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An association between marijuana use and tinnitus

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A B S T R A C T

Objective: While some advocates have argued for marijuana as a treatment for tinnitus, the relationship between marijuana use and tinnitus is unknown. The objective of this study was to evaluate associations between marijuana use and the prevalence, severity, and rate of occurrence of tinnitus.
Study design: Cross-sectional analysis of nationally representative data.
Setting: National Health and Nutrition Examination Survey 2011–2012.
Subjects and methods: Statistical analysis was performed on data collected from 2705 non-institutionalized adults aged 20–69 who underwent audiometric testing and were administered questionnaires about hearing, drug use, current health status, and medical history.
Results: The use of marijuana at least once per month for the previous 12 months was significantly associated with experiencing tinnitus during that 12-month month ($X^2(1) = 19.41$, $p < 0.001$). Subjects who used marijuana were more likely to experience tinnitus after accounting for covariables including age, gender, audiometric hearing loss, noise exposure history, depression, anxiety, smoking, salicylate use, cardiovascular disease, hypertension, and diabetes (OR = 1.75, 95% CI 1.02–3.01, $p = 0.043$). There were no associations between the severity or frequency of tinnitus occurrence and the quantity or frequency of marijuana use. Use of other substances such as alcohol, cocaine, methamphetamine, and heroin was not associated with tinnitus.
Conclusion: Regular marijuana use is associated with prevalent tinnitus. However, no dose response between marijuana use and tinnitus was observed. The relationship between marijuana use and tinnitus is complex and is likely modulated by psychosocial factors.

1. Introduction

Tinnitus is the perception of noise in the absence of acoustic stimulus. While 10–25% of US adults experience tinnitus transiently, 3–8% experience persistent or chronic tinnitus [1,2]. For chronic sufferers, the condition can be frustrating in mild cases to debilitating in extreme cases. Due to its subjective nature, the diagnosis and monitoring of tinnitus relies on self-report and cases are clinically heterogeneous [3]. While its pathophysiology is not completely clear, tinnitus has been associated with numerous risk factors including age, gender, hearing impairment, loud noise exposure, depression, anxiety, smoking, cardiovascular disease, hypertension, and diabetes [1,4,5]. There is no single cure for tinnitus. However, numerous therapies, including masking strategies, hearing amplification, sound/neuromodulation therapy, and cognitive behavioral therapy, have been shown to mitigate its severity [6–8].

In the current climate of medical and recreational marijuana legalization in the US, many sufferers of chronic conditions have begun to explore marijuana as an option for symptomatic relief [9]. Tinnitus is no exception, with some advocates suggesting that medical marijuana may be an emerging treatment [10–12]. However, research in animal models suggests that cannabinoid exposure may in fact promote the development of tinnitus percept behavior [13–15].

The purpose of this investigation is to evaluate associations between marijuana use and the prevalence, severity, and frequency of tinnitus occurrence using data from the National Health and Nutrition Examination Survey, a large nationally representative survey.

2. Methods

Data from subjects aged 20–69 from the National Health and Nutrition Examination Surgery (NHANES) 2011–2012 survey were examined. The survey was conducted by the National Center for Health Statistics (NCHS) of the Centers of Disease Control and Prevention and was approved by the NCHS institutional review board. NHANES is a nationally representative cross-sectional health survey of the US non-institutionalized civilian population. Participants were evaluated with a home interview to determine medical and audiologic history, current medical conditions and health status, medication and drug use, and demographic information. Additionally, each person was randomly assigned to undergo a morning, afternoon, or evening examination at a mobile examination center consisting of a physical examination and audiometric testing.

Age and gender were obtained from the Demographic Variables

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data file (DEMO_G). Use of marijuana, salicylates, alcohol, and other drugs; history of noise exposure, smoking, cardiovascular disease, hypertension, and diabetes; and current anxiety were determined from the survey items detailed in Supplementary Table 1. Participants who have never smoked marijuana were identified by "no" answers to DUQ200 ("Have you ever, even once, used marijuana or hashish?"). Participants who used marijuana at least once a month for the previous 12 months were identified by fulfilling two criteria: 1) "yes" answers to DUQ211 ("Have you ever smoked marijuana or hashish at least once a month for more than one year?") and 2) reporting most recent regular marijuana use in the past 30 days on DUQ215Q ("How long has it been since you last smoked marijuana or hashish at least once a month for one year?"). Mood was calculated using the Patient Health Questionnaire 9 (PHQ-9) data file (DPQ_G). Depression was determined by PHQ-9 score ≥ 10, as this score has a sensitivity of 88% and specificity of 88% for major depression [16].

Audiometry was administered by trained health technicians using a standardized protocol in a sound booth (Acoustic Systems, model Delta 143, Ceder Park, Texas) built into a mobile examination center. Testing was conducted using an audiometer (Interacoustic Model AD226, Assens, Denmark) with standard TDH-39P headphones (Telephonics Corporation, Farmingdale, New York), and insert earphones (EARTone 3A, Etymotic Research, Elk Grove, Illinois). Subjects with an average pure-tone hearing level at 0.5, 1, and 2 kHz of ≥25 dB hearing level were categorized as having hearing loss.

Statistical analysis was conducted using Stata 15 (StataCorp, 2018. *Stata Statistical Software*: *Release 15*. College Station, Tx: StataCorp LP). Univariate analyses were reported as p values derived from t-tests or X^2 tests. Multivariate analysis was reported odds ratio (OR), p values, and 95% confidence interval (CI) derived from a multiple logistic regression. Variables to be included for multiple logistic regression were determined by individual univariable analysis of the following variables: age, gender, hearing loss, work noise exposure, off-work noise exposure, depression, anxiety, smoking, aspirin use, cardiovascular disease, hypertension, and diabetes as defined by Supplementary Table 1. Variables associated with tinnitus at $p \leq 0.05$ were entered into the model. Missing variables were handled by excluding cases from analysis. An estimate was considered statistically significant at $\alpha = 0.05$.

3. Results

The NHANES database collected data from 2160 non-institutionalized adults, whose characteristics are shown in Table 1. The use of marijuana at least once per month for the previous 12 months was significantly associated with experiencing bothersome tinnitus during that 12-month period ($X^2(1) = 19.411$, $p < 0.001$). Amongst marijuana users, prevalent tinnitus was not associated with frequency of marijuana use ($X^2(4) = 6.07$, $p = 0.194$) or quantity of use ($X^2(3) = 1.69$, $p = 0.64$). Amongst respondents with tinnitus, marijuana use was not associated with tinnitus severity ($X^2(4) = 1.60$, $p = 0.809$) or its frequency of occurrence ($X^2(4) = 6.81$, $p = 0.146$). Amongst respondents who experience tinnitus and use marijuana, no dose response was seen with regard to severity of tinnitus and frequency of marijuana use ($X^2(16) = 12.40$, $p = .716$), severity of tinnitus and quantity of marijuana use ($X^2(12) = 10.64$, $p = 0.560$), frequency of tinnitus occurrence and frequency of use ($X^2(16) = 22.73$, $p = 0.121$), or frequency of tinnitus occurrence and quantity of marijuana use ($X^2(12) = 8.95$, $p = 0.707$). Tinnitus was not associated with the use of other substances, including alcohol ($X^2(1) = 2.01$, $p = 0.1.56$), cocaine ($X^2(1) = 0.17$, $p = 0.681$), heroin ($X^2(1) = 2.80$, $p = 0.0.094$), or methamphetamine ($X^2(1) = 2.24$, $p = 0.135$).

To identify variables to be included in the multivariable analysis, univariable analyses were conducted for tinnitus and age, gender, hearing loss, work noise exposure, off-work noise exposure, depression, anxiety, smoking, aspirin use, cardiovascular disease, hypertension, diabetes, and alcohol use. As such, the following variables were included in the multivariate analysis: age (t-test, $p < 0.001$), hearing loss ($X^2(1) = 92.08$, $p < 0.001$), work noise exposure ($X^2(1) = 75.3$, $p < 0.001$), off-work noise exposure ($X^2(1) = 43.62$, $p < 0.001$), depression ($X^2(1) = 179.06$, $p < 0.001$), anxiety ($X^2(1) = 96.71$, $p < 0.001$), smoking ($X^2(1) = 49.32$, $p = 0.001$), cardiovascular disease ($X^2(1) = 41.19$, $p < 0.001$), hypertension ($X^2(1) = 79.18$, $p < 0.001$), aspirin use ($X^2(1) = 4.88$, $p = 0.027$), and diabetes ($X^2(1) = 9.25$, $p = 0.002$). Variables that were excluded from multivariate analysis included: gender ($X^2(1) = 1.66$, $p = 0.197$) and alcohol ($X^2(1) = 2.01$, $p = 0.1.56$).

On multivariate analysis, marijuana use continued to be associated with prevalent tinnitus (OR = 1.75, 95% CI 1.02–3.01, $p = 0.043$; Table 2). Amongst the other variables identified on univariate analysis as being associated with tinnitus, age, off-work noise exposure, smoking, cardiovascular disease, hypertension, aspirin use, and diabetes no longer demonstrated significant associations on multivariate analysis. Presence of hearing loss, history of work noise exposure, depression, and anxiety were each associated with prevalent tinnitus (Table 2).

Table 1
Patient characteristics.

Characteristic	Overall (n = 2705)	Regular marijuana use (n = 118)	Experiences tinnitus (n = 499)
Age	54.28 ± 8.39	48.46 ± 5.34	55.28 ± 8.39
Male gender	1345 (49.72%)	46 (38.99%)	271 (54.31%)
Hearing loss	580 (21.44%)	17 (14.41%)	160 (32.06%)
Work noise exposure	901 (33.76%)	61 (51.69%)	233 (46.79%)
Off-work noise exposure	262 (9.69%)	33 (27.97%)	85 (13.03%)
Depression	316 (11.68%)	27 (22.88%)	129 (25.85%)
Anxiety	278 (10.28%)	31 (26.27%)	104 (20.84%)
Smoking	1200 (44.41%)	93 (78.81%)	273 (54.82%)
Aspirin use	640 (23.66%)	23 (19.49%)	137 (27.45%)
Cardiovascular disease	261 (9.64%)	17 (14.41%)	73 (14.63%)
Hypertension	1127 (41.68%)	50 (42.37%)	254 (50.90%)
Diabetes	510 (19.41%)	12 (10.34%)	96 (19.96%)

4. Discussion

This study shows that regular marijuana use was associated with prevalent tinnitus after controlling for covariables also associated with tinnitus. However, no dose response between the severity or frequency of tinnitus occurrence and the quantify or frequency of marijuana use was observed.

Several animal studies have explored the relationship between cannabinoid receptor agonists and tinnitus-related behavior. Zheng et al. studied tinnitus in rats using salicylate injections and measured

Table 2
Impact of tinnitus risk factors on prevalent tinnitus (multivariable analysis). Asterisks indicate significance ($p < 0.05$).

Variable	Odds ratio (95% CI)	p value
Marijuana use	1.75 (1.02, 3.01)	0.043*
Age	1.00 (0.96, 1.04)	0.983
Hearing loss	2.90 (1.78, 4.72)	< 0.001*
Work noise exposure	1.69 (1.12, 2.55)	0.012*
Off-work noise exposure	1.38 (0.76, 2.5)	0.283
Depression	2.28 (1.30, 4.03)	0.004*
Anxiety	2.48 (1.42, 4.36)	0.002*
Smoking	1.11 (0.71, 1.72)	0.659
Cardiovascular disease	1.24 (0.59, 2.59)	0.573
Hypertension	1.12 (0.73, 1.73)	0.601
Aspirin use	0.70 (0.39, 1.25)	0.232
Diabetes	1.11 (0.62, 1.99)	0.715

tinnitus percept using a conditioned behavioral paradigm [13]. When non-specific cannabinoid CB1 and CB2 receptor agonists (WIN55,212-1 and CP55,940 respectively) were administered to the rats, tinnitus-related behavior significantly increased in both the salicylate and control groups. In a separate study, Zheng et al. studied tinnitus caused by acoustic trauma [15]. Here, tinnitus was induced by exposure to a 16 kHz noise at 115 dB for 1 h. A 1:1 combination of delta-9-tetrahydrocannabinol and cannabidiol was studied. Following acoustic trauma, tinnitus-related behavior was significantly increased in the group that was exposed to cannabinoid solution as compared to those exposed only to the carrier solution. Using a guinea pig model, Berger et al. hypothesized that a cannabinoid CB1 receptor agonist (arachidonyl-2′-chlorethylamide) might prevent salicylate-induced tinnitus due to its protective effect against neurotoxicity in other studies [17]. However, they found no attenuation in tinnitus-related behavior and concluded that CB1 agonists "are not suitable as a potential treatment for tinnitus." In sum, these animal studies suggest that cannabinoid receptor agonists may not be useful in the treatment of tinnitus and may actually exacerbate or promote the development of the condition. These results are consistent with results from the large human sample presented in the current study, where regular marijuana use was associated with prevalent tinnitus.

To our knowledge, this is the first study on the association between marijuana on tinnitus in humans. The main strength of this study lies in its large sample size and diverse patient characteristics. Utilizing the NHANES database allows us to analyze a large and diverse, nationally representative population with outstanding quality control. One limitation in this study is that there is no standardization of marijuana product. Marijuana contains over 400 chemicals with 66 cannabinoid chemicals unique to the genus *Cannabis* [14]. Another limitation is that the results of this study are correlative and causative conclusions are not possible due to its cross-sectional nature. If an association between marijuana use and tinnitus exists, there are three possible causal directions: 1) marijuana use causes increased tinnitus, 2) tinnitus causes increased marijuana use, and 3) an extrinsic factor causes both increased marijuana use and tinnitus. An example of an extrinsic factor is mood disorder, since cross-sectional and prospective studies have consistently shown mood disorders to be correlated with both tinnitus perception and marijuana use [2,18,19]. While our study continued to find a relation between tinnitus and marijuana use even after controlling for depression and anxiety, there is likely a complex interaction between marijuana use, tinnitus, and psychological factors. It is possible that patients with tinnitus tend to use marijuana as a mechanism for self-medication. While we did not find an association with other substances possibly used for self-medication, specifically alcohol, cocaine, methamphetamine, and heroin, the factors driving use of each substance are widely variable and this finding does not exclude the possibility of tinnitus causing increased marijuana use as a mechanism for this association. Finally, a dose response between tinnitus and marijuana use would give insight on the nature of the association, however, no such finding was observed in this sample. This is likely due to the highly subjective nature of tinnitus and heterogeneity in both the marijuana products used and the psychosocial factors driving marijuana use.

In conclusion, we found that regular marijuana use is associated with prevalent tinnitus in our nationally representative sample. However, the relationship between marijuana use and tinnitus is likely complex, and the effects are not fully clear. Future prospective trials may be able to overcome these limitations to determine the effect of cannabinoid receptor agonists and tinnitus.

Supplementary data to this article can be found online at https://doi.org/10.1016/j.amjoto.2019.102314.

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Declaration of competing interest

None.

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