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## Profile of psychiatric symptoms in methamphetamine users in China: Greater risk of psychiatric symptoms with a longer duration of use

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### ABSTRACT

Chronic methamphetamine (MA) use is associated with psychiatric symptoms. This study explored pattern of cooccurring psychiatric symptoms in MA users and their relationship to duration of MA use. A cross-sectional study was conducted among MA users at the Shenzhen Compulsory Drug Detoxification Center from April 2012 to October 2015. The Positive and Negative Syndrome Scale, Hamilton Anxiety Scale, and Beck Depression Inventory were used to assess psychiatric symptoms. Among 1277 MA users, 57.6% participants had any type of psychiatric symptoms including depressive, anxiety and psychotic symptoms. A dose-response relationship was found between duration of MA use and risk of psychiatric symptoms. The odds ratios (OR) of depressive symptoms increased with the duration of MA use (1–5 years vs. < 1 year: 1.74 [95% CI, 1.24–2.42];  $\geq$  5 years vs. < 1 year: 2.07 [1.19–3.61]), so did the ORs of co-occurring anxiety and depressive symptoms (1–5 years: 1.74 [1.20–2.51];  $\geq$  5 years: 3.09 [1.76–5.40]). Methamphetamine-dependent individuals were four-times more likely to experience any type of psychiatric symptoms than non-dependent users. The prevalence of psychiatric symptoms was high in chronic MA users and increased with MA use duration. Early prevention and treatment strategies targeting both MA use and associated psychiatric symptoms are needed.

#### 1. Introduction

The past decade has witnessed a significant increase in the popularity of amphetamine-type stimulants (ATS), particularly methamphetamine (MA), which is an increasing concern worldwide (United Nations Office on Drugs and Crime, 2014). Methamphetamine use continues to rise in most countries in East and Southeast Asia (United Nations Office on Drugs and Crime, 2016). China has experienced changes in patterns of drug abuse in the past few years, with a rapid increase in the use of synthetic drugs, especially ATS abuse (Jia et al., 2015; Lu et al., 2007; Sun et al., 2014). The China National Narcotics Control Commission reported that the number of registered synthetic drug users has exceeded the number of heroin users, mainly attributable to a large increase in MA use. At the end of 2015, among the 2.35

million drug users who were registered in China, 57.1% reported the use of synthetic drugs. Users of ATS accounted for 73.2% of newly identified drug users in 2015 (Office of China National Narcotic Control Commission, 2016). Amphetamine-type stimulants have become the leading drug of abuse in China. Data from the updated National Drug Abuse Monitoring Annual Report indicated that over 70% of ATS users in China began their drug use within the past 5 years (China Food and Drug Administration, 2016).

Chronic MA use can lead to severe neuropsychiatric symptoms (Harro, 2015; Wang et al., 2017). Psychosis, depression, and anxiety are among the most commonly reported symptoms in MA users (Akindipe et al., 2014; Bao et al., 2013; McKetin et al., 2006). Persecutory delusions and auditory hallucinations are frequently present in psychotic MA users, increasing the high risk of violence and criminality

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(Srisurapanont et al., 2003). The presence of anxiety and depression is related to a low quality of life and suicidal behavior (Bolton et al., 2010; Joffe et al., 2012). These psychiatric symptoms are predictive of relapse, cause serious comorbidities, and increase the risk of morbidity and mortality (Eslami-Shahrbabaki et al., 2015; Javadian et al., 2016; Kittirattanapaiboon et al., 2010). Estimates of the prevalence of psychiatric symptoms among MA users have been established in the United States and Australia, among other countries (Glasner-Edwards et al., 2008; McKetin et al., 2006; Salo et al., 2011; Sulaiman et al., 2014). The risk of current and lifetime MA-induced psychosis among MA-dependent individuals was 13.01% and 47.95%, respectively (Sulaiman et al., 2014). High rates of psychiatric disorders(36.0%) were also observed among MA-dependent users in a South African study, including mood disorders (16.0%), psychotic disorders (13.0%), and anxiety disorders (7.0%; Akindipe et al., 2014). Our previous study found that 42% of ATS users in China had depressive symptoms (Bao et al., 2013). However, the profiles of other psychiatric symptoms, including psychosis, depression, and anxiety, have not been comprehensively examined among chronic MA users in China, and the prevalence of their co-occurrence is unclear.

The presence of psychiatric symptoms among MA users was associated with poorer treatment outcomes and greater health service utilization (Glasner-Edwards et al., 2008, 2010a, 2010b). Thus, co-occurring psychiatric symptoms in this population need to be addressed. The World Drug Report indicated that qualified professional treatment for MA dependence and associated psychiatric problems is lacking in some countries in Southeast Asia (United Nations Office on Drugs and Crime, 2015). Considering the heavy burden of ATS abuse and possible consequences of new ATS use that has emerged in recent years, it is necessary to understand the pattern of psychiatric symptoms in MA users in real-world settings to guide healthcare services with regard to prevention and treatment. Despite the well-established prevalence of psychiatric symptoms in MA users and their outcomes, evidence of possible associations between psychiatric comorbidities and the duration of MA use and other risk factors is lacking, especially epidemiological studies with large sample sizes in developing countries. Thus, the primary goal of the present study was to explore patterns of cooccurring psychiatric symptoms in MA users and their relationship to the duration of MA use and other potential risk factors.

#### 2. Methods

#### 2.1. Subjects and setting

A cross-sectional study was conducted at Shenzhen Compulsory Drug Detoxification Center in Guangdong province, China. A total of 1511 MA users who only or primarily used MA in the past (prior to enrollment) were recruited from April 2012 to October 2015. To be included in the study, the subjects had to meet the following inclusion criteria: (1) at least 18 years old, (2) MA was their primary drug ever used, with positive urine test for MA at the time they entered the treatment center, and (3) signed informed consent. Subjects were excluded if they had significant physical illnesses, such as cerebrovascular disease, cardiovascular disease, or stroke.

Of the eligible subjects, we excluded MA users whose information regarding the assessment of psychiatric symptoms was missing (n = 144). Participants with missing information regarding the duration of MA use were also excluded (n = 90). The final sample size in the present study was 1277 MA users, who were divided into three groups based on their duration of MA use (< 1 year, 1–5 years, and  $\geq$  5 years).

The study was approved by the Institutional Ethics Board of Peking University. Written informed consent was obtained from all of the participants.

#### 2.2. Measures

#### 2.2.1. Demographic and drug use characteristics

Face-to-face interviews were conducted by trained interviewers using a self-administered structured questionnaire that included demographic characteristics and drug use history. The demographic characteristics included age, gender, education, ethnicity, marital status, and employment status. Information about MA use included age at first MA use, main route of MA administration, dose, frequency and duration of MA use, and MA dependence in the past year before entering the treatment center. The duration of MA use was defined as the cumulative number of months from the date of initial use to the date of last use. The diagnosis of MA dependence was based on the *Diagnostic* and Statistical Manual of Mental Disorders, 4th edition (Uosukainen et al., 2015). Specifically, individuals who reported two or more of the following symptoms were defined as dependent: craving, tolerance, withdrawal, out-of-control drug use, preoccupation with drug, and use despite significant impairment during the past one year before entering the treatment center. The length of abstinence was based upon selfreported last use of MA, which was divided into three subgroups according to different stages of withdrawal including acute phase ( $\leq 7$ days), sub-acute phase (8-30 days), and beyond one month of abstinence (> 30 days; McGregor et al., 2005; Zorick et al., 2010).

#### 2.2.2. Assessment of psychotic symptoms

Psychotic symptoms were assessed using the Positive and Negative Syndrome Scale (PANSS), which is a combination of the Brief Psychiatric Rating Scale (BPRS) and Psychopathology Rating Scale (Kay et al., 1987). In a previous study, clinically significant psychotic symptoms were defined as the presence of moderate to severe symptoms (score  $\geq$  4) on any of the following BPRS items: suspiciousness, unusual thought content, and hallucinations (McKetin et al., 2013). Unusual thought content on the BPRS consists of descriptors that apply to delusions and unusual thought items on the PANSS (Bell et al., 1992). Therefore, in the present study, a score  $\geq$  4 (moderate to severe) on at least one of the four PANSS items (delusion, hallucinations, suspiciousness, and unusual thought content; e.g., P1, P3, P6, and G9) was characterized as the presence of psychotic symptoms. The validity and reliability of the PANSS (Chinese version) are acceptable for assessing psychotic symptoms, with internal consistency reliability of 0.87 (Si et al., 2004).

#### 2.2.3. Assessment of depressive symptoms

The 13-item short version of the Beck Depression Inventory (BDI) was used to measure depressive symptoms (Beck and Beamesderfer, 1974). Each item is scored from 0 to 3, with cumulative scores that range from 0 to 39. A cutoff value  $\geq 8$  was classified as having depressive symptoms (Bao et al., 2013). Cronbach's  $\alpha$  and the split-half reliability coefficient for the BDI in the Chinese population were 0.890 and 0.879, respectively (Zhang et al., 1990).

#### 2.2.4. Assessment of anxiety symptoms

The Hamilton Anxiety Scale (HAMA) was used to measure anxiety symptoms. This scale consists of 14 items, and each item is scored from 0 to 4, with cumulative scores ranging from 0 to 56 (Tang and Zhang, 1984). A cutoff value  $\geq$  14 was classified as having anxiety symptoms (Eslami-Shahrbabaki et al., 2015). The reliability coefficient of the entire scale assessed in Chinese anxiety patients was 0.93, and the validity was acceptable (Tang and Zhang, 1984).

#### 2.3. Statistical analysis

Numerical variables are reported as mean  $\pm$  SD. Categorical variables are reported as a proportion (%). Differences were analyzed using analysis of variance (ANOVA) for numerical variables and the  $\chi^2$  test for categorical variables across the three duration groups. We used

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