RESEARCH ARTICLE

Increased response conflict in recreational cocaine polydrug users

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Abstract Recent studies suggest that recreational use of cocaine is associated with significant impairments in the same cognitive control functions that are affected by chronic use. Here we tested whether recreational cocaine use can impact the emergence and resolution of response conflict in conflict-inducing tasks. Recreational cocaine polydrug users (n = 17) and cocaine-free controls (n = 17), matched for sex, age, intelligence, and alcohol consumption, performed a Simon task—which is known to induce response conflict. Recreational users showed a larger Simon effect, indicating that they had more difficulty resolving stimulus-induced response conflict. This finding is consistent with the recent literature showing that even small doses of cocaine are sufficient to compromise key cognitive control functions.

Keywords Cocaine · Polydrug · Interference control · Response conflict · Simon effect · Dopamine (DA)

Introduction

Over the last 10 years, taking cocaine by snorting route has become the most common recreational drug habit in Europe after smoking cannabis. The increasing use of cocaine has become a serious public health issue both in Europe and in

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Several studies investigating the long-term effects of cocaine use revealed that chronic (daily) cocaine users show impairments on tasks tapping mental flexibility (Verdejo-Garcia et al. 2006; Verdejo-Garcia and Perez-Garcia 2007), conflict, and cognitive control (Franken et al. 2007; Streeter et al. 2008); have difficulties in inhibiting their overt responses (Fillmore et al. 2002; Verdejo-Garcia et al. 2008; Ersche et al. 2012; but see Vonmoos et al. 2013a) and in controlling and sustaining their attention (Kübler et al. 2005; Hester and Garavan 2009; Vonmoos et al. 2013b); have impairments of inhibitory control processes (Biggins et al. 1997; Bolla et al. 1998, 2000; Fillmore et al. 2002; Hester et al. 2007); make riskier decisions in decision-making tasks (Monterosso et al. 2001; Bolla et al. 2003; Fishbein et al. 2005); and display cognitive impairments in the domains of working memory and declarative memory (Vonmoos et al. 2013b). Interestingly, most of these functions are assumed to rely on dopaminergic functioning (Hershey et al. 2004; Fillmore et al. 2005; Cools 2006; Ghahremani et al. 2012), and previous literature has suggested that the intake of cocaine is associated with a reduced dopamine (DA) receptor availability (Volkow et al. 1993, 1997, 1999; Garavan et al. 2008; Little et al. 2009; Tomasi et al. 2010).

Recent studies extended these findings by showing that even recreational cocaine users, who do not meet criteria for abuse or dependence but take cocaine (preferably by snorting route) on a monthly frequency (1-4 g monthly), show similar cognitive impairments as chronic users consuming cocaine on a much more regular basis (often 1 g daily, but at least 3 g weekly). The first evidence comes from a study by Colzato et al. (2007), who demonstrated that recreational use of cocaine is associated with impaired inhibitory control (but see Vonmoos et al. $2013a^1$), as assessed by performance in the stop-signal task (Logan 1994). Not only took it users longer to abort a prepared response but the size of this inhibitory deficit was also proportional to the amount of cocaine consumption.

In follow-up studies, Colzato and colleagues demonstrated that, compared to cocaine-free controls, recreational cocaine users show impairments in other cognitive control functions, such as the ability to adapt and restructure cognitive representations to changing situational demands (i.e., cognitive flexibility; Colzato et al. 2009a), the ability to inhibit covert attentional responses (Colzato and Hommel 2009), and in early aspects of attentional functioning (Colzato et al. 2009b). Furthermore, recent studies demonstrated that recreational use of cocaine is also associated with impairments on tasks tapping sustained attention and attentional shifting (Soar et al. 2012; Vonmoos et al. 2013b). Interestingly, whereas the ability to update and to actively monitor information in the working memory, as measured by the N-back task (see Kane et al. 2007, for a review), does not seem to be affected by recreational intake of cocaine (Colzato et al. 2009a), the ability to retain spatial information and to maintain remembered items in working memory is compromised (Soar et al. 2012; Vonmoos et al. 2013b).

Finally, Colzato et al. (2008) showed that spontaneous eyeblink rate (EBR), a marker of striatal dopaminergic functioning (Shukla 1985; Karson 1983; Blin et al. 1990; Kleven and Koek 1996; Taylor et al. 1999), was significantly reduced in recreational cocaine users as compared to cocaine-free controls. Importantly, the degree of this reduction was proportional to the peak of cocaine consumption, with higher peaks associated with reduced eyeblinks and, thus, with lower dopaminergic functioning. Taken together, the available studies suggest that even small doses of cocaine (1–4 g monthly) are sufficient to compromise key cognitive control functions.

The present study aimed at complementing demonstrations of impaired cognitive control in recreational cocaine users by focusing on another key cognitive control function: interference control. To this end, we used the Simon task (Simon and Small 1969), a well-known paradigm that has been found to reflect the ability to deal with and resolve response conflict, that is, the ability to select a correct response in face of other, competing responses (cf., Hommel 2011). In this task, participants are required to perform lateralized (left versus right) responses on the basis of a non-spatial stimulus feature, often color. The position of the stimulus varies randomly in such a way that it can spatially correspond or not correspond with the position of the required response. The typical finding is better performance (i.e., faster responses and/or fewer errors) with stimulus– response correspondence than noncorrespondence—the Simon effect (Simon and Small 1969). This effect reflects the difficulty of selecting the correct response between competing responses and, thus, provides a rather direct measure of the efficiency of handling response conflict (Kornblum et al. 1990; Hommel 2011).

Based on the aforementioned findings linking both chronic and recreational cocaine consumption to impaired cognitive control, we considered that recreational users might show impaired conflict management. As the Simon effect can be taken to reflect the quality of conflict management (with smaller effects indicating better control), we thus expected more pronounced Simon effects in recreational users.

Methods

Participants

Thirty-four young healthy adults (26 men and 8 women) participated in the experiment and were compensated for their collaboration. They formed the two experimental groups of 17 recreational users of cocaine and 17 cocaine-free controls. Participants were recruited through advertisements posted on community bulletin boards and by word of mouth. The sample of participants was selected on the basis of a phone interview that, by means of the Mini International Neuropsychiatric Interview (M.I.N.I.; Sheehan et al. 1998; Lecrubier et al. 1997), screened participants for several psychiatric disorders including, post-traumatic stress disorder, ADHD, depression, schizophrenia, mania, and obsessive–compulsive disorder.

Consistent with previous studies (e.g., Colzato et al. 2007), recreational cocaine users met the following criteria: (1) a monthly consumption (1–4 g) by snorting route for a minimum of 2 years; (2) no history of psychopathology and substance use disorder; (3) no use of medication; (4) no clinically significant medical disease. None of the users met more than two of the seven criteria that according to the American Psychiatric Association DSM-IV and the World Health Organization (ICD-10) define addiction: tolerance, withdrawal, difficulty controlling the use, negative consequences for job, family and health, significant time or emotional energy spent in searching/consuming the drug, put off or neglected

¹ It must be said that different stop-signal paradigms might be differentially sensitive in detecting group differences. Thus, specific factors such as the kind of stimuli or signals used, the number of blocks or trials administered, the probability of go trials occurrence as well as pre-existing group differences in RT could account for this discrepancy.

activities because of the use, and desire to cut down the use. Cocaine-free controls met the same criteria with the only difference that they had never consumed cocaine.

In line with previous studies (e.g., Colzato et al. 2007), participants were required to abstain from using any psychoactive drugs for 2 days and from consuming food and beverages containing caffeine for at least 12 h before the test. They were also asked to refrain from consuming alcohol on the night before the experimental session and to have a normal night rest. To increase the likelihood of participants' compliance with these instructions, at the beginning of the session, they were required to provide a saliva sample which, however, was not further analyzed (cf. Colzato et al. 2007).

The two groups were matched for sex, age, IQ (measured by Raven's Standard Progressive Matrices (SPM); Raven et al. 1988), and alcohol consumption. Notwithstanding the fact that cocaine was the preferred drug for users, all cocaine users and cocaine-free controls reported consuming alcohol, cannabis, and MDMA. All participants reported to have never used LSD, barbiturates, steroids, solvents, or opiates. Demographic and drug use information are shown in Table 1. They provided written informed consent after the nature of the study was explained to them. The protocol and the remuneration of 15 euro were approved by the institutional review board (Leiden University, Institute for Psychological Research).

 Table 1
 Demographic
 characteristics
 and
 self-reported
 use
 of

 cocaine
 and
 other
 psychoactive
 drugs

Sample	Cocaine users	Cocaine-free controls	
N (M:F) ^{n.s.}	17 (14:3)	17 (12:5)	
Age (years) ^{n.s.}	24.3 (5.4)	22.1(2.3)	
Raven IQ ^{n.s.}	106.6 (5.4)	106.9 (6.0)	
Monthly drinks ^{n.s.}	66.4 (12.1)	59.8 (7.2)	
Monthly exposure (joints)**	19.2 (7.2)	6.1 (2.7)	
Lifetime exposure (MDMA)**	46.2 (30.0)	17.7 (6.6)	
Monthly exposure (grams cocaine)**	2.4 (0.5)	0	
Lifetime exposure (grams cocaine)**	110.4 (57.1)	0	
Highest regular frequency (times per month)**	3.8 (1.3)	0	
Highest amount in a 12-h period (peak; grams)**	1.4 (0.4)	0	

Standard deviations are shown within parentheses

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

Monthly drinks, monthly number of standard alcoholic drinks

n.s. nonsignificant group difference

**Significant group difference; p < 0.01

Apparatus, stimuli, and procedure

All participants were tested individually and, after having provided the saliva sample, they completed a 30-min reasoning-based intelligence test (SPM) and the Simon task. The SPM provides a measure of IQ by assessing the individual's ability to create perceptual relations and to reason by analogy independent of language and formal schooling. It is a standard, widely used test to measure Spearman's g factor and fluid intelligence in particular (Raven et al. 1988).

In the Simon task, participants were seated in front of a 17-inch monitor screen at a viewing distance of about 60 cm. The task consisted of a 25-min session in which participants were instructed to discriminate the color (green versus blue) of a target circle by pressing one of two lateralized keys on a computer keyboard: the left key in response to the green circle and the right key in response to the blue circle. Target circles were equiprobably presented to the left or to the right of a central fixation point. Participants had to ignore the location of the stimulus and to react as quickly and as accurate as possible to its color.

Trials began with the presentation of the fixation point. Afterward the target stimulus was presented until the response was given but no longer than 1,500 ms. Intervals between subsequent stimuli varied randomly but equiprobably, from 1,750 to 2,250 ms in steps of 100 ms. The task consisted of six blocks of 60 randomly ordered trials, the first of which was a practice block. In half of the trials, stimulus and response positions corresponded, whereas in the other half, stimulus and response positions did not correspond.

Results

First, independent t-tests were performed for all preexperimental measures. No significant group differences were observed for age, t(32) = 1.53, p = 0.14, intelligence, t(32) = 0.15, p = 0.88, and alcohol consumption, t(32) = 1.94, p = 0.06. In contrast, the two groups differed for the consumption of cannabis t(32) = 7.02, p < 0.001and MDMA t(32) = 3.83, p < 0.005, with recreational cocaine users consuming higher quantities than cocainefree controls (see Table 1).

In the Simon task, correct mean reaction times (RTs) and percentages of errors (PEs) were submitted to two separate analyses of variance (ANOVAs) with spatial stimulus– response correspondence (vs. noncorrespondence) as a within-participants factor and group (recreational cocaine users versus cocaine-free controls) as a between-participants factor. Both RT and PE analyses revealed a main effect of correspondence, F(1, 32) = 202.64, p < 0.001, MSE (mean squared error) = 61, $\eta_p^2 = 0.86$ (RTs) and F(1, 32) = 37.91,

Variables	Recreational cocaine users $(n = 17)$	Cocaine-free controls $(n = 17)$
Simon task		
Correspondence		
Reaction times (ms)	366 (11.0)	372 (11.0)
Error rates (%)	3.6 (0.8)	3.0 (0.8)
Noncorrespondence		
Reaction times (ms)	397 (11.3)	395 (11.3)
Error rates (%)	7.7 (1.2)	6.5 (1.2)
Simon effect		
Reaction times (ms)*	32 (2.7)	23 (2.7)
Error rates (%)	4.1 (0.9)	3.5 (0.9)

 Table 2
 Performance on the Simon task as a function of correspond

ence (correspondent vs. noncorrespondent) and group (recreational

Simon effect is calculated as the RTs and the error rates difference between the correspondent and noncorrespondent condition). Standard errors of RTs and error rates are presented in parentheses

Significant group difference; * p < 0.05

cocaine users vs. cocaine-free controls)

Bold values indicate p = 0.02

p < 0.001, MSE = 6.42, $\eta_p^2 = 0.54$ (PEs): Responses were faster and more accurate with stimulus-response correspondence (369 ms and 3.3 %) than with noncorrespondence (396 ms and 7.1 %). Besides that, a significant interaction between correspondence and group was observed in RTs but not in PEs, F(1, 32) = 5.69, p < 0.05, MSE = 61, $\eta_p^2 = 0.15$ (RTs) and F < 1 (PEs). Consistent with our expectations, recreational cocaine users showed a larger Simon effect in RT² than cocaine-free controls (32 vs. 23 ms; see Table 2 for the complete data pattern).

To assess whether the magnitude of cognitive impairment in recreational cocaine users was proportional to the amount of the consumption of cocaine, we computed partial correlations between cocaine-use parameters (the individual lifetime cocaine exposure, peak and monthly cocaine dose), and Simon effect (stimulus-response non-correspondence minus correspondence) in both RT and PE, when controlling for other drugs use. However, no significant correlation was found ($ps \ge 0.06$).

Discussion

In this study, we tested whether recreational use of cocaine affects the efficiency in resolving response conflict in a

Simon task (Simon and Small 1969). As expected, recreational cocaine polydrug users showed a larger Simon effect than cocaine-free controls, thus mirroring a deficit in selecting the correct response in the face of a competing stimulus-induced alternative response. The results of the present study extend previous evidence in suggesting that even the intake of small doses of cocaine for recreational purposes is sufficient to compromise several cognitive control functions, such as inhibitory control, mental flexibility, attentional functioning, and spatial working memory (Colzato et al. 2007, 2008, 2009a, b; Colzato and Hommel 2009; Soar et al. 2012; Vonmoos et al. 2013b). Furthermore, given that DA is thought to play a key role in both signaling and resolving response conflict (Botvinick 2007; Holrovd and Coles 2002), our data are consistent with the hypothesis that cocaine-related cognitive deficits may be dependent on dopaminergic functioning (Volkow et al. 1993, 1997, 1999; Martinez et al. 2009; Tomasi et al. 2010). However, this is not to deny the influence of other potential pre-existing factors. For instance, pre-existing lower D2 receptor densities (Nader et al. 2006), inhibitory deficits (Bechara 2005), or related personality traits like impulsivity (Verdejo-Garcia et al. 2008) have been considered as factors that might either (co-) determine cognitive deficits shown by cocaine users or increase the likelihood to use drugs and/or to become addicted, or both. Thus, we cannot determine for sure whether the impaired response conflict shown by our recreational cocaine sample was preexistent, drug induced, or both.

Recently, Soar et al. (2012) reported that recreational cocaine polydrug users not only showed several neuropsychological impairments on tasks tapping executive functioning but also exhibited higher levels of schizotypy than cocaine-free controls. As the authors did not find any significant correlation between schizotypy scores and the amount of cocaine consumption, they speculated that schizotypy might not be a consequence of cocaine consumption but rather a constitutional trait that might predict the likelihood to start using cocaine or other drugs. That being said, the study design of Soar et al. does not allow telling whether the neuropsychological impairments exhibited by the recreational cocaine users were a cause or a consequence of cocaine consumption. Similarly, even though in our study participants were screened for several psychiatric disorders (e.g., ADHD, schizophrenia, and obsessivecompulsive disorder), we cannot exclude the influence of pre-existing personality group differences. Indeed, previous studies have shown that specific personality traits, such as impulsivity, schizotypy, and depressive symptoms, are exacerbated in individuals prone to use drugs (Morgan 1998; Crews and Boettiger 2009; Barkus and Murray 2010; Herzig et al. 2013). Furthermore, these personality traits, especially impulsivity, seem to be associated with

 $[\]frac{1}{2}$ It is worth noting that although the Simon effect can occur in terms of RT, PE, or both, the effect in terms of RT is the most important (and reliable) one (see Lu and Proctor 1995; Hommel 2011, for a review).

deficits in inhibiting inappropriate responses also in healthy populations without any history of drug use/dependence (Aichert et al. 2012).

Our study has further limitations. First, given that we did not perform any objective assessment of drug use (e.g., urine and/or hair toxicology analyses), it was impossible to verify participants' compliance with the instructions to abstain from taking any drugs during the 48 h preceding the experimental session as well as the undeclared use of other illicit drugs. However, previous studies have shown that self-reports of drug use are quite reliable and strongly correlated with the objective measures of drug use (e.g., Glintborg et al. 2008; Basurto et al. 2009).

Second, we tested a predominantly male sample, a common limitation for studies assessing cocaine-related cognitive deficits since cocaine use is particularly high among young males (see European Monitoring Center for Drugs and Drug Addiction 2012). Accordingly, it is difficult to say whether and to which degree our findings might generalize to female users. Note, however, that this imbalance with respect to gender cannot account for our findings, because the two groups were matched for gender. Given that the ability to resolve response conflict in Simon tasks seems to decline with increasing age (Van der Lubbe and Verleger 2002), it was also important that our participants were matched for age.

Third, and more importantly, we failed to match the two groups in terms of cannabis and MDMA consumption. This should not be surprising given that, especially in recreational settings, the use of cocaine is strongly associated with the consumption of cannabis, MDMA, and alcohol (Kelly and Parsons 2008; Grov et al. 2009; see also European Monitoring Center for Drugs and Drug Addiction 2012). Polydrug use is a common problem in this kind of studies. Indeed, it is frequent for recreational users to combine two or more drugs to enhance, to prolong, and/or to counteract a drug's effect (e.g., Leri et al. 2003). Thus, it is very difficult, though not impossible (see Vonmoos et al. 2013a, b), to find relatively pure cocaine users and to assess solely the specific impact of cocaine on cognitive functioning. Consequently, it is difficult to establish whether the deficit shown by our recreational cocaine sample is due to the consumption of cocaine, of other drugs, or to the combination of two or more drugs.

Among the substances that are commonly used in combination with cocaine, the intake of alcohol seems to play an important role. In particular, the coadministration of cocaine and alcohol produces the so-called cocaethylene, a psychoactive ethyl homolog of cocaine that seems to compromise dopaminergic functioning (Farré et al. 1993). Hence, although we matched the two groups for alcohol consumption, we cannot exclude the possible impact of cocaethylene on the deficit shown by recreational cocaine users. Further studies should extend our preliminary finding by testing the ability to resolve response conflict in relatively pure recreational cocaine users and/or by directly comparing response conflict management in recreational users who differ for the preferred drug.

To conclude, our results are consistent with and extend previous findings in showing that small doses of cocaine, at least in polydrug users, can compromise conflict control a central cognitive control function. Given that decisionmaking under uncertainty (presumably the most common mode in everyday life) is necessarily involving response conflict, this is an alarming observation witnessing that the increasing recreational use of cocaine is really a severe public health issue that deserves attention. One possible implication of our present findings is that decision-making difficulties might represent an important cue for identifying recreational users that are at risk to become addicted.

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