

Neuropsychological impairments in crack cocaine-dependent inpatients: preliminary findings

Paulo J Cunha,^a Sérgio Nicastrí,^{a,b} Luciana P Gomes,^a Renata M Moino^a e Marco A Peluso^a

^a Grupo Interdisciplinar de Estudos de Álcool e Drogas (GREA), Departamento e Instituto de Psiquiatria da Faculdade de Medicina da Universidade de São Paulo (USP)

^b Programa de Álcool e Drogas (PAD) do Hospital Israelita Albert Einstein (HIAE)

**Dados desta pesquisa ("Neuropsychological impairment of cocaine dependent patients" e "Cocaine dependence impaired performance in a new neuropsychological battery sensitive to prefrontal functions -FAB") foram apresentados no Sixty-Sixth Annual Scientific Meeting do College on Problems of Drug Dependence (CPDD) e NIDA International Fórum, realizados de 11 a 17 de Junho de 2004, em San Juan, Puerto Rico (USA).*

Abstract

Objective: Although cocaine use is a significant public health problem, there is relative paucity of scientific data on long-term neurocognitive consequences of the exposure to the substance.

Methods: This study examined the association between crack cocaine dependence and neuropsychological performance. An extended battery of neuropsychological tests was administered to 15 abstinent cocaine abusers, inpatients in abstinence for two weeks, and 15 non-drug-using control subjects matched for age, gender, education, socio-economic status, handedness and IQ.

Results: The preliminary findings showed statistical significance ($p < 0,05$) on differences of performance in attention, verbal fluency, verbal memory, visual memory, learning ability and executive functions.

Conclusions: These results represent evidences that cocaine abuse is associated with decrements in cognitive functioning, similar to cognitive disorders associated to prefrontal and temporal brain impairments. Knowledge of specific cognitive deficits in cocaine abusers may be useful for designing more effective substance abuse prevention and treatment programs.

Keywords: Crack cocaine. Substance-related disorders. Cognition. Neuropsychological tests.

Introduction

Cocaine/crack abuse is associated with several physical, psychiatric and social problems. It is estimated that 14 million people over the world have used cocaine in the last decade.¹ In Brazil, according to the First Home Survey on the use of Drugs, performed at the Brazilian Center of Information on Psychotropic Drugs (CEBRID), it was found that 7.2% of male subjects, aged 25 to 34 years, had already used the drug,² and recent epidemiological data show that cocaine/crack use has been rising among high school and elementary students,³ as well as among patients who seek for treatment in specialized clinics.⁴

Although certain neurological complications can occur in association with the use of cocaine/crack, it seems that there is no consensus among researchers regarding the cognitive impairment related to the use of the drug.^{5,6} Therefore, a better knowledge about these issues will contribute for the development of preventive and treatment programs for cocaine/crack dependent subjects, as they involve cognitive-behavioral approaches.⁷

The objective of this study was to assess the neuropsychological performance of cocaine/crack-dependent subjects, during the second week of abstinence.

Sample and methods

This is a cross-sectional study, with 30 subjects, divided in two groups, one with cocaine/crack-dependent subjects (n=15) and

the other, with normal volunteers (n=15), recruited in the community. Cocaine-dependent subjects were under specialized treatment programs (hospitalization), at the Interdisciplinary Group of Studies on Alcohol and Drugs (GREA), Institute of Psychiatry of the Medical School of the University of São Paulo and at the Therapeutic Community of the APOT (Campinas, SP, Brazil). Groups were matched by variables which could affect the results of the neuropsychological tests: age, gender, education, socioeconomic level and handedness. Exclusion criteria for the study were: significant problems at birth or in the psychomotor development, other DSM-IV axis I psychiatric diagnoses (APA, 1994); use of psychiatric medication; history of head trauma or neurological problems; medical problems which could affect the central nervous system; learning disorder.

Subjects were referred to an initial interview, in order to obtain the informed consent regarding the project and, afterwards, submitted to a neuropsychological battery, and for cocaine/crack-dependent subjects the evaluation was performed in the second week of drug abstinence.

The following areas of the cognitive functioning were assessed: attention (Trail Making Test - TMT, Stroop Color Word Test - SCWT and - Forward Digits FD and Backward Digits - BD, WMS-R),⁸ memory (Logical Memory - LM - I and II - WMS-R, Visual Reproduction - VR - I and II - WMS-R and Recall of the Rey-Osterrieth Complex Figure - ROCF),⁸ learning (Buschke Selective Reminding Test - BSRT),⁸ executive functions (Wisconsin Card Sorting Test - WCST⁸ and Frontal Assessment Battery - FAB⁹),

visuospatial functions (Copy of the ROCF and Block Design – WAIS-R),⁸ language (Vocabulary – WAIS-R, Controlled Oral Word Association Test – COWAT – and Boston Naming Test – BNT)⁸ and intellectual functions (Vocabulary and Block Design, WAIS-R).⁸

Regarding the statistical analysis, comparisons between variables were performed with Student t tests for independent variables (continuous variables) or with Fisher exact test (categorical variables). Statistical significance level was $\alpha = 0.05$ and all tests were two-tailed.

Results

There were no statistically significant differences between patients and controls regarding age, gender, education and socioeconomic level. Cocaine/crack-dependent subjects in average started using the drug at 18.41 years of age and the mean time of use was 10.3 years, and patients used the substance, in average, five days a week. Although all the subjects included in this study had a drinking history, most patients (66.6%) drank little or even had not ingested alcohol in the month prior to the hospitalization.

Regarding the results of the neuropsychological tests (Table 1), the performance of cocaine/crack-dependent subjects was significantly decreased in the FD and BD (WMS-R) tests, which are measures of the attention ability.

Regarding the executive functions, patients had a poorer performance in the FAB and, in language functions, they produced less words started by letters F, A and S, in the COWAT.⁸

In the memory functions, there was difference in the capability of visual recovery, since patients had greater difficulty to recall figures after 30 minutes, both in the VR II (WMS-R) and in the ROCF.⁸

Regarding verbal memory and learning, cocaine/crack-dependent subjects had poorer scores than controls, with statistical significance ($p < 0.05$) in the items Total Recall, Long-Term Retrieval (LTR), Long-Term Storage (LTS), Consistent Long-Term Retrieval (CLTR), Randomic Long-Term Retrieval (RLTR), Reminder and Recall after 15 minutes in BSRT.⁸

Estimated Intellectual Quotient (IQ) in cocaine/crack-dependent subjects was not statistically different from that found in the group of normal controls ($p > 0.05$).

Discussion

In this study, the assessment of the attention ability showed performance differences between cocaine/crack-dependent subjects and normal controls, what has been frequently observed in other investigations.¹⁰ However, after a review on the subject, Horner⁵ claimed that there is still no consistency regarding the findings of attention deficits among cocaine/crack-dependent subjects, due mainly to the different methodologies applied and to the lack of more controlled studies. Further studies are necessary in order to verify the nature and severity of the attention deficits associated with cocaine, as they have a direct clinical implication in the treatment.^{7,10} Alterations in the capability of retaining and manipulating information in the mind (attention and working memory), such as those found in the FD and BD (WMS-R) tests, are related to a poorer retention in the treatment.¹¹

We detected alterations in the performance of cocaine/crack-dependent patients in executive function tests, present in the FAB.⁹ Recent studies have observed pre-frontal alterations in cocaine/crack-dependent subjects, associated with their decision-making deficits¹² and with the neurobiological bases of substance dependences.¹³

The results of this study revealed statistically significant differences in the tests of phonological verbal fluency (letters F, A and S),⁸ showing significant deficits of verbal expression. Although these alterations have already been observed in previous studies,¹⁰ the issue is still unsolved in the literature, as some researches even found a better verbal fluency in subjects dependent on this drug.¹⁴ The hypothesis for that is the probable flaw of these studies regarding the inclusion of outpatients, who could be under the effect of the substance, considering that cocaine/crack intoxication could stimulate the verbal production of these patients.

We also found delayed visual memory deficits (after 30 minutes) in cocaine/crack-dependent patients, both in VR II (WMS-R) and in the ROCF Recall.⁸ Besides, BSRT⁸ showed consistent failures in the memory recovery and verbal learning of dependent subjects, suggesting that these patients have problems in the storage of new verbal information, possibly associated with functional alterations of the frontal and temporal lobes.⁸ Studies have demonstrated that cocaine acts and promotes alterations in hippocampal regions, modifying the Long-Term Potentiation (LTP) mechanism, involved in the process of formation of new memories.¹⁵ The decrease in the availability of dopamine and serotonin in these areas during abstinence has been associated with learning and memory deficits. Similar results regarding memory and learning deficits have already been described in the international literature,¹⁰ and they can impair significantly the patient's ability to incorporate strategies for relapse prevention.^{7,10}

This study was able to detect neuropsychological deficits described in the literature, such as in the attention, language, memory, learning, and executive functions. Despite our cautious delineation of the inclusion and exclusion criteria of participants, the use of a matched control group and the control of abstinence (hospitalization regime), there are limitations in this study. First, the still relatively small size of the sample. Second, the need of a stricter control regarding the existence of neuropsychiatric symptoms which could influence the results. For example, it is believed that the analysis of a previous diagnosis of attention deficit hyperactivity disorder (ADHD), on each of the participants, could provide more evidence regarding the causality of the found alterations. Other information that should be better investigated is the presence and severity of the depressive and anxious symptoms in the subjects. Besides, the cross-sectional delineation of the study prevents the prospective visualization of the found cognitive deficits and to know whether they persist or not during the abstinence.

These data highlight the importance of performing more studies in this area, involving larger samples, a stricter control of the variables which may influence the results, and monitored follow-up of subjects.

Table 1 - Performance of crack/cocaine-dependent subjects (n=15) and normal controls (n=15) in neuropsychological tests used for the evaluation of neurocognitive functions

Neurocognitive Functions	Neuropsychological Tests	Crack/Cocaine Dependent Subjects mean (SD)	Normal Controls mean (SD)	p*	
Attention	Forward Digits (WMS-R)	4.0 (1.64)	6.13 (2.67)	.041**	
	Backward Digits (WMS-R)	3.60 (1.59)	5.53 (2.72)	.025**	
	TMT - A	38.87 (18.53)	32.80 (15.22)	.335	
	TMT - B	100.93 (45.70)	89.60 (60.10)	.566	
	Stroop I	14.87 (4.34)	16.13 (5.73)	.501	
	Stroop II	20.93 (7.69)	18.87 (5.87)	.415	
	Stroop III	31.07 (11.22)	27.13 (10.42)	.328	
Executive Functions	WCST	Correct	44.07 (8.10)	44.87 (8.58)	.795
		Errors	19.7 (8.37)	19.00 (8.47)	.830
		Perseverative Errors	11.13 (5.76)	9.73 (4.93)	.480
		Failures to Maintain set Categories	.73 (.96)	.87 (.92)	.700
	FAB	15.36 (1.65)	17.00 (1.24)	.006**	
Language	COWAT	Animal	17.40 (5.70)	17.40 (5.26)	>.99
		Food	15.40 (4.47)	15.47 (7.15)	.976
		Clothes	15.00 (5.10)	15.13 (5.10)	.943
		Letter F	10.93 (2.69)	13.73 (4.17)	.037**
		Letter A	9.67 (4.13)	13.47 (4.27)	.020**
	Letter S	9.80 (4.11)	13.53 (4.78)	.029**	
	BNT	Correct	56.67 (1.99)	56.47 (3.07)	.416
Memory	Logical Memory I (WMS-R)	22.20 (6.71)	25.93 (6.50)	.133	
	Logical Memory II (WMS-R)	17.07 (5.75)	21.13 (7.44)	.105	
	Visual Reproduction I (WMS-R)	30.53 (6.86)	34.93 (7.00)	.093	
	Visual Reproduction II (WMS-R)	22.87 (10.21)	30.60 (10.80)	.054	
	ROCF	Recal	15.73 (6.89)	21.63 (6.06)	.019**
Memory and Learning	BSRT	Total Recall	105.29 (17.29)	120.07 (13.48)	.016**
		LTR	94.50 (26.81)	114.80 (15.61)	.018**
		STR	11.07 (10.11)	5.93 (3.49)	.075
		LTS	106.36 (25.86)	122.47 (9.51)	.032**
		CLTR	62.79 (29.58)	95.13 (29.22)	.006**
		RLTR	31.86 (14.06)	19.67 (14.67)	.031**
		REMINDER	38.43 (17.65)	22.93 (13.25)	.012**
		Recall after 15 minutes Recognition	9.07 (3.02)	10.87 (1.25)	.044**
Visuospatial Functions	ROCF	Copy	31.77 (5.12)	33.50 (2.38)	.245
	Block Design (WAIS-R)	25.53 (9.36)	28.73 (13.21)	.450	
Intellectual Functions	Estimated IQ (WAIS-R)	91.60 (10.53)	99.47 (16.89)	.137	

NOTES: SD = Standard Deviation; TMT = Trail Making Test; Stroop = Stroop Color Word Test; WCST = Wisconsin Card Sorting Test; FAB = Frontal Assessment Battery; IQ = Intellectual Quotient; WAIS-R = Wechsler Adult Intelligence Scale-Revised; BNT = Boston Naming Test; COWAT = Controlled Oral Word Association Test; WMS-R = Wechsler Memory Scale-Revised; ROCF = Rey-Osterrieth Complex Figure;

Conclusions

The preliminary results of this investigation showed neurocognitive impairment in cocaine/crack-dependent subjects, when compared to normal subjects. We found alterations in attention, verbal fluency, visual memory, verbal memory, learning ability and executive functions. These data show evidence that cocaine abuse is associated with significant neuropsychological deficits, similar to those that occur in cognitive disorders, possibly related to problems in the prefrontal and temporal brain regions. The knowledge of specific neuropsychological impairments can be useful in the planning of more effective preventive and treatment programs for cocaine/crack abuse.

References

1. United Nations Office on Drugs and Crime (UNODC). Global illicit drug trends 2003 [online]. New York: UNODC; 2003. Available from: URL: <http://www.unodc.org>.
2. Carlini EA, Galduróz JCF, Noto AR, Napo SA. I Levantamento Domiciliar sobre o uso de drogas Psicotrópicas no Brasil. São Paulo: [CEBRID] Centro Brasileiro de Informações sobre Drogas Psicotrópicas, Departamento de Psicobiologia, Escola Paulista de Medicina, Universidade Federal Paulista; 2001.
3. Galduróz JCF, Noto AR, Carlini EA. IV Levantamento sobre o uso de drogas entre estudantes de 1^o e 2^o graus em 10 capitais brasileiras (1997). São Paulo: [CEBRID] Centro Brasileiro de Informações sobre Drogas Psicotrópicas, Departamento de Psicobiologia, Escola Paulista de Medicina, Universidade Federal

Paulista; 1997.

4. Laranjeira R, Silveira DX, Formigoni ML, Ferri CP, Dunn J. Crack cocaine: an increase in use among patients attending clinics in São Paulo: 1990-1993. *Subst Use Misuse* 1996;31:519-27.
5. Horner MD. Attentional functioning in abstinent cocaine abusers. *Drug Alcohol Depend* 1999;54:19-33.
6. Cunha PJ, Camargo CHP, Nicastrí S. Déficits Neuropsicológicos e Cocaína: um estudo-piloto. *J Bras Dep Quim* 2001;1(1):31-7.
7. Gottschalk C, Beauvais J, Hart R, Kosten T. Cognitive Function and Cerebral Perfusion During Cocaine Abstinence. *Am J Psychiatry* 2001;158(4):540-5.
8. Spreen O, Strauss EA. *Compendium of neuropsychological tests: administration, norms and commentary*. New York: Oxford University Press; 1998.
9. Dubois B, Slachevsky A, Litvan I, Pillon B. The FAB: A frontal assessment battery at bedside. *Neurology* 2000;55:1621-6.
10. Strickland TL, Mena I, Villanueva-Meyer J, Miller BL, Cummings J, Mehringer CM, et al. Cerebral perfusion and neuropsychological consequences of chronic cocaine use. *J Neuropsychiatry Clin Neurosci* 1993;5:410-27.
11. Teichner G, Horner MD, Harvey RT. Neuropsychological predictors of the attainment of treatment objectives in substance abuse patients. *Int J Neurosci* 2001;106(3-4):253-63.
12. Bechara A, Dolan S, Denburg N, Hindes A, Anderson SW, Nathan PE. Decision-making deficits, linked to a dysfunctional ventromedial prefrontal cortex, revealed in alcohol and stimulant abusers. *Neuropsychologia* 2001;39:376-89.
13. Goldstein RZ, Volkow ND. Drug Addiction and its Underlying Neurobiological Basis: Neuroimaging Evidence for the Involvement of the Frontal Cortex. *Am J Psychiatry* 2002;159:1642-52.
14. Hoff AH, Riordan H, Morris L, Cestaro V, Wieneke M, Alpert R, Wang GJ, Volkow ND. Effects of Crack cocaine on neurocognitive function. *Psychiatry Research* 1996;60:167-76.
15. Smith DA, Browning M, Dunwiddie TV. Cocaine inhibits hippocampal long-term potentiation. *Brain Res* 1993;608:259-65.

Correspondece

Paulo J Cunha - Interdisciplinary Group of Studies on Alcohol and Drugs (GREA)
Departament and Institute of Psychiatry, Medical School,
University of São Paulo (USP)
R. Dr. Ovídio Pires de Campos, nº 785
01060-970 São Paulo, SP, Brazil
Tel./Fax.: (55 11) 3081-8060 / 3064-4973
E-mail: pjcunha@usp.br

Pesquisa realizada no Grupo Interdisciplinar de Estudos de Álcool e Drogas (GREA), Departamento e Instituto de Psiquiatria da Faculdade de Medicina da Universidade de São Paulo (USP) e na Comunidade Terapêutica da Associação Promocional Oração e Trabalho - APOT (Campinas-SP).
Sponsor: Fundação de Amparo a Pesquisa do Estado de São Paulo - FAPESP. Auxílio Pesquisa: Processo nº 00/12081-5.
Received 10.02.2003
Accepted 04.11.2003