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Clinical and demographic characteristics of people who smoke versus inject crystalline methamphetamine in Australia: findings from a pharmacotherapy trial

Running title: Characteristics of people who smoke versus inject methamphetamine

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Abstract

Introduction and Aims: There has been a rapid increase in smoking crystalline methamphetamine in Australia. We compare the clinical and demographic characteristics of those who smoke versus inject the drug in a cohort of people who use methamphetamine. **Methods:** Participants (N=151) were dependent on methamphetamine, aged 18-60 years, enrolled in a pharmacotherapy trial for methamphetamine dependence, and reported either injecting (n=54) or smoking (n=97) methamphetamine. Measures included the Timeline Followback, Severity of Dependence Scale, Amphetamine Withdrawal Questionnaire, Craving Experience Questionnaire and the Brief Psychiatric Rating Scale (symptoms of depression, hostility, psychosis and suicidality). Simultaneous regression was used to identify independent demographic correlates of smoking methamphetamine and to compare the clinical characteristics of participants who smoked versus injected. **Results:** Compared to participants who injected methamphetamine, those who smoked methamphetamine were younger and less likely to be unemployed, have a prison history or live alone. Participants who smoked methamphetamine used methamphetamine on more days in the past four weeks than participants who injected methamphetamine (26 vs. 19 days, $P=0.001$); they did not differ significantly in their severity of methamphetamine dependence, withdrawal, craving or psychiatric symptoms ($P > 0.05$). After adjustment for demographic differences, participants who smoked had lower craving (b (SE)=-1.1 (0.5), $P=0.021$) and were less likely to report psychotic symptoms (b (SE)=-1.8 (0.7), $P=0.013$) or antidepressant use (b (SE)=-1.1 (0.5), $P=0.022$). **Discussion and Conclusion:** Smoking crystalline methamphetamine is associated with a younger less marginalised demographic profile than injecting methamphetamine, but a similarly severe clinical profile.

Keywords: methamphetamine, pharmacotherapy, characteristics, inject, smoke

INTRODUCTION

Australia has experienced a rapid rise in the availability of high purity smokable crystalline methamphetamine (“ice”) over the past decade [1, 2]. This has been associated with a dramatic increase in the popularity of smoking methamphetamine in Australia [3]. Over 90% of people who consume methamphetamine regularly now either smoke or inject this form of the drug [4, 5]. This represents a dramatic shift from the historical situation in Australia, where most harm was associated with injecting use, while non-injecting use consisted of snorting or swallowing low purity powder amphetamine or methamphetamine (referred to as “speed”), this being associated with infrequent use and low levels of harm [6, 7].

Although smoking crystalline methamphetamine is often characterised as a recreational drug use pattern in Australia [3], this route of administration delivers high bioavailability (90%), providing a rapid and intense drug effect similar to that of injection [8]. It is associated with elevated levels of dependence compared to other non-injecting routes of administration [9]. Crystalline methamphetamine smoking has been associated with significant harm and substantial treatment demand in other countries [10, 11], and this same trend is becoming apparent in Australia [3, 12], where methamphetamine smoking now accounts for the majority of amphetamine-related treatment episodes [12].

Currently there are limited data available to understand what implications this shift in the Australian drug market has for providing drug treatment and related health services. Available data suggest that people who smoke the drug have a less marginalised demographic profile than those who inject methamphetamine [3, 13-16]. However, there has not been a detailed characterisation of people who smoke crystalline methamphetamine since the trend became widespread. Nor is there any comprehensive data available on their clinical characteristics (e.g. severity of dependence, harms), which is needed to guide service development.

We provide a contemporary picture of the clinical and demographic characteristics of people who smoke versus inject methamphetamine in Australia by examining participants enrolled in a pharmacotherapy trial [17].

METHODS

Participants were from the N-ICE Trial, a 12-week pharmacotherapy trial for methamphetamine use (ACTRN12618000366257), which is detailed elsewhere [18], and which was implemented via alcohol and other drug services in Geelong, Melbourne and Wollongong, Australia. Participants were recruited in 2018-19 via advertisements (e.g. Facebook, media, and flyers in needle and syringe programs) and word-of-mouth. All participants were dependent on methamphetamine in the past year (assessed using the Composite International Diagnostic Interview [19]), seeking to reduce their methamphetamine use, and not already enrolled in treatment for substance use disorders (including pharmacotherapy). For this analysis, participants were only included if they reported either smoking or injecting as their main route of administration, excluding two participants who reported other routes of administration. All participants provided written consent prior to participation and were reimbursed AU\$30 per assessment. The trial was approved by all relevant human research ethics committees: Eastern Health (E21–2017), Barwon Health (17/202), University of Wollongong and Illawarra Shoalhaven Local Health District Health (2017/549) and Curtin University (HRE2018–0205).

Measures

A face-to-face structured interview was used to obtain information on demographics and substance use history as part of the trial eligibility assessment. Demographics included age, sex, marital status, employment status, highest qualification completed, net legal income in the past fortnight, number of children, accommodation and with whom the person was residing. Methamphetamine use history

included age at first use, first route of use, main route of administration, main form of methamphetamine used in the past month, previous methamphetamine treatment history and the participant's treatment goal for this trial.

Clinical characteristics were obtained at the initial trial assessment (n = 147). Days of methamphetamine use in the past four weeks was assessed using the Timeline Followback method [20]. Days of use in the past 28 days was recorded for all other major drug classes and psychotropic medications (use of which included both prescribed and non-prescribed use). Past week measures included severity of methamphetamine dependence, assessed using the Severity of Dependence Scale [21], methamphetamine craving, assessed using an adaptation of the Craving Experience Questionnaire [22], and methamphetamine withdrawal symptoms, assessed using the Amphetamine Withdrawal Questionnaire [23]. Psychiatric symptoms (depression, suicidality, hostility, suspiciousness, hallucinations, unusual thought content) in the last two weeks were assessed using the Brief Psychiatric Rating Scale [24], where a score of 4 or greater was used to identify clinically significant symptoms. Psychotic symptoms reflected a score of 4+ on any of the items of suspiciousness, hallucinations or unusual thought content.

Further details on the measures can be found in the online appendix.

Analysis

Data were analysed with Stata SE version 16.0 (StataCorp® LLC, College Station, TX, USA). Groups were compared using Pearson's Chi Square tests for categorical data, t-tests for continuous data and median comparison tests for skewed continuous data (where medians and interquartile ranges are reported). A series of regression analyses were used to compare the clinical characteristics of participants who injected versus smoked methamphetamine. Models adjusted for demographic and other substance use variables where these differed significantly between participants who smoked

versus injected. Linear regression was used for continuous outcomes, logistic regression for dichotomous outcomes and a negative binomial model was used for days of methamphetamine use. A sensitivity analysis was undertaken that excluded participants who reported smoking methamphetamine as their main route of administration but who reported having ever injected methamphetamine. All tests were two-sided with significance set at $P < 0.05$.

RESULTS

Demographics

Participants (N = 151) were typically Australian-born (93%) and from English-speaking backgrounds (98%); all used crystalline methamphetamine. Compared to participants who injected methamphetamine (Table 1), participants who smoked methamphetamine were younger and had used methamphetamine for fewer years. They were less likely to be unemployed, have a prison history or live alone, and more likely to live with their parents. With the exception of living with parents, these demographics remained significantly associated with smoking methamphetamine when included in a simultaneous logistic regression model along with duration of methamphetamine use (age, odds ratio 0.89, 95% confidence interval 0.84-0.95; unemployed odds ratio 0.31 95% confidence interval 0.13-0.76; prison history odds ratio 0.40 95% confidence interval 0.17-0.95; living alone odds ratio 0.24 95% confidence interval 0.09-0.66).

Clinical characteristics

Participants who smoked methamphetamine had used the drug on more days in the past four weeks than participants who injected methamphetamine (Table 2). They did not differ significantly from participants who injected methamphetamine on their severity of dependence, craving or withdrawal, or psychiatric symptoms (Table 2). Results were similar after adjustment for demographics that

differed between groups, and years of methamphetamine use (see adjusted results in Table 2), although craving was significantly lower in participants who smoked methamphetamine, as was the likelihood of psychotic symptoms and antidepressant use. Results did not change by excluding participants who smoked methamphetamine who also reported having ever injected it (Table S1). Polysubstance use was similar between groups, with this consisting mostly of tobacco, alcohol and cannabis use (see Table S2 for specific drug categories).

DISCUSSION

Building on earlier observations [14, 25], we confirm that people who smoke crystalline methamphetamine are younger and have less marginalised demographic characteristics than their peers who inject the drug (i.e. less likely to be unemployed, to have been to prison or to live alone). These demographic differences are likely to reflect a birth cohort effect, in that the sharp increase in smoking crystalline methamphetamine over the past decade [1] would have a disproportionate impact on new initiates to substance use, who tend to be in their adolescence and early adulthood. We think it is less likely that these data reflect a transition from injecting to smoking, because the majority of participants who primarily smoked methamphetamine had never injected the drug. The sociodemographic breadth of people who smoke the drug may reflect lower stigma associated with smoking as a route of administration compared to injecting, and/or the social accessibility of smoking drugs (e.g. the common practice of sharing ice pipes in social situations [26]). However, some of the demographic differences between people who smoke and inject the drug may reflect the shorter duration of use amongst people who smoke methamphetamine. It is possible that, as this younger cohort matures, they will experience similar social harms from the drug as those seen amongst people who inject (e.g. unemployment, incarceration). Transition to injecting drug use is also a possibility which we were unable to assess in this cross-sectional analysis.

Despite their more functional demographic profile, people who smoked methamphetamine used the drug more often and had a similarly severe clinical profile, compared to those who injected the drug. Although this finding may seem at odds with reports of recreational crystalline methamphetamine smoking in Australia [27], it is consistent with historical international trends of compulsive use patterns, high dependence and other harms associated with this pattern of drug use [9, 28, 29]. These observations serve as a warning given the increased popularity of methamphetamine use in North America [30] and other parts of the world [31], particularly that both smoking and injecting the drug have the capacity to convey significant harm.

One unexpected finding was slightly lower levels of craving and psychotic symptoms amongst people who smoked methamphetamine compared to those who injected, after adjustment for demographics, which seems at odds with their more frequent use. We also found lower antidepressant use amongst people who smoked methamphetamine. These could be chance findings, or they could reflect other differences between the cohorts not measured in this study (e.g. daily stressors can increase drug cravings [32]), differences in the dose used per occasion, or adjustment for demographics that are related to harms (e.g. psychosis proneness is highest in adolescence and young adulthood and diminishes with age [33]).

The characteristics of people seeking treatment for smoking methamphetamine (cf. injecting the drug) have important implications for how treatment and other health services are provided. These include treatment programs that do not disrupt employment (e.g. appointments outside of work hours, telehealth), and modes of delivery that are better suited to younger people (e.g. outdoor or exercise programs, social media or internet platforms) [34]. Given that much of the focus of harm reduction programming in Australia has been on reducing injection-related harms (e.g. provision of sterile injecting equipment to reduce blood-borne virus risk), further development and evaluation of harm

reduction services that target people who smoke stimulant drugs is required, along with thinking about how these might be delivered (e.g. provision of safer smoking kits [35]).

Limitations

Our findings reflect people entering a pharmacotherapy trial, who are not necessarily representative of people entering conventional drug treatment services, nor are they necessarily typical of people who smoke crystalline methamphetamine in the broader community. All were dependent on methamphetamine and seeking to reduce their use. The exclusion criteria for the trial also shaped the nature of the sample (e.g. the exclusion of people on opioid substitution therapy). The large number of statistical tests conducted may have inflated the type I error rate, leading to chance findings.

Summary

Our findings suggest that people who smoke crystalline methamphetamine in Australia represent a younger generation, with a less marginalised demographic profile, but with a similarly severe clinical profile, to people who inject the drug. Treatment and harm reduction options are needed that provide for this broader client profile.

Supporting Information

Additional Supporting Information may be found in the online version of this article at the publisher's website:

Detailed information on the methods of measurement.

Table S1. Clinical characteristics of participants who smoked methamphetamine and who had no history of injecting methamphetamine versus participants who injected methamphetamine.

Table S2. Other drug and use in the past month at the baseline assessment by smoking vs. injecting methamphetamine.

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Conflict of Interests

OMD has received grant support from the Brain and Behavior Foundation, Simons Autism Foundation, Stanley Medical Research Institute, Deakin University, Lilly, NHMRC and ASBDD/Servier. She has also received in kind support from BioMedica Nutraceuticals, NutritionCare and Bioceuticals. MB has received grant support from Bristol-Myers Squibb, Eli Lilly, GlaxoSmithKline, Organon, Meat and Livestock Board, Novartis, Mayne Pharma and Servier; has been a speaker for AstraZeneca, Bristol-Myers Squibb, Eli Lilly, GlaxoSmithKline, Janssen-Cilag, Lundbeck, Merck, Pfizer, Sanofi Synthelabo, Servier, Solvay and Wyeth; and has served as a consultant to AstraZeneca, Bristol-Myers Squibb, Eli Lilly, GlaxoSmithKline, Janssen-Cilag,

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Table 1. Comparison of participants who smoked versus injected methamphetamine

	Main route of methamphetamine administration		<i>P</i> value	Total sample (N = 151)
	Injecting (n = 54)	Smoking (n = 97)		
<i>Demographics</i>				
Age, median	42	35	< 0.001	38
Male, %	61	59	0.78	60
Unemployed, %	69	48	0.017	56
Prison history, %	38	22	0.034	28
Non-related adult(s)	19	16	0.75	17
Single, %	39	38	0.93	38
Children under 16 years of age, %	37	42	0.53	40
Low income (<\$800/fortnight)	70	56	0.08	62
Years of schooling, median	11	10	0.93	11
Tertiary qualifications, %			0.92	
Nil	29	30		29
University	9	11		11
Trade/technical	62	60		60
Accommodation, %			0.08	
Public housing	22	8		13
Privately rented or owned	50	57		54
Living with family or friends	24	33		30
Temporary or no fixed address	4	2		3
Household residents ^a , %				
Live alone	39	16	0.002	25
Partner	17	26	0.20	23
Children	13	19	0.38	17
Parent(s)	15	32	0.021	26
Other family	9	11	0.69	11
<i>Methamphetamine use</i>				
Age of first use (median years)	21	20	0.34	20
Route of administration on first use, %			< 0.001	
Inject	39	1		15
Smoke	26	55		44
Snort	20	30		27
Swallow	15	14		15
Ever injected methamphetamine, %	100	20	< 0.001	48
Duration of use, median (IQR) years	18 (11–26)	12 (8–19)	0.007	14 (8–22)
Treatment goal of complete abstinence, %	78	87	0.16	83
Methamphetamine treatment history, %	54	57	0.72	56
<i>Study site</i> , %			0.38	
Melbourne	28	37		34
Geelong	37	37		37
Wollongong	35	26		29

^aParticipants could select all options that applied. IQR, interquartile range.

Table 2. Clinical characteristics of the sample

	Total sample ^a (n = 147)	Main route of methamphetamine administration		Unadjusted		Adjusted ^f	
		Injecting (n = 52)	Smoking (n = 95)	b (SE)	P value	b (SE)	P value
Severity of dependence (mean SDS score)	8.1 (3.8)	7.4 (3.8)	8.5 (3.7)	1.08 (0.65)	0.10	0.17 (0.75)	0.82
Craving (mean CEQ score)	5.1 (2.4)	5.6 (2.4)	4.9 (2.3)	-0.75 (0.40)	0.07	-1.11 (0.47)	0.021
Withdrawal (mean AWQ score)	19.9 (7.4)	20.1 (7.4)	19.8 (7.5)	-0.32 (1.29)	0.81	-0.97 (1.47)	0.51
<i>Psychiatric symptoms (BPRS)^b, %</i>							
Hostility	43	35	47	0.53 (0.36)	0.14	-0.07 (0.46)	0.88
Psychotic symptoms	13	15	12	0.21 (0.49)	0.67	-1.77 (0.71)	0.013
Depression	42	37	45	0.36 (0.35)	0.31	0.10 (0.42)	0.82
Suicidality	7	10	5	-0.65 (0.66)	0.32	0.84 (0.83)	0.31
Days of methamphetamine use in past 4 weeks ^c , median	24	19	26	0.21 (0.06)	0.001	0.25 (0.07)	< 0.001
Number of other drug classes used in the past month ^d , %	2.1	2.1	2.1	0.01 (0.18)	0.97	0.08 (0.21)	0.706
<i>Psychotropic medication use in the past month^e, %</i>							
Benzodiazepines	19	23	17	-0.39 (0.43)	0.36	-0.83 (0.56)	0.14
Antidepressants	27	35	22	-0.62 (0.38)	0.10	-1.09 (0.48)	0.022
Antipsychotics	14	19	12	-0.60 (0.48)	0.21	-0.72 (0.58)	0.22

^aAssessed at first trial assessment. ^bClinically significant symptoms (score of 4+ on BPRS items). ^cRegression coefficients are from a negative binomial regression model. ^dIncludes heroin, other opioids, cocaine, ecstasy, hallucinogens, inhalants, cannabis, alcohol and tobacco. ^eIncludes both prescribed and non-prescribed use. ^fAdjusted for duration of methamphetamine use (years) and demographics (prison history, unemployment, accommodation, living alone and living with parents). AWQ, Amphetamine Withdrawal Questionnaire; BPRS, Brief Psychiatric Scale; CEQ, Craving Experience Questionnaire; SDS, Severity of Dependence Scale.

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