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Can symptoms help in differential diagnosis between substance-induced vs independent psychosis in adults with a lifetime diagnosis of cocaine use disorder?

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ABSTRACT

The main goal of this study it is explore the psychopathological differences between IPD and SIPD in a sample of 125 adults with a lifetime diagnosis of cocaine disorder recruited from treatment setting and through street contacts. A secondary analysis of six cross-sectional studies was conducted between 2000 and 2010. SIPD and IPD were diagnosed using the Psychiatric Research Interview for Substance and Mental Disorders (PRISM). 38 subjects (30.4%) were diagnosed with lifetime IPD and 87 (69.6%) with lifetime SIPD. A binomial logistic regression analysis using SIPD as the reference group showed that only previous prison admissions (OR 2.59; 95% CI 1.05, 6.36) and visual hallucinations (OR 5.21; 95% CI 1.54, 17.65) remained significant variables in the group with lifetime SIPD. In the group with lifetime IPD, grandiose delusions (OR 0.19; 95% CI 0.06, 0.60) and disorganized speech (OR 0.16; 95% CI 0.04, 0.61) remained significant. Model predicts the diagnosis of lifetime SIPD with a sensitivity of 80.3% and a specificity of 78.2%. This clinical profile of lifetime SIPD could help distinguish between IPD and SIPD among adults with lifetime diagnosis of cocaine disorder.

1. Introduction

The association between cocaine-use disorders (CUD) and the presence of cocaine-induced psychotic symptoms (CIPS) is widely documented (Fiorentini et al., 2011; Roncero et al., 2014a; Tang et al., 2014). The profiles of the most prevalent CIPS and the risk factors associated with them have been identified (Brady et al., 1991; Satel et al., 1991; Kalayasiri et al., 2006; Tang et al., 2009; Vorspan et al., 2012; Roncero et al., 2013; Vergara-Moragues et al., 2014). However, the correspondence between CIPS and the DSM-IV diagnostic criteria are complex. Three diagnoses are possible on the hypothetical spectrum of comorbid medical conditions. First, in *cocaine intoxication* we typically find perceptual phenomena that disappear with abstinence and intact reality testing. Second, in *cocaine-induced psychotic disorder*, psychotic symptoms are more severe and lasting than in cocaine intoxication and usually accompany altered reality testing (American Psychiatric Association (APA), 1994). Finally, cocaine users diagnosed with a primary or independent psychotic disorder, such as *schizophrenia*, may also experience acute psychotic symptoms induced by cocaine, but it is difficult to differentiate them from the primary psychotic symptoms of schizophrenia.

Studying one side of this clinical spectrum, Roncero et al. (2014b) observed that, in a sample of 143 cocaine users, 27.3% of patients had transient psychotic symptoms and 40.6% had cocaine-induced psychotic disorder. The group of patients with transient psychotic symptoms had a history of more frequent prison admissions, while in the cocaine-induced group, the age of initial cocaine use was lower and the duration of substance dependence was longer.

Most of the studies focusing on the other side of the clinical spectrum have explored the clinical differences between patients diagnosed with schizophrenia and CUD and those without CUD who have received a schizophrenia diagnosis. The prevalence of heavy cocaine use among those suffering from schizophrenia is

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high and ranges from 14% to 50% (Regier et al., 1990; Buckley, 1998; Batel, 2000; Winklbaur et al., 2006; Sara et al., 2014). Individuals with schizophrenia and co-occurring CUD have an earlier onset of schizophrenia than those without CUD (Green et al., 2007), increased rates of arrest for violent crimes (Dermatis et al., 1998), more frequent acute psychiatric inpatient admissions (Dickey and Azeni, 1996; Dermatis et al., 1998), shorter psychiatric hospital stays (Wu et al., 2015), worse prognoses (Seibyl et al., 1993), poorer social functioning (Sara et al., 2014), fewer negative symptoms (Serper et al., 1995, 1999; Lysaker et al., 1994), and more positive symptoms and thought disorders (Serper et al., 1999).

Notably, though the main diagnostic dilemma is whether psychotic disorder in a cocaine user is an independent disorder or whether it is induced by the substance, this issue has received little attention in the literature (Serper et al., 1999). Differential diagnosis between cocaine-induced psychotic disorder (CIPD) and independent psychotic disorder (IPD), such as when schizophrenia is present in cocaine users, is clinically relevant because prognosis and treatment for CIPD and IPD differ, despite their phenomenological similarities (Shaner et al., 1993, 1998; Caton et al., 2000; Sabioni et al., 2013; Tang et al., 2014). To perform this differential diagnosis using the DSM-IV, it is necessary to observe the evolution of the patient's psychotic symptoms over a one-month period. However, this criterion is difficult to fulfil in the routine of clinical practice. Therefore, it would be helpful to have another clinical indicator that can be used to make this differential diagnosis.

Nevertheless, one of the methodological limitations to advancement in this research field has been the lack of valid instruments to assess such patients (Shaner et al., 1998; Fraser et al., 2012). The use of specific standardized instruments for comorbid patients, such as the Psychiatric Research Interview for DSM-IV Substance and Mental Disorders (PRISM), allows researchers to draw distinctions between independent psychotic disorder (IPD) and substance-induced psychotic disorder (SIPD) (Hasin et al., 1996; 2006; Torrens et al., 2004). The research performed so far has focused on samples of substance users rather than the specific sub-sample of cocaine users. These studies have attempted to identify risk factors or clinical indicators that could be associated with IPD or SIPD to guide differential diagnosis. The results show that substance use is more severe among SIPD patients than among IPD patients and that they are more likely to have received treatment for substance use, have a higher prevalence of antisocial personality disorder and worse family support, and are more likely to have a family history of substance use disorder (SUD) (Rosenthal and Miner, 1997; Caton et al., 2005; Fraser et al., 2012). However, from the perspective of clinical practice, it is necessary to identify the phenomenological differences between the two diagnoses in CUD patients. Publications on this topic indicate that SIPD patients experience more visual hallucinations than IPD patients, who have an increased frequency of formal thought disorder, bizarre delusions, and severe positive and negative symptoms (Rosenthal and Miner, 1997; Caton et al., 2005; Fraser et al., 2012). However, none of these studies have compared the frequency of all of the expected psychotic symptoms in both diagnoses using DSM-IV criteria. From the research point of view, we are at the beginning of a personalized psychiatry which seeks to identify treatments and for this it is necessary to demonstrate relationships between biomarkers and endophenotypes (Edwards et al., 2012; De Leon, 2014). Therefore, there is a gap in the field's knowledge that requires further investigation.

The aim of this study is to explore the psychopathological differences between independent psychotic disorder and substance-induced psychotic disorder in adults seeking treatment primarily for cocaine-related problems and from the street (users who were not seeking treatment) with regard to the prevalence of psychotic symptoms. Based on previous studies, we hypothesized that the IPD group would show a higher prevalence of negative symptoms and formal thought disorder than the SIPD group.

2. Methods

2.1. Design, participants, recruitment, and settings

A secondary analysis of 125 cocaine users from six cross-sectional studies performed in cities across Spain was conducted between 2000 and 2010. All of these studies were performed in specific public centres for the treatment of substance abusers and were sponsored by the autonomous governments of Andalusia and Catalonia (Spain). The researchers who conducted these studies are members of the same research network, the "Addictive Disorders RETICs Group", which receives public funding from the Ministry of Health of the Government of Spain (*Carlos III Health Institute*). The Ministry of Health permitted the data from these studies to be shared and authorized this secondary analysis. All of the researchers used the same diagnostic tool and received the same training. To select the subjects for the analysis, we identified those who (a) met the DSM-IV diagnostic criteria for lifetime Cocaine Use Disorder (abuse or dependence) and patients identify cocaine as their primary drug of abuse, and (b) met the DSM-IV criteria for lifetime Psychotic Disorder (IPD or SIPD), excluding those with a history of both types of disorders.

Forty-three subjects were recruited from the Forum Dual Diagnosis Treatment Unit in Barcelona (Mestre-Pintó et al., 2014). Thirty-nine of these subjects had been consecutively admitted to one of six public therapeutic communities of the Andalusian Drug Addiction Plan (Vergara-Moragues et al., 2012). Twenty-one patients were receiving treatment for their addiction to cocaine in an outpatient drug-dependence program in Malaga (Vergara-Moragues et al., 2014). Three subjects were being treated at another outpatient resource in Barcelona (Astals et al., 2008). Twelve patients had been consecutively admitted for detoxification to the inpatient detoxification unit of a teaching hospital in Barcelona (Nocon et al., 2007). Psychiatric disorders were also assessed in a random sample of regular cocaine users, aged 18–30 years, who were recruited from street sites using targeted sampling and nomination techniques as part of a larger study (Herrero et al., 2008). In this study, a total of seven subjects met the selection criteria and were included in our analysis. The selection criteria and recruitment procedures for each of these studies are not specified in this article; for details, please refer to the studies' bibliographical entries (Torrens et al., 2011; Mestre-Pintó et al., 2014). All of the analysed studies strictly adhered to the ethical requirements established by the Declaration of Helsinki, and all participating patients signed an informed consent form. The ethical aspects of this research were approved by the Research Ethics Committee of the Hospital Regional Universitario Carlos Haya of Malaga.

2.2. Measures

2.2.1. Diagnostic assessment

The Spanish version of the *Psychiatric Research Interview for Substance and Mental Disorders* (PRISM) was administered to diagnose lifetime IPD and SIPD, as well as substance use and other psychiatric disorders, according to DSM-IV criteria (Torrens et al., 2004). The PRISM is a semi-structured interview designed to differentiate between the expected effects of intoxication and withdrawal and between primary (independent) and substance-induced disorders (Hasin et al., 1996). The interview assesses the major DSM-IV Axis I diagnostic clusters typically comorbid with drug use (mood, anxiety, psychotic disorders, and eating disorders) and two Axis II disorders (borderline and antisocial