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Association between primary headaches and depression in young adults in southern Brazil☆

Asdrubal Falavigna^{a,*}, Alisson Roberto Teles^b, Gustavo Lisboa Braga^c, Lucas Piccoli Conzatti^c, Leonardo Gilmore Ruschel^c, Pedro Guarise da Silva^c

^a Departmente of Neurology and Neurosurgery, Medical Faculty, Universidade de Caxias do Sul, Caxias do Sul, RS, Brazil

^b Residence of Neurosurgery, Hospital São José, Santa Casa de Porto Alegre, Porto Alegre, RS, Brazil

^c Multidisciplinary Academic League of Neurology and Neurosurgery, Universidade de Caxias do Sul, Caxias do Sul, RS, Brazil

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A B S T R A C T

Objective: To verify the association between depression and headache in young adults, as well as to identify the features of headache associated with depression and the influence of this mood disorder on headache-related disability.

Methods: A cross-sectional study with self-administered questionnaires about headache and depression was conducted at the Universidade de Caxias do Sul. Beck Depression Inventory (BDI) and Migraine Disability Assessment (MIDAS) were used to evaluate depressive symptoms and headache-related disability, respectively. Depression was considered if BDI ≥ 15 .

Results: A thousand and thirteen young adults were included in the study. A clear relationship was observed between headache and depression among the participants. Multivariate analyses demonstrated that nausea or vomiting related to headache and higher headache-related disability scores were independent factors associated with depression. Migraine was more associated with depression than the other types of headache.

Conclusion: The results demonstrate an association between headache and depression. Depressive symptoms are more likely to be found in young adults with more disabling headaches.

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Estudo da relação entre enxaqueca primária e depressão em jovens da região sul do Brasil

R E S U M O

Objetivo: Verificar a associação entre depressão e cefaleia em adultos jovens, assim como identificar as características da cefaleia relacionadas com depressão e a influência da depressão na incapacidade decorrente da cefaleia.

Métodos: Estudo transversal com questionários autoadministrados sobre cefaleia e depressão foi conduzido na Universidade de Caxias do Sul. O Inventário de Depressão de Beck (BDI) e o questionário de avaliação da incapacidade por enxaqueca (MIDAS)

Palavras-chave:

Cefaleia

Depressão

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Cefaleia tensional

☆ Study conducted at the Medical Faculty, Universidade de Caxias do Sul, Caxias do Sul, RS, Brazil.

* Corresponding author.

E-mail: asdrubalmd@gmail.com (A. Falavigna)

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foram utilizados para avaliação dos sintomas depressivos e incapacidade, respectivamente. Depressão foi definida como BDI \geq 15.

Resultados: Foram incluídos no estudo 1.013 adultos jovens. Observou-se uma clara relação entre cefaleia e depressão entre os participantes. Análises multivariadas demonstraram que náuseas ou vômitos relacionados à cefaleia e incapacidade decorrente da dor foram fatores independentes associados à depressão. Enxaqueca foi mais associada com depressão que os outros tipos de cefaleia.

Conclusão: Os resultados demonstram associação entre cefaleia e depressão. Sintomas depressivos são mais comuns em adultos jovens com cefaleias mais incapacitantes.

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Introduction

The association between primary headaches and depression have been reported in the literature.^{1,2} Galego et al.² demonstrated that although there is as yet no logical explanation for this association, it proved to go both ways. Patients with headache have a higher chance of developing depression and patients with depression have a higher chance of developing migraine.

Headache is experienced by 93% of men and 99% of women at some point in life.³ Tension headache is the most common type, being experienced by 69% of the men and 88% of the women³ and it is related to emotional and physical stress. An estimated prevalence of migraine in the worldwide adult population is around 10-12%,⁴ 6-28% in women and 2-19% in men.^{1,5,6} It is a common and disabling primary headache disorder and is considered one of the most common reasons for appointments at neurological centers.²

Our previous study on headache in young adults demonstrated that 74.5% of them had experienced headache in the three months before the interview.⁷ Also, in a preview analysis with young adults, we demonstrated that depression is a common problem in this population, being found in approximately 10%.⁸ In this study, we aimed to verify the association between depression and headache in young adults, as well as to identify the features of headache associated with depression and to verify the influence of this mood disorder on headache-related disability.

Methods

Design

This analysis is part of a large survey about headache, depression and sleep disorders in 1,273 undergraduate students at the Universidade de Caxias do Sul, a private university in the state of Rio Grande do Sul, Brazil. Data were collected from June to September 2007. After mapping all the campus buildings, the researchers were trained to approach all of them during all class periods. Each class was selected randomly by the researcher. After accepting to join the study by signing a letter of consent, the students answered a close-ended instrument to evaluate headache and depressive symptoms. The design and sample are described in detail elsewhere.⁷

The inclusion criteria were to be under 35 years of age and accepting to participate in the study by signing a letter of

consent. Participants who did not answer all the questions about depressive symptoms in the Beck Depression Inventory (BDI) were excluded from this analysis. The study was approved by the Committee on Ethics and Research (n.49/07) of the Universidade de Caxias do Sul.

Instrument

Besides the general characteristics of the sample, all participants answered questions about their headache and its features. This instrument was developed by the researchers and it was demonstrated to have good reliability.⁷ Migraine Disability Assessment (MIDAS) was used to evaluate headache-related disability and BDI assessed depressive symptoms. Both of the instruments are validated for the Brazilian Portuguese language.^{9,10}

The instrument verified headache symptoms in the last three months. Besides several features of pain, the intensity was assessed with a numerical rating scale ranging from 1 (weakest pain) to 10 (strongest pain). Five types of headache were considered: migraine, probable migraine (when only one criterion for migraine was missing), tension headache, probable tension headache (when only one criterion for tension headache was missing), other headaches (which do not enter the classification of any type previously cited). The criteria to characterize migraine and tension headache were based on The International Classification of Headache Disorders by the Headache Classification Subcommittee of the International Headache Society.¹¹

BDI is a self-assessment scale which consists in twenty-one questions, the intensity of each question ranging between 0 and 3. This inventory evaluates the presence of depressive symptoms such as sadness, feeling of discouragement, failure, dissatisfaction, guilt, punishment, disappointment, self-blaming, suicidal thoughts and crying, except question 16 that asks about sleeping pattern and question 18, about changes in appetite. Depression was defined if BDI \geq 15.

MIDAS contains six questions that were used to assess the impact of headache and disability. This questionnaire asks participants to record time lost in days in the last three months due to headache in three domains: paid work, household work, and non-work activities. The six questions did not enter the final score that ranges from 0 to the amount of days of the first five questions. MIDAS is divided into four grades from its score on: 0-5, the person has little or no disability; 6-10: mild disability; 11-20, moderate disability; and > 21, severe disability.

Table 1 – General characteristics of the sample (n = 1,013).

Variables	Total	With no headache (n = 265)	With headache (n = 748)	p
Female gender	638 (63.0)	115 (43.4)	523 (69.9)	<0.001
Age				0.843
17-20	380 (37.5)	104 (39.2)	276 (36.9)	
21-25	397 (39.2)	98 (37.0)	299 (40.0)	
26-30	162 (16.0)	44 (16.6)	118 (15.8)	
31-35	74 (7.3)	19 (7.2)	55 (7.4)	
Socioeconomic class				0.380
A	97 (10.3)	27 (11.2)	70 (10.0)	
B	418 (44.4)	117 (48.3)	301 (43.0)	
C	341 (36.2)	78 (32.2)	263 (37.6)	
D-E	86 (9.1)	20 (8.3)	66 (9.4)	
Ethnicity				0.632
White	949 (94.1)	253 (95.5)	696 (93.5)	
Brown	48 (4.8)	10 (3.8)	38 (5.1)	
Black	10 (1)	2 (0.8)	8 (1.1)	
Asian	2 (0.2)	0 (0.0)	2 (0.3)	
Course				0.658
Biological and health sciences	372 (37)	92 (34.8)	280 (37.7)	
Engineering and exact sciences	480 (47.7)	132 (50.0)	348 (46.9)	
Arts and humans sciences	154 (15.3)	40 (15.2)	114 (15.4)	
Beck Depression Inventory				0.001
No depression	919 (90.7)	256 (96.6)	663 (88.6)	
Mild depression	60 (5.9)	6 (2.3)	54 (7.2)	
Moderate/severe depression	34 (3.4)	3 (1.1)	31 (4.1)	

n (%); Chi-square test.

Statistical analysis

All statistical analyses were conducted with SPSS 18.0 (SPSS, Chicago, IL, EUA). The categorical variables were presented as proportion and the MIDAS score, as median and interquartile range. The age was transformed to a categorical variable.

Bivariate analyses were conducted using the Chi-Square and Mann-Whitney tests, in order to verify factors related to headache and depression. The ANOVA test with Tukey post-hoc analysis was used to determine differences of MIDAS scores among all the subtypes of headache. A logistic regression was performed in order to verify independent features of headache related to depression. The final model of regression was selected by backward deletion method.

Results

This survey included the analyses of 1,013 young adults who meet the inclusion criteria. Female gender comprised 63.0% of the sample and 76.7% were 17-25 years old. Other features of the sample are described in [Table 1](#).

The prevalence of any type of headache in the last three months was 73.8% ([Table 1](#)). There was a clear association between headache and depression among the participants. The prevalence of depression in students with headache was 11.4%, compared with 3.4% of students with no headache ($p = 0.001$). Regarding the depressive paradigm, 90.4% of young adults with highly depressive symptoms reported headache in the last 3 months, compared to 72.1% of the participants with no depression ($p < 0.001$). As to the type of primary headache

and depressive symptoms, it was observed that depression is more likely to be found in participants with migraine or probable migraine. The prevalence of depression in the migraine group was 18.8%.

[Table 2](#) demonstrates bivariate analysis concerning headache features associated with depression. The logistic regression model demonstrated that headache associated with nausea and vomiting and moderate to severe disability assessed by MIDAS were the independent factors related to depression in young adults ([Table 3](#)).

Discussion

Headache is a painful condition related to decreased productivity at work or school, limitation of social activities and impaired quality of life.^{12,13} It is estimated that 47% of the adult population present an active headache disorder,^{14,15} and that most people will experience it at least once in their lives.

Headache is a prevalent and important issue in young adults, being found in approximately 74% of them in our study. In this population, headaches are a serious problem, leading to lost days of study and consequently worse academic performance.^{7,16,17,18} This high rate of headache could be explained by the fact that students are more likely to suffer a high level of stress due to their activities at university. Kumar and Cooney¹⁹ reported that stress and anxiety may activate mechanisms that cause headaches.

Depression is also one of the most important issues in public health, being an important cause of disability worldwide.²⁰ The transition from adolescence to adult life is one of the

Table 2 – Comparative analyses of headache features related to depression.

Variable	Depression		p
	Yes (n = 94)	No (n = 919)	
Median duration of the pain in hours	3 (2-24)	2 (1-4)	<0.001 ^a
Frequency of the headache ($\geq 1x/week$)	52.9%	39.8%	0.073
Holocranian headache	47.0%	36.9%	0.073
Pulsating/throbbing headache	63.9%	56.9%	0.227
Nausea and Vomiting associated with headache	56.5%	33.7%	<0.001
Photophobia associated with headache	65.9%	57.3%	0.130
Phonophobia associated with headache	84.7%	75.9%	0.070
Aura symptoms	37.6%	22.5%	0.002
Headache associated with physical activity	55.3%	38.2%	0.003
Intense headache	25.9%	12.6%	0.001
Limitation in the last three months at work, school or daily activities due to headache	40.0%	26.3%	0.008
Medical consultation for headache	41.2%	29.7%	0.032
Headache related to menstruation	32.9%	48.2%	0.017
Parents and siblings with headache	70.4%	71.3%	0.866
Numerical rating scale of pain	6.20 (± 1.92)	5.35 (± 1.98)	<0.001 ^a
Moderate to severe disability (MIDAS)	39.5%	18.3%	<0.001

Chi-square test.

^a Mann-Whitney U test.**Table 3 – Association between the characteristics of the headache and depression – multiple regression.**

	B	A-OR	95% CI	p
Median duration of the headache	0.008	1.008	0.998-1.019	0.131
Association with nausea or vomiting	0.651	1.917	1.124-3.272	0.017
Moderate to severe disability (MIDAS)	0.861	2.366	1.357-4.127	0.002

95% IC, 95% confidence interval.

periods of higher risk for the development of depression.²¹ In adolescents, depression is not characterized by the classic symptoms; it often presents with a persistent irritable, sad, or bored mood and difficulty with family, school, and work relationships. If not treated correctly, a major depressive episode can last about eight months, with a risk of recurrence of 72% in 5 years.²² In our study, depression was present in approximately 10% of the students, similar to the rates described by Adewuya et al.²³ and Aalto-Setälä et al.,²⁴ who found a rate of 8.3% and 10.7%, respectively.

Our study demonstrated a clear relationship between primary headache and depression in young adults. Also, some features were identified in persons with headache, which would imply greater risk of presenting associated depression. Logistic regression demonstrated that nausea and vomiting and moderate to severe disability are independent factors related to depression. The participants who had nausea or vomiting during a headache crisis were 1.91 times more likely to have depression (95% CI 1.12-3.27; $p=0.017$). Besides, students with moderate or severe disability due to headache had 2.36 times more chance of having depression (95% CI 1.35-4.12; $p=0.002$). These two features are closely related to disability in headaches^{5,7,12} and are more likely to be present in patients with migraine. In fact, our results confirm that young adults with migraine are more likely to present depression than those with tension-type headache, 18.8% and 9.2% respectively ($p<0.001$). Interestingly, Tan et al. found no difference between the prevalence of depression among those

with migraine or tension-type headache in a study involving 95 patients. However, reduced libido, slowness, and nausea were more intense in migraine patients.²⁵

Although the association between depression and headache has been clearly demonstrated, the question about its origin remains unclear. In an epidemiological study, Breslau et al.¹ observed that the risk of first onset migraine in persons with pre-existing major-depression was three times higher than in a person with no history of depression. They also observed that the risk of a person with pre-existing migraine developing a major-depressive episode was more than five times higher than in a person with no history of headaches. All that suggests that migraine and depression co-occur more frequently than could be expected, suggesting that both disorders share molecular or other mechanisms involved.¹

There are some molecular findings that should be mentioned in the association of migraine, anxiety and depression.^{26,27} The disorder that is mostly associated with low levels of serotonin is depression.²⁸ Apparently, serotonin has also been implicated as a key neurotransmitter in migraine.²⁹ The action of serotonin is mediated by 5HT_{1A} receptors, present in greater amounts in the hippocampus. The changes found in this receptor during the process of pain modulation and between migraine attacks have also led to the hypothesis that migraine is involved with low levels of serotonin. This association of low serotonin levels and the occurrence of depression and migraine are supported by

the influence of serotonin in the regulation of mood and pain modulation. On the other hand, recent evidence also indicated that the desensitization of 5HT1A increases the activation of nociceptive pathways, being associated with major depressive disorder.³⁰ Cortisol is a hormone involved in stress response, and when present at high levels, cortisol also desensitizes the serotonin 5HT1A receptor.

Conclusion

Primary headache and depression are frequently found in young adults. Our study demonstrates a clear relationship between headache and depression in this population. Also, depressive symptoms are more likely to be found in young adults with more disabling headaches.

Conflicts of interest

The authors declare no conflicts of interest.

REFERENCES

- Breslau N, Lipton RB, Stewart WF, Schultz LR, Welch KM. Comorbidity of migraine and depression: investigating potential etiology and prognosis. *Neurology*. 2003;60:1308-12.
- Galego JC, Cipullo JP, Cordeiro JA, Tognola WA. Depression and migraine. *Arq Neuropsiquiatr*. 2004;62:774-7.
- Smith RT. Epidemiology and impact of headache: an overview. *Prim Care Clin Office Pract*. 2004;31:237-41.
- Ravishankar N, Demakis GJ. The neuropsychology of migraine. *Dis Mon*. 2007;53:156-61.
- Goldstein M, Chen TC. The epidemiology of disabling headache. *Adv Neurol*. 1982;33:377-90.
- Stewart WF, Lipton RB, Celentano DD, Reed ML. Prevalence of migraine headache in the United States. Relation to age, income, race, and other sociodemographic factors. *JAMA*. 1992;267:64-9.
- Falavigna A, Teles AR, Velho MC, Vedana VM, Silva RC, Mazzocchin T, et al. Prevalence and impact of headache in undergraduate students in Southern Brazil. *Arq Neuropsiquiatr*. 2010;68:873-7.
- Keller MB, Lavori PW, Mueller TI, Endicott J, Coryell W, Hirschfeld RM, et al. Time to recovery, chronicity, and levels of psychopathology in major depression. A 5-year prospective follow-up of 431 subjects. *Arch Gen Psychiatry*. 1992;49:809-16.
- Fragoso YD. MIDAS (Migraine Disability Assessment): a valuable tool for work-site identification of migraine in workers in Brazil. *São Paulo Med J*. 2002;120:118-21.
- Gorestein C, Andrade L. Inventário de depressão de Beck: propriedades psicométricas da versão em português. *Rev Psiquiatr Clin*. 1998;25:245-50.
- The International Classification of Headache Disorders: 2nd ed. *Cephalalgia*. 2004;24(Suppl 1):9-160.
- Lipton RB, Newman IC. Epidemiology, impact, and comorbidities of migraine headaches in the United States. *Neurology*. 2003;60 Suppl 2:S3-8.
- Strine TW, Chapman DP, Balluz LS. Population-based U.S. study of severe headache: adults. *Headache*. 2006;46:223-32.
- Jensen R, Stovner LJ. Epidemiology and comorbidity of headache. *Lancet Neurol*. 2008;7:354-61.
- Stovner L, Hagen K, Jensen R, Katsarava Z, Lipton R, Scher A, et al. The global burden of headache: a documentation of headache prevalence and disability worldwide. *Cephalalgia*. 2007;27:193-210.
- Demirkirkan MK, Ellidokuz H, Boluk A. Prevalence and clinical characteristics of migraine in university students in Turkey. *Tohoku J Exp Med*. 2006;208:87-92.
- Bigal ME, Bigal JO, Bordini CA, Speciali JG. Prevalence and costs of headaches for the public health system in a town in the interior of the state of Sao Paulo. *Arq Neuropsiquiatr*. 2001;59:504-11.
- Curry K, Green R. Prevalence and management of headache in a university undergraduate population. *J Am Acad Nurse Pract*. 2007;19:378-82.
- Kumar KL, Cooney TG. Headaches *Med Clin North Am*. 1995;79:261-86.
- Ustun TB, Ayuso-Mateos JL, Chatterji S, Mathers C, Murray CJ. Global burden of depressive disorders in the year 2000. *Br J Psychiatry*. 2004;184:386-92.
- Kessler RC, Berglund P, Demler O, Jin R, Koretz D, Merikangas KR, et al. The epidemiology of major depressive disorder: results from the National Comorbidity Survey Replication (NCS-R). *JAMA*. 2003;289:3095-105.
- Birmaher B, Ryan ND, Williamson DE, Brent DA, Kaufman J, Dahi RE, et al. Childhood and adolescent depression: a review of the past 10 years. Part I *J Am Acad Child Adolesc Psychiatry*. 1996;35:1427-39.
- Adewuya AO, Ola BA, Aloba OO, Mapayi BM, Oginni OO. Depression amongst Nigerian university students. Prevalence and sociodemographic correlates. *Soc Psychiatry Psychiatr Epidemiol*. 2006;41:674-8.
- Aalto-Setälä T, Marttunen M, Tuulio-Henriksson A, Poikolainen K, Lonnqvist J. One-month prevalence of depression and other DSM-IV disorders among young adults. *Psychol Med*. 2001;31:791-801.
- Tan FU, Ozen NE, Kazezoglu S, Kokoglu F, Boratay C. Depression and anxiety in patients with migraine and tension-type headache. *Gaz Med J*. 2005;16:74-9.
- Papakostas GI, Chuzi SE, Sousa JL, Fava M. 5HT1A-mediated stimulation of cortisol release in major depression: use of non-invasive cortisol measurements to predict clinical response. *Eur Arch Psychiatry Clin Neurosci*. 2010;260:175-80.
- Post RM. Transduction of psychosocial stress into the neurobiology of recurrent affective disorder. *Am J Psychiatry*. 1992;149:999-1010.
- Pytliak M, Vargova V, Mechirova V, Felsoci M. Serotonin receptors - from molecular biology to clinical applications. *Physiol Res*. 2011;60:15-25.
- Cassidy EM, Tomkins E, Dinan T, Hardiman O, O'Keane V. Central 5-HT receptor hypersensitivity in migraine without aura. *Cephalalgia*. 2003;23:29-34.
- Hamel E. Serotonin and migraine: biology and clinical implications. *Cephalalgia*. 2007;27:1293-300.