Substance Use & Misuse, 44:1941–1957

ISSN: 1082-6084 (print); 1532-2491 (online)
DOI: 10.3109/10826080902848897

informa
healthcare

Research Note: Cocaine Users

Neuropsychological Assessment of Current and Past Crack Cocaine Users

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Background: Cognitive changes due to crack cocaine consumption remain unclear. Methods: For clarification, 55 subjects were assigned to three groups: control group, crack cocaine current users, and ex-users. Participants were submitted to Mini-Mental State Examination (MMSE) and tasks evaluating executive functioning and verbal memory. Mood state was also measured. Intergroup comparisons were carried out. Results: Control group performance on the MMSE was better than that of users and ex-users. Verbal memory performance for logical memory of users was impaired. Ex-users scored lower on DSST and Trail Making Test (Part B). Conclusion: Chronic crack cocaine use seems to disrupt general cognitive functioning (MMSE), verbal memory, and attentional resources, but findings suggest that some of these effects could be reversed by abstinence.

Keywords drugs; cocaine; crack cocaine; neuropsychology; cognition; memory; abstinence

The present study was carried out at the Brazilian Center for Information on Psychotropic Drugs (CEBRID) and at the Department of Psychobiology of the Federal University of São Paulo (UNIFESP).

L. G. Oliveira was supported by CAPES – Ph.D. Scholarship and also by the Psychopharmacology Incentive Fund Association (AFIP) and the Foundation for Support to Research in the State of São Paulo (FAPESP; Process no. 04/07153-8).

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Introduction

Several studies have suggested that cocaine, as a vasoconstrictive drug, alters cerebrovascular resistance and has effects on brain perfusion (Herning, King, Better, and Cadet, 1999; Nicastri, Buchpiguel, and Andrade, 2000; Silveira, Fernandes, Barbieri, Labigalini, and Silveira, 2001;; Strickland et al., 1993), metabolism (Volkow et al., 1992), and morphology (Fein, Di Sclafani, and Meyerhoff, 2002; Matochik, London, Eldreth, Cadet, and Bolla, 2003). These data have been assessed through neuroimaging techniques (RM, fMRI, PET, and SPECT) as well as other techniques aimed at understanding drug abuse[1] and its implications.

Through the application of neuropsychological tests, chronic cocaine use (cocaine hydrochloride) has been identified to affect the normal cognition functioning, associated with brain hemodynamic, metabolic, and structural alterations (Horner, 1999; Kosten, 1998). Among brain regions, prefrontal cortex has been the area most commonly affected by cocaine use (Chang, Ernst, Strickland, and Mehringer, 2000; Goldstein et al., 2007; Kelley, Yeager, Pepper, and Beversdorf, 2005; Matochik et al., 2003; Volkow et al., 1992), especially the anterior cingulate gyrus and the orbital frontal cortex (Jovanovski, Erb, and Zakzanis, 2005). Therefore, abilities directly associated to prefrontal cortex activity, such as solving problems, mental flexibility, moral judgment, and speed of information processing have shown impairment, detected in attention and executive functioning tests (Horner, 1999; Kelley et al., 2005; Piatt, Marlowe, and Mountain, 1996).

The interference of cocaine can be easily explained by its mechanism of action on the mesolimbic dopamine pathway, causing a hypoactivity of the prefrontal cortex, among other effects (Dackis and O'Brien, 2001). That would lead to the neurocognitive alterations previously mentioned, as well as a general state of anhedonism culminating in severe self-control deficits, especially concerning the drug pattern of use (Goldstein et al., 2007). The effect of cocaine use is diffuse, not focused on one specific brain area, affecting performance in verbal and visual memories (Jovanovski et al., 2005; Kelley et al., 2005) and causing a slight impairment in verbal fluency and perceptual-sensory functions (Jovanovski et al., 2005), abilities controlled by other cerebral cortical areas.

Among cocaine derivatives, crack cocaine, due to its pharmacokinetic characteristics (Hatsukami and Fischman, 1996), increases the risk of cocaine dependence few occasions after experimentation (Chen and Anthony, 2004). Because it is insoluble in water, crack cocaine is smoked, which allows for a fast pulmonary absorption, immediate and more intense, but short-lasting effects (Hatsukami and Fischman, 1996; Oliveira and Nappo, 2008). Due to the short duration of effects and the great sensation of reward, crack cocaine pattern of use tends to be heavier in terms of both frequency and quantity (Inciardi, Lockwood, and Pottieger, 1993; Nappo, Galduróz, and Noto, 1996; Oliveira and Nappo, 2008; Siegel, 1982), which can set it apart from cocaine hydrochloride regarding brain effects (both mid- and long-term) such as hemodynamic, functional, neurocognitive, and structural alterations.

Few studies about the biological implications arising from the chronic crack cocaine consumption exist. Structurally, it has been identified that this use diminishes the prefrontal cortical volume (Fein et al., 2002), affecting the performance in cognitive abilities in which it is involved, especially executive (Beatty, Katzung, Moreland, and Nixon, 1995; Cunha, Nicastri, Gomes, Moino, and Peluso, 2004; Di Sclafani, Tolou-Shams, Price, and Fein, 2002; Fein et al., 2002; Hoff et al., 1996; Strickland et al., 1993) and attentional functioning

[1]The journal's style utilizes the category *substance abuse* as a diagnostic category. Substances are used or misused; living organisms are and can be *abused.* Editor's note.

(Pace-Schott et al., 2005; Strickland et al., 1993). Hence it is again suggested that cocaine, now as crack cocaine, affects the prefrontal cortex, both structurally and functionally. However, as has already been reported for cocaine hydrochloride, the interference of crack cocaine does not seem to be focused, impairing cognitive performance in measures that reflect the functioning of other brain areas. Deficits in learning, visual and verbal memory, spatial information processing speed, perceptual-motor abilities, and integration, among others, have been reported (Beatty et al., 1995; Cunha et al., 2004; Di Sclafani et al., 2002; Hoff et al., 1996; Pace-Schott et al., 2005).

Even though the neurobiological implications of cocaine hydrochloride and crack cocaine may be similar, there are informal reports that crack cocaine is even more dangerous. Although still controversial, cognitive alterations stemming from chronic crack cocaine consumption have made it difficult for patients to benefit from strategies offered by treatment programs (Aharonovich, Nunes, and Hasin, 2003), with patients becoming quickly frustrated, causing[2] them to give up before completion of the program. Still according to this author, the patients who gave up on the treatment presented more severe cognitive deficits than those who did not, pointing to a necessity of having good understanding capacity and cognitive ability in order to benefit from the program. Taken as a whole, these data indicate the need to clarify the impairing effect of chronic crack cocaine consumption on cognition, so that recognizing users cognitively impaired may increase the chances of them benefiting from the therapeutic intervention.

Another matter that remains controversial and that deserves further studies is that once abstinence is reached, the impairing effects of cocaine (and its derivatives) on cognition would be reversed. In structural terms, when vascular resistance associated with chronic cocaine use is analyzed, it has been observed that neither the blood flow velocity nor the pulsatility of high-caliber arteries is reversed once abstinence is reached (Herning et al., 1999). In functional terms, there were no differences in brain perfusion between cocaine abstinent subjects and current users (Silveira et al., 2001). Although both studies have suggested a stability of the modifications induced by cocaine, a relatively short period of abstinence was considered (only 30 days). The lack of correlation might have possibly been due to the persistence of deficits for considerably longer periods. Thus, it has been suggested that significant brain metabolic alterations are detectable even after 4 months of abstinence (Volkow et al., 1992). In cognitive terms, among cocaine users, cognitive deficit persistence has been identified for as long as 6 months of cocaine abstinence (Strickland et al., 1993), being reversed up to 3 years after substance use cessation (Selby and Azrin, 1998). As to the interference of crack cocaine, it has been suggested that performance in verbal memory measures (both immediate and delayed) is positively correlated to the extension of the cocaine abstinence period, so that the longer this period, the greater the recovery of affected functions (Di Sclafani et al., 2002). These data show that cerebrovascular and neurochemical activities impaired by use/abuse of cocaine and its derivatives may return to the premorbidity state, so the possibility of recovery might not be discarded.

The knowledge about the interference of the effects of crack cocaine on cognition is an urgent matter, and deserves further clarification. This is even more so when one considers that in Brazil, the crack cocaine lifetime use has risen from 0.4% to 0.7% among the general population, in 4 years (from 2001 to 2005) (CEBRID, 2007). Hence, the present study aimed to evaluate the cognitive performance of crack cocaine users (current users) in general cognition, memory, attention, and executive functioning measures and also on

[2]The reader is referred to Hills's criteria for causality which were developed in order to help assist researchers and clinicians determine if *risk factors* were *causes* of a particular disease or *outcomes* or *merely associated* (Hill, 1965).

scales which evaluate mood state (anxiety and depression). The cognitive performance of crack cocaine users was compared to ex-users (that had been abstinent for, at least, a 6-month period), in order to verify the possible reversibility of cognitive and mood state deficits which has been associated with crack cocaine consumption.

Material and Methods

Sample Selection

The study was carried out in the city of Sao Paulo, Brazil, during 2005 and 2006. The research protocol was previously approved by the Research Ethics Committee of the Federal University of São Paulo (UNIFESP). Subject participation was warranted after reading, understanding, and accepting terms of Free and Informed Consent. Participants were rewarded for their time and other expenses (approximately US$15).

Fifty-nine subjects were initially evaluated and divided into three groups according to crack cocaine lifetime use and abstinence: control group (C), crack cocaine current users (U), and ex-users (E). Control subjects ($N = 18$) had never tried crack cocaine nor were they abusers or dependent on other psychotropic substances. Subjects who had reported using tobacco or alcohol during their lifetime, but who were not regular users, were allowed to participate as controls.

Among subjects who reported crack cocaine lifetime use, those who had stopped consumption for a period of time greater than 6 months were named ex-users (E) ($N = 24$), while participants who were currently consuming it were named as users ($N = 17$), whose period of abstinence ranged from 1 to 30 days. Among users and ex-users, crack cocaine consumption should be over 6 months, avoiding the inclusion of subjects that had just tried it. At the time of neuropsychological evaluation, all current users were crack-cocaine-dependent, since all of them filled out at least three of the seven possible *DSM-IV* criteria (APA, 1994).

This study's inclusion criteria were subjects from both genders, aged 18 years or older and with 9–11 years of formal education. On the other side, subjects who filled at least one of the following criteria were excluded: (1) subjects who were intoxicated by crack cocaine or any other psychotropic drug (including tobacco and coffee) at the moment of neuropsychological evaluation; (2) subjects who had a history of medical or psychiatric disorders that were not associated with the use/abuse of crack cocaine; (3) subjects who had a history of cranial or encephalic trauma, epileptic crisis, loss of consciousness for periods longer than 5 min, and other diagnosed neurological disorders; (4) self-reported problems at birth or during childhood and learning disabilities in lifetime (ex: enrollment in special needs classes); (5) lifetime use of injectable drugs or recent use of psychotropic medication including anxiolytics, antipsychotics, narcotics, and barbiturates, for attending either therapeutic or recreational reasons; and finally (6) subjects who were HIV positive. Four of the ex-users were categorized, according to *DSM-IV* criteria (APA, 1994), as being cocaine-dependent (snorted cocaine hydrochloride); they were excluded from the sample. The final sample consisted of 20 ex-users and 55 participants overall.

In a different approach from other studies, this research studied subjects who were current users and who had not attended any therapeutic intervention program. In order to achieve this aim, some special sampling techniques were adopted. So, crack cocaine users were recruited from social circles in which crack cocaine consumption was common. The first contact between researchers and participants was established by key informants, people who had special knowledge of the target population (WHO, 1994). Once this contact was

made, selection progressed through snowball sampling method (Biernacki and Waldorf, 1981) in which one participant indicated an acquaintance, who indicated another, and so forth. Control group subjects were recruited in the neighboring area surrounding UNIFESP, where the research was conducted. Sociodemographic variables, such as age, gender, years of formal education, and socioeconomic status (SES) were balanced among participants in order to make groups as similar as possible. Participants in the users and ex-users groups were paired according to time duration of crack cocaine consumption, expressed in months or years.

Instruments

(a) *Brief interview*: At first, each participant was submitted to a brief interview in order to obtain the signed consent forms and general information such as (1) time duration of crack cocaine consumption (in months or years) and pattern of use (frequency and quantity); (2) ways in which crack cocaine had been used (rock, "*pitilho*": rock mixed with tobacco, and/or "*mesclado*": rock mixed with marijuana) and the average amount per session of use; (3) drug poliuse, focusing mainly on the association of crack cocaine to other substances (both licit and illicit) during the session of consumption; (4) current frequency of other licit (especially alcohol and tobacco) and illicit drug consumption; (5) past or current history of memory, attentional, and/or learning deficits during school life; (6) lifetime infection by sexually transmitted diseases (STDs), including HIV; and finally (7) occurrence of brain trauma, accidents, or any other relevant disorder. When the inclusion criteria were met, participants were then asked to answer questions related to the following scales: (1) Socioeconomic Classification Criteria (ABEP, 2000) to define the subjects' SES; (2) *DSM-IV* criteria (APA, 1994) in order to estimate abuse/dependence to crack cocaine, alcohol, and other drugs; (3) IDATE (Trace and State Anxiety Inventory) (Biaggio, Natalício, and Spielberger, 1979); and (4) Beck Depression Inventory (BDI) (Gorenstein and Andrade, 1996).

(b) *Neuropsychological battery*: A short neuropsychological battery was chosen to evaluate overall cognition and more specifically verbal memory and executive functioning, known to suffer most from the interference brought on by the cocaine (hydrochloride) and chronic crack consumption. Neuropsychological tests, divided according to the cognitive domain they evaluate, were:

I. *Overall mental evaluation:* Mini-Mental State Examination (MMSE) (Brucki, Nitrini, Caramelli, Bertolucci, and Okamoto, 2003);
II. *Evaluation of attentional and executive functions:* (i) Digit span (forward and backward) (Wechsler, 1987); (ii) Verbal fluency, divided into phonemic fluency or FAS (Benton and Hamsher, 1989) and semantic fluency (word categories: animals and fruits) (Brucki and Rocha, 2004); (iii) Stroop Color Word Test (Spreen and Strauss, 1998); (iv) Cancellation Test (Bond and Lader, 1972); (v) Trail Making Test: Trail A and B (Reitan, 1955, 1958); and (vi) Digit Symbol Substitution Test (DSST) (Wechsler, 1987);
III. *Evaluation of learning and memory abilities:* (i) Logical Memory and (ii) Verbal Associated Pairs (both Wechsler, 1987).

Procedures

Subjects were individually evaluated at the Department of Psychobiology at UNIFESP, in neutral and safe rooms, with as little distraction as possible. Each session, ranging from

50 to 75 min, was initiated by a brief interview, and once all the inclusion criteria were met, the neurocognitive evaluation begun. All neuropsychological tests, as well as the scales (BDI and IDATE) were applied in the same order by two health professionals with experience in this type of intervention and PhDs in the drug addiction field. Afterwards, all neuropsychological tests and scales were corrected and the data proceeded to statistical analysis.

Statistical Analysis

Sociodemographic data, time duration of crack cocaine consumption, and scores on the BDI and IDATE (trace and state) were submitted to statistical analysis by one-factor ANOVA, considering the group (according to crack cocaine lifetime consumption and if past or current) as the independent variable. Subject's gender, as a categorical variable, was analyzed separately by χ^2 test. Contrasts between raw data were analyzed with Duncan's test.

For cognitive measures, between-groups differences were analyzed by an adjusted-statistical model in which crack cocaine consumption status (Table 3, letter G) was included as a factor. Otherwise, BDI scores (Table 3, letter B) and a "dummy" variable indicative of alcohol abuse/dependence (Table 3, letter A) were included as covariates. The "backward" method was used. Thus, all variables and correspondent interactions were included in the initial model. Afterwards, nonsignificant variables were removed and the resulting model contained only the significant ones. At first, interactions were removed and, afterwards, the covariates. When interaction was significant, the main effect was kept in the statistical model. Once all covariates were excluded, the final resulting model was a one-factor ANOVA according to crack cocaine consumption status.

Using the BDI scores as a covariate allowed researchers to correct between-subject performance differences according to the possible presence of depressive symptoms. The same was done for alcohol abuse/dependence. When differences reached statistical significance, multiple comparisons were carried out using Duncan's test. The statistical package adopted to carry out performance group comparisons was SAS 9.1. A statistical significance of .05 was considered ($p < .05$).

Results

The results, grouped according to the variables of interest and the participants' groups, are shown in Tables 1–3.

a. *Sociodemographic data* (Table 1): There was no difference among subjects in regards to age ($p = .17$), years of formal education ($p = .16$), and SES ($p = .17$).
b. *Duration of crack cocaine consumption* (Table 1): There was no difference between users and ex-users according to the total duration of crack cocaine consumption ($p = .32$), indicating a homogeneity between groups. Among ex-users, until the neuropsychological evaluation, the total time of crack cocaine consumption ranged from 6 to 96 months (a maximum of 8 years), a period slightly longer among current users, ranging from 12 to 96 months (maximum of 8 years).
c. *Time of crack cocaine abstinence:* Among ex-users, the total time of abstinence ranged from a minimum of 6 months to a maximum of 5 years.
d. *IDATE and BDI scores* (Table 1): Among groups, IDATE performance (trace and state) did not reach statistical significance ($p = .27$ and $p = .14$, respectively) (Table 1).

Table 1
Sociodemographic characteristics, total time duration of crack cocaine consumption (expressed in months), and mood state measures (BDI and IDATE—trace and state) according to participants' group (Average ± SD)

	Average ± SD			
Variable	Control	Current user	Ex-user	*p*
Age	24.2 ± 4.2	22.6 ± 4.3	25.9 ± 6.6	.17
Formal education (years)	11.5 ± 1.0	11.2 ± 0.6	10.9 ± 0.9	.16
SES	18.8 ± 3.3	15.8 ± 5.2	16.8 ± 5.3	.17
IDATE state	40.2 ± 6.3	43.2 ± 8.9	39.0 ± 8.5	.27
IDATE trace	40.9 ± 9.2	47.1 ± 9.2	41.8 ± 10.8	.14
BDI	8.0 ± 6.1	19.4 ± 9.4*/**	11.6 ± 7.7	<.001
Time of crack cocaine use	—	43.8 ± 27.1	34.8 ± 26.3	.32

Note. * indicates difference of performance compared to control group; ** indicates difference of performance between users and ex-users.

On the other hand, difference among groups reached statistical significance for BDI scores ($p < .001$) (Table 1). As current users scored higher than control subjects and ex-users ($p < .05$), it could be suggested that subjects still in use are prone to depressive symptoms. Considering a maximum BDI score of 63 points, the groups' performance ranged from 0 to 18, 0 to 32, and 4 to 39 among healthy subjects, ex-users, and current users, respectively.

e. *Cognitive performance* (Table 2): Regarding performance in MMSE, healthy subjects performed better than current users and ex-users ($p < .05$). Considering 30 points as the maximum possible score for MMSE, groups' performance ranged from 27 to 30, 26 to 30, and 25 to 30 among healthy subjects, ex-users, and users, respectively. Thus, a more detailed interpretation pointed that 5% of healthy subjects, 29% of current users, and 35% of ex-users scored under 28 points, the normal cutoff for Brazilian people with 9–11 years of formal education (Brucki et al., 2003).

   Concerning verbal memory tests, there was no statistical difference among groups in regards to Verbal Associated Pairs performance, both for immediate ($p > .21$) and delayed recall ($p > .12$). However, scores for Logical Memory test, both for immediate ($p = .02$) and delayed recall ($p = .01$) were statistically different among groups. Current users achieved lower scores than healthy subjects and ex-users ($p < .05$) and there was no difference between the performance of the last ones (users and ex-users).

   Executive performance differences among groups were detected for Trail Making Test (Part B) ($p = .038$) and DSST ($p = .003$). Concerning performance on such tests, ex-users had lower scores than control subjects and there was no difference between current crack cocaine user subjects and control ones ($p > .05$). For Trail Making Test (Part B), ex-users performed worse than the current users ($p < .05$).

f. *Covariates interference on cognition:* In order to better understand the real interference of crack cocaine consumption on cognition, the influence of other variables was investigated, such as alcohol abuse/dependence and depressive symptoms presence interference (according to BDI scores). This influence was investigated only on neuropsychological tests whose group difference performance reached statistical significance for crack cocaine consumption interference (Table 2). Thus, as shown in Table 3, cognitive

Table 2
Comparative analysis of cognitive performance according to participants' groups (Average ± SD)

	Average ± SD			
Variable	Control	Current user	Ex-user	*p*
Easy associated pairs (verbal paired associated test)—immediate recall	13.5 ± 1.6	12.6 ± 2.1	12.6 ± 2.3	.475
Difficult associated pairs—immediate recall (PD_RI)	9.8 ± 3.0	8.8 ± 2.6	8.9 ± 3.6	.208
Easy associated pairs—delayed recall (T30_PF)	4.7 ± 0.8	4.5 ± 0.9	4.7 ± 0.5	.820
Difficult associated pairs—delayed recall (T30_PD)	3.6 ± 1.0	3.5 ± 1.4	3.4 ± 1.6	.117
Logical Memory—immediate recall (REC_IF)	8.5 ± 2.6	6.1 ± 2.2*/**	8.3 ± 3.2	.023
Logical Memory—delayed recall (REC_TF)	6.3 ± 2.6	3.7 ± 1.7*/**	5.4 ± 2.8	.011
FAS	31.1 ± 8.9	31.1 ± 10.8	33.7 ± 9.9	.421
Semantic fluency (FL_SEMAN)	30.7 ± 6.5	30.7 ± 6.3	33.6 ± 7.3	.148
Digit span (forward)	5.9 ± 1.2	6.3 ± 1.4	5.8 ± 1.7	.374
Digit span (backward)	4.3 ± 1.4	4.4 ± 0.9	4.0 ± 1.3	.593
Stroop Color Word Test—Trail C (interference) (STR_C)	23.2 ± 5.8	24.4 ± 4.9	26.6 ± 8.5	.291
Trail Making Test—Part A (TRAIL_A)	36.0 ± 6.9	38.7 ± 14.5	40.5 ± 12.5	.136
Trail Making Test- Part B (TRAIL_B)	79.2 ± 21.6	82.2 ± 26.5	101.3 ± 50.1*/**	.038
Cancellation Test (CANC)	87.7 ± 25.3	81.2 ± 19.9	85.8 ± 23.1	.694
DSST	50.9 ± 5.4	46.1 ± 10.6	43.0 ± 9.4*	.003
MMSE	29.1 ± 0.9	28.3 ± 1.2*	28.2 ± 1.3*	.034

Note. *indicates difference of performance compared to control group; **indicates difference of perfomance between users and ex-users.

performance in Logical Memory (immediate and delayed recall) and MMSE suffered a significant interference from crack cocaine consumption but no other relevant interactions. For Trail Making Test (Part B), besides crack cocaine consumption, the presence of depressive symptoms seems to interfere on its performance ($p = .012$). Alcohol abuse/dependence ($p = .033$) and its interaction with BDI scores ($p = .011$) interfered

Table 3
P-values for final adjusted statistical model

Test	G	A	B	G ×A	G ×B	A ×B
REC_IF	0.023	—	—	—	—	—
REC_TF	0.011	—	—	—	—	—
TRAIL_B	0.038	—	0.012	—	—	—
DSST	0.003	0.033	0.430	—	—	0.011
MMSE	0.034	—	—	—	—	—

Note. G indicates condition of crack cocaine use (control, users, and ex-users); A indicates alcohol abuse/dependence; B indicates the interference of the presence of depressive symptoms (according to BDI); G × A indicates the interaction between crack cocaine use and alcohol abuse/dependence; G × B indicates the interaction between crack cocaine use and the presence of depressive symptoms; and A × B indicates the interaction between alcohol abuse/dependence and the presence of depressive symptoms.

on DSST scores. As there was no statistically significant interactions between group (controls, users, and ex-users) and covariates, for none of the cognitive measures mentioned before, results indicate that cognitive deficits shown in Table 2 are exclusively due to crack cocaine consumption. Thus, the covariates studied (alcohol abuse/dependence and BDI scores) did not influence the cognitive measures adopted in this research.

Discussion

The present research findings suggests that chronic crack cocaine consumption interferes negatively on users affective-cognitive domains. Current users scored significantly higher on BDI and showed impaired performance in MMSE and Logical Memory immediate and delayed recall, suggesting a possible overall mental and verbal memory deficits. Crack cocaine ex-users, whose abstinence period of time ranged from 6 months to 5 years, were impaired on MMSE and executive functioning measures (DSST and Trail Making Test, Part B), impairment not observed among crack cocaine current users. The sociodemographic similarity among groups and also similarity between current users and ex-users according to time duration of crack cocaine consumption reflected the homogeneity of samples, allowing a more truthful interpretation of results.

In regards to BDI, crack cocaine current users scored higher than healthy control subjects and ex-users. According to the BDI Brazilian validation (Gorenstein and Andrade, 1996), crack cocaine current users performed similarly to depressed subjects, classifying them as such, corroborating previous studies (Beatty et al., 1995; Di Sclafani et al., 2002). So, the covariated statistical analysis, according to BDI score, was the chosen strategy to eliminate the possible interference of depressive symptoms from the cognitive deficits observed. Thus, deficits presented here may be the result of crack cocaine action on cognition and could not be secondary nor enhanced by comorbidities associated to its consumption (i.e., depressive symptoms nor alcohol abuse/dependence). Regarding depression per se, depressive symptoms are commonest among drug users as evidenced by the higher prevalence of suicidal thoughts and attempts among them (Ardila and Bateman, 1995). In a study that evaluated drug users attending psychiatric emergency services, among different classes of psychotropic drugs, it was suggested that cocaine was the one most often associated to mood disorders, other psychiatric disorders, and suicidal ideations (Garlow, Purselle, and D'Orio, 2003). Among cocaine derivatives, crack has an important role in

the users' emotional turmoil as has been evidenced by a negative association between its frequency of use (or dependence) and mental health (Falck, Wang, Carlson, and Siegal, 2000). This mood instability is thought to be due to cocaine pharmacological action, i.e., its chronic consumption would render mesolimbic pathway cells less responsive to the rewarding dopamine action, and then users would become more prone to depression, irritation, and/or anxiety (Dackis and O'Brien, 2001).

Analyzing neurocognitive functioning in further detail, a performance deficit in MMSE was observed among both crack cocaine current users and ex-users. Considering the MMSE average performance for Brazilian healthy population, with 9–11 years of formal education as 28 points, it is interesting to note that 30% of current users and ex-users scored below this cutoff, pointing to a general impairment in mental functioning. Thus, more detailed evaluation, assessed through other parameters, was essential to determine the specific cognitive deficits due to crack cocaine consumption.

An important verbal memory deficit was found for current crack cocaine users. Because it negatively interfered both on Logical Memory immediate and delayed recall, it is suggested that crack cocaine impairs verbal information processing and also its long-term retention and recovery. So, tasks that require a greater ability or time to elaboration should be affected. By losing the ability to process, associate, consolidate, and recall verbal information, current crack cocaine users may not benefit from therapeutic strategies, becoming less receptive to relapse prevention and, consequently, behavioral changes become more difficult to achieve.

Due to the importance of attentional resources for new verbal memory formation and consolidation (Anderson, Craik, and Naveh-Benjamin, 1998; Baddeley, 1998; Mulligan, 1998), it would be suggested that this mnemonic impairment was mediated by attentional deficits. However, this hypothesis had not been confirmed since no performance impairment was observed in attentional and mental flexibility tests, suggesting that current crack users, still "asymptomatics," are not executive function impaired, but were cognitively impaired only for verbal memory tasks. These results are not confirmed by most available studies, which have pointed to executive function deficits as being the main cognitive implications stemming from the chronic crack cocaine consumption (Beatty et al., 1995; Cunha et al., 2004; Di Sclafani et al., 2002; Fein et al., 2002; Hoff et al., 1996; Strickland et al., 1993). One should, however, highlight the fact that apart from most studies that have investigated cognitive deficits due to chronic crack cocaine consumption, this study was designed to investigate subjects who were neither institutionalized nor have been involved in any therapeutic intervention. Such studies tend to focus on extreme situations in which the crack user or his/her family, motivated by its impairing effects search for treatment, make it more difficult to comprehend the evolution of crack cocaine interference on cognition over time.

Among ex-users, the cognitive interference pattern associated with crack cocaine consumption was different from the one observed among current users. Verbal memory tests and depressive symptoms were seemingly not affected. Thus, among ex-users, cognitive performance was affected mainly in measures of attention and mental flexibility, such as Trail Making Test (Part B) and DSST, pointing to executive function deficits. This result is similar to that reported in a research conducted with crack cocaine users who had been abstinent from 3 to 5 weeks (Beatty et al., 1995). It is important to note, however, that there is an interpretation bias in such test performances, in that, besides measuring executive functions, they tend to measure perceptual ability and motor speed, reflecting deficits in functions other than those of interest. This limitation is inherent to the lack of specificity and sensibility of attentional tests (Horner, 1999). Hence, considering that the performance in those tests is commonly measured by recording the time needed for its execution, it is

possible that the impulsiveness and sensation of urgency brought on by crack cocaine use could have improved the perceptual-motor performance among crack cocaine current users, making possible attentional deficits. Since in the present study no specific tests to evaluate perceptual-motor abilities were employed, other investigations to further understand the specific interference of crack cocaine consumption on executive functions and attentional resources are necessary.

In general, this research has several strengths and limitations. One of its advantages was that it considered, as current users and ex-users, participants who had abused or were crack-cocaine-dependent and not dependent on other cocaine derivatives. Studies concerning the identification of the alterations brought on by cocaine use on brain morphology, perfusion, and function usually include, in the same group, cocaine hydrochloride (snorted or injected) and crack cocaine users, a sampling bias that deserves attention. Since crack cocaine has a high dependence inducing power (Chen and Antony, 2004) it may conduct users to a heavier pattern of use and so to a greater cognitive impairment. Furthermore, in this research, the "user group" was composed by current and asymptomatic subjects who were not under any therapeutic intervention. Thus, present result interpretation is not confined to extreme health conditions (clinical and institutionalized samples) as has been the norm. Finally, current users and ex-users scores were compared to healthy nonuser subjects' performance (control group) with similar sociodemographic characteristics (such as gender, age range, years of formal education, and SES), further enhancing the reliability of results.

Study's Limitations

On the other hand, one of the main limitations of this research was having counted, solely and exclusively, on the subjects' self-reports for determining their past and current drug use. Thus, use (among users) and nonuse (among ex-users) were not confirmed through the detection of cocaine metabolites by any toxicological test. Furthermore, crack cocaine users are usually polydrug users, concurrently or simultaneously combining crack cocaine with other drugs (Oliveira and Nappo, 2008). Although it has been known that polydrug use causes a higher degree of neurological and cognitive impairment, in the present study this condition partially applies since alcohol abuse/dependence was monitored. It is important to note that alcohol has been the substance most commonly associated with cocaine (hydrochloride) and crack cocaine consumption (Gossop, Manning, and Ridge, 2006; Oliveira and Nappo, 2008).

Finally, the crack cocaine quality is poor, mainly due to adulterants and diluents added to it (Bono, 1998; Inciardi et al., 1993; Siegel, 1982), which may make it more difficult to identify, in an evidence-based manner, the pharmacological effects of crack cocaine on a person's neuropsychiatric and neurocognitive domains.

Conclusion

It is suggested that crack cocaine consumption may impair verbal memory and increase the incidence of depressive symptoms among crack cocaine current users. This effect was not observed among ex-users, pointing to a possible reversibility of those deficits. Since the statistical analysis was covariated, cognitive deficits found among users may neither be due to affective disorders nor to alcohol abuse/dependence. Among ex-users, attentional and executive functioning deficits were detected. However, since measures adopted here are not very specific, alterations in perceptual ability and motor speed may have been detected. These alterations were not detected among crack cocaine current users, possibly due to the stimulating effect of crack cocaine.

As the results are still controversial, other neuroimaging, neuropsychological, and neurovascular researches are needed in order to identify the true impairments induced by crack cocaine consumption, evaluating not only their extensions but their persistence through time. Further clarification is necessary to determine whether being abstinent for a period of time seems to influence some neurocognitive functioning.

The presence of neurocognitive deficits points to the need for planning and developing specific treatment programs for crack cocaine current users. This would include a neuropsychological screening for earlier identification of patients who are or may be at greater risk of relapsing in order to better enhance their chance of treatment outcome success.

RÉSUMÉ

Évaluation neuropsychologique d'utilisateurs et ex-utilisateurs de crack

Introduction: Les changements cognitifs en raison de la consommation de crack demeurent controversés. Méthodes: Pour une meilleure compréhension, 55 sujets ont été divisés en un groupe contrôle, un groupe d'utilisateurs actifs de crack, et un groupe d'ex-utilisateurs. Les participants ont été soumis à un Mini Examen de leur état mental (MMSE), ainsi qu'à es tests d'évaluation de leurs fonctions exécutives, mémoire logique et changements d'humeur. Des comparaisons inter-groupes ont été effectuées. Résultats: Les résultats obtenus par le groupe contrôle au MMSE ont été meilleurs que ceux des utilisateurs et des ex-utilisateurs de crack. Les utilisateurs actifs de crack ont présentés un déficit de mémoire logique. Les ex-utilisateurs ont réalisé un score plus faible en DSST et "Trail Making Test" (partie B). Conclusion: La consommation chronique de crack semble perturber le fonctionnement cognitif général (MMSE), la mémoire logique et les ressources attentionnelles, mais certains de ces effets peuvent être inversés par abstinence à la drogue.

RESUMEN

Evaluación neuropsicológica de usuarios y ex-usuarios de crack

Introducción: Los efectos cognitivos debido al consumo de crack siguen en controversias. Métodos: Para una mejor comprensión, 55 sujetos fueron asignados en grupos: controle, usuarios y ex-usuarios de crack. Los participantes fueron sometidos a pruebas para evaluación del estado mental general (MMSE), de funciones ejecutivas, memoria lógica y trastornos del humor. Comparaciones inter-grupo fueron realizadas. Resultados: El desempeño del grupo control en MMSE fue mejor que de usuarios y ex-usuarios de crack. La memoria lógica estuvo deteriorada entre usuarios recientes. Los ex-usuarios tuvieron puntuaciones más bajas en DSST y "Trail Making Test" (Parte B). Conclusión: El uso crónico del crack parece perjudicar las funciones cognitivas generales (MMSE), memoria lógica y atención, pero se sugere que algunos de estos efectos pueden revertir por la abstinencia.

RESUMO

Avaliação neuropsicológica de usuários e ex-usuários de crack

Introdução: Os efeitos cognitivos decorrentes do consumo de crack permanecem controversos. Métodos: Para sua melhor compreensão, 55 sujeitos foram distribuídos em um grupo controle, um grupo de usuários recentes e um grupo de ex-usuários de crack. Os participantes responderam o Mini Exame do Estado Mental (MMSE), assim como testes e escalas de avaliação de funções executivas, memória lógica e transtornos de humor.

Comparações inter-grupo foram realizadas. Resultados: O desempenho do grupo controle no MMSE foi melhor do que o de usuários e ex-usuários de crack. Os usuários recentes de crack apresentaram déficits de memória lógica. Os ex-usuários pontuaram menos nos testes DSST e Trilhas (Parte B). Conclusão: O consumo crônico de crack parece prejudicar o funcionamento cognitivo geral (MMSE), memória lógica e recursos de atenção, mas se sugere que alguns desses efeitos podem ser revertidos pela abstinência à droga.

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