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Factors affecting severity of positive and negative symptoms of psychosis in a polysubstance using population with psychostimulant dependence

Taylor S. Willi [a], William G. Honer [a], Allen E. Thornton [b], Kristina Gicas [b], Ric M. Procyshyn [a], Fidel Vila-Rodriguez [a], William J. Panenka [a], Ana Aleksic [c], Olga Leonova [a], Andrea A. Jones [a], G. William MacEwan [a], Alasdair M. Barr [c,*]

[a] Department of Psychiatry, University of British Columbia, Vancouver, B.C., Canada V6T 1Z3
[b] Department of Psychology, Simon Fraser University, Burnaby, B.C., Canada V5A 1S6
[c] Department of Pharmacology, 2176 Health Sciences Mall, University of British Columbia, Vancouver, B.C., Canada V6T 1Z3

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ABSTRACT

Approximately half of psychostimulant users experience psychotic symptoms, which include both positive and negative symptoms. Prior reports have exclusively used positive symptoms to characterize psychostimulant associated psychosis. Symptoms vary dramatically in severity, though most investigations categorize psychosis as a dichotomous occurrence. To explore the association between different substances of abuse and the severity of psychotic symptoms, we investigated 171 individuals meeting DSM-IV-TR criteria for psychostimulant (cocaine or methamphetamine) dependence in an observational cross-sectional study. Participants were predominantly male (72.5%), recruited from a socially disadvantaged neighborhood in Vancouver, Canada, with a mean age of 45.5($\pm$8.8) years. Of the total sample, 85% were dependent on cocaine, and 28.1% were dependent on methamphetamine. Participants had a median total PANSS score of 63, ranging from 37 to 111. Demographic information, current substance use and early substance exposure were used to predict positive and negative psychotic symptom severity in linear regression models. Increased severity of positive psychotic symptoms was significantly related to greater methamphetamine and marijuana use in the past 28 days, and methadone-abstinence. Negative symptom severity was related to increased opioid use in the past 28 days. There was no overlap between predictors of positive and negative symptom severity.

1. Introduction

Psychostimulants, including amphetamines and cocaine, are the second most commonly used illicit substances worldwide, with an estimated 28–75 million users (World Drug Report, 2014). In urban communities, the rates and heterogeneity of psychostimulant use become even more prevalent (Fischer et al., 2006; Kuramoto et al., 2011). At low doses these drugs generate feelings of increased energy and mood, while frequent exposure and higher doses can lead to a host of adverse effects, including physical (e.g. strokes, seizures, arrhythmias) and psychiatric complications (e.g. dependency, depression, anxiety, psychosis) (Barr et al., 2006).

Approximately 50–75% of cocaine users (Brady, 1991; Mooney et al., 2006; Satel and Edell, 1991; Smith et al., 2009; Vergara-Moragues et al., 2014; Vorspan et al., 2012) and 50–60% of methamphetamine users (Grant et al., 2012; Hall et al., 1996; McKetin et al., 2006; Smith et al., 2009) experience psychotic symptoms during consumption, including paranoia, delusions, and vivid sensory hallucinations (Alam Mehrjerdi et al., 2013; Mahoney et al., 2008). Though high frequencies of psychotic symptoms have been reported in both methamphetamine and cocaine users, direct comparison has shown that methamphetamine users more commonly exhibit psychotic symptoms than cocaine users (Mahoney et al., 2008).

Due to their high prevalence and severity, positive symptoms have been the hallmark of characterizing psychostimulant-associated psychosis (Panenka et al., 2013; Zorick et al., 2008). These positive symptoms are frequently indistinguishable from the positive symptoms of schizophrenia spectrum disorders (Shaner et al., 1998; Zorick et al., 2008). While there is some evidence that

* Corresponding author.
E-mail address: albarr@interchange.ubc.ca (A.M. Barr).

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negative symptoms are also present in psychostimulant-associated psychosis (Srisurapanont et al., 2011), others have theorized that the absence of negative symptoms in psychostimulant-associated psychosis may be a key differentiating factor from schizophrenia spectrum disorders (Zorick et al., 2008). The prevalence and severity of negative symptoms in psychostimulant-associated psychosis is thus an ongoing subject of debate (Panenka et al., 2013; Srisurapanont et al., 2011; Zorick et al., 2008).

The presentation of psychotic symptoms ranges in severity from subclinical psychotic experiences, to psychotic symptoms with varying functional impact, to clinically significant psychotic disorders (Binbay et al., 2012; van Os, 2014). Even though psychostimulant use causes psychosis across a spectrum of severity, most studies report psychosis as a dichotomous categorical occurrence. Only a small number of studies have investigated the severity of current positive symptoms, noting that chronic use (greater than 5 years), weekly use pattern, and injection administration are significant predictors of greater symptom severity (Lichlyter et al., 2011; Vorspan et al., 2012). However, Vorspan et al. was limited to studying only cocaine users, while Lichlyter et al. performed their study in a 30-day stimulant-abstinent sample. Thus, the effect of recent psychostimulant use on psychotic symptom severity is lacking, and has never been evaluated in the context of negative symptoms. When investigated as a categorical outcome (i.e. present or not), identified risk factors for psychostimulant associated psychosis have included earlier age of first use (Chen et al., 2003; Farrell et al., 2002; Kalayasiri et al., 2006a; Roncero et al., 2014), severity of dependence (Farrell et al., 2002; Kalayasiri et al., 2006a; Vergara-Moragues et al., 2014), marijuana dependence (Farrell et al., 2002; Kalayasiri et al., 2010; Roncero et al., 2013, 2014), route of administration (Hall et al., 1996), and recent frequency of use (McKetin et al., 2013). However, categorically defining psychostimulant-induced psychosis may not capture important information when psychosis occurs on a continuum of severity (Binbay et al., 2012; van Os, 2014). Simplifying psychosis to a binary outcome requires the establishment of a threshold, which varies among studies. Some studies define psychostimulant associated psychosis as any lifetime occurrence of a symptom, which may be too broad of an inclusion parameter (Kalayasiri et al., 2006a; Roncero et al., 2014). Other studies require a diagnosis according to standardized criteria (Farrell et al., 2002; Willi et al., 2016), thus excluding moderately symptomatic states, which may overlook risk factors pertinent to moving along the continuum of psychosis (Yung et al., 2003). By utilizing different thresholds for definitions of psychosis, repeatability can be problematic and impede study-to-study comparisons.

The aim of the current study was to identify risk factors that contribute to the spectrum of psychotic severity presenting concurrently with psychostimulant abuse, in both positive and negative dimensions. We hypothesized that variables regarding recent frequency of use would be the strongest predictors of current symptom severity, with greater use associated with greater symptom severity. Here, we describe the results of regression models to help explain the variance of psychosis symptom severity in a psychostimulant dependent population.

2. Methods

2.1. Sample

Participants were selected from the ongoing Hotel Study, an observational longitudinal cohort study of multimorbidity in the Downtown Eastside (DTES) of Vancouver, British Columbia (Vila-Rodriguez et al., 2013). In this cohort of 370 individuals, all cases of past or present psychosis not related to substance abuse were excluded, including schizophrenia, schizoaffective disorder, bipolar with psychosis, major depressive disorder with psychosis, or psychosis not otherwise specified according to DSM-IV-TR criteria. From the remaining 243 participants, inclusion criteria were current psychostimulant dependence at study entry (DSM-IV-TR criteria) and an available Positive and Negative Symptom Syndrome (PANSS) baseline assessment, resulting in the retention of 179 participants. In accordance to Tri-Council policy, the study was approved by the University of British Columbia Clinical Research Ethics Board. All participants provided written informed consent.

2.2. Measures

Demographic information including age, gender, and education were collected. Psychiatric health and substance use disorders were assessed according to DSM-IV-TR diagnostic criteria through consensus with the Best Estimate Clinical Evaluation and Diagnosis (BECED; Endicott, 1988) by an experienced psychiatrist (WGH, OL, or FVR).

Frequency of drug use was retrospectively collected for the 28 days prior to psychiatric assessment with the Time Line Follow Back method (TLFB; Sobell et al., 1986). Drug use frequency was divided by 7 to obtain weeks of use per month. Methadone status was recorded as either positive or abstinent. A urine drug screen was collected at time of psychiatric assessment to validate self-reported data. In instances where no psychostimulant use was reported in the past 28 days, and a urine drug screen was positive, data were omitted from analysis (8 cases, final $n=171$). Years of regular substance usage and age of first usage were provided via self-report.

Severity of psychotic symptomology was assessed using the PANSS (Kay et al., 1987). For the positive dimension, PANSS items P1 (delusions), P3 (hallucinations), P5 (grandiosity), P6 (suspiciousness), G9 (unusual thought content), and G12 (insight) were summed, as previously described using a 5-dimensional factor (potential range: 6–42) (Emsley et al., 2003). For the negative dimension, PANSS items N1 (blunted affect), N2 (emotional withdrawal), N3 (poor rapport), N4 (social withdrawal), N6 (lack of spontaneity), G7 (motor retardation), G13 (disturbance of volition), and G16 (social avoidance) were summed, as previously described (potential range: 7–49) (Emsley et al., 2003).

2.3. Analysis

Data were analyzed using SPSS software version 22 (SPSS Inc., IBM Corp., Armonk, USA). Descriptive statistics were calculated for all variables.

To pre-screen variables of interest before entry into a statistical model, bivariate analyses between variables of interest and the sum of positive symptoms (P1, P3, P5, P6, G9, and G12) or negative symptoms (N1, N2, N3, N4, N6, G7, G13, G16) were performed using a Pearson Correlation.

Pre-screened variables with at least a weak association with the symptom severity outcome ($p<0.20$) were entered into a multiple linear regression model. Model optimization was performed by utilizing a backward elimination model selection approach, where the least significant variable (if $p>0.10$) was dropped from the model. This process was repeated until all variables in the model met criteria ($p<0.10$). Potential interaction effects were explored between the independent variables, and tested for significance at $p<0.05$. Collinearity between independent variables was tested for with the variance inflation factor (VIF).

To investigate possible associations with specific psychotic symptoms, Pearson correlations were performed in a secondary exploratory analysis between significant independent variables from the regression models and the individual PANSS items. Positive symptom PANSS items P1, P3, P5, P6, G9, and G12 were checked for correlations with independent variables of the positive symptom regression, while negative symptom PANSS items N1, N2, N3, N4, N6, G7, G13, G16 were checked for correlations with independent variables of the negative symptom regression.

Potential effects of cocaine use frequency on psychotic symptoms were further investigated in two ways: first, by analyzing individuals with cocaine dependency and concurrent cocaine and methamphetamine dependency (n analyzed $=144$) and second, by excluding all participants dependent on methamphetamine, leaving only cocaine dependent participants ($n=122$). Differences in symptom severity based on type of cocaine (powder or crack) were investigated with a Student's t-test.

The other three dimensions of the 5 factor PANSS model were similarly assessed with optimization of a multiple linear regression model in supplementary analysis, including: Disorganization (sum of P2, N5, N7, G5, G10, G11, and G15), Excitement (sum of P4, P7, G8, and G14), and Anxiety/Depression (G1, G2, G3, G4, and G6) (Emsley et al., 2003).

3. Results

3.1. Descriptive

A total of 171 participants were investigated in this analysis. Table 1 describes the socio-demographic characteristics of the