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Research Submission

Association Between Headaches and Tinnitus in Young Adults: Cross-Sectional Study

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Objective.—To study the association between migraine and tinnitus in a large, cross-sectional study among students.

Background.—Tinnitus has been associated with various pain syndromes, including headaches. However, prior studies were mainly conducted among elderly adults.

Methods.—Cross-sectional study among 5729 participants of the French internet-based Students Health Research Enterprise (i-Share) cohort. Health, personal and lifestyle habits, and socio-demographics characteristics as well as headache/migraine symptoms and tinnitus, were recorded in a standardized questionnaire based on self-reports. Logistic regression models were used to evaluate the association between the students' headache status and tinnitus.

Results.—The 5729 participants had a mean age of 20.8 years (standard deviation 2.8 years), 75.4% were female, and 1645 reported migraine. An association was found between the students' headache status and tinnitus after adjustment for confounding variables. Tinnitus was reported by 8.9% of participants with migraine, 7.3% of patients with migraine without aura, and 10.8% of participants with migraine with aura. The adjusted odds ratios of tinnitus were 1.77 (95% confidence interval, 1.36–2.30) for migraine and 1.38 (0.98–1.92) for non-migraine headache. The association was stronger for students with migraine with aura (odds ratio = 2.10, 95% confidence interval 1.54–2.86) than for migraine without aura (odds ratio = 1.51, 95% confidence interval 1.09–2.07).

Conclusion.—We found an association between migraine and tinnitus among young individuals, which was strongest for the subgroup migraine with aura.

Key words: tinnitus, headache, students, migraine disorders, cohort, epidemiology

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Tinnitus is the perception of sound, typically a ringing, buzzing, or whistling sound, in the absence of a corresponding acoustic external stimulus[1] and is very prevalent in the general population,[2] with an estimated 10% of the adult population being affected. While the prevalence increases with age, still a large proportion of young adults are affected.[3]

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Individual reactions of patients with tinnitus vary from habituation to severe reduction of quality of life.[4] Previous studies have further found associations of tinnitus with depression,[4] insomnia,[5] and chronic pain conditions.[6] Associations between headaches and tinnitus have been described before.[7–11] In a recent cross-sectional study of adult patients with tinnitus aged 18–90 years, headache and particularly migraine were very prevalent.[11] However, associations of headache status and tinnitus in younger individuals and in data not assembled for either headache or tinnitus remain unclear. In addition, it remains unclear whether migraine aura status affects the association between migraine and tinnitus.

Thus, we aimed to investigate the association of non-migraine headache, migraine, and migraine aura status with tinnitus in a large cross-sectional study of French university students.

METHODS

Study Population.—Study subjects were participants in the ongoing internet-based Students Health Research Enterprise (i-Share) project, a prospective population-based cohort study of students of French speaking universities and higher education institutions. The i-Share project was initiated by the Universities of Bordeaux and Versailles Saint-Quentin (France). Due to the high frequency of migraine in young adults, migraine is a main focus of i-Share.

To be eligible to participate, a student had to be officially registered at a university or higher education institute, be at least 18 years of age, able to read and understand French, and provide informed consent for participation. The i-Share project was approved by the "Commission Nationale de l'Informatique et des Libertés" (CNIL – National Commission of Informatics and Liberties) [DR-2013-019].

Data accumulated as part of this study came mainly from participants based in Bordeaux, where active recruitment started in February 2013. Students were informed about the purpose and aims of the study by flyers, information stands at registrations, during lectures, and via social media and newsletters (www.i-Share.fr). Furthermore, a group of trained students informed their peers about the study and collected contact information to initiate the online recruitment process. Enrollment followed a two-step process: first a formal preregistration on the i-Share online portal was required. In the second step, the student finalized the registration process and completed self-administered online questionnaires. Only students who completely filled out the baseline questionnaire without any missing data were eligible for our analyses. The baseline questionnaire asked information on the participant's health status, personal and family medical histories, socio-demographic characteristics, and lifestyle habits. We used data available as of July 13th, 2015. A sample size was not calculated for this specific study, but the study group was, instead, derived from the entire i-Share project set up (www.i-share.fr).

Measures.—*Exposure Variable: Students' Headache Status.*—On the baseline questionnaire, participants were asked: "Have you ever had headache attacks of several hours in the last 12 months?" Participants who did not report headaches during the last 12 months were included in the "no headache" category. Participants who reported headaches were asked further details about their headache symptoms: unilateral location; pulsating quality of pain; inhibition of daily activities; aggravation by routine physical activity; nausea or vomiting; and sensitivity to light or sound. Participants who reported headaches and who reported at least two symptoms of the four first symptoms listed above and at least one symptom of the two last ones were included in the "migraine" category, the other participants were included in the "non-migraine headache" category. Participants who reported headache were further asked whether they had visual, sensory, or motor disturbances before the migraine attack.

To establish migraine classification, we used the "probable migraine" category of the International Classification of Headache Disorders, 3rd edition (beta version).[12]

We defined two outcome measures. The first outcome classified individuals as either "no headache," "non-migraine headache," or "migraine"; the second outcome further dichotomized migraine

into "migraine with aura" and "migraine without aura," resulting in four possible categories (no headache, non-migraine headache, migraine with aura, and migraine without aura).

To validate the self-reported migraine variables, we invited 400 i-Share participants who had indicated having had a headache in the 12 months before the baseline questionnaire to fill out the French version of the ID migraine™ questionnaire.[13,14] Of the 400 students, 7 could not be contacted as their e-mail addresses proved invalid. Of the remaining 393 students, 139 completed the ID migraine™ questionnaire. Using information from these 139 students, we examined the number of students who were classified as having migraine and non-migraine headache based on the baseline i-Share questionnaire and the ID migraine™ questionnaire. On the baseline i-Share questionnaire 88 were classified as having migraine and 51 were classified as having non-migraine headache. Compared to the migraine classification of the i-Share questionnaire, only 8 participants were not classified as having migraine by the ID migraine™ questionnaire, resulting in a predictive value positive of 90.9%. In contrast, 33 participants classified as non-migraine headache by the i-Share questionnaire, were classified as having "migraine" by the ID migraine™ questionnaire (negative predictive value 35.3%), underscoring that the ID migraine™ questionnaire was developed to identify migraine, not to disprove it.

Outcome: Tinnitus.—Participants were asked to report if they had ever been diagnosed with tinnitus (by a medical doctor). In the questionnaire, tinnitus was defined as hearing whistling. Individuals were classified as having or not having tinnitus. Later in this article, we will refer to participants with a diagnosis of tinnitus simply as "tinnitus," using the "yes," or "no" categories. Information on tinnitus was not further validated.

Statistical Methods.—We compared frequency of categorical characteristics of students with respect to their self-reported headache status. We used binary logistic regression models to calculate odds ratio (OR) and 95% confidence intervals of the association between headache status and tinnitus using as reference for the OR the following two categories: participants who did not report headache and participants who had never had a diagnosis of tinnitus. Our main analysis was performed with reported headache status composed by the three categories: "no headache," "non-migraine headache," "migraine." We also ran secondary analyses taking information on migraine aura into account.

The multivariable models controlled for age (18 years, 19 years, 20 years, 21 years or more), gender (male, female), BMI (quartiles, missing indicator variable), study level (1st year, 2nd year, 3rd year, 4th year, or higher year of post-secondary education), sports practice (yes, no), paid employment while being a student (yes, no), sleep quality (good, quite good, neither good nor bad, bad), self-reported physician-diagnosed depression (yes, no), parents' headache status (no headache, one parent has headaches, both parents have headache), parents' marital situation (yes, no), alcohol consumption (never, few times a year, once a month, once a week or less, more than once a week), cannabis consumption (yes, no), current tobacco consumption (yes, no), consumption of other drugs (no, yes). Covariates were chosen based on potential associations with both migraine and tinnitus status.

For the main analysis and the secondary analysis we stratified the association between headache status and tinnitus by gender and tested effect modification by contrasting a main model to a model including the interaction term using the likelihood ratio test.

All P values were two-tailed and we considered $P < .05$ to be statistically significant. We performed all analyses using statistical software (SAS version 9.3; SAS Institute Inc., Cary, NC, USA).

RESULTS

Of the 5729 participants who completed the baseline questionnaire, 3246 (56.7%) reported no headache history, 838 (14.6%) reported non-migraine headache, 1645 (28.7%) reported migraine (of whom 744 [13.0%] reported migraine with aura). A total of 331 (5.8%) reported a medical

Table 1.—Characteristics of the Study Population According to Headache Status

	Headache								Total	
	No Headache		Non-Migraine Headache		Migraine Without Aura		Migraine With Aura			
	n	%	n	%	n	%	n	%	n	%
Tinnitus										
No	3114	95.9	785	93.7	835	92.7	664	89.2	5398	94.2
Yes	132	4.1	53	6.3	66	7.3	80	10.8	331	5.8
Age										
18 years	935	28.8	255	30.4	267	29.6	211	28.4	1668	29.1
19 years	605	18.6	152	18.1	150	16.6	129	17.3	1036	18.1
20 years	454	14.0	120	14.3	137	15.2	114	15.3	825	14.4
21 years or more	1252	38.6	311	37.1	347	38.5	290	39.0	2200	38.4
Gender										
Male	1011	31.1	158	18.9	140	15.5	101	13.6	1410	24.6
Female	2235	68.9	680	81.1	761	84.5	643	86.4	4319	75.4
BMI										
1st quartile	751	23.1	211	25.2	212	23.5	178	23.9	1352	23.6
2nd quartile	765	23.6	191	22.8	215	23.9	182	24.5	1353	23.6
3rd quartile	795	24.5	199	23.7	201	22.3	168	22.6	1363	23.8
4th quartile	775	23.9	194	23.2	218	24.2	165	22.2	1352	23.6
Missing indicator variable	160	4.9	43	5.1	55	6.1	51	6.9	309	5.4
Study level										
1st year	1367	42.1	386	46.1	402	44.6	317	42.6	2472	43.1
2nd year	625	19.3	163	19.5	166	18.4	160	21.5	1114	19.4
3rd year	464	14.3	100	11.9	124	13.8	97	13.0	785	13.7
4th year or more higher year of post-secondary eudcation	790	24.3	189	22.6	209	23.2	170	22.8	1358	23.7
Sports practice										
No	1533	47.2	429	51.2	469	52.1	393	52.8	2824	49.3
Yes	1713	52.8	409	48.8	432	47.9	351	47.2	2905	50.7
Paid employment while being a student										
No	2113	65.1	524	62.5	539	59.8	434	58.3	3610	63.0
Yes	1133	34.9	314	37.5	362	40.2	310	41.7	2119	37.0
Sleep quality										
Good	699	21.5	114	13.6	114	12.7	68	9.1	995	17.4
Quite good	1274	39.2	296	35.3	301	33.4	218	29.3	2089	36.5
Neither good nor bad	726	22.4	225	26.8	231	25.6	197	26.5	1379	24.1
Bad	547	16.9	203	24.2	255	28.3	261	35.1	1266	22.1
Self-reported physician-diagnosed depression										
No	2929	90.2	723	86.3	754	83.7	598	80.4	5004	87.3
Yes	317	9.8	115	13.7	147	16.3	146	19.6	725	12.7
Parents' headache status										
No headache	2417	74.5	524	62.5	469	52.1	355	47.7	3765	65.7
One parent has headaches	788	24.3	285	34.0	394	43.7	343	46.1	1810	31.6
Both parents have headaches	41	1.3	29	3.5	38	4.2	46	6.2	154	2.7
Parents' marital condition										
Not divorced	2283	70.3	562	67.1	611	67.8	479	64.4	3935	68.7
Divorced	963	29.7	276	32.9	290	32.2	265	35.6	1794	31.3
Alcohol consumption										
Never	281	8.7	90	10.7	81	9.0	70	9.4	522	9.1
Several times per year	619	19.1	164	19.6	188	20.9	133	17.9	1104	19.3
Once a month	515	15.9	142	16.9	176	19.5	132	17.7	965	16.8

Table 1.—*Continued*

	Headache								Total	
	No Headache		Non-Migraine Headache		Migraine Without Aura		Migraine With Aura			
	n	%	n	%	n	%	n	%	n	%
Once a week or less	1083	33.4	261	31.1	286	31.7	259	34.8	1889	33.0
More than once a week	748	23.0	181	21.6	170	18.9	150	20.2	1249	21.8
Cannabis consumption										
No	1438	44.3	381	45.5	376	41.7	303	40.7	2498	43.6
Yes	1808	55.7	457	54.5	525	58.3	441	59.3	3231	56.4
Current tobacco consumption										
No	2191	67.5	563	67.2	569	63.2	442	59.4	3765	65.7
Yes	1055	32.5	275	32.8	332	36.8	302	40.6	1964	34.3
Consumption of other drugs										
No	2584	79.6	686	81.9	747	82.9	589	79.2	4606	80.4
Yes	662	20.4	152	18.1	154	17.1	155	20.8	1123	19.6
Total	3246	100.0	838	100.0	901	100.0	744	100.0	5729	100.0

i-Share cohort (n = 5729). Numbers may not add to 100% due to rounding values. BMI = body mass index.

diagnosis of tinnitus. Table 1 summarizes the association between personal characteristics and headache status. Participants with migraine were twice more likely to have at least one parent with headache and to have a bad sleep quality when we compared with participants who did not report headache. Participants with migraine were also more likely to have tinnitus, to be female, to be depressed, and to smoke.

The associations between headache status and tinnitus are summarized in Table 2. Headache status is represented by two explanatory variable, ie, three categories "no headache," "headache," "migraine," ie, four categories "no headache," "headache," "migraine without aura," "migraine with aura." The multivariable model showed that students with migraine had an increased risk of tinnitus. Compared with those who did not report a headache history, the multivariable adjusted OR of tinnitus was 1.77 (95% CI 1.36–2.30) for those who had migraine and 1.38 (0.98–1.92) for those with non-migraine headache. When we took migraine aura status into account, we found a stronger association between migraine with aura and tinnitus (OR 2.10, 95% CI 1.54–2.86) than for migraine without aura (OR 1.51, 95% CI 1.09–2.07). Assuming causality, the attributable risk percent between tinnitus and migraine is 43% and for migraine aura 52%.

We did not find effect modification by gender (*P* for interaction = .52).

DISCUSSION

In this large, cross-sectional study of university students, we found an association of migraine headaches with tinnitus. The association was stronger for individuals reporting migraine with aura. While we also found an association between non-migraine headache and tinnitus in crude models, the association did not remain significant after adjustment for potential confounding factors. We found no significant interaction by gender of the association between headache status and tinnitus.

Comparison With Other Studies.—Few prior studies have described associations of headache status or migraine with tinnitus.[7,8,10,11] In a cross-sectional study of 1817 patients visiting a university hospital

Table 2.—Association Between Headache Status and Tinnitus

	n (%)	Univariate OR (95% CI)*	Multivariable-Adjusted+ OR (95% CI)*
Headache status			
No headache	3246 (56.7%)	1.00	1.00
Non-migraine headache	838 (14.6%)	**1.59 (1.15–2.21)**	1.38 (0.98–1.92)
Migraine	1645 (28.7%)	**2.30 (1.80–2.93)**	**1.77 (1.36–2.30)**
Aura status			
Migraine without aura	901 (15.7%)	**1.86 (1.37–2.53)**	**1.51 (1.09–2.07)**
Migraine with aura	744 (13.0%)	**2.84 (2.13–3.80)**	**2.10 (1.54–2.86)**

i-Share cohort (n = 5729).
*CI = confidence interval; OR = odds ratio. The tinnitus outcome reference is "no tinnitus diagnosis." Odds ratios are calculated from two multinomial logistic regression models, one with the outcomes no headache, non-migraine headache and migraine and the other one making a distinction between migraine with aura and migraine without aura. We considered $P<.05$ to be statistically significant. †Adjusted for age, gender, BMI, study level, sports practice, paid employment while being a student, sleep quality, self-reported physician-diagnosed depression, parents' headache status, parents' marital condition, alcohol consumption, cannabis consumption, current tobacco consumption, and consumption of other drugs.

tinnitus center, 27% reported headaches.[11] A total of 193 patients with both headache and tinnitus (mean age 52 years, 61% women) participated in a sub-study, allowing more detailed assessment of headache symptoms. Forty-five percent had migraine, 13% tension-type headache, 6% both migraine and tension-type headache, and 36 other mostly unclassifiable headache forms. In this study, headache most often preceded tinnitus symptoms,[11] supporting our modeling setup. Other studies found associations between headaches and tinnitus mainly as a result of hypothesis-generating analyses to identify associated factors for tinnitus[7,8,10] or reported about tinnitus symptoms in headache patients only.[9] To the best of our knowledge, there are no other studies reporting associations between headaches and tinnitus in a population-based cohort assembled independent of headache or tinnitus status.

Potential Biological Mechanisms.—Direct biological links between migraine and tinnitus are not known. Based on findings of similar laterality of migraine and tinnitus symptoms[11] as well as findings that tinnitus symptoms are stronger during migraine attacks, it can be hypothesized that central sensitization is a common factor for both conditions.[15,16]

Strengths and Limitations.—Strengths of our study include the large number of participants and large number of students with both migraine and tinnitus, use of a standardized questionnaire to ascertain information about headaches, as well as a large number of personal information, and available information on a large number of potential confounders.

Several limitations should be considered when interpreting our results. First, provided data were self-reported and misclassification is possible. While our migraine assessment could be verified using a different and validated tool (Streel et al[14]), information on migraine aura and tinnitus could not be validated.[17] However, there is little reason to believe that reporting of headache status was depending on tinnitus status (and vice versa) supporting potential random misclassification. Second, our assessment of tinnitus could not be verified and we did not ask questions on severity, laterality, and change over time. Third, despite control of a large number of potential confounders, residual or unmeasured confounding is possible as our study is observational. Fourth, students self-selected to participate in our study and participants were studying at the Universities of Bordeaux, Versailles and Nice. Thus, generalizability to other settings may be limited. However, it would be difficult to argue that the association between migraine and tinnitus would be different in other population-based settings. Lastly, we did not ask participants about

previous ear injuries, which can cause tinnitus and which might be related to migraine.

Potential Implications.—Because migraine and tinnitus are common symptoms in young adults on the population level, patients with migraine should be evaluated for tinnitus and vice versa. Further studies are warranted to evaluate the impact of migraine frequency and treatment on tinnitus and whether treatment strategies for tinnitus positively affect migraine.

CONCLUSIONS

Young adults with migraine report significantly more tinnitus. This association was strongest for individuals with migraine with aura. We did not observe robust associations between non-migraine headache and tinnitus.

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