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ORIGINAL INVESTIGATION

Chronic and recreational use of cocaine is associated with a vulnerability to semantic interference

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Abstract
Rationale Language production requires that speakers effectively recruit inhibitory control to successfully produce speech. The use of cocaine is associated with impairments in cognitive control processes in the non-verbal domain, but the impact of chronic and recreational use of cocaine on these processes during language production remains undetermined.
Objectives This study aims to observe the possible impairment of inhibitory control in language production among chronic and recreational cocaine polydrug users.
Method Two experiments were carried out on chronic (experiment 1) and recreational (experiment 2) cocaine polydrug users performing a blocked-cycled naming task, yielding an index of semantic interference. Participants were matched for sex, age, and intelligence (Raven's Standard Progressive Matrices) with cocaine-free controls, and their performance was compared on the blocked-cycled naming task.
Results Chronic and recreational users showed significantly larger semantic interference effects than cocaine-free controls, thereby indicating a deficit in the ability to inhibit interfering information.
Conclusion Evidence indicates a relationship between the consumption of cocaine, even at recreational levels, and the inhibitory processes that suppress the overactive lexical representations in the semantic context. This deficit may be critical in adapting and responding to many real-life situations where an efficient self-monitoring system is necessary for the prevention of errors.

Keywords Cocaine · Inhibition · Semantic interference · Speech

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Introduction

Taking cocaine by the snorting route is Europe's second preferred recreational drug habit after smoking cannabis (European Centre for Drugs and Drug Addiction 2012). The popularity of cocaine has risen in recent years, and nowadays, it is no longer considered to be an "elite drug," instead being one of the most commonly used drugs, and its use has now been identified as a public health issue in Europe as it is in the USA (EMCDDA 2012; United Nations Office on Drugs & Crime 2013).

Chronic and recreational cocaine users, as well as abstinent cocaine users, are characterized by showing significant decrements in neuropsychological performance when compared to cocaine-free controls (Bolla et al. 2004; Goldstein et al. 2004; Hulka et al. 2013a, b, c; Jovanovski et al. 2005). Several studies have examined the long-term effects of chronic cocaine use on cognitive processes. Commonly observed impairments include deficiencies in cognitive flexibility (Verdejo-García et al. 2006; Verdejo-García and Pérez-García 2007), episodic memory (Manschreck et al. 1990; Mittenberg and Motta 1993; Reske et al. 2010; Vonmoos et al. 2013), social and non-social decision-making (Hulka et al. 2013a), prosodic and cross-modal emotion processing (Hulka et al. 2013b), and inhibitory control processes (Ersche et al. 2012; Fillmore and Rush 2002; Goldstein and Volkow 2002; Rosselli et al. 2001; Volkow et al. 2010). Inhibitory control refers to the processes responsible for suppressing irrelevant and competing information to facilitate the selection

of the correct representation according to the task goal (Anderson 2003; Brainerd and Dempster 1995; Miyake et al. 2000). The frontal regions are proposed as the neural substrate for inhibitory control (Bari and Robbins 2013; Miller and Cohen 2001), and dopamine, the neurotransmitter targeted by cocaine (Hershey et al. 2004), plays an important neuromodulatory role (Arnsten et al. 2012; Previc 1999; Robbins and Arnsten 2009). It is well known that in the long term, chronic (i.e., daily) use of cocaine is associated with reduced functioning of dopamine D_2 (DAD2) receptors in the orbitofrontal cortex, cingulate gyrus, and striatum (Martinez et al. 2009; Tomasi et al. 2010; Volkow et al. 1999) along with dysfunctions in the lateral prefrontal cortex, orbitofrontal cortex, and anterior cingulate gyrus (Bolla et al. 2003, 2004) as well as the cerebellum (Hester and Garavan 2004).

Recent studies have shown that recreational cocaine polydrug users, who do not meet the criteria for abuse or dependence but preferentially take cocaine on a monthly basis (1–4 g monthly) as well as other substances of abuse (e.g., MDMA (ecstasy), alcohol, cannabis), also show cognitive impairments that resemble those of chronic cocaine users. Thus, Colzato et al. (2007) provided evidence that recreational cocaine polydrug users showed impaired response inhibition, measured through a stop-signal task, and inhibition of return, relative to non-cocaine users (Colzato and Hommel 2009). Furthermore, the recreational use of cocaine is associated with impairments on tasks tapping into sustained attention, attentional shifting (Soar et al. 2012; Vonmoos et al. 2013), and resolution of response conflict (Sellaro et al. 2013). Taken together, the available studies suggest that chronic and recreational use of small doses of cocaine may be involved in alterations in inhibitory control functions in the non-verbal domain. Nevertheless, no studies have directly investigated these executive control impairments in the language domain. Although there are some reports of worsened performance on the Stroop task (Rosselli et al. 2001; Verdejo-Garcia et al. 2004), deficits in naming ability (Ardila et al. 1991; Manschreck et al. 1990; Mittenberg and Motta 1993; Rosselli et al. 2001) and in verbal memory and abstraction (Beatty et al. 1995; O'Malley and Gawin 1990; Rosselli and Ardila 1996) observed in chronic and dependent cocaine users compared to non-users, the relationship between inhibitory control and language processing in cocaine users remains undetermined.

The current study aims to explore whether cocaine use is associated with impairments in inhibitory control in language production. To do so, we used the semantic blocking task (Belke et al. 2005; Damian et al. 2001; Kroll and Stewart 1994), where participants are asked to name images presented in a context where all items belong to the same semantic category (homogeneous condition: e.g., train, car, bike) or in a context in which elements belong to different semantic categories (heterogeneous condition: e.g., train, bed, dog). The typical result is slower naming latencies to elements presented in a homogeneous context than in a heterogeneous context. This interference effect is accounted for in terms of competition among the co-activated lexical entries, by virtue of their semantic relatedness. During lexical selection, semantically related concepts receive extra activation and they become potent competitor-distractors, relative to those concepts that are presented in a semantically unrelated context (Roelofs 1992, 2003; Schriefers et al. 1990). In interference paradigms, speakers have to prevent responses corresponding to highly salient competitors and selective inhibition may be involved (Roelofs and Piai 2011; Shao et al. 2013). Further evidence supporting the idea that the semantic blocking task can reflect the ability to inhibit specific unwanted responses comes from neuropsychological studies. For instance, Biegler et al. (2008) observed exaggerated semantic blocking effects in patients with damage to the left inferior frontal gyrus (Biegler et al. 2008), which is thought to be involved in the selection among semantic competing representations (Thompson-Schill 2003; Thompson-Schill et al. 1997, 2002).

In the present study, we investigated whether the abuse of cocaine predisposes an individual to show a possible deficit in verbal inhibitory control in chronic (experiment 1) and recreational cocaine polydrug users[1] (experiment 2). The focus of experiment 1 was to examine if chronic cocaine users, who have not been using drugs other than cocaine (except alcohol and tobacco), show higher vulnerability to semantic interference—if so, we would expect larger semantic blocking effects in users than in cocaine-free controls. In experiment 2, we hypothesized that the abuse of small amounts of cocaine predisposes to a greater semantic blocking effect with respect to cocaine-free controls, and therefore, we expected to find larger semantic blocking effects in the recreational cocaine polydrug users due to inefficient inhibitory mechanisms at lexical selection.

General method

Apparatus, stimuli, and procedure

All participants were tested individually in a session that lasted approximately 60 min. They first completed a drug use questionnaire, before performing the screening tasks, followed by a Spanish version of the semantic blocking task. This task consisted of 20 images belonging to different semantic categories (faces, vehicles, vegetables, instruments,

[1] Chronic cocaine users were screened for other drug use. We found that they only used cocaine except for one participant that had also used MDMA. Recreational cocaine users, on the other hand, sporadically used other drugs such as MDMA or cannabis, but they mainly and preferably used cocaine. As the recreational users were not "pure" cocaine users, this group of users was called "recreational cocaine polydrug users."

and clothes) shown on a computer screen. The exemplars were selected to minimize within-category visual similarity, associative relations between exemplars, and overlap of initial phonemes of the names of the stimuli. The frequency and number of letters were controlled. The stimuli were arranged in a 5×5 item matrix. Columns corresponded to categories and formed homogeneous groups of five items, while rows formed groups of five items from different categories. Thus, there were five blocks with five items each from the same category and five blocks with the same number of items from different categories. Each block contained four repetitions (four presentations cycles), a total of 20 trials per block. Each presentation cycle contained five different items, and each item occurred once in each position within a cycle. The last item of a cycle was never the same as the first of the next cycle to avoid repetition of items on successive trials (Belke et al. 2005).

For counterbalancing purposes, we created five different homogeneous lists and five different heterogeneous lists from the combination of the ten blocks in a Latin square design. Homogeneous and heterogeneous lists were presented in alternating orders, with a pause after each list.

The participants were instructed to name each item as quickly and accurately as possible. We presented images on a screen using a computer, and an electronic device recorded verbal responses. The experimenter recorded errors and equipment failures. Before the naming task, participants were familiarized with the complete set of stimuli with the corresponding name printed below. A trial consisted of the following: a fixation cross at the center of the screen for 500 ms, the stimulus which remained on the screen until the response or for a maximum of 3000 ms, and a blank interval for 500 ms. Response latencies were measured from the presentation of the stimulus to the onset of the response.

In both experiments, participants were matched for race, age, and IQ [measured by Raven's Standard Progressive Matrices (Raven et al. 1988)]. Furthermore, to ensure intact verbal and memory functions, the participants preformed a Boston Naming Test (Kaplan et al. 1983), a modified version of the verbal fluency test (VFT) for native Spanish speakers from the Screen for Cognitive Impairment in Psychiatric (SCIP) patients (Pino et al. 2006), and a memory span test (Daneman and Carpenter 1980). Participants filled in a self-report questionnaire on recent use, amounts, and patterns of alcohol and drug consumption during the last 6 months (cf. Colzato and Hommel 2009, Colzato et al. 2007). To encourage participants' compliance with the instructions, saliva samples were obtained (not further analyzed) at the beginning of the experiment (cf. Colzato et al. 2004). We obtained written informed consent from all participants after providing them with explanations about the nature of the experiment. The local ethics committee approved the protocol and the compensation of 20 euro for participation in the study.

Experiment 1

Participants

Thirty-two adults (30 men and 2 women) participated in the experiments. They formed the two experimental groups of 16 chronic cocaine users and 16 cocaine-free controls. Chronic cocaine users were recruited from the *Proyecto Hombre Granada* rehabilitation center. The inclusion criteria were as follows: (1) meeting the DSM-IV criteria for cocaine dependence as assessed by the clinician version of the Structured Clinical Interview for DSM-IV Disorders (SCID) (American Psychological Association 2000) (First et al. 1996) and (2) a minimum abstinence interval of 2 days for all abuse substances except nicotine, observed by periodic urine toxicology tests, therapist reports, or self-reports. The exclusion criteria were (1) the presence of any Axis I or Axis II disorders except substance abuse, determined by the Mini International Neuropsychiatric Interview (MINI) (Lecrubier et al. 1997), a brief diagnostic tool that screens for several psychiatric disorders; (2) the presence of history of brain injury or central nervous system diseases; and (3) an excessive intake of alcohol (>280 g/week for men and >168 g/week for women) (Foster and Marriott 2006). Four of the chronic cocaine users were using prescribed benzodiazepines, but they were asked not to use the medication 2 days before the assessment. Sixteen healthy adults formed the control group. We recruited the control participants via notes posted on community bulletin boards and by word of mouth. The control group did not meet any criteria for Axis I or Axis II psychiatric disorders, including substance abuse, and had no clinically significant medical disease (e.g., multiple sclerosis or brain injury). In the last 6 months, prior to participation, three chronic cocaine users and three cocaine-free users also smoked marijuana, while one chronic cocaine user reported having used MDMA (ecstasy). Although participants in the chronic group were engaged in the detoxification program, they were periodically (every 30 days) screened for drug use through urine analysis, and we asked them to refrain from taking all types of psychoactive drugs for at least 2 days before the experiment. In addition, all participants were asked not to consume alcohol the night before the experimental session and to have a normal night of rest. Researchers were also instructed to observe if participants had used alcohol prior to the experimental session.

Results

Demographic and drug use statistics are provided in Table 1. As mentioned, we assessed the alcohol habits of the participants through a self-reported questionnaire enquiring about their weekly intake of alcoholic drinks. Since the strengths of different types of alcoholic beverages vary significantly, we adopted the definitions of standard "drinks" or "units," equal

Table 1 Demographic characteristics and self-reported use of cocaine and other psychoactive drugs in experiments 1 and 2

Sample	Experiment 1		Experiment 2	
	Chronic cocaine users	Cocaine-free controls	Recreational cocaine polydrug users	Cocaine-free controls
N (M:F)[a]	16 (15:1)	16 (15:1)	20 (10:10)	20 (10:10)
Age (years)[a]	33.75 (4.46)	31.25 (4.97)	24.70 (4.26)	23.35 (3.24)
Raven IQ[a]	98 (5.43)	101 (8.60)	103 (9.2)	101 (9.5)
Cigarettes (unit/day)	12.13 (7.44)*	1.69 (3.38)*	7.60 (8)**	1.95 (3.30)**
Alcohol (units/week)	24.40 (18.3)**[b]	1.8 (3.7)**	15.0 (5.31)**	4.75 (9.89)**
Monthly cannabis (joints)	2.75 (6.64)*	0.75 (1.61)*	25.6 (26.57)**	1.2 (4.51)**
Years of using cocaine	10.31 (4.88)	0	4 (2.43)	0
Monthly exposure (grams of cocaine)	15.37 (16.96)	0	2.56 (1.74)	0
Maximum amount in a 12-h period (grams)	2.81 (1.52)	0	1.61 (0.76)	0
Mean weeks in abstinence	24.71 (17.68)	0	1.89 (1.43)	0
Money spent monthly (euro)	922.5 (1017.96)	0	98 (46.29)	0
MDMA (grams/last 6 months)	0.40 (1.62)	0	1.95 (1.92)	0

Raven IQ IQ measured by means of the Raven's Standard Progressive Matrices

*$p<0.05$, significant group difference; **$p<0.01$, Significant group difference;

[a] No significant difference

[b] Unit equals to 10 ml or 8 g of pure ethanol (International Center for Alcohol Policies 2005; Spanish Ministry of Health 2007). Chronic cocaine users are alcohol abstinent once they are engaged in the rehabilitation program

to 10 ml or 8 g of pure ethanol (International Center for Alcohol Policies 2005; Spanish Ministry of Health 2007). As can be observed in Table 1, users differed from controls in the amount of tobacco, alcohol, and cannabis consumed before they entered into the rehabilitation program, although all of them were not consuming alcohol or cannabis once they entered into the program.

No significant group differences were obtained for IQ, $t(30)=1.10$, $p=0.27$; verbal functions in Boston Naming Test, $t(30)=-0.10$, $p=0.29$; verbal fluency test, $t(30)=1.04$, $p=0.30$; and memory span test, $t(30)=1.54$, $p=0.13$. Table 2 shows the performance on the neuropsychological tests.

Separate analyses were performed using IBM SPSS Statistics® 20 for participants and items, yielding F_1 and F_2 statistics, respectively. Given the traditional logic in the psycholinguistics field, we report both analyses to check whether the findings could be generalized not only across participants but also across similar stimulus materials.

We carried out a repeated measures ANOVA to compare the response latencies (RLs) and errors with context (homogeneous vs. heterogeneous) as a within-subjects factor and group (chronic cocaine users vs. cocaine-free controls) as a between-groups factor.

Three types of responses were excluded from the analysis (5.14 %): (1) naming errors, hesitations, and microphone failures; (2) responses longer than 1500 ms or shorter than 250 ms; and (3) trial pictures that accounted for more than 15 % of errors on overall task performance. In addition, as context effects are being targeted, following the procedure of analysis adopted by Damian et al. (2001), the first occurrence of each stimulus on each block was first excluded (first cycle), and the data from the other three cycles were collapsed.

Table 2 Mean scores obtained in neuropsychological test performance in experiments 1 and 2

Test	Experiment 1		Experiment 2	
	Chronic cocaine users	Cocaine-free controls	Recreational cocaine polydrug users	Cocaine-free controls
BNT[a]	50.94 (4.64)	49 (5.5)	50.25 (3.1)	51.75 (4.74)
VFT[a]	40.25 (7.2)	43.25 (8.9)	43.20 (10.43)	46.7 (9.22)
MST[a]	2.68 (0.92)	3.12 (0.64)	3.23 (0.90)	3.50 (0.76)

Standard deviation in parentheses

BNT Boston Naming Test, *VFT* verbal fluency test, *MST* memory span test

[a] No significant difference

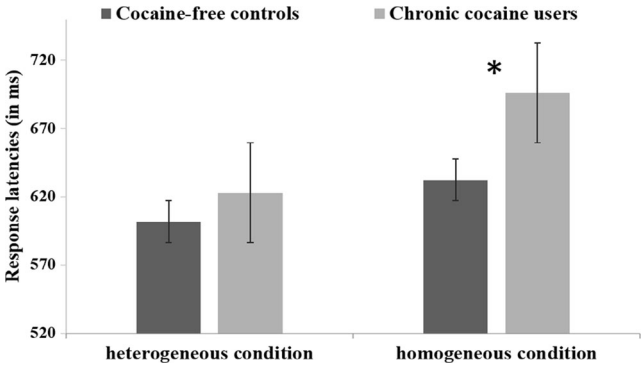

Fig. 1 Mean response latencies (in milliseconds) by conditions in Experiment 1

Figure 1 reports the mean RLs for correct responses, and error means are reported in Table 3.

Response latencies

The RL analysis showed a significant effect of context [$F_1(1, 30)=66.19$, $p<0.001$, $\eta^2_p=0.68$; $F_2(1, 48)=44.19$, $p<0.001$, $\eta^2_p=0.47$], indicating that the homogeneous condition led to longer naming latencies ($M=664$, SD=80) than the heterogeneous condition ($M=612$, SD=65). The main effect of group was significant in the item analysis [$F_1(1, 30)=3.14$, $p=0.86$, $\eta^2_p=0.09$; $F_2(1, 48)=26.3$, $p<0.001$, $\eta^2_p=0.35$], showing that chronic cocaine users need more time to name the stimuli ($M=660$, SD=89) than the cocaine-free control group ($M=617$, SD=57). Most importantly, the context×group interaction was significant [$F_1(1, 30)=11.19$, $p=0.002$, $\eta^2_p=0.27$; $F_2(1, 48)=7.07$, $p=0.011$, $\eta^2_p=0.12$], showing that chronic users had larger semantic interference effects than the cocaine-free controls. Post hoc Newman-Keuls analyses showed a reliable difference between the homogeneous and heterogeneous condition (both $p<0.05$) for the group of chronic users (73 ms) and cocaine-free group (30 ms).

Errors

The main effect of context was significant in the analysis by items [$F_1(1, 30)=3.28$, $p=0.07$, $\eta^2_p=0.09$; $F_2(1, 48)=4.26$, $p=0.04$, $\eta^2_p=0.08$], indicating that the homogeneous condition produced more errors than the heterogeneous condition. Neither the main effect of group nor the context×group interaction was significant [$F<1$].

Correlations

To test whether the magnitude of semantic interference was proportional to the amount of cocaine consumed, we computed partial correlation coefficients between relevant cocaine use variables (e.g., lifetime amount, times per week of cocaine use, maximum peak in 12 h, and monthly cocaine consumption in grams) and both semantic blocking (the result of the subtraction between homogeneous and heterogeneous response latencies) and error, when controlling for the use of other drugs (tobacco, MDMA, and alcohol). The variable error commission correlated positively with times per week of cocaine use ($r=0.681$, $p=0.01$) (Fig. 2) and maximum peak of cocaine used in 12 h ($r=0.718$, $p=0.006$) (Fig. 3). Although the variable semantic effect followed the same trend, no correlations reached significance ($r\leq0.41$, $p\geq0.15$). Thus, it seems that the heavy cocaine usage (more times per week and high peaks in 12 h) may impair performance on the semantic blocking task. No other significant correlations were found ($p>0.05$).

Discussion

Experiment 1 tested the hypothesis that chronic cocaine users have an impairment in inhibitory processes in the verbal domain. If so, chronic cocaine users would show a more pronounced semantic blocking effect due to an inefficient selection mechanism when items became stronger competitors during lexical selection. This is exactly what we observed: both groups showed similar performance in naming items in a semantically unrelated condition, but chronic cocaine users showed larger naming latencies for the items to be named in a semantically related condition in comparison to the cocaine-free controls. In addition, partial correlations showed that heavy cocaine (more times per week and high peaks in 12 h)

Table 3 Mean error execution (in percentage) by conditions in experiments 1 and 2

Condition	Experiment 1		Experiment 2	
	Chronic cocaine users	Cocaine-free controls	Recreational cocaine polydrug users	Cocaine-free controls
Homogeneous	3.37	2.12	3.04	0.95
Heterogeneous	1.76	1.74	1.65	1.16

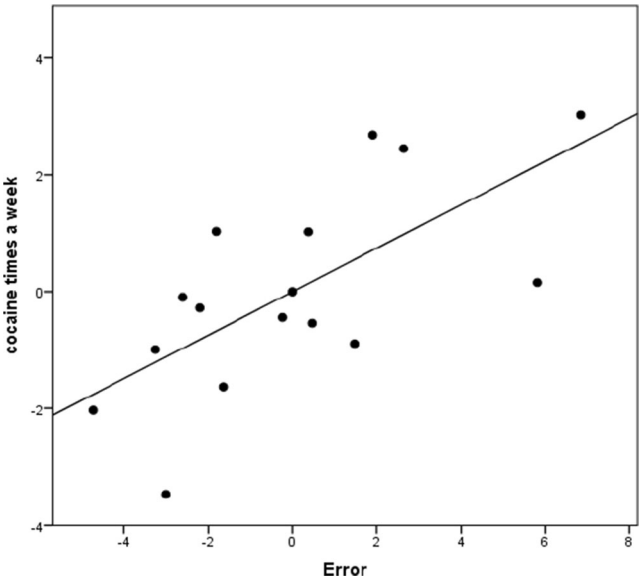

Fig. 2 Scatter diagram of the partial correlation between error commission and weekly consumption of cocaine (residuals) in experiment 1, controlling for the use of other drugs

seems to contribute to the greater semantic effect. Based on the assumption that there are impaired inhibitory processes in long-term cocaine users (Ersche et al. 2012; Fillmore and Rush 2002; Goldstein and Volkow 2002; Rosselli et al. 2001; Volkow et al. 2010), we consider that the greater semantic interference that chronic cocaine users show reflects a deficit in the inhibitory mechanism involved during lexical selection.

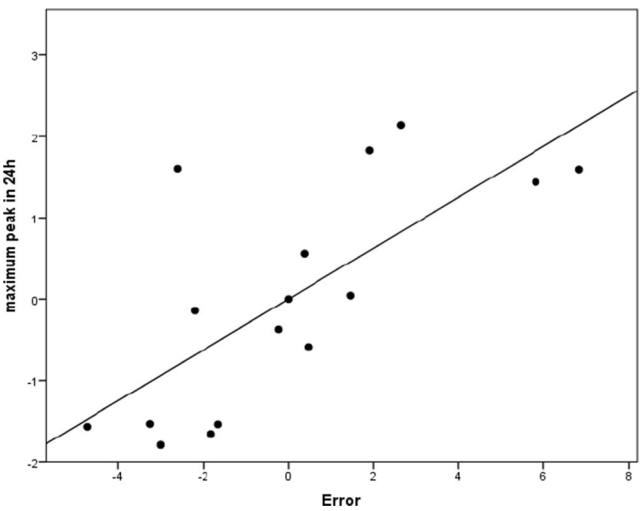

Fig. 3 Scatter diagram of the partial correlation between the error commission and maximum consumption of cocaine in 12 h (residuals) in experiment 1, controlling for the use of other drugs

Experiment 2

Participants

Forty healthy adults (20 men and 20 women) served as participants for partial fulfillment of course credits or financial compensation. They formed the two experimental groups of 20 recreational cocaine polydrug users and 20 cocaine-free controls. We recruited the participants via notes posted on community bulletin boards and by word of mouth. Recreational cocaine polydrug users met the following criteria: (1) a monthly consumption (1 to 4 g) by the snorting route for a minimum of 2 years; (2) no Axis I or Axis II psychiatric disorders DSM-IV (American Psychological Association 2000), including substance abuse; (3) no clinically significant medical disease; (4) no use of prescription medication; and (5) non-excessive below-risk intake of alcohol (>280 g/week for men and >168 g/week for women) (Foster and Marriott 2006). Cocaine-free controls met the same criteria, but they reported no history of past or current cocaine use.

In the 6 months prior to participation, 14 recreational cocaine polydrug users and 2 cocaine-free users also smoked marijuana, while 14 recreational users reported having used MDMA (ecstasy) and 6 reported using ketamine. Participants were asked to refrain from taking all psychoactive drugs for at least 2 days, not to consume alcohol the night before the experimental session, and to have a normal night of rest. Researchers were instructed to observe if participants had used alcohol prior to the experimental session. Participants were selected by means of a telephone interview using the MINI (Lecrubier et al. 1997). The sample was obtained from a pool of 50 potential volunteers who responded to the advertisements for studies conducted in our lab over a period of 6 months. Within this pool of potential participants, the most common reason for excluding an individual from the study was meeting criteria for psychiatric disorders, alcohol abuse, or medication.

Results

Demographic and drug use statistics are provided in Table 1. Recreational cocaine polydrug users significantly used more tobacco, alcohol, and cannabis than the control group in the last 6 months prior to the test. No significant group differences were obtained for intelligence, $t(38)=0.66$, $p=0.51$; Boston Naming Test, $t(38)=1.18$, $p=0.24$; memory span test, $t(38)=0.99$, $p=0.32$; or verbal fluency test, $t(38)=1.12$, $p=0.26$. Table 2 shows performance on the neuropsychological tests.

As for experiment 1, three types of responses were excluded from the analysis (3.56 %): (1) naming errors, hesitations, and microphone failures; (2) responses longer than 1500 ms or

shorter than 250 ms; and (3) trial pictures that accounted for more than 15 % of errors on overall task performance.

Response latencies

The RL analysis showed a significant effect of context [$F_1(1, 38)=40.15$, $p<0.001$, $\eta^2_p=0.51$; $F_2(1, 48)=22.26$, $p<0.001$, $\eta^2_p=0.31$], indicating that the homogeneous condition led to longer naming latencies ($M=604$, SD=80) than the heterogeneous condition ($M=572$, SD=78.5). The main effect of group was marginally significant in the item analysis [$F_1(1, 38)=0.37$, $p=0.54$, $\eta^2_p=0.009$; $F_2(1, 48)=3.62$, $p=0.063$, $\eta^2_p=0.07$], showing that recreational polydrug cocaine users needed more time to name the stimuli (M=595, SD=87.6) than cocaine-free control group ($M=580$, SD=73.6). Most importantly, the context×group interaction reached significance [$F_1(1, 38)=6.95$, $p=0.012$, $\eta^2_p=0.15$; $F_2(1, 48)=4.02$, $p=0.05$, $\eta^2_p=0.07$], showing that recreational polydrug cocaine users had stronger semantic interference than the cocaine-free controls. Post hoc Newman-Keuls analyses showed a reliable difference between the homogeneous and heterogeneous condition (both $p<0.05$) for the group of recreational cocaine polydrug users (46 ms) and cocaine-free group (19 ms). Figure 4 reports the mean RLs for correct responses.

Errors

The main effect of context was not significant in both the subject and item analysis. The main effect of group was significant in the item analysis [$F_1(1, 38)=8.43$, $p=0.006$, $\eta^2_p=0.18$; $F_2(1, 48)=12.35$, $p<0.001$, $\eta^2_p=0.20$], showing a higher rate of errors in the recreational cocaine polydrug group compared to the cocaine-free control group. Interestingly, the context×group interaction reached significance in the item analysis [$F_1(1, 38)=3.76$, $p=0.06$, $\eta^2_p=0.08$; $F_2(1, 48)=5.6$, $p=0.022$, $\eta^2_p=0.10$]. Post hoc Newman-Keuls analyses showed that the recreational cocaine polydrug users committed a higher rate of errors for semantically related items than the control group. Error means are reported in Table 3.

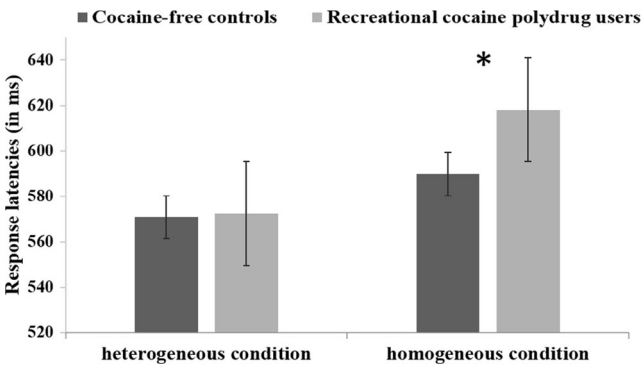

Fig. 4 Mean response latencies (in milliseconds) by conditions in experiment 2

Correlations

To test whether the magnitude of semantic interference is proportional to the amount of cocaine consumed, we computed partial correlation coefficients between relevant cocaine use variables (such as lifetime amount, maximum peak in 12 h, and monthly cocaine consumption in grams) and both the semantic blocking effect and error commission, when controlling for the use of other drugs (tobacco, MDMA, and alcohol). However, no correlation reached significance ($r\leq 0.41$, $p\geq 0.10$).

Discussion

As expected in experiment 1, recreational cocaine polydrug users showed larger semantic blocking effects in comparison with a cocaine-free group, reflecting vulnerability to semantic interference in a language production task. The results are in line with those studies in which recreational cocaine polydrug users show decreased performance in tasks tapping inhibition (Colzato and Hommel 2009; Colzato et al. 2007; Sellaro et al. 2013). Taken together, these results suggest that even small amounts of cocaine may predispose to inefficient selection mechanisms for lexical selection during language production. However, the possible causal role of drug consumption in language selection has to be taken with caution since recreational cocaine polydrug users significantly used more tobacco, alcohol, and cannabis than the control group, and partial correlations between cocaine use and semantic blocking did not reach significance. It is also important to note the possibility that preexistent endophenotypes that are known to contribute to behavioral performance in cocaine users may have a role to play in the impairment of language competition in recreational users (Ersche et al. 2012; Verdejo-Garcia et al. 2008).

General discussion

This study investigated for the first time whether the chronic and recreational use of cocaine leads to a detectable increase in semantic interference. The magnitude of the semantic effect was substantially larger in the chronic and recreational cocaine groups relative to cocaine-free controls during the naming of semantically related objects. This semantic interference can be accounted for by the competition between co-activated lexical entries in a homogeneous context that affects selection latencies (Roelofs 1992; Schriefers et al. 1990). To ensure the success of the lexical selection, the inhibitory system must

act to selectively suppress semantically related lexical entries that are strong competitors for the correct answer (Roelofs and Piai 2011; Shao et al. 2013). Following the study of Biegler, Crowther and Martin (2008), patients with left inferior frontal gyrus damage showed an exaggerated semantic blocking effect, suggesting that this brain adjusts the weight derived from the co-activation of semantic-related items (Biegler et al. 2008). Thus, we propose that the chronic and recreational cocaine users may suffer from the same deficit, albeit in a milder form. Our results are in line with the available studies on recreational and chronic users of cocaine, which report impairments on tasks measuring inhibition in non-verbal domains (Colzato et al. 2007; Fillmore and Rush 2002; Sellaro et al. 2013; Verdejo-García et al. 2007). However, this is the first study in which a semantic blocking task is used as an indicator of interference resolution in the verbal domain in cocaine users. Both chronic and recreational cocaine users showed larger semantic blocking, probably due to inefficient use of verbal inhibitory processes.

The design of our study allows us to reject alternative accounts of our observations in terms of age, IQ, and sex, since the two user groups were matched with the controls on these variables. Similarly, the present results cannot be explained by factors related to preexisting psychiatric disorders which are known to affect response inhibition (Rosenberg et al. 1997; Schachar and Logan 1990; Thoma et al. 2007) since we conducted extensive screening using the MINI to exclude any preexisting psychiatric disorders (e.g., ADHD).

Nevertheless, the results of the study for the recreational polydrug group do not allow us to completely rule out an account of their deficit in terms of preexistent underlying neurocognitive endophenotype for stimulant drug addiction that may contribute to task performance (Ersche et al. 2012; Verdejo-Garcia et al. 2008). However, the fact that the impairment was found for both chronic and recreational users with very different social and personal profiles may suggest that recreational cocaine use is also related to the larger blocking effects found in the recreational polydrug users relative to the controls.

Another possible shortcoming of our study is that, given the abuse rate of other drugs when consuming cocaine among recreational users (Grov et al. 2009; Kelly and Parsons 2008), it is difficult to separate the cognitive deficit produced by cocaine use from the effect of the use of other drugs. It should be noted that the difference in significance in the use of tobacco, alcohol, and cannabis between the groups may also be influencing the difference in the semantic effect. We tried to minimize this fact by selecting a sample of users who predominantly used cocaine and avoiding as far as possible the selection of people that also abuse other stimulant drugs. We based our selection on self-report measures, since previous studies have shown that self-reports of drug abuse are quite reliable and strongly correlated with objective measures of drug abuse (Glintborg et al. 2008; Zaldívar Basurto et al. 2009). Since our participants reported very low consumption of cannabis and MDMA, we doubt that our results may be attributed to the effects of the use of any of these two drugs. Moreover, studies that have examined the effect of MDMA and cannabis on executive functions have provided conflicting results. Whereas deficits in working memory appear to be likely consequences of chronic MDMA and impairments in cognitive flexibility due to cannabis use (Verdejo-García et al. 2005), less consistent results were found in studies investigating inhibitory control in the abuse of both substances (Crean et al. 2011; Kalechstein et al. 2007).

A more important limiting factor of our study is the fact that cocaine and alcohol are more often than not consumed together, and our sample of cocaine users was not an exception (see Table 1). Given the fact that acute alcohol use impairs inhibitory control (Fillmore and Vogel-Sprott 2000; Fillmore 2007; Noël et al. 2010), it is difficult to determine whether the obtained effects are the result of cocaine or of alcohol and cocaine together (Jatlow et al. 1996). In this regard, the screening of alcohol consumption in both groups was particularly important, so that participants selected for the study reported an average long-term consumption below the criteria for high alcohol use (280 g/week for men and 168 g/week for women). In addition, the group of chronic users was undergoing regular urine toxicology screens as part of their treatment. However, while we used self-report measures and provided specific instructions not to consume alcohol or other drugs before the experimental session, we cannot be sure that participants in experiment 2 may have actively used either alcohol or cocaine shortly before the session, with 24 to 48 h prior to the experimental session potentially affecting performance on the semantic-blocked naming task. Although this suggestion should be treated with caution, the fact that the impairment appeared in both recreational and chronic users (urine tested) suggests that this might not have been the case.

The outcomes from both experiments show that the use of high and low amounts of cocaine may be influencing the vulnerability to interference in verbal cognitive processes in which inhibitory control is required. Although the role of some preexisting factor such us impulsiveness, risky behavior, driving, or illegal activity (Verdejo-Garcia et al. 2008) cannot be ruled out, the present results support the broader notion that cocaine use may impair inhibitory processes including those that subserve speech production.

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Conflict of interest All authors declare that they have no conflicts of interest.

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