Associations between headache and stress, alcohol drinking, exercise, sleep, and comorbid health conditions in a Japanese population

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Abstract We conducted a cross-sectional survey of 12,988 subjects aged 20–79 years (5,908 men and 7,090 women) receiving health checkups at a Tokyo clinic. They filled out a self-administered structured questionnaire, and 5.4% of the men and 15.4% of the women reported having headaches. Younger subjects were more prone to having headaches. The likelihood of having headaches increased with stress level and decreased ability to relieve stress in both genders. There was an inverse dose–response relationship between having headaches and alcohol consumption, and less walking/exercise and sleep problems increased the likelihood of headaches in both genders. Headache sufferers of both genders were more likely to report multiple additional poor health conditions. A multivariate stepwise logistic analysis showed that age, self-estimated degree of stress, reported number of additional poor health conditions, and less alcohol consumption were independently correlated with having headaches. In conclusion, although women were more susceptible to headache, Japanese men and women in Tokyo shared factors associated with headache, including age, stress, having other poor health conditions, alcohol consumption, sleep, and exercise.

Keywords Alcohol · Gender · Headache · Poor health condition · Stress

Introduction

Headaches rank among the most frequent complaints in the general and working populations [1] and they can affect the quality of life and work productivity [2] Headache sufferers tend to complain of other pains in various parts of the body [3, 4] and a wide range of lifestyle choices, including drinking, smoking, and exercise, may be involved in headache occurrence. Stress and poor sleep are frequently cited on lists of headache triggers. Headache sufferers often report that drinking alcohol is related to some of their headaches. Headaches are also a frequent symptom of both alcohol-induced flushing responses and hangover in the Japanese with inactive acetaldehyde dehydrogenase-2 (ALDH2), who fail to promptly eliminate acetaldehyde, a toxic metabolite of ethanol [5, 6]. The genetic variation prevalent in the Japanese may modify the interaction between headache and alcohol consumption. In the present study, we investigated the associations between headaches and various lifestyle choices and comorbid conditions in a very large Japanese general population in Tokyo.

Subjects and methods

The reference population of this study consisted of 16,290 Japanese who came to Mitsukoshi Clinic of Tokyo for an annual health checkup between January 2004 and December 2004. They were workers or residents of Tokyo or of neighboring areas, who had been registered on the clinic lists for annual health checkups. They were routinely
asked to fill out a self-administered structured question-
naire concerning their physical condition, stress, exercise,
sleep, and drinking and smoking habits for clinical use,
and 13,001 of them completed all items related to stress,
exercise, sleep, and drinking and smoking habits. After
excluding the three persons aged 80 years or more, 12,988
persons (5,908 men and 7,090 women) who were aged
20–79 years were adopted as the subjects of this study.

Each subject was asked to indicate from the following,
the poor health conditions that applied to them: I have
headaches; I have lost weight; I get tired easily; I have little
energy; I have little appetite; I have pain in my upper
abdomen; I have pain in my lower abdomen; food sticks in
my throat; I have heartburn; I have a heavy feeling in my
stomach; I have nausea or vomiting; I have blood in my
stools; I feel tightness in my chest; I have palpitations or
shortness of breath; I have a cough or cough up sputum;
I have blood in my sputum; I have low back pain; my limbs
feel numb; my limbs hurt; my limbs are swollen; my hands
shake; I sometimes feel dizzy; I have ringing in my ears; I
get up to urinate at night; I am anxious sometimes; and I
cannot sleep well.

The questionnaire asked the subjects to estimate their
degree of stress in comparison with others by choosing from:
little or none; low; average; somewhat high; very
high, and their ability to relieve stress by choosing from:
good; fairly good; little; and none. The choices for the
average duration of sleep were: less than 5 h; 5 h to less than
6 h; 6 h to less than 8 h; and 8 h or more. The questionnaire
also asked the subjects to report alcohol intake as frequency
of consumption per week and the usual amount(s) and
type(s) of alcoholic beverage(s) consumed per day. Subjects
were classified as non-drinkers or as current drinkers who
consumed less than 1 unit/day (1 unit = 22 g ethanol, the
ethanol content of one serving of sake), 1 unit to less than
2 units/day, 2 units to less than 3 units/day, and 3 units/day
or more. The subjects were asked to report on smoking and
weekly frequency of walking or exercise for at least 20 min
at a time or at least a total of 1 h a day. The choices for
frequency of walking or exercise were: seldom; 1 day/week;
2 days/week; 3–4 days/week; and 5 days/week or more.
Blood pressure measurements were made in the arm, with an
automated sphygmomanometer (BP-103iII, Omron
Healthcare Co. Ltd., Kyoto) between 9:00 am and 11:00 am
and with the subjects in the sitting position. The subjects
were requested to refrain from eating and drinking for at
least 12 h and from smoking for at least 30 min before the
examination. The subjects were divided into four groups
according to systolic pressure measured at the time of
the health checkup: under 100, 100–119, 120–139, and
140 mmHg and over.

This study was conducted following the Ethical Guide-
lines for Epidemiological Research in Japan and reviewed
and approved by the Ethics Committee of Mitsukoshi
Health and Welfare Foundation.

Statistical analysis

Data are summarized as percentage values, and the chi-
squared test was used for comparisons between groups.
The relationships between headache and lifestyle and
health conditions are expressed as odds ratio (OR) and
95% confidence interval (CI) estimated by a multiple
logistic regression model with adjustment for age and
other confounding factors. The stepwise procedure with
P < 0.05 for entry and removal was used to select inde-
dependent significant factors. All statistical analyses were
performed using SAS software (version 9.1, SAS Institute,
Cary, NC).

Results

Prevalence of headache

Table 1 shows the proportions of subjects who reported
having headaches according to gender and age group. Of
the 12,998 subjects, 1,411 (5.4% of the men and 15.4% of
the women) reported having headaches. A significantly
higher rate of women reported having headaches than the
men in all age brackets. The younger subjects were more
prone to having headaches, regardless of gender. Headache
ranked 3rd in women and 11th in men among the poor
physical conditions asked in the questionnaire.

Headaches and stress

The likelihood of having headaches increased in stepwise
fashion with stress level and decreased ability to relieve
stress, in both men and women (Table 2). The subjects
whose self-estimated degree of stress was “little or none”
had the lowest rate of headache (1.5% of men and 6.1% of
women) among all the subcategories of lifestyles evaluated
in this study, in contrast to the highest rate (18.1% of men
and 30.7% of women) among the subjects whose ability to
relieve stress was “none”. The age-adjusted ORs for the
highest versus lowest level of stress and the lowest versus
highest ability of stress release in men were approximately
twofold stronger than in women (11.74 vs. 4.9 and 6.96 vs.
3.52, respectively).

Headaches and alcohol

Current drinkers, both men and women, had a lower
likelihood of headaches than non-drinkers, regardless of
the amount consumed (ORs = 0.51–0.76 for men and
There was an inverse dose–response relationship in both the men and the women.

Headaches and exercise

There was an inverse association between having headaches and walking/exercise that was significant among the men and marginally significant among the women. When “seldom” was used as the referent, the lowest significant risk for headache for both men and women was in the “2 days/week” category (OR = 0.53 for men and 0.71 for women).

Headaches and sleep

When 6 h to less than 8 h sleep was used as the referent, both less sleep (ORs = 1.63–2.04) and excessive sleep (OR = 1.89) in men, and less sleep (ORs = 1.31–1.33) in women were positively associated with having headaches.

Headaches and smoking

There was no association between having headaches and smoking.

Headaches and blood pressure

There was no association between having headaches and systolic blood pressure.

Headaches and poor health condition

Headache sufferers of both genders were more likely to report multiple other poor health conditions (Tables 3, 4). The multivariate stepwise logistic regression model showed that the physical conditions that were significantly and independently associated with headaches were fatigability, upper abdominal pain, lower abdominal pain, heavy feeling in the stomach, lower back pain, palpitations or shortness of breath, dizziness, ringing in the ears, and anxiety in both men and women, and heartburn, nausea, chest tightness, swollen limbs, getting up to urinate at night, and sleep disturbance in women alone. The likelihood of having headaches increased greatly with the number of poor health conditions reported.

Analysis in a multivariate logistic regression model, of which independent variables were selected from all the factors by a stepwise procedure showed that age, self-estimated degree of stress, reported number of additional poor health conditions, and less alcohol consumption were independently related to having headaches in both men and women and that the effects of the remaining factors no longer reached significance (Table 5).

Discussion

This cross-sectional large survey of headaches in a Tokyo population showed that men and women shared several factors associated with headache, but that women were much more susceptible to headaches. A multivariate analysis demonstrated that age, self-estimated degree of stress, reported number of comorbid poor health conditions, and less alcohol consumption were independently related to having headaches in both men and women. Since we used a simple questionnaire to ask subjects to indicate if the item “I have headaches” applied to them, it is impossible to classify the types of headaches in this study. One of the authors (M.Y.), a board-certified neurologist, informed the workers of a Tokyo company about the results of the health checkup and interviewed all 99 workers (29 men and 70 women aged 20–59 years; 7.0% of the present headache sufferers) who had replied that the questionnaire item “I have headaches” applied to them during the health checkup.
### Table 2 Relationship between headache and lifestyle choices

| Stress         | Men  |           | Age-adjusted OR | 95%CI     | Women |           | Age-adjusted OR | 95%CI     |
|----------------|------|-----------|-----------------|-----------|-------|-----------|-----------------|-----------|
|                | N    | Proportion of headache sufferers (%) |                  |           |       | Proportion of headache sufferers (%) |                  |           |
| Very high      | 305  | 16.7      | 11.74           | 4.16–33.15| 484   | 25.4      | 4.90            | 2.75–8.75 |
| Somewhat high  | 1,364| 8.4       | 5.37            | 1.96–14.76| 1,706 | 22.2      | 4.10            | 2.36–7.13 |
| Average        | 3,307| 3.9       | 2.56            | 0.94–6.99 | 4,001 | 12.8      | 2.15            | 1.24–3.72 |
| Low            | 662  | 3.5       | 2.39            | 0.81–6.94 | 666   | 8.9       | 1.48            | 0.81–2.71 |
| Little or none | 270  | 1.5       | 1.00            | Referent  | 231   | 6.1       | 1.00            | Referent  |

| Ability to relieve stress | Men  |           | Age-adjusted OR | 95%CI     | Women |           | Age-adjusted OR | 95%CI     |
|----------------------------|------|-----------|-----------------|-----------|-------|-----------|-----------------|-----------|
| Good                       | 2,489| 3.0       | 1.00            | Referent  | 2,728 | 10.9      | 1.00            | Referent  |
| Fairly good                | 2,272| 6.3       | 2.11            | 1.58–2.81 | 2,824 | 15.0      | 1.41            | 1.21–1.66 |
| Little                     | 1,074| 8.3       | 2.76            | 2.00–3.80 | 1,416 | 22.9      | 2.39            | 2.01–2.84 |
| None                       | 72   | 18.1      | 6.96            | 3.63–13.34| 114   | 30.7      | 3.52            | 2.32–5.34 |

| Drinking                  | Men  |           | Age-adjusted OR | 95%CI     | Women |           | Age-adjusted OR | 95%CI     |
|----------------------------|------|-----------|-----------------|-----------|-------|-----------|-----------------|-----------|
| Non-drinker               | 1,410| 7.5       | 1.00            | Referent  | 4,366 | 16.5      | 1.00            | Referent  |
| Less than 1 unit/day      | 1,688| 6.2       | 0.76            | 0.57–1.01 | 1,883 | 14.0      | 0.77            | 0.66–0.90 |
| 1 to less than 2 units/day| 1,287| 4.2       | 0.56            | 0.40–0.79 | 585   | 13.0      | 0.72            | 0.56–0.93 |
| 2 to less than 3 units/day| 789  | 3.9       | 0.55            | 0.36–0.83 | 154   | 7.8       | 0.39            | 0.22–0.71 |
| 3 units/day or more       | 734  | 3.5       | 0.51            | 0.32–0.79 | 99    | 11.1      | 0.59            | 0.31–1.11 |

| Walking or exercise       | Men  |           | Age-adjusted OR | 95%CI     | Women |           | Age-adjusted OR | 95%CI     |
|----------------------------|------|-----------|-----------------|-----------|-------|-----------|-----------------|-----------|
| 5 days/week or more       | 2,042| 4.9       | 0.68            | 0.50–0.92 | 2,297 | 14.7      | 0.85            | 0.72–1.01 |
| 3–4 days/week             | 1,069| 5.2       | 0.77            | 0.54–1.10 | 1,658 | 15.4      | 0.93            | 0.77–1.13 |
| 2 days/week               | 859  | 3.7       | 0.53            | 0.35–0.81 | 889   | 12.5      | 0.71            | 0.56–0.90 |
| 1 day/week                | 745  | 6.3       | 0.88            | 0.61–1.28 | 665   | 15.5      | 0.88            | 0.68–1.12 |
| Seldom                    | 1,193| 7.2       | 1.00            | Referent  | 1,579 | 17.7      | 1.00            | Referent  |

| Sleep                     | Men  |           | Age-adjusted OR | 95%CI     | Women |           | Age-adjusted OR | 95%CI     |
|----------------------------|------|-----------|-----------------|-----------|-------|-----------|-----------------|-----------|
| Less than 5 h              | 305  | 9.2       | 2.04            | 1.33–3.14 | 510   | 17.1      | 1.33            | 1.03–1.70 |
| 5 to less than 6 h         | 2,127| 7.0       | 1.63            | 1.28–2.08 | 2,957 | 17.2      | 1.31            | 1.15–1.50 |
| 6 to less than 8 h         | 3,279| 4.0       | 1.00            | Referent  | 3,476 | 13.7      | 1.00            | Referent  |
| 8 h or more                | 196  | 6.1       | 1.89            | 1.02–3.51 | 142   | 10.6      | 0.76            | 0.44–1.32 |

| Smoking                   | Men  |           | Age-adjusted OR | 95%CI     | Women |           | Age-adjusted OR | 95%CI     |
|----------------------------|------|-----------|-----------------|-----------|-------|-----------|-----------------|-----------|
| Never smoker              | 2,370| 5.4       | 1.00            | Referent  | 5,559 | 15.0      | 1.00            | Referent  |
| 1–19 cigarettes/day       | 1,016| 6.3       | 1.07            | 0.78–1.46 | 884   | 16.9      | 1.05            | 0.87–1.28 |
| 20–29 cigarettes/day      | 1,304| 5.4       | 0.98            | 0.73–1.33 | 216   | 14.8      | 0.92            | 0.63–1.35 |
| ≥30 cigarettes/day        | 493  | 5.7       | 1.09            | 0.71–1.67 | 30    | 20.0      | 1.42            | 0.58–3.49 |
| Ex-smoker                 | 725  | 4.1       | 0.75            | 0.50–1.14 | 400   | 17.0      | 1.07            | 0.82–1.41 |

| Blood pressure, systolic  | Men  |           | Age-adjusted OR | 95%CI     | Women |           | Age-adjusted OR | 95%CI     |
|----------------------------|------|-----------|-----------------|-----------|-------|-----------|-----------------|-----------|
| <100 mm Hg                 | 525  | 5.9       | 1.00            | 0.67–1.50 | 2,374 | 15.7      | 0.98            | 0.85–1.14 |
| 100–119 mm Hg              | 2,304| 6.0       | 1.00            | Referent  | 3,008 | 15.4      | 1.00            | Referent  |
| 120–139 mm Hg              | 2,254| 5.1       | 0.92            | 0.71–1.19 | 1,343 | 15.3      | 1.13            | 0.94–1.36 |
| ≥140 mm Hg                 | 825  | 4.6       | 1.03            | 0.70–1.50 | 365   | 12.9      | 1.04            | 0.75–1.45 |

*P* values are for homogeneity among the subcategories of each factor by the age-adjusted logistic regression model.
checkup. Based on the information obtained during the interview, the author classified their headaches according to the International Classification of Headache Disorders, 2nd edn (ICHD-II) [7]. Migraine was diagnosed in 67% of them, tension-type headache in 20%, migraine with tension-type headache in 11%, and unspecified in 3%. The proportion of the subjects of this study who reported headaches was 5.4% of men and 15.4% of women. Large Japanese population-based studies have reported migraine headaches in 2.3–3.6% of men and 9.1–12.9% of women [8, 9], and the distribution of the subjects with headaches according to age in the present study was similar to that of

Table 3 Relationship between having headaches and other poor health conditions in men

| Other poor health conditions | Men Absent | Men Present | Age-adjusted model | Multivariate model* |
|-----------------------------|-----------|------------|---------------------|---------------------|
|                             | N         | N          | Proportion of headache sufferers (%) | Proportion of headache sufferers (%) | OR | 95%CI | P | OR | 95%CI | P |
| Poor appetite                | 5,849     | 58         | 5.3                  | 58                  | 19.0 | 3.76  | 1.91–7.41 | 0.0001 | 1.00 Referent |
| Weight loss                  | 5,654     | 253        | 5.4                  | 94                   | 14.9 | 3.71  | 2.07–6.67 | <0.0001 |
| Feeling of food sticking in the throat | 5,813 | 5,3 | 5.3 | 94 | 14.9 | 3.71 | 2.07–6.67 | <0.0001 | 1.00 Referent |
| Upper abdominal pain         | 5,799     | 108        | 5.1                  | 108                 | 20.4 | 4.77  | 2.93–7.77 | <0.0001 | 1.81 1.02–3.21 0.0435 |
| Lower abdominal pain         | 5,819     | 88         | 5.2                  | 88                  | 20.5 | 4.99  | 2.91–8.56 | <0.0001 | 2.48 1.32–4.67 0.0047 |
| Easy fatigability            | 5,038     | 869        | 3.9                  | 869                 | 14.2 | 3.65  | 2.87–4.65 | <0.0001 | 2.20 1.68–2.88 <0.0001 |
| Heartburn                   | 5,648     | 259        | 5.0                  | 259                 | 13.9 | 3.52  | 2.41–5.13 | <0.0001 |
| Heavy feeling in the stomach | 5,556     | 351        | 4.8                  | 351                 | 14.3 | 3.27  | 2.36–4.53 | <0.0001 | 1.80 1.25–2.59 0.0017 |
| Chest tightness              | 5,757     | 150        | 5.1                  | 150                 | 60.16 | 3.65  | 2.31–5.76 | <0.0001 |
| Lower back pain              | 4,621     | 1,286      | 4.2                  | 1,286               | 9.6  | 2.68  | 2.11–3.40 | <0.0001 | 1.86 1.44–2.41 <0.0001 |
| Numbness                    | 5,513     | 394        | 5.2                  | 394                 | 7.6  | 1.81  | 1.22–2.69 | 0.0035 |
| Palpitations/shortness of breath | 5,626 | 281        | 4.9                  | 281                 | 16.0 | 4.35  | 3.07–6.16 | <0.0001 | 1.84 1.23–2.76 0.0033 |
| Edema                       | 5,710     | 197        | 5.1                  | 197                 | 14.7 | 3.44  | 2.27–5.22 | <0.0001 |
| Tremor                      | 5,847     | 60         | 5.3                  | 60                  | 16.7 | 3.78  | 1.88–7.59 | 0.0002 |
| Loss of energy              | 5,394     | 513        | 5.3                  | 513                 | 6.8  | 1.76  | 1.21–2.56 | 0.0032 |
| Limb pain                   | 5,703     | 204        | 5.1                  | 204                 | 12.8 | 3.24  | 2.10–5.01 | <0.0001 |
| Dizziness                   | 5,681     | 226        | 4.7                  | 226                 | 23.5 | 6.83  | 4.87–9.58 | <0.0001 | 3.25 2.21–4.78 <0.0001 |
| Cough/sputum                | 5,225     | 682        | 5.1                  | 682                 | 7.9  | 1.75  | 1.29–2.38 | 0.0004 |
| Bloody sputum               | 5,892     | 15         | 5.4                  | 15                  | 20.0 | 4.81  | 1.33–17.38 | 0.0165 |
| Nausea/vomiting             | 5,844     | 63         | 5.2                  | 63                  | 20.6 | 4.18  | 2.23–7.84 | <0.0001 |
| Ringing in the ears         | 5,509     | 398        | 4.9                  | 398                 | 11.8 | 3.41  | 2.43–4.79 | <0.0001 | 1.82 1.24–2.68 0.0023 |
| Bloody stools               | 5,821     | 86         | 5.3                  | 86                  | 12.8 | 2.73  | 1.43–5.23 | 0.0024 |
| Urination during the night  | 5,569     | 338        | 5.4                  | 338                 | 6.2  | 1.84  | 1.14–2.98 | 0.0131 |
| Anxiety                     | 5,452     | 456        | 4.8                  | 456                 | 12.5 | 2.67  | 1.97–3.63 | <0.0001 | 1.43 1.01–2.02 0.0449 |
| Sleep disturbance           | 5,458     | 449        | 5.0                  | 449                 | 10.9 | 2.28  | 1.65–3.15 | <0.0001 |

Number of other poor health conditions

| 0 | 2,448 | 1.8 | 1.00 Referent |
| 1 | 1,453 | 5.5 | 3.49 2.39–5.10 |
| 2 | 929   | 7.4 | 4.96 3.35–7.34 |
| 3 | 501   | 6.8 | 4.67 2.93–7.43 |
| 4-5 | 405 | 12.6 | 10.01 6.52–15.36 |
| 6 or more | 171 | 24.6 | 24.28 15.10–39.02 |

* Variables were selected by a stepwise procedure with P < 0.05 for entry and removal; age was forced to enter into the model (OR for age was not shown)
the subjects who had migraine in these studies. Although we did not ask the time frame of the headache, these findings suggest that chronic headache sufferers tended to report that the item “I have headaches” applied to them and that a high proportion of the headache sufferers in our study had migraine. The subjects in this study consisted of workers or residents of Tokyo or neighboring areas, who had received an annual health checkup and who were more likely to be middle-aged women, probably in the middle-to-high socioeconomic bracket. These background factors at least partially explain the somewhat high headache prevalence in the subject population.

We confirmed that stress is a major precipitating factor of headaches, a finding consistent with the results of

| Other poor health conditions | Absent | Present |
|------------------------------|--------|---------|
| N                                           | Proportion of headache sufferers (%) | Proportion of headache sufferers (%) | Age-adjusted model | Multivariate model* |
| Poor appetite                 | 7,004 15.1 | 72 25.0 | 1.75 | 1.02–3.00 | 0.0416 |
| Weight loss                   | 6,870 15.1 | 206 17.0 | 1.20 | 0.83–1.74 | 0.3370 |
| Feeling of food sticking in the throat | 6,926 14.9 | 150 29.3 | 2.47 | 1.72–3.54 | <0.0001 |
| Upper abdominal pain          | 6,920 14.7 | 157 36.3 | 3.37 | 2.41–4.70 | <0.0001 |
| Lower abdominal pain          | 6,801 14.5 | 276 32.3 | 2.68 | 2.06–3.48 | <0.0001 |
| Easy fatigability             | 5,643 11.7 | 1,441 29.4 | 3.05 | 2.65–3.52 | <0.0001 |
| Heartburn                     | 6,784 14.6 | 292 29.8 | 2.85 | 2.18–3.71 | <0.0001 |
| Heavy feeling in the stomach  | 6,454 13.8 | 628 30.6 | 2.80 | 2.33–3.37 | <0.0001 |
| Chest tightness               | 6,836 14.5 | 240 35.4 | 3.41 | 2.59–4.49 | <0.0001 |
| Lower back pain               | 5,344 12.1 | 1,740 25.1 | 2.52 | 2.20–2.89 | <0.0001 |
| Numbness                      | 6,542 14.4 | 541 25.7 | 2.29 | 1.86–2.82 | <0.0001 |
| Palpitations/shortness of breath | 6,607 14.0 | 472 32.8 | 3.30 | 2.68–4.06 | <0.0001 |
| Edema                         | 6,273 13.8 | 808 26.5 | 2.19 | 1.84–2.60 | <0.0001 |
| Tremor                        | 7,007 15.0 | 69 34.8 | 3.03 | 1.83–5.01 | <0.0001 |
| Loss of energy                | 7,015 15.0 | 61 32.8 | 3.01 | 1.75–5.17 | <0.0001 |
| Limb pain                     | 6,698 14.7 | 380 24.7 | 2.23 | 1.74–2.86 | <0.0001 |
| Dizziness                     | 6,365 12.9 | 713 36.2 | 3.89 | 3.28–4.61 | <0.0001 |
| Cough/sputum                  | 6,598 15.0 | 479 18.2 | 1.34 | 1.05–1.70 | 0.0197 |
| Bloody sputum                 | 7,067 15.2 | 9 22.2 | 1.79 | 0.37–8.68 | 0.4713 |
| Nausea/vomiting               | 6,964 14.7 | 113 47.8 | 5.11 | 3.51–7.45 | <0.0001 |
| Ringing in the ears           | 6,446 13.7 | 632 30.4 | 3.05 | 2.53–3.68 | <0.0001 |
| Bloody stools                 | 7,028 15.1 | 49 26.5 | 2.06 | 1.08–3.91 | 0.0273 |
| Urination during the night    | 6,868 14.8 | 209 29.2 | 2.88 | 2.10–3.94 | <0.0001 |
| Anxiety                       | 6,083 13.6 | 997 25.4 | 2.15 | 1.83–2.53 | <0.0001 |
| Sleep disturbance             | 6,350 14.0 | 730 25.6 | 2.25 | 1.87–2.70 | <0.0001 |
| Number of other poor health conditions |        |        |        |        |        |
| 0                             | 2,494 5.3 | 1.00 | Referent |
| 1                             | 1,813 13.5 | 2.87 | 2.29–3.58 |
| 2                             | 1,085 18.1 | 4.10 | 3.24–5.18 |
| 3                             | 709 20.7 | 4.83 | 3.75–6.23 |
| 4–5                           | 637 30.9 | 8.72 | 6.82–11.15 |
| 6 or more                     | 338 47.0 | 17.71 | 13.37–23.45 |
| P                             | <0.0001 |

* Variables were selected by a stepwise procedure with \( P < 0.05 \) for entry and removal; age was forced to enter into the model (OR for age was not shown)
previous cross-sectional studies [10, 11] and a recent prospective study [12]. The present study also demonstrated a stepwise inverse relationship with ability to relieve stress as well as a positive association with stress level in both men and women. The two self-estimated aspects of stress had the greatest impact of all of the factors associated with having headaches in this study. Although in contrast to other quantifiable variables, self-estimated classification of stress may differ between men and women, the association between stress and headache was stronger in men than in women.

Previous studies have shown an association between the occurrence of headaches and the presence of pain elsewhere in the body [3, 4]. The present study demonstrated that headache sufferers not only tended to complain of other pain, but to report a variety of poor health conditions, and that having headaches was clearly associated with the number of poor health conditions in a stepwise fashion in both men and women. Increasing numbers of other painful areas [4] and combinations of chronic musculoskeletal complaints, gastrointestinal complaints, and psychiatric symptoms [13] have been reported to have a greater impact on the likelihood of headache occurrence. Whether the association is causal or the poor health conditions and headache share common background factors are topics for future research. However, since the comorbid conditions were all self-reported in a questionnaire, some of the strong associations between headache and poor health conditions may have been partly influenced by a tendency to answer all questions regarding complaints in a similar way.

| Table 5 | Multivariate analysis of risk factors for headache |
|---------|--------------------------------------------------|
|         | Men                                              | Women                                           |
|         | Multivariate OR* 95%CI                            | Multivariate OR* 95%CI                          |
| Age (year) |                                                 |                                                 |
| 20–29    | 1.00 Referent                                   | 1.00 Referent                                   |
| 30–39    | 0.63 0.39–1.01                                  | 0.63 0.39–1.01                                  |
| 40–49    | 0.42 0.26–0.67                                  | 0.42 0.26–0.67                                  |
| 50–59    | 0.31 0.19–0.49                                  | 0.31 0.19–0.49                                  |
| 60–69    | 0.19 0.10–0.35                                  | 0.19 0.10–0.35                                  |
| 70–79    | 0.36 0.08–1.60                                  | 0.36 0.08–1.60                                  |
|          | $P < 0.0001$                                     | $P < 0.0001$                                    |
| Stress   |                                                 |                                                 |
| Very high| 3.71 1.28–10.77                                  | 1.75 0.94–3.25                                  |
| Somewhat high | 2.41 0.86–6.72                              | 2.23 1.24–4.03                                  |
| Average  | 1.70 0.62–4.68                                  | 1.66 0.93–2.97                                  |
| Low      | 1.81 0.62–5.34                                  | 1.42 0.75–2.69                                  |
| Little or none | 1.00 Referent                        | 1.00 Referent                                   |
|          | $P = 0.0010$                                     | $P = 0.0003$                                    |
| Number of other poor health conditions |                                             |                                                 |
| 0        | 1.00 Referent                                   | 1.00 Referent                                   |
| 1        | 3.32 2.27–4.86                                  | 2.74 2.19–3.43                                  |
| 2        | 4.23 2.83–6.32                                  | 3.85 3.03–4.88                                  |
| 3        | 4.07 2.53–6.54                                  | 4.50 3.47–5.82                                  |
| 4–5      | 7.82 5.00–12.24                                 | 7.87 6.11–10.14                                 |
| 6 or more| 17.68 10.66–29.34                               | 15.78 11.75–21.18                               |
|          | $P < 0.0001$                                     | $P < 0.0001$                                    |
| Alcohol drinking |                                         |                                                 |
| Non-drinker | 1.00 Referent                              | 1.00 Referent                                   |
| Less than 1 unit/day | 0.80 0.60–1.08                        | 0.79 0.67–0.93                                  |
| 1 to less than 2 units/day | 0.61 0.43–0.87                        | 0.69 0.53–0.91                                  |
| 2 to less than 3 units/day | 0.59 0.39–0.91                        | 0.37 0.20–0.68                                  |
| 3 units/day or more | 0.40 0.25–0.63                        | 0.50 0.26–0.96                                  |
|          | $P = 0.0004$                                     | $P < 0.0001$                                    |

* Variables except age were selected by a stepwise procedure with $P < 0.05$ for entry and removal

$P$ values are for homogeneity among the subcategories of each factor.
immune system disturbance, toxic effects of congeners, vasculature, altered cytokine pathways [24], endocrine and [22, 23] include a vasodilatory effect on the intracranial susceptible mechanisms by which alcohol induces headache than those without it [21]. Pos- individuals with migraine have a higher risk of delayed cation and drinking habit is needed. The present study demonstrated an inverse dose–response relationship between headaches and alcohol consumption in both men and women. Previous data for the association have been less clear [4, 9–11, 14, 15], but a large population-based cross-sectional study in Norway showed a tendency for the prevalence of headache to decrease with increasing alcohol consumption [16], and another large population-based cross-sectional study in the Netherlands showed that migraine sufferers were less likely to consume alcohol [17]. A recent prospective analysis of migraine sufferers in Austria showed that consumption of beer reduced the risk of headache and migraine, as well as the risk of headache persistence [12]. Our findings are consistent with the results of these studies. In the Norwe- gian study only 3% of the subjects reported drinking >14 standard units of alcohol per 2 weeks, whereas in our study 48% of the men and 12% of the women reported drinking ≥22 g ethanol per day. The drinking behavior of the Japanese is strongly governed by the Asian genetic polymorphism of ALDH2. ALDH2 genotyping among a subgroup of the present study population showed a much higher frequency of ALDH2-deficient individuals among the non/rare drinkers than the drinkers (75 vs. 33% of the men and 57 vs. 20% of the women). ALDH2-deficient individuals are more sensitive to alcohol flushing responses [18] and hangover [5, 6], in both of which headache is a major symptom. Intake of alcoholic beverages has been reported to be an aggravating factor of headache [4], especially migraine [19] and cluster headache [20]. Indi- viduals with migraine have a higher risk of delayed alcohol-induced headache than those without it [21]. Possible mechanisms by which alcohol induces headache [22, 23] include a vasodilatory effect on the intracranial vasculature, altered cytokine pathways [24], endocrine and immune system disturbance, toxic effects of congeners, and acetaldehyde-mediated changes [5, 6, 18]. Japanese headache sufferers with inactive ALDH2 may be more vulnerable to severe alcohol-induced or hangover head- ache, than those without inactive ALDH2, and must avoid alcohol drinking. Another possible explanation of the inverse association between headache and alcohol drinking is related to the development of tolerance for headache in drinkers. Habitual drinking leads to the development of tolerance for alcohol-induced headache [6], which may affect the mechanisms by which common headaches occur. Third, non-drinking may influence other lifestyle factors associated with headache, since alcoholic beverages serve as a stress reliever or sleep aid in some persons. Further in- depth study of the association between headache classification and drinking habit is needed. Furthermore, possible interactions between the ALDH2 genotype, alcohol consumption, and headache prevalence in Japanese subjects may differ according to the headache classification. We have developed a screening test for inactive ALDH2 that consists of the following two questions about current and past facial flushing: (1) Do you have a tendency to flush in the face immediately after drinking a glass (approximately 180 ml) of beer? (2) Did you have a tendency to flush in the face immediately after drinking a glass of beer during the 1st to 2nd year after you started drinking? When current or former flushing individuals were assumed to have inactive ALDH2, both the sensitivity and specificity of the test were approximately 90% among both Japanese men and women 40 years of age or more [25]. We are now conducting a large cross-sectional study in Tokyo workers by using the simple flushing questionnaire, a drinking questionnaire, and a headache questionnaire designed to diagnose headache type according to the ICHD-II criteria.

An inverse association between headaches and walking/exercise was observed in the present study, and the strength of association was somewhat greater in men than in women and was most prominent among the subjects who reported a walking/exercise frequency of “2 days/week”. A study conducted in Denmark reported a significant association between low physical activity and tension-type headache in men, but not in women or in subjects with migraine [10]. Physical activity influences several factors, including stress, stress release, muscle strength, and prostaglandin and hormone levels [26], and further epidemiological and mechanistic studies are required. In our study, both less sleep and excessive sleep in men and less sleep in women were positively associated with having headaches, findings consistent with those of previous studies [27, 28].

In conclusion, although women were more susceptible to headache, Japanese men and women in Tokyo shared factors associated with headache, including age, stress, having other poor health conditions, alcohol consumption, sleep, and exercise.

Conflict of interest None.

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