

Brief report

Preliminary evidence of behavioral predictors of recurrent drug-induced psychosis in methamphetamine abuse

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Abstract

The goal of this study was to examine behavioral characteristics of currently drug-abstinent methamphetamine (MA)-dependent subjects ($n=39$) who experienced psychotic symptoms associated with MA abuse. All participants completed the Wender Utah Rating Scale (WURS), which retrospectively assesses Attention Deficit Hyperactivity Disorder-relevant childhood behaviors. The results suggest the existence of possible behavioral markers reflecting an early cognitive vulnerability to the development of frequent MA-induced psychotic symptoms as well as increased vulnerability associated with a family history of psychiatric illness. © 2007 Elsevier Ireland Ltd. All rights reserved.

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1. Introduction

In the past decade the use of the stimulant methamphetamine (MA) has increased in the general population, with worldwide abuse of amphetamines surpassing that of cocaine and opiates combined (United Nations, 2004). It is now estimated that approximately 5% of the adult population in the United States have used MA on at least

one occasion with worldwide use estimated to be 33 million users (Roehr, 2005). A subset of individuals who chronically abuse MA also develop severe recurrent psychotic symptoms commonly termed MA psychosis. These symptoms are often associated with high levels of psychiatric hospitalization and serious social dysfunction (Chen et al., 2003). The nature and severity of MA psychosis can be debilitating, often persisting long after cessation of drug use and in some cases eventually meet criteria for a primary psychotic disorder, suggesting that MA use may be a risk factor for schizophrenia in vulnerable individuals (Chen et al., 2005).

Although psychotic symptoms are well documented in a subset of MA abusers, little is known about the behavioral and neural mechanisms underlying the

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vulnerability to develop psychosis in MA users (Broome et al., 2005). The goal of the present study was to examine demographic and clinical characteristics of a sample of currently drug-abstinent MA-dependent subjects who experienced psychotic symptoms associated with MA abuse. This approach will be a first step in identifying possible behavioral predictors that may represent risk factors for developing recurrent psychotic symptoms associated with MA abuse.

2. Methods

2.1. Setting and sample

The MA-dependent group comprised 18 men and 21 women meeting criteria for lifetime MA dependence according to DSM-IV criteria. The MA abusers were recruited from substance abuse treatment centers and residential housing programs in the Sacramento area. All subjects had been drug abstinent for a minimum period of 4 weeks (range 4 weeks to 10 years) by self-report and random urine drug screens performed at referring sites. All subjects were literate and completed a standardized measure of verbal IQ (National Adult Reading Test; NART) (Nelson, 1982). The MA-dependent subjects reported symptoms associated with MA psychosis that included paranoid delusions, and visual, auditory and tactile hallucinations. Exclusionary criteria were: 1) history of neurological disorder; 2) co-existing current non-substance related Axis I disorder; 3) substance dependence (other than MA and excluding nicotine) within the past year; and 4) self-reported history of a seropositive test for HIV. All subjects signed informed consent approved by the University of California Davis Institutional Review Board and were paid a modest stipend for study participation.

2.2. Assessments

2.2.1. Semi-structured interviews

2.2.1.1. Structured Clinical Interview for DSM-IV. All participants were interviewed by trained clinicians using the Structured Clinical Interview for DSM-IV [SCID] and a consensus diagnosis was obtained for each participant. The SCID was used as an adjunctive measurement to assess the presence and frequency of psychotic episodes associated with MA use.

2.2.1.2. Methamphetamine Experience Questionnaire.

All participants were interviewed using the Methamphetamine Experience Questionnaire (MEQ), which is an

interview based on the Cocaine Experience Questionnaire (Gelernter et al., 1994). The MEQ is designed to assess the frequency of psychotic episodes associated with MA use, conditions in which psychotic episodes occur, and the persistence of these symptoms.

Sample MEQ questions include:

- 1) How often have you had paranoid experiences while using methamphetamine, using a 0 to 5 scale?
- 2) Were you more likely to get paranoid when you used greater amounts of methamphetamine?
- 3) Did paranoia ever persist after you came down from methamphetamine?

2.2.2. Questionnaires

2.2.2.1. Wender Utah Rating Scale. All participants completed the Wender Utah Rating Scale (WURS), which retrospectively assesses Attention Deficit Hyperactivity Disorder-relevant childhood behaviors and symptoms in adults (Ward et al., 1993; Wender, 1985).

2.3. Study rationale

As previous studies have reported an association between attentional dysfunction and psychosis proneness

Table 1
Demographic and clinical characteristics of 39 methamphetamine-dependent individuals

	Methamphetamine abusers with frequent psychosis (n=22)	Methamphetamine abusers with non-frequent psychosis (n=17)
<i>Demographic variables</i>		
Age, years, mean (SEM)	37.14 (1.8)	36.41 (2.2)
Females	11	10
Subject's education, years, mean (SEM)	12.68 (0.35)	13.0 (0.48)
Parental education, years, mean (SEM)	12.91 (0.54)	14.29 (0.98)
NART	106.05 (1.16)	106.0 (1.34)
Right-handed	22	16
Family history of psychiatric disorder	8	4
<i>Clinical variables</i>		
<i>Methamphetamine use</i>		
Duration, years, mean (SEM)	16.68 (1.82)	13.62 (1.58)
Months abstinent, mean (SEM)	18.73 (6.22)	23.29 (9.56)
Age of first use, years, mean (SEM)	17.36 (1.37)	18.0 (1.16)
Tobacco smokers	17	15

in persons at high risk for developing schizophrenia (Keshavan et al., 2003), we tested the hypothesis that a history of impaired attention function may also represent a vulnerability factor for developing recurrent psychotic symptoms associated with MA use. Furthermore, we examined additional premorbid risk factors for MA psychosis including familial history of psychiatric illness and age of first MA use (Chen et al., 2003).

3. Results

Based on a split of their MEQ responses, the 39 MA-dependent subjects were either classified as having frequent psychotic episodes (FP) while under the influence of MA (>2 on a 5-point Likert scale) or having non-frequent psychotic episodes (NFP) (1–2 on a 5-point Likert scale). The NFP group reported that they rarely experienced psychotic symptoms, while the FP group reported that they experienced psychotic episodes on a regular basis following MA use, in some cases every time they used MA. Using this classification, we identified 22 FP subjects (11 men and 11 women) and 17 NFP subjects (7 men and 10 women). An analysis of the demographic statistics revealed that on average the FP and the NFP groups did not differ in age [$F(1,37)=0.06$, $P=0.79$], years of education [$F(1,37)=0.29$, $P=0.58$], years of parental education [$F(1,37)=1.70$, $P=0.20$], or estimates of premorbid intelligence as assessed by the NART (Nelson, 1982) [$F(1,37)=0.001$, $P=0.98$]. An examination of the drug use patterns revealed that the MA-dependent subjects who experienced frequent psychotic episodes did not differ in duration of drug use [$F(1,37)=0.15$, $P=0.23$], time drug abstinent [$F(1,37)=17$, $P=0.68$], or age of first use [$F(1,37)=0.12$, $P=0.73$], from those who did not experience recurrent psychotic episodes. Substance use characteristics of the methamphetamine abusers are outlined in Table 1.

Further analyses revealed significant correlations between frequency of psychotic episodes and scores on the WURS ($r=0.56$, $P=0.0002$). See Fig. 1. Those individuals who reported having attentional problems early in childhood were the ones who exhibited a pattern of frequent psychotic episodes associated with MA abuse. Based on the work of others (Chen et al., 2003), we also examined the prevalence of family history of psychiatric disorders in our sample. Thirty-eight (97%) of our subjects were able to provide information on history of psychiatric illness in their biological families.¹ Compared with the others, the 12 subjects (32%)

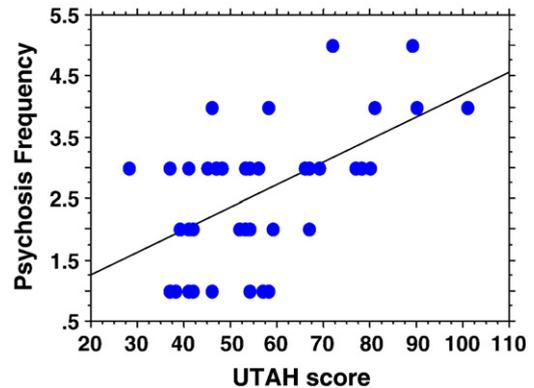


Fig. 1. Scatterplot of correlation between frequency of drug-induced psychotic episodes and self-reported scores on the Wender Utah Rating Scale of childhood attention function in 39 methamphetamine-dependent individuals.

who reported psychiatric illness in family members showed both an increased frequency of psychotic episodes [$F(1,36)=5.63$, $P=0.025$] and higher scores on the WURS [$F(1,36)=5.41$, $P=0.026$].² Of the 12 subjects who reported a family history of psychiatric illness, 67% reported experiencing psychotic episodes on a frequent basis.

4. Discussion

The data in the current study reveal significant positive correlations between frequency of MA-related psychotic episodes and scores on the WURS, a scale that retrospectively measures childhood attention function and hyperactivity. It should be noted that all of the subjects reported at least one occurrence of MA-related psychosis. MA-dependent subjects who never experienced psychosis were not included, primarily because of small sample size. Nevertheless, looking for differences within a population of MA-dependent subjects who experience psychotic symptoms is consistent with other studies in the field (Suzuki et al., 2006). The current study differs from others, however, in that the subjects were all individuals residing in the community, without other psychiatric disorders, and without active psychosis at the time of clinical assessment.

Although the correlational patterns reported within the current study cannot imply causality, the data nonetheless reveal an interesting relationship between measures of early attention/hyperactivity and the emergence of frequent psychotic episodes in individuals who abuse MA heavily in adulthood and reach criteria for

¹ One MA abuser was unable to provide information related to family history as this subject was adopted at an early age.

² A broad range of psychiatric disorders was included: schizophrenia, anxiety, and depression.

dependence. These patterns do not appear to result from a self-report bias as post-hoc analyses of other variables within the MEQ (i.e. persistence of paranoia when not using and distress levels) failed to reveal a significant correlation with the WURS rating scale. The WURS also failed to correlate with other personality self-report scales that were administered as part of a larger battery ($P=0.18$) (Buss and Durkee, 1957).

Consistent with other studies (Chen et al., 2003), these data suggest that a familial history of psychiatric illness may further increase the risk of developing recurrent psychotic symptoms associated with MA abuse. Those MA-dependent subjects with a familial history of psychiatric disorder reported that they experienced psychotic episodes more frequently than those MA-dependent subjects without a family history of psychiatric illness. Recent epidemiological studies have also shown that early substance use (i.e. cannabis) among individuals who are at genetic risk may increase the likelihood of developing psychotic symptoms in adulthood. Data collected in a large cohort of individuals provided evidence that those who carry the ValVal allele of the COMT gene and consume marijuana at an early age are at greater risk for developing psychotic symptoms later in life (Caspi et al., 2005). As other studies have reported cognitive risk factors for psychosis (Wood et al., 2003), the data in the current study also suggest the existence of behavioral markers reflecting an early cognitive vulnerability to the development of frequent psychotic symptoms.

4.1. Limitations

As the WURS retrospectively measures hyperactivity in childhood as well as attentional impairment, future studies are needed to evaluate the separate contribution of these factors (Lynskey and Hall, 2001). Other factors such as family interactions and parental attachment may also play a role. Although the data in the current study are selectively associated with chronic MA use, the identification of cognitive and behavioral markers linked to psychosis proneness may be applicable to a broad spectrum of psychiatric disorders. Other studies have also reported increased WURS ratings in chronic substance abusers (Clure et al., 1999; Matsumoto et al., 2005a,b), but this is the first study to our knowledge to link measures of childhood ADHD to drug-induced psychoses. Further studies are needed to determine if this cognitive vulnerability is linked to abnormal brain function in regions such as the prefrontal cortex, a neural region often implicated in the development of psychotic symptoms.

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