Differential effects of MDMA, cocaine, and cannabis use severity on distinctive components of the executive functions in polysubstance users: A multiple regression analysis

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Abstract

Executive functioning impairments have been demonstrated following consumption of drugs of abuse. These executive impairments could play an important role on the development of the addictive process and rehabilitation of substance abusers. Recent neuropsychological models of executive functioning assume a multicomponent organization of these processes, suggesting different functions could contribute differentially to performance on executive tasks. The aim of this study was to analyze the relationship between severity of consumption of different drugs and neuropsychological performance on tasks sensitive to impairment in the executive subprocesses of working memory, response inhibition, cognitive flexibility, and abstract reasoning. Instruments sensitive to impairment in these four components were administered to 38 polysubstance abusers along with a severity of drug consumption interview. Multiple regression analyses were used. Results showed a differential impact of severity of MDMA abuse on working memory and abstract reasoning indices, of cocaine severity on an inhibitory control index and of cannabis on a cognitive flexibility index. Metabolic reorganization of monoamine frontal–subcortical pathways after drug exposure are proposed as possible explanations for these impairments.

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Keywords: Executive functions; Substance abuse; Severity; MDMA; Cocaine; Cannabis
1. Introduction

Drug use and addiction continue to be phenomena requiring a complex approach on the part of psychological practice and research. From a neuropsychological point of view, the use of drugs has historically been regarded from a double perspective. On the one hand, several studies have suggested the existence of neuropsychological alterations prior to drug use that could act as causal or vulnerability factors (Verheul, 2001). On the other hand, there has been an abundance of neuropsychological research on impairments that can result from drug misuse. In this sense, seminal studies in this area have shown the damaging effects of drugs, like alcohol, cannabis, cocaine, amphetamines, methamphetamines, and opioids on diverse cognitive functions, like attention, memory, or learning (for review, see Rogers & Robbins, 2001).

Nevertheless, in the past few years, several lines of research in neuropsychology have become increasingly interested in the study of executive functions, among the several neuropsychological functions whose impairment stems from the prolonged use of drugs. The executive functions are a group of superior abilities of organization and integration that have been neuroanatomically associated with different neural interaction pathways involving the prefrontal cortex (Roberts, Robbins, & Weiskrantz, 1998). These include anticipating and establishing goals, designing plans and programs, self-regulation and monitoring of tasks, and effective execution and feedback (Lezak, 1995).

The results yielded by these neuropsychological studies have shown the existence of significant impairments in the executive functioning of users of a number of substances. Roselli and Ardila (1996) reported significant correlations between the chronicity of use of cocaine and other drugs and moderate executive performance deteriorations, evaluated by the Wisconsin Card Sorting Test (WCST). In a similar fashion, Bolla, Funderburk, and Cadet (2000), using regression analyses, correlated cocaine cumulative dose effects with response inhibition impairment in a Go/No-Go Task. More recently, Fillmore and Rush (2002), and Fillmore, Rush, and Hays (2002) have demonstrated the existence of impairments in the control of response suppression inhibitory processes, both in controlled dosing studies and in studies with chronic cocaine users.

With regard to opioid and amphetamine users, Ornstein et al. (2000) showed the existence of alterations in the executive processes of attentional set shifting and sequence generation. Similarly, Lyvers and Yakimoff (2003) detected significant impairments on WCST performance related to severity of methadone use. Mintzer and Stitzer (2002), and Pau, Lee, and Chan (2002) have also found a significant correlation between opioid abuse and executive functioning impairment.

Finally, various studies have attempted to correlate cumulative dose effects of MDMA consumption with cognitive impairments, often by using regression techniques that have shown the existence of significant alterations in episodic and working memory (Bolla, McCann, & Ricaurte, 1998; Gouzoulis-Mayfrank et al., 2000; Wareing, Fisk, & Murphy, 2000), verbal fluency (Bhattachary & Powell, 2001), and planning and execution of strategies (Fox, Parrot, & Turner, 2001). The majority of these studies indicate that the degree of
executive impairment increases with the severity of use, and that the impairments are relatively lasting over time.

It is worth pointing out the effort made in many of these studies to relate quantity and chronicity measures of drug use with the magnitude of the neuropsychological impairments. Due to the absence of a more profound knowledge about the cause–effect relationships in the area of the neuropsychology of drug dependence, and the considerable methodological difficulties associated to longitudinal studies, these chronicity and severity-related measures can provide important support for the hypothesis that drugs generate neuropsychological alterations, and not the other way around.

In accord to this research line, the present work is aimed, in the first place, at determining the presence of clinically significant alterations in the executive functioning of polysubstance users in rehabilitation and, secondly, at determining whether the magnitude of the alterations depends on the severity of use of several drugs. The main hypotheses that stem from these objectives are, first, that the neuropsychological evaluation of these participants will show significant executive functioning impairments, and, second, that the greater the dose and frequency of drug use, and the more time elapsed since the onset of drug use, the greater the magnitude of these impairments will be.

2. Methods

2.1. Participants

The sample was composed of 38 detoxified polysubstance abusers (32 of which were male). All of them had passed a withdrawal period from the diverse drugs, and were recruited as soon as they joined a rehabilitation program. None of them was participating in any ambulatory substitution treatment with methadone or other pharmacological treatments (e.g., naltrexone) during the course of the neuropsychological evaluation. Potential participants that had previously been diagnosed of any other disorder, or showed signs of any disorder from DSM-IV axes I and II in the course of a clinical interview were not included in the target sample. Those potential participants who had been previously diagnosed of neurological disorders or HIV infection were also excluded. The participants belonged to the Proyecto Hombre Recovery Center in Granada (Spain) and collaborated voluntarily in this study. All of them met the following criteria: (1) to be a polysubstance user, (2) to overcome a minimum abstinence period of 2 weeks, and (3) to be literate enough to write and read, and correctly complete the tests. All the participants signed a written consent form that corroborated their voluntary participation, and urine analyses for cannabis, benzodiazepines, cocaine, and heroin metabolites were carried out to assure the abstinence period. Their age varied from 23 to 44 years, with an average of 30.55, and they had attended school in a range from 6 to 15 years, with an average of 10.05 (see Table 1). Quantity and chronicity parameters, and abstinence period duration, for each participant, are displayed in Table 1.
2.2. Materials and evaluation procedure

The Interview for Research on Addictive Behavior (Lopez-Torrecillas, Godoy, Pérez-Garcia, Godoy, & Sanchez-Barrera, 2001) was used to evaluate the severity of drug use. This instrument evaluates, by means of a brief interview, the quantity (dosing), frequency (consumption episodes by month), and chronicity (years of duration) of the use of a series of substances that can produce physical or psychological dependence, including cannabis, cocaine, MDMA, heroin, and alcohol, which were the drugs of abuse considered in the present study. For every substance, the participant had actually consumed, the following information was requested: (1) the average amount of each target drug ingested in each episode of use (number of fags for cannabis; number of pills for MDMA; number of grams for cocaine and heroin; and number of units for alcohol, considering that a glass of scotch equals 1 unit, while a glass of wine or beer equals 0.5 units); (2) the frequency of these consumption episodes per month: daily, between one and three times upon a week, once a week, between one and three times upon a month, or once a month; and (3) the number of

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Sociodemographic characteristics, average dose, frequency, duration of drug use, and abstinence in the sample</th>
</tr>
</thead>
<tbody>
<tr>
<td>Variable</td>
<td>Frequency</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>32</td>
</tr>
<tr>
<td>Female</td>
<td>6</td>
</tr>
<tr>
<td></td>
<td>Average</td>
</tr>
<tr>
<td>Age</td>
<td>30.55</td>
</tr>
<tr>
<td>Years of schooling</td>
<td>10.05</td>
</tr>
<tr>
<td>Substance Average Dose (per episode) × Frequency (per month)</td>
<td>Average</td>
</tr>
<tr>
<td>Cannabis (fags)</td>
<td>232.18</td>
</tr>
<tr>
<td>Cocaine (g)</td>
<td>25.72</td>
</tr>
<tr>
<td>Heroin (g)</td>
<td>33.82</td>
</tr>
<tr>
<td>MDMA (pills)</td>
<td>6.47</td>
</tr>
<tr>
<td>Alcohol (units)</td>
<td>308.12</td>
</tr>
<tr>
<td>Substance Duration of drug use (years)</td>
<td>Average</td>
</tr>
<tr>
<td>Cannabis (fags)</td>
<td>8.10</td>
</tr>
<tr>
<td>Cocaine (g)</td>
<td>6.86</td>
</tr>
<tr>
<td>Heroin (g)</td>
<td>5.88</td>
</tr>
<tr>
<td>MDMA (pills)</td>
<td>0.80</td>
</tr>
<tr>
<td>Alcohol (units)</td>
<td>11.68</td>
</tr>
<tr>
<td>Abstinence (months)</td>
<td></td>
</tr>
</tbody>
</table>

2.2. Materials and evaluation procedure

The Interview for Research on Addictive Behavior (Lopez-Torrecillas, Godoy, Pérez-Garcia, Godoy, & Sanchez-Barrera, 2001) was used to evaluate the severity of drug use. This instrument evaluates, by means of a brief interview, the quantity (dosing), frequency (consumption episodes by month), and chronicity (years of duration) of the use of a series of substances that can produce physical or psychological dependence, including cannabis, cocaine, MDMA, heroin, and alcohol, which were the drugs of abuse considered in the present study. For every substance, the participant had actually consumed, the following information was requested: (1) the average amount of each target drug ingested in each episode of use (number of fags for cannabis; number of pills for MDMA; number of grams for cocaine and heroin; and number of units for alcohol, considering that a glass of scotch equals 1 unit, while a glass of wine or beer equals 0.5 units); (2) the frequency of these consumption episodes per month: daily, between one and three times upon a week, once a week, between one and three times upon a month, or once a month; and (3) the number of
years that elapsed since the onset of the use. A composite severity score was obtained for each substance, according to Eq. (1):

\[
\text{Composite Severity Score} = (1) \text{ average dosing (per episode)} \times (2) \text{ frequency (per month)} \times (3) \text{ chronicity (years)}. \tag{1}
\]

To evaluate executive functioning, a selective protocol was designed, composed of tests sensitive to impairments in different components of the executive functions according to most recent theoretical models (Barkley, 2001; Miyake, Friedman, Emerson, Witzky, & Howerther, 2000). We focused on the following four executive components: (a) monitoring and updating of incoming information in the working memory (working memory), (b) deliberate controlled suppression of prepotent responses (response inhibition/selective attention), (c) shifting back and forth between multiple operations or mental sets (cognitive flexibility), and (d) processing information and forming judgements about the relation between abstract concepts (analogical reasoning). Tasks were presented alternating between difficult and easy ones, and verbal and nonverbal ones, as listed below:

- Letter number sequencing, from the Wechsler Adult Intelligence Scale (WAIS III; Wechsler, 1997; TEA, 1999).
- Stroop: test of colors and words (Golden, 1978; TEA, 1999).
- Arithmetic (WAIS III; Wechsler, 1997; TEA, 1999).
- Similarities (WAIS III; Wechsler, 1997; TEA, 1999).
- Changes, test of cognitive flexibility (“Cambios: Test de Flexibilidad Cognitiva”; Seisdedos, 1994): The 27 items in the test contain simple geometric figures, with regard to which three types of simple transformations can be requested. Each requested transformation consists of an increase or decrease in one or several figure’s features (number of sides, size, and the intensity of the internal design). Each item contains three geometric figures. In the blank space between two figures, a small circle with arrows or triangles in it indicates the type of transformation requested. The user is asked to decide whether the change indicated by the circle between two figures makes them fit to each other.
- Digits forward and backward (WAIS III; Wechsler, 1997; TEA, 1999).

Data from the three subtests of the WAIS III: letter number sequencing, arithmetic, and digits were transformed to obtain a single index of working memory performance. The Stroop test was used as an index of response inhibition, Changes was used as an index of cognitive flexibility and similarities as an analogical reasoning index.

The participants were evaluated individually between November 2001 and March 2002, in a single session each, that lasted approximately 40 min. The evaluations were carried out in the Proyecto Hombre installations in Granada (Spain). The evaluation consisted of the
selective protocol of neuropsychological evaluation of the executive functions previously described (including the six tests listed above) and the Interview for Research on Addictive Behavior (López-Torrecillas et al., 2001). There was no need to take a break during the evaluation in any case.

2.3. Variables and statistical analysis

Once the participants had been evaluated, their scores were recorded and their performance levels on the neuropsychological tests were classified according to Heaton, Grant, and Mathews (1991). This classification is based on $t$ scores. Thus, direct measures from neuropsychological test were previously transformed into this type of standardized scale.

The composite scores from the Interview for Research on Addictive Behavior were transformed into standardized $Z$ scores. Five severity $Z$ scores were obtained in this way for cannabis, cocaine, heroine, MDMA, and alcohol.

To check the main hypothesis, a multiple regression analysis was carried out, with the aim of determining the capacity of the several severity measures to predict executive functioning impairments. Our main goal was to establish whether the severity of use of the five substances correctly predicts the level of performance on the neuropsychological tests selected to measure executive functioning. Consequently, four measures, transformed into $t$ scores, were used as dependent variables directly related to executive functioning: the WAIS III working memory index (obtained from letter number sequencing, arithmetic, and digits scores), the Stroop interference Index, the Changes cognitive flexibility index, and the WAIS III similarities analogical reasoning index. The five standardized scores of severity (for cannabis, cocaine, heroine, MDMA, and alcohol) were introduced in the analysis as predictor variables.

3. Results

3.1. Proportion of participants with deterioration in the executive functions

The participants were classified into three categories, depending on their degree of executive functioning impairment (slight, moderate, or no impairment). Cutoff points were established according to the standardized criteria proposed by Heaton et al. (1991): $t$ scores above 39 were considered as no impairment, $t$ scores between 30 and 39 were considered as slight impairment, and $t$ scores below 30 were considered as moderate impairment. The frequency and proportion of participants in each of the three levels of impairment—defined independently by means of the four executive functioning measures described above—are displayed in Table 2. The evaluated sample showed some degree of impairment (slight and moderate) in the four measures. Moreover, all the tests, except the Stroop-interference, yielded a greater percentage of impaired participants than intact ones.

Participants who showed a moderate impairment ($t$ scores below 30) in two or more executive functioning measures were labelled as significantly impaired, whereas those
who did not meet this criterion were labelled as nonimpaired. Adopting this criterion, 44.7% of the participants presented clinically significant impairments in their executive functioning.

3.2. Relationship between severity of use and neuropsychological performance

First, we used bivariate correlation analyses to detect possible overlapping between the components tapped by the four different indices of executive functioning. Results showed only the working memory and similarities indices, both from the WAIS III were significantly correlated ($r = .432; N = 38; P < .05$; see Table 3).

Second, four multiple regression analyses were carried out, one for each of the four measures of executive functioning: The WAIS III working memory index, the Stroop-interference score, the Changes score and WAIS III similarities Index. The severity scores for cannabis, cocaine, heroin, MDMA, and alcohol consumption were used as predictor variables. Age and number of schooling years were also included as independent variables in those regression analyses in which nonstandardized dependent measures (Stroop and Changes) were used.

The results showed that the regression function ($R^2$) was statistically significant for the dependent variables working memory, $F(5,37) = 4.344, P < .01$, Changes, $F(5,37) = 4.037, P < .01$, and similarities, $F(5,37) = 3.304, P < .05$, and marginally significant for the dependent variable Stroop-interference, $F(5,37) = 2.237, P = .059$. Collinearity diagnoses showed the predictor variables were moderately independent among each other for all the different performance indices.

A detailed analysis of the $\beta$ coefficients of the significant or marginally significant regression functions showed that the severity of use of MDMA is the best predictor of

<table>
<thead>
<tr>
<th>Variable</th>
<th>Degree of impairment</th>
<th>Without impairment</th>
<th>Slight impairment</th>
<th>Moderate impairment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Working memory</td>
<td>12 (31.6%) 18 (47.4%) 8 (21.1%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Similarities</td>
<td>14 (36.8%) 18 (47.4%) 6 (15.8%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Changes</td>
<td>7 (18.4%) 13 (34.2%) 18 (47.4%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stroop-interference</td>
<td>22 (57.9%) 13 (34.2%) 3 (7.9%)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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Table 2
Frequency and percentage of impaired participants in the four indices of executive functioning

<table>
<thead>
<tr>
<th>Variable</th>
<th>Without impairment</th>
<th>Slight impairment</th>
<th>Moderate impairment</th>
</tr>
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<td>3 (7.9%)</td>
</tr>
</tbody>
</table>

Table 3
Correlations between the four different indices of executive functioning

<table>
<thead>
<tr>
<th></th>
<th>Working memory</th>
<th>Stroop-interference</th>
<th>Changes</th>
<th>Similarities</th>
</tr>
</thead>
<tbody>
<tr>
<td>Working memory</td>
<td>1</td>
<td>.025</td>
<td>.279</td>
<td>.432*</td>
</tr>
<tr>
<td>Stroop-interference</td>
<td>1</td>
<td></td>
<td>.029</td>
<td>.220</td>
</tr>
<tr>
<td>Changes</td>
<td>1</td>
<td></td>
<td></td>
<td>.291</td>
</tr>
<tr>
<td>Similarities</td>
<td>1</td>
<td></td>
<td></td>
<td>1</td>
</tr>
</tbody>
</table>

* $P < 0.05$. 
performance on the working memory index, $\beta = -0.634$, $t(1,37) = -4.429$, $P < .001$, and on
the similarities analogical reasoning index, $\beta = -0.498$, $t(1,37) = -3.311$, $P < .01$. As
expected, in both cases, severity and performance variables were inversely correlated. The
severity of use of cocaine is also inversely related to performance on the Stroop-interference
test, $\beta = -0.360$, $t(1,35) = -2.035$, $P = .05$. Finally, the severity of cannabis use is the best
predictor of performance on Changes, $\beta = -0.437$, $t(1,35) = -2.666$, $P < .05$, a cognitive
flexibility index (see Table 4).

As Table 4 shows, alcohol, MDMA, and heroin severity appear to be relatively important
predictor variables for Changes performance, along with the severity of cannabis which
appears as the main predictor. Similarly, heroin severity seems to be an important predictor
variable on similarities performance, along with the main predictor variable, which is MDMA
severity. For both dependent variables, the combination of all drug severity regression
functions were statistically significant.

4. Discussion

The main objective of this study was to determine the presence of impairments in the
executive functioning of a sample of detoxified drug-dependent participants, as well as the
possible influence of the severity of the use of diverse drugs on the magnitude of these
neuropsychological alterations.

The results of the neuropsychological tests reveal the existence of executive functioning
impairments in this sample. The tests detected the existence of slight or moderate impair-
ments in all the measures registered. The working memory, Changes, and similarities indices
identified a greater percentage of impaired participants than intact ones, whereas the
interference measure detected a lower percentage of impaired participants than intact ones.
The global impairment criterion described in the procedure section, which required the
presence of clinically significant impairments in a minimum of two functions, allowed to
classify a 44.7% of the sample as clinically impaired individuals.

What are the clinical implications than can be derived from our results? In our opinion, the
presence of these significant alterations in several executive subprocesses could considerably
affect both the course of the treatment and its results, as far as these participants may find

<table>
<thead>
<tr>
<th>Impairment indices</th>
<th>Model ($R^2$)</th>
<th>Predictor variables ($\beta$ coefficients)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Working memory</td>
<td>.404*</td>
<td>Alcohol (.083) Cannabis (.131) Cocaine (-.092) Heroine (-.136) MDMA -.634*</td>
</tr>
<tr>
<td>Stroop</td>
<td>.343</td>
<td>Alcohol (.314) Cannabis -.092 Cocaine -.360* Heroine -.158 MDMA -.318 MDMA -.338 Age -.108</td>
</tr>
<tr>
<td>Changes</td>
<td>.485*</td>
<td>Alcohol -.227 Cannabis -.437* Cocaine .129 Heroine -.147 MDMA -.176 MDMA -.211 Age -.290</td>
</tr>
<tr>
<td>Similarities</td>
<td>.340*</td>
<td>Alcohol (.219) Cannabis .127 Cocaine -.117 MDMA -.314 MDMA -.498*</td>
</tr>
</tbody>
</table>

* $P < 0.05.$
difficult to comprehend and assimilate the constituent contents of the program, to generate new behaviors directed toward desirable goals, to motivate themselves, to plan behaviors based on objectives that do not involve an immediate reward, and to inhibit inappropriate impulsive responses. The adaptation of rehabilitation programs to the time constraints of a possible recovery of these functions, the development of specific neuropsychological assessment and rehabilitation protocols for these functions, and the incorporation of such tools into the therapeutic process could improve the effectiveness of drug-dependence rehabilitation programs.

These alterations, however, are far from being uniform across the several substances considered. Our results are, therefore, congruent with a multicomponent approach, based on the independent evaluation of distinct subprocesses, through a series of neuropsychological tests for the assessment of executive functions. Although this assumption could induce some overlap among the domains tapped by the different tests (Bolla et al., 2000), the most recent studies in the field defend the validity of this fragmented approach, capable of discriminating between different subprocesses or components (Barkley, 2001; Miyake et al., 2000).

A second objective of this study was to establish whether the existence of these executive alterations was related to the severity of drug use. The regression analyses used to determine the effects of the severity of different substances on the performance on different subprocesses of the executive function showed that the severity of drug use was inversely related to performance on a number of neuropsychological tests of working memory, response inhibition, cognitive flexibility, and abstract reasoning.

These neuropsychological alterations may be related to the existence of persistent metabolic alterations produced by the intermittent stimulation of the action pathways of diverse neurotransmitters, concretely the projection systems of dopamine and serotonin (Kish, 2002; Obrocky et al., 2002; Volkow & Fowler, 2000). Most recent studies in neuropsychology and neuroimaging have placed the target areas of drug action in prefrontal and subcortical regions of the brain. These areas overlap the dopamine and serotonin projection pathways, and are supposed to be the regions responsible for regulating the distinct components of the executive functions. Along with these studies, our results suggest that the severity of use of drugs that affect dopamine and serotonin pathways can produce significant and relatively long-lasting neuropsychological impairments of diverse components of the executive functions.

In more detail, our study suggests a significant effect of MDMA on the working memory and analogical reasoning components, a relatively specific effect of cocaine on the response inhibition component, and a significant effect of cannabis on the cognitive flexibility component, which could be explained by the involvement of distinct metabolic pathways. From a clinical perspective, these neuropsychological impairments could be contributing to the high dropout rates presented by the specific treatments of stimulant users, by producing deficits that preclude the high content assimilation and behavior organization necessary in these treatment programs.

It is well known that MDMA does affect both dopamine and serotonin systems (Kish, 2002; Semple, Ebmeier, Glubus, O’Carroll, & Johnsione, 1999). These data are consistent with functional neuroimaging studies that indicate that the majority of metabolic reductions
produced as a result of the use of ecstasy are concentrated in dorsolateral and parietal prefrontal regions (Cohen, Bonvento, Lacombe, & Hamel, 1996). The dorsolateral region of the prefrontal cortex is an area traditionally associated with the working memory executive component, whereas the involvement of superior parietal regions on working memory processes has been highlighted by recent neuroimaging studies (Collette & Van der Linden, 2002). Furthermore, a number of neuropsychological studies, by using regression techniques similar to that used in the present work, have showed cumulative dosing damaging effects of ecstasy on the working memory component (Bolla et al., 1998; Fox et al., 2001; Gouzoulis-Mayfrank et al., 2000). Therefore, both the functional neuroimaging and neuropsychological studies support the results obtained in the neuropsychological tests used in the present study, and the hypothesis that the severity of use of MDMA can distinctively affect working memory.

The analogical reasoning component appears to be affected by the combination of several substance use severity measures, with MDMA appearing as main predictor, and severity of heroin appearing as an important contributing factor. Possibly, maintenance, coding, and updating components of working memory are also involved in making judgements of similarity between abstract concepts, as suggested by the significant correlation detected among these tests. Additionally, recent neuroimaging works have shown common neuronal substrates for both working memory and reasoning (Ruff, Knauff, Fangmeier, & Spreer, 2003). Therefore, we hypothesise that the impairment patterns produced by MDMA on working memory processes might be also involved in performance deterioration on the similarities test. Moreover, the most recent neuropsychological research has related the use of opioids with the existence of executive alterations in abstract reasoning (Lyvers & Yakimoff, 2003; Ornstein et al., 2000), a subprocess that is mainly involved in performance on this test. Our results therefore suggest a combined effect of these drugs on the common neuronal circuits involved in working memory and reasoning, principally the dorsolateral prefrontal cortex.

Our results also suggest a relatively specific effect of the severity of cocaine use on performance in the interference condition of the Stroop task, which is traditionally considered an instrument for the study of selective attention and inhibitory processes. The Stroop-interference condition is sensitive to damage of the anterior cingulate and the orbitofrontal cortex (Peterson et al., 1999). Functional neuroimaging studies in cocaine addict participants show the existence of abnormally low metabolic levels in the orbital–frontal cortex (Goldstein & Volkow, 2002). On the other hand, some controlled dosing neuropsychological studies have shown that the inhibitory control can become reduced by acute minimum doses of cocaine (Fillmore, Rush, & Hays, 2002), indicating that this component may be particularly sensitive to the effects of the drug on the nervous system. Moreover, dose-dependent studies in chronic cocaine users have shown a significant impairment of response inhibition (Bolla et al., 2000; Fillmore & Hays, 2002).

Our results also showed the existence of significant relationships between combinations of several drug use severity measures introduced into the regression model and the impairment in the cognitive flexibility component. The considerable influence of cannabis use severity on this test is worth noting. Although THC, like the active components of most
of the drugs studied, has also shown clear effects on frontal metabolic indices, it must be kept in mind that it is not a particularly toxic substance except in chronic and severe use patterns (Solowij, 1998). This is congruent with the presence of very heavy cannabis users in our sample. Along with cannabis, MDMA and alcohol appear to exert synergic effects on changes performance that is congruent with recent works that have suggested additive neuropsychological and brain functional induced impairments resulting from concurrent consumption of cannabis and MDMA (Croft, MacKay, Mills, & Gruzelier, 2001) and cannabis and alcohol (Nixon, 1999).

Together, these findings suggest the existence of differential neuropsychological impairments on four well-defined executive subprocesses as a function of severity of consumption of distinct drugs. In spite of these selective patterns of impairment related to specific drugs of abuse, additive or synergic effects cannot be discarded in any case.

Several possible limitations of our study should be considered and addressed by future research. In the first place, we decided to carried out independent regression analyses for different executive components, although it is quite likely that some of these subprocesses might be overlapped in the different tests. Preliminary correlational analyses among different executive indices supported this strategy, that have been assumed by recent theoretical models defending a fragmented organization of the executive functions (Miyake et al., 2000) and is clinically useful considering the specific information that each of these separate executive indices could provide us (Bolla et al., 2000). Secondly, we should highlight that the size of our sample might not be large enough to obtain conclusive outcomes by means of regression analyses. Further research using larger sample sizes would be necessary to confirm the relationship between severity of consumption of certain drugs and executive impairments. Finally, although the results obtained by the present study let us suggest that the use of drugs can generate impairments in the executive functions of the user participants, we cannot discard the possibility that certain neuropsychological alterations, possibly related to these functions, may predate the initiation of drug use. Future research of a prospective nature would be necessary to definitively clarify the direction of the causal relationships between the use of drugs and the neuropsychological alterations.

References


