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Is there a discrete negative symptom syndrome in people who use methamphetamine?

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ABSTRACT

Background: Positive psychotic symptoms have consistently been associated with methamphetamine use but the presence of a negative symptom cluster remains unclear. We used exploratory factor analysis to examine whether a discrete negative syndrome could be delineated among methamphetamine users, and to examine the clinical correlates of this syndrome.

Method: Participants ($N = 154$) were people who used methamphetamine at least monthly and did not meet DSM-IV diagnostic criteria for lifetime schizophrenia. Scores on the Brief Psychiatric Rating Scale for the past month were subject to exploratory factor analysis. Latent class analysis was applied to resultant factor scores to determine whether negative and positive factors were experienced by the same participants. Past-month substance use measures were days of use for each drug type and methamphetamine dependence assessed using the Severity of Dependence Scale.

Results: We articulated a three-factor model including 'positive/activation symptoms' (e.g. suspiciousness, hallucinations, conceptual disorganisation, tension), 'affective symptoms' (e.g. depression, anxiety) and 'negative symptoms' (e.g. blunted affect, motor retardation). Positive-activation and affective symptoms (but not negative symptoms) were positively correlated with past month days of methamphetamine use ($r = 0.16$; $r = 0.25$) and severity of dependence ($r = 0.24$; $r = 0.41$). Negative symptoms were correlated with heroin ($r = 0.24$) and benzodiazepine use ($r = 0.21$). Latent class analysis revealed a three-class model comprising a positive-symptom class (44%, high positive-activation, low negative symptoms), a negative-symptom class (31%, low positive-activation, high negative symptoms), and a low-symptom class (38%, low on all factors).

Conclusions: A negative symptom syndrome exists among people who use methamphetamine, but this appears related to polysubstance use rather than forming a part of the psychotic syndrome associated with methamphetamine use. Overlooking the role of polysubstance use on negative symptoms may conflate the profiles of methamphetamine-associated psychosis and schizophrenia.

1. Introduction

Differentiating between schizophrenia and substance-induced psychosis in methamphetamine users is notoriously difficult [1], and previous researchers have argued that these two disorders manifest a common symptom profile [2]. Robust evidence exists for a positive psychotic syndrome (i.e. delusions and hallucinations) precipitated by acute methamphetamine exposure in people without schizophrenia [1,3–8], and the presence of these positive symptoms are core diagnostic features for both substance-induced psychosis and schizophrenia (diagnostic and statistical manual for mental disorders fifth edition; DSM-V [9]). However, unlike for schizophrenia, the diagnostic criteria for substance-induced psychosis does not include negative psychotic symptoms, which are characterised by absences or reductions in movement, speech, affect and motivation (i.e. poverty of speech, psychomotor retardation, and flattened or incongruous affect). The absence of negative symptoms in the methamphetamine-associated psychosis

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may be a potentially crucial point of distinction from schizophrenia. However, the literature has been mixed regarding the relationship between methamphetamine use and negative psychotic symptoms.

A recent systematic review [7] found that <20% of studies examining the symptom profile of methamphetamine-associated psychosis report negative symptoms. In the studies that do report negative symptoms, the prevalence rate is typically 20% - 26% of patients [8,10]. However, McKetin et al. [6] examined psychiatric symptom exacerbation associated with methamphetamine use and found no evidence for a negative psychotic syndrome. This suggests that negative symptoms are not acutely precipitated by methamphetamine use but may instead result from various confounding factors occurring in this population. This may include the primary or secondary effects of other substances, notably antipsychotic medication use [11], or methamphetamine-related depression which can manifest as affective blunting and social withdrawal [12]. These hypotheses have not been tested empirically in the methamphetamine user population.

A lack of association between acute methamphetamine use and negative symptoms is supported by the schizophrenia literature. A systematic review of 32 experimental studies involving the administration of psychostimulants in people with schizophrenia indicated that whilst positive symptoms increased in 30–70% of patients, negative symptoms typically decreased or remained stable [13]. Accordingly, neurobiological studies of schizophrenia indicate increased dopamine in the striatum occurs with the emergence of positive symptoms, whereas negative symptoms have been associated with reductions in dopamine, particularly in mesocortical tracts [14,15]. Although this research focuses on individuals with schizophrenia, it suggests that the surge of dopamine released during acute methamphetamine exposure would likely result in a symptom profile characterised by positive – rather than negative – psychotic symptoms.

The current study aimed to determine whether a discrete negative symptom syndrome exists in the psychiatric profile of methamphetamine users who did not meet diagnostic criteria for schizophrenia, and to understand how this syndrome relates to methamphetamine use. Exploratory factor analysis of current psychiatric symptoms was used to identify whether a negative symptom syndrome exists in this population. We then examined whether the derived factors were associated with measures of methamphetamine and other substance use, familial morbidity for psychotic disorders, and other sociodemographic risk factors for psychosis (e.g., younger age, male gender, and immigration). Latent class analysis was then used to identify subgroups of participants based on their scores across the derived factors. We hypothesised that if negative symptoms are part of an acute methamphetamine-associated psychosis syndrome then we would expect that same group of people who experience negative symptoms would also experience positive psychotic symptoms, and that these syndromes would both be correlated with methamphetamine use.

2. Method

2.1. Procedure

Participants were recruited in Canberra, Australia, through word-of-mouth, online and print media advertisements, and flyers placed at needle and syringe programs and on public notice boards. Inclusion criteria were use of methamphetamine on at least six occasions over the past 6 months and being at least 18 years of age. To measure typical patterns of substance use in the past month, participants were excluded if they had been incarcerated, hospitalised or in residential drug treatment during the month prior to interview. All participants were volunteers who provided informed consent and were reimbursed AU$40 for their time and travel expenses. Interviews were one-hour in duration and were conducted in public locations convenient to the participant (e.g., cafes, shopping malls). The study was approved by the Australian National University's Human Research Ethics Committee.

Participants were excluded from analyses if they (i) had not used methamphetamine in the past month ($n = 10$), (ii) met the DSM-IV diagnostic criteria for lifetime schizophrenia ($n = 20$) assessed using the Composite International Diagnostic Interview (CIDI [16]), or (iii) had missing data on the Brief Psychiatric Rating Scale (BPRS [17]) or the CIDI ($n = 6$). The CIDI module did not measure negative and disorganised symptoms (DSM-V criteria A3-A5 for schizophrenia), and did not screen for bipolar disorder or schizoaffective disorder (DSM-V criteria D for schizophrenia).

2.2. Measures

2.2.1. Psychiatric symptoms

Psychiatric symptoms in the past month were assessed using the BPRS, in which symptom severity is rated from (1) “not present” to (7) “extremely severe” [17]. A selection of interviews was audiotaped, with consent the participants ($n = 21$), and rated by a second interviewer (R.M) to calculate interrater reliability. Cohen's kappa values were at an acceptable level for all symptoms other than elevated mood and bizarre behaviour (< 0.40) [18], and therefore these items were excluded from analyses. After excluding elevated mood and bizarre behaviour, interrater agreement for categorical ratings of psychiatric symptoms was substantial (kappa = 0.69, range = 0.44–0.90).

2.2.2. Substance use and other measures

Self-reported days of use in the past four weeks was assessed for methamphetamine, alcohol, tobacco, heroin, other opioids, cocaine, ecstasy, cannabis, other hallucinogens, inhalants, benzodiazepines, antidepressants, and antipsychotic medication (“How many days have you used [substance] in the past month?”). Other measures of methamphetamine use included age of first use and dependence in the past month. Dependence was defined as a score of 4 or greater on the Severity of Dependence Scale (SDS [19]), which yields 71% sensitivity and 77% specificity against a DSM-IV diagnosis of severe amphetamine dependence [20]. Demographic measures included age in years, sex, years of education, employment status, and current living arrangement. Family history of psychiatric illness was measured using adapted modules from the Diagnostic Interview for Psychosis (DIP [21]).

2.3. Statistical analyses

Factor analysis and latent class analysis were conducted in MPlus version 7.2 [22]. Exploratory factor analysis was used to examine current psychiatric symptoms and their inter-correlations, and was estimated with the principal axis factors method and an oblique oblimin rotation. Only factor loadings of 0.32 or higher were considered [23] as this reflects 10% of the variance accounted for by the latent factor. Factor analysis models with increasing numbers of extracted latent factors were compared with a series of goodness of fit indicators, including Akaike Information Criterion (AIC) and Bayesian Information Criterion (BIC), with lower values reflecting a better fitting model. Once the optimal number of latent factor dimensions to be extracted were identified, latent class analysis was applied to the extracted factor scores for each participant.

The five-class mixture model could not be estimated with 1000 random starts, and thus, indices of model fit were compared across two-class, three-class and four-class models. The best-fitting model was selected based on higher entropy, lower AIC and BIC. The Vuong-Lo-Mendell-Rubin Likelihood Ratio Test (VLMR LRT) and the parametric bootstrapped likelihood ratio test (BLRT) were used to examine whether each additional class significantly improved the fit of the model to the data [24,25]. Descriptive analyses were undertaken in Stata version 14.1 [26], with medians (*mdn*) reported for skewed data. Comparisons of median factor scores between each class were conducted with Wilcoxon rank-sum test, with an alpha value of $p < .01$ used to adjust for multiple testing. Two-way independent samples *t*-

tests (or Wilcoxon rank-sum test for skewed data) was used to compare factors between sample subgroups ($p < .05$ considered statistically significant). Correlates between factor scores and continuous variables (i.e. age) were examined using Pearson's pairwise correlations for normally distributed data (or Spearman's rank correlation for skewed continuous data).

3. Results

3.1. Sample characteristics

The sample consisted of 154 participants, with a median age of 39.4 years (SD = 10.1). The majority were male (69%), unemployed (67%) and single (64%). The median age of first methamphetamine use was 19.3 years (SD = 7.1) and participants had used for a median of 20.1 years (SD = 9.5). The highest endorsements for primary route of methamphetamine administration in the past month were for injection (74%) and for smoking (20%). Participants had used methamphetamine on a median of 11.5 days (interquartile range = 5–20) in the past month, and 42% were dependent on methamphetamine. Participants had used a median of 5 different drug classes (IQR = 4–6) in the past month, most commonly tobacco (98%), cannabis (79%), alcohol (65%), benzodiazepines (51%), and heroin (48%). The most prevalent BPRS symptoms included anxiety (71%), depression (64%), hostility (52%), suspiciousness (36%), and self-neglect (34%), while relatively few participants reported disorientation (1%), motor retardation (1%), mannerisms and posturing (2%), or uncooperativeness (2%).

3.2. Exploratory factor analysis

Indices of model fit were compared across one-, two-, three-, four- and five-factor models for the 22 BPRS items. The three-factor model reported the lowest BIC value and the two-factor solution reported the lowest AIC value (Supplementary Table 1). The three-factor model was selected as the most parsimonious factor model with the highest factor loadings (Table 1). Disorientation, self-neglect and uncooperativeness demonstrated poor discrimination between the factors and were excluded from the final three-factor solution. Disorientation failed to significantly load on any factor, self-neglect cross-loaded across factor two (0.59) and three (0.75); and uncooperativeness loaded moderately first (0.59) and the second factor (0.64).

The first identified factor encompassed grandiosity, unusual thought content, hallucinations, tension, conceptual disorganisation, hyperactivity, distractibility, excitement, and mannerisms (labelled 'positive/activation symptoms'). A second 'affective symptoms' factor comprised of depression, anxiety, suicidality, guilt, somatic concern, and hostility. The third 'negative symptoms' factor was characterised by blunted affect, emotional withdrawal, and motor retardation. Internal reliability for each factor ($\alpha = 0.73–0.78$) was at an acceptable level (Cortina, 1993). Positive-activation symptoms shared a moderate positive correlation with the affective symptoms ($r = 0.41$, $p \leq 0.001$), and a large negative correlation with negative symptoms ($r = -0.63$, $p \leq 0.001$). There was no statistically significant correlation between negative and affective symptoms ($r = 0.04$, $p = .591$). Inter-item correlations for each factor are provided in Supplementary Tables 2–4.

Table 1
Exploratory factor analysis results.

	Factor 1: Positive/activation	Factor 2: Affect	Factor 3: Negative	Unadjusted median (interquartile range)[a]
Factor correlations, *r* (*p*-value)				
Positive/activation	–	0.410 (<0.001)	−0.630 (<0.001)	–
Affect	–	–	0.044 (0.591)	–
Item loadings				
Grandiosity	0.995			1.0 (1–1)
Distractibility	0.987			1.0 (1–1)
Unusual thought con.	0.980	0.455		2.0 (1–3)
Suspiciousness	0.918	0.653		2.0 (1–4)
Hallucinations	0.889	0.689		2.0 (1–3)
Mannerisms	0.861	0.449		1.0 (1–1)
Conceptual disorg.	0.775			1.0 (1–1)
Tension	0.415			1.0 (1–2)
Excitement	0.412			1.0 (1–1)
Hyperactivity	0.395			1.0 (1–1)
Suicidality		0.998		2.0 (1–4)
Anxiety		0.996		4.0 (2–5)
Depression		0.995		4.0 (3–5)
Guilt		0.979		1.0 (1–3)
Somatic concern		0.953		2.0 (1–2.5)
Hostility		0.951		3.0 (2–5)
Blunted affect			0.995	1.0 (1–2)
Motor retardation			0.993	1.0 (1–1)
Emotional with.			0.989	1.0 (1–2)
Disorientation				1.0 (1–1)
Self-neglect		0.586	0.749	2.0 (1–4)
Uncooperativeness	0.640		0.595	1.0 (1–2)
Alpha reliability	0.79	0.73	0.77	–
Explained variance[b]	0.35	0.25	0.21	–

Note. Factor loadings below 0.30 have been suppressed. Unusual thought con. = Unusual thought content. Conceptual disorg. = Conceptual disorganisation. Emotional with. = Emotional withdrawal.
[a] Median (IQR) for item across total sample.
[b] Cumulative explained variance = 0.81.

3.3. Correlations between factors and substance use

Correlates of each factor are shown in Table 2. Scores on both the positive-activation and affective symptom dimensions were positively correlated with median days of methamphetamine use in the past month, as well as with median dependence score and median days of antipsychotic medication use (Table 2). Participants with a familial history of affective disorder scored higher on positive-activation symptoms and affective symptoms. Negative symptoms were positively correlated with days of heroin use and days of benzodiazepine use in the past month. Affective symptoms were positively correlated with a median of drug classes used in the past month. Unemployed participants scored higher on the positive-activation symptoms, and female participants scored higher on affect.

3.4. Latent class analysis

LCA was applied to factor scores to identify classes of participants who had similar scores across the positive-activation, affective and negative symptoms. Indices of model fit (BIC and AIC) across two, three and four-class models were compared. Likelihood ratio tests indicated that goodness-of-fit was significantly improved with each successive model (Table 3). Relative to the three-class model, the four-class model included a very small fourth class ($n = 9$) which shared a largely overlapping symptom profile with the third class. The most parsimonious model was the three-class model (Fig. 1, Supplementary Table 4), with adequate entropy (0.785) and low BIC/AIC. Class one (44%, $n = 68$) is referred to as the positive-symptom class and reported high positive-activation symptoms compared to class two ($p \leq 0.001$) and three ($p \leq 0.001$). Class two (31%, $n = 47$), referred to as the negative-symptom class, reported comparatively higher negative symptoms factor scores compared to class one ($p \leq 0.001$) and three ($p \leq 0.001$). Class three (38%, $n = 25$) reported low scores on all three factors, and is thus referred to as the low-symptom class (Fig. 1, Supplementary Table 4). All three classes had similar affective symptom scores. Participants in the negative-symptom class reported significantly more days of benzodiazepine use ($z = -2.32$, $p = .020$, *mdn* difference = 15.5 days), and

Table 2
Sociodemographic, drug use and psychiatric correlates of factor dimensions.

	Positive-activation	Affect	Negative
Spearman's rank correlation (*p* value)			
Age in years	0.01 (0.931)	−0.04 (0.593)	0.023 (0.777)
Years of education	−0.01 (0.861)	−0.01 (0.903)	0.004 (0.960)
Age of first methamphetamine use	−1.57 (0.119)	−1.54 (0.126)	0.86 (0.389)
Years of methamphetamine use	0.07 (0.366)	−0.01 (0.948)	−0.02 (0.756)
Wilcoxon rank-sum test value (*p* value)			
Male sex	1.20 (0.231)	2.31 (0.022)*	−0.64 (0.518)
Currently unemployed	2.12 (0.035)*	1.18 (0.238)	0.24 (0.806)
Single and never married	−0.44 (0.656)	−0.13 (0.893)	0.17 (0.862)
Immigrant background	0.36 (0.717)	0.98 (0.325)	0.01 (0.993)
Family history of affective disorder	1.97 (0.050)*	3.29 (0.001)*	1.24 (0.217)
Family history of schizophrenia	−1.57 (0.119)	−1.54 (0.126)	0.86 (0.389)
Substance use in past month, *r* (*p*-value)			
Median SDS score	0.24 (0.003)*	0.41 (<0.001)*	−0.05 (0.531)
Days of methamphetamine use	0.16 (0.043)*	0.25 (0.002)*	0.001 (0.995)
Days of heroin use	−0.30 (0.004)*	−0.03 (0.753)	0.24 (0.019)*
Days of other opioid use[a]	−0.10 (0.408)	−0.08 (0.493)	−0.15 (0.189)*
Days of benzodiazepines use	−0.13 (0.200)	0.114 (0.270)	0.213 (0.037)*
Days of alcohol use	−0.10 (0.328)	0.11 (0.249)	0.14 (0.135)
Days of cannabis use	−0.03 (0.699)	0.02 (0.860)	0.03 (0.714)
Days of antipsychotic use	0.18 (0.031)*	0.15 (0.059)	0.02 (0.772)
Days of antidepressant use	−0.14 (0.338)	−0.06 (0.689)	0.229 (0.118)
Median number of drug classes used[b]	0.02 (0.756)	0.25 (0.002)*	0.08 (0.314)

[a] Other opioids includes methadone, morphine, and prescription pain killers.
[b] Drug classes includes methamphetamine, alcohol, tobacco, heroin, other opioids, cocaine, ecstasy, cannabis, other hallucinogens, inhalants, benzodiazepines, antidepressants, and antipsychotic medication.
* $p < .05$.

marginally more days of heroin use ($z = -1.73$, $p = .084$, *mdn* difference = 7.0 days) in the past month compared to the positive-symptom class. These two classes did not differ on days of methamphetamine use in the past month ($z = -0.661$, $p = .508$, *mdn* difference = 2.0 days). A supplementary three-class latent model was conducted on the original 22 BPRS items (Table S6; Fig. S1).

Table 3
Criterion for model selection in latent class analysis.

	Two-class	Three-class	Four-class
Entropy	0.869	0.785	0.817
AIC/Adjusted BIC	1180/1179	1144/1142	1119/1117
BLRT (*p-value*)	−614.8 (<0.001)	−580.1 (<0.001)	−558.2 (<0.001)
VLMR LRT (*p-value*)	−614.8 (0.044)	−580.1 (0.031)	−558.2 (0.0202)

Note. AIC = Akaike Information Criterion, BIC = Bayesian Information Criterion, BLRT = parametric bootstrapped likelihood ratio test, VLMR LRT = Vuong-Lo-Mendell-Rubin Likelihood Ratio Test.

4. Discussion

We identified a negative symptom syndrome in methamphetamine users without a diagnosis of schizophrenia, which unlike the positive-activation or affective symptoms, was not correlated with current methamphetamine use or related to familial risk for psychosis. These results suggest that negative symptoms are unlikely to be due to the direct effect of acute methamphetamine use. In addition, negative symptoms were reported by a subpopulation of methamphetamine users which differed from the subgroup of participants who experienced positive psychotic symptoms. This suggests that negative symptoms are not occurring within the same syndrome as methamphetamine-associated psychosis. The negative syndrome was not correlated with methamphetamine-related depression (i.e. the affect factor), nor was it related to the secondary side effects of antipsychotic medication. Several alternative explanations are considered below.

Negative symptoms may be a consequence of neurotoxic impairment in long-term methamphetamine users. Prolonged or heavy methamphetamine use impacts normal brain function and prompts changes in brain structure [27,28], which in turn, may indirectly precipitate negative symptoms [14]. Longitudinal evidence into methamphetamine users indicates that negative symptoms become increasingly prominent as positive symptoms subside over time [29,30]. This 'residual state' is observed in other psychotic disorders [31]. This explanation is not reflected in the current findings because negative symptoms were not associated with duration of methamphetamine use (in years) or frequency of methamphetamine use. Nonetheless, it would be informative for future longitudinal studies to assess whether these psychiatric factors alternate or interact over time, and whether negative symptoms may have prognostic utility in predicting clinical course and treatment response [32–34].

Alternatively, negative symptoms in the current sample may reflect a pre-existing neurobiological or genetic vulnerability found in some individuals, and these symptoms are antecedent to – rather than induced by – methamphetamine use. Although not tested directly, the self-medication hypothesis [35] suggests that people with premorbid negative symptoms [36] may subsequently use substances (such as methamphetamine) to temporarily alleviate the distress and suffering associated with these symptoms. People with negative symptoms may use methamphetamine to increase sociability and reduce blunted affect, and indeed, amphetamine does appear to obscure negative symptoms in experimental studies of schizophrenia [13]. A self-medication approach does not explain why individuals in the negative-symptoms class do not report positive symptoms. We would expect to these individuals to either report positive symptoms alone, with negative symptoms masked by methamphetamine use, or to manifest both negative and positive symptoms which vary based on fluctuating patterns of methamphetamine use over the past month.

Finally, negative symptoms measured in this study may be an artefact of polysubstance use. The current study found that the negative syndrome was positively correlated with days of heroin use and days of benzodiazepine use in the past month. Heroin and benzodiazepine use was common among the current sample, and this polysubstance use pattern is common among people who inject drugs [37]. In contrast to the psychostimulant effects of methamphetamine, heroin and benzodiazepines are central nervous system depressants which produce reduced neurophysiological processing, impaired motor movements, and respiratory and cardiovascular depression [38]. The intoxication effects of these depressant drugs correspond to the observed negative symptoms in the current study, including slowed movements and speech, social withdrawal, and blunted emotional expressiveness [39–41]. Our results align with a recent Canadian study of polysubstance users [42], in which frequency of opioid use was associated with emotional withdrawal, social withdrawal, and motor retardation, but was not associated with measures of positive psychotic symptoms. Likewise, the current study found that frequency of methamphetamine use was

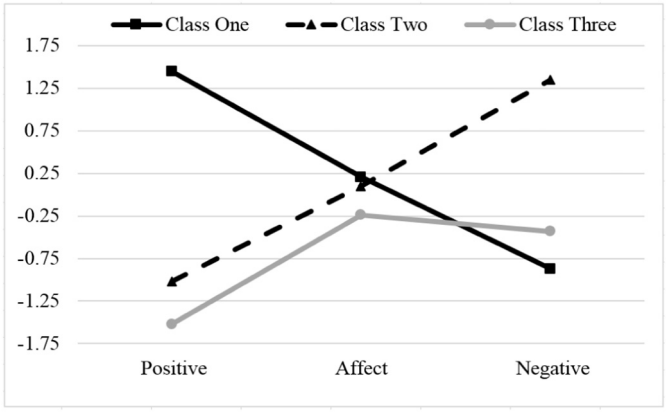

Fig. 1. Median factor scores by class membership. *Note*. Median factor score coefficients for each dimension are zero for the total sample. Statistical comparison between latent classes is available in Supplementary Table 4.

associated with positive – but not negative – symptomology. Prospective longitudinal research is needed to explore a causal relationship between intoxication effects of depressant drugs and negative symptoms in methamphetamine users.

4.1. Clinical implications

Overlooking the role of polysubstance use in the manifestation of negative symptoms may lead people with methamphetamine-associated psychotic symptoms to be misdiagnosed as having schizophrenia. A common clinical scenario may involve a patient who reports positive symptoms (i.e. delusions of persecution) precipitated by heavy methamphetamine use, as well as diminished emotional expression due to intermittent opioid use. Although these symptoms are substance-induced, such a patient would meet the symptom criteria for schizophrenia in presenting with both delusions and negative symptoms during a one-month period. Clinicians are often inclined to attribute psychotic symptoms to primary psychotic disorders rather than to substance use [43], and such misdiagnosis may result in the inappropriate prescription of long-term antipsychotic medications [44] rather than focusing on the management of substance use disorders. The findings of the current study support the need for clinicians to carefully assess each patient's drug history across all classes of substances, including licit prescription medications (such as benzodiazepines) to inform decisions about differential diagnoses. This would involve considering the number of drug types used, the timing and quantity of most recent use for each drug type, and recent changes in drug use patterns [45].

4.2. Limitations

First, the CIDI Schizophrenia module [16,46] did not include a measure of negative or disorganised psychotic symptoms [9], and therefore, some participants with a diagnosis of schizophrenia may not have been properly excluded have been captured in the negative-symptom class. Similarly, we did not screen for participants who met criteria for other primary psychotic disorders, such as bipolar disorder or schizoaffective disorder, who would report delusions or hallucinations that were not better explained by methamphetamine use (i.e. persisted for one month beyond intoxication). In the current study, these methamphetamine users would have been incorrectly identified as meeting the diagnostic criteria for SZ and confounded the symptoms profiles observed. Second, in recruiting from the community rather than clinical settings, the extracted factors may not generalise to methamphetamine users who require hospitalisation for more acute or complex psychotic symptomatology. Third, factor analysis typically requires a sample of at least 200 participants, and although this risk is reduced due to the high number of observed items and sufficient inter-item communality [47]. Finally, the current study could be strengthened with the use of a standardised tool to quantify drug use frequency in the past month, such as the Timeline Followback method [48].

4.3. Conclusions

We identified a negative symptom factor in people who use methamphetamine and who do not meet diagnostic criteria for schizophrenia. This negative syndrome was not correlated with methamphetamine use, and instead may be an artefact of depressant or sedative use. Overlooking the role of polysubstance use in people who use methamphetamine may have obfuscated diagnostic differences methamphetamine-associated psychosis and schizophrenia in prior research. Clinicians should carefully assess each patient's drug history to allow for greater accuracy when differentiating between methamphetamine-associated psychosis and schizophrenia in community settings.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.comppsych.2019.06.002.

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