Hypertension

EPIDEMIOLOGY/POPULATION SCIENCE

Association Between Lifetime Classic Psychedelic Use and Hypertension in the Past Year

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ABSTRACT: Using data from the National Survey on Drug Use and Health (2005–2014), weighted to be representative of the US adult population, the present study investigated the association between lifetime classic psychedelic use and hypertension in the past year among adults in the United States. The results showed that respondents who reported having used a classic psychedelic at least once in their lifetime had significantly lower odds of hypertension in the past year after adjusting for several potential confounders (adjusted odds ratio, 0.86 [0.81–0.91]; $P<0.0001$). Notably, when analyzing the associations between hypertension in the past year and lifetime use of the main classes of classic psychedelics, namely tryptamines (N,N-dimethyltryptamine, ayahuasca, and psilocybin), lysergic acid diethylamide (a lysergamide), and phenethylamines (mescaline, peyote, and San Pedro), only the association with lifetime tryptamine use was significant (adjusted odds ratio, 0.80 [0.73–0.89]; $P=0.0001$). Though these associations are novel, rigorous randomized controlled trials are warranted to investigate potential causal pathways of classic psychedelics on blood pressure. **(*Hypertension*. 2021;77:1510–1516. DOI: 10.1161/HYPERTENSIONAHA.120.16715.)** • **Data Supplement**

Key Words: adults ■ blood pressure ■ hypertension ■ odds ratio ■ psilocybin

The prevalence and costs of hypertension are rising worldwide, and the mechanisms underlying its development and progression are complex.[1–4] For example, several modifiable risk factors contributing to hypertension have been identified, including cigarette smoking, diet and salt intake, lack of physical exercise/sedentary lifestyle, and alcohol consumption.[5] There are also associations between chronic stress, internalizing disorders such as depression, anxiety, and addiction, and the subsequent diagnosis of hypertension.[6,7] Further, recent evidence suggests that low-grade inflammation and divergent serotonin system activation are important factors in the pathophysiology of hypertension.[8–13]

While healthy lifestyle choices can prevent or delay the onset of hypertension and can reduce cardiovascular risk,[14] a major drawback of current lifestyle modification intervention is poor adherence to behavior change over time.[15,16] Hence, new preventive interventions (including more profound and persistent lifestyle changes) are warranted.

Research into the therapeutic potential of serotonin 2A receptor agonist classic psychedelics has reemerged in the past 2 decades, but it has focused primarily on mental rather than physical health outcomes. The evidence to date suggests that classic psychedelic-mediated experiences can disrupt engrained thinking and behavioral patterns and can be effective in the treatment of internalizing disorders.[17] For example, 2 oral doses of psilocybin administered together with psychological support significantly decreased depressive symptoms for patients with treatment-resistant depression at 1 week, 3 months, and 6 months post-treatment.[18,19] Participants were interviewed long after the classic psychedelic-mediated experiences, and many of them reported significant changes in behavior associated with favorable effects on cardiovascular risk factors, including improvements to diet and exercise and reduced alcohol consumption.[20]

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Novelty and Significance

What Is New?

- To date, the long-term effects of classic psychedelics on blood pressure remain unknown. This is the first study to evaluate the association between lifetime classic psychedelic use and hypertension in the past year.

What Is Relevant?

- In the present study, lifetime classic psychedelic use was associated with lower odds of hypertension in the past year. Our results serve as a springboard for rigorous randomized controlled trials on the long-term effects of classic psychedelics on blood pressure.

Summary

In conclusion, lifetime classic psychedelic use was associated with lower odds of hypertension in the past year, with several potential confounding variables controlled for in the analyses.

Nonstandard Abbreviations and Acronyms

DMT	N,N-dimethyltryptamine
LSD	lysergic acid diethylamide
NSDUH	National Survey on Drug Use and Health

There are 3 main classes of classic psychedelics (tryptamines, lysergamides, and phenethylamines) that have unique structural features and neurochemical mechanisms.[21] Most notably, tryptamines include N,N-dimethyltryptamine (DMT), the DMT-containing admixture ayahuasca, and psilocybin; lysergic acid diethylamide (LSD) comprises the lysergamide class; and phenethylamines include mescaline and the mescaline-containing cacti peyote and San Pedro.[22] There have been randomized, placebo-controlled clinical trials to evaluate the mental health effects of classic psychedelics such as psilocybin, ayahuasca, and LSD,[23] but findings from a recent population study suggest that the effects might vary across classes, with tryptamine use associated with the greatest therapeutic potential with regard to mental health.[22]

There is little evidence of physiological toxicity for classic psychedelics, and the risk of harm to oneself and others is considered low.[24–27] In fact, research suggests that classic psychedelics could have both immunomodulatory and anti-inflammatory properties, which could be contributing factors to both mental and cardiovascular health.[10,28] While classic psychedelics can induce transient increases in heart rate and systolic and diastolic blood pressure,[29–31] the long-term effects of classic psychedelic use on hypertension remain unknown.

The present study analyzed pooled data from the National Survey on Drug Use and Health (NSDUH; 2005–2014) to investigate the association between lifetime classic psychedelic use and hypertension in the past year. Based on the evidence to date, we hypothesized that lifetime classic psychedelic use would be associated with lower odds of hypertension in the past year. Further, in light of recent evidence from a recent population study,[22] we also hypothesized that lifetime tryptamine use would have the strongest association with hypertension in the past year among the main classes of classic psychedelics.

MATERIALS AND METHODS

Data and Population

The NSDUH is a nationally representative survey in the United States, conducted annually in all 50 states and the District of Columbia. The survey is designed to provide up-to-date information on mental health issues and tobacco, alcohol, and drug use in the general population. The present study used pooled data from NSDUH survey years 2005 to 2014, which contained responses from 381 682 (unweighted) adults aged ≥18 years. The data were weighted to reflect the civilian noninstitutionalized population. The NSDUH public use data files are available on their homepage: https://www.datafiles.samhsa.gov/study-series/national-survey-drug-use-and-health-nsduh-nid13517.

Variables

The dependent variable was hypertension in the past year. This variable was dichotomous (hypertension reported and hypertension not reported) and derived from the following question:

Which, if Any, of These Conditions Did a Doctor or Other Medical Professional Tell You That You Had in the Past 12 Months?

Consistent with prior research,[32] the independent variable was lifetime classic psychedelic use. Respondents reporting that they had ever, even once, used DMT, ayahuasca, LSD, mescaline, peyote or San Pedro, or psilocybin were coded as positive for lifetime classic psychedelic use, whereas those indicating that they had never used any of these substances were coded as negative.

In addition, control variables included age, sex, ethnoracial identity, educational attainment, annual household income, marital status, self-reported engagement in risky behavior, lifetime use of cocaine, other stimulants, sedatives, tranquilizers, heroin, pain relievers, marijuana, phencyclidine,

3,4-methylenedioxymethamphetamine (ecstasy), inhalants, smokeless tobacco, pipe tobacco, cigar and cigarettes daily, and age of first alcohol use (see the Data Supplement for more details on variables).

Statistical Analyses

The present study used weighted descriptive statistics to report the baseline characteristics of lifetime classic psychedelic users versus nonlifetime classic psychedelic users (Table 1), as well as the percentage of respondents with hypertension in the past year, divided into lifetime classic psychedelic use and lifetime use of the main classes of classic psychedelics: tryptamines (DMT, ayahuasca, or psilocybin), LSD, and phenethylamines (mescaline, peyote, or San Pedro; Table 2). Logistic regression was used to calculate adjusted odds ratios with 95% CIs and examine the association between lifetime classic psychedelic use and hypertension in the past year (model 1), as well as the association between lifetime use of the main classes of classic psychedelics (tryptamines, LSD, and phenethylamines) and hypertension in the past year (model 2; Table 3).

The analyses used weights provided by the NSDUH, and each of the control variables listed above were included as covariates in the regression models to control for potential sources of confounding. There was no control for multiple comparisons in the present study, but exact *P* values are reported to the fourth decimal place, which allows for the application of conservative Bonferroni-type corrections of the reader's choosing. The analyses were conducted using Stata, version 16.

RESULTS

Descriptive Statistics

Table 1 displays weighted descriptive statistics of lifetime classic psychedelic users versus nonlifetime classic psychedelic users. Consistent with prior research,[32,33] lifetime classic psychedelic use was more common among middle-aged adults, men, non-Hispanic Whites and non-Hispanic Native Americans/Alaska Natives, individuals with greater educational attainment and income, individuals who had never been married and individuals who were divorced/separated, individuals with greater self-reported engagement in risky behavior, and individuals who reported lifetime use of each of the other illicit substances. Furthermore, lifetime classic psychedelic use was more common among individuals who reported lifetime use of each of the tobacco types, individuals who reported first using alcohol before 20 years of age, and individuals with a history of depression or anxiety.

Table 2 displays the percentage of respondents reporting hypertension in the past year. As seen in the table, the prevalence of hypertension in the past year among respondents who had ever used a classic psychedelic was ≈67% of that among respondents who had never used a classic psychedelic. Notably, the prevalence of hypertension in the past year among respondents who had ever used a tryptamine (DMT, ayahuasca, or psilocybin) was ≈56% of that among respondents who had never used a tryptamine.

Regression Models

Table 3 presents results from regression models testing the association between lifetime classic psychedelic use and hypertension in the past year (model 1), as well as the association between lifetime use of the main classes of classic psychedelics and hypertension in the past year (model 2). As illustrated in the table, lifetime classic psychedelic use was associated with a 14% lower odds of hypertension in the past year, but among the main classes of classic psychedelics, only lifetime tryptamine use was significantly associated with hypertension in the past year, with a 20% lower odds.

Robustness Checks

To check the robustness of the findings in the present study, we tested whether the association between lifetime classic psychedelic use and hypertension in the past year differed as a function of mental health history, but the association was broadly similar among those with and without a history of depression and those with and without a history of anxiety. We also included mental health history variables as covariates in additional analyses, without observing major differences from the main findings (see Tables S1 through S5 in the Data Supplement for analyses with mental health history variables). In addition, we tested whether the association between lifetime classic psychedelic use and hypertension in the past year differed as a function of recency of classic psychedelic use. Among the variables analyzed in the present study, the NSDUH only assessed recency of use for LSD, but there were no significant associations between recency of LSD use and hypertension in the past year. The main findings remained broadly unchanged when recency of LSD use was included in the regression model (see Table S6 for analysis with recency of LSD use).

DISCUSSION

The present study investigated the association between lifetime classic psychedelic use and hypertension in the past year. The results showed that respondents who reported having tried a classic psychedelic at least once in their lifetime had significantly lower odds of hypertension. Notably, when analyzing the associations between hypertension in the past year and lifetime use of the main classes of classic psychedelics, namely tryptamines (DMT, ayahuasca, and psilocybin), LSD (a lysergamide), and phenethylamines (mescaline, peyote, and San Pedro), only the association with lifetime tryptamine use was significant.

The novel findings in the current study may be explained by multiple factors, including (1) long-term

Table 1. Characteristics of Lifetime Classic Psychedelic Users vs Nonlifetime Classic Psychedelic Users

Variable	Lifetime classic psychedelic users	Nonlifetime classic psychedelic users	
	Weighted, %	Weighted, %	*P* value
Age, y			<0.0001
18–25	14.2	14.8	
26–34	21.2	15.0	
35–49	34.1	26.5	
50–64	28.3	24.2	
≥65	2.3	19.5	
Sex			<0.0001
Male	62.7	45.9	
Female	37.3	54.1	
Race			<0.0001
Non-Hispanic White	83.6	65.3	
Non-Hispanic African American	3.9	12.7	
Non-Hispanic Native American/Alaska Native	1.0	0.4	
Non-Hispanic Native Hawaiian/Pacific Islander	0.2	0.4	
Non-Hispanic Asian	1.3	5.2	
Non-Hispanic >1 race	2.0	1.0	
Hispanic	8.0	15.0	
Education			<0.0001
Fifth grade or less	0.3	1.7	
Sixth grade	0.2	1.5	
Seventh grade	0.2	0.6	
Eighth grade	0.9	1.8	
Ninth grade	1.8	2.5	
Tenth grade	3.1	3.0	
Eleventh grade	4.7	4.5	
Twelfth grade	28.2	30.8	
Freshman college year	10.2	8.6	
Sophomore or junior college year	20.3	16.7	
Senior college year or more	30.1	28.4	
Annual household income			<0.0001
<$20 000	17.0	18.7	
$20 000–$49 999	30.3	33.3	
$50 000–$74 999	17.8	17.3	
≥$75 000	34.9	30.7	
Marital status			<0.0001
Married	47.0	54.9	
Widowed	1.7	6.8	
Divorced/separated	18.4	12.9	
Never married	33.0	25.4	
Self-reported engagement in risky behavior			<0.0001
Never	27.3	55.5	
Seldom	44.8	32.4	
Sometimes	25.0	11.1	
Always	2.8	1.1	
Age of first alcohol use			<0.0001
<13 y	19.0	5.2	
13–19 y	76.9	58.6	
>20 y	3.4	21.7	
Never used alcohol	0.7	14.4	
Lifetime tobacco use			
Lifetime smokeless tobacco use	41.6	15.6	<0.0001
Lifetime pipe tobacco use	29.7	13.1	<0.0001
Lifetime cigar use	68.8	32.7	<0.0001
Lifetime daily cigarette use	70.2	35.6	<0.0001
Lifetime illicit substance use			
Lifetime cocaine use	71.2	7.3	<0.0001
Lifetime other stimulant use	37.6	3.8	<0.0001
Lifetime sedative use	18.1	1.2	<0.0001
Lifetime tranquilizer use	37.6	5.0	<0.0001
Lifetime heroin use	10.8	0.4	<0.0001
Lifetime pain reliever use	45.9	9.3	<0.0001
Lifetime marijuana use	98.0	36.2	<0.0001
Lifetime MDMA/ecstasy use	32.8	2.0	<0.0001
Lifetime PCP use	17.9	0.4	<0.0001
Lifetime inhalant use	40.0	3.8	<0.0001
Mental health history			
Lifetime depression	21.9	11.3	<0.0001
Lifetime anxiety	15.6	7.4	<0.0001
Total	13.6	86.4	

All percentages were rounded to the nearest 0.1%; cumulative percentages may not add to 100.0. Pearson χ^2 tests were used to examine the characteristics of lifetime classic psychedelic users vs nonclassic psychedelic users. Lifetime depression and lifetime anxiety were included as covariates in the robustness checks (see the Data Supplement for robustness checks). MDMA indicates 3,4-methylenedioxymethamphetamine; and PCP, phencyclidine.

health behavior changes induced by classic psychedelic use[20,34,35]; (2) improvements in mental health and decreases in chronic stress, which are known risk factors for hypertension[6,36]; (3) several immunomodulatory and anti-inflammatory effects that are of importance for the development and progression of hypertension[8,10,21,37,38]; and (4) high affinity of some classic psychedelics to serotonin 2A receptors, conferring antihypertensive effects.[9,10,12,13] However, caution should be exercised in inferring causality. The present results are primarily conceptualized as a catalyst for further research on the link between classic psychedelic use and long-term trends in

Table 2. Percentage of Respondents With Hypertension in the Past Year

	Hypertension in the past year	
	%	N
Lifetime classic psychedelic use		
Yes	13.3	4488
No	19.9	34454
Lifetime tryptamine use		
Yes	11.0	2686
No	19.8	36256
Lifetime LSD use		
Yes	14.1	3478
No	19.6	35464
Lifetime phenethylamine use		
Yes	17.9	1724
No	19.1	37218

The number of observations was 381682 (unweighted). Percentage estimates calculated using weights for national representativeness provided by the NSDUH. N refers to the unweighted counts of respondents in each row. LSD indicates lysergic acid diethylamide; and NSDUH, National Survey on Drug Use and Health.

Table 3. Lifetime Classic Psychedelic Use Predicting Hypertension in the Past Year

Variable	aOR (95% CI)	*P* value
Hypertension in the past year		
Model 1		
Lifetime classic psychedelic use	0.86 (0.81–0.91)	<0.0001
Model 2		
Lifetime tryptamine use	0.80 (0.73–0.89)	0.0001
Lifetime LSD use	0.96 (0.87–1.05)	0.3361
Lifetime phenethylamine use	0.97 (0.87–1.08)	0.5595

The number of observations was 375362 (unweighted). Odds ratios were adjusted for age, sex, ethnoracial identity, educational attainment, annual household income, marital status, self-reported engagement in risky behavior, lifetime use of cocaine, other stimulants, sedatives, tranquilizers, heroin, pain relievers, marijuana, PCP, MDMA/ecstasy, inhalants, smokeless tobacco, pipe tobacco, cigar and cigarettes daily, and age of first alcohol use. aOR indicates adjusted odds ratio; LSD, lysergic acid diethylamide; MDMA, 3,4-methylenedioxymethamphetamine; and PCP, phencyclidine.

blood pressure, with rigorous randomized controlled trials needed to better test cause-and-effect relationships.

The reason that lifetime tryptamine use may be particularly associated with lower risk of hypertension is not easily answerable by the present study. The main classes of classic psychedelics might typically be taken in unique contexts, with varying frequency and dose, with different intentions, and with varying degrees of psychological support, which could lead to divergent outcomes on health behavior and mental health. It is also possible that the different anti-inflammatory effects, immunomodulatory functions, and pharmacology of each class of classic psychedelics produce unique outcomes on specific measures of physical health. For example, tryptamines have been shown to have affinity for and agonist activity at serotonin 1A receptors. The serotonin 1A receptor has been associated with antidepressant (but possibly also antihypertensive[39]) effects when activated and could offer a pharmacological explanation for the results in the present study. In addition, previous research suggests that tryptamine use may hold the greatest therapeutic potential with regard to mental health,[22] which might also help to explain why lifetime tryptamine use had the strongest association with hypertension in the past year among the three classes of classic psychedelics.

Limitations inherent in the study design warrant consideration. First, causal inference was limited with the cross-sectional design in the current study. While the analysis controlled for multiple plausible confounders, the association between lifetime classic psychedelic use and hypertension in the past year could have been obscured by unmeasured variables that were not included in the NSDUH (eg, a shared factor that predisposes respondents to healthy lifestyle behaviors associated with cardiovascular health might also predispose them to classic psychedelic use). Second, the NSDUH did not contain information on the set and setting of classic psychedelic use, including context, frequency, dose, intentions, and psychological support. The analysis could, therefore, not evaluate set and setting-specific associations between classic psychedelic use and hypertension in the past year. Third, the dependent variable was derived from a question based on an indirectly referred opinion from a physician or other medical professional, which could have biased the results. Future research should investigate associations between lifetime classic psychedelic use and clinical measurements of blood pressure, as well as delineate mechanisms that explain the effect of such use on blood pressure. It would also be important to assess whether potential causal effects vary across different populations.

Conclusions

There has been extensive research on prevention and treatment of hypertension in recent decades, including multiple interventions designed to address modifiable risk factors. Meanwhile, research has also reemerged on the therapeutic effects of classic psychedelics, but the effects of classic psychedelics on hypertension remain largely unknown. The novel findings in the present study suggest an association between lifetime classic psychedelic use and lower odds of hypertension in the past year, which demonstrates the need for more rigorous research to investigate potential causal pathways of classic psychedelics on blood pressure.

Perspectives

The results showed that lifetime classic psychedelic use was associated with a 14% lower odds of hypertension in

the past year and that lifetime tryptamine use was associated with a 20% lower odds of hypertension in the past year. These findings may prove valuable for understanding the physical health outcomes of classic psychedelic use, with rigorous randomized controlled trials warranted to investigate potential causal pathways of classic psychedelics on blood pressure.

ARTICLE INFORMATION

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