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Diagnosis of methamphetamine-induced psychotic disorder: Findings of an expert consensus panel

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Abstract

Aim: We define criteria for methamphetamine-induced psychotic disorder (MIPD) to aid in accurate and reliable diagnosis.

Method: An expert panel was recruited and engaged in an iterative consensus process. A literature search supported this work. The a priori level for consensus was considered $\geq 80\%$ of voting panellists.

Results: The final expert panel included 22 physicians from different backgrounds and practice environments. The panel produced two consensus diagnoses: (1) acute MIPD and (2) persisting MIPD, which is further separated into subacute and chronic timeframes. Although certain characteristics differentiate methamphetamine-induced psychosis shortly after use, identification of persisting MIPD depends largely on a history of symptom onset. All respondents voted in the final round, and both criteria were fully endorsed by 91% (20/22) of respondents. Panellists further recommended next steps in validation and research on this topic.

Conclusion: These diagnostic criteria aid clinicians in differentiating methamphetamine-induced psychotic symptoms from psychosis because of other psychiatric disorders and can guide future studies. Future research might examine these criteria's prognostic significance, interrater

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CONFLICT OF INTEREST STATEMENT

The authors declare no conflicts of interest.

reliability and acceptability including among persons in recovery. This work is a necessary and vital step in advancing the science of methamphetamine addiction treatment.

Keywords

addiction; consensus process; diagnosis; methamphetamine; methamphetamine psychosis; methamphetamine use disorder

1 | INTRODUCTION

Methamphetamine is a highly addictive psychostimulant that adversely affects users' physical, mental and social wellbeing (Jones et al., 2022). In the United States, overdose death rates from psychostimulants increased over 300% from 2013 to 2019, and by 2019 it was the second leading cause of overdose deaths after opioids (Lecomte et al., 2018). Among methamphetamine's most consequential psychiatric symptoms is the development of psychosis—hallucinations, delusions, or disorganized thinking. Approximately one third of methamphetamine users develop methamphetamine-induced psychosis, which may occur without long-standing addiction or use disorder and correlates with poor outcomes and treatment engagement (Courtney & Ray, 2014). Methamphetamine psychosis is also strongly correlated with an elevated risk of mortality and healthcare utilization (Barbic, Whyte, Sidhu, Luongo, Chakraborty, et al., 2022; Barbic, Whyte, Sidhu, Luongo, Stenstrom, et al., 2022; Hajebi et al., 2018; Hjorthoj et al., 2021). Despite this growing prevalence and severity of methamphetamine use, relatively few users seek treatment (Jones et al., 2020).

To improve its treatment, methamphetamine-induced psychosis must first be identified early and appropriately. Making the diagnosis is challenging: comorbid substance use is common among patients with existing severe mental illness (Jones et al., 2020), and there is a considerable overlap of symptoms between methamphetamine psychosis and schizophrenia (Medhus et al., 2013). In addition, there is uncertainty in how to characterize psychotic symptoms occurring during periods of methamphetamine intoxication or withdrawal (Glasner-Edwards & Mooney, 2014). The diagnostic and statistical manual, Fifth Edition-Text Revision (DSM-5-TR) states that substance-induced psychosis should not be considered if symptoms persist after 1 month of intoxication or withdrawal (American Psychiatric Association, 2022). However, it is recognized that methamphetamine-induced psychotic symptoms last well beyond 1 month of abstinence (Hajebi et al., 2018). Better diagnostic guidance can facilitate clinicians' abilities in offering evidence-based treatment for methamphetamine use disorder; educating patients and families; and avoiding iatrogenic harm of unwarranted treatments. In addition, accurate identification of methamphetamine-induced psychosis is needed to inform public health surveillance, interventions, policymaking, research and service delivery (Simpson et al., 2023).

In this study, we utilized an expert panel process to define the diagnosis of methamphetamine-induced psychotic disorder (MIPD). The a priori instructions to the panel were to produce guidance to inform diagnostic criteria and write specific criteria if possible. These proposed diagnostic criteria are intended to aid clinicians in differentiating MIPD from psychotic illnesses with similar presentations.

2 | METHODS

An expert consensus process was utilized to develop diagnostic criteria. Methods were based on best practices, applying Delphi techniques for developing clinical guidelines using electronic and remote communication (Cole et al., 2013; Colton & Hatcher, 2004; Institute of Medicine (US) Committee on Standards for Developing Trustworthy Clinical Practice Guidelines, 2011). The process and results are reported here using previously published guidance (Junger et al., 2017; Rethlefsen et al., 2021). Data were collected using RedCap, a secure web-based research collection instrument (Harris et al., 2009).

2.1 | Recruitment and panel selection

We recruited clinicians with expertise in managing methamphetamine addiction, intoxication, withdrawal and psychosis. An initial email invitation was sent to multiple national listservs used by psychiatrists with relevant expertise; listserv leaders gave permission prior to recruitment. There were approximately 1200 listserv recipients; recipients were also invited to forward the invitation. The email invitation briefly described the study aims and instructed interested parties to complete a secure electronic screening form.

The a priori inclusion criteria required participants to have at least 5 years of experience working with patients who are using methamphetamine and to be currently treating at least three patients per week who have problematic methamphetamine use. Physicians were expected to have a board certification in a relevant specialty. Participants uploaded a curriculum vitae and provided demographic information. Participants were allowed to consent to being publicly recognized for participation.

Study investigators then reviewed applicants for the panel using a previously described consensus approach (Colton & Hatcher, 2004). Applicants meeting inclusion criteria were scored as being 'Not useful,' 'Moderately useful' or 'Very useful' for the panel's work. All applicants who were scored as 'Very useful' were included, and applicants who were scored as 'Moderately useful' were included if their inclusion added experiential diversity to the panel. The selection criteria and process were not disclosed to panel applicants in order to reduce the risk of misrepresentation in the application process.

2.2 | Consensus process

The a priori threshold for consensus was set at $\geq 80\%$ of panel respondents. The panel planned up to four rounds of web-based voting and at least one web-based teleconference between votes. The conferences were meant to be informative and collaborative, whereas voting took place during surveys sent out between conferences. These survey results were used to determine consensus. The initial survey round solicited qualitative feedback on panellists' practice and opinions. This feedback and communication among panellists were reviewed by the lead investigators to inform more specific subsequent surveys. At the outset of the panel process, panellists were polled as to preferred communication and shared digital platforms, and it was decided to use an email listserv for ongoing communication, a shared web drive for documents, and an online bibliographic reference system, Zotero

(Corporation for Digital Scholarship, Vienna, VA), for sharing literature. These platforms all allow secure communication among multiple participants. A study research assistant (RA) provided technical support.

2.3 | Literature search

A literature search was conducted in support of panellists' work. This search sought to make relevant scientific literature accessible to panellists without biasing their opinions due to article selection. The search included literature indexed in PubMed, which was selected for his broad reach; additional databases were not included as we expected this one database would provide a large number of articles. From a key word combination search in PubMed for all results up to May 2022, 1923 unduplicated articles were identified. An RA and the senior author (SS) reviewed article titles and abstracts to exclude 185 articles that were not in English and 695 articles that did not appear relevant to the panel's goals. The remaining 1043 were electronically organized in Zotero, which allowed panellists to search and organize articles of interest. Given the volume of papers and a desire to err on the side of article inclusion without biasing participants, articles were not rated by quality, and no full text review was conducted to exclude articles. Panellists were advised that they could access the Zotero library and full text of articles to complement the consensus process but otherwise did not receive instructions for reviewing this literature. Panellists could access full text articles via Zotero, their local institutions, or the study research assistant, who was available to obtain full text articles. No panellists requested articles of the assistant, and we did not ask panellists how often they requested full text articles from other sources or accessed literature outside of this review. Panellists did not receive additional training in reviewing literature for this study. A PRISMA diagram, search keywords and organizational categories are described in Figure S1.

2.4 | Ethical considerations

This study was authorized by the Colorado Multiple Institutional Review Board. All patients consented to participation.

3 | RESULTS

3.1 | Participants

The final expert panel included 22 physicians. One participant withdrew early in the study for personal reasons, and their data are excluded from reporting. Table 1 describes the expert panel group. Panellist engagement was excellent: Figure 1 describes activities of the panel and participation rates at each step. All panellists participated in at least one meeting and one round of voting. Missing data are reported as such throughout the manuscript.

3.2 | Diagnostic criteria

The panel produced two diagnoses intended to help clinicians distinguish methamphetamine-induced psychotic symptoms from psychotic symptoms because of other etiologies. The diagnoses are (1) acute methamphetamine-induced psychotic disorder (AMIPD) and (2) persisting methamphetamine-induced psychotic disorder (PMIPD). The criteria include a brief narrative description and enumerated criteria; criteria are in Table 2.

All respondents voted in the final round, and both criteria were endorsed by (20/22) 91% of respondents.

AMIPD should be considered when there is concurrent methamphetamine intoxication or withdrawal. The DSM-5-TR describes stimulant intoxication as occurring after use of any stimulant, causing clinically significant behavioural or psychological changes, and occurring with at least two of nine physical symptoms, such as tachycardia, mydriasis, perspiration, or nausea; stimulant withdrawal is characterized by dysphoric mood and two or more of five symptoms including fatigue and increased appetite. After the period of intoxication and/or withdrawal and if patients remain psychotic, patients are at risk of PMIPD. PMIPD may be subacute up to 1 month after the last use of methamphetamine, or chronic when psychosis persists beyond 1 month of sobriety. The criteria emphasize that certain characteristics of psychotic symptoms may increase the likelihood of AMIPD and substance PMIPD: persecutory delusions, auditory or visual hallucinations, tactile hallucinations and parasitosis. Parasitosis is a delusional belief that one is infested with parasites (Laidler, 2018).

In the final vote, panellists who did not endorse criteria were allowed to endorse only part of the criteria or provide feedback. All respondents endorsed at least some of the criteria, and dissenting panellists shared reasons for not approving other portions of the criteria. Concerns included that 'significant distress' may be inadequate for a disease where insight is so often impaired; that visual hallucinations should not be included; or that the criteria should contain wording that explicitly excludes other disorders such as schizophrenia.

In developing these criteria, the panel considered multiple alternative formats, language and content. The panel opted against defining criteria for methamphetamine intoxication and withdrawal syndromes. Although it was agreed these syndromes might vary somewhat for methamphetamine than for other stimulants, the panel was satisfied with application of existing DSM-5-TR stimulant criteria in clinical practice. The panel also decided against other forms for criteria such as paragraph-length patient descriptions or ordinal ratings of severity. The panel felt that including the term 'disorder' was important to highlight the chronic, substantial and treatable nature of MIPD.

3.3 | Secondary findings

Panellists voted on specific reasons that these criteria are important and suggestions for future research. The most endorsed reasons for developing these criteria were importance for affecting prognosis (100%) or level of care (91%). In voting on suggestions for future research, 'Studying the likelihood of progression from acute MIPD to persisting MIPD' was considered a 'High' or 'Very High' priority by $\geq 80\%$ of panellists (86%). Other reasons for future research were also frequently endorsed: 'Describing the validity of the proposed diagnoses' (77%), 'Identifying the best medication treatments for MIPD' (77%) and 'Describing psychometric reliability of the proposed diagnoses' (72%). Tables S1 and S2 report these secondary findings.

3.4 | Panellist experience

During the final round of voting, panellists were asked to rate their experience with the panel process using a 5-point Likert scale. Ninety-six percent reported accessing scientific literature as part of the consensus process, and all panellists felt their 'opinion was respected in this process.' Full participant feedback is described in Table 3.

4 | DISCUSSION

Using a consensus process, this expert panel produced novel diagnostic criteria for MIPDs. Our findings highlight some of the clinical features, progression and outcomes of methamphetamine-induced psychosis at even early stages of presentation. These criteria can guide clinicians, patients, families, scientists and policymakers who are seeking to improve the care of those with methamphetamine addiction.

This work poses important issues for the clinical management of methamphetamine psychosis. The panel repeatedly raised the importance of considering symptom timing in the treatment of MIPD. Panellists agreed that psychotic symptoms of methamphetamine use merit recognition whether they occur during intoxication, withdrawal or thereafter. These symptoms may vary somewhat over the course of recovery: acute MIPD is characterized by specific hallucinations and delusions, whereas the psychotic content seen in chronic PMIPD cannot be differentiated from primary psychosis. The patient's prior history of use and symptom onset are important for the diagnosis of both AMIPD and PMIPD, albeit more so for PMIPD. In addition, it is important for providers to recognize other physical, psychological and behavioural symptoms of methamphetamine intoxication beyond psychosis, as these could be crucial clues that the patient is experiencing AMIPD. These conclusions can be considered a clinically expert interpretation of prior scientific literature and topic reviews that have posed a range of nuanced and conflicting reports on the nature of methamphetamine psychosis.

These criteria are an important step in advancing the science of methamphetamine addiction. Panellists' backgrounds reflected a variety of practice settings, regions, and personal and professional backgrounds; several members reported having lived experience with addiction. Nevertheless, future work can improve the validity and usefulness of these criteria. This work may include tests of interrater reliability between providers; review of criteria by larger groups of clinicians or persons with lived experience; and study of the criteria's use in clinical practice. Notwithstanding the importance of these next steps, the panel more strongly felt that other research topics were of greater importance: understanding risk factors for progression from acute to persisting MIPD or examining medication treatments for MIPD. These highly experienced panellists likely felt urgency to advance the science of addiction treatment for their patients. These results also suggest the importance of early identification and management in clinical care.

Our methodology likely contributed to the high consensus achieved for the final diagnostic criteria. Iterative web-based survey voting began with open-ended themes and was increasingly targeted towards the specific form and content of potential final criteria. Panel surveys were complemented by email and conference discussion. Participants had access

to scientific literature and assistance for problem-solving technical barriers to participation. The specific content of the final criteria reflects terminology, symptoms and timeframes that attained high rates of endorsement through preceding surveys. The high response rates and positive experiences reported by panellists obviate the risk of participation bias.

There are limitations to these findings. Given the highly specific task of the panel in developing diagnostic criteria related to psychiatric and psychotic symptoms, we recruited psychiatrists likely to work closely with patients who have methamphetamine psychosis, including in emergency and crisis settings. The strict criteria for panel inclusion may have promoted homogeneity of panellists' experience and led to a higher likelihood of developing consensus; an intentionally high bar of $\geq 80\%$ was thus set for endorsing criteria. This work only included English-speaking clinicians and English literature notwithstanding a long history of methamphetamine addiction science occurring in other countries, notably in Asia. Results of the literature search were not judged or curated for quality, as our intent was to provide a range of references with minimal risk of biasing participants. A large electronic library was available for participants, but we did not review the full text of all articles prior to making them available to panellists. Moreover, panellists likely have variable expertise in reviewing and interpreting scientific literature, and we did not examine individual panellists' reasoning behind their opinions or literature assessments. These criteria reflect an important expert consensus on this topic, but ongoing study of their use in practice and correlation with patient outcomes will be needed.

5 | CONCLUSION

Methamphetamine-induced psychotic disorder is a highly prevalent, dangerous and complex disorder that is difficult to identify and treat. This panel poses specific diagnostic criteria for acute MIPD and persisting MIPD that will inform patient care and support researchers in studying this disease. Many clinicians and staff struggle to treat persons with difficult symptoms of methamphetamine addiction; these criteria can help providers understand and manage the most severe manifestations of patients' methamphetamine use. Ultimately, these criteria represent a necessary initial step in improving the care of millions worldwide with methamphetamine addiction.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

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Recruitment

May 2022

- Email invitations
- Consent to possible participation and ongoing communication
- Selection of 23 panelists; 1 dropped and following rates are reported out of 22 panelists

Orientation Meeting

September 2022; 100% participation

- Introduction to group members, expectations, and study subject rights
- Review of expert panel methodology
- Discussion of best means for communication among panelists including via brief follow-up survey
- Description of expert panel goals

Round 1 Survey

September 2022; 96% participation

- Open-ended prompts on approach to identifying and managing methamphetamine-induced psychosis

Round 1 Meeting

October 2022; 82% participation

- Review of response themes from Round 1 Survey
- Open discussion of challenges these themes raise for developing criteria
- Open discussion of possible criteria

Round 2 Survey

October 2022; 96% participation

- Survey on importance of developing criteria
- Vote on specific symptoms that may suggest methamphetamine-induced psychosis at different time frames
- Vote on format of eventual diagnostic criteria

Round 2 Meeting

November 2022; 77% participation

- Review of Round 2 Survey results
- Discussion on defining criteria based on timeframe relative to methamphetamine use
- Discussion on terminology for criteria and organization

Round 3 Survey

December 2022; 100% participation

- Vote on diagnostic criteria
- Feedback on future research priorities
- Feedback on quality of panel process

Round 3/ Final Meeting

January 2023; 54% participation

- Review of final endorsed criteria and other results from Round 3 Survey
- Discussion of future collaboration opportunities
- Closure of panel process

FIGURE 1.

Expert panel process and participation rates.

TABLE 1

Description of Panellists.

Characteristic	Panellists, <i>n</i> (%) total <i>n</i> = 22
Gender	
Female	14 (64%)
Male	8 (36%)
Race	
White	17 (77%)
Asian	4 (18%)
Other	1 (5%)
Ethnicity	
Hispanic	1 (5%)
Non-Hispanic	21 (95%)
Lived experience with substance use	
Yes	2 (9%)
No	14 (64%)
Prefer not to answer	6 (27%)
Profession	
Physician	22 (100%)
Board certifications	
Addiction medicine	4 (18%)
Emergency medicine	2 (9%)
Internal medicine	1 (5%)
Psychiatry	22 (100%)
Another ABMS board	3 (14%)
Primary practice environment	
Urban	18 (82%)
Rural	2 (9%)
Suburban	2 (9%)
How would you describe your primary practice environment	
Academically affiliated	9 (41%)
Academic medical center	8 (36%)
Community hospital	6 (27%)
Emergency/urgent care	15 (68%)
Regions/countries of practice	
United States (US) Midwest	3 (14%)
US South	9 (41%)
US West	9 (41%)
Canada	1 (5%)
Clinical practice experience	
Mean (SD) number of years treating patients with methamphetamine use disorder	10 (± 7) years; 226 total years
Mean (SD) number of patients treated weekly over the prior 2 years with active or remitted methamphetamine use disorder	25 (± 40)

Characteristic	Panellists, <i>n</i> (%) total <i>n</i> = 22
Mean (SD) number of patients treated weekly over the prior 2 years with methamphetamine-induced psychosis	13 ($\pm$ 11)

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TABLE 2
Diagnostic Criteria for Methamphetamine-induced psychotic disorders.

Acute methamphetamine-induced psychotic disorder
Acute MIPD is a clinical presentation of psychosis that emerges shortly after methamphetamine use.
A. There is evidence of recent methamphetamine use based on one of the following:
1. Report by patient or informant of recent methamphetamine use
2. Positive toxicology test
3. Clinical presentation of methamphetamine intoxication or withdrawal
B. The presence of any of the following psychotic symptoms:
1. Persecutory or paranoid delusions
2. Auditory hallucinations
3. Visual hallucinations
4. Parasitosis, including with tactile hallucinations
5. Tactile hallucinations, without parasitosis
C. The psychotic symptoms cause clinically significant distress, impairment, or dangerousness.
Persisting methamphetamine-induced psychotic disorder
Persisting MIP is a presentation of psychosis due to methamphetamine use in which psychosis persists beyond the initial period of intoxication or withdrawal. Persisting MIP should be considered whenever a patient with psychosis has a history of methamphetamine use.
A. The patient has a history of methamphetamine use.
B. The onset of symptoms occurred during a period of methamphetamine use and persists after the patient has stopped using.
C. The psychotic symptoms cause clinically significant distress or impairment.
D. Two timeframes describe the course of the disorder:
1. Subacute PMIPD describes symptoms persisting after the period of acute intoxication or withdrawal until 1 month of abstinence from methamphetamine. Psychotic symptoms likely to indicate subacute PMIPD:
i. Persecutory or paranoid delusions
ii. Auditory hallucinations
iii. Visual hallucinations
iv. Parasitosis, including with tactile hallucinations
v. Tactile hallucinations, without parasitosis
2. Chronic PMIPD describes symptoms persisting after 1 month of sobriety from methamphetamine. No specific psychotic symptoms differentiate PMIPD from those of primary psychotic disorders.