# Typologies of positive psychotic symptoms in methamphetamine dependence

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## Abstract

**Background and Objectives**—Understanding methamphetamine associated psychotic (MAP) symptom typologies could aid in identifying individuals at risk of progressing to schizophrenia and guide early intervention.

**Methods**—Latent class analysis (LCA) of psychotic symptoms collected from 40 methamphetamine dependent individuals with a history of psychotic symptoms but no history of a primary psychotic disorder.

**Results**—Three typologies were identified. In one, persecutory delusions dominated (Type 1), in another persecutory delusions were accompanied by hallucinations (Type 2), and in the third a high frequency of all the assessed hallucinatory and delusional symptoms was observed (Type 3).

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The authors have no conflicts of interest to disclose.

The views expressed in this article are those of the authors and do not reflect the official policy or position of the United States Government.

**Discussion and Conclusion**—MAP is a heterogeneous syndrome with positive symptom typologies.

**Scientific Significance**—This study represents the first attempt at identifying typologies of MAP and highlights the potential utility of LCA in future large-scale studies.

### Keywords

psychosis; stimulant; profile; structure; latent class

## 1. INTRODUCTION

Methamphetamine (MA) can result in a transient psychosis, methamphetamine psychosis (MAP) [1]. An estimated 30% of people diagnosed with a stimulant-induced psychosis will be re-diagnosed with schizophrenia within eight years [2]. This situation indicates a need to identify those MAP cases that are at risk of progressing to schizophrenia, so that early intervention can be provided and subsequent risk of transition to schizophrenia reduced.

One way of identifying which cases are likely to progress to schizophrenia is to examine their symptom patterns. In particular, positive symptoms such as bizarre thinking (i.e. phenomenon that the person's culture would regard as totally implausible) have been shown to predict psychosis onset among prodromal/high-risk individuals.[3] As such the type of positive symptoms experienced may provide an indication of which individuals with MAP are more at risk of progressing to schizophrenia. Although numerous studies have documented the prevalence of psychotic symptoms in MAP, primarily persecutory delusions and hallucinations (usually visual and auditory), the structure or typologies of psychotic symptoms in MAP has yet to be undertaken.

The current study explored the use of latent class analysis to see whether this method could identify groups, or classes, of MA dependent individuals who had similar psychotic symptom typologies, as such typologies may have potential diagnostic and/or prognostic utility.

## 2. METHODS

### 2.1 Participants

Participants met DSM-IV criteria for lifetime MA dependence and either MA abuse or dependence within the last 18 months. All participants were selected from a larger cohort study that was designed to elucidate the combined effects of MA, HIV infection, and aging on the central nervous system.[4] Exclusion criteria included: (1) a self-reported history of primary psychotic disorder not related to substance use; (2) alcohol dependence within a year of participation in the study; (3) dependence on any substance (other than MA or marijuana) within 5 years of participation; (4) abuse of a substance other than MA, cannabis or alcohol within the past year; (5) history of Hepatitis C virus infection confirmed with an on-site diagnostic test; (6) a history of comorbid neurological illness or injury (e.g. seizure disorder, closed head injury with loss of consciousness for longer than 30 minutes, central nervous system neoplasms); and (7) Wide Range Achievement Test-4 reading subtest

standard scores 80. All substance abuse/dependence criteria were assessed by trained research assistants using the Composite International Diagnostic Interview (CIDI version 2.1).

## 2.2 Measures

**2.2.1 Psychotic experiences—**Psychotic experiences were assessed using a 14-item questionnaire adapted from the Mini International Neuropsychiatric Interview and other previously developed psychotic symptom assessments [5]. Items assessed lifetime occurrence (yes/no) of hallucinations (Q1–2), persecutory delusions (Q3–6), a subset of Schneiderian first-rank symptoms (e.g. passivity of thought and delusions of control)[6] (Q7–12), and other delusional experiences (e.g. delusions of reference) (Q13–14) (Supplementary Table). Internal consistency (Cronbach's alpha) of the 14-items was 0.912.

**2.2.2 Methamphetamine use parameters—**MA dependence was assessed using the CIDI. The timeline follow-back [7] was used to assess other methamphetamine use patterns.

**2.2.3 Premorbid/comorbid conditions—**Lifetime DSM-IV diagnoses of substance dependence and mood disorders were obtained via the CIDI. DSM-IV diagnoses of lifetime antisocial personality disorder and attention-deficit/hyperactivity disorder were obtained using modules of the Diagnostic Interview Schedule-IV.

## 2.3 Statistical Analysis

Latent class models were estimated using a maximum likelihood estimator with robust standard errors and were implemented in Mplus software (version 7.0). Models were fitted using 500 random starting values to ensure replication of the final log-likelihood value. Modeling was done sequentially, fitting a model with one latent class followed by fitting models with one additional class than was estimated in the previous model. The Bayesian Information Criterion (BIC), Akaike Information Criterion (AIC), Lo-Mendell-Rubin log-likelihood ratio test (LMR-LRT) statistic, and the parametric bootstrapped likelihood ratio test statistic were used to assess and compare model fit.

# 3. RESULTS

Of participants who met the inclusion criteria (n = 57), 40 had experienced psychotic symptoms and were included in further analysis. The MAP sample consisted of predominately white (73%, n=29), high-school educated (mean = 13 years education, SD = 2 years) men (95%, n=38) in their late 30s (mean = 39 years, SD = 10). The mean age of first MA use was 25 years (SD = 8 years) and the median total days of use over the previous 18 months was 1456 (interquartile range = 430 – 2483 days). Lifetime prevalence of alcohol, cannabis, nicotine, cocaine, hallucinogen, inhalant, and opioid dependence/abuse was 68%, 47%, 33%, 25%, 17%, 11%, and 8%, respectively. Lifetime prevalence of major depressive disorder, antisocial personality disorder, attention deficit hyperactivity disorder, and Bipolar I disorder was 60%, 38%, 18%, and 13%, respectively.

### 3.1 Lifetime prevalence of psychotic symptoms

The lifetime prevalence of each specific psychotic symptom ranged from 23% to 88% (Supplementary Table). Persecutory delusions (i.e. being followed, 88%; spied on, 83%; plotted against, 73%) were most prevalent followed by both visual (63%) and auditory (60%) hallucinations. Prevalence of first-rank symptoms ranged from 23% (somatic passivity, Q7) to 38% (passivity of volition, Q12) and other delusions ranged from 28% (delusions of reference, Q14) to 40% (delusions of mind being read, Q13).. The total number of psychotic symptoms endorsed ranged from 1 to 14 (median=5, interquartile range=3–10).

### 3.2 Latent class analysis

AIC values indicated comparable fit between the 3- and 4-class models. The BIC and the LMR LRT indicated superior and equivalent fit for the 2- and 3-class models, respectively. Whereas, the Parametric Bootstrapped likelihood ratio test indicated superior fit for a model with 4 classes, which did not differ significantly from a 5-class model. Balancing this, it appeared that either a 3- or 4-class model should be extracted. However, the 4-class model included a class with a membership of only two participants so we choose the more parsimonious 3-class model.

The probability of endorsing each of the 14-items by the 3 classes is shown in Figure 1. The largest class (Type 1) comprised 43% (n=17) of the sample and as a group its members had relatively high probability of three of the four items relating to persecutory delusions (Q3–5, 41–77%) compared with other symptoms, with low probabilities for hallucinations (<20%), first-rank symptoms (<10%), and other delusional symptoms (< 20%). The second class (Type 2) represented 35% (n=14) of the sample. This class had high probability of endorsing the same three persecutory delusion items as the Type 1 class but also endorsed the hallucination items (>90%). This class had low-moderate probabilities for first-rank symptoms and other delusional symptom items (7–43%) but their probability of experiencing these symptoms was greater than the Type 1 class. The final and smallest class (Type 3) comprised 22% (n = 9) of the sample. Members of this class had high probabilities for hallucination and persecutory delusion items similar to that of other two classes but notably greater probabilities for first-rank symptoms and other delusional symptoms.

## 4. DISCUSSION

Our results suggest MAP is a heterogeneous syndrome. We found three typologies based on endorsement patterns of 14 psychotic symptoms experienced by MA dependent individuals. Consistent with previous observations all three typologies featured persecutory delusions [8–11] with the exception of question 6 (being tested or experimented on), which only featured in Type 3 class and may be secondary to other delusions (e.g. ideas of reference) that were of high prevalence in Type 3 but not in Types 1 and 2 classes. Previous characterizations of MAP have included hallucinations as a core symptom, however, our results suggest there is a subset of individuals with MAP that may not experience hallucinations (Type 1). In addition, we identified a small subset of individuals (Type 3) with a symptom typology characterized by persecutory delusions and hallucinations together

with first-rank symptoms and other delusional symptoms (e.g. delusions of reference). This is aligned with previous research that has documented between 33% – 63% of MAP cases involve first-rank symptoms [8,9,11].

The high prevalence of first-rank symptoms among individuals classified in the Type 3 class is particularly interesting given research that suggests first-rank symptoms are more often than not bizarre[12] and that bizarre thinking has been associated with risk for psychosis onset.[3] Thus, individuals in the Type 3 class may be at greater risk for or have an undiagnosed psychotic disorder. However, first-rank symptoms are present in a minority of cases of schizophrenia and are known to poorly differentiate schizophrenia from other psychotic disorders.[10] As such, prospective cohort studies are required before symptom typologies can be used for identification and targeted interventions of MAP.

Our results are based on a relatively small sample for a latent class analysis but they represent the first attempt at identifying typologies of MAP and highlight the potential utility of this method in future large scale studies. As such, the present results are preliminary and are meant to stimulate the generation of hypotheses and future research aimed at replicating and clinically describing the identified MAP typologies. Future research should include the measurement of negative symptoms (e.g. flattened affect, apathy) and neurocognitive symptoms, as these have been observed in the MAP syndrome [8,9,11,13]. These results also need to be replicated with more robust measures of psychotic symptoms. There is a range of factors that may impact on symptom typology, which were not assessed in the current study, and which could be explored in future research. These include the influence of familial morbidity for psychotic disorders, the temporal relationship between methamphetamine use and psychotic symptoms, the impact of concurrent cannabis use on psychotic symptoms, and the potential relationship with co-occurring mood disorders.

## Supplementary Material

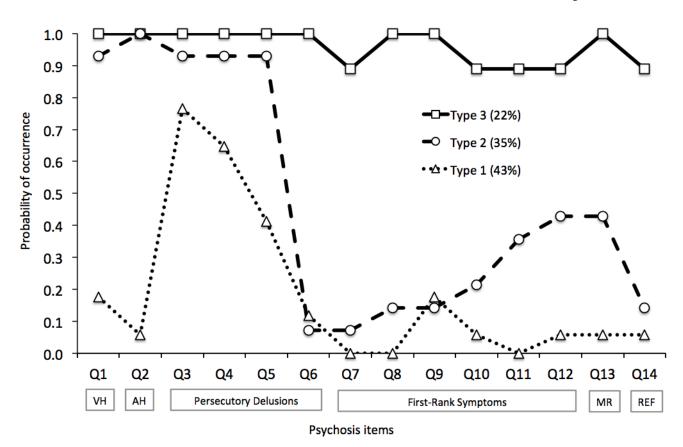Refer to Web version on PubMed Central for supplementary material.

## Acknowledgments

Director), William Perry, Ph.D., Mark Geyer, Ph.D., Brook Henry, Ph.D.; Project 2: Amanda B. Grethe, Ph.D. (Project Director), Martin Paulus, M.D., Ronald J. Ellis, M.D., Ph.D.; Project 3: Sheldon Morris, M.D., M.P.H. (Project Director), David M. Smith, M.D., M.A.S., Igor Grant, M.D.; Project 4: Svetlana Semenova, Ph.D. (Project Director), Athina Markou, Ph.D., James Kesby, Ph.D.; Project 5: Marcus Kaul, Ph.D. (Project Director).

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**Figure 1.**
Estimated probabilities for the occurrence of 14 psychotic symptoms by latent class. AH, auditory hallucinations; MR, delusions of mind being read; REF, delusions of reference; VH, visual hallucinations