Original Paper

The epidemiology of 5-methoxy-*N*,*N*-dimethyltryptamine (5-MeO-DMT) use: Benefits, consequences, patterns of use, subjective effects, and reasons for consumption

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Alan K Davis[1], Joseph P Barsuglia[2], Rafael Lancelotta[3], Robert M Grant[4] and Elise Renn[2]

Abstract

Background/aim: 5-Methoxy-*N*,*N*-dimethyltryptamine (5-MeO-DMT) is a psychoactive compound found in several plants and in high concentrations in *Bufo alvarius* toad venom. Synthetic, toad, and plant-sourced 5-MeO-DMT are used for spiritual and recreational purposes and may have psychotherapeutic effects. However, the use of 5-MeO-DMT is not well understood. Therefore, we examined patterns of use, motivations for consumption, subjective effects, and potential benefits and consequences associated with 5-MeO-DMT use.

Methods: Using internet-based advertisements, 515 respondents (M_{age}=35.4. SD=11.7; male=79%; White/Caucasian=86%; United States resident=42%) completed a web-based survey.

Results: Most respondents consumed 5-MeO-DMT infrequently (≤once/year), for spiritual exploration, and had used less than four times in their lifetime. The majority (average of 90%) reported moderate-to-strong mystical-type experiences ($M_{intensity}$=3.64, SD=1.11; range 0–5; e.g., ineffability, timelessness, awe/amazement, experience of pure being/awareness), and relatively fewer (average of 37%) experienced very slight challenging experiences ($M_{intensity}$=0.95, SD=0.91; range 0–5; e.g., anxiousness, fear). Less than half (39%) reported repeated consumption during the same session, and very few reported drug craving/desire (8%), or legal (1%), medical (1%), or psychiatric (1%) problems related to use. Furthermore, of those who reported being diagnosed with psychiatric disorders, the majority reported improvements in symptoms following 5-MeO-DMT use, including improvements related to post-traumatic stress disorder (79%), depression (77%), anxiety (69%), and alcoholism (66%) or drug use disorder (60%).

Conclusion: Findings suggest that 5-MeO-DMT is used infrequently, predominantly for spiritual exploration, has low potential for addiction, and might have psychotherapeutic effects. Future research should examine the safety and pharmacokinetics of 5-MeO-DMT administration in humans using rigorous experimental designs.

Keywords

Epidemiology, tryptamines, 5-MeO-DMT, 5-methoxy-*N*,*N*-dimethyltryptamine

Introduction

5-Methoxy-*N*,*N*-dimethyltryptamine (5-MeO-DMT; also known as '5-MeO-DMT,' 'Toad,' or 'The God Molecule') is a natural psychoactive indolealkylamine substance (Szabo et al., 2014; Yu, 2008). 5-MeO-DMT is the most prominent psychoactive ingredient of *Bufo alvarius* toad venom (Lyttle et al., 1996; Weil and Davis, 1994) and is also found in a number of plants and shrubs (e.g., virola resin, peregrina seeds, *Dictyoloma incanescens*) (Agurell et al., 1969; Pachter et al., 1959; Torres and Repke, 2006). 5-MeO-DMT was first synthesized in 1936 (Hoshino et al., 1936), but plant extracts and other botanical 5-MeO-DMT preparations (e.g., Yopo snuff) have reportedly been used among indigenous cultures in the Americas dating back to pre-Columbian times (Ott, 2001b; Weil and Davis 1994). Although some reports also suggest that *Bufo alvarius* toad venom may have been used historically by indigenous cultures (Weil and Davis, 1994), little evidence supports this claim and it may be that use of toad venom is a more recent development (VICELAND, 2017).

Despite anecdotal reports on the Internet, which describe current spiritual, recreational, and therapeutic use of 5-MeO-DMT in the USA and elsewhere (Erowid, n.d.), prevalence and use characteristics are largely unknown because use of this specific substance is not included in most national epidemiological surveys (Palamar et al., 2015). Nevertheless, recent data from the USA

[1]Behavioral Pharmacology Research Unit, Department of Psychiatry, Johns Hopkins School of Medicine, Baltimore, MD, USA
[2]Crossroads Treatment Center, Rosarito, Mexico
[3]School of Counseling, Leadership, Advocacy, and Design, University of Wyoming, Laramie, WY, USA
[4]Department of Medicine, University of California, San Francisco, CA, USA

Corresponding author:
Alan K. Davis, Johns Hopkins University School of Medicine, 5510 Nathan Shock Drive, Baltimore, MD 21224, USA.
Email: alan.kooi.davis@gmail.com

indicate that only 1.2% of adults in the general population reported any 'psychedelic tryptamine' use (e.g., N, N-dimethyltryptamine, 5-methoxy-diisopropyltryptamine) between 2009 and 2013 (Palamar et al., 2015). If US adults reported 5-MeO-DMT use within this category of substances, then prevalence appears to be quite low. Additionally, estimates of the global prevalence of 5-MeO-DMT use are limited by lack of inclusion in epidemiological surveys (United Nations Office on Drugs and Crime, 2014). However, when it has been included, 5-MeO-DMT is categorized with other psychoactive tryptamines and synthetic cathinones and cannabinoids as a group of 'novel psychoactive substances,' thus limiting ability to estimate global prevalence (Khaled et al., 2016).

In terms of its pharmacological effects, 5-MeO-DMT is a potent, fast-acting, psychedelic substance (Ott, 2001a). In animal models, 5-MeO-DMT acts as a non-selective 5-HT agonist (Shen et al., 2011), active at both the 5-HT_{1A} and 5-HT_{2A} receptors (Jiang et al., 2016). 5-MeO-DMT appears to have a higher affinity for the 5-HT_{1A} receptor subtype (Spencer et al., 1987) and also inhibits the reuptake of 5-HT (Nagai et al., 2007). This pattern of neurotransmitter binding affinity is similar to that of structurally similar psychedelic tryptamines (e.g., N,N-dimethyltryptamine, 5-methoxy-diisopropyltryptamine; Fantegrossi et al., 2006; Rabin et al., 2002; Sadzot et al., 1989; Winter, 2009), and somewhat different from tryptamines with stronger affinity for the 5-HT_2 receptor family (e.g., *O*-phosphoryl-4-hydroxy-*N,N*-dimethyltryptamine or 'psilocybin'; McKenna et al., 1990). 5-MeO-DMT is metabolized through oxidative deamination by MAO-A, and its active metabolite, bufotenine, has been shown to be a potent ligand of 5-HT_{2A} receptors (Roth et al., 1997; Shen et al., 2010), although it is unknown whether this metabolite has any discernable psychoactive effect.

Published studies of human self-experiments describe a range of subjective effects of 5-MeO-DMT that vary depending on the dose and route of administration (Ott, 2001a; Shulgin and Shulgin, 1997). Such effects include auditory, visual, and time perception distortions and emotional experiences, as well as memory impairment, with peak effects between 35 and 40 minutes after insufflation or within seconds-to-minutes when smoked (Ott, 2001a; Shulgin and Shulgin, 1997). Furthermore, current unpublished reports of 5-MeO-DMT use describe inhalation (e.g., smoking or vaporizing) as a common means of consumption with initial onset of effects within 60 seconds and peak total duration of effect between 5 and 20 minutes (Erowid, n.d.). Although there is limited evidence about the scope of 5-MeO-DMT use, safety, or its effects, the Drug Enforcement Administration nonetheless placed 5-MeO-DMT in Schedule I of the US Controlled Substances Act in 2011 (Drug Enforcement Administration, Department of Justice, 2010), in large part due to being similar in molecular structure to *N,N*-dimethyltryptamine and evidence that it was four to five times more potent (Ott, 2001a). Although the legal status of 5-MeO-DMT varies by country, most primarily English-speaking countries have placed restrictions on its use (e.g., Misuse of Drugs Act 1971).

Despite the fact that 5-MeO-DMT use is illegal in the USA and elsewhere, anecdotal reports indicate that consumption continues in a variety of underground ceremonial settings as a form of spiritual exploration (Psychedelic Times, 2016). Additionally, 5-MeO-DMT use continues among individuals who might purchase 5-MeO-DMT sold on the Internet or from other sources, extract 5-MeO-DMT from natural sources, for the purpose of spiritual exploration or recreation (Reddit, 2011). There is also anecdotal and empirical evidence that some people use 5-MeO-DMT for the purpose of treating psychiatric conditions, including symptoms related to depression, anxiety, post-traumatic stress disorder, and problematic substance use, either by self-administration (Psychedelic Times, 2016) or through visiting treatment facilities that provides 5-MeO-DMT in locations where the substance is unregulated (Lancelotta, 2017; Thoricatha, 2015).

Although the basic pharmacology of 5-MeO-DMT has been examined in animal models (e.g., Jiang et al., 2016; Nagai et al., 2007; Shen et al., 2011; Spencer et al., 1987), and the subjective effects have been published in case reports of self-administration (Ott, 2001a; Shulgin and Shulgin, 1997) and provided in anecdotal reports posted on the Internet (Erowid, n.d.), we could find no epidemiological studies examining the patterns of use, subjective effects, motivations for use, or potential medical and psychiatric harms/benefits of consuming 5-MeO-DMT. The relative absence of information about the scope of 5-MeO-DMT use limits understanding of the safety and risk profile of this substance, which is needed to inform the design of future clinical trials. Therefore, the primary aim of this study is to examine the epidemiology of 5-MeO-DMT use among English-speaking adults who have consumed 5-MeO-DMT at least once in their lifetime. As a secondary aim, we examined whether there were changes in medical and psychiatric functioning following 5-MeO-DMT use. Aim 3 involved an examination of differences in the subjective effects and the patterns and motivations for use as a function of the type of 5-MeO-DMT consumed (i.e., synthetic vs toad venom vs plant extracts/yopo snuff).

Methods

Procedure

From April 2017 to August 2017 we posted written recruitment advertisements on the Internet (e.g., at 5meodmt.org, reddit.com, bluelight.org), created a Facebook group for the study (i.e., 5-MeO-DMT Research Project) and posted several advertisements in this Facebook group page and on other pages on Facebook related to 5-MeO-DMT use. All recruitment advertisements contained information regarding the purpose of the study, the estimated amount of time required to complete the survey (approximately 20 minutes), and the anonymity of completing the survey. Additionally, we informed potential respondents that we would donate US$2 per person, up to US$250, to the Multidisciplinary Association for Psychedelic Studies as a way to 'pay it forward' for their time. We also created website banner advertisements that were shown to visitors at erowid.com and bluelight.org. Upon clicking any of our advertisments, potential respondents were sent to the secure survey site (hosted by surveygizmo.com), where they viewed the informed consent document which repeated the purpose of the study and described eligibility criteria, including being at least 18 years old, able to read and understand English, and having used 5-MeO-DMT at least once in their lifetime. No personal identifying information was collected in the survey. All study procedures were approved by the human subject's review board at Bowling Green State University.

Measures

5-MeO-DMT survey. We began the survey by describing the various types of 5-MeO-DMT (i.e., chemical/synthetic, toad venom,

plant extract, yopo, other). We also asked respondents to report which of these types of 5-MeO-DMT they had *ever* used and with which type of 5-MeO-DMT they had *the most* experience. The survey also included items that asked about frequency of use, typical dose, and motives for using 5-MeO-DMT (e.g., recreation, spiritual exploration, healing from trauma, treatment for addiction, treatment for depression, because my friends tried it). Additionally, the survey included questions examining the most common routes of administration (e.g., smoking/vaporizing, insufflation, injecting), age at first use, stability of recent consumption (e.g., use in the past 12 months increased, stayed the same, or decreased), and whether there were other people present when they consumed 5-MeO-DMT, and if so, how many people were also using 5-MeO-DMT and how many were not also using.

We also asked respondents questions about the typical location of 5-MeO-DMT use (e.g., own home/apartment, friend's home/apartment) and who (if anyone) has administered the 5-MeO-DMT to them (versus self-administration). In addition, we included variables assessing several aspects of addiction potential, such as the frequency of repeated consumption in the same session, craving/desire, possible consequences they may have experienced related to 5-MeO-DMT use (e.g., psychiatric problems, medical treatment, or legal problems associated with use), and whether they ever attempted to quit, reduce, or increase their consumption. Moreover, we asked from where or from whom they obtained their 5-MeO-DMT, the potential clinical or spiritual applications of 5-MeO-DMT, and we asked them to compare the intensity of 5-MeO-DMT to other psychedelic substances with which they were familiar (e.g., LSD, psilocybin). Finally, we included a series of questions about respondents' history of being diagnosed with several medical (e.g., asthma, coronary artery disease) or psychiatric (e.g., depression, anxiety) conditions and whether their symptoms associated with each condition had improved, stayed the same, or worsened following 5-MeO-DMT use. The full survey is available from the corresponding author.

Acute Mystical experiences. We included the Mystical Experiences Questionnaire (MEQ30), a 30-item self-report measure developed to assess the subjective mystical experiences one might have after taking a hallucinogen (Maclean et al., 2012). Respondents were asked to reflect on the first experience they had with 5-MeO-DMT and to describe the intensity with which they experienced each mystical effect using a 6-point scale from 'None; not at all' to 'Extreme.' Previous research (Maclean et al., 2012) has found that the measure produces four subscales: (1) Mystical; (2) Positive mood; (3) Transcendence of time/space; and (4) Ineffability. The MEQ also yields an MEQ total scale score which can be used to rate the overall intensity of mystical experiences. Furthermore, similar to Griffiths et al. (2006), we also calculated the proportion of the sample who experienced a 'complete mystical experience' (i.e., the proportion of the sample whose mean score for each of the four MEQ subscales was at least three-fifths of the total possible score = 60%). Internal consistency of the total scale and each subscale in the current sample was: Total scale (Cronbach's alpha = 0.97), Mystical (Cronbach's alpha = 0.96), Positive Mood (Cronbach's alpha = 0.90), Transcendence (Cronbach's alpha = 0.93), and Ineffability (Cronbach's alpha = 0.91).

Acute Challenging experiences. We included the Challenging Experiences Questionnaire (CEQ), a 26-item self-report measure developed to assess the intensity of challenging experiences one might have after taking a hallucinogen (Barrett et al., 2016). Respondents were asked to reflect on the first experience they had with 5-MeO-DMT and to describe the intensity with which they experienced each challenging psychological or physical experience using a 6-point scale from 'None; not at all' to 'Extreme.' Previous research (Barrett et al., 2016) has found that the measure produces seven subscales: (1) Fear; (2) Grief; (3) Physical distress; (4) Insanity; (5) Isolation; (6) Death; and (7) Paranoia. We also calculated a CEQ total scale score to rate the overall intensity of challenging experiences. Internal consistency of the total scale and each subscale in the current sample was: Total Scale (Cronbach's alpha = 0.94), Fear (Cronbach's alpha = 0.93), Grief (Cronbach's alpha = 0.85), Physical distress (Cronbach's alpha = 0.79), Insanity (Cronbach's alpha = 0.78), Isolation (Cronbach's alpha = 0.87), Insanity (Cronbach's alpha = 0.78), Death (Cronbach's alpha = 0.88), and Paranoia (Cronbach's alpha = 0.63).

Drug use history. We designed this measure to examine the frequency of past 3-month use of alcohol, tobacco, and a variety of other substances (e.g., MDMA/ecstasy, cocaine, methamphetamine, marijuana/cannabis, synthetic cannabinoids, mushrooms, ayahuasca, iboga/ibogaine, LSD/Acid, synthetic cathinones, etc.) on a scale from 0 to 90 days.

Demographic questionnaire. We designed this measure to examine the age, gender, ethnicity, sexual orientation, country/region of residence, employment status, level of education, and relationship status of each respondent.

Data analyses. We began by conducting frequency counts and descriptive analyses of demographic characteristics, patterns of using 5-MeO-DMT, motivations for consumption, subjective mystical and challenging effects, and medical/psychiatric harms/benefits variables. Next, using a series of chi-square and oneway ANOVAs, we examined differences in demographic characteristics, subjective mystical and challenging effects, patterns of use, and motives for consumption as a function of the type of 5-MeO-DMT that respondents reported they had the most experience with (i.e., synthetic vs toad venom vs plant extract/yopo). Because of the limitations of using a Bonferroni-corrected alpha (e.g., testing of an irrelevant null hypothesis (study-wide error rate) and increasing the likelihood of Type II error in a large sample; Perneger, 1998), an alpha of 0.05 was used to determine the significance of statistical tests. All analyses were conducted using SPSS v.24 (IBM Corp, New York, NY, USA).

Results

Respondent characteristics

During recruitment, 2207 people clicked one of the recruitment ads and were presented with information about the study. Of these individuals, 569 consented to participate, began filling out the survey, and completed all of the main study questionnaires related to 5-MeO-DMT consumption. Of these respondents, we excluded 46 because they did not know or were unable to identify what form of 5-MeO-DMT they had used (i.e., synthetic, toad venom, plant extract/yopo) and thus would have been eliminated in analyses of subgroup differences. Of the remaining 523, we excluded 4

Table 1. Demographic characteristics of total sample and each subsample of 5-MeO-DMT users.

Characteristic	Total sample	Synthetic	Toad	Plant Extract/Yopo	*F* or χ^2	Post hoc
	n=515[a]	*n*=284[b]	*n*=148[c]	*n*=83[d]		
	M(SD) or %	M(SD) or %	M(SD) or %	M(SD) or %		
Age	35.63 (11.65)	34.14 (11.71)	40.27 (9.97)	32.51 (11.94)	17.84***	S=P<T
Gender					47.80***	
Female	20%	12	40	15		S=P<T
Male	80	88	60	85		S=P>T
Ethnicity					2.98	
White/Caucasian	86%	88	82	86		
Non-White/Caucasian (e.g., Black/African, Asia/Pacific Islander, Latino(a), other)	14	12	18	15		
Sexual orientation					1.25	
Heterosexual	82%	80	84	85		
Non-heterosexual (e.g., homosexual, bisexual, asexual)	18	20	16	15		
Country[e]					3.65	
USA	41%	44	34	47		
Non-USA	59	56	66	53		
US region					16.70*	
West	49%	45	65	41		S=P<T
South	22	23	20	20		S=P=T
Midwest	17	19	5	23		S=P>T
Northeast	13	13	10	16		S=P=T
Employment status					5.64	
Full time	48%	49	51	43		
Part time	18	17	19	21		
Unemployed	12	14	7	13		
Other (e.g., retired, disabled)	22	20	23	23		
Highest education level					29.42***	
High school or less	16%	19	7	18		S=P>T
Some college, no degree	26	26	20	37		T<P
Trade/technical school/Associates degree	13	11	15	13		S=P=T
Bachelor's degree	24	25	24	20		S=P=T
Advanced degree (MA, PhD, MD)	22	19	33	12		S=P<T
Relationship status					6.25*	
Married/partnered	48%	44	51	49		S<P
Single/divorced	52	56	49	41		S>P

*$p < 0.05$; ** $p < 0.01$; *** $p < 0.001$.
S: Synthetic/Chemical; T: Toad Venom; P: Plant Extract/Yopo.
[a]Range is 497–515.
[b]Range is 273–284.
[c]Range is 140–148.
[d]Range is 81–83.
[e]*n* by condition (Total sample = 396; Synthetic = 218; Toad = 120; Plant Extract/Yopo = 58).

because of duplicate IP addresses, 1 for careless responding, 2 for reporting that they were under age 18 at the time of survey, and 1 for reporting that they had never used 5-MeO-DMT. The final sample was comprised of 515 respondents.

As examination of Table 1 reveals, the majority of respondents were Caucasian (86%), heterosexual (82%), and male (79%), with a mean age of 35.4 years (SD = 11.7), and resided outside the USA (58%). See Table 1 for further demographic characteristics of the sample. Respondents also reported consuming a variety of substances in the 3 months prior to the survey, with marijuana/cannabis (M_{days}=34.22; SD=37.43), tobacco (M_{days}=25.12; SD=36.99), and alcohol (M_{days}=16.22; SD=23.59) being consumed the most frequently. See Table 2 for more details about frequency of other substance use.

Patterns of 5-MeO-DMT use and motivations for consumption

Overall, respondents reported having the most experience with synthetic 5-MeO-DMT (55%; *n*=284), and almost one-third

Table 2. Proportion of sample using each substance in the past 3 months, and the average number of days using alcohol and other substances in the past 3 months in total sample and each substance-specific subsample.

Scale	Proportion Total sample	Mean Total sample	Synthetic	Toad	Plant Extract/ Yopo	*F*	Post hoc
	n=515	*n*=515 [a]	*n*=284[b]	*n*=148[c]	*n*=83[d]		
	%	M(SD)	M(SD)	M(SD)	M(SD)		
Alcohol	77%	16.22 (23.59)	16.96 (24.06)	14.33 (21.72)	16.94 (25.13)	0.63	
MDMA/ecstasy	32	0.80 (4.27)	0.65 (1.47)	0.51 (1.15)	1.76 (10.21)	2.49	
Cocaine	23	1.06 (5.09)	1.24 (5.88)	0.67 (3.91)	1.07 (3.66)	0.57	
Methamphetamine	21	2.67 (11.74)	2.73 (11.25)	1.86 (10.73)	3.95 (14.88)	0.76	
Marijuana/cannabis	78	34.22 (37.43)	37.11 (38.37)	24.33 (32.77)	41.60 (38.82)	7.43**	S = P > T
Synthetic cannabinoids	9	0.09 (0.98)	0.09 (0.97)	0.01 (0.09)	0.25 (1.65)	1.49	
Mushrooms/psilocybin	41	1.22 (4.63)	1.07 (5.66)	1.19 (1.98)	1.80 (3.78)	0.73	
Ayahuasca	19	0.52 (3.19)	0.36 (3.70)	0.87 (2.70)	0.48 (1.62)	1.12	
DMT	34	1.37 (5.29)	1.16 (4.02)	1.05 (2.58)	2.67 (10.34)	2.77	
San Pedro	15	0.14 (0.83)	0.05 (0.21)	0.25 (1.39)	0.31 (0.90)	4.43*	NS
Peyote	13	0.11 (0.67)	0.06 (0.34)	0.09 (0.34)	0.32 (1.49)	4.43*	S < P
Iboga/ibogaine	10	0.08 (0.81)	0.06 (0.92)	0.10 (0.66)	0.08 (0.59)	0.09	
LSD/Acid	44	1.87 (5.56)	1.58 (3.19)	1.82 (7.56)	3.00 (7.78)	1.92	
Other psychedelics	25	0.60 (1.98)	0.69 (2.21)	0.14 (0.43)	1.07 (2.53)	5.86**	S = P > T
Psychedelic res. chem.	25	0.76 (3.13)	1.09 (3.88)	0.11 (0.58)	0.66 (2.41)	4.39*	S > T
Opioid res. chem.	11	0.07 (0.60)	0.08 (0.73)	0.02 (0.26)	0.10 (0.51)	0.47	
Benzo res. chem.	18	1.09 (5.86)	1.61 (7.49)	0.13 (0.96)	0.86 (3.15)	2.89	
Dissociative res. chem.	16	0.67 (4.52)	0.90 (5.29)	0.04 (0.26)	0.93 (5.32)	1.72	
Stimulant res. chem.	14	0.35 (2.01)	0.51 (2.54)	0.14 (0.94)	0.07 (0.35)	2.33	
Synthetic cathinones	13	0.23 (1.71)	0.37 (2.24)	0.02 (0.26)	0.04 (0.20)	2.34	
Street opioids	16	1.06 (7.43)	1.33 (9.26)	0.67 (4.15)	0.69 (2.51)	0.44	
Prescription opioids	29	4.15 (15.37)	4.12 (14.95)	2.41 (10.75)	7.38 (22.26)	2.40	
Prescription stimulants	25	4.37 (15.80)	4.79 (16.32)	2.01 (10.64)	6.94 (20.41)	2.47	
Tobacco	56	25.12 (36.99)	23.72 (36.12)	19.92 (34.46)	40.10 (41.28)	7.50**	S = T < P
Benzos	35	4.57 (14.07)	6.28 (16.71)	0.84 (3.22)	4.79 (13.88)	6.67**	S > T
Ketamine	23	0.97 (5.40)	1.40 (6.89)	0.37 (2.24)	0.46 (1.65)	2.00	
Inhalants	16	0.35 (2.01)	0.46 (2.55)	0.04 (0.26)	0.48 (1.26)	2.07	
PCP	11	0.25 (4.10)	0.36 (5.36)	0.09 (0.88)	0.17 (0.88)	0.21	

Note: When the standard deviation is greater than the mean the data are skewed due to a large proportion of zeros.
Res. chem.: research chemicals; PCP: phencyclidine; Benzo: benzodiazapine; LSD: lysergic acid diethylamide; DMT: dimethyltryptamine; MDMA: 3,4-methylenedioxymethamphetamine.
*$p < 0.05$; **$p < 0.01$; ***$p < 0.001$.
[a]Range 466–505.
[b]Range 267–282.
[c]Range 126–141.
[d]Range 70–82.

(29%; *n*=148) reported having the most experience with toad venom. The remainder of the sample (16%; *n*=83) reported that they had the most experience with plant extracts or other botanical preparations containing 5-MeO-DMT (e.g., yopo snuff). As Table 3 reveals, most respondents (60%) had consumed 5-MeO-DMT in the past year, had consumed 5-MeO-DMT through a smoking/vaporizing route of administration (81%), had consumed 5-MeO-DMT less than four times in their lifetime (59% 1–4 times total), with less than one-quarter (21%) reporting lifetime use of more than 10 occasions. Of those who had used 5-MeO-DMT more than one time, most (54%) used 5-MeO-DMT at a frequency of about once per year or less. Of all respondents, most used in the setting of their own or a friend's apartment/home (64%), and had obtained the substance from a guide/session leader (30%), a friend (29%), or the Internet (26%). Regarding their motivations for consumption, the majority of the sample (68%) reported spiritual exploration as their top reason, with small proportions reporting that recreation (18%) or healing/psychological treatment (14%) as the primary reason for use.

Regarding addiction potential, most respondents (61%) reported that they never re-dosed immediately after taking 5-MeO-DMT, although approximately one-quarter (28%) reported sometimes re-dosing, and a notably small proportion (11%) reporting that they frequently or always re-dosed. Additionally, very few respondents reported craving/desire for 5-MeO-DMT (8%), ever being arrested or in legal trouble due to 5-MeO-DMT use (1%),

ever being in therapy or psychiatric treatment (1%), or seeking medical attention (1%) as a result of 5-MeO-DMT use. Moreover, most respondents (86%) reported that their use in the past year had decreased or stayed the same, and almost all (~95%) reported that they never attempted to reduce or quit their use of 5-MeO-DMT, suggesting that use is moderated in large part without a need for personal or medical/psychiatric interventions, and is not associated with behaviors requiring law enforcement.

Subjective effects of 5-MeO-DMT

As Table 4 reveals, large proportions of respondents (average of 90%) reported experiencing moderate-to-strong mystical-type experiences after consuming 5-MeO-DMT ($M_{intensity}$=3.64, SD=1.11; range 0–5). For example, more than 90% reported on individual items of the MEQ that they experienced freedom from the limitations of their personal self and feeling a unity or bond with what was felt to be greater than their personal self, experience of pure being or awareness, experience of oneness in relation to an inner world within, and gained insightful knowledge experienced at an intuitive level. Large proportions (84–96%) also experienced a variety of moderate-to-strong euphoric and positive mood experiences, including amazement, tenderness and gentleness, peace and tranquility, ecstasy, awe or awesomeness, and joy. Transcendent experiences (e.g., loss of sense of time, sense of space, awareness of location) were also very common (87–97% of sample), as were the endorsement of ineffable qualities of their experience such as a sense that the experience could not adequately be described in words. Approximately one-half (57%) of the sample had a 'complete mystical experience' characterized by endorsement of ≥ 60% of the total possible score across all four subscales of the MEQ30.

Although relatively less common compared with mystical effects, some respondents (average of 37%) reported experiencing challenging psychological and somatic experiences ($M_{intensity}$=0.95, SD=0.91; range 0–5; see Table 5). For example, between 40% and 66% of respondents reported experiences of feeling their heart beat, fear, frightened, their body shake/tremble, anxious, as if they were dead or dying, shaky inside, that something horrible would happen, like crying, pressure or weight in their chest or abdomen, and panic, and having the profound experience of their own death. Despite endorsement of these challenging experiences, the overall intensity of these experiences was rated as 'very slight' (1) on a scale from 'None; not at all' (0) to 'Extreme' (5).

Compared with other psychedelic substances that respondents reported having used (i.e., LSD (53% had used), mushrooms (19% had used), and ayahuasca/DMT (15% had used)), almost two-thirds (60%) considered the subjective effects of 5-MeO-DMT to be 'more intense' than these other familiar psychedelic substances.

Subjective effect of 5-MeO-DMT use on medical and psychiatric functioning

Very few respondents reported being diagnosed with medical conditions (see Table 6), including asthma (12%), high blood pressure (9%), or chronic fatigue syndrome (8%), but almost all of these respondents (73–78%) reported that there were no changes in medical functioning following 5-MeO-DMT use. Interestingly, small proportions (15–24%) reported that symptoms associated with these medical conditions were better after 5-MeO-DMT use, and notably small proportions (4–7%) reported that their symptoms had worsened. The incidence of self-reported lifetime psychiatric disorders in this sample included anxiety (63%), depression (61%), drug use disorder (33%), alcoholism or hazardous drinking (22%), attention deficit hyperactivity disorder (22%), post-traumatic stress disorder (21%), eating disorder (10%), obsessive compulsive disorder (11%), and bipolar disorder (8%). Similar to those with medical conditions, psychiatric symptoms were rarely reported as worsened following 5-MeO-DMT use (average of 4% reporting worsening of symptoms across all psychiatric conditions), but comparatively larger proportions reported that their psychiatric conditions were improved following 5-MeO-DMT use, including those experiencing improvements in depression (77%), post-traumatic stress disorder (79%), anxiety (69%), substance use problems (~63%), and obsessive compulsive disorder (53%). Moreover, smaller proportions, but often more than one-third of the sample (35–50%), reported improvements in symptoms related to attention deficit hyperactivity disorder, autism, bipolar disorder, and eating disorder.

Comparison of patterns of use, motivations for consumption, and subjective effects by subtype of 5-MeO-DMT

As Table 1 reveals, the Synthetic 5-MeO-DMT group was similar in age and gender distribution to the Plant Extract/Yopo group, both groups being significantly younger and comprised of fewer females compared with the Toad group. Additionally, as shown in Table 2, there were few differences in the number of days (in the past 3 months) that respondents used other substances, regardless of the subtype of 5-MeO-DMT consumed. When significant differences were found, it was typically those in the Synthetic group who used other substances more frequently (e.g., marijuana/cannabis, benzos, psychedelic research chemicals, other psychedelics) compared with those in the Toad group. As Table 3 reveals, almost all of the Toad group smoked/vaporized 5-MeO-DMT and significantly larger (but still small) proportions in the Synthetic and Plant Extract/Yopo groups consumed by other means (i.e., swallowed or snorted). Additionally, those respondents in the Synthetic and Plant Extract/Yopo groups had higher numbers of total lifetime use of 5-MeO-DMT compared with the Toad group, but the Synthetic group consumed less frequently than the Toad or Plant Extract/Yopo groups. Frequency of re-dosing immediately after consumption was also different between groups, wherein more people in the Toad group reported never re-dosing compared with the Synthetic and Plant Extract/Yopo groups. Moreover, there were no significant group differences in addiction potential or safety variables including no differences in the proportion experiencing craving/desire, legal trouble, medical treatment, or psychiatric treatment associated with 5-MeO-DMT use, and notably small and statistically equivalent proportions in each group reported ever attempting to reduce or quit using 5-MeO-DMT.

As Table 3 also reveals, although most respondents in each group reported spiritual exploration as their top reason for using 5-MeO-DMT, significantly larger proportions of those in the

Table 3. Patterns of 5-MeO-DMT use in the total sample and in each subtype of 5-MeO-DMT subsample.

Characteristic	Total sample	Synthetic	Toad	Plant Extract/Yopo	χ^2	Post hoc
	n=515[a]	*n*=284[b]	n=148[c]	*n*=83[d]		
	M(SD) or %	M(SD) or %	M(SD) or %	M(SD) or %		
Type of 5-MeO-DMT ever used						
Chemical/synthetic	64%	99%	14%	33%	348.94***	S > P > T
Toad venom/bufotoxin	34	9	99	5	392.31***	S = P < T
Plant extract/yopo	27	15	12	95	236.43***	S = T < P
Other	3	4	1	2	2.28	
Unsure	3	2	3	5	2.47	
Typical route of administration					51.64***	
Swallowed	6%	7%	1%	10%		T<S=P
Snorted	10	13	0	17		T<S=P
Smoked/vaporized	81	76	98	70		S=P<T
Other (e.g., injected, sublingual, rectal)	3	4	1	4		
Age at first use					105.68***	
Less than 18	6%	8%	2%	7%		S>T
18–29	49	62	19	61		S=P>T
30–39	22	15	34	22		S<T
40–49	15	11	29	7		S=P<T
50–69	8	5	16	2		S=P<T
Number of lifetime uses of 5-MeO-DMT					51.12***	
1–2	38%	31%	59%	27%		S=P<T
3–4	21	20	23	19		NS
5–10	20	23	11	25		S=P>T
11+	21	26	7	29		S=P>T
Frequency of use^					25.40***	
Once per month or more	13%	14%	10%	15%		NS
Less than once per month but more than once per year	32	27	41	37		S<T
About once per year	16	12	23	23		S<T
Less than once per year	38	48	26	25		S>T=P
Location used					121.37***	
Own apartment/house	50%	62%	15%	68%		T<S=P
Friend's apartment/house	14	14	16	12		NS
Outdoors	19	12	34	13		T>S=P
Church/spiritual location	7	3	17	5		T>S=P
Other	10	8	19	2		T>S=P
Source of 5-MeO-DMT					266.72***	
A guide/session leader	30%	9%	79%	15%		S=P<T
The Internet	26	41	2	17		T<P<S
A friend	29	36	7	46		T<S=P
Other (e.g., family member)	15	15	12	23		NS
Average number of other people using at the same time	2.09 (3.28)	1.26 (1.73)	4.02 (4.78)	1.48 (2.63)	41.64***	S=P<T
Average number of other people around but not using	1.60 (6.88)	0.94 (3.60)	1.93 (1.90)	3.24 (15.50)	3.87*	S<P
Stability of past-year consumption					24.01***	
Decreased	40%	48%	25%	36%		S>T
Stayed the same	46	41	56	51		S<T
Increased	14	11	20	13		S<T

(Continued)

Table 3. (Continued)

Characteristic	Total sample	Synthetic	Toad	Plant Extract/Yopo	χ^2	Post hoc
	n=515[a]	*n*=284[b]	n=148[c]	*n*=83[d]		
	M(SD) or %	M(SD) or %	M(SD) or %	M(SD) or %		
	Total Sample	**Synthetic**	**Toad**	**Plant/Other/Unsure**	***F* or χ^2**	**Post hoc**
Proportion of sample who ranked each reason for taking 5-MeO-DMT as their top reason					45.05***	
Spiritual exploration	68%	64%	77%	68%		S<T
Recreation	18	27	2	17		T<S=P
Healing/psychological treatment	14	9	21	16		S<T
Types of administration (all that apply)						
Self-administer	61%	81%	15%	75%	188.62***	T<P=S
Shamanic practitioner	34	15	76	23	167.44***	T>P=S
Friend or peer sitter	28	32	16	33	13.82**	T<S=P
Other (e.g., clergy, clinical professional)	2	3	15	1	4.87	
Milligrams typically used (based on type of 5-MeO-DMT they have the most experience with)					84.20***	
Unknown	38%	25%	56%	48%		S<T=P
0–10	25	34	10	22		T<P=S
11–50	29	37	16	23		S>T
51+	9	5	18	7		S<T
Frequency of re-dosing immediately after coming down from first dose					20.88**	
Never	61%	59%	74%	47%		S=P<T
Sometimes	28	30	18	40		S=P>T
Frequently	5	5	3	8		NS
Always	6	7	5	5		NS
Most experience with which other psychedelic substance					45.61***	
LSD/Acid	53%	57%	39%	62%		S=P>T
Mushrooms	19	17	20	20		NS
Ayahuasca/DMT	13	7	29	7		S=P<T
Other	15	18	13	11		NS
Frequency of using other psychedelic substance					14.85	
Less than once per year	27%	26%	32%	21%		
About once per year	10	14	5	6		
Once every 6 months	20	19	21	21		
About once every other month	18	17	19	20		
About once per month	25	24	23	32		
Total lifetime doses of other psychedelic substance					15.99*	
1–10	28%	26%	36%	22%		NS
11–30	30	28	33	31		NS
31–100	22	22	20	25		NS
101 or more	20	25	10	22		S=P>T
Intensity of 5-MeO-DMT compared to other psychedelic substance					8.34	
Less intense	22%	24%	19%	21%		
Same intensity	14	17	9	14		
More intense	64	59	72	65		
Experienced craving/desire for 5-MeO-DMT					0.11	
Yes	8%	7%	7%	8%		

(Continued)

Table 3. (Continued)

Characteristic	Total sample	Synthetic	Toad	Plant Extract/Yopo	χ^2	Post hoc
	n=515[a]	*n*=284[b]	n=148[c]	*n*=83[d]		
	M(SD) or %	M(SD) or %	M(SD) or %	M(SD) or %		
	Total Sample	**Synthetic**	**Toad**	**Plant/Other/Unsure**	***F* or χ^2**	**Post hoc**
Number of past reduction attempts					3.61	
0	95%	94%	97%	95%		
1	4	5	2	2		
2+	1	1	1	2		
Number of increase attempts					5.69	
0	68%	66%	75%	64%		
1	16	16	16	18		
2+	15	18	10	18		
Number of quit attempts					4.52	
0	96%	94%	98%	95%		
1	4	5	2	4		
2+	<1	<1	0	1		
Last time used 5-MeO-DMT					45.21***	
Within the past month	24%	19%	27%	35%		S<P
Between 1 and 6 months ago	23	18	32	24		S<T
Between 6 and 12 months ago	13	11	18	8		NS
More than 1 year ago	41	53	23	33		S>T=P
Ever arrested/in legal trouble due to 5-MeO-DMT use					1.63	
Yes	1%	1%	0%	1%		
Therapy or psychiatric services as a result of 5-MeO-DMT use					0.20	
Yes	1%	1%	1%	1%		
Medical treatment as a result of 5-MeO-DMT use					2.09	
Yes	1%	1%	1%	2%		
Potential psychological or spiritual applications of 5-MeO-DMT						
Personal growth	90%	88%	94%	92%	4.04	
Spiritual growth	89	85	96	92	12.28**	S<T
Psychotherapeutic work	84	81	87	87	2.90	

Note: When the standard deviation is greater than the mean the data are skewed due to a large proportion of zeros.
*p < 0.05; **p < 0.01; ***p < 0.001.
S: Synthetic/Chemical; T: Toad Venom; P: Plant Extract/Yopo; 5-MeO-DMT: 5-Methoxy-N,N-Dimethyltryptamine.
[a]Range is 504–515.
[b]Range is 279–284.
[c]Range is 144–148.
[d]Range is 81–83.
^Only responded if lifetime use was > 1 time (Total sample = 398; Synthetic = 231; Toad = 92; Plant Extract/Yopo = 75).

Synthetic and Plant Extract/Yopo groups reported recreation as a top motivation compared with those in the Toad group. Conversely, significantly larger proportions of those in the Toad group reported their top motivation for use was spiritual exploration or psychological healing/treatment compared with those in the Synthetic group. Regarding mystical experiences reported in this sample, Table 4 reveals that most of the statistically significant differences in the proportion of those who experienced mystical effects were between the Synthetic and Toad groups, with people in the Toad group endorsing more intense mystical effects. Despite these statistically significant differences, the overall mean scores on the mystical experiences subscales indicate that most respondents experienced these subjective effects at a strong intensity.

Similarly, Table 5 shows the most common statistical differences in the proportions of each group reporting challenging experiences were between the Synthetic and Toad groups, but the direction of effect was opposite to that found in reporting of mystical experiences. Specifically, when statistically significant differences were found it was typically those in the Synthetic group

Table 4. Proportion of sample experiencing each subjective effect reported on the Mystical Experiences Questionnaire and comparison of mean subscale scores by type of 5-MeO-DMT consumed.

Mystical experiences	Total sample	Synthetic	Toad	Plant Extract/Yopo	*F* or χ^2	Post hoc
	n=515[a]	*n*=284[b]	*n*=148[c]	*n*=83		
	M(SD) or %	M(SD) or %	M(SD) or %	M(SD) or %		
Mystical Subscale	3.43(1.40)	3.10(1.49)	4.07(1.07)	3.44(1.21)	25.75***	S=P<T
Freedom from the limitations of your personal self and feeling a unity or bond with what was felt to be greater than your personal self	91%	87%	98%	95%	16.92***	S<T
Experience of pure being and pure awareness (beyond the world of sense impressions)	92	90	95	98	6.93*	NS
Experience of oneness in relation to an inner world within	90	87	92	95	6.21*	NS
Experience of the fusion of your personal self into a larger whole	90	85	98	94	20.28***	S<T
Experience of unity with ultimate reality	89	84	96	93	15.97***	S<T
Feeling that you experienced eternity or infinity	88	84	94	90	9.38**	S<T
Experience of oneness or unity with objects and/or persons perceived in your surroundings	78	75	83	82	4.27	
Experience of the insight that all is One	84	80	93	84	13.71**	S<T
Awareness of the life or living presence in all things	81	74	89	95	27.76***	S<T=P
Gain of insightful knowledge experienced at an intuitive level	90	84	97	98	23.10***	S<T=P
Certainty of encounter with ultimate reality (in the sense of being able to know and see what is really real) at some point during your experience	82	77	89	88	11.60**	S<T
You are convinced now, as you look back on your experience, that in it you encountered ultimate reality (i.e., that you knew and saw what was really real)	81	74	91	84	17.30***	S<T
Sense of being at a spiritual height	88	83	94	94	13.89**	S<T=P
Sense of reverence	88	83	93	95	13.49**	S<T=P
Feeling that you experienced something profoundly sacred and holy	85	79	95	92	24.93***	S<T=P
Positive Mood Subscale	3.55(1.31)	3.28(1.39)	4.04(1.08)	3.61(1.26)	17.56***	S=P<T
Experience of amazement	96%	94%	97%	99%	3.67	
Feelings of tenderness and gentleness	84	78	93	93	21.78***	S<T=P
Feelings of peace and tranquility	87	82	93	92	10.63**	S<T
Experience of ecstasy	87	82	92	92	11.02**	S<T
Sense of awe or awesomeness	94	91	97	99	10.28**	S<T
Feelings of joy	90	87	92	95	6.21*	NS
Transcendence of Time and Space Subscale	3.72(1.37)	3.53(1.47)	4.11(1.13)	3.68(1.26)	9.02***	S<T
Loss of your usual sense of time	97%	96%	97%	99%	1.64	
Loss of your usual sense of space	95	93	97	96	4.46	
Loss of usual awareness of where you were	88	86	93	86	4.23	
Sense of being outside of time, beyond past and future	89	86	93	92	4.55	
Being in a realm with no space boundaries	87	80	95	94	21.82***	S<T=P
Experience of timelessness	90	88	94	92	4.41	
Ineffability Subscale	4.07(1.23)	3.88(1.38)	4.39(0.93)	4.14(1.04)	8.79***	S<T
Sense that the experience cannot be described adequately in words	95%	92%	98%	98%	7.62*	S<T
Feeling that you could not do justice to your experience by describing it in words	95	93	98	99	8.49*	NS
Feeling that it would be difficult to communicate your own experience to others who have not had similar experiences	96	94	97	99	3.13	
MEQ Total Mean Score	3.58(1.22)	3.30(1.31)	4.10(0.92)	3.59(1.00)	23.20***	S=P<T
Complete mystical experience	57%	50%	74%	53%	22.97***	S=P<T

*p < 0.05; **p < 0.01; ***p < 0.001.

S: Synthetic/Chemical; T: Toad Venom; P: Plant Extract/Yopo.

[a]Range is 512–515.

[b]Range is 283–284.

[c]Range is 145–148.

Table 5. Mean subscale scores of the Challenging Experiences Questionnaire, and proportion of sample experiencing each subjective effect reported on the CEQ across the total sample and each substance specific subsample.

Challenging experiences	Total sample	Synthetic	Toad	Plant Extract/Yopo	*F* or χ^2	Post hoc
	n=515[a]	*n*=284[b]	*n*=148[c]	*n*=83[d]		
	M(SD) or %	M(SD) or %	M(SD) or %	M(SD) or %		
Fear Subscale	1.22(1.38)	1.44(1.46)	0.94(1.29)	0.97(1.14)	8.23***	S>T=P
I felt frightened	53%	59%	43%	51%	10.52**	S>T
Panic	40	45	33	35	6.78*	S>T
I had the feeling something horrible would happen	41	47	32	35	10.91**	S>T
Experience of fear	63	69	51	63	12.75**	S>T
Anxiousness	49	59	35	42	24.01***	S>T=P
Grief Subscale	0.69(1.00)	0.74(1.06)	0.62(0.85)	0.60(1.03)	1.10	
Sadness	30%	35%	25%	24%	6.37*	NS
Feelings of despair	20	25	15	12	10.51**	S>T=P
Feelings of grief	26	29	23	21	3.12	
I felt like crying	40	38	43	41	1.20	
Despair	17	21	12	13	7.16*	S>T
Emotional and/or physical suffering	25	30	21	18	6.55*	NS
Physical Distress	1.15(1.09)	1.28(1.14)	0.89(0.91)	1.13(1.11)	6.40**	S>T
Feeling my body shake/tremble	50%	55%	39%	52%	9.49**	S>T
Feeling my heart beating	66	66	59	77	7.81*	T<P
I felt shaky inside	43	47	35	41	8.01*	S>T
I felt my heart beating irregularly or skipping beats	26	28	19	30	4.42	
Pressure or weight in my chest or abdomen	40	47	26	40	18.40***	S>T
Insanity	0.85(1.21)	0.98(1.28)	0.71(1.16)	0.69(1.02)	3.24*	NS
Fear that I might lose my mind or go insane	36%	38%	36%	30%	1.76	
I experienced a decreased sense of sanity	36	42	26	34	11.40**	S>T
I was afraid that the state I was in would last forever	27	29	22	29	2.77	
Isolation	0.76(1.23)	0.90(1.28)	0.54(1.10)	0.67(1.22)	4.67*	S>T
Feeling of isolation from people and things	31%	36%	21%	31%	10.16**	S>T
Isolation and loneliness	35	43	23	28	18.67***	S>T=P
I felt isolated from everything and everyone	24	29	19	18	7.05*	NS
Death	1.75(1.90)	1.74(1.91)	1.99(1.94)	1.40(1.74)	2.56	
I felt as if I was dead or dying	48%	48%	50%	48%	0.31	
I had the profound experience of my own death	52	51	58	42	5.32	
Paranoia	0.18(0.60)	0.20(0.62)	0.16(0.56)	0.18(0.57)	0.18	
I had the feeling that people were plotting against me	9%	8%	8%	11%	0.64	
Experience of antagonism toward people around me	9	11	6	9	2.31	S>T
CEQ Total Mean Score	0.95(0.91)	1.06(0.97)	0.80(0.79)	0.82(0.86)	4.93**	

Note: When the standard deviation is greater than the mean the data are skewed due to a large proportion of zeros.
*$p < 0.05$; **$p < 0.01$; ***$p < 0.001$.
S: Synthetic/Chemical; T: Toad Venom; P: Plant Extract/Yopo.
[a]Range is 511–515.
[b]Range is 282–284.
[c]Range is 144–148.
[d]Range is 82–83.

who endorsed slightly more intense challenging experiences compared with the Toad group. Despite these statistically significant differences, the overall mean scores on the challenging experiences subscales indicate that most respondents experienced these challenging subjective effects to only a very slight degree.

Table 6. Medical and psychiatric conditions and change in symptoms (better, same, worse) following 5-MeO-DMT use.

Condition	% had condition[a]	% better[b]	% same[b]	% worsened[b]
High blood pressure	9	15	78	7
Coronary artery disease	1	0	100	0
Asthma	12	24	73	4
Other lung disease	2	22	78	0
Chronic fatigue syndrome	8	58	37	5
Forgetfulness	28	27	69	4
Depression	61	77	22	2
Anxiety	63	69	27	5
Shyness	48	60	37	3
Chronic anger	21	76	20	4
Eating disorder	10	39	59	2
Bipolar disorder	8	50	47	3
PTSD	21	79	18	3
ADHD	22	35	61	4
Autism	4	48	52	0
OCD	11	53	37	10
Alcoholism or hazardous drinking	22	66	31	3
Drug use disorder	33	60	35	5

PTSD: post-traumatic stress disorder; ADHD: attention deficit hyperactivity disorder; OCD: obsessive compulsive disorder.
[a]Proportion is out of the total sample (ns range from 476–490).
[b]Only including responses from those who endorsed having the condition.

Discussion

This study appears to be the first investigation of the epidemiology of 5-MeO-DMT use. Despite some statistically significant differences in the patterns of use and subjective effects as a function of the type of 5-MeO-DMT used (i.e., synthetic, toad venom, plant extract/yopo), these data suggest that most people who consume 5-MeO-DMT use a synthetic source and vaporization/smoking as the route of administration. The majority of the sample used 5-MeO-DMT for the purpose of spiritual exploration, and used infrequently, consuming 5-MeO-DMT less than four times in their lifetime. Similar to other hallucinogens (McCabe et al., 2017), there were also very low rates of addiction-related symptoms including craving/desire or legal consequences following 5-MeO-DMT use, as well as low rates of repeated consumption in the same session and psychiatric or medical complications related to use. Similar to people who use other tryptamines (Barrett et al., 2016; Griffiths et al., 2006; MacLean et al., 2012), most respondents also reported a variety of moderate-to-strong mystical experiences (e.g., awe or awesomeness, amazement, loss of time and space, and difficulty putting experience into words) and relatively fewer experienced very slight challenging experiences (e.g., fear, anxiousness).

Furthermore, large proportions of respondents in this study reported that 5-MeO-DMT use contributed to improvements in symptoms related to several psychiatric conditions, including anxiety, depression, substance use problems, and post-traumatic stress disorder, suggesting that 5-MeO-DMT may have psychotherapeutic effects under optimal conditions. These positive self-reported psychotherapeutic effects across a variety of psychiatric conditions are consistent with anecdotal reports on the Internet (Psychedelic Times, 2016), pharmacological effects in animals (Jiang et al., 2016; Nagai et al., 2007; Shen et al., 2011; Spencer et al., 1987), findings from population-based surveys (Krebs and Johansen, 2013), and findings with related psychoactive tryptamines (e.g., psilocybin) in individuals with problems associated with addiction, anxiety, or depression (for a review see Johnson and Griffiths, 2017).

Such therapeutic potential of tryptamines appears to be due, at least in part, to their ability to occasion mystical experiences, which has been demonstrated to have lasting beneficial effects (Garcia-Romeu et al., 2015). However, this study is cross-sectional, lacked a validated measure of psychiatric symptoms and assessment of prior psychiatric treatment, and included many poly-substance users, which limits any causal inferences in the relation between the use of 5-MeO-DMT and an improvement in symptoms. Thus, the associations of psychiatric benefits remain observational. Nevertheless, that 5-MeO-DMT appears to have a safety/risk profile similar to that of tryptamines, producing moderate-to-strong mystical, and very slight challenging (e.g., anxiety, fear), experiences at a similar intensity as moderate to high-dose psilocybin administered in laboratory settings (Barsuglia et al., 2017; Griffiths et al., 2006), and that the duration of effect is substantially shorter (20-40 minutes compared to 4-6 hours; Erowid, n.d.; Ott, 2001a), suggests that it might be worth examining the possibility of 5-MeO-DMT administration as an adjunct to psychotherapy. These efforts may contribute to the scalability of psychedelic-assisted psychotherapy in that they could substantially reduce the costs associated with treatment if and when psychedelic-assisted psychotherapy is made available to the public.

Limitations of this study include the cross-sectional nature of the data, which precludes any interpretation of causality with regard to the short- or long-term effects of 5-MeO-DMT consumption, and the self-report of 5-MeO-DMT use (e.g., dose, frequency) and related experiences, which are subject to retrospective recall bias and subjective estimates. Additionally, the

sample was recruited using Internet advertisements and thus is subject to selection bias. Although there are several practical and methodological advantages to using web-based recruitment (King et al., 2014), and evidence supports the validity and reliability of anonymous reports of substance use and use-related consequences provided via the Internet (Ramo et al., 2012), we cannot rule out the likelihood that people who use 5-MeO-DMT but who did not access the sites from which we recruited respondents, or those who decided not to participate in online research, may have different patterns of use, subjective effects, and other experiences related to their 5-MeO-DMT use.

The study is also limited by the use of a donation to a psychedelic research organization, instead of providing monetary compensation to encourage participation, which may have created unique volunteer biases or otherwise influenced the composition of the sample. Similar to other web-based studies of people who use licit and illicit substances (Ashrafioun et al., 2016; Davis and Rosenberg, 2016), the sample was comprised mostly of white, heterosexual men, which could reflect a limitation in recruitment method, or it could be that the population of people who use 5-MeO-DMT is similarly comprised. Regardless, future studies should attempt to recruit samples comprised of individuals that identify as being from a diverse background, perhaps specifically by recruiting non-English-speaking individuals. This study also lacks validated measures of alcohol and other drug use and medical/psychiatric functioning, thus, more research is needed to determine whether the results from this study are generalizable to the population of people who consume 5-MeO-DMT.

To the extent that these results are generalizable to the international English-speaking population of people who use 5-MeO-DMT, findings highlight the infrequent pattern of use and the moderate-to-strong subjective mystical and very slight challenging effects of 5-MeO-DMT consumption. Similar to other psychedelic tryptamines, 5-MeO-DMT also appears to have a relatively good safety profile of use in spiritual and recreational settings, with little likelihood of producing an addictive or problematic syndrome of consumption in most users. This is especially evident when compared with the prevalence of past-year and lifetime medical, psychiatric, social, and legal problems associated with drugs in other classes (e.g., alcohol, cannabis, cocaine; McCabe et al., 2017). Furthermore, these data suggest that there may be psychotherapeutic effects associated with 5-MeO-DMT consumption, including catalyzing transformative mystical experiences and self-reported reductions in symptoms related to depression, anxiety, substance use problems, and post-traumatic stress disorder. However, there is at least one report of a fatal intoxication associated with ayahuasca containing 5-MeO-DMT and other substances (Sklerov et al., 2005), and there have been no published laboratory studies examining the safety of synthetic 5-MeO-DMT administration in humans, thus limiting understanding of the risk/benefits of consumption. Therefore, we recommend that future research examine the safety and pharmacokinetics of 5-MeO-DMT administration in humans using rigorous experimental designs.

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Author contributions

AKD and JPB were responsible for study conceptualization. All authors contributed to further conceptualization and study design. AKD, JPB, and RL were responsible for coordinating study recruitment. AKD was responsible for primary data analyses and AKD and RL were responsible for drafting the first manuscript. Remaining authors assisted with refining analyses and manuscript editing. All authors approve submission of this manuscript.

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ORCID iD

Rafael Lancelotta https://orcid.org/0000-0002-7789-3463

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