



## Familial occurrence of headache disorders: A population-based study in mainland China



Mianwang He<sup>a</sup>, Shengyuan Yu<sup>a,\*</sup>, Ruozhuo Liu<sup>a</sup>, Xiaosu Yang<sup>b</sup>, Gang Zhao<sup>c</sup>, Xiangyang Qiao<sup>d</sup>, Jiachun Feng<sup>e</sup>, Yannan Fang<sup>f</sup>, Xiutang Cao<sup>g</sup>, Timothy J. Steiner<sup>h</sup>

<sup>a</sup> Department of Neurology, Chinese PLA General Hospital, Fuxing Road 28, Haidian District, 100853 Beijing, China

<sup>b</sup> Department of Neurology, Xiangya Hospital, Central-South University, Changsha, Hunan Province, China

<sup>c</sup> Department of Neurology, The Fourth Military Medical University, Xian, Shaanxi Province, China

<sup>d</sup> Department of Neurology, Affiliated Huashan Hospital of Fudan University, Shanghai, China

<sup>e</sup> Department of Neurology, The First Hospital of Jilin University, Changchun, Jilin Province, China

<sup>f</sup> Department of Neurology, The First Affiliated Hospital of Sun Yat-sen University, Guangzhou, Guangdong Province, China

<sup>g</sup> Department of Health and Economics, Chinese PLA General Hospital, Beijing, China

<sup>h</sup> Department of Neuroscience, Norwegian University of Science and Technology, Trondheim, Norway

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### ABSTRACT

**Background:** Headache disorders are highly prevalent worldwide, and familial occurrence and heredity are contributory factors attracting the interest of epidemiological researchers. Our purpose, in a large sample drawn nationwide from the Chinese general population, was to evaluate the frequency of similar headache in first-degree relatives (FDRs) of those with different headache types.

**Methods:** This was a questionnaire-based nationwide cross-sectional door-to-door survey using cluster random-sampling, selecting one adult (18–65 years) per household. Headache was diagnosed by ICHD-II criteria. Participants with headache were asked whether or not any FDRs had similar headache to their own. Chi-squared test and multivariate logistic regression analysis were used to assess the strength and significance of associations.

**Results:** Of 5041 survey participants (participation rate 94.1%), 1060 (21.0%) were diagnosed with headache (migraine 469 [9.3%], tension-type headache [TTH] 543 [10.8%], headache on  $\geq 15$  days/month 48 [0.95%]). From these, 31 were excluded because of missing data about FDRs, leaving 1029 for analysis (male 350 [mean age:  $46.7 \pm 11.4$  years]; female 679 [mean age  $46.3 \pm 11.2$  years]). Similar headache in one or more FDRs was reported by 22.2% (95% CI: 19.6–24.7%) overall, by 25.1% (21.1–29.1%) of those with migraine, by 19.1% (15.7–22.4%) with TTH and by 29.2% (16.3–42.0%) with headache on  $\geq 15$  days/month. The differences was significant between migraine and TTH (OR = 1.4,  $p = 0.023$ ), but were not significant between headache on  $\geq 15$  days/month and TTH (OR = 1.7,  $p = 0.093$ ), migraine and headache on  $\geq 15$  days/month (OR = 1.2,  $p = 0.534$ ). In multivariate analysis: for migraine versus TTH, AOR = 1.2 ( $p = 0.015$ ); for headache on  $\geq 15$  days/month versus TTH, AOR 2.3 ( $p = 0.018$ ).

**Conclusion:** Headache was highly prevalent in China and common among FDRs of those with any type of headache (headache on  $\geq 15$  days/month > migraine > TTH). Against the background of the general-population prevalence of each disorder, familial occurrence was a very highly influential factor in headache on  $\geq 15$  days/month. There are important implications in this for public health and education.

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### 1. Background

Many studies in recent years by validated questionnaire have further verified that headache disorders are highly prevalent worldwide [1]. Headache in China is in lack of healthcare utilization [2]. Differences in headache classification, perception of headache severity and health-seeking behaviour between Chinese and non-Chinese had been found in Singapore [3]. Familial occurrence,

\* Corresponding author.

E-mail addresses: [hemianwang@hotmail.com](mailto:hemianwang@hotmail.com) (M. He), [yusy1963@126.com](mailto:yusy1963@126.com) (S. Yu), [liurz301@sina.com](mailto:liurz301@sina.com) (R. Liu), [sjnk\\_xy@yahoo.com.cn](mailto:sjnk_xy@yahoo.com.cn) (X. Yang), [fmmuzhaogang@163.com](mailto:fmmuzhaogang@163.com) (G. Zhao), [qiaoxy@yahoo.com](mailto:qiaoxy@yahoo.com) (X. Qiao), [fengjcfank@yahoo.com.cn](mailto:fengjcfank@yahoo.com.cn) (J. Feng), [fangyannan@21cn.com](mailto:fangyannan@21cn.com) (Y. Fang), [xtcao@sina.com](mailto:xtcao@sina.com) (X. Cao), [t.steiner@imperial.ac.uk](mailto:t.steiner@imperial.ac.uk) (T.J. Steiner).

whether as a consequence of heredity or of common lifestyles, behaviours and environment, is a contributory factor which attracts the interest of epidemiological researchers. Studies suggest a high risk of migraine in first-degree relatives (FDRs) of those with migraine [4,5], and perhaps especially of migraine with aura (MA) in the FDRs of MA probands [6,7]. One study found that FDRs of probands with migraine without aura (MO) had increased risks of MO and MA, while FDRs of those with MA had increased risk of MA but not of MO [8]; another study suggested that FDRs of MA and MO probands had significantly increased risks of both MA and MO [9]. Early onset and severe migraine may be associated with higher levels of familial occurrence [10]. Studies also suggest that FDRs of those with chronic tension-type headache (CTTH) have significantly increased risk of themselves having CTTH [11–13]. Currently there are no reports of familial occurrence of episodic TTH, or of the group of disorders characterised by headache on  $\geq 15$  days/month (which include CTTH and medication-overuse headache [MOH]). No studies have been conducted among the population of China.

In the context of a cross-sectional population-based nationwide survey of headache prevalence [14], we collected data on similar headache affecting FDRs of those with migraine, TTH and headache on  $\geq 15$  days/month. Here we present the analysis of these data.

## 2. Methods

### 2.1. Ethics

The study protocol was approved by the Chinese Ministry of Health and the ethics committee of the Chinese PLA General Hospital, Beijing.

### 2.2. Study design

The original study performed during 2009–2010 was a cross-sectional door-to-door survey throughout China. A representative sample of the adult population was obtained by randomised cluster-sampling according to the EPI method established by the World Health Organization [15]. Households were visited by cold-calling, and one adult was randomly selected from each. These methods have been described in detail previously [14,16].

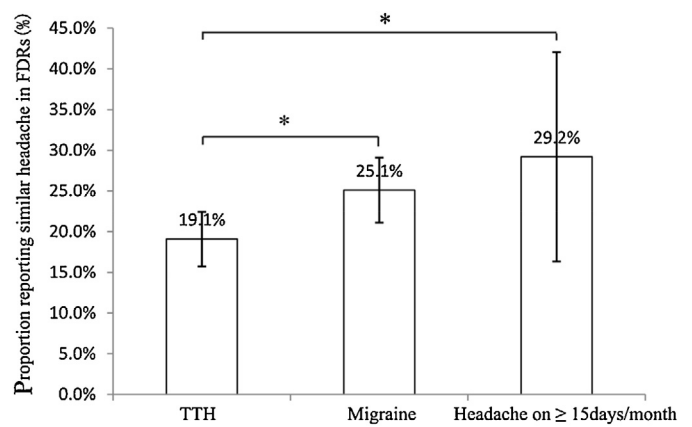
### 2.3. Enquiry

Interviewers employed a structured questionnaire developed for population-based studies [1] by *Lifting The Burden* [17], translated into Chinese from the English version and validated within the target population in a sub-study [16]. Demographic enquiry included age, gender, habitation, marital status, occupation and educational level. Anthropometric data included weight and height, recorded using a portable calibrated digital scale, from which body mass index (BMI) was calculated. Headache diagnoses were based on the criteria of the International Classification of Headache Disorders 2nd edition (ICHD-II) [18]. Participants identifying more than one headache type were asked to focus only on the one they recognised as most bothersome.

Of those with headache, we asked whether or not any FDRs (parents, siblings or children) had similar headache to their own. We assumed such headache was diagnostically the same as that described by the respondent.

### 2.4. Statistical analysis

We categorised demographic variables and summarised them as percentages by headache type. Age was also expressed as means  $\pm$  standard deviations (SDs). The occurrence of similar headache in FDRs was recorded as “yes” or “no” and proportions



\* $p < 0.05$  (adjusted odds ratio from multivariate analysis)

**Fig. 1.** Proportions of participants reporting similar headache in first-degree relatives according to headache type.

estimated with 95% confidence intervals (CIs). We used independent chi-squared tests for significant differences between headache types, regarding  $p \leq 0.05$  as significant. We then calculated adjusted odds ratios (AORs) with 95% CIs by multivariate logistic regression taking into account the following variables: age, gender, habitation, marital status, occupation, educational level, body weight.

## 3. Results

There were 5,041 survey participants (participation rate 94.1%), of whom 469 (9.3%) were diagnosed with migraine, 543 (10.8%) with TTH and 48 (0.95%) with headache on  $\geq 15$  days/month. We excluded 18 with migraine and 13 with TTH because of missing data about FDRs; therefore we analysed 1029 participants reporting headache (mean age:  $46.5 \pm 11.3$  years; male 350 [ $46.7 \pm 11.4$  years]; female 679 [ $46.3 \pm 11.2$  years]; 451 with migraine, 530 with TTH and all 48 with headache on  $\geq 15$  days/month). Table 1 shows the distribution of demographic, BMI data.

Overall, 22.2% (95% CI: 19.6–24.7%) of participants with headache reported similar headache in FDRs: 25.1% (21.1–29.1%) of those with migraine, 19.1% (15.7–22.4%) with TTH and 29.2% (16.3–42.0%) with headache on  $\geq 15$  days/month (Fig. 1). These proportions were significantly higher in migraine (chi-squared = 5.141, OR = 1.4,  $p = 0.023$ ; AOR = 1.2,  $p = 0.015$ ) and headache on  $\geq 15$  days/month (chi-squared = 2.823, OR = 1.7,  $p = 0.093$ ; AOR = 2.3,  $p = 0.018$ ) than in TTH, but the difference between headache on  $\geq 15$  days/month and migraine was not significant (chi-squared = 0.386, OR = 1.2,  $p = 0.534$ ; AOR = 1.2,  $p = 0.237$ ).

We calculated ratios of the proportions reporting similar headache in FDRs to the observed general-population 1-year prevalence of each headache type (migraine 9.3%, TTH 10.8%, CDH 1.0%) [14,19]. These were for migraine 2.7:1, for TTH 1.8:1 and for headache on  $\geq 15$  days/month 30.7:1.

## 4. Discussion

Our study found high proportions (19.1–29.2%) of FDRs of participants with headache were reported as having similar headache. They were significantly higher in both migraine and headache on  $\geq 15$  days/month than in TTH. However, when related to the general-population prevalence of each headache type, the proportion for headache on  $\geq 15$  days/month was an order of magnitude higher than those for migraine or TTH. It is essential to recognise here that these proportions do not represent prevalences because

**Table 1**  
Demographic, anthropometric data in participants with headache according to headache type.

Variable	Category	Migraine (n = 451)	Tension-type headache (n = 530)	Headache on $\geq 15$ d/m (n = 48)
Gender	male	146 (32%)	191 (36%)	13 (27%)
	female	305 (68%)	339 (64%)	35 (73%)
Age (years)	18–39	123 (27%)	157 (30%)	6 (13%)
	40–65	328 (73%)	373 (70%)	42 (87%)
Habitation	urban	160 (35%)	207 (39%)	13 (27%)
	rural	291 (65%)	323 (61%)	35 (73%)
Educational level	secondary school or less	323 (72%)	369 (70%)	43 (90%)
	high school or above	127 (28%)	157 (30%)	5 (10%)
Marital status	single, widowed or divorced	31 (7%)	61 (12%)	6 (13%)
	married	420 (93%)	469 (88%)	42 (87%)
Body mass index (kg/m <sup>2</sup> )	<25	325 (72%)	390 (74%)	28 (58%)
	$\geq 25$	126 (28%)	139 (26%)	20 (42%)
Occupation	unemployed	40 (9%)	62 (12%)	4 (8%)
	working (employee or other)	408 (91%)	454 (88%)	44 (92%)

Some data were missing; d/m: days/month.

the denominators are unknown: each participant would have had multiple FDRs. We did not collect data on numbers of FDRs, but in most cases there would realistically be up to 3–4: two parents and  $\leq 1$  sibling and/or child, as one child family plan policy had implemented in mainland China for 4 decades. There is no reason to believe that number of FDRs might vary significantly between different headache disorders, meaning that comparisons between headache types are valid.

It is also important to note that the family unit in China is tight because of oriental Confucius value. Accordingly, participants would almost certainly be aware of similar headache symptoms among all FDRs. The probability is therefore good of a high level of case ascertainment, while the assumption is a reasonable one that headache described as similar is in fact so. The further assumption that headache described as similar in FDRs was diagnostically the same as the headache in the proband can be justified on this basis, although some uncertainty has to be admitted in the absence of direct interrogation of FDRs. This would have been a resource-consuming enquiry, which we did not have the means to undertake.

This study was not able to distinguish between heredity and lifestyle, behavioural or environmental factors that might promote familial occurrence of these headache disorders. Multiple epidemiological studies showing FDRs of migraine probands are at high risk of themselves having migraine [4–9], and one relating this risk to early onset and severity of migraine in the proband [10], have suggested heredity is important in this disorder. In fact, migraine – even in its common forms (MO and MA) – has long been argued to have a genetic basis [8,20]. No such evidence supports the notion of heredity as a factor in episodic TTH, although this may be because the issue has not been studied. On the other hand, several studies (all from Denmark) suggest heredity has a role in CTTH [11–13]. In our survey, CTTH was included among disorders characterised by headache on  $\geq 15$  days/month, although as a minority – two thirds of such cases were probable MOH [14].

The extraordinary finding was the very high proportion of participants with headache on  $\geq 15$  days/month (29.2%) who reported similar headache in one or more FDRs against a general-population prevalence of 0.95% estimated in the same survey (a ratio of over 30:1). Again it must be emphasised that the 29.2% did not represent a prevalence, but the extreme magnitude of the ratio (especially compared with those for migraine [2.7:1] and TTH [1.8:1]) nonetheless suggests that headache on  $\geq 15$  days/month is highly familial. MOH is essentially a consequence of behaviour, which might be genetically determined, but we suggest it is more likely that overuse of medication is learnt (or taught) within families. This suggestion has been made before [19], and, if true, has important implications for public health and the need for public education.

The strengths of our study lie in the large representative sample from a nationwide study, selected and engaged using established methodology, and with a high participation rate, avoiding selection bias [21]. Diagnoses in the participants were made using a validated translation [16] of a widely used instrument [1]. Underreporting of family history in FDRs has been noted in the United States and Denmark with regard to “severe headache” and migraine [22,23] and CTTH [13]; this may not have occurred herein view of the tight family unit in China but, if it did, our findings would be conservative. It is unlikely to have affected headache types differentially. The principal limitations have been referred to above: we did not count, or interview, FDRs; proportions reporting similar headache do not therefore represent prevalences, and diagnoses of similar headache are attended by a degree of imprecision, probable bias may exist. We did not include, for comparative purposes, the non-headache general population since we did not further question participants who had reported being headache-free.

## 5. Conclusion

Headache is highly prevalent in China, and common among FDRs of those with any type of headache (headache on  $\geq 15$  days/month > migraine > TTH). Against the background of the general-population prevalence of each disorder, familial occurrence was a very highly influential factor in headache on  $\geq 15$  days/month. There are important implications for public health and education.

## Competing interests

The authors declare no conflicts of interest.

## Authors' contributions

SY and TS conceived the study, and SY organized the national survey. RL, XY, GZ, XQ, JF and YF participated in the design and coordination of the study, and in the data collection. XC was responsible for sample selection and assisted in the statistical analysis. MH performed the statistical analysis and drafted the manuscript. TS assisted in drafting and revising the manuscript. All authors approved the final version.

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