Original Paper

Classic psychedelic use is associated with reduced psychological distress and suicidality in the United States adult population

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Journal of Psychopharmacology
1–9

DOI: 10.1177/0269881114565653
jop.sagepub.com

Abstract

Mental health problems are endemic across the globe, and suicide, a strong corollary of poor mental health, is a leading cause of death. Classic psychedelic use may occasion lasting improvements in mental health, but the effects of classic psychedelic use on suicidality are unknown. We evaluated the relationships of classic psychedelic use with psychological distress and suicidality among over 190,000 USA adult respondents pooled from the last five available years of the National Survey on Drug Use and Health (2008–2012) while controlling for a range of covariates. Lifetime classic psychedelic use was associated with a significantly reduced odds of past month psychological distress (weighted odds ratio (OR)=0.81 (0.72–0.91)), past year suicidal thinking (weighted OR=0.86 (0.78–0.94)), past year suicidal planning (weighted OR=0.71 (0.54–0.94)), and past year suicide attempt (weighted OR=0.64 (0.46–0.89)), whereas lifetime illicit use of other drugs was largely associated with an increased likelihood of these outcomes. These findings indicate that classic psychedelics may hold promise in the prevention of suicide, supporting the view that classic psychedelics' most highly restricted legal status should be reconsidered to facilitate scientific study, and suggesting that more extensive clinical research with classic psychedelics is warranted.

Keywords

Psychedelic, hallucinogen, lysergic acid diethylamide, psilocybin, mescaline, mental health, suicide, prevention

Introduction

Almost half of a billion people worldwide suffer from mental health problems, at substantial cost to society (World Health Organization, 2001). Suicide is among the many deleterious consequences of poor mental health and accounts for approximately one million deaths across the globe annually (Hawton and van Heeringen, 2009). Despite advances in mental health treatment over the past 60 years, suicide rates have not significantly declined in much of the world during this time (Varnik, 2012), suggesting the need for more innovative and effective mental health treatments. In response to this trend the National Institute of Mental Health has called for research on novel interventions that address the mechanisms underlying suicidal phenomena (National Action Alliance for Suicide Prevention: Research Prioritization Task Force, 2014). Treatments involving classic psychedelics may represent one such approach.

Classic psychedelics can occasion mystical-type experiences and have been used in sacramental healing contexts across cultures since time immemorial (Johnson et al., 2008; Nichols, 2004). Among the most prominent of these substances are dimethyltryptamine (DMT; widespread in the plant kingdom), the semi-synthetic lysergic acid diethylamide (LSD; derived from the ergot fungus), mescaline (the primary active constituent of peyote and other cacti), and psilocybin (the primary psychoactive constituent of *Psilocybe* and other mushroom genera), with primary effects caused by their action as agonists on serotonin 2A (5-HT_{2A}) brain receptors (Vollenweider and Kometer, 2010). Western science devoted significant attention to classic psychedelics from the 1950s through the early 1970s, and though a lack of modern methodological rigor complicates interpretation, results suggested that classic psychedelics might potentiate psychotherapeutic effectiveness (Johnson et al., 2008; Nichols, 2004; Vollenweider and Kometer, 2010). To the dismay of responsible investigators, sensationalized media coverage of recreational classic psychedelic use in the 1960s led to the most severe legal restrictions, which all but eliminated the possibility of future study that might have yielded more conclusive findings. These legal restrictions were enacted in the absence of a compelling medical or scientific rationale, and contemporary analysis suggests that classic psychedelics are among the least harmful of misused drugs, with limited dependence potential (Nutt et al., 2007, 2010).

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The past three decades have witnessed a gradual return to research on classic psychedelics. Though limited in number, these studies indicate that classic psychedelics may warrant the attention they received five decades ago, not least in part because they appear to target a number of factors that modulate suicide risk. For instance, affective disturbance is one of the most prominent contributors to suicidality (Hawton and van Heeringen, 2009). Under carefully controlled conditions, a single administration of psilocybin can occasion profoundly meaningful experiences that bring about persisting elevations in mood among healthy, hallucinogen-naïve volunteers (Griffiths et al., 2006, 2008, 2011). In a pilot trial among individuals with advanced-stage cancer a single dose of psilocybin was associated with long-term reductions in anxiety and depression (Grob et al., 2011), and in a pilot trial among individuals with life-threatening diseases two administrations of LSD produced lasting reductions in anxiety (Gasser et al., 2014; in press). Substance misuse also is robustly related to suicide risk (Borges et al., 2000; Britton and Conner, 2010; Center for Substance Abuse Treatment, 2008; Hawton and van Heeringen, 2009; Wilcox et al., 2004), and several lines of research suggest that classic psychedelics have anti-addictive effects (Bogenschutz and Pommy, 2012). For example, a recent meta-analysis of six randomized clinical trials of treatment for alcoholism conducted between 1966–1970 found that a single dose of LSD reduced the probability of alcohol misuse almost two-fold relative to comparison conditions (Krebs and Johansen, 2012). Furthermore, a single-arm trial of smoking cessation involving up to three administrations of psilocybin yielded abstinence rates of 80% at long-term follow-up, more than doubling abstinence rates typical of approved contemporary tobacco dependence interventions (Johnson et al., 2014). Moreover, naturalistic hallucinogen use predicted a reduced likelihood of recidivism among more than 25,000 individuals under community corrections supervision with a history of substance involvement (Hendricks et al., 2014). Additional prominent suicide risk factors include impulsive-aggressive personality characteristics and early traumatic life events (Hawton and van Heeringen, 2009). Psilocybin may occasion enduring improvements in inner peace, patience, good-natured humor/playfulness, interpersonal regard, anger, and compassion (Griffiths et al., 2006, 2011), and may facilitate processing of prior trauma by enhancing recall of autobiographical memories (Carhart-Harris et al., 2012a). Finally, classic psychedelics may boost spirituality (Bogenschutz and Pommy, 2012; Griffiths et al., 2011), which has been shown to protect against suicidality (Rasic et al., 2009, 2011; Weber and Pargament, 2014). Although sample sizes in recent medical administration studies have been limited, no serious adverse events were reported, consistent with historical data indicating that these substances can be administered safely in medical contexts by using appropriate safeguards (Johnson et al., 2008).

Neurobiological experiments echo clinical findings, adding further evidence to suggest that classic psychedelics may modify processes implicated in suicidality. Increased 5-HT_{2A} receptor density in the prefrontal cortex is associated with suicide risk factors (e.g. major depression) and suicidal behavior, and may reflect compensatory up-regulation of 5-HT_{2A} receptors stemming from dysfunctional serotonergic transmission (Bhagwagar et al., 2006; Carballo et al., 2008; Meyer et al., 2003; Shelton et al., 2008). Classic psychedelic use down-regulates 5-HT_{2A} receptors in the prefrontal cortex which may, in turn, normalize limbic hyperactivity associated with affective disturbance (Baumeister et al., 2014, Kraehenmann et al., in press; Vollenweider and Kometer, 2010). Reduced neuroplasticity (i.e. expression of brain-derived neurotrophic factor) is also associated with affective disturbance and suicide, and classic psychedelic use may elicit neuroplastic adaptation via glutamatergic transmission (Baumeister et al., 2014; Bogenschutz and Pommy, 2012; Dwivedi, 2010; Dwivedi et al., 2003; Vollenweider and Kometer, 2010). Furthermore, the default mode network (DMN) is hyperactive and hyperconnected among those with affective disorders, a state that may underpin negative rumination and rigid pessimism characteristic of these conditions (Carhart-Harris et al., 2014; Whitfield-Gabrieli and Ford, 2012). Classic psychedelics may normalize the DMN, thereby reducing this cognitive fixedness (Carhart-Harris et al., 2012b; Carhart-Harris et al., 2014; Muthukumaraswamy et al., 2013; Roseman et al., 2014; Tagliazucchi et al., 2014). In support of this view, a single dose of psilocybin increased personality openness 14 months post-administration (MacLean et al., 2011). Some studies show that openness may protect against suicide in older adults, though findings are mixed (Segal et al., 2012). Finally, emerging evidence suggests that classic psychedelics might reduce markers of central nervous system inflammation that are implicated in a host of mental health conditions and suicidal behavior (Black and Miller, in press; Szabo et al., 2014).

Despite evidence suggesting safety and efficacy, the legal status of classic psychedelics has not changed since 1971. Classic psychedelics remain Schedule I substances (designated as having a high potential for abuse, no currently accepted medical use, and a lack of accepted safety under medical supervision), rendering clinical research with these drugs extremely difficult to conduct (Nutt et al., 2013). Consequently, an understanding of the impact of classic psychedelics on mental health and suicidality remains incomplete. Given the regulatory difficulty associated with administering classic psychedelics to humans, population-based survey studies represent one means for examining the relationships of classic psychedelic use with mental health and suicidality. What population-based survey studies sacrifice in internal validity afforded by experimental methodology, they gain in external validity provided by large samples, minimal inclusion and exclusion criteria, and assessment of subjects in real-world settings (Kelley et al., 2003). To our knowledge, only one prior investigation has evaluated the population-level associations of classic psychedelic use with mental health. Using data drawn from 2001–2004 of the National Survey on Drug Use and Health (NSDUH), Krebs and Johansen (2013) tested the relationships of lifetime classic psychedelic use with worst month of the past year psychological distress, past year mental health treatment use, and past year *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition* (DSM-IV; American Psychiatric Association, 1994) symptom indicators among over 130,000 USA adults. They found that lifetime classic psychedelic use was largely unassociated with these outcomes, though some findings indicated that lifetime classic psychedelic use was associated with a decreased likelihood of certain mental health indices (e.g. past year mental health treatment utilization). The purpose of the current study was to examine the relationships of lifetime classic psychedelic use with past month psychological distress and past year suicidality using data drawn from the last five available years of the NSDUH at the time of analysis (2008–2012).

Considering multiple lines of research indicating that classic psychedelics may be protective with regard to mental health problems and suicidality, we hypothesized that lifetime classic psychedelic use would be associated with a decreased likelihood of past month psychological distress, past year suicidal thinking, past year suicidal planning, and past year suicide attempt.

Methods

The NSDUH survey of the Substance Abuse and Mental Health Services Administration of the United States Department of Health and Human Services is conducted annually to estimate the prevalence of substance use and mental illness in the general USA civilian non-institutionalized population using a complex, probability sampling design (United States Department of Health and Human Services, 2009, 2010, 2011, 2012, 2013). NSDUH interviewers met with individuals in their homes, who listened to prerecorded survey questions on headphones and provided responses via computer. Participants in the current study were adult (≥18 years old) respondents of the NSDUH survey pooled across years 2008–2012 with valid data on the primary independent variable (lifetime classic psychedelic use) and all covariates (see below). These cross-sectional data were pooled across years 2008–2012 because standardized assessment procedures introduced in 2008 yielded the same variables for analysis. Weighted interview response rates were approximately 75%. Detailed information on NSDUH methodology is available elsewhere (https://nsduhweb.rti.org/respweb/homepage.cfm). The NSDUH survey was approved by the institutional review board of the Research Triangle Institute and the current analyses were approved by the institutional review board of the University of Alabama at Birmingham.

Data analysis

A unique identifier was created for each unique NSDUH respondent from years 2008–2012 using the Cantor pairing function. Respondents reporting they had ever, even once, used DMT (code 616 from variables HALNEWA, HALNEWB, HALNEWC, HALNEWD, or HALNEWE=1), ayahuasca (a South American drink that contains DMT; code 6103 from variables HALNEWA, HALNEWB, HALNEWC, HALNEWD, or HALNEWE=1), LSD (variable LSDFLAG=1), mescaline (variable MESC2=1), peyote or San Pedro (cacti that contain mescaline; variable PEYOTE2=1 or code 6077 from variables HALNEWA, HALNEWB, HALNEWC, HALNEWD, or HALNEWE=1), or psilocybin (variable PSILCY2=1) were coded as positive for lifetime classic psychedelic use; those indicating that they had never used any of these substances were coded as negative. We considered coding individuals who responded in the affirmative to a query concerning use of DMT, alpha-methyltryptamine (AMT), and 5-methoxy-N, N-diisopropyltryptamine (5-MeO-DIPT) ("Have you ever, even once, used any of the following: DMT, also called dimethyltryptamine, AMT, also called alpha-methyltryptamine, or Foxy, also called 5-MeO-DIPT?"; variable TRYPTM=1) as lifetime classic psychedelic users, but since DMT use in particular could not be determined from this query, and because the classification of AMT and 5-MeO-DIPT as classic psychedelics is inconclusive, this query was not used to classify lifetime classic psychedelic users (post-hoc analyses determined that doing so contributed only 362 additional individuals to the group of lifetime classic psychedelic users and had no meaningful impact on the results). A single variable corresponding to lifetime classic psychedelic use (yes =1 or no=0) was the primary independent variable in analyses.

The primary outcome variables included past month psychological distress (variable SPDMON; yes=1 or no=0) as measured by the widely used and well-validated Kessler Psychological Distress Scale (K6; Kessler et al., 2002, 2010; Khan et al., 2014), past year suicidal thinking ("At any time in the past 12 months… did you seriously think about trying to kill yourself?"; variable MHSUITHK; yes=1 or no=0), past year suicidal planning ("During the past 12 months, did you make any plans to kill yourself?"; variable MHSUIPLN; yes=1 or no=0), and past year suicide attempt ("During the past 12 months, did you try to kill yourself?"; variable MHSUITRY; yes=1 or no=0). Multivariate logistic regression was used to test the associations between lifetime classic psychedelic use and the primary outcomes while controlling for the following covariates: age in years (18–25, 26–34, 35–49, 50–64, or 65 or older); gender (male or female); ethnoracial identity (non-Hispanic White, non-Hispanic African American, non-Hispanic Native American/Alaska Native, non-Hispanic Native Hawaiian/Pacific Islander, non-Hispanic Asian, non-Hispanic more than one race, or Hispanic); educational attainment (5th grade or less, 6th grade, 7th grade, 8th grade, 9th grade, 10th grade, 11th grade, 12th grade, freshman college year, sophomore or junior college year, or senior college year or more); annual household income (less than $20,000, $20,000–$49,999, $50,000–$74,999, or $75,000 or more); marital status (married, divorced/separated, widowed, or never married); self-reported engagement in risky behavior ("How often do you like to test yourself by doing something a little risky?"; never, seldom, sometimes, or always) and lifetime illicit use of cocaine, other stimulants, sedatives, tranquilizers, heroin, pain relievers, marijuana, 3,4-methylenedioxymethamphetamine (MDMA)/ecstasy, phencyclidine (PCP), and inhalants (each aforementioned drug category coded as separate covariates). All analyses were conducted in SAS version 9.3 using PROC SURVEYLOGISTIC and accounted for the complex study design variables and sampling weights as recommended by the NSDUH.

Results

Of the 191,382 respondents, 27,235 reported lifetime classic psychedelic use (13.6% weighted). Of these, 391 reported lifetime DMT use (0.1% weighted), 26 reported lifetime ayahuasca use (0.008% weighted), 18,152 reported lifetime LSD use (10.2% weighted), 4687 reported lifetime mescaline use (3.5% weighted), 3540 reported lifetime peyote or San Pedro use (2.4% weighted), and 20,274 reported lifetime psilocybin use (8.9% weighted). In addition, 12,657 of the respondents reported past month psychological distress (4.8% weighted), 10,445 reported past year suicidal thinking (3.8% weighted), 3157 reported past year suicidal planning (1.1% weighted), and 1716 reported past year suicide attempt (0.5% weighted).

Table 1 displays the characteristics of lifetime classic psychedelic users versus non-lifetime classic psychedelic users. Lifetime classic psychedelic use was concentrated among 26–64 year olds and rare among those aged 65 years and older. Furthermore, lifetime classic psychedelic use was more common among men,

Table 1. Characteristics of lifetime classic psychedelic users versus non-lifetime classic psychedelic users.

Feature	Lifetime classic psychedelic users	Non-lifetime classic psychedelic users	*p* value
	Weighted %	Weighted %	
Age, years			<0.0001
18–25	13.6	14.9	
26–34	21.3	14.9	
35–49	33.7	26.3	
50–64	29.4	24.4	
65 and older	2.0	19.4	
Gender			<0.0001
Male	62.8	46.0	
Female	37.2	54.0	
Race			<0.0001
Non-Hispanic White	83.3	65.2	
Non-Hispanic African American	3.9	12.7	
Non-Hispanic Native American/Alaska Native	1.1	0.4	
Non-Hispanic Native Hawaiian/Pacific Islander	0.2	0.4	
Non-Hispanic Asian	1.3	5.2	
Non-Hispanic more than one race	2.0	1.1	
Hispanic	8.3	15.0	
Education			<0.0001
5th grade or less	0.3	1.6	
6th grade	0.1	1.5	
7th grade	0.2	0.6	
8th grade	1.0	1.8	
9th grade	2.0	2.5	
10th grade	3.2	2.9	
11th grade	4.8	4.5	
12th grade	28.1	30.9	
Freshman college year	10.1	8.7	
Sophomore or junior college year	20.0	16.4	
Senior college year or more	30.3	28.7	
Annual household income			<0.0001
Less than $20,000	16.9	18.5	
$20,000–$49,999	30.0	33.3	
$50,000–$74,999	17.8	17.2	
$75,000 or more	35.3	31.0	
Marital status			<0.0001
Married	47.3	54.5	
Divorced/separated	18.3	13.1	
Widowed	1.8	6.7	
Never married	32.6	25.7	
Self-reported engagement in risky behavior			<0.0001
Never	27.8	55.6	
Seldom	44.1	32.4	
Sometimes	25.3	11.0	
Always	2.8	1.0	
Lifetime illicit substance use			
Lifetime cocaine use	71.4	7.5	<0.0001
Lifetime other stimulant use	37.1	3.7	<0.0001
Lifetime sedative use	17.9	1.2	<0.0001
Lifetime tranquilizer use	37.5	5.0	<0.0001
Lifetime heroin use	10.6	0.4	<0.0001
Lifetime pain reliever use	46.5	9.5	<0.0001
Lifetime marijuana use	97.7	36.2	<0.0001
Lifetime MDMA/ecstasy use	33.0	2.1	<0.0001
Lifetime PCP use	18.0	0.4	<0.0001
Lifetime inhalant use	39.5	3.8	<0.0001

All percentages were rounded to the nearest 0.1%. Rao-Scott chi-square tests were used to examine the characteristics of lifetime classic psychedelic users versus non-lifetime classic psychedelic users. MDMA: 3, 4-methylenedioxymethamphetamine; PCP: phencyclidine.

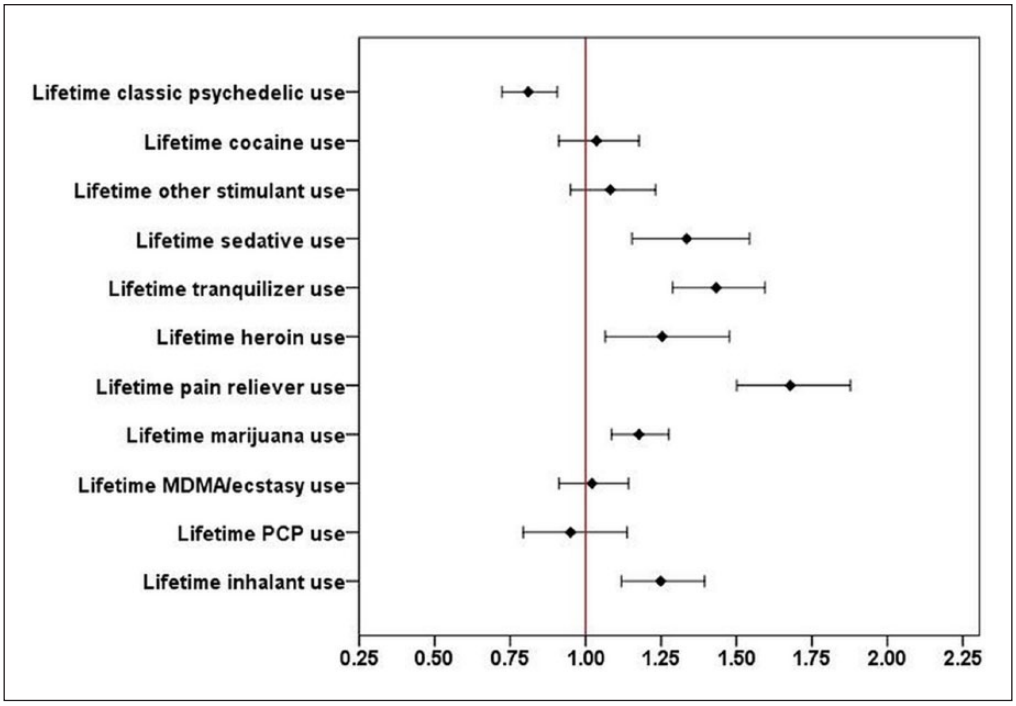

Figure 1. Result of multivariate logistic regression model predicting past month psychological distress. Diamonds are weighted odds ratio point estimates and error bars are 95% confidence intervals. Associations of demographic variables and self-reported engagement in risky behavior with psychological distress are not presented. *n*=191,369 due to missing data on the dependent variable. MDMA: 3, 4-methylenedioxymethamphetamine; PCP: phencyclidine.

non-Hispanic Whites and Native Americans/Alaska Natives, those with greater educational attainment and income, individuals who were divorced/separated or who had never been married, those with greater self-reported engagement in risky behavior, and those who reported lifetime illicit use of each of the other substances. Among lifetime classic psychedelic users, only 240 (0.9% weighted) reported never having used any other illicit substance whereas among non-lifetime classic psychedelic users, 85,601 (58.2% weighted) reported never having used any other illicit drug. Figures 1–4 show the results of multivariate logistic regression models predicting past month psychological distress, past year suicidal thinking, past year suicidal planning, and past year suicide attempt. As shown in these figures, lifetime classic psychedelic use was associated with a decreased likelihood of past month psychological distress (weighted OR=0.81 (0.72–0.91), p=0.0002), past year suicidal thinking (weighted OR=0.86 (0.78–0.94), p=0.001), past year suicidal planning (weighted OR=0.71 (0.54–0.94), p=0.01), and past year suicide attempt (weighted OR=0.64 (0.46–0.89), p=0.008). Conversely, lifetime illicit use of other substances was either not related with or associated with an increased odds of these outcomes, with odds ratios (ORs) for all relationships exceeding 1.0 except lifetime PCP use and past month psychological distress, and lifetime MDMA/ecstasy use and past year suicidal thinking, past year suicidal planning, and past year suicide attempt (no OR significantly different than 1.0).

Discussion

The objective of the current study was to evaluate the associations of classic psychedelic use with psychological distress and suicidality in a large sample generalizable to the USA adult population. Consistent with hypotheses, lifetime classic psychedelic use was associated with a 19% reduced likelihood of past month psychological distress, a 14% reduced likelihood of past year suicidal thinking, a 29% reduced likelihood of past year suicidal planning, and a 36% reduced likelihood of past year suicide attempt. These findings comport with the accumulating literature indicating that classic psychedelics may remediate a number of risk factors associated with suicide. Indeed, if the current results reflect a direct causal chain between classic psychedelic use and decreased suicidality, the mechanisms described in the introduction may have explanatory value. By contrast, lifetime illicit use of all other substances was by and large associated with an increased likelihood of psychological distress and suicidality at or above the trend level. These results align with data indicating that non-psychedelic substance use is a suicide risk factor (Borges et al., 2000; Britton and Conner, 2010; Center for Substance Abuse Treatment, 2008; Hawton and van Heeringen, 2009; Wilcox et al., 2004).

An obvious limitation of the current research is its reliance on self-report. Biases in responding may have obscured the true relationships of classic psychedelic use with psychological distress and suicidality. Also, analyses were restricted to the available data, which precluded testing more nuanced associations (e.g. dose-response relationships). Furthermore, as with any cross-sectional study, the associations reported here may not necessarily indicate causation. Population survey studies cannot control for all possible sources of confounding and therefore we cannot rule out that a shared underlying factor may have contributed to both classic psychedelic use and decreased psychological distress and

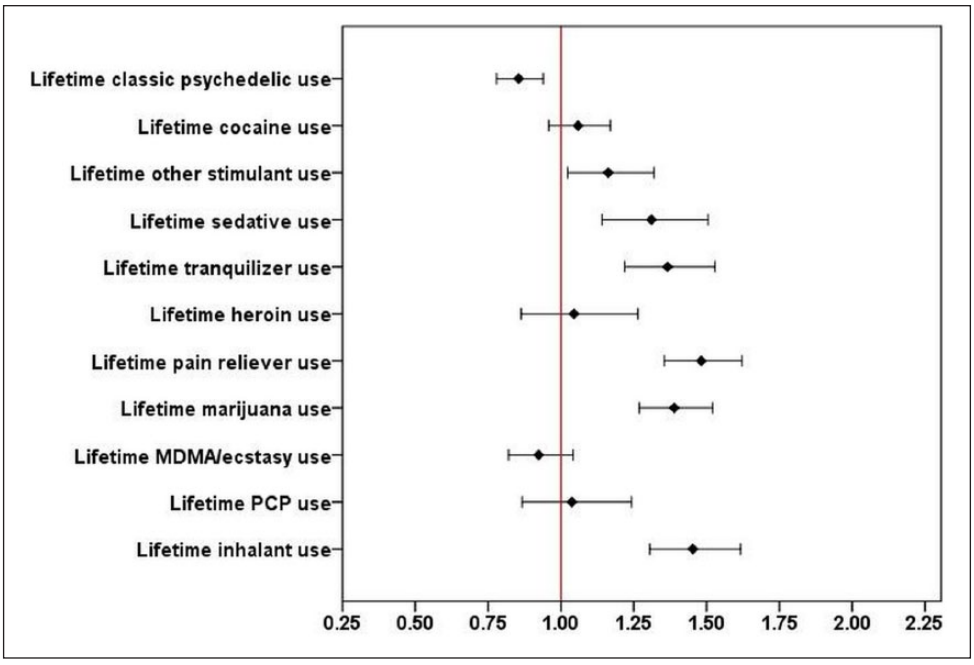

Figure 2. Result of multivariate logistic regression model predicting past year suicidal thinking. Diamonds are weighted odds ratio point estimates and error bars are 95% confidence intervals. Associations of demographic variables and self-reported engagement in risky behavior with suicidal thinking are not presented. *n*=190,728 due to missing data on the dependent variable. MDMA: 3, 4-methylenedioxymethamphetamine; PCP: phencyclidine.

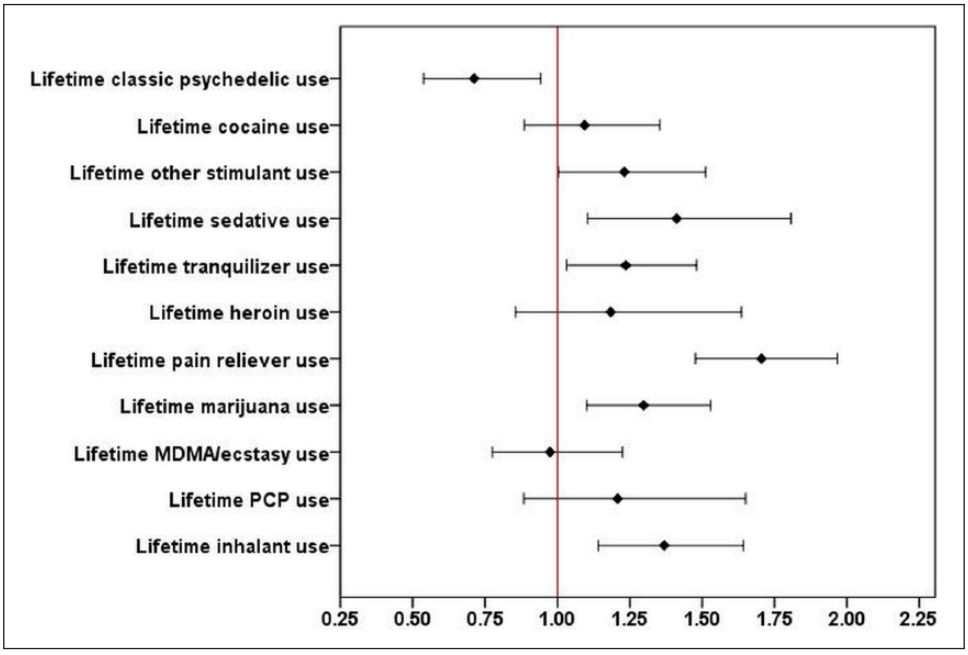

Figure 3. Result of multivariate logistic regression model predicting past year suicidal planning. Diamonds are weighted odds ratio point estimates and error bars are 95% confidence intervals. Associations of demographic variables and self-reported engagement in risky behavior with suicidal planning are not presented. *n*=190,713 due to missing data on the dependent variable. MDMA: 3,4-methylenedioxymethamphetamine; PCP: phencyclidine.

suicidality. Psychedelic drug users commonly report autognostic (Móró et al., 2011), "mind expansion," spiritual, and curiosity motives for such use (Lyvers and Meester, 2012). Although these interests may be lasting effects of classic psychedelic drug use, they may also represent predrug characteristics among classic psychedelic users that might protect against suicide as well (e.g. openness, curiosity, and spiritual tendencies; Carhart-Harris et al., 2014; Kashdan et al., 2004; Rasic et al., 2009, 2011; Weber and Pargament, 2014). Lerner and Lyvers (2006) found that classic psychedelic users reported less materialistic values and greater

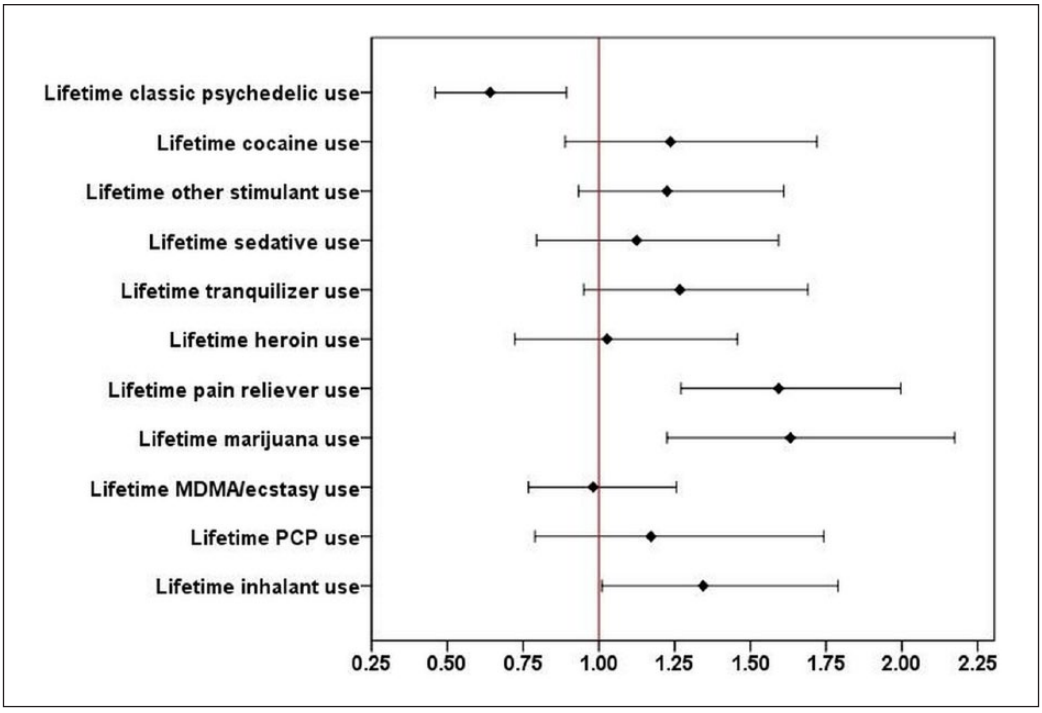

Figure 4. Result of multivariate logistic regression model predicting past year suicide attempt. Diamonds are weighted odds ratio point estimates and error bars are 95% confidence intervals. Associations of demographic variables and self-reported engagement in risky behavior with suicide attempt are not presented. *n*=190,709 due to missing data on the dependent variable. MDMA: 3,4-methylenedioxymethamphetamine; PCP: phencyclidine.

mysticism, spirituality, and concern for others than non-classic psychedelic drug users, and speculated that both predrug factors and classic psychedelic drug effects contributed to group differences. This too may be the case with regard to the present findings. However, as classic psychedelic use was associated with self-reported engagement in risky behavior and illicit substance use, some who use classic psychedelics may also have a premorbid liability for suicidality. The picture is undoubtedly complex. Nevertheless, future research should attempt to delineate longitudinal predictors of classic psychedelic use that also relate to mental health and suicidal behavior.

We also cannot rule out the possibility that classic psychedelic use may have caused harm at the individual level. Indeed, classic psychedelic use may exacerbate schizophrenia or other psychotic disorders, can be dangerous in hazardous physical environments, and can sometimes elicit feelings of anxiety, fear, panic, and paranoia (Johnson et al., 2008). Nevertheless, the associations reported here suggest that if individual-level harms occurred, they failed to obscure the apparent protective effect of classic psychedelic use on psychological distress and suicidality at the population level. Considering that carefully controlled conditions are ideal in the administration of classic psychedelics (Johnson et al., 2008), it is noteworthy that naturalistic classic psychedelic use demonstrated evidence of benefit. Not only could classic psychedelic users have used in suboptimal settings, they could have ingested substances of unknown purity and/or at sub- or supratherapeutic doses. If the results do reflect salubrious effects of classic psychedelic use, these may very well be potentiated in specialized treatment settings designed to maximize safety and efficacy (Johnson et al., 2008).

Given the grave and chronic nature of suicide (Hawton and van Heeringen, 2009; Varnik, 2012) and the call for research on innovative treatments that target suicide pathogenisis (National Action Alliance for Suicide Prevention: Research Prioritization Task Force, 2014), the current findings set the stage for more extensive clinical research with classic psychedelics. Despite millennia of use in sacred healing rituals, and accruing scientific evidence suggesting safety and efficacy when administered in clinical settings with appropriate safeguards (Johnson et al., 2008), classic psychedelics remain Schedule I substances. Accordingly, evaluating the clinical application of classic psychedelics remains an arduous challenge secondary to regulatory hurdles and scarce funding, among other obstacles (Nutt et al., 2013). The present results reinforce the perspective that the designation of these substances should be reconsidered to allow further scientific inquiry. Regardless, priorities for future investigation include evaluating the efficacy of classic psychedelics in treating suicidality as well as pathologies associated with increased suicide risk including affective disturbance, substance misuse, dysfunction marked by impulsive-aggressive personality traits, trauma sequelae, and neurocognitive deficits. Mediators of classic psychedelics' effects should be carefully evaluated so as to better understand their mechanisms of action. Elucidating such mechanisms is critical to optimizing the benefits of classic psychedelics and their concomitant psychotherapeutic components.

Conclusion

Classic psychedelics carry a contentious recent history and barriers to their clinical evaluation remain. Growing evidence

including the present research suggests that classic psychedelics may have the potential to alleviate human suffering associated with mental illness. Further rigorous research is warranted to better understand these substances, with the ultimate goal of taking full advantage of their latent therapeutic capacity.

Acknowledgements

NSDUH data are available to the public and archived at http://www.icpsr.umich.edu/icpsrweb/SAMHDA/series/64. The authors thank Mallory Cases, Michael Scott Crawford, Noah Wiles Sweat, and Jacqueline Upp for their work on the project.

Declaration of Conflicting Interests

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The authors received no financial support for the research, authorship, and/or publication of this article.

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