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Cognition and impulsivity in adults with attention deficit hyperactivity disorder with and without cocaine and/or crack dependence

Carmen S. Miguel[a,*], Paula A. Martins[b], Nathalya Moleda[c], Margarete Klein[a], Tiffany Chaim-Avancini[d], Maria A. Gobbo[a], Tania M. Alves[a], Maria A. Silva[a], Mario R. Louzã[a,b]

[a] Research Program for Attention Deficit Hyperactivity Disorder in Adults, Department of Psychiatry, University of São Paulo School of Medicine, Rua Dr. Ovídio Pires de Campos, 785—3° Andar, 05403-010 São Paulo, SP, Brazil
[b] Program for Early Evaluation and Treatment of Psychosis, Department of Psychiatry, University of São Paulo School of Medicine, Rua Dr. Ovídio Pires de Campos, 785—3° Andar, 05403-010 São Paulo, SP, Brazil
[c] Mackenzie Presbyterian University, Rua da Consolação, 930, 01302-907 São Paulo, SP, Brazil
[d] (LIM-21, Laboratory for Medical Research 21), specializing in Neuroimaging, Department of Psychiatry, University of São Paulo School of Medicine, Rua Dr. Ovídio Pires de Campos, 785, 05403-010 São Paulo, SP, Brazil

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ABSTRACT

Background: Substance use disorder (SUD) is a common comorbidity in adults with attention deficit-hyperactivity disorder (ADHD). However,there have been few studies on cognitive profiles of these patients. Impulsivity is also commonly increased in both disorders. The central aim of this study was to compare cognition and impulsivity in subjects who had ADHD and cocaine dependence (ADHD + COC group) to those with ADHD only (ADHD-noSUD group). We hypothesized that the ADHD + COC group would show more marked cognitive dysfunction and greater impulsivity than their counterparts with ADHD only.
Methods: A total of 70 adult patients diagnosed with ADHD according to (DSM-IV-TR) criteria were enrolled; 36 with ADHD + COC and 34 with ADHD-noSUD. All study participants were evaluated with a sociodemographic questionnaire; the Mini International Neuropsychiatric Interview; the Adult ADHD Self-Report Scale; the Addiction Severity Index; the Alcohol, Smoking and Substance Involvement Screening Test; the Barratt Impulsiveness Scale; and a comprehensive neurocognitive battery.
Results: Compared to individuals with ADHD-noSUD, ADHD + COC individuals had significantly lower mean IQ and higher motor impulsivity. On average, the ADHD + COC group also performed more poorly on tasks assessing verbal skills, vigilance, implicit learning during decision making, and ADHD-noSUD performed more poorly on selective attention, information processing, and visual search.
Conclusions: Our results support the integrative theory of ADHD based on the cognitive and affective neuroscience model, and suggests that ADHD-noSUD patients have impairments in cognitive regulation, while ADHD + COC patients have impairments in both cognitive and affective regulation.

1. Introduction

Attention deficit-hyperactivity disorder (ADHD) and substance use disorder (SUD) are common and often coexist in adults. The risk of developing cocaine (COC) abuse is two times higher in individuals with (vs. without) ADHD (Lee et al., 2011). The prevalence of ADHD is high among patients with COC dependence, reaching 23.1% (Van-Emmerick-Van Oortmerssen, 2012). Two recent studies of adults with COC dependence demonstrated considerable frequencies of comorbid ADHD: 20.5% (Pérez de los Cobos et al., 2011) and 25.0% (Daigre et al., 2013). Compared to their counterparts without ADHD, COC-dependent adults with ADHD are more severe in different aspects of the disorder: they initiated drug use at a younger age, were younger at first hospitalization, used COC more frequently or

* Corresponding author. Fax: +55 011 2661 7656.
E-mail address: carmen1sil@yahoo.com.br (C.S. Miguel).

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intensely, and were more likely to abandon treatments (Carroll and Rounsaville, 1993; Levin et al., 2007; Arias et al., 2008; Pérez de los Cobos et al., 2011).

Both patients with ADHD or SUD show deficits in executive function and high impulsivity and preference for immediate (versus delayed) rewards can promote drug addiction among individuals with ADHD (de Wit, 2009).

Studies of patients with both ADHD and SUD demonstrated cognitive impairments compared to those with ADHD alone or healthy controls. These include lower intelligence-quotient (IQ) scores, fewer years of education, as well as more marked deficits in working memory, verbal comprehension, perceptual organization, processing speed, and attention (Ginsberg et al., 2010; Bihlar Muld et al., 2013). On the other hand, COC-dependent patients with ADHD did not show differences in interference control (Stroop Test), time reproduction (visual time reproduction paradigm), attentional set-shifting (Trail Making Tasks A and B) and working memory (n-back Task) compared to their counterparts with ADHD only or healthy controls. Nevertheless, they had higher motor impulsivity with lower response inhibition (Stop Signal Task) and cognitive impulsivity (Delayed Discounting Test; Crunelle et al., 2013). Using the Barratt Impulsiveness Scale (BIS-11) Crunelle et al. (2013) also demonstrated higher attention impulsivity in the COC-dependent patients with ADHD compared to ADHD-only and healthy-control groups. Pérez de los Cobos et al. (2011), who compared patients with probable adult ADHD and concomitant COC dependence with COC dependence patients, reported that the former group had higher scores in the BIS-11 than the latter.

Two other studies investigated the impact of ADHD in COC use or dependence. Vonmoos et al. (2013), using a neuropsychological battery, observed that the presence of ADHD as a comorbidity either to recreational cocaine users or to dependent cocaine users worsened the scores of a global cognitive index in comparison to their counterparts without ADHD. Vergara-Moragues et al. (2011) used Barkley's Current Behavior Scale Self-Report to measure executive function in patients with COC dependence and ADHD, compared to COC dependence without ADHD.

The neuropsychological model proposed by Nigg and Casey (2005), considers that children with the ADHD-combined subtype have deficits in cognitive and affective control. This model posited that they have impairments in cognition related to executive control, in tasks that require prolonged effort and concentration. Such disruptions could weaken self-control (i.e., impaired cognitive regulation). In fact, a study showed that patients with ADHD or with SUD had deficits in executive function (Martínez-Raga and Knecht, 2012).

Nigg and Casey (2005) also suggested, however, that impairments in affective regulation, reward expectation, and delay aversion are observed in children with ADHD. These disruptions could lead to enhanced impulsivity and more marked emotional dysregulation (i.e., impaired affective regulation) in ADHD (Martel et al., 2009).

Although Nigg and Casey (2005) proposed their model in the context of childhood development, it seems to accommodate observations on adults with ADHD as well as SUD. One study has evaluated deficits in cognition and impulsivity in patients with both ADHD and COC dependence; but the study involved relatively small patient sample of ADHD and COC dependence ($n = 11$; Crunelle et al., 2013).

In order to address this knowledge gap, we undertook the present study to evaluate potential differences in executive function, verbal memory, and impulsivity between adults with ADHD and COC dependence (i.e., ADHD + COC group) or ADHD without substance use disorder (i.e., ADHD-noSUD group). We hypothesized that cognitive and emotional profiles would differ between the two groups, with the ADHD-noSUD group showing marked impairments in cognitive control and the ADHD + COC group exhibiting greater deficits in cognitive as well as emotional and motivational control.

2. Materials and methods

2.1. Participants

From May, 2010 through October, 2012, we included 70 patients with ADHD according to criteria from the *Diagnostic and Statistical Manual of Mental Disorders Fourth Edition (Text Revision;* DSM-IV-TR*;* American Psychiatric Association (APA), 2000). Cocaine-dependent patients with ADHD (designated the ADHD + COC group) were recruited from among those under treatment at a therapeutic community (Associação para Promoção da Oração e do Trabalho – APOT [Association for Promotion of Prayer and Work]) in the city of Campinas, Brazil, or from one of two inpatient units in the city of São Paulo, Brazil. These comprised the Detoxification Unit of Taipas General Hospital; and the Interdisciplinary Group for Alcohol and Drug Studies Clinic (GREA) at the Institute of Psychiatry of the Clinical Hospital of the Faculty of Medicine, University of São Paulo (Hospital das Clínicas da Faculdade de Medicina da Universidade de São Paulo; IPQ–HCFMUSP). We recruited patients who had ADHD but not SUD (designated the ADHD-noSUD group) from among those seeking treatment at the outpatient clinic of the Research Program for Attention Deficit Hyperactivity Disorder in Adults at the IPQ–HCFMUSP.

Eligible patients were between 18 and 60 years of age; had completed at least the fourth grade of elementary school; had IQ $\geq$ 80; and had received a diagnosis of ADHD according to DSM-IV-TR criteria but had no history of using ADHD medications. Also excluded in both subgroups were patients who had a history of: 1) a neurological conditions leading to loss of consciousness for >10 min (e.g., stroke, epilepsy, head trauma, ecc) and other neurological conditions that could impair cognition or 2) any serious medical condition.

Additional criteria for inclusion in the ADHD + COC group were: 1) receiving a diagnosis of powder or crack cocaine dependence (based on DSM-IV-TR criteria) and 2) having been abstinent for $\geq$15 days (as verified by urine testing). To be included in the ADHD-noSUD group, patients could not have a history of drug abuse or dependence.

2.2. Sociodemographic and clinical assessments

Sociodemographic data, including, age, gender, race, marital status, years of education, number of school-grades repeated, and employment status were collected in all patients. In the ADHD + COC subgroup, we collected data related to the preference and frequency of using powder or crack cocaine.

The diagnostic interview was based on the Structured Clinical Interview for DSM-IV-TR (APA 2000) and the Schedule for Affective Disorders and Schizophrenia for School-Age Children Present and Lifetime Version (KSADS-PL; Kaufman et al., 1997). All patients completed the 18-item Adult ADHD Self-Report Scale (ASRS; Mattos et al., 2006). The Mini International Neuropsychiatric Interview (MINI), version 5.0.0. (Amorim, 2000) was administered to both groups to verify the presence of 21 other psychiatric diagnosis and SUD. The Alcohol, Smoking, and Substance Involvement Screening Test (ASSIST), Henrique et al. (2004) was used to screen the level of risk of the involvement with different substances (Lower, Moderate, and High). Only the module Drugs and Alcohol Use from version 6 of the Addiction Severity Index (ASI; Kessler and Pechansky, 2006), was employed in both groups. The Barratt Impulsiveness Scale, version 11 (BIS-11; von Diemen et al., 2007), was administered to determine impulsivity (a detailed description can be found in Supplementary Material[1] - Methods CL).

2.3. Assessment of abstinence from psychoactive substance use

To verify abstinence from psychoactive-substance use, a urine drug screen kit was administered (Rapid Drug Screen; American Bio Medica Corporation, Kinderhook, NY, USA http://www.abmc.com/products/rapiddrugscreen.html) (For further details see Supplementary Material[2] – Methods UR).

2.4. Neuropsychological assessments

Neuropsychological assessments were conducted individually, in a fixed order, and in two sessions (to prevent fatigue). The complete assessment lasted an average of 2 h and was conducted at the institution from which the patient was recruited.

The neuropsychological battery comprised fourteen tests: Vocabulary and Matrix Reasoning subtests Wechsler Abbreviated Scale of Intelligence—WASI (Wechsler, 1999), Stroop Color-Word Interference Test (Strauss et al., 2006), Continuous Performance Test (CPT II; Multihealth Systems Inc., North Tonawanda, NY, USA), Trail Making Test —TMT (Strauss et al., 2006), Wisconsin Card-Sorting Test (WCST; Odessa FL, USA), Iowa Gambling Task (IGT; PAR Psychological Assessment Resources, Inc., Lutz, FL, USA), Digit Span and Letter-Number Sequencing subtests of the Wechsler Adult Intelligence Scale-Third Edition (WAIS III; Nascimento, 2004), Rey Auditory Verbal Learning Test—RAVLT (Strauss et al., 2006), Controlled Oral Word Association Test—FAS (Strauss et al., 2006), Logical Memory subtest Wechsler Memory Scale-Third Edition (Wechsler, 1997), Tower of Hanoi task (Spreen and Strauss, 1998), Reading the Mind in the Eyes Test (Sanvicente-Vieira et al., 2014; a detailed description can be found in Supplementary Material[3] – Methods NP).

2.5. Statistical analysis

To determine whether data were normally distributed, the Kolmogorov–Smirnov test was applied. A descriptive analysis of sociodemographic and clinical parameters included measures of central tendency and dispersion. Chi-square tests were used to compare categorical variables, and Student's *t*-test or the Mann-Whitney test to compare continuous variables, between the ADHD + COC and ADHD-noSUD groups.

Neuropsychological variables and BIS-11 subscale scores were compared in the ADHD+ COC and ADHD-noSUD groups via a logistic regression analysis. The *a priori* two-tailed α was 0.05. Data were processed and analyzed using the Statistical Package for the Social Sciences, version 14.0 for Windows (SPSS Inc., Chicago, IL, USA).

2.6. Ethical considerations

The study protocol and informed-consent document were approved by the Research Ethics Committee of FMUSP *Hospital das Clínicas* (Protocol no. 0788/09) in 2009. All study procedures used in this study were in accordance with the Helsinki Declaration of 1975 as revised in 2013. All participants provided written informed consent before any study assessment.

[1] Supplementary material can be found by accessing the online version of this paper at http://dx.doi.org and by entering doi:. . .

[2] Supplementary material can be found by accessing the online version of this paper at http://dx.doi.org and by entering doi:. . .

[3] Supplementary material can be found by accessing the online version of this paper at http://dx.doi.org and by entering doi:. . .

3. Results

3.1. Participants

Of 242 individuals screened, 70 subjects were included in the study: 36 in the ADHD + COC group and 34 in the ADHD-noSUD group (Fig. 1).

3.2. Sociodemographic characteristics

More than 70% of patients in each group were men. There were no statistically significant between-group differences in gender, age, or race. All subjects in the ADHD-noSUD group had ≥8 years of education, compared to 75% of those in the ADHD + COC group. A significantly higher proportion of subjects in the ADHD + COC group were married, whereas educational attainment and employment status were significantly (or borderline-significantly) inferior in this group compared to the ADHD-noSUD group variables (Table 1).

3.3. Clinical characteristics

In the ADHD + COC group compared to the ADHD-noSUD group, respectively, the ADHD subtype was categorized as predominantly inattentive (30.6% vs. 48.5%), predominantly hyperactive-impulsive (11.1% vs. 3.0%), or combined (58.3% vs. 48.5%). There was no significant difference between the groups in these three subtypes ($P = 0.194$). Psychiatric comorbidities were more common in the ADHD + COC group (Table 2). The risk of suicide was overall significantly higher in the ADHD + COC group: none (38.9% vs. 97.0%); low (38.9% vs. 3.0%); moderate (5.6% vs. 0%), and high (16.7% vs. 0%). Table 2 shows that proportions of subjects with current suicidality, lifetime antisocial personality disorder, current manic episodes, and/or current (within the past 2 years) dysthymia were significantly higher in the ADHD + COC (vs. the ADHD-noSUD) group (each $P \leq 0.007$). No tics- and Tourette syndrome were observed in our samples.

3.4. Psychoactive substance use

Use of tobacco was detected in 47.0% of the ADHD-noSUD group and 86.1% in the ADHD + COC group ($p < 0.001$). No patient had tobacco dependence. 94% of the ADHD-no SUD group reported use of alcohol and none had alcohol abuse or dependence (exclusion criteria for this group). In the ADHD +COC group, 22.2% had alcohol abuse and 63.9%, alcohol dependence.

Tobacco was the first substance to be consumed by both groups, at 13.32 ± 2.59 years and 14.26 ± 2.81 years, for the ADHD + COC and ADHD-noSUD groups respectively. The initiation of alcohol use was at 13.88 ± 1.90 years and 14.93 ± 1.94 years for the ADHD + COC and ADHD-noSUD groups respectively (no significant differences in both substances).

For the ADHD + COC group, the mean ±SD age at initiation of powdered cocaine use was 17.1 ± 2.4 years and crack use, 22.3 ± 6.8 years. The overall mean duration of abstinence was 83.8 ± 55.3 days; the mean number of treatment admissions was 2.6 ± 2.4; and the mean age on first admission was 25.6 ± 6.5 years. Table 3 shows the characteristics of other SUDs.

3.5. Neuropsychological characteristics and impulsivity

The ADHD + COC group had a significantly lower IQ compared with the ADHD-noSUD group: a mean ± SD of 92.44 ± 10.72 (range: 80–119) compared with 102.52 ± 12.32 (range: 80–126) ($P = 0.001$). Given this difference, we included IQ as a covariate in further statistical analyses (Table 4).

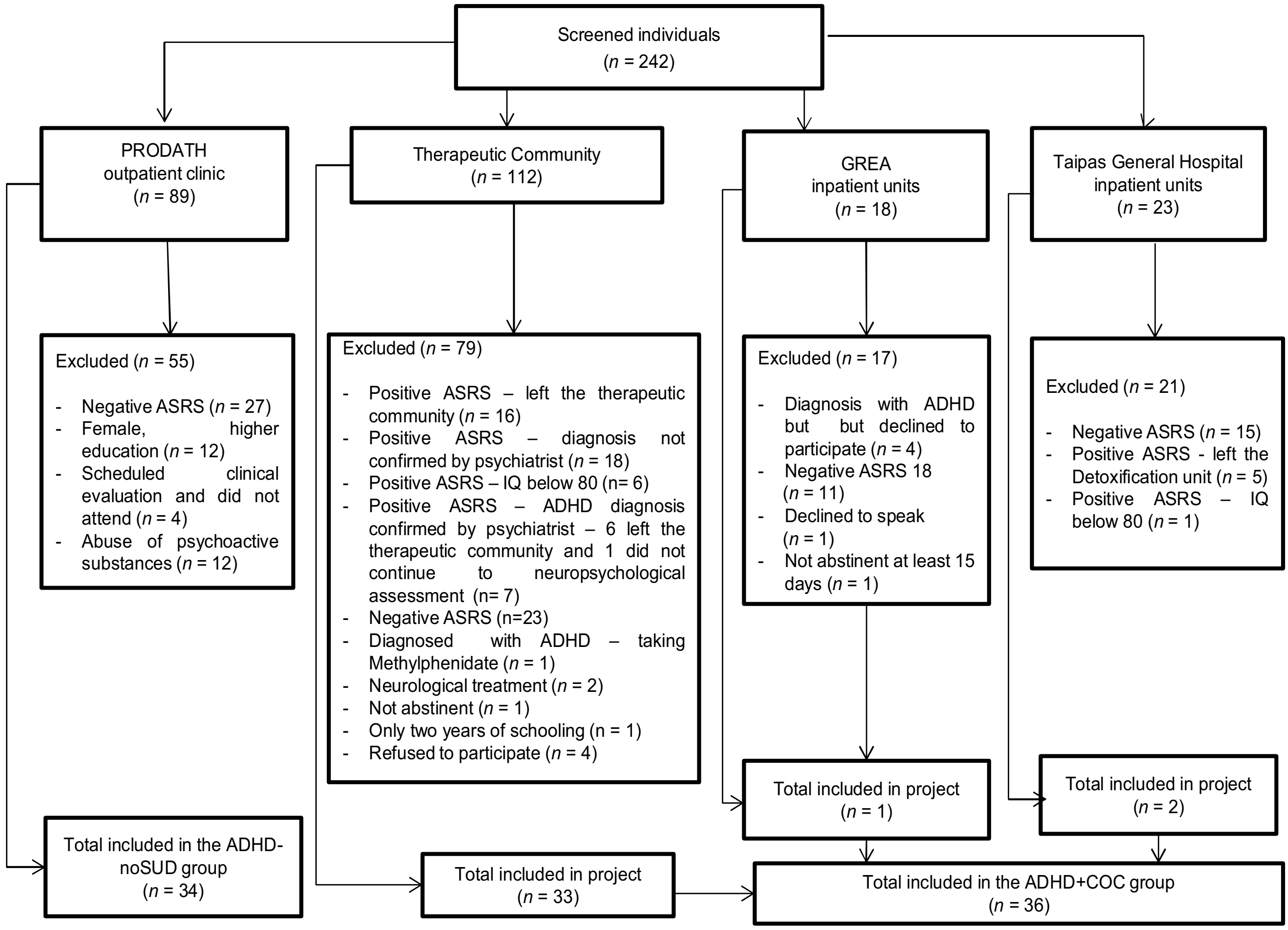

Fig. 1. Flow chart of screening procedures, diagnostic assessments, and subject enrollment.

Table 1
Sociodemographic characteristics.

Variable	ADHD + COC	ADHD-noSUD	*P value*
	(*n* = 36)	(*n* = 34)	
Male gender, *n* (%)	28 (77.7)	24 (70.6)	0.584
Age, mean ± SD	30.1 ± 7.5	28.2 ± 6.9	0.276
Race			
White, *n* (%)	25 (69.4)	21(61.8)	0.603
Black, *n* (%)	10 (27.8)	13 (38.2)	
Asian, *n* (%)	1 (2.8)	0 (0)	
Marital status			**0.020**
Single, *n* (%)	19 (52.8)	27 (79.4)	
Married, *n* (%)	16 (44.4)	6 (17.6)	
Divorced, *n* (%)	1 (2.8)	1 (2.9)	
Years of education, mean ± SD	11.3 ± 3.0	12.5 ± 1.7	0.051
School grades repeated (*n*), mean ± SD	1.9 ± 1.5	1.2 ± 1.3	**0.029**
Ever employed, *n* (%)	17 (47.2)	29 (85.3)	**0.020**

ADHD + COC: subjects with both attention deficit-hyperactivity disorder (ADHD) and cocaine dependence; ADHD-noSUD: subjects with ADHD but no substance use disorder. Bold: statistically significant values.

On the Stroop Test, trial 1 (color naming), the ADHD-noSUD group exhibited slower responses than did the ADHD + COC group (17.42 ± 4.37 vs. 14.73 ± 3.73 ms, respectively; $P = 0.002$). The ADHD-noSUD group also had slower responses in visual search and psychomotor speed (41.35 ± 13.60 vs. 36.00 ± 12.17 ms; $P = 0.016$). On the other hand, the ADHD + COC group showed longer reaction times and greater variability (hit reaction time block change) compared to the ADHD-noSUD group on the CPT (78.76 ± 157.97 vs. 46.92 ± 9.53 ms; $P = 0.017$).

Subjects in the ADHD + COC group on average, chose fewer advantageous cards than did individuals in the ADHD-noSUD group in Block 2 of the IGT (draws 21–40), (−0.70 ± 6.41 vs. 2.88 ± 6.34; $P = 0.039$).

On the BIS–11 subjects in the ADHD + COC group scored significantly higher than did those in the ADHD-noSUD group only in the motor impulsivity subscale (29.28 ± 5.23 vs. 26.12 ± 5.19; $P = 0.037$).

The comparative neurocognitive characteristics between ADHD + COC and ADHD-no SUD groups is presented in Fig. 2.

Table 2
Clinical characteristics (scores and diagnoses).

Variable	ADHD + COC	ADHD-noSUD	*P value*
	(*n* = 36)	(*n* = 34)	
ASRS: Inattention dimension score, mean ± SD	24.89 ± 4.34	29.09 ± 3.13	**<0.001**
ASRS: Hyperactivity/impulsivity dimension score, mean ± SD	24.33 ± 5.29	22.82 ± 5.93	0.265
MINI: Antisocial personality disorder— lifetime, *n* (%)	25 (69.4)	0 (0.0)	**<0.001**
MINI: Suicidality—current, *n* (%)	22 (61.1)	1 (2.9)	**<0.001**
MINI: Manic episode—current, *n* (%)	14 (38.9)	0 (0.0)	**<0.001**
MINI: Dysthymia—current (last 2 years), *n* (%)	10 (27.8)	1 (2.9)	**0.007**
MINI: Major depression episodcurrent (last 2 weeks), *n* (%)	16 (44.4)	12 (35.3)	0.625
MINI: Major depression episode—past, *n* (%)	8 (22.2)	7 (20.6)	1.000
MINI: Major depression episode with melancholic features, *n* (%)	9 (25.0)	8 (23.5)	1.000
MINI: Panic disorder—current, *n* (%)	5 (13.9)	0 (0.0)	0.550
MINI: Social phobia—current, *n* (%)	9 (25.0)	6 (17.6)	0.568
MINI: Posttraumatic stress disorder—current, *n* (%)	1 (2.8)	0 (0.0)	1.000
MINI: Generalized anxiety disorder—current, *n* (%)	6 (16.7)	8 (23.5)	0.553

ADHD + COC: subjects with both attention deficit-hyperactivity disorder (ADHD) and cocaine dependence; ADHD-noSUD: subjects with ADHD but no substance use disorder. ASRS, Adult ADHD Self-Report Scale; MINI: Mini International Neuropsychiatric Interview, version 5.0.0. Bold: statistically significant values.

Table 3
Characteristics of current substance use.

Variable	ADHD + COC	ADHD = noSUD
	(*n* = 36)	(*n* = 34)
MINI: Powder cocaine dependence, *n* (%)	28 (77.8)	0 (0.0)
MINI: Powder cocaine abuse, *n* (%)	8 (22.2)	0 (0.0)
MINI: Crack cocaine dependence, *n* (%)	21 (58.3)	0 (0.0)
MINI: Crack cocaine abuse, *n* (%)	1 (2.8)	0 (0.0)
MINI: Alcohol dependence, *n* (%)	23 (63.9)	0 (0.0)
MINI: Alcohol abuse, *n* (%)	8 (22.2)	0 (0.0)
MINI: Marijuana dependence, *n* (%)	8 (22.2)	0 (0.0)
MINI: Marijuana abuse, *n* (%)	2 (5.6)	0 (0.0)
ASSIST: Had smoked marijuana at least once, *n* (%)	0 (0.0)	5 (14.7)
MINI: Inhalant dependence, *n* (%)	2 (5.6)	0 (0.0)
MINI: Inhalant abuse, *n* (%)	1 (2.8)	0 (0.0)
MINI: Tranquilizer dependence, *n* (%)	1 (2.8)	0 (0.0)
MINI: Daily use of illicit psychoactive substance, *n* (%)	27 (77.1)	0 (0.0)
Q: Preference for powder cocaine and alcohol, *n* (%)	19 (52.8)	0 (0.0)
Q: Preference for powder cocaine exclusively, *n* (%)	8 (22.2)	0 (0.0)
Q: Preference for crack cocaine use, *n* (%)	12 (33.3)	0 (0.0)
Q: Did not use crack cocaine, *n* (%)	14 (38.9)	0 (0.0)

ADHD + COC: subjects with both attention deficit-hyperactivity disorder (ADHD) and cocaine dependence; ADHD-noSUD: subjects with ADHD but no substance use disorder; ASSIST: Alcohol, Smoking, and Substance Involvement Screening Test; MINI: Mini International Neuropsychiatric Interview, version 5.0.0; Q: sociodemographic questionnaire.

We found no significant differences between groups in: 1) reasoning, conceptualization, and mental flexibility when confronted with new situations created by the environment (WCST); 2) auditory attention and verbal working memory (Digit Span and SLN); 3) verbal learning and memory (RAVLT, Logical Memory); 4) planning and problem-solving abilities (Tower of Hanoi); 5) inferring the mental states of others (Reading the Mind in the Eyes Test) and 6) verbal fluency (FAS).

4. Discussion

These findings support our hypothesis that there are significant differences in executive function and impulsivity between patients with ADHD + COC compared to the ADHD-noSUD patients. Subjects in our ADHD + COC group had significantly lower verbal IQ, verbal skills, vigilance, and poorer implicit learning in an affective decision making task, as well as greater motor impulsivity as measured by both neuropsychological tasks and the BIS-11. On the other hand, subjects in our ADHD-noSUD group showed more prominent deficits in selective attention, visual search, and processing speed.

Although the lower mean IQ in our ADHD + COC group was an unexpected finding, it corroborates reported data on children with ADHD (Biederman et al., 2012; Tsai et al., 2013) as well as prison inmates with ADHD and a history of SUD (Ginsberg et al., 2010). One possible explanation for our observation of lower IQ scores in our ADHD + COC group is that vigilance deficits impaired mental efforts to perform tasks such as the WASI Vocabulary subtest. Other possibility is that lifetime substance use could have reduced IQ as shown by Meier et al. (2012) in a longitudinal study with persistent cannabis users.

The impaired verbal skills of the ADHD + COC group reflect on the significant differences between the groups in relation to formal crystallized intelligence but not on fluid intelligence. This is consistent with an overall lower level of education and higher frequency of grade repetition, also described in patients with ADHD (Kuriyan et al., 2013). On the other hand, we did not find differences in verbal learning between the groups, suggesting that our results could be explained in part by differences in executive function.

Children with ADHD and executive dysfunction were twice as likely to repeat a grade as those without such dysfunctions (Biederman et al., 2004). It is also possible that a greater impulsivity and impatience among subjects in the ADHD + COC group could led these patients to provide shorts and less elaborated answers to the tests questions. The relationship between lower IQ and impaired verbal skills in the ADHD + COC group also might be influenced by multiple, interacting factors related to ADHD and/or SUD, such as age of onset of substance use (Capella et al., 2015) and the presence of conduct disorder that is frequently observed in ADHD, anxiety and SUD patients (Burton, 2014) and antisocial personality disorder is present in a high percentage in our ADHD + COC sample.

Table 4
Results (mean ± standard deviation) of the neuropsychological tests and Barratt Impulsivity Scale (BIS-11) and of the logistic regression (groups as dependent variable).

Variable	ADHD + COC M (SD)	ADHD-no SUD M (SD)	β	S.E.	*P value*
WASI: Vocabulary	48.08 (8.91)	55.44 (7.34)	0.115	0.035	**0.001**
WASI: Matrix Reasoning	24.00 (4.58)	27.50 (6.48)	−0.062	0.094	0.512
Stroop: task 1	14.73 (3,73)	17.29 (4,37)	0.301	0.95	**0.002**
Stroop: task 1 errors	0.00 (0.00)	0.17 (0.75)	9.849	10265.06	0.999
Stroop: task 2	18.70 (5.50)	19.76 (4.36)	0.090	0.056	0.108
Stroop: task 2 errors	0.00 (0.00)	0.02 (0.17)	22.222	40192.96	1.000
Stroop: task 3	29.35 (10.28)	28.50 (9.68)	0.025	0.028	0.360
Stroop: task 3 errors	0.38 (0.65)	0.50 (1.13)	0.178	0.305	0.560
TMT-A	36.00 (12.17)	41.21 (13.40)	0.062	0.026	**0.016**
TMT-B	96.00 (46.03)	84.65 (32.10)	0.001	0.008	0.871
CPT: omission	5.42 (7.20)	3.73 (5,34)	−0.051	0.042	0.232
CPT: commission	20.74 (9,34)	16.91 (7.72)	−0.039	0.031	0.212
CPT: perseverations	1.82 (2.97)	1.05 (1.70)	−0.131	0.118	0.268
CPT: Hit RT	376.19 (56.39)	374.30 (50.07)	−0.001	0.005	0.832
CPT: Hit RTBC	27.75 (166.49)	−0,006 (0,024)	−32.210	13.448	**0.017**
CPT: Hit SEBC	27.76 (166.49)	0.014 (0.076)	−1.455	3.757	0.699
CPT: Hit RTIS	27.80 (166.49)	0.042 (0.028)	−14.615	8.899	0.101
CPT: Hit SEIS	27.76 (166.49)	−0.015 (0.091)	−3.007	2.525	0.234
IGT: Block 1 (1–20)	−3.16 (6.21)	−2.29 (3.58)	0.066	0.057	0.243
IGT: Block 2 (21–40)	−0.70 (6.41)	2.88 (6.34)	0.098	0.047	**0.039**
IGT: Block 3 (41–60)	3.67 (6.45)	3.17 (7.06)	−0.040	0.044	0.368
IGT: Block 4 (61–80)	1.93 (8.84)	4.94 (7.61)	0.029	0.034	0.394
IGT: Block 5 (81–100)	1.61 (9.08)	4.76 (8.47)	0.027	0.032	0.397
IGT: total net score	3.35 (22.54)	13.47 (22.45)	0.017	0.013	0.195
BIS-11: attentional	23.74 (3.49)	23.60 (3.16)	0.004	0.083	0.958
BIS-11: motor	29.28 (5.23)	26.12 (5.19)	−0.115	0.055	**0.037**
BIS-11: non-planning	31.00 (6.10)	30.78 (5.06)	−0.009	0.048	0.859
BIS-11: total	84.02 (11.67)	80.51 (9.76)	−0.031	0.026	0.244

ADHD + COC: subjects with both attention deficit-hyperactivity disorder (ADHD) and cocaine dependence; ADHD-noSUD: subjects with ADHD but no substance use disorder; BIS–11: Barratt Impulsiveness Scale, version 11CPT: Continuous Performance Test, computerized version; IGT: Iowa Gambling Task, computerized version; RT, reaction time; RTBC, reaction time by block change; SEBC, Standard Error by block change; RTIS, Reaction Time by Inter-Stimulus Interval; SEIS, Standard Error by Inter-Stimulus Interval; TMT: Trail Making Test. WAIS: Wechsler Adult Intelligence Scale-Third Edition Bold: statistically significant values.

The two groups show differences in their attentional profile, suggesting differences in their strategies and efforts to finish their tasks with success. In our study, the ADHD-noSUD group, compared to the ADHD + COC group, is slower in the execution of some tasks that are time-dependent, maybe a strategy to reduce errors due to distraction.

Our ADHD-noSUD (vs. ADHD + COC) group had greater difficulty in sensorial and perceptual processing when only color naming is required (Stroop test, part A), but we did not observe differences in the congruent word-color naming (Stroop test, part B) and the interference word-color naming (Stroop test, part C). This is also described in children with ADHD and suggests that they have impairments in sensorial and perceptual processes because color naming is more complex than word-color naming when semantic and perceptual processing occur simultaneously (Tannock et al., 2006).

Subjects in our ADHD-noSUD group has performed more poorly on psychomotor speed and visual search compared to the ADHD + COC group. This finding is compatible with results from other studies (Holdnack et al., 1995; Johnson et al., 2001) and suggests that individuals with ADHD may reduce their psychomotor speed as a strategy to help them understand the requirements of a task.

Otherwise, the ADHD + COC group was faster in the execution of tasks requiring selective and divided attention, but their higher variability of response in vigilance suggests difficulty in maintaining vigilance while executing tasks over time. A study with ADHD patients showed that variability in reaction time during task performance was linked to hyperactivity and impulsivity (Epstein et al., 2003). The greater motor impulsivity observed in the ADHD + COC group might exacerbate this difficulty. The poorer performance of our ADHD + COC group in Block 2 of the IGT, which requires strategic skills at the initial stage of implicit learning (Brand et al., 2007), suggests that COC-dependent individuals with ADHD are essentially gambling but unaware of the punishment ("loss of money") they receive. This inference is consistent with data from Kjome et al. (2010), in which COC-dependent patients were strongly responsive to rewards during early learning stages; compromising their decision-making ability. Learning processes are also linked to affective and emotional systems (Stocco and Fum, 2008; Wagar and Ixon, 2006) so that the higher impulsivity observed during the IGT could be related to learning difficulties (Upton et al., 2011). Conversely, qualitative assessments showed that children with ADHD alone were less sensitive to penalties, as assessed via the IGT (Humphreys and Lee, 2011). Toplak et al. (2005), applying the IGT, reported that adolescents with ADHD and conduct disorder, learning disability, anxiety, depression or oppositional-defiant disorder exhibited more risk-taking behaviors than did healthy controls, what was also observed in our ADHD + COC group, that presented a high frequency of other comorbidities besides SUDs.

Studies in children with ADHD demonstrated that learning mechanisms interacted with cognitive and emotional processes, so that such children have difficulties in detecting regularities and irregularities in their environment, potentially impairing cognitive control (Nigg and Casey, 2005). Taken together with the evidence of poor performance by our ADHD + COC group on Block 2 of the IGT, these difficulties could explain differences in learning processes between our ADHD + COC and ADHD-noSUD groups only at the IGT task onset. This intergroup disparity could also be related to greater variability in vigilance processes among patients in our ADHD + COC group, suggesting that such individuals need time to adjust their performance in a monotonous and lengthy task. The greater motor impulsivity in our ADHD + COC group is indicative of difficulty in thinking before acting, what might also influence the decision making process. Cocaine craving has been associated with greater motor impulsivity subscore in the BIS-11, although not with

Variables	ADHD+COC	ADHD-no SUD
Estimated IQ	↓	↑
Vigilance	↓	↑
Implicit learning in affective decision making	↓	↑
Verbal skills	↓	↑
Visual search, psychomotor speed	↑	↓
Color naming	↑	↓
Motor impulsiveness	↑	↓

Fig. 2. Comparative neurocognitive characteristics between the ADHD + COC and the ADHD-no SUD groups.

the total BIS-11 score (Moeller et al., 2001). In terms of the model proposed by Nigg and Casey (2005), which included cognitive and affective domains, our ADHD-noSUD patients showed impairment only in the cognitive (i.e., self-control), whereas our ADHD + COC group showed deficits in both cognitive and affective mechanisms.

Our results are in some aspects not comparable with those of Crunelle et al. (2013), who did not find differences between ADHD and ADHD + COC in relation to most of the neuropsychological tasks used, except in motor and cognitive impulsivity. In our study, comparatively, the ADHD + COC group showed a more impaired profile in impulsivity and vigilance while the ADHD-noSUD were more impaired in some attentional characteristics. The differences between our studies could be related to differences in sample sizes and in some characteristics of our sample (e.g., our ADHD + COC were inpatients, probably more severe than her outpatients). The presence of other comorbidities as well the lower IQ in our sample could suggest that our ADHD + COC patients have a more severe disorder (Arias et al., 2008; Bihlar Muld et al., 2013). Duration of abstinence could also influence the results. Potvin et al. (2014) in a review, conclude that cognitive deficits are more intense in the first weeks of abstinence but show a trend to improve after 5 months of maintained abstinence.

4.1. *Study strengths and limitations*

Strengths of our study include the sample size, the inclusion of male and female patients and a comprehensive neuropsychological battery. Otherwise, the predominance of male subjects in our sample precluded stratification of patients by gender; our sample size also did not allow to examine the ADHD subtypes and type of cocaine used (powder or crack). It was also not possible to exclude the influence of other comorbidities besides SUD on the neuropsychological evaluation (Zulauf et al., 2014). The main limitation of our study is that our analysis is restricted because we did not include a group of healthy controls and COC-dependent subjects without ADHD.

Our results should be generalized with caution, because the ADHD + COC participants were hospitalized and therefore likely to present with more severe symptoms compared to their community-dwelling counterparts.

Future studies should include in the investigation groups of healthy controls and COC dependent patients (without ADHD) and other methods besides neuropsychological testing (e.g. neuroimaging) in order to better understand possible neurobiological differences among these groups of subjects.

4.2. *Conclusions*

According to the neurocognitive model proposed by Nigg and Casey (2005) we may conclude that patients with ADHD-noSUD have impairments in cognitive regulation while in patients with ADHD + COC both cognitive and affective regulation are impaired.

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Conflict of interest

No competing interests.

Contributors

C.S. Miguel designed the study, collected the data, interpreted the results, and wrote the first draft, M. R. Louzã contributed to designing the study, collected the data, analyzed the data, and participated in writing the manuscript. P. A. Martins, N. Moleda, M. Klein, M. A. Gobbo, T. Chaim-Avancini, T. M. Alves, and M. A. Silva collected the data. All authors contributed to and approved the final manuscript.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.drugalcdep.2015.12.040.

References

American Psychiatric Association (APA), 2000. Diagnostic and Statistical Manual of Mental Disorders, fourth ed. Text Revised (DSM-IV-TR), APA, Washington.

Amorim P., 2000. Mini International Neuropsychiatric Interview (MINI): Validação de entrevista breve para diagnóstico de transtornos mentais. [Mini International Neuropsychiatric Interview (MINI): validation of a short structured diagnostic psychiatric interview] Rev. Bras. Psiq. 22, 106-115. Portuguese.

Arias, A.J., Gelernter, J., Chan, G., Weiss, R.D., Brady, K.T., Farrer, L., Kranzler, H.R., 2008. Correlates of co-occurring ADHD in drug-dependent subjects: prevalence and features of substance dependence and psychiatric disorders. Addict. Behav. 33, 1199–1207.

Biederman, J., Fried, R., Petty, C., Mahoney, L., Faraone, S.V., 2012. An examination of the impact of attention-deficit hyperactivity disorder on IQ: a large controlled family-based analysis. Can. J. Psychiatry 57, 608–616.

Biederman, J., Monuteaux, M.C., Doyle, A.E., Seidman, L.J., Wilens, T.E., Ferrero, F., Morgan, C.L., Faraone, S.V., 2004. Impact of executive function deficits and attention-deficit/hyperactivity disorder (ADHD) on academic outcomes in children. J. Consult. Clin. Psychol. 72, 757–766.

Bihlar Muld, B., Jokinen, J., Bolte, S., Hirvikoski, T., 2013. Attention deficit/hyperactivity disorders with co-existing substance use disorder is characterized by early antisocial behaviour and poor cognitive skills. BMC Psychiatry 13, 336.

Brand, M., Recknor, E.C., Grabenhorst, F., Bechara, A., 2007. Decisions under ambiguity and decisions under risk: correlations with executive functions and comparisons of two different gambling tasks with implicit and explicit rules. J. Clin. Exp. Neuropsychol. 29, 86–99.

Burton, M., 2014. Children and young people's mental health. In: Burton, M., Pavord, E., Williams, B. (Eds.), An Introduction To Child And Adolescent Mental Health. SAGE Publications Ltd, London, pp. 1–38.

Carroll, K.M., Rounsaville, B.J., 1993. History and significance of childhood attention deficit disorder in treatment-seeking cocaine abusers. Compr. Psychiatry 34, 75–82.

Crunelle, C.L., Veltman, D.J., van Emmerik-van Oortmerssen, K., Booij, J., van den Brink, W., 2013. Impulsivity in adult ADHD patients with and without cocaine dependence. Drug Alcohol Depend. 129, 18–24.

Daigre, C., Roncero, C., Grau-López, L., Martínez-Luna, N., Prat, G., Valero, S., Tejedor, R., Ramos-Quiroga, J.A., Casas, M., 2013. Attention deficit hyperactivity disorder in cocaine-dependent adults: a psychiatric comorbidity analysis. Am. J. Addict 22, 466–473.

de Wit, H., 2009. Impulsivity as a determinant and consequence of drug use: a review of underlying processes. Addict. Biol 14, 22–31.

Epstein, J.N., Erkanli, A., Conners, C.K., Klaric, J., Costello, J.E., Angold, A., 2003. Relations between Continuous Performance Test performance measures and ADHD behaviors. J. Abnorm. Child Psychol. 31, 543–554.

Ginsberg, Y., Hirvikoski, T., Lindefors, N., 2010. Attention Deficit Hyperactivity Disorder (ADHD) among longer-term prison inmates is a prevalent, persistent and disabling disorder. BMC Psychiatry 10, 112.

Henrique, I.F.S., De Micheli, D., Lacerda, R.B., Lacerda, L.A., Formigoni, M.L.S., 2004. Validação da versão brasileira do teste de triagem do envolvimento com álcool, cigarro e outras substâncias (ASSIST) [Validation of the Brazilian version of Alcohol, Smoking and Substance Involvement Screening Test (ASSIST)]. Rev. Assoc. Med. Bras. 50, 199–206, Portuguese.

Holdnack, J.A., Moberg, P.J., Arnold, S.E., Gur, R.C., Gur, R.E., 1995. Speed of processing and verbal learning deficits in adults diagnosed with attention deficit disorder. Cogn. Behav. Neurol. 8, 282–292.

Humphreys, K.L., Lee, S.S., 2011. Risk taking and sensitivity to punishment in children with ADHD, ODD, ADHD + ODD, and controls. J. Psychopathol. Behav., Assess. Availabe from. http://www.kathrynhumphreys.com/uploads/4/3/0/6/43065295/humphreys_2011_risk_taking.pdf; Last accessed: (11.09.15.).

Johnson, D.E., Epstein, J.N., Waid, L.R., Latham, P.K., Voronin, K.E., Anton, R.F., 2001. Neuropsychological performance deficits in adults with attention deficit/hyperactivity disorder. Arch. Clin. Neuropsychol. 16, 587–604.

Kaufman, J., Birmaher, B., Brent, D., Rao, U., Flynn, C., Moreci, P., Williamson, D., Ryan, N., 1997. Schedule for Affective Disorders and Schizophrenia for school-age children-present and lifetime version (K-SADS-PL): initial reliability and validity data. J. Am. Acad. Child Adolesc. Psychiatry 36, 980–988.

Kessler, F., Pechansky, F., 2006. Escala de Gravidade de Dependência (ASI6) para o Brasil [The Addiction Severity Index (ASI) Version 6 to Brazil]. Portuguese. Available from http://www.cpad.org.br/site2/br/asi6-apresentacao Last accessed: 11/09/2015.

Kjome, K.L., Lane, S.D., Schmitz, J.M., Green, C., Ma, L., Prasla, I., Swann, A.C., Moeller, F.G., 2010. Relationship between impulsivity and decision making in cocaine dependence. Psychiatry Res. 178, 299–304.

Kuriyan, A.B., Pelham Jr., W.E., Molina, B.S.G., Waschbusch, D.A., Gnagy, E.M., Sibley, M.H., Babinski, D.E., Walther, C., Cheong, J., Yu, J., Kent, K.M., 2013. Young adult educational and vocational outcomes of children diagnosed with ADHD. J. Abnorm. Child Psychol. 41, 27–41.

Lee, S.S., Humphreys, K.L., Flory, K., Liu, R., Glass, K., 2011. Prospective association of childhood attention-deficit/hyperactivity disorder (ADHD) and substance use and abuse/dependence: a meta-analytic review. Clin. Psychol. Rev. 31, 328–341.

Martel, M.M., Nigg, J.T., von Eye, A., 2009. How do trait dimensions map onto ADHD symptom domains? J. Abnorm. Child Psychol. 37, 337–348.

Martínez-Raga, J., Knecht, C., 2012. Patológía Dual –Protocolos de intervención –TDAH. Sociedad Española de Patologia Dual. Available from http://www.patologiadual.es/docs/protocolos_patologiadual_modulo5. pdf Last accessed 07/18/2015.

Mattos, P., Segenreich, D., Saboya, E., Louzã, M., Dias, G., Romano, M., 2006. Adaptação transcultur para o portugués da escala Adult Self-Report Scale para avaliação do Transtorno de Déficit de Atenção/Hiperatividade (TDAH) em adultos [Transcultural adaptation of the Adult Self-Report Scale into Portuguese for evaluation of adult attention-deficit/hyperactivity disorder (ADHD)]. Rev Psiq Clin. 33,188-194. Available from http://www.scielo.br/scielo.php?script=sci_arttext&pid=S0101-60832006000400004>. Last accessed 11/09/2015.al.

Meier, M.H., Caspi, A., Ambler, A., Harrington, H., Houts, R., Keefe, R.S., McDonald, K., Ward, A., Poulton, R., Moffitt, T.E., 2012. Persistent cannabis users show neuropsychological decline from childhood to midlife. Proc. Natl. Acad. Sci. U. S. A. 109, E2657–E2664.

Moeller, F.G., Dougherty, D.M., Barratt, E.S., Schmitz, J.M., Swann, A.C., Grabowski, J., 2001. The impact of impulsivity on cocaine use and retention in treatment. J. Subst. Abuse Treat. 21, 193–198.

Nascimento E., 2004. WAIS-III –Escala de Inteligência Wechsler para adultos. 3º ed. Manual para administração e avaliação –Adaptação e padronização de uma amostra brasileira. [WAIS III Wechsler Intelligence Scale for adults. 3rd ed. Administration and Scoring Manual]. São Paulo: Casa do Psicólogo. Portuguese.

Nigg, J.T., Casey, B.J., 2005. An integrative theory of attention-deficit/hyperactivity disorder base don the cognitive and affective neurosciences. Dev. Psychopathol. 17, 785–806.

Pérez de los Cobos, J., Siñol, N., Puerta, C., Cantillano, V., López Zurita, C., Trujols, J., 2011. Features and prevalence of patients with probable adult attention deficit hyperactivity disorder who request treatment for cocaine use disorders. Psychiatry Res. 185, 205–210.

Potvin, S., Stavro, K., Rizkallah, E., Pelletier, J., 2014. Cocaine and cognition: a systematic quantitative review. J. Addict Med. 8, 368–376.

Sanvicente-Vieira, B., Kluwe-Schiavon, B., Wearick-Silva, L.E., Piccoli, G.L., Scherer, L., Tonelli, H.A., Grassi-Oliveira, R., 2014. Revised Reading the Mind in the Eyes Test (RMET) –Brazilian version. Rev Bras Psiquiatr., 60–67.

Spreen, O., Strauss, E., 1998. Compendium of Neuropsychological Tests: Administration. In: Norms and Commentary. Oxford University Press, New York.

Stocco, A., Fum, D., 2008. Implicit emotional biases in decisión making: the case of the Iowa Gambling task. Brain Cogn. 66, 253–259.

Strauss, E., Sherman, E.M.S., Spreen, O.A., 2006. Compendium Of Neuropsychological Tests: Administration. In: Norms and Commentary. Oxford University Press, New York.

Tannock, R., Banaschewski, T., Gold, D., 2006. Color naming deficits and attention-deficit/hyperactivity disorder: a retinal dopaminergic hypothesis. Behav. Brain Funct. 27, 2–4.

Toplak, M.E., Jain, U., Tannock, R., 2005. Executive and motivational processes in adolescents with Attention-Deficit Hyperactivity Disorder (ADHD). Behav. Brain Funct. 27, 1–8.

Tsai, C.S., Huang, Y.S., Wu, C.L., Hwang, F.M., Young, K.B., Tsai, M.H., Chu, S.M., 2013. Long-term effects of stimulants on neurocognitive performance of taiwanese children with attention-deficit/hyperactivity disorder. BMC Psychiatry 4, 330, 13.

Upton, D.J., Bishara, A.J., Ahn, W.Y., Stout, J.C., 2011. Propensity for risk taking and trait impulsivity in the Iowa Gambling Task. Pers. Individ. Dif. 50, 492–495.

Vergara-Moragues, E., González-Saiz, F., Lozano Rojas, O., Bilbao Acedos, I., Fernández Calderón, F., Betanzos Espinosa, P., Verdejo García, A., Pérez García, M., 2011. Diagnosing adult attention deficit/hyperactivity disorder in patients with cocaine dependence: discriminant validity of Barkley executive dysfunction symptoms. Eur. Addict. Res. 17, 279–284.

von Diemen, L., Szobot, C.M., Kessler, F., Pechansky, F., 2007. Adaptation and construct validation of the Barratt Impulsiveness Scale (BIS 11) to Brazilian Portuguese for use in adolescents. Rev. Bras. Psiquiatr. 29, 153–156.

Vonmoos, M., Hulka, L.M., Preller, K.H., Jenni, D., Baumgartner, M.R., Stohler, R., Bolla, K.I., Quednow, B.B., 2013. Cognitive dysfunctions in recreational and dependent cocaine users: role of attention-deficit hyperactivity disorder, craving and early age at onset. Br. J. Psychiatry 203, 35–43.

Wagar, B.M.D., Ixon, M., 2006. Affective guidance in the Iowa Gambling Taskn. Cogn. Affect. Behav. Neurosci. 6, 277–290.

Wechsler, D., 1997. Wechsler Memory Scale –III: Administration And Scoring Manual. The Psychological Corporation, San Antonio, TX.

Wechsler, D., 1999. Wechsler Abbreviated Scale of Intelligence (WASI) Manual. The Psychological Corporation, San Antonio, TX.

Zulauf, C.A., Sprich, S.E., Safren, S.A., Wilens, T.E., 2014. The complicated relationship between attention deficit/hyperactivity disorder and substanace use disorders. Curr. Psychiatry Rep. 16, 436.