Published in final edited form as:

Headache. 2008 ; 48(10): 1451–1459. doi:10.1111/j.1526-4610.2008.01175.x.

Are Sleep Difficulties Associated With Migraine Attributable to Anxiety and Depression?

Angeliki Vgontzas, BS, Lihong Cui, MS, and Kathleen R. Merikangas, PhD

National Institute of Mental Health—Section on Developmental Genetic Epidemiology, Bethesda, MD, USA.

Abstract

Objective—To examine whether sleep complaints reported by migraineurs can be attributed to comorbid anxiety and/or depression.

Background—A consistent association between migraine and sleep complaints has been reported in community and clinical studies. However, anxiety and depression are often comorbid with migraine. Thus, it may be possible that the increased prevalence of sleep problems in migraineurs is attributable to comorbid anxiety and depression. To our knowledge, no previous studies have demonstrated that the associations are not solely attributed to comorbid anxiety and depression.

Design and Methods—Controlled family study of anxiety disorders and substance use disorders in a community in New Haven County, CT. The sample included 221 probands (41 migraineurs) and their 261 directly interviewed first-degree relatives (39 migraineurs), including parents, siblings, and offspring over age 18. A lifetime history of migraine was obtained using the Diagnostic Interview for Headache Syndromes. A lifetime history of psychiatric disorders was obtained using the semi-structured Schedule for Affective Disorders and Schizophrenia which was modified to incorporate Diagnostic and Statistical Manual diagnostic criteria. Several sleep items on current and lifetime sleep complaints were included as a subset of the interview.

Results—There was a significant association between migraine and the number of sleep problems as well as several specific sleep symptoms among probands and their adult relatives. Adults with migraine reported having significantly more lifetime sleep problems (OR [CI] = 2.3 [1.1–4.6]), and more current sleep difficulties, specifically, inadequate sleep (2.5 [1.2–5.0]), difficulty falling asleep (3.0 [1.5–6.3]), and persistent nightmares of childhood onset (4.3 [1.8–9.9]) than those without migraine. The associations between sleep problems and migraine persisted after controlling for both lifetime and current anxiety and mood disorders.

Conclusions—The association between sleep problems and migraine that is not solely explained by comorbid anxiety disorders or depression suggests that sleep problems should be evaluated among people with migraine.

Keywords

sleep; migraine; anxiety; depression

INTRODUCTION

Migraine and sleep disturbances are two common conditions in the United States, affecting approximately 12% and 40% of the population, respectively.^{1,2} Their association has been investigated in numerous clinical and community studies of adults³⁻¹⁴ and children.¹⁵⁻¹⁹ Migraineurs report a host of sleep disturbances, most notably, increased trouble falling asleep,^{8,9,11,19} which affects as many as 50% of migraineurs.⁹ Other complaints include: waking up during the night, fears or anxiety when falling asleep, falling asleep sweating, lack of refreshing sleep, feeling tired upon awakening, snoring and restless movements while asleep.¹⁰⁻¹² With respect to diurnal rhythm, migraineurs are more likely to be morning type (28%) than evening type (16%), and are more likely to have a diurnal preference compared with non-migraineurs.⁸ Although the specific explanations for the association between sleep disturbances and migraine are not well understood, greater understanding of the mechanisms for these associations could have both clinical and theoretical significance.

The high comorbidity of migraine with anxiety and depression established in studies of both community²⁰⁻²⁵ and clinical samples²⁶ complicates our understanding of comorbidity of sleep complaints and migraine because sleep disturbances are also core features of mood and anxiety disorders.^{2,27-29} Therefore, it is important to discriminate between sleep problems which may be attributable to comorbid anxiety or depression compared with those that may be specifically associated with migraine. Although some studies have investigated the links between headaches, anxiety/depression and sleep problems,³⁰⁻³² none of these studies have investigated these associations specifically among those with migraine. Moreover, studies which have investigated the association between sleep difficulties and migraine have not considered the possible role of anxiety and depression.

This study aims to examine the association between migraine and sleep problems in the context of a family study of anxiety disorders and migraine. Because relatives of case and control probands have been shown to be equivalent to a quasi epidemiologic sample,³³ the associations in relatives provide a more valid test of these associations. Therefore, the specific goals of this paper are: (1) to examine the association between migraine and sleep problems in probands and their adult relatives; (2) to evaluate the extent to which the association between sleep problems and migraine is attributable to comorbid anxiety and/or depression, particularly among relatives.

METHODS

Sample

Data for this analysis were collected from a large family study of the familial aggregation of anxiety and substance use disorders. Participants were also characterized according to other mental and physical conditions including mood disorders and migraine. The study was approved by the Institutional Review Board of Yale University.

Probands—The study was originally designed to investigate the familial aggregation and coaggregation of mood disorders, anxiety disorders, and substance use disorders. Therefore, 262 probands were ascertained from outpatient anxiety and substance abuse clinics at the Connecticut Mental Health Center (New Haven, CT) or through a random digit dialing procedure in the greater New Haven area. All of the controls and 47.4% of the probands were recruited from the community. Forty-one probands had a lifetime history of migraine.

Adult Relatives—Two-hundred and sixty-one directly interviewed first-degree relatives (approximately one per family) including parents (40.8%), siblings (47.3%), and offspring over age 18 (11.9%) were also included in these analyses. All adult relatives were assessed for a

lifetime history of migraine. Diagnostic information on first-degree relatives was obtained by direct interview and structured family history interviews. Family history information was obtained using a modified version of the Family History-Research Diagnostic Criteria developed by Andreasen and colleagues (1977) to collect diagnostic spectrum information and to obtain both Diagnostic and Statistical Manual (DSM)-III and DSM-III-R diagnoses. Sixty-five percent of eligible relatives were interviewed (see Headache Classification Committee of the International Headache Society JO³⁴). Thirty-nine relatives had a lifetime history of migraine.

Measures

Headache Interview—A lifetime history of migraine was obtained using the Diagnostic Interview for Headache Syndromes (DIHS); DIHS is a semi-structured diagnostic interview that is comprised of an open-ended interview regarding the lifetime history of headache to identify the headache subtypes. Criteria for migraine were based on the symptom criteria used in an earlier population twin study of migraine as defined according to the International Headache Society Criteria for Headache Syndromes.³⁴ All headache interviews were conducted by trained clinical interviewers and reviewed by a neurologist. Best estimate diagnoses based on the DIHS with the relative as well as reports from family members were used in the current study. We did not include information on the frequency, age of onset, or specific migraine subtypes in these analyses.

Psychiatric Interview—A lifetime history of psychiatric disorders was obtained using the semi-structured Schedule for Affective Disorders and Schizophrenia (SADS),³⁵ which was modified to incorporate DSM diagnostic criteria (American Psychiatric Association, 1988; 1990; 1994). Probands were excluded from the study if there was evidence of significant organic mental impairment, schizoaffective disorder, schizophrenia, or a significant history of drug dependence, particularly intravenous drug use. Interviews were systematically reviewed by psychiatrists and clinical psychologists. The final psychiatric diagnoses were based upon all available information, including the diagnostic interview (SADS), family history reports, and medical records using a best estimate diagnostic procedure.

Sleep Problems—The sleep questions included in this analysis were drawn from (1) a sleep subsection inserted into the modified SADS interview; (2) a short section on childhood and developmental health problems in the medical history of the interview. The initial probe “Have you ever had sleep problems?” was followed by the following items assessing current sleep complaints: difficulty falling asleep, difficulty staying asleep, inadequate sleep, and oversleeping. These items were similar to those included in the International Sleep Society criteria for Insomnia.³⁶ The items on sleep problems of child onset included questions on nightmares, bedwetting, and sleepwalking. With the exception of the child-onset sleep problems, the time period for these questions may be considered lifetime.

Analysis

For the purposes of these analyses, probands and relatives were assessed separately. Standard chi-square tests were used for the 2-way tables of categorical variables. Odds ratios were estimated using Logistic Regression models for probands and Generalized Estimating Equation (GEE) models for relatives to investigate the association between lifetime history of migraine (0 = no migraine, 1 = migraine) and sleep problems while controlling for age, sex, anxiety (0 = no anxiety, 1 = anxiety), mood (0 = no, 1 = yes), and substance use (0 = no, 1 = yes) disorders. GEE accounts for the correlations of members from the same family. The dependent variables are the individual sleep symptoms as well as an aggregate variable for any sleep problems (0 = no sleep problem, 1 = sleep problem).

RESULTS

The demographic characteristics of migraine and control probands and adult relatives are shown in Table 1. There were more female probands in the migraine group (65.9%) than in the non-migraine group (47.5%). The mean age of the probands did not differ by migraine status. With respect to the three ascertainment groups (anxiety, substance abuse, and controls), there was no overall difference between the probands with migraine and without migraine. The probands with migraine reported significantly higher rates of both lifetime and current anxiety disorders.

Relatives had similar demographic profiles to those of the probands. There were more females in the migraine group (82.0%) than in the non-migraine group (60.8%), but the mean age in the 2 groups was similar. Lifetime diagnoses of anxiety or depression were not significantly higher in the migraine group; however, current diagnosis of depression was higher in the migraine group.

Table 2 shows the frequencies of sleep complaints by migraine status. The percentage of probands with migraine who reported any (one or more) sleep problem was 85.4% vs 65.3% for controls. The most frequent sleep complaints of migraine probands were: inadequate sleep (46.3%), difficulty falling asleep (48.8%), and oversleeping (43.9%). Oversleeping was the most common complaint reported by probands without migraine (43.8%). The percentage of relatives with migraine who reported sleep problems was 79.5% vs 61.7% for controls. Their most frequent sleep complaints were also inadequate sleep (41.0%), difficulty falling asleep (41.0%), and oversleeping (41.0%).

Table 3 shows the association between migraine and sleep problems with and without controlling for lifetime and current anxiety or mood disorders. The odds ratios and confidence limits are adjusted for sex and age. Probands with migraine reported having significantly more lifetime history of sleep problems in general (OR [CI] = 2.3 [1.1-4.6]) as well as current complaints of inadequate sleep (2.5 [1.2-5.0]) and difficulty falling asleep (3.0 [1.5-6.3]). The associations for inadequate sleep and difficulty falling asleep persisted when the models were adjusted for comorbid lifetime anxiety and depression. When the models were adjusted for current anxiety or depression, difficulty falling asleep became marginally significant while the association for inadequate sleep persisted. Additionally, the effects of comorbid substance use disorders were included in the models, but there were no significant effects on any of the sleep problems. Difficulty staying asleep and oversleeping were not significantly associated with migraine in the probands.

Similar results were found among the adult relatives. Adult relatives with migraine reported having significantly more lifetime sleep problems (OR [CI] = 3.2 [1.5-6.7]), and current complaints, including inadequate sleep (2.5 [1.3-4.7]) and difficulty falling asleep (3.3 [1.7-6.7]), and additionally, difficulty staying asleep (2.5 [1.2-5.4]) than adult relatives without migraine. When the models were adjusted for lifetime anxiety or depression (column 4) and substance use disorders (data not shown) and current anxiety or depression, all of the sleep problems were still associated with migraine.

The last row of Table 3 presents the association between nightmares and migraine with similar adjustment for lifetime and current anxiety and depression, age and sex. There was a significant association between migraine and persistent nightmares in both the probands (4.3 [1.8-9.9]) and relatives (4.1 [2.0-8.3]). This association persisted when the models were adjusted for lifetime anxiety or depression and current anxiety or depression. Not shown, bedwetting and sleepwalking were not found to be significantly associated with migraine in the probands or the relatives.

The association between the number of sleep problems and migraine in probands and relatives is shown in Table 4. We did not control for co-occurring anxiety and depression because of the sparse cell sizes. However, these results show that migraine is associated not only with sleep problems in general but also with the number of sleep problems. About 60% of the probands with migraine reported multiple (more than 2) sleep problems whereas only 18% of the controls. Likewise, twice as many of the relatives with migraine compared with those without migraine reported multiple sleep problems (61.5% vs 35.5%). There is substantial overlap among the adult current sleep problems, particularly inadequate sleep, difficulty falling asleep, and difficulty staying asleep (data not shown).

DISCUSSION

This study confirms prior reports of a strong association between migraine and sleep difficulties, with an approximately 3-fold increase in sleep problems among those with migraine. Not only did more people with migraine report specific sleep disturbances but they also had a greater number of sleep problems than their non-migraine counterparts. These findings contribute to current knowledge by demonstrating that the associations between migraine and sleep problems are not solely attributable to either current or lifetime comorbid anxiety and depression. The finding that relatives with migraine reported the same current sleep complaints as probands with migraine suggests that there may be a direct association between sleep disturbances and migraine.

Consistent with prior findings,^{8,9,11,12} probands with migraine reported that their sleep in general is inadequate, particularly with respect to difficulty falling asleep. In addition, the finding that those with migraine were characterized by multiple sleep problems suggests that migraine may be associated with poor sleep quality in general. Although anxiety and depression did not explain the sleep complaints of migraineurs, anxiety and depression were associated with difficulty falling asleep and inadequate sleep in the probands, and with difficulty falling asleep and staying asleep in the relatives. Persistent nightmares were not related to anxiety and/or depression in both the probands and relatives. This was not surprising as previous studies have reported little or no association between anxiety and nightmare frequency.³⁷

Our finding that migraineurs reported more persistent nightmares has been recently reported in the child literature.³⁸ Migraine attacks at night occur most frequently during late stages of sleep^{10,39} and transitions from rapid eye movement (REM) sleep periods,⁶ which may facilitate dream recall.⁴⁰ In fact, one study found that dreams which culminate in migraine headaches were characterized by the presence of negative affect (ie, nightmares).⁴¹ Even in the absence of a nighttime headache attack, migraineurs may be more likely to remember their dreams since they are more likely to wake up during the night.¹¹

Although the design and measures of the present study limit speculation on the possible explanations for the association between sleep problems and migraine, the 2 major classes of explanations for comorbidity are that one disorder is etiologically associated with the second or that the 2 conditions are manifestations of the common underlying pathways.⁴² In terms of causal mechanisms, migraine attacks that occur at night or during early morning hours could cause sleep problems, or conversely, a lack of sleep could provoke migraine attacks.^{43,44} Conversely, our finding of lifetime co-occurrence of migraine and childhood-onset nightmares and multiple sleep problems would be consistent with a common diathesis explanation. This mechanism would provide a compelling explanation in light of the persistent personality characteristics, autonomic lability,²¹ and hyperresponsiveness that tend to be stable characteristics of people with migraine.⁴⁵

Irrespective of the explanations for the association between sleep problems and migraine, our findings have important clinical implications. First, the recognition and treatment of sleep problems in migraine patients may diminish the impact of migraine on daily functioning.⁴⁶ Pharmacologic, relaxation, and cognitive behavioral treatments aimed to improve sleep as well as strategies to improve sleep hygiene may benefit migraine patients. Furthermore, if changes in sleep herald the onset of migraine, early intervention in this process could actually reduce the incidence of acute attacks of migraine.

The strengths of this study include: the recruitment of probands from both clinical and community settings, the systematic assessment of migraine, sleep problems and anxiety and mood disorders, and the inclusion of relatives, which constitutes a quasi epidemiologic sample. The original focus of this family study resulted in several limitations in the present analysis. Specifically, there was a lack of recruitment of migraine probands from clinical settings, a lack of information on migraine subtypes, severity and recency, and relatively small numbers. Furthermore, the cross-sectional design precluded evaluation of possible explanations for the order of onset of migraine, sleep problems, and anxiety and depression.

Nevertheless, these findings are intriguing and suggest that future studies should evaluate sleep problems in the context of both migraine and comorbid mood and anxiety disorders systematically. Prospective studies that seek to investigate the order of onset and persistence of these findings would provide insight into the possible explanations for these associations. For example, sleep problems were found to herald the onset of depression in a prospective study of a large population-based cohort by Dryman et al.⁴⁷ Confirmation of these findings in other samples generated systematic intervention studies of sleep problems to reduce the incidence of episodes of major depression.⁴⁸ However, no comparable studies of migraine and sleep problems have been conducted. Studies using tools such as actigraphy and daily headache diaries could provide insight into the associations found in this study.

REFERENCES

1. Lipton RB, Stewart WF, Diamond S, Diamond ML, Reed M. Prevalence and burden of migraine in the United States: Data from the American Migraine Study II. *Headache* 2001;41:646–657. [PubMed: 11554952]
2. Bixler EO, Kales A, Soldatos CR, Kales JD, Healey S. Prevalence of sleep disorders in the Los Angeles metropolitan area. *Am J Psychiatry* 1979;136:1257–1262. [PubMed: 314756]
3. Biondi DM. Headaches and their relationship to sleep. *Dent Clin North Am* 2001;45:685–700. [PubMed: 11699236]
4. Blau JN. Resolution of migraine attacks: Sleep and the recovery phase. *J Neurol Neurosurg Psychiatry* 1982;45:223–226. [PubMed: 7086442]
5. Marca, G Della; Vollono, C.; Rubino, M.; Di Trapani, G.; Mariotti, P.; Tonali, PA. Dysfunction of arousal systems in sleep-related migraine without aura. *Cephalalgia* 2006;26:857–864. [PubMed: 16776702]
6. Dexter JD, Weitzman ED. The relationship of noc-turnal headaches to sleep stage patterns. *Neurology* 1970;20:513–518. [PubMed: 4314825]
7. Dexter JD. The relationship between stage III + IV + REM sleep and arousals with migraine. *Headache* 1979;19:364–369. [PubMed: 229086]
8. Gori S, Morelli N, Maestri M, Fabbrini M, Bonanni E, Murri L. Sleep quality, chronotypes and preferential timing of attacks in migraine without aura. *J Headache Pain* 2005;6:258–260. [PubMed: 16362680]
9. Kelman L, Rains JC. Headache and sleep: Examination of sleep patterns and complaints in a large clinical sample of migraineurs. *Headache* 2005;45:904–910. [PubMed: 15985108]
10. Rasmussen BK. Migraine and tension-type headache in a general population: Precipitating factors, female hormones, sleep pattern and relation to lifestyle. *Pain* 1993;53:65–72. [PubMed: 8316392]

11. Egilius L. Fatigue and sleep in chronic headache sufferers: An age-and sex-controlled questionnaire study. *Headache* 1997;37:549–552. [PubMed: 9385751]
12. Calhoun AH, Ford S, Finkel AG, Kahn KA, Mann JD. The prevalence and spectrum of sleep problems in women with transformed migraine. *Headache* 2006;46:604–610. [PubMed: 16643555]
13. Goder R, Fritzer G, Kapsokalyvas A, et al. Polysomnographic findings in nights preceding a migraine attack. *Cephalalgia* 2001;21:31–37. [PubMed: 11298661]
14. Jennum P, Hein HO, Suadicani P, Gyntelberg F. Headache and cognitive dysfunctions in snorers. A cross-sectional study of 3323 men aged 54 to 74 years: The Copenhagen Male Study. *Arch Neurol* 1994;51:937–942. [PubMed: 8080395]
15. Aaltonen K, Hamalainen ML, Hoppu K. Migraine attacks and sleep in children. *Cephalalgia* 2000;20:580–584. [PubMed: 11075842]
16. Bille BS. Migraine in school children. A study of the incidence and short-term prognosis, and a clinical, psychological and electroencephalographic comparison between children with migraine and matched controls. *Acta Paediatr* 1962;136:1–151.
17. Lanzi G, Zambrino CA, Balottin U, Tagliasacchi M, Vercelli P, Termine C. Periodic syndrome and migraine in children and adolescents. *Ital J Neurol Sci* 1997;18:283–288. [PubMed: 9412852]
18. Miller VA, Palermo TM, Powers SW, Scher MS, Hershey AD. Migraine headaches and sleep disturbances in children. *Headache* 2003;43:362–368. [PubMed: 12656707]
19. Bruni O, Fabrizi P, Ottaviano S, Cortesi F, Giannotti F, Guidetti V. Prevalence of sleep disorders in childhood and adolescence with headache: A case-control study. *Cephalalgia* 1997;17:492–498. [PubMed: 9209768]
20. Breslau N, Davis GC, Andreski P. Migraine, psychiatric disorders, and suicide attempts: An epidemiologic study of young adults. *Psychiatry Res* 1991;37:11–23. [PubMed: 1862159]
21. Merikangas KR, Merikangas JR, Angst J. Headache syndromes and psychiatric disorders: Association and familial transmission. *J Psychiatr Res* 1993;27:197–210. [PubMed: 8366469]
22. Lanteri-Minet M, Radat F, Chautard MH, Lucas C. Anxiety and depression associated with migraine: Influence on migraine subjects' disability and quality of life, and acute migraine management. *Pain* 2005;118:319–326. [PubMed: 16289799]
23. Oedegaard KJ, Neckelmann D, Mykletun A, et al. Migraine with and without aura: Association with depression and anxiety disorder in a population-based study. The HUNT Study. *Cephalalgia* 2006;26:1–6. [PubMed: 16396660]
24. Lipton RB, Hamelsky SW, Kolodner KB, Steiner TJ, Stewart WF. Migraine, quality of life, and depression: A population-based case-control study. *Neurology* 2000;55:629–635. [PubMed: 10980724]
25. Merikangas KR, Angst J, Isler H. Migraine and psychopathology. Results of the Zurich cohort study of young adults. *Arch Gen Psychiatry* 1990;47:849–853. [PubMed: 2393343]
26. Mitsikostas DD, Thomas AM. Comorbidity of headache and depressive disorders. *Cephalalgia* 1999;19:211–217. [PubMed: 10376165]
27. Ford DE, Kamerow DB. Epidemiologic study of sleep disturbances and psychiatric disorders. An opportunity for prevention? *JAMA* 1989;262:1479–1484. [PubMed: 2769898]
28. Mellinger GD, Balter MB, Uhlenhuth EH. Insomnia and its treatment. Prevalence and correlates. *Arch Gen Psychiatry* 1985;42:225–232. [PubMed: 2858188]
29. Roth T, Jaeger S, Jin R, Kalsekar A, Stang PE, Kessler RC. Sleep problems, comorbid mental disorders, and role functioning in the national comorbidity survey replication. *Biol Psychiatry* 2006;60:1364–1371. [PubMed: 16952333]
30. Ohayon MM. Prevalence and risk factors of morning headaches in the general population. *Arch Intern Med* 2004;164:97–102. [PubMed: 14718329]
31. Boardman HF, Thomas E, Millson DS, Croft PR. Psychological, sleep, lifestyle, and comorbid associations with headache. *Headache* 2005;45:657–669. [PubMed: 15953298]
32. Maizels M, Burchette R. Somatic symptoms in headache patients: The influence of headache diagnosis, frequency, and comorbidity. *Headache* 2004;44:983–993. [PubMed: 15546261]
33. Avenevoli S, Merikangas KR. Familial influences on adolescent smoking. *Addiction* 2003;98:1–20. [PubMed: 12752359]

34. Headache Classification Committee of the International Headache Society. Chairman classification and diagnostic criteria for headache disorders, cranial neuralgias, and facial pain. *Cephalalgia* 1988;8 (Suppl 7):1–96.
35. Endicott J, Spitzer RL. A diagnostic interview: The schedule for affective disorders and schizophrenia. *Arch Gen Psychiatry* 1978;35:837–844. [PubMed: 678037]
36. American Academy of Sleep Medicine. International Classification of Sleep Disorders, Revised: Diagnostic and Coding Manual. American Academy of Sleep Med; Chicago, IL: 2001.
37. Wood JM, Bootzin RR. The prevalence of nightmares and their independence from anxiety. *J Abnorm Psychol* 1990;99:64–68. [PubMed: 2307768]
38. Isik U, Ersu RH, Ay P, et al. Prevalence of headache and its association with sleep disorders in children. *Pediatr Neurol* 2007;36:146–151. [PubMed: 17352946]
39. Fox A. Migraine chronobiology. *Headache* 1998;38:431–441.
40. Dement W, Kleitman N. The relation of eye movements during sleep to dream activity: An objective method for the study of dreaming. *J Exp Psychol* 1957;53:339–346. [PubMed: 13428941]
41. Levitan H. Dreams which culminate in migraine headaches. *Psychother Psychosom* 1984;41:161–166. [PubMed: 6463182]
42. Merikangas, KR. Comorbidity for anxiety and depression: A review of family and genetic studies. In: Maser, JD.; Cloninger, CR., editors. *Comorbidity of Mood and Anxiety Disorders*. American Psychiatric Press; Washington, DC: 1990. p. 331–348.
43. Ulfberg J, Carter N, Talback M, Edling C. Headache, snoring and sleep apnoea. *J Neurol* 1996;243:621–625. [PubMed: 8892061]
44. Poceta JS, Dalessio DJ. Identification and treatment of sleep apnea in patients with chronic headache. *Headache* 1995;35:586–589. [PubMed: 8550358]
45. Bonnet MH, Arand DL. Heart rate variability in insomniacs and matched normal sleepers. *Psychosom Med* 1998;60:610–615. [PubMed: 9773766]
46. Stovner LJ, Hagen K. Prevalence, burden, and cost of headache disorders. *Curr Opin Neurol* 2006;19:281–285. [PubMed: 16702836]
47. Dryman A, Eaton WW. Affective symptoms associated with the onset of major depression in the community: Findings from the US National Institute of Mental Health Epidemiologic Catchment Area Program. *Acta Psychiatr Scand* 1991;84:1–5. [PubMed: 1927557]
48. Eaton WW, Badawi M, Melton B. Prodromes and precursors: Epidemiologic data for primary prevention of disorders with slow onset. *Am J Psychiatry* 1995;152:967–972. [PubMed: 7793466]

Table 1
Demographic Characteristics of Probands and Relatives by Migraine Status

	Migraine	No migraine	Total	P value
Probands	41	221	262	
Female (%)	65.9	47.5	50.4	.031
Age (mean years, range)	39.5 (24.0-56.0)	39.7 (25.0-55.0)	39.7 (24.0-56.0)	N.S.
Proband Ascertainment Group (%)				
Anxiety *	78.0	50.7	55.0	N.S.
Substance abuse only	9.8	25.3	23.2	N.S.
Control	12.2	24.0	21.8	N.S.
Lifetime psychiatric diagnoses (%)				
Depression **	58.5	42.5	45.0	.059
Anxiety *	82.9	53.4	58.0	<.001
Both	53.7	33.0	36.3	.012
None	12.2	37.1	33.2	.002
Current psychiatric diagnoses (%)				
Depression **	12.2	8.1	8.8	N.S.
Anxiety *	70.7	33.5	39.3	<.001
Both	12.2	5.0	6.1	.077
None	29.3	63.4	58.0	<.001
Adult relatives	39	222	261	
Female (%)	82.0	60.8	64.0	.011
Age (mean years, range)	44.3 (19.0-76.0)	42.3 (18.0-80.0)	42.6 (18.0-80.0)	N.S.
Lifetime psychiatric diagnoses (%)				
Depression **	41.0	35.1	36.0	N.S.
Anxiety *	51.3	38.8	40.6	N.S.
Both	33.3	20.7	22.6	.083
None	41.0	46.9	50.0	N.S.
Current psychiatric diagnoses (%)				
Depression **	10.3	3.2	4.2	.042
Anxiety *	25.6	21.6	22.2	N.S.
Both	7.7	2.7	3.5	N.S.

	Migraine	No migraine	Total	P value
None	71.8	77.9	77.0	N.S.

* Anxiety disorders include: agoraphobia, social phobia, generalized anxiety disorder, panic disorder, separation anxiety, and overanxious disorder.

** Depression includes: major depressive disorder, and dysthymia.

Table 2
Proportions of Probands and Relatives With Sleep Problems by Migraine Status

	Probands			Relatives		
	Migraine (n = 41)	No migraine (n = 221)	P value	Migraine (n = 39)	No migraine (n = 222)	P value
Any sleep problem (%)	85.4	65.3	.008	79.5	61.7	.033
Inadequate sleep (%)	46.3	25.3	.006	41.0	24.8	.035
Difficulty falling asleep (%)	48.8	23.5	.001	41.0	18.0	.001
Difficulty staying asleep (%)	39.0	27.1	NS	33.3	14.4	.073
Oversleeping (%)	43.9	43.8	NS	41.0	43.2	NS
Persistent nightmares (%)	30.8	9.3	.001	30.8	10.4	.001
Bedwetting (%)	21.9	16.0	NS	15.4	11.3	NS
Sleepwalking (%)	11.3	7.3	NS	17.9	8.5	.004

Table 3

Associations Between Migraine and Sleep Problems With and Without Adjustment for Lifetime and Current Anxiety and/or Depression (Odd Ratios and 95% Confidence Intervals)

Sleep problems	Probands (N = 262)			Relatives (N = 261)		
	Migraine [*]	Migraine adjusted for lifetime anxiety or depression ^{**}	Migraine adjusted for current anxiety or depression ^{***}	Migraine [*]	Migraine adjusted for lifetime anxiety or depression ^{**}	Migraine adjusted for current anxiety or depression ^{***}
Inadequate sleep	2.5 (1.2-5.0)	2.2 (1.1-4.5)	2.3 (1.1-4.7)	2.5 (1.3-4.7)	2.4 (1.3-4.5)	2.4 (1.3-4.6)
Anxiety disorder		2.6 (1.4-5.1)	1.3 (0.7-2.4)		1.3 (0.7-2.5)	0.9 (0.4-2.0)
Depression		0.6 (0.3-1.0)	1.5 (0.6-3.7)		0.8 (0.4-1.4)	1.4 (0.4-5.2)
Difficulty falling asleep	3.0 (1.5-6.3)	2.2 (1.1-4.7)	2.1 (0.9-4.7)	3.3 (1.7-6.7)	3.3 (1.6-6.6)	3.1 (1.5-6.3)
Anxiety disorder		3.4 (1.6-7.0)	3.4 (1.8-6.2)		1.7 (0.9-3.4)	2.4 (1.1-4.8)
Depression		1.4 (0.8-2.7)	3.1 (1.1-8.7)		2.8 (1.4-5.2)	3.3 (1.0-10.4)
Difficulty staying asleep	1.5 (0.8-3.1)	1.2 (0.6-1.5)	1.1 (0.5-2.5)	2.5 (1.2-5.4)	2.3 (1.1-4.8)	2.3 (1.1-5.0)
Anxiety disorder		2.4 (1.2-4.6)	2.2 (1.2-3.9)		1.5 (0.8-2.8)	2.2 (1.0-4.6)
Depression		1.4 (0.8-2.7)	2.8 (1.0-7.4)		2.1 (1.1-3.9)	2.1 (0.7-6.9)
Oversleeping	0.9 (0.5-1.8)	0.9 (0.4-1.8)	0.9 (0.4-1.9)	1.1 (0.5-2.2)	1.0 (0.5-2.1)	1.0 (0.5-2.1)
Anxiety disorder		1.3 (0.7-2.3)	1.1 (0.6-1.9)		1.8 (1.0-3.5)	1.3 (0.7-2.3)
Depression		0.9 (0.5-1.6)	1.1 (0.5-2.8)		0.6 (0.3-1.2)	1.8 (0.5-6.0)
Sleep problems	2.3 (1.1-4.6)	1.7 (0.9-3.6)	1.7 (0.8-3.6)	3.2 (1.5-6.7)	3.0 (1.4-6.3)	3.0 (1.5-6.3)
Anxiety disorder		2.7 (1.4-5.0)	2.6 (1.5-4.5)		1.9 (1.0-3.5)	2.7 (1.4-5.4)
Depression		1.3 (0.8-2.4)	2.7 (1.0-7.3)		2.1 (1.2-3.8)	3.1 (1.0-10.2)
Persistent nightmares	4.3 (1.8-9.9)	3.7 (1.5-8.7)	3.2 (1.3-8.1)	4.1 (2.0-8.3)	3.9 (1.8-8.2)	4.1 (2.0-8.4)
Anxiety disorder		1.4 (0.6-3.8)	1.9 (0.8-4.6)		2.3 (1.0-5.1)	1.7 (0.8-4.1)
Depression		1.8 (0.8-4.1)	1.7 (0.5-5.7)		1.8 (0.8-4.2)	0.7 (0.2-2.3)

The item "Sleep problems" was used as a probe and describes lifetime presence of problems.

* Adjusted for age and sex.

** Adjusted for age, sex, and lifetime history of: anxiety (agoraphobia, social phobia, generalized anxiety disorder, panic disorder, separation anxiety, and overanxious disorder), and depression (major depressive disorder and dysthymia).

*** Adjusted for age, sex, and current: anxiety (agoraphobia, social phobia, generalized anxiety disorder, panic disorder, separation anxiety, and overanxious disorder), and depression (major depressive disorder and dysthymia).

Table 4
Number of Sleep Problems Among Probands and Relatives by Migraine Status

Number of sleep problems	Probands (N = 262)		Relatives (N = 261)	
	Migraine (%) (n = 41)	No migraine (%) (n = 221)	Migraine (%) (n = 39)	No migraine (%) (n = 222)
None	25.9	54.2	11.5	45.6
+1 symptom	0	11.0	0	5.1
+2 symptoms	7.4	16.9	26.9	13.8
+ >2 symptoms	59.3	17.8	61.5	35.5
Chi-square (4 df) = 20.12, P = .0005				
Chi-square (4 df) = 13.77, P = .0032				