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Cocaine polydrug use and its impact on intentional harm recognition: a high-density EEG study

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Abstract

Background Cocaine and stimulant consumption constitute a significant global issue and are associated with impaired social skills. However, the relationship between substance abuse and intentional harm recognition remains unclear. Intentional harm recognition is a crucial social cognitive ability that allows individuals to determine whether a harmful action performed by another person is deliberate or accidental.

Methods The present study examined self-reported, behavioural, and neural responses associated with intentional harm recognition in $n=19$ cocaine polydrug users (COC) and $n=19$ healthy controls (HC). High-density electroencephalography (hdEEG) was used to measure brain activity during an Intentional Inference Task (IIT), which assesses fast intention recognition in scenarios involving deliberate or unintentional harm to people and objects. This study took place between 2014 and 2015 in Santiago, Chile.

Results Behaviorally, COC exhibited slower reaction times (RT) than HC. Event-related potential (ERP) analysis revealed late frontal differences in HC when attributing intentional harm, while these differences were absent in COC.

Conclusions These findings suggest a potential shift in COC towards emotional over-involvement and away from rational cognitive assessment of social information. The present results provide new insights into the recognition of intentional harm processing in cocaine polydrug users and highlight the potential clinical benefits of interventions focused on socio-emotional regulation training.

Keywords Substance use disorder, Social cognition, Intentional harm recognition, Intentional inference task (IIT), HdEEG

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Introduction

Estimates suggest that 296 million people use drugs, which represents an increase of 23% in the decade from 2011 to 2021. 39.5 million individuals suffer from a substance use disorder (SUD), and twenty-two million people have problems with cocaine [1]. Within South America, the annual prevalence of cocaine use is highest among Chile (1.1%), Argentina & Uruguay (1.6%), and Costa Rica (1.2%) [1].

Substance use has important implications for broader indicators of well-being. While 9.3% of the general population in Brazil has experienced some form of violence, exposure to violence is more than twice that (19.7%) among cocaine users [2]. The likelihood of being involved in violent crimes increases by a factor of 4 among cocaine users [2]. While causal links cannot be ascertained from these statistics, it is worrying that individuals who use cocaine are at greater risk of being the victims and perpetrators of violent crimes. Given the evidence that certain drugs lead to disinhibition [3, 4], cocaine use may be directly linked to violent crime [5, 6]. However, it is also possible that socio-economic status accounts for the link between substance use and violence [7].

The same factors underpinning exposure to violence and drug abuse among those of low socioeconomic status (SES) may also be related to other deficits in daily life functioning. People with substance use disorder (SUD) have been shown to exhibit deficits in socio-affective and cognitive function [8–11]. These deficits may be the precipitant to or consequence of regular drug use. The effects of frequent drug use, such as blunted reward and general disinhibition, may put specific individuals at a greater likelihood of using greater quantities and a larger variety of drugs. Lack of social support and adaptive coping strategies, along with easy access to drugs, is likely to promote and maintain use among individuals from lower socio-economic strata [12]. Lack of rewarding social encounters, along with insufficient social support, may impact initial and continued drug use [13, 14]. Continued usage is expected to dynamically interact with vulnerability factors, creating further social and functional impairments. This can be due to or potentiated by a number of contextual reasons, such as social stressors or socioeconomic status.

Intentional harm recognition is a critical component of effective social interaction, which implies understanding the goals, intentions, and mindset of others (i.e., Theory of Mind) [15]. Misunderstanding the choices of others is likely to lead to miscommunication, arguments, and unpleasant interpersonal experiences. Specifically, intention recognition or inference is critical to empathy and moral decision-making processes [16, 17]. Intention recognition refers primarily to the ability to cognitively determine if an action performed by another person is accidental or voluntary [18, 19]. Intentional recognition detection involves early and late brain responses involving the amygdala and frontotemporal coupling [20]. Intentional harm recognition requires integrating.

complex processes such as emotion and cognition and is moderated by individual psychological traits [21–23]. Intention recognition has been studied in the context of moral decision research [24], the development of social abilities in young people [18], and dementia [19]. Despite impaired socio-cognitive function among stimulant drug users [25, 26] and the potentially critical role that lack of intentional harm recognition may play in facilitating interpersonal deficits and heightened violence exposure among drug-affected individuals, no one has investigated intentional harm recognition in a sample of individuals who misuse cocaine.

More importantly, such work has not been conducted while controlling SES (an essential potential confound).

The Intentional Inference Task (IIT) [18] assesses fast intention inference regarding actions involving harm to others (intentional vs. unintentional) with different targets (Object vs. Person) (See Fig. 1). The IIT task has primarily been implemented as an examination of moral behaviour and its brain correlates in healthy people [24]. Also, it has been used to study the effects of early social deprivation on the intention inference capabilities and the extent of deficits due to frontotemporal dementia and frontal lesions [27]. While the IIT is typically used to study moral decisions, it is also ideally designed to differentiate how individuals perceive the perpetration of violent behaviour against objects and individuals, intentionally and unintentionally [28]. Given the links mentioned above between substance use (cocaine use in particular) and violent behaviour, as well as known deficits in socio-cognitive processes among individuals with SUD [25, 26], we employed the IIT to explore the potential influence of chronic cocaine use as well as numerous psychological factors (i.e., empathy, sensation-seeking, executive function) on intention inference. Alterations to the brain's early and late temporal dynamics have been observed among event-related potentials (ERPs) during this task [24]. Different amplitude modulations have been apparent for intentional vs. unintentional conditions, likely reflecting functions such as emotion processing, arousal activation, and cognitive evaluation. The most pronounced effects of this task have been reported in frontal electrodes [18].

For this study, we aimed to examine the neural signatures (i.e., event-related potential - ERP) linked to behaviour during the IIT. Given the number of factors influencing socio-cognitive processes, especially among individuals with varied socio-economic backgrounds, it is critical to control for potential confounds. In the present study, Cocaine polydrug users (COC) were compared

Fig. 1 Intentional Inference Task. **A**: Person Intentional (PI) represents an intentional harm to a person. **B**: Person Unintentional (PU) represents unintentional harm to a person. **C**: Object Intentional (OI) represents intentional harm to an object. **D**: Object Unintentional (OU) represents unintentional harm to an object

to a demographically and socioeconomically matched healthy control group (HC). To ascertain possible influences of early childhood upbringing, we assessed individual differences in parental bonding. We also collected measures of empathy, sensation-seeking, and executive function; these variables may constitute confounds and indirect ways individuals with SUD exhibit socio-cognitive impairments.

Given that attention is affected in periods of abstinence and related to behavioural performance [29, 30], we predicted that COC would be slower and less accurate than HC in the intentional inference task. Also, we predicted that COC would exhibit worse performance than HC for executive functions, consistent with impairments in general executive function [31]. We also predicted group differences in empathy and sensation-seeking (COCs exhibiting less empathy and more sensation-seeking than HCs).

At the neural level, based on previous research that has explored the late positive potential (LPP) in substance use populations, including cocaine users. For instance [32], investigated ERPs in individuals with cocaine use disorders (CUD) and found that cocaine-related images elicited increased LPP amplitudes, particularly in early (400–1000 ms) and late (1000–2000 ms) time windows. This suggests sustained attentional engagement with drug-related cues but not necessarily with social cues. Additionally, another study [33] examined behavioural and neural responses to drug-related and non–drug-related emotional stimuli in methamphetamine addicts. They observed that drug-related images elicited increased electrocortical measures of motivated attention, like affectively pleasant and unpleasant pictures, in both abstinent and current users. While these studies engage in late event-related responses, they focus on motivation, not social cognition. We expected a difference in HC ERP modulation relative to COC in predefined frontal regions of interest (ROI) [18]. Specifically, we predicted that COC would exhibit less amplitude modulation than HC, corresponding to less emotional arousal [34]. We expected group differences to be significantly pronounced for intentional vs. unintentional condition comparisons.

Methods

Participants

Our sample comprised two groups: Cocaine polydrug users (COC) and Healthy controls (HC). At the time of evaluation, the COC group was engaged in outpatient treatment for substance use problems at the *National Service for the Prevention and Rehabilitation of Drug and Alcohol Consumption (SENDA).* In our study, all participants in COC condition had a documented history of substance use; however, they were in an abstinence period of at least six months at the time of assessment. This study took place between 2014 and 2015 in Santiago, Chile. The study was conducted at the Laboratory of Social Neuroscience at the University of Diego Portales, a specialised research centre in social cognition. Participant's care is delivered by a multidisciplinary team composed of clinical psychologists and neuropsychologists. Healthy control participants were recruited from the community through advertisements and word of mouth and were screened to exclude any history of substance use disorder or significant psychiatric conditions. All assessments were conducted in the same neuroscience centre previously described. A team of trained psychologists and neuropsychologists affiliated with the research centre evaluated participants individually in a controlled, quiet environment. These professionals received specific training in administering the cognitive tasks and EEG procedures used in the present study under the supervision of senior researchers from the same centre. To reduce potential confounding effects, participants were instructed to abstain from caffeine-containing substances (e.g., coffee and energy drinks) starting the evening before the assessment. No other medications or substances were systematically withheld, but participants were screened for recent substance use as part of the intake procedure.

In our study, individuals classified as *cocaine polydrug users* were those with a history of regular cocaine use and, at the time of participation, had been abstinent for a minimum of 6 months. Occasional or experimental users were not included in this group. The term *polydrug* refers to the use of multiple substances either concurrently or sequentially. In this study, the identification of polydrug use was operationalised using the World Health Organization – Alcohol, Smoking, and Substance Involvement Screening Test (WHO-ASSIST).

Table 1 Abuse and dependence on substances

Substance	Abuse		Dependence	
	HC *n*	COC *n*	HC *n*	COC *n*
Tobacco	1	13	6	18
Alcohol	8	16	0	14
Marijuana	0	18	0	14
Cocaine	0	19	0	19
Amphetamines	0	11	0	3
Sedatives	0	7	0	1
Opiates	0	1	0	0

COC = Cocaine polydrug users; HC = Healthy Group; n = Number of the sample who have the risk for abuse and dependence related to a specific substance

Participants were given the WHO-ASSIST [35] to assess the amount and extent of use of 10 different drugs. In our study, the WHO-ASSIST was used as a screening tool to assess the level of substance involvement, but the classification of abuse and dependence presented in Table 1 was based on clinical diagnoses made by trained professionals. Diagnoses of substance abuse and dependence were established according to DSM-IV criteria by licensed clinicians. The HC group was matched for age, sex, and educational level. A neuropsychologist evaluated all participants; participants with any history of medical conditions (other than substance use problems in COC) were excluded. All participants provided written informed consent following the Declaration of Helsinki.

Neuropsychology and self-reported measures

Drug use, cognitive and socio-emotional assessment

Participants performed several tasks and self-report measures to assess general cognitive processes (executive functions), socio-emotional skills (empathy; sensation seeking), and self-reported drug patterns. Performance on these measures was compared between groups. Finally, a correlation test was performed between ERP amplitudes and the empathic self-report measure.

Drug use

1. World Health Organization – Alcohol, Smoking, and Substance Involvement Screening Test (WHO-ASSIST) The WHO-ASSIST (v3.0) assesses lifetime substance use and use in the past three months in addition to providing estimates of risk for future substance use problems and the likelihood of substance use disorder diagnoses (i.e., abuse and dependence). Version 3.0, from an adapted and validated test used in Chile [36], covers ten substances: tobacco, alcohol, cannabis, cocaine (including base paste and cocaine hydrochloride), amphetamines, inhalants, sedatives, hallucinogens, opiates, and other drugs. The final scores for each substance are classified into three levels of risk (low, intermediate, and high) [35].

Cognitive skills

2. INECO Frontal Screening: The INECO Frontal Screening (IFS) is a relatively quick way to assess executive functions and has been mainly used as a screening tool. This battery has shown good internal consistency, high reliability, and concurrent validity [37]. The tasks included in the IFS are Luria motor series (3 points), Conflicting instructions (3 points), Go-no goes (3 points), Calendar months backward (2 points), Backwards digit span (6 points), Modified Corsi tapping test (4 points), Proverb interpretation (3 points) and Modified Hayling Test (6 points). The IFS has a maximum possible score of 30 points. High scores indicate the preservation of executive functions, with a cut point of 18 points for the Chilean version showing a typical performance in global executive functions for this population [38].

Socio-emotional skills

3. Interpersonal Reactivity Index: The interpersonal reactivity index (IRI) was developed to assess four dimensions of empathy (Empathetic concern, perspective-taking, personal distress, and fantasy). Each subscale contains seven items. The Empathic Concern subscale assesses emotional Empathy or feelings of compassion for others in pain. The Perspective Taking subscale considers cognitive Empathy, or the tendency to see the world from others' viewpoints. The Personal Distress subscale assesses self-focused responses to others' suffering. The Fantasy subscale assesses Empathy for fictional characters. The first three subscales have exhibited relationships to more adaptative interpersonal (e.g., prosocial behaviour) and intrapersonal (e.g., mental well-being) functioning [39, 40].

4. Sensation Seeking Scale: The Sensation Seeking Scale (SSS) was developed to provide a trait measure of sensation-seeking. Form V of this scale (SSS-V) is a forced-choice questionnaire that yields four subscale scores: (a) adventure seeking (TAS), (b) experience seeking (ES), (c) disinhibition (DIS), and boredom susceptibility (BS). The SSS-V scale contains 40 items, with 10 items for each subscale [41].

Behavioural task and procedure

5. Intention inference task (IIT) Electroencephalography (EEG; see below for details) was recorded while participants completed a modified version of the Intention Inference Task [18, 24, 42]. The IIT assesses fast intention inference regarding actions involving harm to others (intentional vs. unintentional) with different targets (object vs. Person) (See Fig. 1). Participants were asked to evaluate whether the actions they saw were intentional or unintentional. In this study, participants were presented with a series of three-frame videos (total 300 ms, 100 ms each frame) on a computer screen. The first frame (T1) shows the start of the action. The second frame (T2) presented either intentional or unintentional harm images. The third frame (T3) showed the result of the action. The trials began with a fixation cross presented for 800 ms, and the inter-trial interval was fixed to 500 ms. During the experiment, accuracy and reaction times were recorded. There were 184 trials (46 per condition: Person Intentional, Person Unintentional, Object Intentional, and Object Unintentional). The IIT was adapted from previously validated paradigms designed to assess rapid social cognitive processes related to intention attribution in the context of harm [18, 24, 42]. The task was originally developed through iterative experimental designs aimed at distinguishing intentional vs. unintentional actions using dynamic visual stimuli that minimise verbal and cultural biases. The specific version used in this study has been previously employed in EEG by our group and fMRI studies [18, 24] and has demonstrated good construct validity, with differentiation of neural responses to intentional vs. unintentional harm (e.g., modulation of early components and LPP).

Brain recording

6. EEG recordings and pre-processing EEG data were recorded with 128-channel HydroCel Sensors using a GES300 Electrical Geodesic amplifier at a sampling rate of 500 Hz. The vertex was used as the reference during the recording, but signals were re-referenced offline to the mastoids. ERP analyses were conducted using MATLAB R2017b, EEGLAB 13.15.4b, and ERPLAB 5.0.0. The data was digitally filtered offline from 0.5 Hz to 30 Hz and down-sampled to 250 Hz to remove unwanted frequency components. Also, Trials that contained voltage fluctuations exceeding ± 200 µV were rejected. Eye movement, other artifacts, and trial rejection were removed from further analysis using visual inspection and Independent Component Analysis (ICA). Continuous EEG data was segmented using a temporal window that began 200 ms before the onset of the stimulus and concluded 800 ms after the offset of the stimulus.

Data analysis

Neuropsychological and self-reported measures: independent samples t-tests were used to compare cognitive skills and psychological traits between groups

Behavioural performance: Repeated measure ANOVAs and Tukey HSD post-hoc comparisons were performed to analyse behavioural IIT data (i.e., reaction time (RT) and accuracy (ACC)). Analysis was conducted in Jamovi (Jamovi project, 2018). Jamovi (Version 0.9) [Computer Software]. Retrieved from https://www.jamovi.org).

*ERP analysis: R*epeated measure ANOVAs and Tukey HSD post-hoc comparisons were performed to analyse ERP IIT data. We used a previously defined group of electrodes for ROI analyses, comprising a frontal, central, and posterior zone (FZ, CZ, and PZ, respectively). Social cognition studies have previously reported time-series analysis in these representative ROIs. Past work has focused on three time windows for stimulus processing the IIT (early–middle–late) [18, 24]. A Shapiro-Wilk normality test was conducted to assess the normality of the data distribution. The tests revealed that the data did not

Table 2 Lifetime substance use by group

Substance	COC *n*	HC *n*
Tobacco	18	6
Alcoholic drinks	16	16
Marijuana	17	0
Cocaine	19	0
Amphetamines or other stimulants	10	0
Inhalants	7	0
Tranquilisers or sleeping pills	6	0
Hallucinogens	4	0
Opiates	1	0
Others-specify	1	0

COC = Cocaine polydrug users; HC = Healthy Group n = The number of the sample that reported the use of some substance in the list

Table 3 Health, social, legal, or financial problems related to substance use

Substance	COC *n*	HC *n*
Tobacco	10	1
Alcoholic drinks	13	0
Marijuana	12	0
Cocaine	16	0
Amphetamines or other stimulants	3	0
Inhalants	2	0
Tranquilisers or sleeping pills	0	0
Hallucinogens	0	0
Opiates	0	0
Others-specify	0	0

COC = Cocaine polydrug users; HC = Healthy Group; n = number of the sample who have experienced this event at least once in the last three months

Table 4 Neuropsychological and Socio-emotional assessment

	HC	COC	
Neuropsychological assessment	M (SD)	M (SD)	*t* (d)
IFS	26.00 (2.28)	20.15 (3.93)	5.59 (1.81)***
IFS-Working Memory	7.53 (1.30)	5.63 (1.67)	3.89 (1.26)***
IFS-Similarities	2.94 (0.22)	2.05 (0.97)	3.91 (1.26)***
IFS-Verbal Fluency	3.00 (0.00)	2.89 (0.31)	1.45 (0.47)
IFS-Motor control	3.00 (0.00)	2.89 (0.31)	1.45 (0.47)
Socio-emotional assessment			
IRI	92.78 (9.39)	93.47 (12.03)	-0.20 (-0.06)
IRI–PT	27.73 (4.13)	24.21 (4.42)	2.54 (0.82)*
IRI–PD	13.00 (3.94)	17.42 (6.22)	-2.62 (-0.84)*
IRI–EC	30.52 (4.58)	29.94 (5.38)	0.36 (0.11)
IRI–F	21.52 (4.94)	21.89 (4.14)	-0.25 (-0.08)
SSS-V	17.15 (5.42)	23.63 (5.84)	-3.53 (-1.14)***
SSSV–TAS	4.94 (2.51)	7.05 (2.64)	-2.50 (-0.81)*
SSSV–ES	6.36 (1.70)	7.00 (1.60)	-1.14 (-0.37)
SSSV–D	3.15 (1.70)	4.63 (2.01)	-2.44 (-0.79)*
SSSV–BS	2.68 (1.60)	4.94 (2.41)	-3.41 (-1.10)**

COC = Cocaine poly-drug users; IFS = Ineco Frontal Screening; IFS-WM = Ineco Frontal Screening Working Memory; IRI = Interpersonal Reactivity Index; IRI–PT = Interpersonal Reactivity Index-Perspective Taking; IRI–PD = Interpersonal Reactivity Index–Personal Distress; IRI–EC = Interpersonal Reactivity Index–Empathic Concern; IRI–F = Interpersonal Reactivity Index-Fantasy; SSSV = Sensation Seeking Scale form V; SSSV–TAS = Thrill and adventure seeking; SSSV–ES = Experience seeking; SSSV–D = Disinhibition; SSSV–BS = Boredom susceptibility; * $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$

significantly deviate from normality, p-value > 0.05, indicating that the normality assumption was met.

Results

Sample characteristics

Participants

The sample consisted of 19 COC (7 female, 12 males; mean age 32.2, SD = 8.7) and 19 HC (7 female, 12 males; mean age 31.8, SD = 8.0) individuals. A priori power analysis was conducted to determine the minimum sample size required to detect a between-group difference, assuming a significance level of α = 0.05 and statistical power of 0.70. The analysis indicated that a total sample size of ~ 40 participants (~ 20 per group) would be sufficient, assuming a standard deviation of ~ 1.2.

Self-reported and neuropsychological results

Substance abuse Consistent with group selection, the COC group showed that all the participants in this group are at risk for cocaine abuse and risk for cocaine dependence relative to the HC group, in which no participant reported a risk for cocaine abuse or dependence (see Table 1). Lifetime substance use was comparable across groups for alcohol, but only COC showed use of other drugs (see Table 2). Only COC exhibited drug-related impairment in daily life (see Table 3).

Socio-emotional results The Socio-emotional evaluation did not show significant differences in the total score of Empathy, but HC exhibited a higher score than COC on the Perspective-taking subscale (cognitive dimension) of the IRI. In contrast, COC showed higher scores on the personal distress subscale (affective dimension) of the IRI. Thrill and adventure-seeking, Disinhibition, and Boredom susceptibility subscales of the SSS-V were higher in COC than in HC. No significant differences between groups were observed for the Empathic Concern or Fantasy subscales of the IRI Experience seeking subscale of the SSS-V (See Table 4).

Neuropsychological results Neuropsychological evaluation using the IFS test showed that HC performed better than COC on the total score of Executive Functions (t [35] = 5.59, $p < 0.001$, two-tailed); Working Memory subscale (t [35] = 3.88, $p < 0.001$, two-tailed).

Behavioural results

Accuracy measure There are no differences between groups, but global effects across all subjects being Person intentional is more accurate than Person unintentional. A 2 (Target: Person vs. Object) x 2 (Intention: Intentional vs. Unintentional) ANOVA was conducted, including a between-subjects factor of group (HC vs. COC). Comparable to prior work (Escobar et al., 2014), an interaction between target and intentionality was observed [F [1, 35] = 21.64, $p < 0.001$, $\eta_p^2 = 0.37$]. Post-hoc analysis (Tukey HSD $p < 0.001$) showed greater accuracy for Person intentional ($M = 0.83$ $SEM = 0.02$) than Person unintentional ($M = 0.55$ $SEM = 0.03$). Post-hoc tests also showed greater accuracy under Person intentional ($M = 0.83$ $SEM = 0.02$) than object unintentional ($M = 0.67$ $SEM = 0.03$; Tukey HSD $p = 0.004$). Despite not finding differences between groups, global differences are a good indicator of the sensitivity of the task.

Reaction times HC performance is faster than the COC group. A 2 (Target: Person vs. Object) x 2 (Intention: Intentional vs. Unintentional) ANOVA was performed for RT, including a between-subjects factor of group (HC vs. COC). A main effect was observed between subjects [F [1, 35] = 8.79, $p = 0.005$, $\eta_p^2 = 0.19$; HC had faster reaction times ($M = 465$ ms; $SEM = 47.1$) than COC ($M = 702$ ms; $SEM = 64.7$). See Fig. 2.

ERP results

ERP ROI analyses. Based on previous reports of ERPs evoked by socio-affective stimuli related to painful images, we choose three regions of interest, frontal, central, and posterior, as well as different time windows, early 100–200 ms, 200–400 ms and late 400–600, 600–700 ms and 700–800 ms [18]. A 2 (Target: Person vs. Object) x 2 (Intentionality: Intentional vs. Unintentional) x 3 (ROI: frontal vs. central vs. posterior) ANOVA was conducted, including a between-subject factor of group (HC vs. COC).

The most critical effects observed in our data occurred at 400–600 ms; Target and ROI interacted (F [2, 43] = 5.10, $p = 0.009$, $\eta^2 = 0.14$). A posthoc analysis (Tukey HSD) revealed that the difference was in the frontal ROI for Person vs. object ($p < 0.001$); here, Person ($M = 0.29$; $SE = 1.03$) showed a more positive amplitude than the object (M = -1.33; $SE = 1.04$). Also, at 600–700 ms: An interaction of Target x Intentionality x ROI (F [2, 43] = 3.27, $p = 0.04$, $\eta^2 = 0.08$) was observed. A posthoc analysis (Tukey HSD) revealed that the difference was at frontal ROI for Person intentional vs. object unintentional condition ($p < 0.001$); here, Person intentional ($M = 1.68$; $SE = 1.29$) showed a more positive amplitude than object unintentional (M = -0.37; $SEM = 1.22$). See Fig. 3a and b.

Significantly, given the absence of group differences and the interactions at frontal ROI, we performed a separate analysis for each group, considering the same factors and time windows.

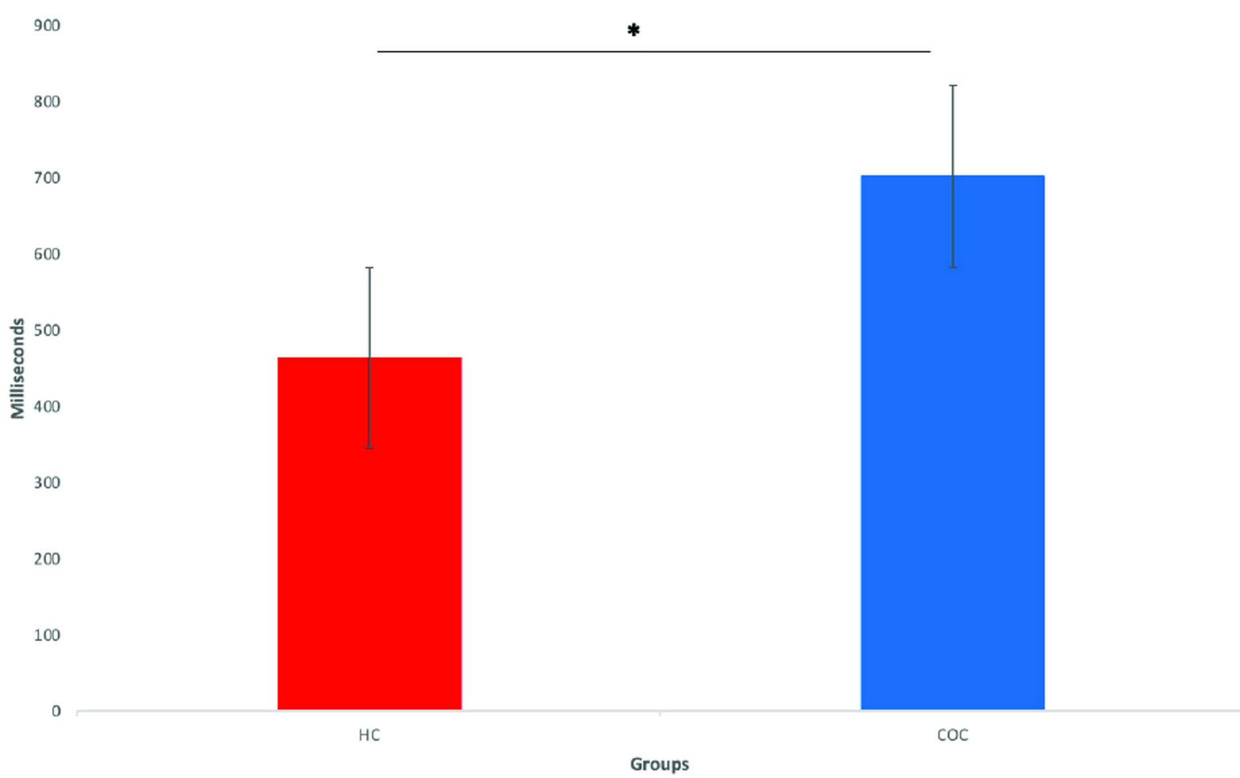

Fig. 2 Reaction Time for the Intentional Inference Task. Reaction times in milliseconds for both groups HC: Healthy Control Group; COC: Cocaine Polydrug Users, across all conditions

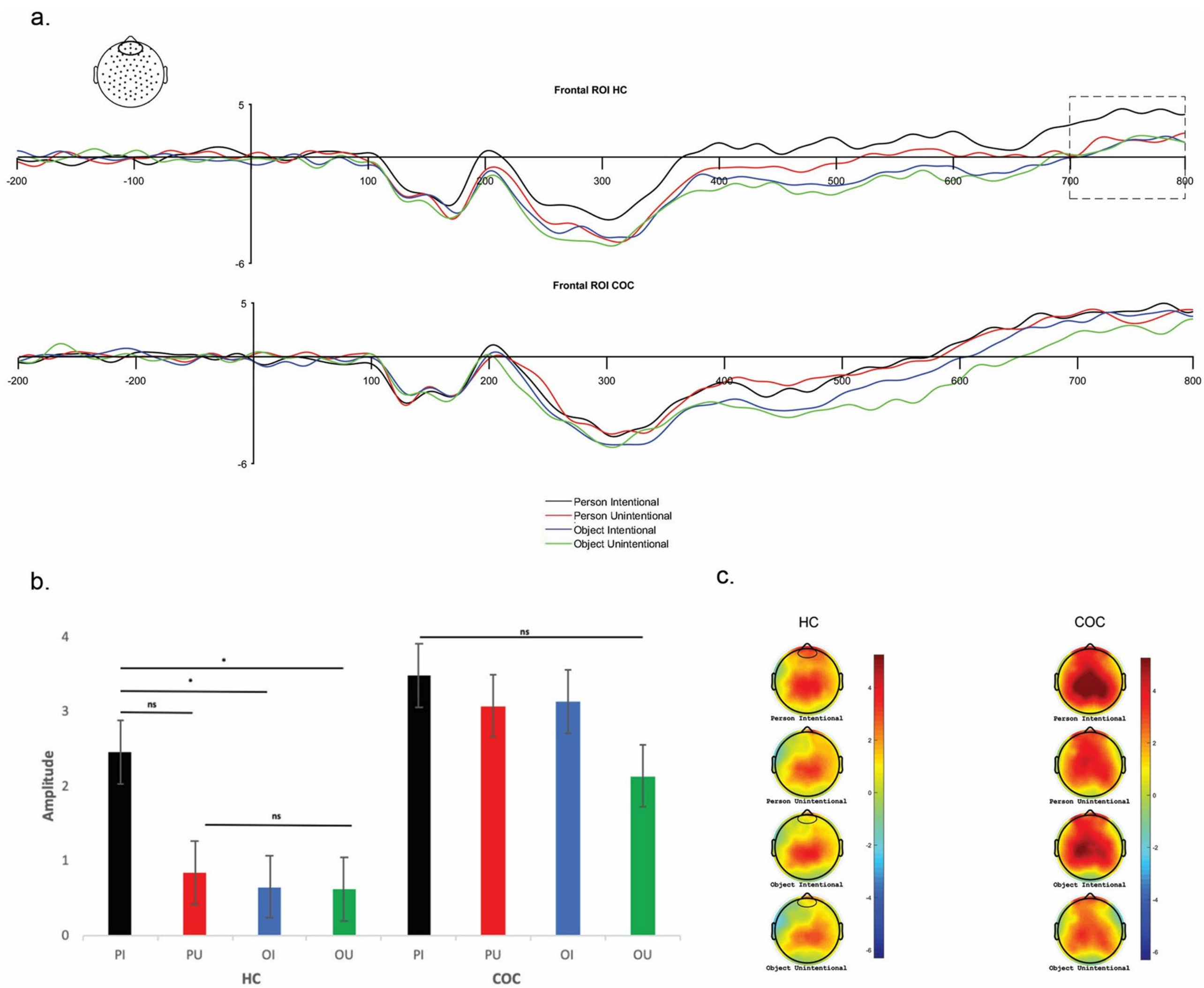

Fig. 3 ERP for frontal ROI by group. Comparison between conditions for the amplitude of ERP at Frontal (700–800 ms) in both groups. ERP map 700–800 ms for both groups. (**a**) Plot of the frontal ROI for all conditions and both groups; (**b**) Comparison of amplitude in microvolts from the ERP at the Frontal ROI for both groups; (**c**) ERP map at 700–800 ms. Remarked areas represent the differences in the ERP. HC: Healthy Control Group; COC: Cocaine Polydrug Group

The most important effects observed in our data occurred at 700–*800 ms* (Fig. 4a-b). Here, an interaction of Target x Intentionality x ROI [F [2, 30] = 4.00, $p = 0.02$, $\eta^2 = 0.20$] was observed in HC. A posthoc analysis (Tukey HSD) revealed that the difference was at frontal ROI for person intentional v/s object intentional ($p = 0.02$); here Person intentional ($M = 2.43$; $SE = 1.06$) showed a more positive amplitude than object intentional condition ($M = 0.70$; $SE = 0.85$) and for Person intentional v/s object unintentional condition ($p = 0.01$); here Person intentional ($M = 2.43$; $SE = 1.06$) show more positive amplitude than object unintentional condition ($M = 0.74$; $SE = 1.16$). This interaction was not observed in the COC group [F [2, 28] = 1.32, $p = 0.2$, $\eta^2 = 0.08$] (Fig. 3c represents topological activity).

Correlation between erp's amplitude and empathy To explore the relation between the evoked related potential response with Empathy (another critical component in social cognition), we perform a correlation test between the amplitude difference (Δ amplitude) among conditions at Frontal ROI 700–800 ms and the empathic self-report measure (IRI). First, we analyse if there is a difference between the Δ amplitudes of groups; no differences were found here (t [30] = -1.43, $p = 0.17$, two-tailed). However, we observed a positive correlation between Δ amplitude for Person Intentional – Person Unintentional and the total score of the empathy scale in HC, $r = 0.54$, $p = 0.01$. No correlation was found in the COC group for this ROI at this time window (See Fig. 4).

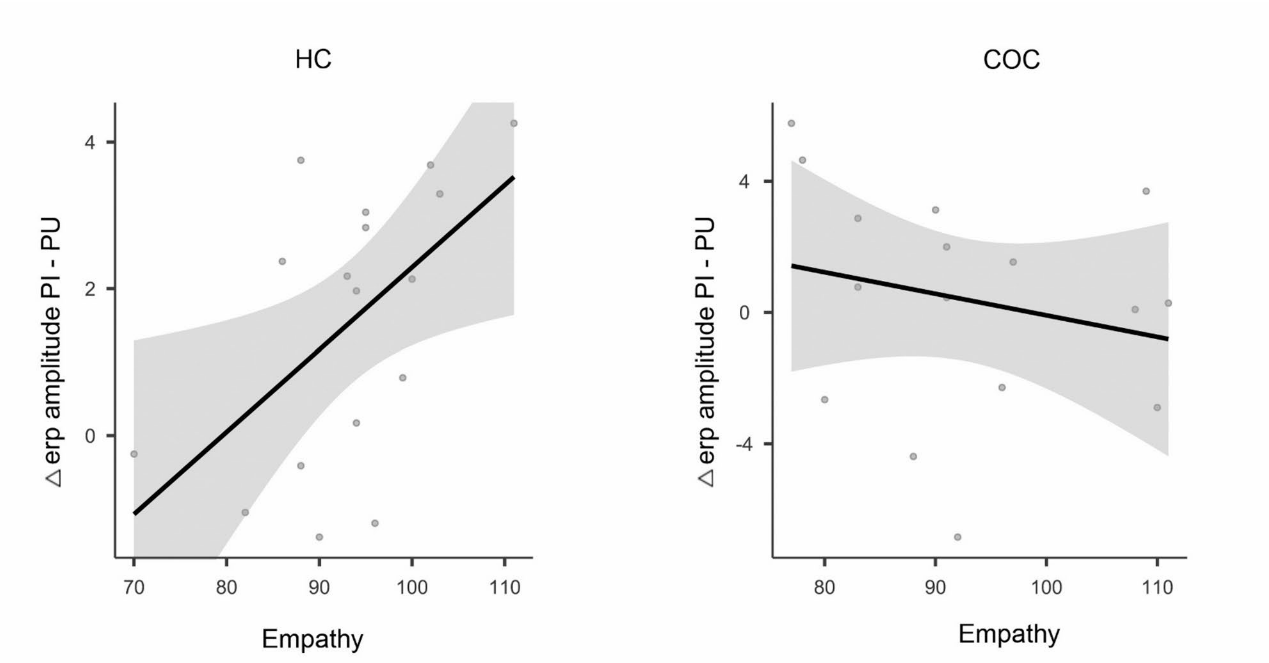

Fig. 4 Correlation between Δ ERP amplitude at frontal ROI (700–800 ms) and IRI total score in both groups. Correlation between Δ PI – PU (difference between amplitudes in Person intentional and Person Unintentional condition) and Empathy (total score from Interpersonal Reactivity Index), in both groups, HC and COC

Discussion

The consequences of cocaine and stimulant abuse on social and cognitive skills have been well-documented [10, 11, 44–46]. However, no prior work has investigated the neural evoked response of intentional harm recognition in cocaine polydrug users, which may reflect a socio-cognitive skill underpinning interpersonal behaviour. Critically, cocaine abuse and the use of other stimulant drugs have been associated with disruptive social behaviour, including violence and rule-breaking [10, 47–51]. Thus, impaired intention inference may partially underpin the relationship between cocaine abuse and maladaptive interpersonal behaviour. This study assessed the ERP response to harm intention recognition, considering persons and objects while controlling for gender, age, educational level, and sociocultural background. We also evaluated other cognitive, social, and psychological traits (executive functions, empathy, and sensation seeking).

There were no observed group differences in brain activity. However, separate group brain analysis showed that during a late time window (700-800ms) for cortical ERPs at the frontal and central ROI as a marker associated with intentional vs. unintentional harm depicted in visual stimuli, HC exhibited a marked amplitude increase for person intentional relative to object intentional and unintentional (frontal ROI), no such difference was present among COCs. Nevertheless, at 600–700 ms, COCs show a difference associated with an increase for person intentional relative to object unintentional at central ROI. These results are consistent with other studies showing impairment in frontal brain circuits related to contextual evaluation and decision-making [18, 20, 52]. While early temporal ERP activity has been associated with automatic brain responses and reflects arousal activity [53–55], later temporal ERP activity has been associated with more effortful stimulus evaluation and classification. Also, the amplitudes observed at the frontal ROI positively correlated with the total score of empathy in HC. In contrast, in the case of the COC group, an association was not evident. It is possible that neural dynamics related to empathic processes could be altered by drug abuse.

Behaviourally, a significant difference was found between groups in reaction time (RT); COC were slower overall than HC. Impaired reaction time has been reported among cocaine users in other experimental settings as well [56].

There was a significant difference between groups in the total score of executive functions (EF), with COC performing worse than HC. Thus, the observed behavioral differences on the IIT could have resulted from general differences in EF and specific differences in socio-affective functions. Within the EF, there were differences in working memory and on the similarities test (a measure of abstraction skill), consistent with impairments in global EF. In contrast to previous works [57, 58], there were no differences in Verbal Fluency or Motor Control. One possible explanation is that affected EF are those related to social skills, such as working memory, inhibition, and abstraction abilities, which could be reflected in social-affective behavior [59].

Consistent with prior work [60], groups also had significant differences in sensation seeking. Across all domains of sensation seeking (thrill and adventure seeking, experience seeking, Disinhibition, and boredom susceptibility), COC were higher than HC. This is very consistent with previous observations among those with substance abuse, in which disinhibition and risk decisions are some of the most characteristic features [43].

Given that IIT differences were not solely attributable to differences in EF, other possible disparities are important avenues for understanding altered behavior among cocaine and stimulant drug users. Interestingly, while there was no significant group difference in global empathy (measured using the IRI), there was a dissociation between perspective-taking (PT) and personal distress (PD). While HCs exhibited significantly greater PT, COCs exhibited significantly greater PD. Perspective-taking is a cognitive dimension of empathy, primarily of understanding another person's inner experience [61]. Personal distress refers to an aversive, self-focused emotional reaction to the apprehension or comprehension of another's emotional state or condition [39, 62]. The present findings may suggest that altered neurobehavioral patterns among cocaine drug users (i.e., slower RTs, poor differentiation classification of social cues as indexed by late ERP activity) are potentially related to a shift towards emotional over-involvement and away from rational cognitive assessment of social information. Cognitive control and inhibition have a direct impact on behaviour.

Limitations

This study investigates the neural evoked response of intentional harm recognition in cocaine polydrug users. This is a growing field in social neuroscience, and several new lines of investigation need to be developed and applied in this population. One limitation of the present study is the small sample size. Further studies with larger samples are needed. Interaction effects may have been absent due to insufficient statistical power. It is challenging to recruit patients and socio-demographically matched participants who fulfil the necessary conditions for this research. However, the same task has been reported using no more than ten subjects and shown to be sensitive [24]. On the other hand, while these findings suggest impaired cognitive evaluation of social signals and heightened emotional involvement in cocaine polydrug users—potentially leading to maladaptive social responses—they do not establish this as the sole underlying mechanism. Future research should further examine behavioral responses in ecologically valid social settings. Another limitation of this study was the absence of a biological marker to confirm recent drug abstinence or use. The medical staff did characterise the drug use behaviour of each participant, somewhat mitigating this concern.

Conclusion

In sum, this study provides evidence of the difference in ERP correlates of intentional harm recognition in a cocaine polydrug sample relative to a sociodemographically matched healthy control group. The COC group showed a diminished performance in perspective-taking and elevated scores for personal distress vs. the control group; this difference could be interpreted as a poor cognitive evaluation of social cues and an emotional over-involvement. These findings provide a new perspective to study critical social cognitive skills as intention inference in this population, suggesting that work in training socio-emotional regulation may be of clinical benefit. Finally, social context plays a vital role in addictive behaviour, and strategies for prevention and treatment should include a socio-emotional focus.

Abbreviations

COC	Cocaine poly-drug users
HC	Healthy Controls
IIT	Intentional Inference Task
PU	Person Unintentional
PI	Person Intentional
OU	Object Unintentional
OI	Object Intentional
SUD	Substance use disorder
WHO-ASSIST	World Health Organization Alcohol, Smoking, and Substance Involvement Screening Test
SES	Socioeconomic Status
IFS	Ineco Frontal Screening
IFS-WM	Ineco Frontal Screening Working Memory
IRI	Interpersonal Reactivity Index
IRI-PT	Interpersonal Reactivity Index-Perspective Taking
IRI-PD	Interpersonal Reactivity Index–Personal Distress
IRI-EC	Interpersonal Reactivity Index–Empathic Concern
IRI-F	Interpersonal Reactivity Index-Fantasy
SSSV	Sensation Seeking Scale Form V
SSSV-TAS	Thrill and Adventure Seeking
SSSV-ES	Experience Seeking
SSSV-D	Disinhibition
SSSV-BS	Boredom Susceptibility
ERP	Event-related potential
ROI	Region of Interest (EEG analysis)
SD	Standard Deviation
SE	Standard Error
SEM	Standard Error of the Mean

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Author contributions

Juan-Pablo Morales: Conceptualization, Methodology, Formal analysis, Investigation, Data curation, Writing - Original Draft. Nicholas T. Van Dam: Conceptualization, Writing - Original Draft. Daniela Huepe-Artigas: Writing - Review & Editing. Consuelo San-Martin: Conceptualization, Writing - Original Draft. Álvaro Rivera: Software, Writing - Review & Editing. Felipe Rojas: Writing - Review & Editing, Formal analysis. Joaquín Valdés: Writing - Review & Editing, Formal analysis. Agustín Ibáñez: Writing - Review & Editing, Conceptualization. David Huepe: Conceptualization, Resources, Writing - Review & Editing, Supervision, Funding acquisition.

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Data availability
Data will be available on the GitHub platform once the manuscript has been accepted.

Declarations

Ethics approval and consent to participate
The study received prior approval from the ethics committee of Diego Portales University N°1140114 and followed the protocol of the Declaration of Helsinki. Finally, all participants provided a signed consent after reading the information with detailed procedure information.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

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