The frontal assessment battery (FAB) reveals neurocognitive dysfunction in substance-dependent individuals in distinct executive domains: Abstract reasoning, motor programming, and cognitive flexibility

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ARTICLE INFO

ABSTRACT

Substance-dependence is highly associated with executive cognitive function (ECF) impairments. However, considering that it is difficult to assess ECF clinically, the aim of the present study was to examine the feasibility of a brief neuropsychological tool (the Frontal Assessment Battery — FAB) to detect specific ECF impairments in a sample of substance-dependent individuals (SDI). Sixty-two subjects participated in this study. Thirty DSM-IV-diagnosed SDI, after 2 weeks of abstinence, and 32 healthy individuals (control group) were evaluated with FAB and other ECF-related tasks: digits forward (DF), digits backward (DB), Stroop Color Word Test (SCWT), and Wisconsin Card Sorting Test (WCST). SDI did not differ from the control group on sociodemographic variables or IQ. However, SDI performed below the controls in DF, DB, and FAB. The SDI were cognitively impaired in 3 of the 6 cognitive domains assessed by the FAB: abstract reasoning, motor programming, and cognitive flexibility. The FAB correlated with DF, SCWT, and WCST. In addition, some neuropsychological measures were correlated with the amount of alcohol, cannabis, and cocaine use. In conclusion, SDI performed more poorly than the comparison group on the FAB and the FAB's results were associated with other ECF-related tasks. The results suggested a negative impact of alcohol, cannabis, and cocaine use on the ECF. The FAB may be useful in assisting professionals as an instrument to screen for ECF-related deficits in SDI.

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1. Introduction

There is a growing and consistent body of research showing that substance-dependent individuals (SDI) usually show abnormal functioning in specific neural networks of the prefrontal cortex (PFC) related to executive cognitive function (ECF), decision-making, and emotional control (Dolan, Bechara, & Nathan, 2008; Fein, Di Sclafani, & Meyerhoff, 2002; Goldstein et al., 2004; Grant, Contoreggi, & London, 2000; Liu, Matochik, Cadet, & London, 1998; Matochik, London, Eldreth, Cadet, & Bolla, 2003; Rogers & Robbins, 2001; Verdejo-García, Bechara, Recknor, & Perez-Garcia, 2006; Verdejo-García, López-Torrecillas, Arcos, & Pérez-García, 2005; Verdejo-García, Perales, & Pérez-Garcia, 2007; Volkow et al., 1992). PFC dysfunction may impair response inhibition, impulse control, conflict/error monitoring and goal-driven behaviors, as well as contribute to poor decision-making and to the maintenance of the drug-seeking behavior, despite negative consequences (Bartzokis et al., 2000; Bechara et al., 2001; Bolla et al., 2003, 2004; Dolan et al., 2008; Fishbein et al., 2005; Goldstein & Volkow, 2002; Grant et al., 2000; Verdejo-García et al., 2006; Volkow & Fowler, 2000).

However, it is difficult to assess ECF clinically (Anderson, Damasio, Jones, & Tranel, 1991; Miller et al., 1991). Traditional ECF-related tests (i.e., Wisconsin Card Sorting Test) may fail to detect ECF deficits in SDI (Aharonovich et al., 2006; Bartzokis et al., 2000; Cunha, Nicastri, Gomes, Moino, & Peluso, 2004; Cunha, Bechara, Andrade, & Nicastri, in press; Gillen et al., 1998; Grant et al., 2000; Toomey et al., 2003) and even in neurological patients with known PFC injury (Anderson et al., 1991; Bechara, Damasio, Damasio & Anderson, 1994). In addition, there is no gold standard neuropsychological test exclusively designed to detect ECF deficits. Consequently, searching for ECF deficits usually includes time-consuming tests and extensive neuropsychological batteries, which may be difficult to tolerate by SDI and involve relatively high financial costs to substance abuse treatment providers.

The need for an efficient tool to promptly explore different domains of ECF motivated Dubois et al. to devise the Frontal Assessment Battery (FAB) (Dubois, Slachevsky, Litvan, & Pillon, 2000), a neuropsychological battery composed of six subtests which evaluate different ECF-

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related functions. The performance on the six subtests of the FAB gives a composite global score, which evaluates the severity of the dysexecutive syndrome and suggests a descriptive pattern of ECF in a given patient (Dubois et al., 2000). The FAB subtests significantly correlated with frontal metabolism in a PET study of patients with frontal lobe damage of various etiologies (Sarazin et al., 1998). The FAB's authors studied patients with varying degrees of frontal lobe dysfunction (Parkinson Disease, multiple system atrophy, corticobasal degeneration, progressive supranuclear palsy, and frontotemporal dementia) and the FAB presented good psychometric properties (internal consistency, optimal interrater reliability, and concurrent validity) (Dubois et al., 2000). The FAB has been shown to have good psychometric properties in a series of other neuropsychiatric disorders such as Attention-Deficit Hyperactivity Disorder (ADHD) (Lima, Meireles, Fonseca, Castro, & Garrett, 2008; Nakaaki et al., 2007; Rodriguez del Alamo, Catalán Alonso, & Carrasco Marín, 2003; Slachevsky et al., 2004). The recent neuroimaging study performed by Guedj and collaborators (2008) found a significant correlation between the FAB performance and brain perfusion in the PFC. The authors suggest that these findings confirm that the FAB is an adequate tool for assessing PFC functions, and is thus useful for the evaluation of diseases associated with frontal dysfunction. Although substance use disorders (SUD) have been frequently associated with frontal dysfunction, the FAB has only been used to assess ECF in a small sample of SDI (Cunha, Nicastri, et al., 2004) and in a group of alcohol-dependent patients (Pombo, Levy, Bicho, Ismail, & Cardoso, 2008). Both studies have compared the FAB's Global Score in SDI with control groups. However, the FAB may be used to assess different subtypes of ECF such as abstraction, mental flexibility, motor programming, sensitivity to interference, inhibitory control, and environmental autonomy. Curiously, to our knowledge, there are no studies focusing on examination of different FAB's subtests in abstinent SDI. We believe that studies with FAB in SDI would help not only to detect generalized and unspecific ECF impairments (Cunha, Nicastri, et al., 2004; Pombo et al., 2008), but also help us to identify neurocognitive deficits in distinct ECF domains of these patients. Second, there is no consensus about the frontal sensitivity of the FAB (Lezak, Howieson, & Loring, 2004), and no studies have been done to establish a link between the FAB and other traditional frontal tasks in SDI. Third, there is an absence of studies searching for possible dose-related ECF impairments with the FAB in SDI. Investigation of dose-related neurocognitive effects of SDI in different subtests of the FAB would provide further evidence of causality between substance use and executive dysfunction using a brief instrument such as the FAB. Therefore, the main goal of the present study was to assess whether the FAB can detect different types of ECF-deficits in a sample of SDI. A secondary aim of this study was to test the frontal sensitivity of the FAB in SDI, by comparing with results in other traditional ECF-related instruments. The third aim was to analyze if there were dose-related neurocognitive effects of substance use on FAB's results. We hypothesized that: SDI would show significant abnormalities on the FAB's total score and on different subcomponents of the FAB; that the neurocognitive alterations detected by the FAB would be correlated with results in other traditional ECF-related instruments; and that the neurocognitive deficits detected by the FAB would be dose-related, meaning that the heavier the substance use, the lower the neurocognitive performance detected by the FAB.

2. Methods

2.1. Participants

Sixty-two male individuals participated in this study. Thirty SDI who met the two following criteria were enrolled: 1) DSM-IV-TR criteria (American Psychiatric Association, APA, 2000) for cocaine dependence at time of admission to the treatment program; 2) self-report of drug use at least six times in the month prior to admission. The SDI were recruited from two inpatient units: 1) the Interdisciplinary Group of Studies on Alcohol and Drugs (GREA) at the University of São Paulo; 2) the Association for the Promotion of Prayer and Work (APOT) in Campinas (São Paulo state, Brazil). At the time of the data collection, the treatment units where the study was conducted did not have any women. The exclusion criteria for the SDI were: 1) past or current major psychiatric disorders (i.e., bipolar disorder, depression, and mania); 2) history of neurological disorders such as head injuries, with loss of consciousness for longer than 30 min, strokes, and intracranial hemorrhages; 3) prior diagnosis of learning disorder; 4) IQ less than 70. The SDI were all treatment-seeking substance-dependent patients who had been abstinent from drugs for an average of two weeks before their evaluation. The abstinence period was verified by self-report and supervised by the clinical staff.

The neurocognitive performance of the SDI was compared to the results of a control group, which consisted of 32 healthy volunteers, recruited in the city of São Paulo. The control group consisted of employees from the public hospital where the research center (GREA) is located ($n = 2$) and the local police department ($n = 12$). We also recruited adult students from a public school ($n = 18$). The exclusion criteria for the control group were: 1) DSM-IV-TR criteria for any psychoactive substance dependence other than nicotine; 2) the same exclusion criteria of the SDI.

2.2. Procedure

The research protocol satisfied the Helsinki Declaration and was approved by the University of Sao Paulo Research Review Board (CAPPesq-HC-FMUSP). After signing an informed consent, participants were assessed by either a clinical psychologist or a psychiatrist. The interview questions covered demographics, drug use, and their consequences on psychosocial functioning. The Cocaine Addiction Severity Test (CAST) and Cocaine Assessment Profile (CAP) (Washton, 1989) were used to assess alcohol, tobacco, and other drug use. Psychiatric symptoms were assessed by the SRQ-20 (Mari & Williams, 1986).

A trained neuropsychologist (P.J.C.) administered the neuropsychological tests, drug use questionnaires, and psychiatric rating scales, in one single session, usually in the morning. The sequence of neuropsychological tests followed the same pattern in both groups. The intellectual quotient (IQ) was estimated based on the two subtests of the Wechsler Adult Intelligence Scale – Revised – WAIS-R (Wechsler, 1981), Vocabulary and Block Design (Silverstein, 1982).

2.3. Neurocognitive measures

The authors used four standard neuropsychological instruments and the FAB to assess ECF. The traditional ECF-related instruments were chosen based on adaptation and validation studies for our population (Portuguese-language). They were:

2.3.1. Stroop Color Word Test (SCWT) (Lezak et al., 2004; Stroop, 1935)

This test was designed to measure selective attention, cognitive flexibility, and inhibitory control (Lezak et al., 2004; Stroop, 1935). In this study, we used a version of the SCWT that was translated into Portuguese and adapted to Brazilian population. It is a version of the SCWT, designed by Camargo et al. (unpublished results), a senior neuropsychologist from our research center. The SCWT we used has three parts: Part I) the patient is invited to name different colors, printed in 20 small rectangles, as fast as he/she can; the randomly-assigned colors used in the three parts of this version of the SCWT were: green, blue, brown, and pink; Part II) the subjects have to name the color of the ink of non-color printed words, such as "each", "never", "today", and "everything" — in Portuguese: "cada", "nunca", "hoje", e "tudo", respectively; Part III) the patient has to name the

color of the ink in which a color name is printed when the print ink is one of the colors above mentioned (Stroop, 1935). The score is measured by the time in seconds - until the patient has completed each part of the SCWT (I, II, and III).

2.3.2. Wisconsin Card Sorting Test (WCST) (Heaton, Chelune, Talley, Kay, & Curtiss, 1993; Lezak et al., 2004), 64 card version (Haaland, Vranes, Goodwin, & Garry, 1987)

Four "stimulus cards" are placed in front of the subject. All cards used in the game have a color, a geometric shape, and a quantity. The subject then receives a deck of 64 cards and is asked to pick a card and match it to one of the four stimulus cards. After each trial, the examiner says whether the response is correct or not. The patient has to deduce the sorting principle from the examiner's feedback and then maintain a consistent pattern of responses. However, the sorting principle is changed by the examiner, after the subject gives 10 consecutive correct answers. The sequence of changing is: color, shape, and number. The WCST evaluates abstraction ability, mental flexibility and sustained attention (Haaland et al., 1987; Heaton et al., 1993; Lezak et al., 2004); it was already translated into Portuguese and validated to Brazilian population (Cunha, Trentini, et al., 2004). Four measures of performance were analyzed: 1) correct responses; 2) categories; 3) perseverative errors; and 4) failure to maintain set.

2.3.3. Digits forward (DF) and backward (DB), from the revised version of the Wechsler Adult Intelligence Scale (WAIS-R) (Wechsler, 1981)

Both tests consist of seven pairs of random sequences of numbers that the examiner reads aloud at the rate of one per second (Lezak et al., 2004; Wechsler, 1981). DF consists of repeating series of numbers in the same order and DB in the reverse order. Each correct sequence is equivalent to 1 point. The scoring ranges from 0 (none sequence of number was correctly repeated) to 14 (all the 7 pairs of sequences of numbers were correctly repeated). The DF and DB are commonly used for measuring span of immediate verbal recall (Lezak et al., 2004), but DF and DB demands different mental abilities and they are subserved by specific brain regions (Gerton et al., 2004; Lezak et al., 2004).

2.3.4. Frontal Assessment Battery (FAB) (Dubois et al., 2000)

The administration of the FAB takes approximately 10 min; each subtest is scored from 0 (minimum score) to 3 (maximum score) and the total score of the FAB is the sum of the scores in the 6 subtests (the FAB's total score ranges from 0 to 18) (Dubois et al., 2000). The FAB has already been translated into Portuguese (Cunha & Novaes, 2004) and detailed information about instructions of the FAB are described elsewhere (Dubois et al., 2000). The 6 subtests are:

Conceptualization: it is based on the traditional similarities subtests included in the intelligence scales designed by Wechsler (1981). This subtest evaluates the subject's ability to generate similarities between: *1) banana-orange*, *2) table-chair*, *3) tulip-rose-daisy*. The examiner asks: "In what way are they alike?" In the case of total or partial failure in the first item (i.e., "they are not alike"), the examiner may help the subject saying "both a banana and an orange are…" but doesn't give any credit for him/her. The patient cannot be helped in the other items (*table-chair, tulip-rose-daisy*). Full correct responses are fruits, furniture, and flowers, respectively. Each right response is associated to one credit (none correct: 0; one correct: 1; two correct: 2; three correct: 3).

Mental flexibility: the subject has to recall as many words as he/she can beginning with the letter "S" in a 1-minute trial. The examiner says: "Say as many words as you can beginning with the letter 'S,' any words except surnames or proper nouns" (Dubois et al., 2000). The examiner may help, if no response is given during the first 5 s: "for instance, salt". Each correct word is scored as one point. The score in mental flexibility may be 0 (less than 3 words), 1 (3 to 5 words), 2 (6 to 9 words), and 3 (more than 9 words).

Motor programming: the examiner, sitting in front of the patient, asks him/her to watch carefully the Luria's fist-palm-edge motor series (Dubois et al., 2000; Luria, 1966) The examiner repeats three times the Luria's motor sequences with his left hand. Then, he asks the patient to repeat the movement with his/her right hand, initially accompanying the examiner's movement, and then alone. The examiner performs the series three times with the patient, and then asks the patient to do it on his/her own. The patient who cannot perform three correct consecutive series even with the examiner receives no point. The subject who is able to perform three correct consecutive series with the examiner, but fails alone, receives 1 point. Two points are given to the patient who performs at least three correct consecutive series alone, and the full score (three points) is given for six correct consecutive series.

Sensitivity to interference: this is a subtest similar to the SCWT (Dubois et al., 2000). The examiner requires the patient to tap twice on a table upon hearing a single tap. The examiner then performs a sequence of three trials (1-1-1) and the patient should respond appropriately. Next, the examiner asks the patient to tap once on the table upon hearing two taps. Then, a series of three trials is given: 2-2-2. Finally, the examiner performs the following series: 1-1-2-1-2-2-2-1-1-2. If the patient taps like the examiner at least four consecutive times, receives 0 point. One point is given when the patient makes more than 2 errors, and two points are given if the subject makes 1 or 2 errors. The full score (three points) is given when the patient executes without any error.

Inhibitory control: this task is based on the traditional go-no go paradigm. It is similar to the previous subtest, but here the patient should inhibit what he/she had just learned: the subject is required to tap once upon hearing a single tap. A series of three trials is run: 1-1-1. Then, the examiner asks the patient to do not tap upon hearing two taps. The examiner performs three trials (2-2-2). Next, the examiner taps the following sequence: 1-1-2-1-2-2-2-1-1-2. The scoring is identical to the previous subtest.

Environmental autonomy: this subtest evaluates the abnormal spontaneous tendency to adhere to the environment through the prehension behavior. The examiner sits in front of the patient and places the patient's hands palm up on his/her knees. Then, without saying anything, the examiner touches the patient's palms of his/her hands. The examiner evaluates if the patient spontaneously takes his/her hands. If the patient takes the examiner's hands, the examiner will try again asking: "Now, do not take my hands". If the patient takes the examiner's hands even after he/she has been told not to do so, he/she receives zero points. One point is given to the patient who takes the examiner's hands without hesitation. Two points are given to the patient who hesitates and the full score (three points) is obtained when the patient does not take the examiner's hands.

2.4. Data analyses

Statistical comparisons were made using the unpaired Student's *t*-test or Mann–Whitney test for quantitative variables. The Fisher's Exact Test was used for categorical variables. The normality of observations was verified by the Kolmogorov–Smirnov test. The level of statistical significance was $\alpha = .05$ and all statistical tests were two-tailed. Correlations between the FAB scores, other frontal neuropsychological measures (i.e., DF, DB, SCWT, and WCST), and drug use variables were assessed by the Spearman correlation coefficient (r_s). Statistical Package for the Social Sciences (SPSS) for Windows, version 14.0 (SPSS inc., 2005) was used to perform all statistical analyses.

3. Results

There were no statistically significant differences between the SDI and the control group in variables such as age, education (years),

economic level (family income), ethnicity, and handedness (Table 1). The estimated IQ of the subjects in the control group was slightly higher than that of the subjects in the SDI group, but the difference was not statistically significant ($p > .05$). In addition, performance on vocabulary subtest of the WAIS-R was not statistically different between the SDI and the control group.

The lifetime duration (years) and recent frequency (weekly) of cocaine use was very high among the SDI (Table 2). The daily use of psychoactive substances other than cocaine was higher among the SDI; alcohol doses ($M = 4.61$; $SD = 2.02$), joints of marijuana ($M = .69$; $SD = .16$), and tobacco cigarettes ($M = .67$; $SD = .12$). The control group did not report any lifetime use of cocaine, but some of them reported recent use (in the past month) of other substances, such as alcohol ($M = .28$; $SD = .29$), nicotine ($M = .12$; $SD = .31$), and marijuana ($M = .04$; $SD = .02$). Neither group reported any recent use of LSD, heroin, amphetamine, methamphetamine, or ecstasy (MDMA).

The results obtained by the SDI did not differ from those of the control group on the SCWT (Parts I, II, and III) or WCST (i.e., correct responses, perseverative errors, failure to maintain set, and number of categories). However, the results of the SDI in the DF and DB (Table 3) were significantly lower than those of the control group ($p < .05$).

The overall score of the FAB was lower in the SDI than in the control group ($p < .01$). On average, they had greater impairments in three cognitive domains: abstract reasoning, motor programming, and cognitive flexibility ($p < .01$) (Fig. 1 and Table 4).

There were no significant correlations between drug use variables, FAB scores and other traditional frontal neuropsychological measures in the control group. However, in the SDI, the FAB's mental flexibility subtest was negatively correlated with the number of perseverative errors in the WCST ($r_s = -.44$, $p < .05$) and positively correlated with the DF ($r_s = .57$, $p < .01$) (Table 5): the better the performance on mental flexibility, the fewer the perseverative errors on the WCST and the better the performance on DF. The FAB's total score was negatively correlated with the Part III of the SCWT ($r_s = -.41$, $p < .05$): the better the performance on the FAB, the lower the time to complete the third part of the SCWT. Motor programming was positively associated with the number of failures to maintain set in the WCST ($r_s = .41$, $p < .05$): the better the performance on motor programming, the greater the number of failures to maintain set.

The daily cannabis consumption (number of joints) was negatively correlated with the FAB's inhibitory control subtest ($r_s = -.45$, $p < .05$): the more joints per day smoked in the last 30 days, the lower the performance on inhibitory control. The daily amount of alcohol use (doses) during the past 30 days was positively associated with the number of perseverative errors in the WCST ($r_s = .38$,

$p < .05$): the greater amount of alcohol used, the more perseverative errors in the WCST. Finally, the lifetime cocaine use (years) was negatively correlated with DB ($r_s = -.39$, $p < .05$): the more years the SDI consumed cocaine, the lower the performance on DB (Table 6).

4. Discussion

The SDI evaluated in the present study performed significantly worse than a healthy control group in the FAB, a very brief instrument designed for the evaluation of ECF. The SDI were cognitively impaired in half (50%) of all cognitive domains assessed by the FAB, including abstract reasoning, cognitive flexibility, and motor programming. In addition, the SDI underperformed the control group in standard ECF-related tasks; the digits forward and backward, which are measures of attention and working memory, respectively (Braver et al., 1997). To our knowledge, this is the first scientific report showing neurocognitive alterations by different subtests of the FAB in SDI, as well as correlations between the FAB's results (total score and subtests' scores) and other traditional frontal tasks, such as digits, SCWT, and WCST, thus suggesting that the FAB is a valid instrument to assess ECF in SDI. Furthermore, the neuropsychological measures were mildly associated with alcohol, cannabis, and cocaine consumption, suggesting a negative impact of recent and lifetime substance use on the ECF of SDI.

Our findings are consistent with the recent data on neuroimaging, neuropsychology, and neurophysiology, which showed strong evidence of ECF impairments and PFC abnormalities on both structure

Table 1
Sociodemographic variables, intellectual functioning, and substance use of the SDI ($n = 30$) and healthy controls ($n = 32$).

	SDI	Controls	p
	Mean ($\pm$ SD)	Mean ($\pm$ SD)	
Age[*]	27.17 (7.64)	26.75 (5.55)	.80
Education (years)[*]	9.93 (2.74)	10.78 (2.20)	.18
Family income[*] (monthly, in R$[***])	2,452 (1,918)	2,135 (1,711)	.49
Ethnicity (Brazilian White/ African Brazilian)[**]	27/3	27/5	.70
Handedness (right handed/left handed)[**]	28/2	26/6	.25
Estimated Intellectual Quotient (IQ)[*]	95.87 (11.62)	101.06 (12.82)	.10
Vocabulary (WAIS-R)[*]	43.37 (10.52)	47.31 (8.79)	.11

Notes: SDI = substance-dependent individuals; SD = Standard Deviation ($\pm$). WAIS-R = Wechsler Adult Intelligence Scale-Revised.
  [*] Student's *t* test for independent samples.
  [**] Fisher's Exact Test.
  [***] Values are described in Brazilian currency − each American dollar (US$ 1.00) was equivalent to 1.75 Brazilian Reais (R$ 1.75) at the time of the submission of the article (April, 2010).

Table 2
Cocaine, alcohol, and other drug use among the SDI and the control group.

	SDI ($n = 30$)	Controls ($n = 32$)
	Mean ($\pm$ SD)	Mean ($\pm$ SD)
Cocaine		
Days/week	5.03 (.35)	–
Grams/week	18.73 (14.94)	–
Duration (years)	8.23 (5.27)	–
Abstinence (days)	14.00 (.82)	–
Alcohol		
Drinks/day	4.61 (2.02)	0.28 (.29)
Marijuana		
Joints/day	.69 (.16)	.04 (.02)
Tobacco		
20 cigarettes/day (packs)	.67 (.12)	.12 (.31)

Notes: SDI = substance-dependent individuals; data are presented as means ± standard deviations (SD).

Table 3
Performance of SDI ($n = 30$) and healthy controls ($n = 32$) in traditional neuropsychological tests designed to evaluate executive cognitive functioning (ECF).

Neurocognitive functions	Neuropsychological tests		SDI	Controls	p
			Mean ($\pm$ SD)	Mean ($\pm$ SD)	
Attention and executive functioning	SCWT	Part I[*] (sec)	16.06 (9.09)	14.58 (4.22)	.42
		Part II[*] (sec)	19.40 (6.10)	17.29 (4.71)	.13
		Part III[*] (sec)	29.46 (9.69)	26.08 (8.88)	.15
	WCST (64-cards)	Correct[*]	44.03 (7.73)	43.84 (9.15)	.93
		Perseverative errors[*]	10.03 (4.96)	10.22 (5.57)	.89
		Failure to maintain set[*]	.73 (.87)	.63 (.79)	.61
		Categories[*]	2.63 (1.25)	2.72 (1.30)	.79
	Digits (WAIS-R)	Forward (DF)[**]	5.30 (2.09)	6.63 (2.51)	.03
		Backward (DB)[**]	4.60 (1.90)	6.25 (2.36)	.01

Notes: SDI = substance-dependent individuals; SD = Standard Deviation [$\pm$]; SCWT = Stroop Color Word Test; sec = seconds; WCST = Wisconsin Card Sorting Test; WAIS-R = Wechsler Adult Intelligence Scale-Revised.
  [*] Student's *t* test for independent samples.
  [**] Mann–Whitney test for independent samples.

Executive Cognitive Functioning (ECF) as measured by the FAB
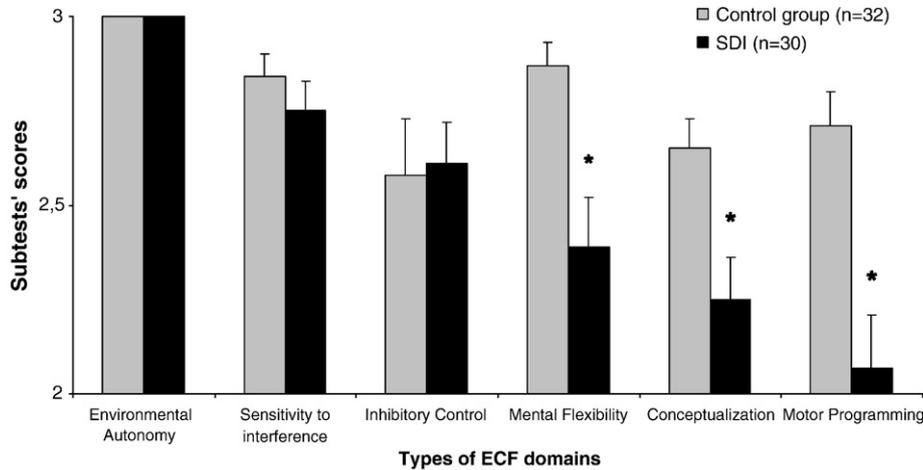
Fig. 1. Neurocognitive performance of SDI and healthy controls in the six cognitive domains of the Frontal Assessment Battery (FAB). Notes: SDI = substance-dependent individuals; FAB = Frontal Assessment Battery; ECF = executive cognitive functioning; [*] indicate ECF domains significantly different between groups by Mann–Whitney test for independent samples ($p < .01$); vertical lines represent standard errors SE ($\pm$).

and metabolism among SDI (Bartzokis et al., 2000; Bechara et al., 2001; Bolla et al., 2003, 2004; Cunha et al., in press; Fillmore & Rush, 2002; Fishbein et al., 2005; Glass et al., 2009; Goldstein & Volkow, 2002; Goldstein et al., 2007; Volkow & Fowler, 2000). The three FAB's subtests in which the SDI were found to have ECF-related impairments (i.e., abstract reasoning/conceptualization, mental/cognitive flexibility, and motor programming), are tasks that have been associated with the functioning of medial, dorsolateral, and posterior areas of the PFC (Dubois et al., 2000; Sarazin et al., 1998). Although the "frontal" sensitivity of the FAB has not been established totally (Guedj et al., 2008; Lezak et al., 2004; Pombo et al., 2008), most of the

correlations between FAB's results and other standard ECF-related tasks indicate that the FAB is a good indicator of severity of the executive dysfunction in SDI. However, it is possible that lower cerebellar hemispheric gray and white matter volumes may also contribute to neuropsychological deficits and motor dysfunction observed in these patients (Sim et al., 2007).

4.1. Clinical implications

Because the FAB is a very easy and quick neuropsychological instrument to administer, potentially all mental health professionals could apply it in the day-by-day setting. The FAB is a paper-and-pencil instrument, so the examiner does not need complex materials or even a computer while administering the battery. We believe that the FAB promises to be an important addition to the field of addiction. Specifically, the results in the FAB could represent indicators of how well the patients will perform in the treatment setting, since cognitive deficits have been associated with low retention in SDI (Aharonovich, Nunes, & Hasin, 2003; Aharonovich et al., 2006; Gottschalk, Beauvais, Hart, & Kosten, 2001; Teichner, Horner, Roitzsch, Herron, & Thevos, 2002). Moreover, recent research findings have suggested that ECF impairments may be both predisposing factors and/or negative consequences of SUD (Dolan et al., 2008; Fillmore & Rush, 2002; Glass et al., 2009; Verdejo-García et al., 2006). Therefore, the use of a brief tool to investigate ECF in humans would be very relevant not

Table 4

Neurocognitive performance of SDI and healthy controls in the six cognitive domains of the FAB.

Frontal Assessment Battery (FAB)	SDI Mean ($\pm$SE)	Control group Mean ($\pm$SE)	p
Conceptualization**	2.25 (.08)	2.65 (.11)	< .01
Mental Flexibility**	2.39 (.13)	2.87 (.06)	< .01
Motor Programming**	2.07 (.14)	2.71 (.09)	< .01
Sensitivity to Interference**	2.75 (.08)	2.84 (.06)	.40
Inhibitory Control**	2.61 (.11)	2.58 (.15)	.56
Environmental Autonomy**	3.00 (.00)	3.00 (.00)	1.00
Total score*	15.07 (.27)	16.65 (.23)	< .01

Notes: SDI = substance-dependent individuals; SE = Standard Errors ($\pm$).
* Student's t test for independent samples.
** Mann–Whitney test for independent samples.

Table 5

Correlation between the Frontal Assessment Battery (FAB) and the other neuropsychological tests among the SDI.

Correlations (r_s)	SCWT part III	WCST cat.	WCST pers. er.	WCST fail. set.	D.F. WAIS-R	D.B. WAIS-R
Frontal Assessment Battery (FAB)						
Mental Flexibility	−.16	.35	−.44*	.11	.57**	.19
Motor Programming	−.27	−.06	−.15	.41*	−.08	−.24
FAB's total score	−.41*	.03	−.36	.35	.15	−.11

Notes: SDI = substance-dependent individuals; r_s = Spearman correlation coefficient; SCWT = Stroop Color Word Test; WCST Cat. = Categories completed in the Wisconsin Card Sorting Test; WCST Pers. Er. = Perseverative errors in the WCST; WCST Fail. Set = Failure to maintain set in the WCST; D.F. = Digits Forward; WAIS-R = Wechsler Adult Intelligence Scale-Revised; D.B. = Digits Backward; correlations were considered statistically significant if $p < .05^*$ and $p < .01^{**}$.

Table 6

Correlation between drug use variables and neuropsychological measures among the SDI.

Correlation (r_s)	Cocaine, alcohol, cannabis, and tobacco use				
	Cocaine	Cocaine	Alcohol	Cannabis	Tobacco
	Grams/week	Lifetime/years	Daily use	Daily use	Daily use
Neuropsychological measures					
FAB's Inhibitory Control	.003	−.15	−.29	−.45*	−.12
WCST—Pers. Er.	−.09	.01	.38*	.20	−.14
D.B.—WAIS-R	.03	−.39*	−.34	−.06	.05

Notes: SDI = substance-dependent individuals; r_s = Spearman correlation coefficient; The daily use of substances other than cocaine was evaluated considering the amount of doses for alcohol, the number of joints for cannabis, and the quantity of cigarettes for tobacco; FAB = Frontal Assessment Battery; WCST Pers. Er. = perseverative errors; WAIS-R = Wechsler Adult Intelligence Scale-Revised; D.B. = Digits Backward; correlations were considered statistically significant if $p < 0.05^*$.

only to help tailor specific treatment strategies to SDI (Teichner et al., 2002), but also for early detection of ECF deficits in children and adolescents with adverse events (i.e., childhood abuse, or exposure to violent crime) at a higher risk for SUD (Douglas et al., 2010).

Nevertheless, it is important to bear in mind that we do not presume that the FAB should substitute for other standard ECF-related tasks in the neuropsychological evaluation of SDI. For example, the FAB is not able to evaluate decision-making, such as the Iowa Gambling Task (IGT), designed by Bechara et al. (1994). In addition, the FAB does not seem to be sensitive to OFC functioning (Guedj et al., 2008) and the FAB's Inhibitory Control was not sensitive to deficits in response inhibition, which are frequently observed in SDI (Fillmore & Rush, 2002; Glass et al., 2009; Verdejo-García et al., 2005). The FAB's Sensitivity to Interference and Environmental Autonomy subtests were also not sensitive to neurocognitive alterations in our sample of SDI. Moreover, our findings reveal that the FAB has ceiling effects in the two samples (SDI and Control Group), which may have compromised the sensitivity of 3/6 FAB subtests to show significant group differences in our sample. Finally, we did not have data on the ecological validity of the FAB. Therefore, we argue that the FAB must serve as a screening neurocognitive method for the evaluation of ECF in SDI. In the future, perhaps some subtests of this battery might be changed or substituted to target the specificities of neurocognition among SDI.

4.2. Limitations

Despite the important strengths, some limitations of this study should be considered. First, we evaluated only male SDI and one cannot assume that these results are valid for women. In fact, conditions associated with female gender (e.g., hormonal) may partially protect the brain from drug-induced damage (Chang, Ernst, Strickland, & Mehringer, 1999) making direct comparisons problematic (Glass et al., 2009). Second, this study was conducted based on self-reported alcohol, cocaine, and other drug use, for both the SDI and the control group. However, the SDI enrolled in this protocol were predominantly inpatients and under the supervision of the clinical staff to verify and to exclude eventual subjects showing behavioral alterations associated with acute drug use. The reliability of self-report data regarding substance use has often been questioned. However there has been significant evidence that for treatment-seeking SDI, self-reported drug use has been shown be valid, and the level of cognitive functioning did not influence the validity of self-reports (Brown, Kranzler, & Del Boca, 1992; Rice, 2007). Future research, preferentially prospective studies, which use the FAB, neuroimaging techniques (PET, SPECT, and fMRI), and neurophysiologic evaluation, with a larger sample of SDI, consisting of both genders, are required to investigate the correlation between SUD, predisposing factors, and consequences on PFC functioning.

4.3. Conclusion

The present findings have shown that the FAB was sensitive to ECF and PFC-related dysfunction in a sample of SDI. The FAB may represent an efficient tool for neurocognitive screening in SDI by clinicians who tackle the challenge of addiction on a daily basis. These findings may have several implications on diagnosis, treatment, and early prevention interventions.

Contributors

Cunha, Bolla, Guerra, and Nicastri designed the study and Cunha and Nicastri wrote the protocol. Cunha, Guerra, and Nicastri oversaw recruitment and assessment of subjects. Cunha oversaw the development and maintenance of the database. Cunha and Bolla managed the literature searches and summaries of previous related work. Cunha, Bolla, and Nicastri undertook the statistical analysis, and Cunha wrote the first draft of the manuscript. All authors reviewed the manuscript for scientific content and approved the final manuscript.

Conflict of interest

None for any of the authors.

References

Aharonovich, E., Hasin, D. S., Brooks, A. C., Liu, X., Bisaga, A., & Nunes, E. (2006). Cognitive deficits predict low treatment retention in cocaine dependent patients. *Drug and Alcohol Dependence, 81*, 313–322.

Aharonovich, E., Nunes, E., & Hasin, D. (2003). Cognitive impairment, retention and abstinence among cocaine abusers in cognitive-behavioral treatment. *Drug and Alcohol Dependence, 71*, 207–211.

American Psychiatric Association (2000). Diagnostic and Statistical Manual of Mental Disorders, 4th ed. . Washington, DC: Author (text revision).

Anderson, S. W., Damasio, H., Jones, R. D., & Tranel, D. (1991). Wisconsin card sorting test performance as a measure of frontal lobe damage. *Journal of Clinical and Experimental Neuropsychology, 13*, 909–922.

Bartzokis, G., Lu, P. H., Beckson, M., Rapoport, R., Grant, S., Wiseman, E. J., et al. (2000). Abstinence from cocaine reduces high-risk responses on a gambling task. *Neuropsychopharmacology, 22*, 102–103.

Bechara, A., Damasio, A. R., Damasio, H., & Anderson, S. (1994). Insensitivity to future consequences following damage to human prefrontal cortex. *Cognition, 50*, 7–15.

Bechara, A., Dolan, S., Denburg, N., Hindes, A., Anderson, S. W., & Nathan, P. E. (2001). Decision-making deficits, linked to a dysfunctional ventromedial prefrontal cortex, revealed in alcohol and stimulant abusers. *Neuropsychologia, 39*, 376–389.

Bolla, K. I., Eldreth, D. A., London, E. D., Kiehl, K. A., Mouratidis, M., Contoreggi, C., et al. (2003). Orbitofrontal cortex dysfunction in abstinent cocaine abusers performing a decision-making task. *Neuroimage, 19*, 1085–1094.

Bolla, K. I., Ernst, M., Kiehl, K., Mouratidis, M., Eldreth, D., Contoreggi, C., et al. (2004). Prefrontal cortical dysfunction in abstinent cocaine abusers. *The Journal of Neuropsychiatry and Clinical Neurosciences, 16*, 456–464.

Braver, T. S., Cohen, J. D., Nystrom, L. E., Jonides, J., Smith, E. E., Noll, D. C., et al. (1997). A parametric study of prefrontal cortex involvement in human working memory. *Neuroimage, 5*, 49–62.

Brown, J., Kranzler, H. R., & Del Boca, F. K. (1992). Self-reports by alcohol and drug abuse inpatients: Factors affecting reliability and validity. *British Journal of Addiction, 87*, 1013–1024.

Chang, L., Ernst, T., Strickland, T., & Mehringer, C. M. (1999). Gender effects on persistent cerebral metabolite changes in the frontal lobes of abstinent cocaine users. *The American Journal of Psychiatry, 156*, 716–722.

Cunha, P. J., Nicastri, S., Gomes, L. P., Moino, R. M., & Peluso, M. A. (2004). Neuropsychological impairments in crack cocaine-dependent inpatients: Preliminary findings. *Revista Brasileira de Psiquiatria, 26*, 103–106.

Cunha, P. J., & Novaes, M. A. (2004). Neurocognitive assessment in alcohol abuse and dependence: Implications for treatment. *Revista Brasileira de Psiquiatria, 26*, S23–S27 (suppl).

Cunha, P.J., Bechara, A., Andrade, A.G., Nicastri, S, in press. Decision-Making Deficits Linked to Real-Life Social Dysfunction in Crack-Cocaine Dependent Individuals. *American Journal on Addictions.*

Cunha, J. A., Trentini, C. M., Argimon, I. L., Oliveira, M. S., Werlang, B. G., & Prieb, P. G. (2004). *Teste Wisconsin de classificação de cartas.* São Paulo, SP: Casa do Psicólogo.

Dolan, S. L., Bechara, A., & Nathan, P. E. (2008). Executive dysfunction as a risk marker for substance abuse: The role of impulsive personality traits. *Behavioral Sciences & the Law, 26*, 799–822.

Douglas, K. R., Chan, G., Gelernter, J., Arias, A. J., Anton, R. F., Weiss, R. D., et al. (2010). Adverse childhood events as risk factors for substance dependence: Partial mediation by mood and anxiety disorders. *Addictive Behaviors, 35*, 7–13.

Dubois, B., Slachevsky, A., Litvan, I., & Pillon, B. (2000). The FAB: a Frontal Assessment Battery at bedside. *Neurology, 55*, 1621–1626.

Fein, G., Di Sclafani, V., & Meyerhoff, D. J. (2002). Prefrontal cortical volume reduction associated with frontal cortex function deficit in 6-week abstinent crack-cocaine dependent men. *Drug and Alcohol Dependence, 68*, 87–93.

Fillmore, M. T., & Rush, C. R. (2002). Impaired inhibitory control of behavior in chronic cocaine users. *Drug and Alcohol Dependence, 66*, 265–273.

Fishbein, D. H., Eldreth, D. L., Hyde, C., Matochik, J. A., London, E. D., Contoreggi, C., et al. (2005). Risky decision making and the anterior cingulate cortex in abstinent drug abusers and nonusers. *Cognitive Brain Research, 23*, 119–136.

Gerton, B. K., Brown, T. T., Meyer-Lindenberg, A., Kohn, P., Holt, J. L., Olsen, R. K., et al. (2004). Shared and distinct neurophysiological components of the digits forward and backward tasks as revealed by functional neuroimaging. *Neuropsychologia*, *42*, 1781—1787.

Gillen, R. W., Kranzler, H. R., Bauer, L. O., Burleson, J. A., Samarel, D., & Morrison, D. J. (1998). Neuropsychologic findings in cocaine-dependent outpatients. *Progress in Neuro-psychopharmacology & Biological Psychiatry*, *22*, 1061—1076.

Glass, J. M., Buu, A., Adams, K. M., Nigg, J. T., Puttler, L. I., Jester, J. M., et al. (2009). Effects of alcoholism severity and smoking on executive neurocognitive function. *Addiction*, *104*, 38—48.

Goldstein, R. Z., Leskovjan, A. C., Hoff, A. L., Hitzemann, R., Bashan, F., Khalsa, S. S., et al. (2004). Severity of neuropsychological impairment in cocaine and alcohol addiction: Association with metabolism in the prefrontal cortex. *Neuropsychologia*, *42*, 1447—1458.

Goldstein, R. Z., Tomasi, D., Rajaram, S., Cottone, L. A., Zhang, L., Maloney, T., et al. (2007). Role of the anterior cingulate and medial orbitofrontal cortex in processing drug cues in cocaine addiction. *Neuroscience*, *144*, 1153—1159.

Goldstein, R. Z., & Volkow, N. D. (2002). Drug addiction and its underlying neurobiological basis: Neuroimaging evidence for the involvement of the frontal cortex. *The American Journal of Psychiatry*, *159*, 1642—1652.

Gottschalk, C., Beauvais, J., Hart, R., & Kosten, T. (2001). Cognitive function and cerebral perfusion during cocaine abstinence. *The American Journal of Psychiatry*, *158*, 540—545.

Grant, S., Contoreggi, C., & London, E. D. (2000). Drug abusers show impaired performance in a laboratory test of decision making. *Neuropsychologia*, *38*, 1180—1187.

Guedj, E., Allali, G., Goetz, C., Le Ber, I., Volteau, M., Lacomblez, L., et al. (2008). Frontal Assessment Battery is a marker of dorsolateral and medial frontal functions: A SPECT study in frontotemporal dementia. *Journal of the Neurological Sciences*, *273*, 84—87.

Haaland, K. Y., Vranes, L. F., Goodwin, J. S., & Garry, P. J. (1987). Wisconsin Card Sort Test performance in a healthy elderly population. *Journal of Gerontology*, *42*, 345—346.

Heaton, R. K., Chelune, G. J., Talley, J. L., Kay, G. G., & Curtiss, G. (1993). *Wisconsin Card Sorting Test (WCST) — manual revised and expanded.* Odessa, FL: Psychological Assessment Resources.

Lezak, M. D., Howieson, D. B., & Loring, D. W. (2004). *Neuropsychological assessment*, 4th ed. New York, NY: Oxford University Press.

Lima, C. F., Meireles, L. P., Fonseca, R., Castro, S. L., & Garrett, C. (2008). The Frontal Assessment Battery (FAB) in Parkinson's disease and correlations with formal measures of executive functioning. *Journal of Neurology*, *255*, 1756—1761.

Liu, X., Matochik, J. A., Cadet, J. L., & London, E. D. (1998). Smaller volume of prefrontal lobe in polysubstance abusers: a magnetic resonance imaging study. *Neuropsychopharmacology*, *18*, 243—252.

Luria, A. R. (1966). *Higher cortical functions in man.* New York, NY: Basic Books.

Mari, J. J., & Williams, P. (1986). A validity study of a Psychiatric Screening Questionnaire (SRQ-20) in primary care in the city of Sao Paulo. *The British Journal of Psychiatry*, *148*, 23—26.

Matochik, J. A., London, E. D., Eldreth, D. A., Cadet, J. L., & Bolla, K. I. (2003). Frontal cortical tissue composition in abstinent cocaine abusers: a magnetic resonance imaging study. *Neuroimage*, *19*, 1095—1102.

Miller, B. L., Cummings, J. L., Villanueva-Meyer, J., Boone, K., Mehringer, C. M., Lesser, I. M., et al. (1991). Frontal lobe degeneration: clinical, neuropsychological, and SPECT characteristics. *Neurology*, *41*, 1374—1382.

Nakaaki, S., Murata, Y., Sato, J., Shinagawa, Y., Matsui, T., Tatsumi, H., et al. (2007). Reliability and validity of the Japanese version of the Frontal Assessment Battery in patients with the frontal variant of frontotemporal dementia. *Psychiatry and Clinical Neurosciences*, *61*, 78—83.

Pombo, S., Levy, P., Bicho, M., Ismail, F., & Cardoso, J. M. N. (2008). Neuropsychological function and platelet monoamine oxidase activity levels in type I alcoholic patients. *Alcohol and Alcoholism*, *43*, 423—430.

Rice, C. (2007). Retest reliability of self-reported daily drinking: form 90. *Journal of Studies on Alcohol and Drugs*, *68*, 615—618.

Rodriguez del Alamo, A., Catalán Alonso, M. J., & Carrasco Marín, L. (2003). FAB: a preliminar Spanish application of the frontal assessment battery to 11 groups of patients. *Revista de Neurologia*, *36*, 605—608.

Rogers, R. D., & Robbins, T. W. (2001). Investigating the neurocognitive deficits associated with chronic drug misuse. *Current Opinion in Neurobiology*, *11*, 250—257.

Sarazin, M., Pillon, B., Giannakopoulos, P., Rancurel, G., Samson, Y., & Dubois, B. (1998). Clinicometabolic dissociation of cognitive functions and social behavior in frontal lobe lesions. *Neurology*, *51*, 142—148.

Silverstein, A. B. (1982). Two and four-subtest short forms of the Wechsler Adult Intelligence Scale-Revised. *Journal of Consulting and Clinical Psychology*, *50*, 415—418.

Sim, M. E., Lyoo, I. K., Streeter, C. C., Covell, J., Sarid-Segal, O., Ciraulo, D. A., et al. (2007). Cerebellar gray matter volume correlates with duration of cocaine use in cocaine-dependent subjects. *Neuropsychopharmacology*, *32*, 2229—2237.

Slachevsky, A., Villalpando, J. M., Sarazin, M., Hahn-Barma, V., Pillon, B., & Dubois, B. (2004). Frontal Assessment Battery and differential diagnosis of frontotemporal dementia and Alzheimer disease. *Archives of Neurology*, *61*, 1104—1107.

SPSS inc. (2005). SPSS for Windows, 14.0. Chicago, IL: SPSS inc.

Stroop, J. R. (1935). Studies of interference in serial verbal reaction. *Journal of Experimental Psychology*, *18*, 643—662.

Teichner, G., Horner, M. D., Roitzsch, J. C., Herron, J., & Thevos, A. (2002). Substance abuse treatment outcomes for cognitively impaired and intact outpatients. *Addictive Behaviors*, *27*, 751—763.

Toomey, R., Lyons, M. J., Eisen, S. A., Xian, H., Chantarujikapong, S., Seidman, L. J., et al. (2003). A twin study of the neuropsychological consequences of stimulant abuse. *Archives of General Psychiatry*, *60*, 303—310.

Verdejo-García, A., Bechara, A., Recknor, E. C., & Perez-Garcia, M. (2006). Executive dysfunction in substance dependent individuals during drug use and abstinence: An examination of the behavioral cognitive and emotional correlates of addiction. *Journal of the International Neuropsychological Society*, *12*, 405—415.

Verdejo-García, A. J., López-Torrecillas, F., Arcos, F. A., & Pérez-García, M. (2005). Differential effects of MDMA, cocaine, and cannabis use severity on distinctive components of the executive functions in polysubstance users: A multiple regression analysis. *Addictive Behaviors*, *30*, 89—101.

Verdejo-García, A. J., Perales, J. C., & Pérez-Garcia, M. (2007). Cognitive impulsivity in cocaine and heroin polysubstance abusers. *Addictive Behaviors*, *32*, 950—966.

Volkow, N. D., & Fowler, J. S. (2000). Addiction, a disease of compulsion and drive: involvement of the orbitofrontal cortex. *Cerebral Cortex*, *10*, 318—325.

Volkow, N. D., Hitzemann, R., Wang, G., Fowler, J. S., Wolf, A. P., Dewey, S., et al. (1992). Long-term frontal brain metabolic changes in cocaine abusers. *Synapse*, *11*, 184—190.

Washton, A. M. (1989). *Cocaine addiction: treatment, recovery and relapse prevention.* New York, NY: WW Norton & Company.

Wechsler, D. (1981). *Wechsler Intelligence Scale for Adults-Revised (WAIS-R).* New York, NY: The Psychological Corporation.