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ORIGINAL INVESTIGATION

Negative mood induction normalizes decision making in male cocaine dependent individuals

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Abstract
Rationale Decision making is thought to play a key role in psychostimulant relapse, but very few studies have addressed the issue of how to counteract decision-making deficits in addicted individuals. According to the somatic marker framework, pervasive decision-making problems in addicted individuals may relate to abnormalities in the processing of emotional signals that work to anticipate the prospective outcomes of potential decisions.
Objective The present study was conducted to test whether the induction of different emotional states (positive, negative, or drug-related) could either normalize or further impair decision-making performance in male cocaine polysubstance-using individuals (CPSI), as indexed by the Iowa gambling task (IGT).
Methods Forty-two CPSI and 65 healthy control individuals (all males) were randomly allocated in four affective conditions using a parallel-group design. Participants in the different conditions performed the IGT during exposure to neutral, positive, negative, or drug-related sets of affective images.
Results The results showed that the CPSI exposed to the negative affective context showed a preference for the risk-averse safe choices of the IGT and had a net performance indistinguishable from that of controls. On the other hand, CPSI exposed to positive, drug-related, and neutral contexts showed the typical pattern of disadvantageous performance in the IGT and performed significantly poorer than controls. The impact of the negative mood induction could not be explained in terms of baseline differences in decision-making skills, personality traits related to sensitivity to reward/punishment, or trait positive/negative affect.
Conclusions We conclude that negative mood induction can normalize decision-making performance in male CPSI, which may have important implications for the treatment of cocaine use-related disorders.

Keywords Cocaine · Decision making · Negative mood · Emotion · Somatic markers · Cognition

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Introduction

The somatic marker theory of addiction posits that persistent drug use may relate to defective engagement of emotion-related signals (somatic markers) that normally operate to anticipate the prospective outcomes of potential decisions. In addicted individuals, emotional signals linked to drug experiences may override adaptive emotional signals in driving decisions, thus promoting decision styles based on the endorsement of immediately reinforcing

options (Verdejo-García et al. 2009). This notion is also embedded in other current neurobiological models of addiction which posit that inflated affective valuation of reward-like expectancies can foster maladaptive choices in addicted individuals (Goldstein and Volkow 2002; Redish et al. 2008). Support to these notions stems both from behavioral studies showing that individuals with substance use disorders show abnormal performance on affective-based decision-making tests (indexed by the Iowa gambling task or other similar risk-based decision probes; see review in Verdejo-García et al. 2008) and psychophysiological studies showing abnormal enactment of somatic signals during decision making in these groups (Bechara and Damasio 2002; Bechara et al. 2002; Fishbein et al. 2005). Importantly, growing research indicates that decision making is a reliable marker of clinical outcomes in addiction. In opiate and alcohol groups, individuals with impaired performance on decision-making tests are at a considerably higher risk of drug relapse (Bowden-Jones et al. 2005; Passetti et al. 2008). Similarly, in individuals with psychostimulant dependence, the patterns of brain activations during decision making are predictive of relapse after 1-year follow-up (Paulus et al. 2005).

The apparent implication of this notion for addiction treatment is that adequate training of emotional signals may improve decision-making skills in addicted individuals. However, although spontaneous somatic markers and anticipatory affect are hard-wired to drive decisions according to homeostatic aims (Damasio 1994; Knutson and Greer 2008), the effects of particular affective states (positive, negative, or drug-related) or "external" manipulations of affect (like those employed in psychological interventions) on adaptive guidance on decision making is rather less known. Classic cognitive models about the effects of mood on risk-based decision making support the main assumption that positive affect tends to increase risk-taking behavior, whereas negative affect tends to promote risk aversion (Knutson and Greer 2008). The findings from studies using the Iowa gambling task (IGT) and other risk-sensitive decision-making tests broadly support this effect in healthy individuals, especially with regard to the influence of negative affect. In mood induction experiments, risk-averse decisions are increased when participants are exposed to highly arousing personal moral dilemmas (Overman et al. 2006) or emotions of fear and anger (Heilman et al. 2010); interestingly, risk-averse decisions tend to extinguish when these negative emotions are effectively reappraised (Heilman et al. 2010). Recent electrophysiological evidence indicates that induction of negative mood increases the amplitude of the error-related negativity potential following mistakes in a conflict task (Wiswede et al. 2009); hence, it is possible that moderate levels of negative mood foster adaptive (risk-averse) decisions by boosting sensitivity to punishment. In accordance, elevated scores in trait anxiety and depression are positively correlated with better decision-making performance in the IGT (Smoski et al. 2008; Werner et al. 2009). On the other hand, extreme levels of trait anxiety (Miu et al. 2008), acute social stress (Starcke et al. 2008), or chronic pain (Verdejo-García et al. 2009) actually impair decision-making performance in the IGT and analogous measures.

Although literature in healthy individuals is relatively neat, predictions about the effects of particular mood states on the decision-making skills of individuals with substance use disorders are hard to be made for a number of reasons. First of all, drug addiction is associated with the consolidation of unique affective states, such as craving, which might by itself promote risk-prone decisions (Verdejo-García et al. 2009). Moreover, emotion processing systems become persistently altered in addiction, with relative insensitivity to positive stimuli (Aguilar de Arcos et al. 2005) and hypersensitivity to negative arousing stimuli and stress (Aguilar de Arcos et al. 2008; Li and Sinha 2008), both findings being related to higher probability of drug relapse (Lubman et al. 2009; Sinha et al. 2006). These notions raise the hypothesis that addicted individuals would tend to make riskier decisions under craving-related states, but could be more sensitive to negative mood induction in counteracting risk-prone tendencies. The aim of this study was to test these hypotheses by probing the decision-making performance of cocaine polysubstance-dependent individuals exposed to positive, negative, and drug-related affective contexts as compared to healthy controls performing under the same conditions.

Materials and methods

Participants

Forty-two cocaine polysubstance-dependent individuals (CPSI), aged 19–44 years (M=28.93, SD=6.39), and 65 healthy control subjects, aged 23–41 years (M=30.17, SD=4.98), participated in this study. All participants were male; this was intended to avoid well-known gender differences in experiments using emotional induction paradigms (Lang et al. 1993) and taking into account the low prevalence of women entering drug treatment during recruitment. CPSI were recruited in an inpatient therapeutic community —"Proyecto Hombre"—in the city of Granada, Spain. All of them reported cocaine as their main drug of choice and the drug for which they actually demanded treatment; however, they also had regular use of alcohol, cannabis, and MDMA (see Table 1). CPSI should have a minimum abstinence duration of 15 days (for any drug) to be able to enter the study; indeed, the mean duration of abstinence in the group was of 34.28 (SD=22.01) weeks so that it was possible to

Table 1 Descriptive scores for patterns of quantity and duration of substance use in the CPSI

Substances	Substance use parameters		
	Units	Mean	SD
Cannabis	Joints per month	100.64	101.70
	Duration (years)	18.78	71.50
Cocaine	Grams per month	18.96	29.18
	Duration (years)	4.13	2.91
MDMA	Tablets per month	10.19	10.26
	Duration (years)	2.81	2.39
Alcohol	Standard units per month	87.48	85.27
	Duration (years)	8.52	9.68

rule out general alert or cognitive alterations linked to the acute or short-term effects of any drug. None of them were currently following pharmacological substitution treatments. Urine analyses for cannabis, benzodiazepines, cocaine, and alcohol metabolites were conducted at the time of the study to confirm abstinence. Potential participants who had previously been diagnosed with any disorder from DSM-IV Axes I and II (other than substance dependence) were not included in the target sample. Those potential participants who had been previously diagnosed with traumatic brain injury, neurological or systemic disorders, or HIV were also excluded.

Control participants were selected by means of adverts distributed through a local employment agency, so they were also matched to CPSI in terms of unemployment status. Selection criteria for these control participants were: (1) absence of current or past substance abuse, excluding past or current social drinking (less than ten drinks per week); (2) absence of documented major psychiatric disorders; (3) absence of documented head injury or neurological disorder; and (4) not being on any medication affecting the central nervous system. The mean amount of alcohol use in control participants was 25.52 units/month (SD=30.82), and the mean duration of alcohol consumption was 10.63 years (SD=5.57).

Instruments and assessment procedures

Patterns of drug use

Data regarding lifetime amount and duration of use of the different drugs were self-reported by participants and collected using the Interview for Research on Addictive Behaviour (Verdejo-García et al. 2005). This interview provides an estimation of monthly use of each substance (amount per month) and total duration of use of each substance (in years). The descriptive scores for these variables in the present sample are presented in Table 1.

Questionnaire measures of positive and negative affect, sensitivity to reward and punishment, and craving

Positive and Negative Affect Scale The Positive and Negative Affect Scale (PANAS; Watson et al. 1988) comprised two 10-item self-report scales designed to measure positive and negative affect. Ratings of 20 mood adjectives are made on a five-point scale that includes "very slightly or not at all," "a little," "moderately," "quite a bit," and "extremely." Participants were requested to rate these adjectives and their own affect during the last week; the scale has shown appropriate stability across a 2-month period and strongly correlates with trait measures of temperament and personality so that it can be reliably used as a measure of long-term individual differences in affect (Watson and Clark 1994). The Spanish adaptation of the PANAS, used in this study, has shown adequate psychometric properties and external validity (Sandín et al. 1999).

Hamilton scales of depression and anxiety These are semi-structured interviews aimed to assess a broad spectrum of symptoms related to depression and anxiety, which are rated by the examiner and yield an overall score of severity (Hamilton 1959, 1960). Assessments referred to symptoms of depression and anxiety during the last month. In this study, we used the Spanish adaptations of both scales, which have shown adequate psychometric properties and external validity (Ramos-Brieva et al. 1994; Lobo et al. 2002).

Sensitivity to Punishment and Sensitivity to Reward Questionnaire This is a self-report measure assessing a participant's appetitive (sensitivity to reward, SR) and aversive (sensitivity to punishment, SP) motivational system functioning levels (Torrubia et al. 2001). The Sensitivity to Punishment and Sensitivity to Reward Questionnaire (SPSRQ) comprised 48 items, of which 24 assess SR and 24 assess SP. The SR and the SP scales are reported to show adequate internal consistency, as well as convergent, construct, and discriminate validity (Caseras et al. 2003).

Cocaine Craving Scale This is composed of five items requesting participants to: (1) rate how strong their desire was to use cocaine right at the time of the assessment, (2) rate how often had they felt to use cocaine during the last 24 h, (3) rate how strong their desire was to use cocaine during the last 24 h, (4) imagine themselves in the environment in which they previously used drugs and/or alcohol and then estimate the likelihood that they would use cocaine, and (5) rate how strong their urges were for cocaine when something in the environment reminded them of it (Weiss et al. 1995). Response options ranged from 0 for "no desire/likelihood of use" to 9 for "strong desire/

likelihood of use." The composite score was a sum of these five items, ranging from 0 to 45. This scale has shown optimal levels of reliability (Weiss et al. 1997) and ecological validity (Weiss et al. 2003).

Emotional version of the Iowa gambling task

We created four different experimental versions of the IGT (see Bechara et al. 2000 for a description of the original task) in order to induce different conditions of sustained affective context (i.e., neutral, positive, negative, and cocaine-related affective states) during decision-making performance. The rationale was to probe decision-making performance (indexed by the IGT) under the influence of these four different affective contexts (manipulated between subjects) in both groups (CPSI and controls). Therefore, the variation with regard to the original IGT consisted on the insertion of three blocks of 21 affective images presented in a random order at three different points during the task: immediately before trials 40 (onset of block 3 of the IGT), 60 (onset of block 4 of the IGT), and 80 (onset of block 5 of the IGT). Images were presented for 6 s each, making up a total duration of 126 s for each block of images. This duration is optimal to create a "sustained affective context" that is thought to last at least for the following 2 min (Bradley et al. 1996); this is approximately the time needed to complete each IGT block of 20 trials (pilot studies observations). Images were inserted from trial 40 on because the first 40 trials are regarded to index early learning of task contingencies, whereas the last three blocks index decision-making abilities (Bechara et al. 2005). The images were extracted from the International Affective Picture System (Lang et al. 2001) and were selected and grouped according to their content (neutral, positive, negative, or cocaine-related). Additional images were required to complete the cocaine-related set of images, so we developed some of them and obtained some others from free available resources in the Internet. Importantly, the positive, negative, and cocaine-related images, although differing in their valence, had statistically matched mean arousal values.

The main aim of this selection process was to create the four sets of images intended to induce the affective context of the four distinct affective conditions: neutral, positive, negative, and drug cue. Once the images were selected, four different versions of the IGT were programmed, each of which contained a different set of images (neutral, positive, negative, or cocaine-related).

We used a parallel-group design where participants were randomly allocated in these four different conditions (neutral, positive, negative, and drug cue IGTs). This procedure formed eight subgroups of participants, four belonging to the CPSI group (neutral, $n=11$; positive, $n=10$; negative, $n=10$; drug cue, $n=11$) and four belonging to controls (neutral, $n=16$; positive, $n=17$; negative, $n=16$; drug cue, $n=16$).

In order to control for possible baseline differences on decision-making skills irrespective of the affective manipulation, we also administered a parallel version of the IGT (the KLMN IGT version; see Verdejo-García et al. 2006). This parallel IGT version was always administered after the emotional IGT version and participants performed it under standard testing conditions (i.e., without any affective manipulation).

Procedure

Participants were assessed individually between November 2008 and September 2009. Assessments were conducted across two sessions separated by <1 week. During the first session, we administered the trait affect questionnaire measures, followed by the emotional IGT version. During this first session, participants also rated the valence and arousal of the images presented during the emotional IGT version (see Electronic supplementary material (ESM) Table SA1). CPSI also rated the desire evoked by the drug-related pictures. The IGT parallel version was administered in a second session, along with a battery of cognitive tests whose results will be reported elsewhere. The study was approved by the Ethical Committee for Research in Humans of the University of Granada. All participants signed an informed consent form certifying their voluntary participation. Control participants, but not CPSI, received a €40 compensation for collaborating.

Statistical analysis

Our main hypothesis was that affective condition would influence decision-making performance in different ways in both groups. This hypothesis was tested using a 2 (group—CPSI vs. controls)×4 (affective condition—neutral vs. positive vs. drug cue vs. negative) univariate analysis of variance (ANOVA) on IGT net scores. This test was followed by planned t tests contrasting performance between both groups on each of the four affective conditions. This way, we were able to test whether potential performance differences between the groups vary as a function of the affective context conditions. We also conducted post hoc one-way ANOVAs to test performance differences between the different affective condition subgroups within each group (CPSI and controls).

Two series of Pearson product moment correlation analyses were conducted to examine the associations between personality and trait affect scores (SPSRQ, PANAS, and Hamilton Depression and Anxiety Scales)

and decision-making performance in the CPSI and control groups separately.

Results

Demographic, drug use, and trait affect characteristics of CPSI and control individuals allocated in the different affective conditions

CPSI allocated in the different affective conditions did not significantly differ in terms of cocaine regular use or duration of use. CPSI across the different affective conditions were also statistically matched for patterns of use of alcohol, cannabis, and MDMA, which were the other drugs used by more than 15% of the sample (see ESM Table SA2). They also showed statistically equivalent levels of VAS-indexed subjective craving (Table 2). Both groups (CPSI vs. controls) were statistically matched for age, but controls had significantly more years of education (M=17, SD=4.25 vs. M=11.87, SD=3.40). However, we found no significant differences in years of education as a function of group and affective condition (F for the interaction effect=1.37, p>0.2); indicating that years of education were evenly distributed across the different experimental conditions of interest in this study. In addition, we found no significant differences in sensitivity to reward and punishment (SPSRQ), positive and negative affect (PANAS), or depression (Hamilton Depression Scale) as a function of group and affective condition (p>0.1 for the interaction effect in all cases), meaning these variables were evenly distributed across the different experimental conditions. For anxiety scores (Hamilton Anxiety Scale), there was a group × affective condition significant interaction (p=0.004), and post hoc analyses revealed that this was driven by group differences within the positive, negative, and neutral conditions (CPSI having higher scores than controls), but not within the drug cue condition (both groups statistically matched). However, there were no differences between CPSI and controls allocated across the four experimental conditions (within-subject contrasts). Descriptive scores for all affective measures are displayed in Table 2.

Emotional IGT performance of CPSI and controls in the different affective conditions

We first performed a 2 (group)×4 (affective condition) ANOVA on the IGT net score. According to the initial hypothesis, the results showed a trend to significant effects of the group × affective condition interaction (F=2.42, df= 3, 99, p=0.07). This analysis was followed up by a series of paired t tests aimed to compare IGT performance between the CPSI vs. controls allocated in the four different affective conditions (neutral, positive, drug cue, and negative). The results showed that the CPSI individuals had significantly worse IGT performance than controls in the neutral (t=−2.07, df=25, p=0.049, Cohen's d=0.8); positive (t=−3.29, df=25, p=0.003, Cohen's d=1.08); and drug cue conditions (t=−2.88, df=25, p=0.008, Cohen's d=1.12). However, both groups showed non-significant performance differences in the negative condition (t=0.48, df=24, p=0.63). Inspection of descriptive scores (see Fig. 1) indicates that CPSI individuals allocated in the neutral, positive, and drug cue conditions had average performances within the disadvantageous range (below 0, indicating overall preference for risky decks), whereas controls displayed normal performance, indexed by positive mean scores. In sharp contrast, CPSI individuals allocated in the negative condition actually outperformed controls, scoring both groups within the advantageous range.

A post hoc one-way ANOVA conducted only in the CPSI group in order to compare IGT performance between CPSI individuals allocated in the four experimental

Table 2 Descriptive scores for measures of affect, personality, and craving in CPSI and controls

Measures of affect, personality and craving	Affective condition							
	Neutral		Positive		Negative		Drug cue	
	CPSI	Controls	CPSI	Controls	CPSI	Controls	CPSI	Controls
PANAS positive	27.33 (7.29)	21.91 (4.23)	26.25 (6.40)	23.60 (6.63)	26.70 (5.27)	21.50 (7.93)	25.30 (4.52)	25.63 (5.71)
PANAS negative	15.89 (6.75)	10.36 (1.81)	14.63 (8.28)	13.20 (3.29)	16.60 (6.15)	10.30 (1.56)	13.20 (3.55)	12.50 (4.87)
Depression	5.58 (3.52)	0.65 (1.53)	5.80 (5.02)	1.82 (2.21)	6.40 (4.24)	1.38 (2.57)	3.25 (2.70)	1.50 (2.36)
Anxiety	8.58 (6.68)	0.65 (1.11)	9.90 (7.71)	1.65 (1.83)	7 (6.01)	1.63 (2.81)	3.33 (3.20)	2.75 (3.21)
SP	12.44 (3.04)	7.18 (4.95)	12.38 (6.71)	11.24 (6.75)	10.14 (5.69)	7.50 (4.74)	14.45 (6.08)	7.44 (3.51)
SR	16.11 (3.48)	9.88 (3.35)	14.88 (3.98)	10.71 (4.41)	11.14 (4.74)	9 (3.93)	13.64 (5.88)	10.94 (3.27)
CCS	8.67 (4.97)		8.75 (6.86)		8.78 (3.07)		10.10 (6.15)	

PANAS Positive and Negative Affect Scale, *SP* sensitivity to punishment, *SR* sensitivity to reward, *CCS* Cocaine Craving Scale

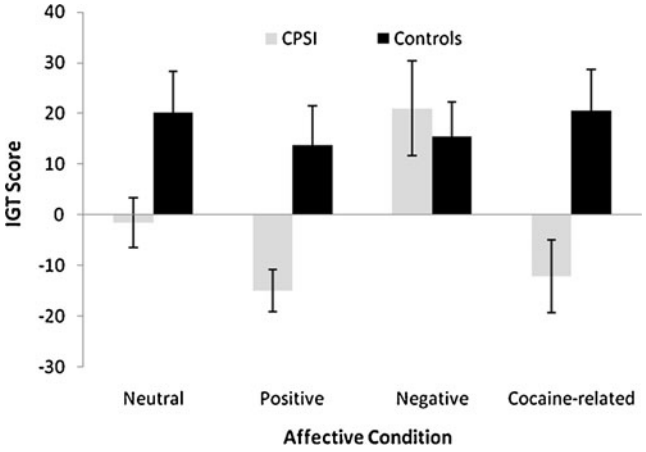

Fig. 1 IGT performance between the cocaine polysubstance-using individuals (*CPSI*) vs. controls allocated in the four different affective conditions

conditions yielded a main effect of the affective manipulation (F=5.79, df=3, 38, p=0.02). Post hoc DMS tests showed that this effect was driven by a significantly better performance in CPSI exposed to the negative condition as compared to neutral (p=0.02), positive (p=0.001), and drug cue conditions (p=0.001).

Performance of CPSI and controls on the IGT parallel version

We conducted a 2 (group)×4 (affective condition) ANOVA on the parallel IGT version scores. Although this task was performed under standard conditions (without affective manipulation), we kept the affective condition factor to test whether the group differences reported above were driven by baseline differences in the decision-making skills of individuals allocated in the different subgroups. Nonetheless, the ANOVA failed to show a significant interaction effect for IGT parallel version scores (F=0.56, df=3,87, p=0.65). A post hoc one-way ANOVA conducted only in the CPSI group in order to compare IGT performance between CPSI individuals that were previously allocated in different experimental conditions also failed to show any significant difference on performance across CPSI subgroups (F=0.24, df=3,36, p=0.86).

Correlations

We conducted a series of Pearson product moment correlation analyses for each group in each affective condition entering emotional IGT net score, PANAS scores, and Hamilton's anxiety and depression scores. In the CPSI subgroup performing the negative affective condition, there was a significant positive correlation between anxiety and IGT performance (r=0.72, p=0.02). Furthermore, in the CPSI subgroup performing the drug cue affective condition, there was a significant negative correlation between PANAS negative affect scores and IGT performance (r=−0.82, p=0.006). No other significant correlations emerged within the CPSI. We found no correlations between these variables in the case of controls.

Discussion

This study shows for the first time that negative mood induction can normalize decision-making performance in male cocaine polysubstance-using individuals (CPSI). Male CPSI exposed to the negative affective context showed a preference for the risk-averse safe choices of the IGT, and their net performance was indistinguishable from that of controls. On the other hand, male CPSI exposed to positive, drug-related, and neutral images showed the typical pattern of disadvantageous performance in the IGT (i.e., preference for the high-risk decks), and their net performance was significantly decreased with respect to that of controls; effect sizes for these decrements were large, especially for the positive and drug cue conditions (>1). Importantly, the impact of negative mood induction cannot be explained in terms of baseline differences in decision-making skills, personality traits related to sensitivity to reward/punishment, or trait affect. Nonetheless, there was a significant positive correlation between greater anxiety and better IGT performance that was specific for the CPSI subgroup exposed to the negative affective context. These results have outstanding implications for the clinical treatment of addictive disorders, especially when considering that decision-making ability is a reliable marker of drug relapse.

According to the somatic marker framework, the impact of the negative affect induction on the decision-making performance of CPSI may be explained by a boosting effect of negative mood on the emotional signals that normally work to anticipate the prospective outcomes of different choices (Bechara 2004; Bechara and Damasio 2005). This view is also consistent with a component process account of decision making which posits that altered performance in the IGT could relate to a failure to rapidly learn from negative feedback (Fellows 2007); hence, the negative mood induction may have facilitated punishment-based learning. Both views are supported by electrophysiological evidence showing that negative mood induction increases error-related negativity (Wiswede et al. 2009), a brain potential purported to reflect punishment-based signals through the enactment of phasic dopamine signals (Nieuwenhuis et al. 2004). Along similar lines, the negative mood induction may have put this subgroup of CPSI in a "hot" state, during which decisions are more easily driven by emotions (Loewenstein et al. 2001). During this "hot" negative state, the triggering of "risk as feelings" that are

related to negative consequences may be exaggerated, thus favoring risk aversion (Bechara 2004; Loewenstein et al. 2001). This effect is also predicted by the anticipatory affect model which posits that negative arousal should promote avoidance behavior (Knutson and Greer 2008). This effect could be further fostered by the congruency between their background affect and the content of the affective manipulation, as suggested by the positive correlation between anxiety and decision-making performance in this particular group. This notion is consistent with a mood congruency model by which background feelings serve as a filter for incoming stimuli, amplifying the attention to information that is consistent with the person's mood (Bower 1981). Accordingly, a recent study found a positive significant association between trait anxiety and IGT performance (Werner et al. 2009).

Interestingly, the impact of negative affect was evident among male CPSI, but not among controls. This could partially reflect a ceiling effect in the case of control individuals, which displayed optimal decision-making strategies irrespective of the valence of mood induction. However, it is also plausible that CPSI have a greater sensitivity to negative arousing stimuli, as shown by previous studies (Aguilar de Arcos et al. 2008; Chapin et al. 2010) and in accordance with stress and allostatic models of addiction (Koob and Le Moal 2001; Li and Sinha 2008). Although this hypersensitivity is not reflected in statistical differences in subjective ratings, CPSI actually rated negative images as mildly more arousing. In fact, we would expect this quite subtle effect for hypersensitivity to negative stimuli to be beneficial for decision making since very high levels of negative affect actually worsen decision-making performance (Miu et al. 2008; Starcke et al. 2008). Another unexpected result was the lack of significant effects of the drug cue mood induction in the decision-making performance of CPSI. In this case, results might be partially explained by a floor effect since CPSI showed a quite disadvantageous decision-making performance irrespective of mood induction. However, these results argue against the hypothesis that cue-induced craving plays a major role on risky decision making. This finding is also in agreement with recent evidence showing that non-specific positive or stress-related feelings are better predictors of drug relapse than cue-induced craving (Epstein et al. 2009; Sinha et al. 2006).

The impact of negative mood on decision-making performance, which is regarded as a relevant indicator of drug relapse (see Passetti et al. 2008), may thus have relevant implications for cocaine addiction treatment. According to our results, the induction of a short-term negative state of moderate intensity could contribute to decrease risk-prone decision tendencies in cocaine-dependent individuals, which could achieve enormous significance if able to reduce drug-seeking tendencies in everyday situations. For example, future studies should examine the effects of including short infusions of negative affective images on real-time electronic devices like those employed on ecologically momentary assessments (Epstein et al. 2009). Emotion regulation techniques could also work to reappraise typical negative emotions into "risk as feelings" (Loewenstein et al. 2001), facilitating their role in signaling the long-term consequences of potentially risky choices. Although we believe that the study is rich in clinical implications, we are also cognizant about relevant limitations, including the lack of psychophysiological or neuroendocrine measures that may had clarified the biological substrates of the impact of the negative mood induction and the relatively small sample size, which might have potentially blurred possible subtle effects of the positive and drug-related manipulations. The relatively small sample size in the different subgroups may also account for the fact that the negative mood effect is only readily statistically significant in the direct comparisons between CPSI and controls under different affective conditions. In addition, caution should be taken in attempting to generalize these results to female cocaine users; evidence indicates that negative mood states are a relevant factor in predicting substance relapse in women, whereas men are more likely to have positive experiences prior to relapse (Walitzer and Dearing 2006). Along the same lines, there is evidence of enhanced frontolimbic activation in response to stress in female vs. male cocaine users (Li et al. 2005), which may confer higher risk for detrimental effects of negative emotion on cognitive control among women (Li et al. 2009; de Visser et al. 2010). Therefore, it is plausible that the effects of negative mood induction on risk-averse decision making are specific to men.

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Conflict of interest The authors have no conflicts of interest to declare.

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