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The association between stress and headache: A longitudinal population-based study

Sara H Schramm[1], Susanne Moebus[1], Nils Lehmann[1], Ursula Galli[2], Mark Obermann[3], Eva Bock[1], Min-Suk Yoon[4], Hans-Christoph Diener[3] and Zaza Katsarava[5]

Abstract

Introduction: We studied the association between stress intensity and headache frequency for tension-type headache (TTH), migraine and migraine with coexisting TTH (MigTTH).

Method: We studied a population-based sample of 5159 participants (21–71 years) who were asked quarterly between March 2010 and April 2012 about headache and stress. Log-linear regression in the framework of generalized estimating equations was used to estimate regression coefficients presented as percent changes to describe the association between stress intensity (modified visual analog scale (VAS) from 0 to 100) and headache frequency (days/month) stratified by headache subtypes and age groups and adjusted for sex, age, frequent intake of acute pain drugs, drinking, smoking, BMI and education.

Results: TTH was reported in 31% participants (48.1 ± 12.5years, 51.5% women, 2.2 ± 3.9 mean headache days/month, 52.3 ± 26.7 mean stress), migraine in 14% (44.8 ± 11.3years, 73.3%, 4.5 ± 5.2 days/month, 62.4 ± 23.3), MigTTH in 10.6% (43.5 ± 11.5 years, 61.0%, 3.6 ± 4.8 days/month, 58.6 ± 24.1), 23.6% were unclassifiable, and 20.8% had no headache. In participants with TTH an increase of 10 points on VAS was associated with an increase of headaches days/month of 6.0% (adjusted). Higher effects were observed in younger age groups (21–30/31–40/41–50/51–60/61–71 years: 9.8/10.2/7.0/6.5/3.5%). Slightly lower effects were observed for migraine (4.3%, 8.1/5.1/3.4/6.3/0.3%) and MigTTH (4.2%, 5.5/6.8/6.9/5.8/–0.7%).

Conclusion: Our study provides evidence for an association between stress intensity and headache frequency.

Keywords

Stress, migraine, tension-type headache, epidemiology, longitudinal, headache

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Introduction

Headache patients frequently report stress to be one of their main activators or aggravators for headache (1–4). It is supposed that stress can be a predisposing factor contributing to the onset of headache disorders, that it accelerates the progression to chronic headache, provokes and exacerbates headache episodes and that the headache experience itself can serve as a stressor (5,6). Tension-type headache (TTH) and migraine are the most common primary headache disorders, affecting up to 80% of the general population (7). The stress system has components of the central and peripheral nervous system. The central components are located in the hypothalamus and the brainstem. The peripheral

[1]Institute for Medical Informatics, Biometry and Epidemiology, University Hospital of University Duisburg-Essen, Germany
[2]Department of Psychology, Center for Psychotherapy, University of Zurich, Switzerland
[3]Department of Neurology, University Hospital of University Duisburg-Essen, Germany
[4]Department of Neurology, St. Joseph Hospital, Ruhr-University of Bochum, Germany
[5]Department of Neurology, Evangelisches Krankenhaus Unna, Germany

Corresponding author:
Sara H Schramm, Institute for Medical Informatics, Biometry and Epidemiology, University Hospital of University Duisburg-Essen, Hufelandstr. 55, 45122 Essen, Germany.
Email: sara.schramm@uk-essen.de

components include the peripheral limbs of the hypothalamic-pituitary-adrenal axis, the efferent sympathetic-adrenomedullary system and components of the parasympathetic system. The principal effectors of the stress system include corticotropin-releasing hormone; arginine vasopressin; the proopiomelanocortin-derived peptides α-melanocyte-stimulating hormone and β-endorphin, the glucocorticoids and the catecholamines norepinephrine and epinephrine (8,9). Signals of the stress system arrive through distinct pathways and impact a diversity of cognitive, emotional, neurosensory, and peripheral somatic functions. Stress itself is an ill-defined term and can refer to a number and magnitude of experienced life events or daily hassles, a set of physiological responses that occur under pressure, a state of emotional distress or the inability to deal with demands of life (5). Psychological stress originates from perceived threats to physical well-being or from challenges that are cognitive or emotional in nature (5). The concrete biological mechanisms by which stress contributes to TTH or migraine, and whether these mechanisms are similar or different for TTH and migraine, are currently unknown. The biopsychosocial model attempts to explain the complex genesis of headache by the multidirectional relationship between biological (physiological), psychological (cognitive, emotional, behavioral), and social (environmental) factors (10,11) The ethiopathogenetic model for TTH suggests that stress may contribute to TTH by aggravating abnormal pain processing (6,12,13). Genetic (14), epigenetic (15), psychosocial (16), physiological and biochemical (17) predispositions in combination with habitual dysfunctional stress management (18) have been suggested as influencing the occurrence and severity of migraine. Neurophysiological studies in migraine patients have detected abnormal cortical excitability and information processing between attacks, whereas cortical habituation was seen as a protective mechanism against overstimulation of physiological stress (19,20). Stress might produce additional chemical changes in the cerebral cortex of sufficient degree to promote migraine attacks (20). It is supposed that behavioral interventions and coping strategies reduce stress by promoting a balanced, regular lifestyle (21–24). Evidence is missing that stress has an influence on primary headache disorders or that stress-based lifestyle changes reduce the frequency or severity of headaches. To the best of our knowledge, longitudinal population-based studies evaluating the association between stress on headache frequency with regard to particular subtypes of primary headaches and age have not been performed until now. Therefore, the longitudinal population-based German Headache Consortium (GHC) study investigated the association between stress intensity and headache frequency for the main headache subtypes TTH, migraine and migraine with coexisting TTH and for different age groups.

Methods

Study design and study population

The GHC study has been described in detail elsewhere (25). Briefly, the GHC study is a population-based cohort study, started in 2003 and supported by the German Federal Ministry of Education and Research. The study was approved by the ethics committee of the University of Duisburg-Essen, Germany. Informed written consent was obtained from all participants prior to enrollment. Between 2003 and 2005, about 18,000 men and women with German citizenship, aged 18 to 65 years, were randomly selected from statutory lists of residents in three German cities: Essen (585,481 residents), Muenster (272,890 residents) and Sigmaringen (16,501 residents). We obtained baseline information from 9944 participants; of those, 843 were lost to follow-up before 2010 (Figure 1). Between March 2010 and April 2012, the remaining 9101 participants received quarterly one of two different follow-up questionnaires (short, long) via postal mail (Figure 2). A short questionnaire was sent six times (three times a year) and a long questionnaire once in the first year. For logistic reasons, the short questionnaire was sent to three-quarters of the study population each quarter over two years and the long version to one-quarter of the study population each quarter of the first year. Participants who did not respond were called at least eight times to be interviewed by telephone. Interviews were performed by trained medical students using the identical mailed questionnaire. Overall, we obtained follow-up information on 5159 (56.7%) participants.

Questionnaire

A detailed description and validation of the headache-screening questionnaire was published previously (26,27).

Short questionnaire. The short questionnaire assessed perceived stress using a modified visual analog scale (VAS), ranging from 0 to 100 and included questions about the number of days associated with headache and the frequency of intake of acute pain medication. Regarding stress we asked the following question: ''Please estimate your personal stress. Mark the line according to your perceived stress in the last three months.'' Respondents specified their level of stress by indicating a position along a discrete linear scale between 0 (no stress) and 100 (very high stress).

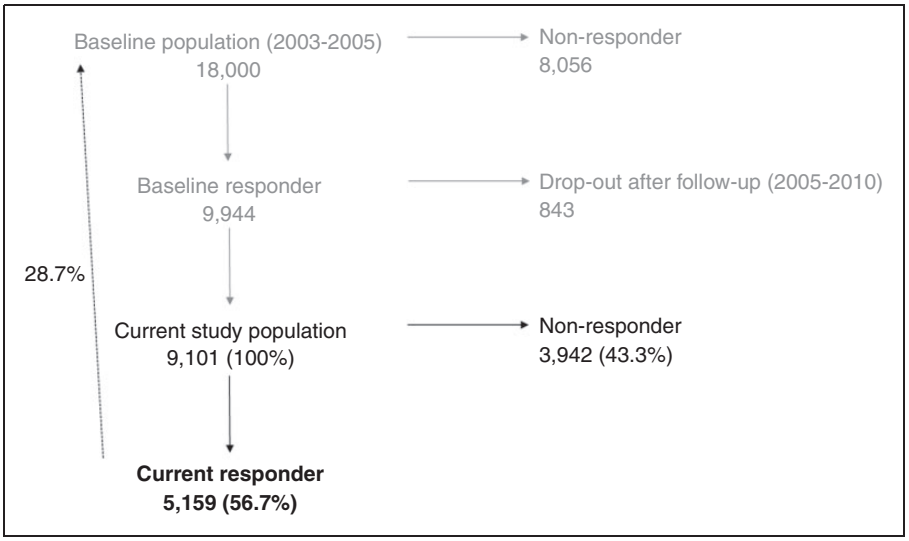

Figure 1. Screening procedure.

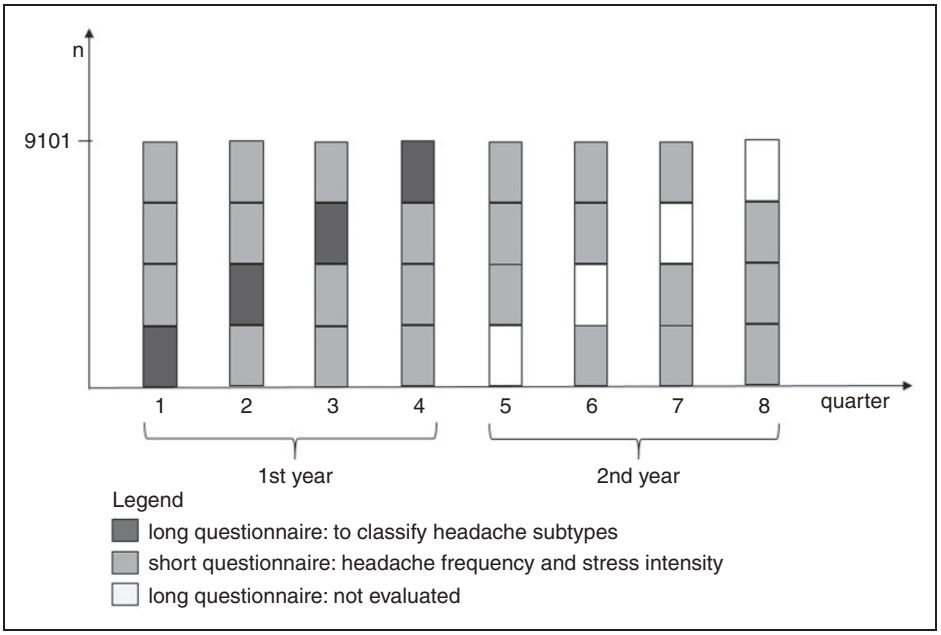

Figure 2. Study design.

Regarding headache frequency we asked: ''Did you suffer from headache in the last three month? If yes, on how many days/month on average?''

Long questionnaire. The long questionnaire included inquiries to diagnose headache according to the International Classification of Headache Disorders, second edition (ICHD-2) classification criteria of the International Headache Society (IHS) (28) and questions about height, weight and behavior with regard to smoking and drinking alcoholic beverages.

The covariate ''education'' was collected at baseline by questionnaire or telephone interview.

Diagnostic criteria

Headache subtypes were defined according to the criteria of the IHS (28).

- Diagnosis of TTH: Respondents who met ICHD-2 criteria for definitive or probable TTH, but did not fulfill the IHS criteria for migraine.

- Diagnosis of migraine: Respondents who met ICHD-2 criteria for definitive or probable migraine, but did not fulfill the IHS criteria for TTH.
- Diagnosis of migraine with coexisting TTH: Respondents who met ICHD-2 criteria for definitive or probable migraine and fulfilled the IHS criteria for TTH.
- Diagnosis of unclassifiable headache: All other participants with headache that did not match any of these classifications for primary headache and participants with headache but missing long questionnaire.
- Diagnosis of no headache: Respondents with none of the above headache subtypes who reported no headache in all short questionnaires.

Definition of covariates

- Overuse of acute pain drugs (yes) was defined as intake of acute pain drugs (including any pain and migraine drugs) on $\geq$15 days/month. Overuse of acute pain drugs (no) was defined as intake of acute pain drugs on <15 days/month. No medication was defined as no pain medication at all.
- Drinking (yes) was defined as daily or almost daily drinking of alcoholic beverages and drinking (no) was defined as no or casual drinking of alcoholic beverages.
- Smoking (yes) was defined as current smoking or quit smoking in the last 12 months and smoking (no) was defined as never or past smoking.
- Normal body mass index (BMI) was defined as BMI $< 25\,kg/m^2$, overweight as BMI between $25\,kg/m^2$ and $30\,kg/m^2$ and obesity as BMI $> 30\,kg/m^2$.
- High education was defined as general qualification for university entrance or completion of university, and low education was defined as any other response.

Statistical analyses

Results are based on the analysis of data from participants, who responded to at least one short questionnaire ($n = 5159$). Descriptive statistics characterized participants by quarter and headache subtype. Mean stress and mean headache frequency were presented stratified by headache subtype and age groups (21–30, 31–40, 41–50, 51–60 and 61–71 years). We investigated the association between stress intensity (VAS from 0 to 100) and headache frequency (days/month) stratified by different headache subtypes and age groups (21–30, 31–40, 41–50, 51–60 and 61–71 years). To account for the correlation structure in the data that results from repeated questioning, log-linear regression in the framework of generalized estimating equations (GEEs) was used. We used the negative binomial link function, which accounts for overdispersion and which has been proposed to account for excess zeros.[29] GEE modelling estimates averaged regression coefficients of the population. They are interpreted just as in a cross-sectional analysis. Results are presented as percent changes with 95% confidence intervals (95% CI), adjusting for sex, age and overuse of acute pain drugs, drinking, smoking, BMI and education. All statistics were completed in SAS, version 9.2 (Statistical Analysis Systems Corp., Cary, NC, USA).

Results

Response

Of the 9101 baseline participants, 57% ($n = 5159$, mean age 47.7 ± 12.5 years, 53.2% women) responded to at least one short questionnaire. Response for the eight quarters ranged between 42% and 78% (Table 1). The sample size decreased from 3841 in quarter 1 to 2992 in quarter 8. The main reason for non-response was refusing to continue participation (between 64% and 99%). Of 5159 participants, 3735 (72.4%) responded to all six short questionnaires, 443 (8.59%) responded to five, 129 (2.50%) to four, 146 (2.83%) to three, 187 (3.62%) to two and 519 (10.1%) only to one short questionnaire. A detailed table that describes type and proportion of response of the short questionnaire as well as the reasons for non-response is presented in the supplementary materials. The long questionnaire was answered once by 4515 participants (78.4%).

Characteristics of the study population

Table 1 shows the characteristics of the study population by quarter. From quarter 1 to 8, the percentage of women (range 50.5%–60.1%), mean age (47.0–50.2 years), headache frequency (2.2–2.7 days/month), stress (50.8–55.1) and overuse of acute pain drugs (2.9%–5.0%) were similar. In the later quarters, slightly more participants reported headache (quarter 1: 55.3%; quarter 8: 61.3%). Women and men reported similar mean stress over all quarters (women: 53.9 ± 26.5; men: 52.2 ± 27.7). Table 2 shows the distribution of headache subtypes and the characteristics of the study population per headache subtype. TTH was reported in 1598 (31%) participants (aged 48.1 ± 12.5 years, 51.5% women) with 2.2 ± 3.9 mean headache days/month, and a mean stress intensity of 52.3 ± 26.7. Participants with migraine (14.0%) were younger on average (44.8 ± 11.3 years), more likely women

Table 1. Characteristics of the study population by short questionnaire and quarter.

Quarter	1	2	3	4	5	6	7	8
Period	26.3.–25.6.10	26.6.–25.9.10	26.9.–26.12.10	27.12.–27.3.11	28.3.–25.6.11	26.6.–5.10.11	6.10.–19.1.12	20.1.–19.4.12
n	9101	5664	4793	4,607	4509	4356	4302	4100
Responder, *n* (%)	3841 (42.2)	3700 (78.4)	3110 (64.9)	3219 (69.9)	3437 (76.2)	3265 (75.0)	2908 (67.6)	2992 (73.0)
Women, *n* (%)	2047 (53.3)	1966 (63.1)	1886 (60.6)	1616 (50.2)	1824 (53.2)	1768 (54.2)	1748 (60.1)	1513 (50.6)
Age, years								
Mean ± SD	47.0 ± 12.5	49.8 ± 11.5	46.7 ± 13.2	48.3 ± 12.3	46.8 ± 12.4	50.2 ± 11.2	47.0 ± 13.0	48.5 ± 12.1
Missing, *n*	1	1	1	0	1	0	0	0
Headache, *n* (%)								
Yes,	2080 (54.3)	1965 (53.2)	1887 (60.8)	1924 (59.9)	2069 (60.4)	1899 (58.3)	1822 (62.7)	1829 (61.23)
Missing, *n*	8	5	6	5	10	5	4	6
Headache days/month								
Mean ± SD	2.3 ± 4.5	2.2 ± 4.2	2.7 ± 4.6	2.4 ± 4.2	2.3 ± 3.9	2.3 ± 4.1	2.5 ± 4.0	2.3 ± 4.0
Q1/Q2/Q3	0/1/3	0/1/3	0/1/3	0/1/3	0/1/3	0/1/3	0/1/3	0/1/3
Missing, *n*	18	21	16	26	17	24	20	16
Stress (VAS)								
Mean ± SD	50.8 ± 28.0	51.5 ± 27.9	53.0 ± 27.2	53.5 ± 27.1	55.1 ± 25.9	53.4 ± 27.2	54.6 ± 26.2	53.6 ± 26.2
Q1/Q2/Q3	30/50/75	30/50/75	30/60/75	30/60/75	35/60/75	30/60/75	35/60/75	30/60/75
Missing, *n*	24	13	19	14	17	19	26	16
[a]Medication overuse, *n* (%)								
No	1422 (37.6)	1544 (42.1)	1516 (49.3)	1593 (50.0)	1617 (47.4)	1473 (45.5)	1371 (47.4)	1423 (48.0)
Yes	108 (2.9)	161 (4.4)	138 (4.5)	150 (4.7)	148 (4.3)	155 (4.8)	143 (5.0)	144 (4.9)
[b]No medication	2257 (59.6)	1960 (53.5)	1420 (46.2)	1441 (45.3)	1646 (48.3)	1613 (49.8)	1377 (47.6)	1397 (47.1)
Missing, *n*	54	35	36	35	26	24	17	28

Q1: first quartile; Q2: median; Q3: third quartile. [a]Medication overuse was defined as intake of acute pain drugs on ≥ 15 days per month. [b]No pain medication at all.

Table 2. Characteristics of the study population by headache subtype.

	Total	TTH	Migraine	MigTTH	Unclassifiable headache	No headache
n (%)	5159 (100)	1598 (31.0)	724 (14.0)	548 (10.6)	1215 (23.6)	1074 (20.8)
Women, *n* (%)	2746 (53.2)	823 (51.5)	531 (73.3)	334 (61.0)	652 (53.7)	405 (37.8)
Age, years						
Mean ± SD	47.7 ± 12.5	48.1 ± 12.5	44.8 ± 11.3	43.5 ± 11.5	46.7 ± 12.3	52.4 ± 12.6
Missing, *n*	1	0	0	0	0	1
Stress (VAS)						
Mean ± SD	53.1 ± 27.1	52.3 ± 26.7	62.4 ± 23.3	58.6 ± 24.1	54.0 ± 26.6	41.1 ± 29.1
Q1/Q2/Q3	30/60/75	30/55/75	50/70/80	40/60/80	30/60/75	15/40/70
Headache days/month						
Mean ± SD	2.4 ± 4.2	2.2 ± 3.9	4.5 ± 5.2	3.6 ± 4.8	2.2 ± 4.1	0
Q1/Q2/Q3	0/1/3	0/1/3	2/3/5	1/2/4	0/1/2.5	0
[a]Drinking						
Yes, *n* (%)	27 (0.7)	11 (0.7)	2 (0.3)	2 (0.4)	6 (1.0)	6 (1.0)
Missing, n	1161	43	24	14	627	451
[b]Smoking						
Yes, *n* (%)	1099 (27.4)	397 (25.4)	209 (29.8)	157 (29.1)	162 (27.6)	174 (28.0)
Missing, *n*	1145	35	22	9	627	450
BMI, *n* (%)						
$<25\ kg/m^2$	1990 (50.0)	782 (50.4)	385 (55.6)	279 (52.4)	294 (50.3)	250 (40.6)
$25–30\ kg/m^2$	1396 (35.1)	548 (35.3)	196 (28.3)	178 (33.4)	200 (34.3)	274 (44.5)
$>30\ kg/m^2$	592 (14.9)	222 (14.3)	112 (16.2)	76 (14.3)	90 (15.4)	92 (14.9)
Missing, *n*	1181	46	31	15	631	456
[c]Education						
High, *n* (%)	1728 (34.7)	612 (39.2)	237 (34.0)	193 (36.8)	423 (36.3)	262 (25.3)
Missing, *n*	177	37	27	24	51	38

TTH: tension-type headache; MigTTH: migraine with coexisting tension-type headache; Q1: first quartile; Q2: median; Q3: third quartile; BMI: body mass index. [a]Drinking (yes) was defined as daily or almost daily drinking of alcoholic beverage. [b]Smoking (yes) was defined as current smoking or quit smoking in the last 12 months. [c]High education was defined as general qualification for university entrance or completion of university.

(73.3%), reported a higher frequency of headaches (4.5 ± 5.2 days/month) and greater stress intensity (62.4 ± 23.3). Similar results could be observed for those with migraine with coexisting TTH (10.6%, 43.5 ± 11.5 years, 61.0% women), however with a lower frequency of headaches (3.6 ± 4.8 days/month), and lower stress intensity (58.6 ± 24.1); in 23.6% of the participants the headache type was not classifiable. Participants with migraine and migraine with coexisting TTH were more likely to smoke (29.8% and 29.1%) and less likely to be highy educated (34.0% and 36.8%) compared to participants with TTH (smoking: 25.4%, high education: 39.2%). Few participants reported daily or almost daily drinking of alcoholic beverages and there was no difference between headache subtypes (0.29%–0.71%). Participants with no headache (20.8%) were older on average (52.4 ± 12.6 years), less likely women (37.8%), more often reported a normal BMI (40.6%), less often reported high education (25.3%) and perceived less stress (41.1 ± 29.1) than participants with headaches. Stratified by age groups (Table 3) we observed a similar prevalence of TTH in each age group (range 27.5%–32.7%). The prevalence of migraine and migraine with coexisting TTH increased more or less from age group 21–30 to 31–40 years and then it decreased by age (migraine: (21–30/31–40/41–50/51–60/61–71 years) 14.7/20.7/15.5/12.7/7.3%; migraine with coexisting TTH: 14.4/14.6/13.1/8.0/4.3%). Older participants experienced less headache (prevalence of ''no headache'': 14.4/11.8/16.2/22.9/37.4%). In all age groups participants with migraine and migraine with coexisting TTH reported more stress than those with TTH followed by those without headache. On average the highest stress scores were reported by younger respondents (TTH: 56.8/60.1/59.2/52.7/32.2; migraine: 65.9/64.8/62.3/63.6/48.7; migraine with coexisting TTH: 58.4/60.8/60.1/56.8/49.8; no headache: 49.8/52.8/50.9/

46.3/26.5). In participants with TTH there was no trend in mean headache days/month by age group (range 2.1–2.3 days/month). In migraine and migraine with coexisting TTH mean headache days increased by age (migraine. 4.0/4.4/4.2/4.8/5.9 days/month; migraine with coexisting TTH: 3.3/3.1/3.1/4.0/7.5 days/month).

Association between stress intensity and headache frequency

Table 3 shows the percent increase in headache days/month and the corresponding 95% CI intervals for each 10-point stress increase on the VAS stratified by headache subtypes and age groups in decades. An increase in headache frequency was positively correlated with increasing stress intensity independent of headache subtype. Highest effects were observed in participants with TTH: In the fully adjusted model, each 10-point increase in stress intensity was associated with a 6.4% (95% CI: 4.4%–8.5%) increase in headache days/month. In participants with migraine and in participants with migraine with coexisting TTH, the increase was almost identical, with 4.3% (2.4%–6.2%) and 4.2% (1.9%–6.6%), respectively. The association between stress and headache frequency was most prominent in young study respondents of all headache subtypes; participants between 61 and 71years with migraine or migraine with coexisting TTH experienced no increase in headache days/month with stress increase (fully adjusted; TTH: (21–30/31–40/41–50/51–60/61.71 years) 9.8/10.2/7.0/6.5/3.5%; migraine: 8.1/5.1/3.4/6.3/0.3%; migraine with coexisting TTH: 5.5/6.8/6.9/5.8/–0.7%). Estimates and 95% CI of the covariates without stratification by age groups are presented in supplementary materials.

Discussion

We found that participants who reported headache experienced more stress compared to participants without headache. Participants with migraine experienced more stress than participants with TTH. Increasing stress was associated with increasing headache frequency for all headache subtypes, which was particularly pronounced in participants with TTH and younger headache sufferers. Women and men reported almost the same mean stress level.

Published evidence is insufficient to determine whether individuals who are afflicted with primary headache experience a greater number of life stressors or are more reactive to life stressors than individuals who do not experience headaches (5). Data on this topic have been presented from the American Migraine Prevalence and Prevention (AMPP) Study. Individuals with chronic migraine reported more major life events and were more likely to perceive events as stressful compared to those with episodic migraine (30). A cross-sectional study with 1260 adolescents reported that adolescents who experienced headache reported higher levels of stress measured with the Trier Inventory of Chronic Stress and adolescents diagnosed with migraine reported higher levels of stress than those with TTH (19). These results are in line with our longitudinal study, which shows that participants with headache experienced more stress than participants with no headache, and participants with migraine experienced more stress than participants with TTH. There are multi-faceted sex differences in stress responsiveness (31). Boardman at al. (2) indicated that women were more likely to report stress, whereas in our study, women and men reported almost the same mean stress score. Antithetic results of studies might be due to different stress measurement. Our investigation contributes to evidence that individuals with primary headache experience more stress.

It is currently unknown if variations in stress intensity influence headache frequency and whether the impact of stress on headache frequency differs for migraine and TTH (32). An investigation of 114 headache sufferers observed for 28 days showed that the frequency of stressful events is positively and significantly correlated with the frequency of headache (33). This is compatible with our findings. Additionally, we differentiated for headache subtypes and age groups. Increasing stress was positively correlated with increasing headache frequency for all headache subtypes, but pronounced in younger participants and in participants with TTH. Participants between 61 and 71 with migraine or migraine with coexisting TTH experienced no increase in headache frequency with stress increase. The reason why older participants do not generally have higher headache frequency in relation to stress levels might be that older people generally experience less stress, and because of experience of life they might know better how to handle it. A 9.6% magnitude of effect in a person with TTH between 21 and 30 years who reports headaches on three days/month translates to an increase of 6.9 hours headache per month (9.6% × 3 days) with each 10-point increase on the VAS or even an increase of 17.0 hours in a person with migraine between 21 and 30 years reporting headache on 10 days/month (7.1% × 10 days). It was surprising that the highest number of headache days for migraine, migraine with coexisting TTH and unclassifiable headache occurred in the oldest age group. A reason might be selection bias. By trend, more affected old people participated than those with few headache days. Several variables are likely to influence the association between headache frequency and stress intensity, including age, female sex, smoking, drinking,

Table 3. Association between stress increase on VAS and headache frequency.

	Age groups, years	21–30	31–40	41–50	51–60	61–71	Total
Total	*n*	619	807	1478	1351	904	5159
	$\%_r$, $\%_c$	12.0, 100	15.6, 100	28.7, 100	26.2, 100	17.5, 100	100, 100
TTH	*n*	193	222	453	442	288	1,598
	$\%_r$, $\%_c$	12.1, 31.2	13.9, 27.5	28.4, 30.6	27.7, 32.7	18.0, 31.9	100, 31.0
	Stress (VAS), mean ± SD	56.8 ± 23.5	60.1 ± 23.3	59.2 ± 23.9	52.7 ± 26.2	32.2 ± 25.5	52.3 ± 26.7
	Headache days/month, mean ± SD	2.3 ± 2.9	2.3 ± 3.5	2.1 ± 3.7	2.2 ± 4.2	2.2 ± 4.7	2.2 ± 3.9
	Increase in headache days in % for 10-point stress increase on VAS						
	Crude (95%CI)	10.1. (7.3–12.9)	10.5 (5.1–16.0)	5.0 (–0.1 to 10.1)	6.7 (3.3–10.1)	4.9 (0.3–9.4)	6.4 (4.4–8.5)
	Fully adjusted (95%CI)	9.8 (6.8–12.8)	10.2 (4.6–15.8)	7.0 (3.6–10.4)	6.5 (3.3–9.7)	3.5 (−1.0 to 8.0)	6.0 (4.0–8.0)
Migraine	*n*	91	167	229	171	66	724
	$\%_r$, $\%_c$	12.6, 14.7	23.1, 20.7	31.6, 15.5	23.6, 12.7	9.1, 7.3	100, 14.0
	Stress (VAS), mean ± SD	65.9 ± 21.2	64.8 ± 21.9	62.3 ± 23.6	63.6 ± 22.3	48.7 ± 26.0	62.4 ± 23.3
	Headache days/month, mean ± SD	4.0 ± 4.8	4.4 ± 4.7	4.2 ± 4.9	4.8 ± 5.5	5.9 ± 6.7	4.5 ± 5.2
	Increase in headache days in % for 10-point stress increase on VAS						
	Crude (95% CI)	8.4 (5.0–11.9)	6.9 (3.1–10.7)	3.6 (0.4–6.8)	5.8 (0.7–10.9)	−0.4 (−3.5 to 2.8)	4.3 (2.4–6.2)
	Fully adjusted (95% CI)	8.1 (3.8–12.3)	5.1 (1.2–9.0)	3.4 (0.1–6.6)	6.3 (1.4–11.2)	0.3 (−3.5 to 4.1)	4.3 (2.4–6.3)
MigTTH	*n*	89	118	194	108	39	548
	$\%_r$, $\%_c$	16.2, 14.4	21.5, 14.6	35.4, 13.1	19.7, 8.0	7.1, 4.3	100, 10.6
	Stress (VAS), mean ± SD	58.4 ± 24.4	60.8 ± 23.1	60.1 ± 23.1	56.8 ± 24.4	49.8 ± 28.2	58.6 ± 24.1
	Headache days/month, mean ± SD	3.3 ± 3.6	3.1 ± 3.7	3.1 ± 3.6	4.0 ± 5.5	7.5 ± 8.9	3.6 ± 4.8
	Increase in headache days in % for 10-point stress increase on VAS						
	Crude (95% CI)	4.5 (0.8–8.2)	8.9 (4.3–13.5)	6.7 (3.7–9.7)	7.4 (2.3–12.6)	−1.0 (−7.4 to 5.5)	4.7 (2.2–7.1)
	Fully adjusted (95% CI)	5.5 (1.3–9.8)	6.8 (2.3–11.2)	6.9 (4.1–9.6)	5.8 (1.9–9.7)	−0.7 (−10.5 to 9.1)	4.2 (1.9–6.6)
Unclassifiable headache	*n*	157	205	360	320	173	1215
	$\%_r$, $\%_c$	12.9, 25.4	16.9, 25.4	29.6, 24.4	26.3, 23.7	14.2, 19.1	100, 23.6
	Stress (VAS), mean ± SD	58.2 ± 23.9	59.8 ± 23.9	59.9 ± 24.2	53.5 ± 25.9	34.6 ± 27.4	54.0 ± 26.6
	Headache days/month, mean ± SD	1.8 ± 3.3	2.2 ± 3.3	2.3 ± 3.7	2.1 ± 4.3	2.5 ± 5.6	2.2 ± 4.1
	Increase in headache days in % for 10-point stress increase on VAS						
	Crude (95% CI)	13.3 (6.4–20.1)	7.9 (4.2–11.5)	10.1 (6.1–14.2)	8.6 (3.7–13.4)	6.7 (0.9–12.4)	7.7 (5.2–10.1)
	Fully adjusted (95% CI)	19.9 (11.5–28.3)	9.1 (3.2–14.9)	8.5 (3.8–13.2)	9.3 (4.1–14.6)	1.5 (−5.6 to 8.5)	8.4 (5.3–11.5)
No headache	*n*	89	95	240	310	338	1074
	$\%_r$, $\%_c$	8.3, 14.4	8.9, 11.8	22.4, 16.2	28.9, 22.9	31.5, 37.4	100, 20.8
	Stress (VAS), mean ± SD	49.8 ± 26.5	52.8 ± 25.6	50.9 ± 27.1	46.3 ± 28.2	26.5 ± 26.2	41.1 ± 29.1

TTH: tension-type headache; MigTTH: migraine with coexisting tension-type headache; r: row; c: column; VAS: visual analog scale; CI: confidence interval.

obesity, education and overuse of acute pain drugs. Female sex has been demonstrated as an important risk factor for migraine (34), and it has been reported that women are more likely to report stress (2). Smoking, drinking, obesity and education are related to lower socioeconomic status, which has been discussed as being associated with headache (35) and stress (36,37). For this reason, we adjusted for the above-mentioned factors in our analysis. However, these factors did not significantly influence the model. The present systematic investigation of individual experience of stress and headache frequency revealed considerable differences between patients with TTH and migraine. This might reflect different biopsychosocial mechanisms.

Lipton et al. reported that reduction in stress from one day to the next was associated with migraine onset the next day (38). On the surface this suggests very opposite results to our study. But we asked a very different question. Our participants were asked about average stress and headache days of a three-month period whereas Lipton et al. analyzed headache diaries and compared time periods of several hours. Mapping the results would require studies that combine diary methods with three-month survey methods.

Behavioral treatments (i.e. cognitive behavioral therapy, biofeedback (22,39), relaxation training) have demonstrated clinical efficacy when practiced correctly (40,41). Yoga (42) or tai chi (43) are mentioned to improve headache as well. Behavioral treatments may be used individually or in conjunction with pharmacologic and other interventions and may augment the effectiveness of other treatments, or minimize the need for their use (23,24,41). Our results underline the need for stress management strategies in people with headache.

We identified several strengths and limitations of our study. Strengths are: the large-scale population-based longitudinal design, which included participants from three different regions of Germany; the large sample size, which provided enough power to test a number of predefined covariates; and the use of validated questionnaires that were published prior to the study. A limitation of our study is the use of ICHD-2 criteria and not ICHD third edition beta (ICHD-3) beta because of the timing and the possible incorrect classification of headache subtypes. Headache features were detected only once retrospectively by questionnaire, which is not as robust as clinical assessment with headache diary. Another limitation is the overall response rate of the survey of 57%, which is satisfactory in comparison with other large-scale population-based studies in Western Europe and the United States, but selection bias cannot be ruled out. One hint of selection bias is that the fraction of people with headache increased by follow-up. These limitations are not unique to our study, as most large-scale, questionnaire-based surveys face these challenges. Another limitation is the fact that the primary variable is a single, global question regarding reported stress over a three-month period. It is likely that peaks in stress over three months can be moderated by valleys, and so ratings do not truly reflect the experience of stress but rather show an average. Another limitation is the use of a simple VAS scale to measure stress and not a validated scale, but the VAS was reported to be a relatively efficient tool for assessing stress and to measure perceived stress (44). In the current investigation (2010–2012) there was a shift of prevalence from ''no headache'' to TTH compared to baseline (2003–2005) (25). We believe this shift is most likely due to selection bias and a different definition of ''no headache'' and not to an actual shift in the study population. However, this should not affect our observation with regard to the reported positive association between headache and stress intensity. Because we questioned several thousand people every three months we could ask only a limited number of questions. For further investigations it would be interesting to classify the headache subtypes more precisely and to collect more information about the episodes of migraine in a smaller study population. At the same time, it would be interesting to have more details regarding the evaluation of perceived stress. Overall, our study provides essential data for more detailed insight into the association between stress and headache subtypes.

Conclusions

This longitudinal population-based cohort study quantitatively shows that increasing stress was associated with increasing headache days, which was particularly pronounced in participants with TTH and younger headache sufferers. The benefit from psychological interventions for stress might be slightly higher in patients with TTH than in migraine or migraine with coexisting TTH patients and might be higher in younger headache patients. This should be validated in further clinical studies that distinguish between headache subtypes and age. Our findings are important to support the tailoring of stress-management approaches in patients with different headache subtypes.

Clinical implications

1. Patients with migraine and tension-type headache (TTH) may benefit from psychological interventions for stress.
2. The benefit may be higher in younger headache sufferers.
3. The benefit may be slightly higher in patients with TTH.

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Conflict of interest

Sara Schramm, Nils Lehmann, Ursula Galli, Min-Suk Yoon, Eva Bock and Susanne Moebus have nothing to declare. Mark Obermann has received scientific support and/or honoraria from Biogen Idec, Novartis, Sanofi-Aventis, Pfizer, and Teva. Hans-Christoph Diener has been a consultant for and is a member of the speakers' bureau of Allergan Inc. Zaza Katsarava has received grants and research support, been a consultant for, and is a member of the speakers' bureau of Allergan Inc.

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