug use histories, so progression of the substance use disorder could also explain the discrepancy. Another important difference between the present study and Preller's (2014b) study was regarding general cognition, because our samples had lower mean IQ values. However, our values are equivalent to those reported in Latin American samples (Lynn & Meisenberg, 2010) and replicate IQ values identified in previous studies, including Brazilian CDU participants (Kluwe-Schiavon et al., 2016; Viola et al., 2013). Given such contrasting findings, someone could hypothesize the existence of culturally dependent effects in social cognition, which may be a focus for future research. Our results for RMET also contrast with those of Kemmis et al. (2007). One difference, however, is that Kemmis et al. deliberately excluded dependent users, investigating only nondependent cocaine users, which may had accounted for the differences in results. Consequently, ToM deficits might not develop before severe cocaine addiction, which is in line with findings of Preller et al. (2014b) showing that only dependent cocaine users displayed deficits in mental perspective-taking, but not regular recreational cocaine users.

We found negative correlations between some drug use parameters and ToM performance, which is consistent with previous research on substance use disorders (Kornreich et al., 2002; McDonald et al., 2013) and provides corroboration for the hypothesis that the extension of the neurotoxic effects due to drug use may be directly associated with the severity of the behavioral and cognitive impairments within the disorder (Kuhar & Pilotte, 1996; Makris et al., 2008). However, sociocognitive deficits in substance use disorders might not be understood merely as consequences of drug use; they may also be implicated in the initiation of drug use (Kuhar & Pilotte, 1996; Volkow et al., 2011a).

Our study is subject to certain limitations. First, we investigated a women-only sample. Since there are sex-based differences in cocaine dependence (Elman et al., 2001), our findings cannot be generalized to men. Second, we cannot rule out nicotine- or alcohol-exposure effects as possible explanations for the effects we observed, because groups differed in these variables. In particular, clinical participants had been abstinent from nicotine for about 20 days, whereas control participants (although only 25% reported to use tobacco) did not have a period of required abstinence. Given the impact of nicotine on cognitive processing, we cannot exclude potential nicotine effects among the HC group, despite no differences being found between tobacco users and nonusers within controls (all ps > .005). Third, we employed a cross-sectional design and used correlations and general linear models to assess effects, so it is not possible to make causal inferences about the associations among variables. Fourth, we did not assess the severity of tobacco dependence or personality disorders, which would have provided a more detailed characterization of our sample.

Fifth, our sample came from a low-education background, which is representative of the majority of Latin American populations, especially among substance users. In this regard, we suggest caution when comparing our results with those of other studies, including study results from highly educated samples. Sixth, we found lower MMSE and IQ scores in comparison to those values reported for the participants from European and North American studies (Sanvicente-Vieira et al., 2017). It is important to recognize that there were no group-wide differences regarding general intelligence in our study. Moreover, the low IQ scores observed in this sample may reflect the relatively poor educational opportunities and overall poor socioeconomic conditions common in developing countries (Victora et al., 2015; Yassuda et al., 2009). Future intercultural investigations will help to elucidate whether our results can only be generalized to Latin American samples or if ToM deficits are in fact applicable to all cocaine users.

Seventh, our results could be related to other cognitive functions not assessed here; thus, a wider cognitive battery might have revealed specific cognitive domains to be associated with ToM impairment. In spite of these limitations, this study has unique strengths: we used stringent inclusion/exclusion criteria to avoid potential bias effects, and we included three different and widely used classical measures of ToM. This is important because restricting testing to a single ToM paradigm has been cited as an important limitation of ToM research (Harrington et al., 2005; Sprong et al., 2007). Thus, our results provide evidence that CDU women have ToM impairments, particularly when a higher cognitive demand is required. They also suggest that therapeutic strate-

gies focusing on sociocognitive functioning could have the potential to improve secondary outcomes related to drug use.

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