



Distinct cognitive performance and patterns of drug use among early and late onset cocaine users



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ABSTRACT

Introduction: Adolescence is a crucial period for neurodevelopment, but few studies have investigated the impact of early cocaine use on cognitive performance and patterns of substance use.

Methods: We evaluated 103 cocaine dependent inpatients divided in two groups: early-onset users (EOG; n = 52), late-onset users (LOG; n = 51), and 63 healthy controls. Neuropsychological functioning was evaluated using Digits Forward (DF) and Backward (DB), Trail Making Test (TMT), Stroop Color Word Test (SCWT), Controlled Oral Word Association Test (COWAT), Wisconsin Card Sorting Test (WCST), Rey Osterrieth Complex Figure Test (ROCF), Frontal Assessment Battery (FAB), and Iowa Gambling Test (IGT). Use of alcohol and other drugs was assessed with the Addiction Severity Index (ASI-6).

Results: Analyses of covariance controlling for age, IQ and years of education showed that EOG presented worse performance in attention span (DF, p = 0.020), working memory (DB, p = 0.001), sustained attention (WCST, p = 0.030), declarative memory (ROCF, p = 0.031) and general executive functioning (FAB, p = 0.003) when compared with the control group. LOG presented impairments on divided attention (TMT, p = 0.003) and general executive functioning (FAB, p = 0.001) in relation to the control group. EOG presented higher use of cannabis and alcohol than LOG (p ≤ 0.001).

Conclusion: Early-onset cocaine users display more pronounced neuropsychological alterations than controls, as well as a greater frequency of polydrug consumption than LOG. The prominent cognitive deficits in EOG probably reflect the deleterious interference of cocaine use with early stages of neurodevelopment. This may be related to more severe clinical characteristics of substance disorder in this subgroup, including polysubstance abuse.

1. Introduction

Substance use disorder is mainly characterized by a problematic pattern of continuous drug use, despite negative consequences (APA, 2013). Cocaine is one of the most addictive substances (UNODC, 2015) so its excessive and repeated use is considered a major public health issue (National Institute on Drug Abuse, 2010; UNODC, 2015).

Cocaine dependent individuals (CDI) usually presents with impairments in cognitive functioning that may negatively impact their behavior (Lubman, Yücel & Pantelis, 2004; Vonmoos et al., 2013; Vonmoos et al., 2014; Cunha, Bechara, de Andrade & Nicastrì, 2011). Longer periods of drug use are associated with worse neuropsychological performance (Madoz-Gúrpide, Blasco-Fontecilla, Baca-García & Ochoa-Mangado, 2011). Furthermore, both recreational and

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chronic cocaine users show evidence of cognitive impairments, more specifically in executive functioning (EF) (Vonmoos et al., 2013). EF is characterized by the ability to adapt to new situations through different domains such as cognitive flexibility, response inhibition, conflict monitoring and working memory (Collette, Hogge, Salmon & Van der Linden, 2006). Recently, our group reported some improvement in attention and EF after one month of abstinence (Gonçalves et al., 2014).

Adolescence is known as a transition period from childhood to adulthood, which represents a significant step for neurodevelopment and it includes significant opportunities and vulnerabilities (Dahl, 2004; Monti et al., 2005). In this period, the brain is under prominent changes and continues to develop until it reaches its maturity (Shaw et al., 2008). These changes occur due to a refinement in the neural structure (Blakemore, 2012), mainly guided by the development of the circuitry of the prefrontal cortex (PFC) (Liston et al., 2005). The PFC is known to be critical to EF and difficulties in impulse control in adolescents occur due to an increased sensitivity to motivational cues that challenge the less mature cognitive control system, represented by the PFC itself (Somerville & Casey, 2010). Therefore, it is plausible to suppose that excessive and repeated use of cocaine particularly in this period may negatively impact the complex process of brain maturation outlined above. However, only a limited number of studies to date have assessed whether an early abuse of substances leads to greater risk of cognitive dysfunction (Cannizzaro, Elliott, Stohl, Hasin & Aharonovich, 2014; Gruber, Dahlgren, Sagar, Gönenç & Lukas, 2014; Vonmoos et al., 2013; Fontes et al., 2011). Vonmoos et al. (2013) observed that cocaine use before 19 years of age may significantly contribute to a general worsening of cognitive performance in comparison to the cognitive profile seen in individuals with a later onset of cocaine use. However, they used a global cognitive index integrating attention, working memory, declarative memory and EF, therefore precluding the evaluation of each specific cognitive domain in that group of patients.

There is also evidence that earlier-onset drug users may be at a higher risk of developing more severe drug abuse or dependence when compared to late onset users (Hall & Lynskey, 2005; Lynskey et al., 2003). For example, adolescents with recent onset cocaine use are more likely to experience problems related to drug dependence than adult recent-onset users (Chen, Storr & Anthony, 2009). Furthermore, earlier substance use predicts later polydrug use (EMCDDA, 2009; Lynskey et al., 2003).

It is highly relevant to understand if early cocaine use would be associated with greater cognitive impairments and polydrug use, especially in developing countries where cocaine use is substantially increasing, and the first cocaine use is decreasing in age – almost half of the users have tried cocaine before 18 years old (Abdalla et al., 2014). Also, studies have neglected a relevant aspect that is the association between age of onset of cocaine and impairments in specific cognitive domains, such as attention, working memory, declarative memory, and general EF.

The objectives of this study were two-fold: to investigate whether people who started using cocaine earlier (before 18 years of age) would present worse performance on specific neuropsychological functions such as attention, working memory, declarative memory, divided attention, inhibitory control, mental flexibility, verbal fluency, declarative memory, decision making and EF than patients with later onset of drug abuse (after 18 years); and to evaluate patterns of drug use, in order to identify if an early use of cocaine would be associated to the consumption of other substances (focusing on recent use of alcohol, cannabis, and tobacco). We hypothesized that earlier cocaine use would be associated with worse EF and higher use of other drugs.

2. Materials and methods

2.1. Participants, ethical aspects and procedures

One hundred and sixty-six subjects were included in this study. The

CDI were recruited from two inpatient units: (1) The Interdisciplinary Group of Studies on Alcohol and Drugs (GREA); (2) The Association for the Promotion of Prayer and Work (APPW). All CDI were evaluated according to the DSM-IV-TR criteria (DSM-IV; American Psychiatry Association, 2000) at the time of admission to the treatment programs. Patients from GREA were in a four-week standard medical inpatient program for the treatment of cocaine dependence, which requires hospitalization on the impulsive behavior ward of the GREA, Institute of Psychiatry, University of São Paulo, in the city of Sao Paulo, Brazil. Patients from APPW were in a therapeutic community, located in the city of Campinas (Sao Paulo state, Brazil), where the treatment program includes a longer period for detoxification (~8 months), and use of 12 steps strategies, Cognitive-Behavioral Therapy (CBT) and religious-based activities. The CDI were all treatment-seeking inpatients evaluated after at least one week of abstinence. The abstinence was verified by self-report and supervised by the clinical staff of the inpatient units. In a subgroup of patients (n = 73), two urine tests were used to verify recent cocaine use (if positive), and afterwards to verify their abstinence (if negative). In total, 103 CDI were evaluated and separated in two groups: early onset group (EOG), with individuals who started to use crack-cocaine when they were < 18 years of age (n = 52), and the late onset group (LOG), with subjects who initiated cocaine use at 18 years or older (n = 51).

We excluded patients with: (1) past or current major diagnosis of mental disorders according to the DSM-IV-TR, including schizophrenia, dementia, severe depressive disorder, and bipolar disorder; (2) DSM-IV criteria for opioid dependence; (3) history of any neurological conditions or any medical condition that could affect the central nervous system; (4) history of head traumas with loss of consciousness for longer than 30 min; (5) prior diagnosis of learning disorder; and (6) intellectual quotient (IQ) < 70.

The control group (CG, n = 63) comprised volunteers actively recruited in the city of Sao Paulo, including employees from the public hospital where the research center (GREA) is located, as well as people from the community and from the local police department. We also recruited adult students from a local public school. The exclusion criteria for the control group were: (1) DSM-IV criteria for any psychoactive substance dependence disorder other than nicotine; (2) the same exclusion criteria of the CDI group outlined above.

The majority of our participants (73 CDI and 31 controls) were evaluated with the Structured Clinical Interview for DSM Disorders (SCID, Del-Ben et al., 2001). The remaining participants (30 CDI and 32 controls) underwent interviewing by an experienced clinical psychiatrist using a list of questions covering symptoms of major psychiatric disorders, as well as the validated instrument to screen for psychiatric disorders in primary care called Self-Reporting Questionnaire (SRQ-20) (Cunha, Bechara, de Andrade & Nicastrí, 2011; Cunha, Nicastrí, de Andrade & Bolla, 2010). Socioeconomic levels were classified according to Brazilian Association of Research Enterprises (ABEP, 2010). The study was approved by the University of Sao Paulo Review Board (CAPPesq). All participants gave written informed consent after understanding the procedures of the study.

2.2. Mood, anxiety, childhood ADHD symptoms and patterns of drug use

All subjects were assessed by the Beck Depression Inventory (BDI) (Beck, Steer & Garbin, 1988) and the State-Trait Anxiety Inventory (STAI) (Spielberger, Gorsuch & Lushene, 1970). Childhood attention deficit/hyperactivity disorder (ADHD) symptoms were assessed by the abbreviated version of the Wender-Utah Rating Scale (WURS - McCann, Scheele, Ward & Roy Byrne, 2000), comprising 25 of the 61 items from the original scale. Patterns of alcohol, tobacco and other drug use were assessed using the Addiction Severity Index (ASI-6) (Kessler et al., 2012). Recent use of other substances (alcohol, tobacco, cannabis, sedatives) was defined as substance use for at least three times a week in the last 30 days.

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