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Neuropsychological effects associated with recreational cocaine use

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Abstract

Rationale: Recent evidence suggests that recreational cocaine use is on the increase, with the UK reporting one of the highest levels of use in the EU (EMCDDA, 2010). Nevertheless, very few studies have addressed the neuropsychological effects associated with non-dependent recreational cocaine use.

Objectives: The current study aimed to assess whether recreational cocaine users show neuropsychological deficits on a battery of tests, previously shown to be sensitive to cocaine dependent and psychosis-prone individuals. Schizotypal traits were also measured.

Methods: Recreational cocaine users (n=17) were compared with controls (n=24) on drug use patterns, the General Health Questionnaire (GHQ-12), the Brief Schizotypal Personality Questionnaire (SPQ-B) and four neuropsychological tasks: spatial working memory, Intra/extra dimensional set-shifting, the Stocking of Cambridge, and the Rapid Visual Processing.

Results: Relative to controls, recreational cocaine users produced significantly more errors on the intra/extra dimensional set shift task and completed fewer stages; made significantly more 6 box stage errors on the spatial working memory task; and made significantly more errors and fewer hits, with overall poorer detection rates on the rapid visual processing task. Recreational cocaine users reported significantly higher scores on the cognitive-perceptual and disorganised thinking SPQ-B subscales and total SPQ-B scores compared to controls.

Conclusions: Recreational cocaine users displayed impairments on tasks tapping sustained attention, attentional shifting and spatial memory and reported higher schizotypal trait expression. These findings are consistent with the emerging literature suggesting subtle cognitive deficits, putatively reflecting underlying dopaminergic dysfunction, in non-dependent, recreational cocaine users.

Keywords: recreational cocaine, neuropsychological, schizotypy, deficits, attention, working memory

Introduction

Recreational cocaine use is on the increase and the UK has the highest levels of reported use in the EU (EMCDDA, 2010). Last year the prevalence of cocaine use among young adults (aged 15-34 years) in the UK was 6.2%, well above the EU average of 2.3% (EMCDDA, 2010). Lifetime prevalence amongst 16-59 year olds is estimated at 9.4%, even higher in young adults (15-34 years) at 14.9%; higher than other known recreational substances such as ecstasy (8.6% in 16-59 years and 13.8% in 15-34 years; EMCDDA, 2010).

Cocaine is a dopaminergic stimulant, but long term chronic use has been associated with a number of neuropharmacological abnormalities. These include a depletion, and reduced functioning of D2 receptors in the orbitofrontal cortex, cingulate gyri and striatum (Volkow et al, 1993, 1997, 1999; Martinez et al, 2007, 2009), dysfunctions in frontal brain regions including orbitofrontal, lateral prefrontal and anterior cingulate cortex (Bolla et al, 2001, 2003, 2004), as well as anterior cingulate and cerebellum (Hester and Garava, 2004). A reduced uptake of l-dopa (the precursor to dopamine) has also been reported in abstinent cocaine users (Volkow et al, 1996). Some recent evidence suggests that cocaine may even be a dopaminergic neurotoxin within the mid brain (Little et al 2009).

The above implicated areas are commonly associated with the control of goal-directed behaviour; the anterior cingulate gyrus is heavily implicated in attentional function (Yamaski et al 2005) and response inhibition (Hester and Garavan, 2004), and the orbitofrontal cortex is associated with decision making (Bolla et al, 2003). That cocaine dependence and abuse has been frequently associated with neuropsychological and cognitive deficits (e.g. Bolla et al, 1999; Hester and Garavan, 2004; Verdejo-Garcia and Perez-Garcia, 2007) is therefore not surprising. According to one meta-analysis assessing cognitive deficits in abstinent cocaine abusers, the largest effect sizes were found in attentional measures, with moderate effect sizes shown in visual and working memory and some aspects of executive functioning (Jovanovski et al, 2005).

Nevertheless, whether recreational levels of drug use can also cause long-term reductions in dopaminergic functioning and subsequent neuropsychological effects has been relatively unexplored. Evidence to suggest that recreational, rather than chronic use of cocaine may be associated with altered dopaminergic functioning (particularly in the striatum) stems from a study assessing spontaneous eye-blink - a known clinical marker for dopaminergic functioning. Colzato et al (2008) demonstrated that recreational cocaine users (monthly intranasal consumption of 1-4 grams for a minimum of 2 years) displayed a significantly reduced eye-blink rate relative to non-cocaine users. The amount of cocaine consumed, moreover, was negatively correlated with the degree of dopaminergic alteration (as indexed via reduced eye-blink rate). Given these putative alterations in dopaminergic functioning associated with a recreational level of use, one might expect to see parallel alterations in cognitive performance.

To date only a handful of studies have addressed the neuropsychological or cognitive effects associated with recreational or non-dependent cocaine use. Rahman and Clarke (2005) demonstrated neurocognitive impairments in areas of attention and verbal recognition (but also improvements in category fluency) in a sample of recreational cocaine users relative to non-drug using controls, with the duration and intensity of use correlating with some aspects of functioning. Their cocaine users, however, predominantly used crack cocaine, a derivative of powdered cocaine which is not

representative of the majority of 'recreational' users (who tend to snort powdered cocaine). Indeed, crack cocaine is commonly associated with a different pattern of usage (Chen and Anthony, 2004), abuse potential (Gossop et al, 1994) and behavioural differences (Gossop et al, 2006) and as such, may be associated with a different profile of cognitive impairment.

In another study primarily aimed at assessing the cognitive effects of ecstasy (MDMA) use, Groth-Marnat et al (2007) reported that a greater lifetime use of cocaine, rather than ecstasy, was associated with the severity of decrement in general memory and delayed verbal memory. More recently, Colzato and colleagues (2007, 2008, 2009a, 2009b) have reported a number of studies solely addressing recreational cocaine use. Recreational cocaine users were defined as those who did not meet the DSM-IV criteria for abuse or dependence and had a monthly consumption of 1-4grams (often consumed in only a few sessions, so that peak use often equated to monthly use; Colzato et al, 2008). They demonstrated a range of cognitive impairments amongst the recreational cocaine users (relative to non-cocaine polydrug users) in areas of cognitive flexibility, response inhibition, inhibition of return (IOR) and visual attention, but not in working memory (Colzato et al, 2009a). Deficits did not appear to be related to other drug use (e.g. ecstasy/MDMA, cannabis, alcohol and nicotine) and in some cases (inhibitory control for example) deficits were related to lifetime cocaine exposure (Colzato et al, 2007). Impairments were similar, but smaller in magnitude, to those observed in chronic users which are commonly attributed to dopaminergic malfunction (Bolla et al, 2001; Tomasi et al, 2010) suggesting that even recreational use of cocaine might begin to compromise dopaminergic pathways.

Although there are many compelling arguments for cocaine-induced impairments in cognitive functioning via direct alteration of the dopamine system (e.g. Volkow et al, 1993; Volkow et al, 1997; Volkow et al, 1999; Martinez et al, 2007, 2009; Tomasi et al, 2010), as highlighted by Colzato et al (2009a) it is also possible that a number of pre-existing factors might account for the observed cognitive deficits either directly or via increasing the likelihood that certain individuals will use the drug. Such vulnerability factors might include cognitive disturbance (Bechara, 2005), dopaminergic receptor dysfunction (Nader et al, 2006) or preexisting personality traits, such as impulsivity (Verdejo-Garcia et al, 2008) or schizotypy.

Schizotypy has received little attention in the recreational drug use literature. It can be measured in both clinical and normal populations using psychometric measures such as the Schizotypal Personality Questionnaire (SPQ; Raine, 1991a) and the trait is generally considered to provide an index of psychosis-proneness (e.g. Chen et al, 1997; Tsakanikos and Reed, 2004; Berigda and Lenzenweger, 2006). Schizotypy scores are generally higher in adolescents and young adults (Raine, 1991; ages at which drug use is usually initiated) and among recreational drug users including current cannabis users (Skosnik et al, 2001; Schiffman et al, 2005; Fridberg et al 2011) and recreational ketamine users (Morgan et al, 2004). Whilst little attention has been given to assessing whether cocaine users also report higher schizotypy levels, cocaine use has been associated with aspects of schizotypy - psychosis and paranoia (e.g. Cubells et al, 2005; Floyd et al, 2006; Kalaysariri et al, 2006). Levels of schizotypy traits in general population samples have also been associated with cognitive performance including sustained attention (Berigda and Lenzenweger, 2006) and working memory (Schmidt-Hansen and Honey, 2009). Given the above, it is likely that schizotypy may be a confounding personality trait when assessing potential cognitive effects associated with recreational cocaine use. Thus, the current study aimed to assess whether recreational cocaine users show neuropsychological deficits on a battery of tests previously shown either to be sensitive to dopaminergic functioning and/or, to be impaired in dependent

cocaine users whilst controlling for schizotypy and other drug use. Given the high rate of polydrug use among recreational users (e.g. Kelly and Parsons, 2008; Grov et al, 2009), isolating the effects of cocaine on cognitive functioning is a difficult task. Here we will minimize polydrug effects in the cocaine group by not excluding participants who reported other drug use (with the exception of cocaine).

Methodology

Participants

Cocaine users

Seventeen recreational cocaine users were recruited (5 male, 12 female). Recreational cocaine use was defined as using intranasal cocaine within the last year, but on no more than 10 occasions within the last month. Polydrug use was also reported within this group (see table 2). The mean age of the group was 28.6 ± 5.3 years. 59% (n=10) classified themselves as white, 35% (n=6) as black, and 6% (n=1) mixed ethnicity. 18% (n=3) of participants were educated to GCSE level only, 29% (n=5) to A-level, 12% (n=2) to NVQ level, 29% (n=5) to degree level and 12% (n=2) to postgraduate level

Controls

Twenty-four participants (8 male, 16 female) who reported no cocaine use within the last year were recruited as a control group. 38% (n=9) reported use of other recreational drugs within the last month (see table 2). The mean age of the group was 25.6 ± 4.5 years. 50% (n=12) classified themselves as white, 13% (n=3) as black, 17% (n=4) as mixed and 21% (n=5) as asian. 4% (n=1) of participants were educated to GCSE level only, 38% (n=9) to A-level, 4% (n=1) to NVQ level, 33% (n=8) to degree level and 13% (n=3) to postgraduate level. A further 8% (n=2) indicated 'other'.

All participants were recruited either through advertisements placed around the University of East London (UEL) grounds or via the snowball technique (Solowji et al, 1992). Self-reported exclusion criteria for both groups were 1) current use of psychiatric medication, 2) epilepsy, 3) current treatment for any psychological problem or substance/alcohol dependency, 4) sustained head injury, 5) current pregnancy and 6) drug use within 24 hours prior to testing. All participants gave written informed consent and the study was approved by the UEL Ethics Committee.

Questionnaire assessment:

All participants provided demographic details, and information regarding personal and family psychiatric histories. They also completed the UEL drug use questionnaire (Parrott, Sisk and Turner, 2000) to assess drug use within the last month with additional questions pertaining to patterns of cocaine use, subjective effects associated with their cocaine use and a measure of dependence. Dependence was measured using the Severity of Dependence Scale (SDS; Gossop et al, 1995). This is a 5-item questionnaire; each item is rated on a 4-point scale; 'never', 'sometimes', 'often' and 'nearly always', with scores awarded from 0-3 respectively. Total scores therefore ranged from 0-15, with a higher score reflecting a higher level of dependence.

The Brief Schizotypal Personality Questionnaire (SPQ-B; Raine, 1991b) was used to assess levels of schizotypy traits. This 22 item questionnaire uses a yes/no response with scores awarded for every 'yes' response. As well as a total score, the scale comprises 3 subscales; cognitive perceptual, interpersonal and disorganized schizotypy. A higher score indicates higher schizotypal proneness.

The General Health Questionnaire (GHQ-12; Goldberg and Williams, 1988) was used for a general measure of psychological health. The scale consists of 12 items utilizing a four point Likert scale; 'less than usual', 'no more than usual', 'rather more than usual' and 'much more than usual', with scores awarded from 0-3 respectively. Total scores range from 0 to 36; with a higher score reflecting poorer psychological health.

Neuropsychological assessment:

All tasks were administered from the CANTAB (Cambridge Cognition, CeNeS Ltd. Cambridge UK) via a portable computer with a Datalux touch-sensitive screen. All participants were given verbal as well as written instructions (via the CANTAB) on how to complete each task. The tasks were administered in the following order:

Spatial working memory task (SWM)

The SWM task tests the ability to retain spatial information and to manipulate remembered items in working memory. Participants are required to find a number of blue tokens (dependent on the trial) in one of several boxes (a search) and move that token to a column on the right side of the screen, whilst not returning to a box which previously contained that token. Participants have to find all the blue tokens to fill the column. The number of boxes increases over the test period, until there are 8 boxes to search in. The colour and position of the boxes change over consecutive trials. On each trial, returning to an empty box which has already contained a blue token constitutes an error. Errors are broken down into the number of between errors (times the participant revisits a box in which a token has previously been found) and the number of within errors (number of times a participant revisits a box already found to be empty during the same search) for total trials and 4-, 6- and 8-box trials; as well as total errors; and a strategy score (the number of times a new search begins with the same box).

Intra-Extra Dimensional Set Shift (IED)

The IED is an executive functioning task, which tests rule acquisition and reversal. It features visual discrimination, attentional set formation and maintenance, shifting and flexibility of attention. Simple stimuli are made up of one of two artificial dimensions; colour-filled shapes and white lines. Compound stimuli comprise white lines overlying colour-filled shapes. Participants are initially presented with two simple coloured shapes and must learn which one is correct by touching it. Once criterion is reached the contingencies are reversed, i.e. the incorrect stimulus becomes the correct stimulus. A second dimension is then introduced, initially lying adjacent to, and then overlapping, the first dimension. The contingencies remain the same as at the end of the simple discrimination. Again once criterion has been reached with the overlapping compound stimulus, the contingencies are again reversed. When the participants have learnt this compound discrimination, new compound stimuli are presented and

participants are required to learn which of the new dimensions are correct (the intra-dimensional shift). Participants are then required to shift attention to the previously irrelevant dimension and learn which of the two exemplars in this dimension is now correct (the extra-dimensional shift). Criterion for each stage is 6 consecutive correct responses and, if at any stage the criterion isn't reached, the test is terminated after 50 trials. The following performance indices for this task were recorded: the number of errors made on stages successfully completed (completed stage errors), the number of trials on all successfully completed stages (completed stage trials), the number of errors made prior to the extra-dimensional shift (pre-ED errors), number of stages completed (out of a total 9), total errors adjusted (a measure of performance efficiency, adjusted to account for each stage not completed due to failure), and number of trials completed on all attempted stages adjusting for stage not attempted due to failure at an earlier stage (total trials adjusted).

The Stockings of Cambridge (SOC)

The SOC is a measure of spatial planning. Participants are shown two displays consisting of three coloured balls which appear to be stacked on top of one another. The participant must move the balls in the lower display, by touching the required ball and moving it to the desired location, to mimic the upper display. Participants' planning abilities are measured by a) the time, and b) the number of moves required to complete the pattern. As the test continues the number of moves required to match the upper display increases, such that planning problems consist of 2, 3, 4 and 5 moves. The difference in time taken to complete each problem is indicative of the additional time taken to plan the solution. If the participant takes more than double the required number of moves to complete the solution, the trial is terminated. The test is ended in the event of three consecutive terminations. Outcome measures for each of the 2-, 3-, 4- and 5- move problems are: a) the time taken to plan the solution (mean initial thinking time), b) the number of moves required to solve the problem, c) the speed of movement after the initial move has been made (subsequent thinking time) and d) the number of occasions the trial has been successfully completed in the minimum number of possible moves (problems solved in minimum moves).

Rapid visual processing (RVP)

The RVP is a measure of sustained attention. Participants are required to detect consecutive odd or even sequences of digits (e.g. 2-4-6, 5-7-9), presented one digit at a time in a white box in the centre of the screen. Digits are presented in pseudo-random order at a rate of 100 digits per minute, with 16 target sequences occurring every 2 minutes. The first 4 minutes of the test constitutes a 'warm up' and the final 3 minutes are scored. The number of correct responses is recorded (total hits), along with the number of total misses (occasions where there has been a failure to respond to a target sequence), the mean response latency and a measure of how good the participant is at detecting target sequences (RVP A'); using the probability of both a hit and false alarm – thus a measure of sensitivity to errors regardless of error tendency (ranging from 0-1; bad to good).

Data analysis

All data was processed and analysed using the Statistical Package for Social Science (SPSS) version 18 in Windows Vista. Chi-square analyses were conducted on all categorical demographic and drug use

data. The remaining demographic and drug use data were analysed using independent t-tests; where Levene's homogeneity of variance was significant 'equal variances not assumed' values are presented. ANOVAs were performed on all neuropsychological test data. Observed power and effect sizes are also reported. There were missing data for 2 cocaine users and 3 control participants on the intra-extra dimensional shift and rapid visual processing tasks, therefore group analyses were conducted on the smaller sample of 15 cocaine users and 21 controls for these tests only. Further ANCOVAs, with age and total schizotypy scores were used as separate covariates on test data where significant group differences were found. Whilst cannabis and benzodiazepine (BDZ) use differed significantly between groups, data violated the assumption for use as a covariate because a) use was very low for BDZ use, and b) data was subjective (Tabachnick and Fidell 2007). Correlation analyses were conducted on measures of cocaine use and schizotypy scores and task data. The threshold for statistical significance for all main effects and correlations was set at the more stringent level of $p < 0.01$ given the multiple comparisons.

Results

Participant and drug use data

Tables 1 and 2 present a summary of participant characteristics and drug use for the two groups. There were no significant differences in frequencies between groups for gender, ethnicity and education [$\chi^2(1) = 0.71, p = 0.79$], [$\chi^2(5) = 4.30, p = 0.51$] and [$\chi^2(3) = 6.99, p = 0.07$] respectively. There was no significant group difference in age, [$t(39) = 2.15, p = 0.037$].

There were no significant group differences between cocaine users and non-cocaine users on all other drug use except duration of cannabis use (in years) [$t(37) = -0.52, p \leq 0.001$]; cocaine users reported using cannabis for significantly more years.

There were no significant group differences on psychological health as measured by the GHQ, [$t(39) = 0.30, p = 0.77$]. There were significant group differences in schizotypy levels with cocaine users reporting significantly higher total scores [$t(39) = 3.28, p = 0.002$] and higher scores on the cognitive perceptual and disorganised subscales [$t(39) = 2.64, p = 0.012$], [$t(39) = 4.06, p < 0.001$] respectively. There were no significant correlations between measures of cocaine use and total schizotypy scores.

Table 3 summarises the pattern of cocaine use amongst the recreational cocaine group. The measure of dependence to cocaine indicated a low dependence level (mean = 2.59).

Neuropsychological data

Table 4 summarises the task data from all four CANTAB tasks.

Spatial Working Memory (SWM)

Relative to controls, recreational cocaine users made more total between errors, and more between errors at each box stage (4, 6 and 8) of the spatial working memory task (see table 3) indicating more visits to

boxes previously revealed to hold targets . This difference was statistically significant only at the 6 box stage [$F(1,39) = 9.08, p=0.005$] and remained significant after covarying for both age and total schizotypy ($p<0.05$).

No significant correlations were found between patterns of cocaine use and SWM performance on any of the indices.

Intra/extra dimensional shift set (IED)

Recreational cocaine users were significantly less efficient at completing the IED task, making more errors in the extra-dimensional stage of the task (EDS errors; $F(1,34)= 12.32, p=0.001$) and completed significantly fewer stages within the task [$F(1,34)=7.57, p=0.009$] relative to controls. All group differences remained statistically significant after covarying for both age and schizotypy ($p<0.05$).. Average cocaine use was also shown to significantly correlate with IED on pre-extra dimensional errors [$r=0.64, p=0.01$].

Stockings of Cambridge (SOC)

As can be seen from table 3, recreational cocaine users took longer to plan the solution (initial thinking time) and subsequently execute the task (subsequent thinking time) on problems consisting of 2 and 3 moves, however they were quicker for problems consisting of 4 and 5 moves relative to non-users . However, these differences were not statistically significant. Amount of cocaine use in the last month and year, correlated negatively with the mean initial thinking time on 3-move problems [$r=-0.64, p<0.01$ and [$r=-0.62, p<0.01$ respectively].

Rapid Visual Processing (RVP)

Relative to controls, recreational cocaine users made significantly fewer hits [$F(1,39)=12.73, p=0.001$]and more misses [$F(1,39)=19.34, p<0.001$] thus demonstrating a significantly poorer performance at detecting target sequences [$F(1,39)=21.67, p<0.001$]. With the exception of mean latency, these differences remained significant after covarying for both age and schizotypy ($p<0.01$). No significant correlations were found between RVP performance indices and measures of cocaine use.

Discussion

Relative to controls, the recreational cocaine users in this sample displayed impairments on a number of tasks tapping executive functioning: spatial working memory, sustained attention and attentional shifting but were unimpaired on spatial planning.

In relation to spatial working memory, cocaine users made more between errors on the 6-box trial. That is, they revisited boxes in which they had already located a target, significantly more times than non-cocaine users indicating an inability to monitor and maintain the memory of previously located targets. It is interesting to note that there were no significant differences on the same trial for within errors

(number of times a participant revisits a box already found to be empty during the same search). The literature on working memory and cocaine use is inconsistent. In recreational cocaine users Colzato et al (2009a) failed to show any significant differences in the maintenance of information in working memory (as measured by the digit span, mental counters task and the N-Back task; mainly non-spatial tasks in nature) relative to controls, despite showing impairments on tasks assessing cognitive flexibility (WCST and the Dots triangles task; mainly spatial tasks). Pace-Schott et al (2008) conversely, found impaired attention and delayed verbal recognition memory in abstinent cocaine abusers, whilst working memory was unaffected. In Jovanoski et al's (2005) meta-analysis assessing cognitive function in abstinence cocaine abusers, only moderate effect sizes were found on aspects of working memory. This is mirrored in the current study which demonstrated only small effect sizes (<2 ; Cohen, 1988) on those aspects which were significant. The fact that a significant effect was found on the 6-box trial but not the 4- and 8-box is difficult to explain but findings on these trials (and indeed on other task indices) were in the same direction; indicating recreational cocaine users were showing poorer performance on most measures on this task; perhaps given greater power such significant findings in recreational cocaine users may be evident.

Recreational cocaine users also showed impairments on the intra/extra dimensional shift task (IED), successfully completing fewer stages and making more total errors compared to controls. Errors were made specifically during the extra-dimensional shift stage. This pattern of findings suggests impairments in rule acquisition and reversal, as well as visual discrimination, attentional set formation and maintenance and flexibility of attention. There is also some evidence to suggest that these deficits relate to the amount of cocaine use, with greater average amounts correlating significantly with errors on this task. Again, these impairments are in accord with the findings reported by Colzato and colleagues (2007, 2008, 2009a, 2009b), who have consistently shown that recreational cocaine users display deficits in areas of cognitive flexibility, response inhibition, (IOR) and visual attention.

The lack of significant group differences on the Stockings of Cambridge (SOC) task, tapping spatial planning is inconsistent with studies in chronic and dependent cocaine users, where evidence has shown motor abilities and planning to be impaired (e.g. Hoff et al, 1996; Bolla et al, 1999). These findings suggest that this area of cognitive functioning may only be affected by chronic, dependent cocaine use. Nevertheless, given that this is the first study to specifically address spatial planning within recreational cocaine users, this remains speculative

Recreational cocaine users demonstrated deficits in sustained attention, indicated by significantly more incorrect hits and misses on the Rapid Visual Processing task (RVP) than controls, and a poorer score on the RVP A'. Thus, cocaine users were significantly poorer at detecting target sequences relative to controls. This particular sustained attention task is sensitive to dysfunction in the parietal and frontal lobe regions of the brain (e.g. Lawrence et al, 2003), areas also shown to be deficient in dopaminergic activity in chronic cocaine users (e.g. Volkow et al, 1993, 1997, 1999; Martinez et al, 2007, 2009). Attention itself is one cognitive domain which has consistently been shown to be impaired in chronic abstinent cocaine abusers; showing large effects sizes (Jovanovski et al, 2005). The existing evidence, although limited also suggests that attention is compromised in recreational cocaine users (Rahman and Clarke, 2005; Colzato and Hommel, 2009; Colzato et al, 2009b) and is not accounted for by other recreational drug use such as MDMA and cannabis (Colzato et al, 2009b). Interestingly, the effects of recreational cocaine use on sustained attention in the current study were not associated with amount and duration of use. This parallels Colzato and Hommel's finding (2009), in users with similar patterns of

cocaine use; the magnitude of the inhibition of return effect (which involves attentional focus) was not proportional to cocaine consumption.

As a group, recreational cocaine users reported higher schizotypal trait expression than controls; on the total score, and the 'cognitive perceptual' and 'disorganised schizotypy' sub-scales. Although previous research has shown a link between other recreational drug use and schizotypy (e.g. Fridberg et al, 2011; Morgan et al, 2004), this is the first time higher levels of schizotypy have been reported in recreational cocaine users. That there were no significant correlations between measures of cocaine use and schizotypy scores implies that this is a constitutional trait associated with cocaine consumption rather than an effect of cocaine use. Indeed this has also been shown within cannabis users; Schiffman et al, (2005) reported that schizotypy proceeded, but was not causally related to, cannabis use.

It is possible that the higher levels of schizotypy in our cocaine users, rather than cocaine use per se, could independently result in the neuropsychological deficits evidenced in this group. Prior evidence suggests that schizotypy in the normal population is associated with impaired motor control and cognitive function (e.g. Lezenweger and Maher, 2002) particularly sustained attention (Bergida and Lenzenweger, 2006), working memory (Schmidt-Hansen and Honey, 2009), spatial working memory (Park et al, 1995) and inhibitory functioning (e.g. Migo et al, 2006; Taskanikos and Reed, 2004). Nevertheless, given that schizotypy itself did not emerge as a significant covariate in the analyses conducted here, lends weight to the hypothesis that recreational cocaine use itself affects neuropsychological performance in the absence of schizotypal traits.

The recreational cocaine users in this sample were using, on average, once a month and just under 2 grams on each occasion, which equates to their self-reported amounts of money spent on cocaine per occasion (one gram of cocaine on average costs £40; DrugScope, 2009). This level of usage is similar to that reported in other studies assessing recreational cocaine users (Colzato and colleagues, 2007, 2008, 2009a, 2009b). One advantage of the current study over previous studies assessing recreational cocaine users is the utilisation of a brief screening measure for psychological dependence to cocaine. Scores on this measure indicated that participants were not dependent on cocaine. A common problem in recreational drug research is polydrug use (the use of more than one drug); isolating the effects of cocaine use (or any other single drug) on cognitive functioning therefore, is a challenge. In the current study, minimal other drug use was reported by both controls and cocaine users, with the exception of cannabis. Recreational cocaine users reported using cannabis for a longer duration, but their current monthly cannabis use was similar to controls. Thus it is unlikely that current cannabis use can account for the deficits seen in recreational cocaine users particularly given that cannabis is not known to be a long-term neurotoxin.

The current study lends support to the notion that recreational cocaine use results in subtle but significant neuropsychological deficits in areas of attentional functioning and spatial working memory. These impairments do not appear to be due to other drug use and may not necessarily be dose related given the lack of significant correlations between levels of cocaine use and neuropsychological performance. Given that recreational cocaine use has previously been associated with altered dopaminergic functioning using the eye-blink marker (Colzato et al, 2008), one might tentatively

conclude that recreational cocaine use is sufficient in hampering dopamine-mediated cognitive functions.

There are however, a number of other possible explanations for these deficits which need to be considered including amotivation in the cocaine users and ischemic strokes which have been shown to be associated with cocaine use (Westover, McBride & Haley, 2007); both issues could potentially account independently for the neuropsychological impairments shown in these recreational cocaine users. In addition, the participants of this study reported high weekly alcohol consumption (approximately 18 units per week). Whilst groups didn't differ on alcohol consumption, the co-administration of alcohol and cocaine has been shown to produce cocaethylene (Farre et al, 1993), a psychoactive metabolite with toxic effects similar to cocaine (McCance et al 1995). The neuropsychological impairments shown in the cocaine users could therefore be a result of cocaethylene or indeed a combination of both psychoactive substances.

The current study relied on self-report data of current and past drug use and there was no objective confirmation (i.e. drug screen) of drug abstinence prior to assessment. However, based on reported patterns of recent cocaine use (on average recent use was over 1 week prior to assessment), it is likely that participants were abstinent from the drug. Furthermore, self report and objective indices of drug use in previous studies have shown strong associations, indicating self-report drug use to be reliable (e.g. Glinborg et al, 2008; Basurto et al, 2009). Despite the reliability of self-report data there still remains the issue concerning the purity of cocaine that has been consumed in these users. Within the UK (and most of Europe) the purity of cocaine has been in decline, with purity levels down to 20.3% in 2009 (EMCDDA, 2011). Cocaine is often 'cut' with other substances such as lidocaine and caffeine (EMCDDA, 2010) which could have partially contributed to the neuropsychological effects observed in the cocaine users.

There are several other preexisting factors which might also account for the group differences observed here including dopaminergic vulnerability (Nadar et al, 2006), inhibitory control, impulsivity (Bechara, 2005; Verdejo-Garcia et al, 2008) and IQ. Future studies thus need to control for such pre-existing factors through statistical means or ideally through the use of a longitudinal studies. A limitation of the current study worth noting is that there was no measure of pre-morbid IQ, therefore there may be pre-existing group differences in IQ. However given that the two groups did not differ on level of educational achievement indicates that group differences in performance were not due to lower IQ in the cocaine group.

The relative low power in this study is also worth noting (see table 4). Whilst there was insufficient power to detect some differences between cocaine users and controls, others were low (<80%) which may account for the lack of ability to detect further subtle differences between the groups. Effect sizes here are also very small (<0.03), with the exception of some of the RVP indices. Thus whilst there are significant differences between controls and recreational cocaine users on various indices of cognitive functioning (with sufficient power to detect them), clinically these deficits may not be immediately apparent, and more importantly, may not manifest themselves to the extent that they impact on a recreational cocaine user's everyday life. It would be of interest to assess the impact of these cognitive deficits on recreational cocaine users' everyday functioning.

To conclude, relative to non-users, recreational cocaine users in this study displayed poorer performance on aspects of sustained attention, flexibility of attention, spatial working memory and rule acquisition and reversal (executive functioning) whilst spatial planning remained intact. These impairments, moreover, did not appear to be mediated by other drug use or levels of schizotypy. This study has also demonstrated, for the first time, elevated levels of schizotypy in a sample of recreational cocaine users. These findings are consistent with the emerging literature suggesting subtle cognitive deficits, putatively reflecting underlying dopaminergic dysfunction, in non-dependent, recreational cocaine users.

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Table 1: Mean (SD) for participant characteristics, GHQ-12 and SPQ-B measures in recreational cocaine users and controls

	Recreational Cocaine Users	Controls
N	17	24
Age	28.59 (5.27)	25.29 (4.50)
Gender (M/F)	5/12	8/16
GHQ	15.06 (8.00)	14.29 (8.24)
SPQ-B Total	9.29 (4.06)***	4.79 (4.50)
Cognitive Perceptual	3.35 (1.93)***	1.71 (1.99)
Interpersonal	2.88 (2.20)	2.88 (2.20)
Disorganised	3.06 (1.25)**	1.17 (1.61)

p<0.001; *p<0.01

Table 2: Drug use: number reporting use and mean (SD) times per month consumed (unless otherwise stated) in recreational cocaine users and controls.

	Recreational Cocaine Users		Controls	
	Mean (SD)	N	Mean (SD)	N
Tobacco (cigarettes per day)	7.71 (7.33)	13	3.58 (6.01)	8
Alcohol (units per week)	18.81 (15.31)	16	17.58 (32.08)	19
Cannabis use (occasions per month)	21.44 (29.87)	15	21.67 (81.09)	9
Cannabis: length of use (years)	9.93 (5.76)**	15 ^a	2.63 (4.76)	8
Cannabis: days since used	26.29 (87.62)	17	65.0 (297.36)	12
Ecstasy/MDMA	0.53 (1.07)	5	0.17 (0.64)	2
Amphetamine	0.06 (0.24)	1	0.04 (0.20)	1
Mushrooms	0.12 (0.49)	1	-	0
Amyl-nitrate	0.059 (0.24)	1	-	0
Ketamine	0.12 (0.33)	2	-	0
Benzodiazepines	0.76 (1.09)	7	0.08 (0.28)	2

**p<0.001;

^a 2 missing data

Table 3: Self-reported Patterns of Cocaine use for the Recreational Cocaine Users

	Mean (SD)	Range
Age of first use (years)	20.82 (3.54)	17-27
Duration since last used (weeks)	3.00 (2.68)	0-9
No. occasions used in last month	2.35 (2.23)	0-7
No. occasions used in last year	20.18 (19.08)	0-70
Lifetime consumption (no. of occasions)	264.57 (437.55)	3-1500
Average use (grams) on each occasion	1.90 (1.07)	0.25-4
Amount spent (£) on each occasion	58.82 (45.23)	0-150
Severity of Dependence Mean Score	2.59 (3.30)	0-13
Frequency of use:	%	
Weekly	17.6	
Monthly	52.9	
Every 3 months	11.8	
Yearly	17.6	

Table 4: Mean (SD) scores for each CANTAB task

	Recreational Cocaine Users	Controls	P	Effect size	Observed power
Spatial Working Memory					
Between errors	28.18 (18.71)	18.38 (18.62)	0.11	0.07	0.37
4 boxes	1.41 (2.00)	0.67 (1.31)	0.16	0.05	0.30
6 boxes	9.71 (6.40)	4.00 (5.67)	0.005	0.19	0.84
8 boxes	17.06 (12.40)	12.04 (12.96)	0.22	0.04	0.23
Strategy	33.76 (4.10)	30.50 (8.04)	0.13	0.06	0.32
Total errors	31.24 (20.76)	18.75 (19.14)	0.05	0.09	0.50
Within errors	0.82 (2.43)	0.83 (1.97)	0.99	>0.001	0.05
4 boxes	0.06 (0.24)	0.04 (0.20)	0.81	0.002	0.06
6 boxes	0.35 (1.22)	0.08 (0.28)	0.30	0.03	0.18
8 boxes	0.41 (1.06)	0.75 (1.98)	0.53	0.10	0.10
IED					
Completed stage errors	12.60 (9.59)	15.52 (16.74)	0.55	0.01	0.09
Complete stage trials	69.00 (21.03)	70.62 (26.60)	0.85	0.01	0.05
EDS errors	14.93 (9.61)	5.24 (6.99)	0.001	0.27	0.93
Pre ED errors	5.20 (3.03)	5.33 (2.69)	0.89	0.001	0.05
Stages Completed	8.20 (0.94)	8.86 (0.48)	0.01	0.18	0.76
Total errors ¹	32.67 (19.32)	17.86 (18.78)	0.03	0.14	0.61
Total trials ¹	109.00 (34.43)	101.86 (108.37)	0.81	0.002	0.06
SOC					
Mean initial thinking time					
2 moves	1598.89 (1916.64)	849.83 (650.29)	0.08	0.08	0.41
3 moves	2151.56 (1694.34)	1671.13 (1014.03)	0.26	0.03	0.20
4 moves	2595.60 (1996.68)	3143.44 (3853.12)	0.60	0.007	0.08
5 moves	2771.59 (2508.36)	3657.41 (3297.79)	0.36	0.02	0.15
Mean moves					
2 moves	2.24 (0.44)	2.06 (0.22)	0.11	0.07	0.07
3 moves	3.21 (0.36)	3.29 (0.66)	0.63	0.06	0.08
4 moves	5.59 (1.26)	5.58 (0.93)	0.99	<0.001	0.05
5 moves	6.96 (1.26)	6.53 (2.06)	0.46	0.01	0.11
Mean subsequent thinking time					
2 moves	165.97 (356.00)	149.85 (360.77)	0.89	0.001	0.05
3 moves	156.49 (503.43)	88.81 (229.47)	0.57	0.01	0.08
4 moves	445.55 (629.68)	504.57 (818.96)	0.81	0.002	0.06
5 moves	220.46 (180.68)	382.01 (621.30)	0.31	0.03	0.17
Problems solved in minimum moves	7.76 (1.64)	8.21 (2.17)	0.48	0.01	0.11
RVP					
RVP A'	0.89 (0.04)	0.95 (0.04)	<0.001	0.36	0.995
RVP Mean latency	474.55 (90.56)	396.80 (114.35)	0.03	0.12	0.62
Total hits	15.41 (4.40)	20.71 (4.87)	0.001	0.25	0.94
Total misses	11.59 (4.40)	5.74 (4.05)	<0.001	0.33	0.99

¹adjusted indices – adjusted to account for failed stage attempts