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Relationship between Headache status and Chronotype

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Relationship between Headache status and Chronotype

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by

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학위논문원문제공서비스에대한동의서

본인의학위논문에대하여서울대학교가아래와같이학위논문제공하는것에동의합니다.

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논문제목: Relationships between Headache status andChronotype

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Abstract

Background: The associations between headacheand sleep are complex. Migraine significantly impairs daytime function. Most cross-sectional studies based on small clinical population showed disrupted sleep pattern was associated with migraine. Information about the association with circadian rhythm is, however, rare. In this study, we aimed to explore evaluate the association of migraine or other headaches with chronotypesin the general population. Correlations with insomnia, sleepiness, and sleep quality were also investigated.

Methods:A total of 2886 Korean general population were recruited, and they filled out the questionnaires after instructions of interviewer. The questionnaires included questions related sleep parameters involving sleep time, Pittsburgh Sleep Quality Index (PSQI), Insomnia Severity Index (ISI) and Epworth Sleepiness Scale (ESS). The final sample included 2550 participants (51.2% females;19-69 years), which were divided into three groups as migraine group, non-migrainous headache group and headache-free group, based on ICHD-2 criteria.

Results: According to ICHD-2 criteria, we classified 5.2% of study population as migraine. Migraine group significantly showed late circadian preference ($p=0.036$), poor sleep quality (<0.001), daytime sleepiness ($p=0.028$) and insomnia (<0.001), after adjustment of covariates. Correlation with late chronotypeswas not related to headache severity.

Conclusions: The aim of the study was to evaluate associations between chronotype and headache in a large non-clinical population.Migraine was significantly associated with late chronotype. Correlation with insomnia, daytime sleepiness and poor sleep quality was documented.

Keywords: Chronotype, headache, migraine, insomnia, sleep quality.

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LIST OF ABBREVIATIONS

ICHD-2 :international classification of headache disorders second edition

HIT-6 :headache impact test-6

PHQ-9 :Personal health questionnaire depression scale

MCTQ :MunichChronoType Questionnaire

MEQ :Morningness-EveningnessQuestionnaire

SDW :total sleep time on workdays

SDF :total sleep time on free days

MSW :mid sleep time on workdays

MSF : mid sleep time on free days

MSFsc :corrected mid sleep time on free days

SDAvg :Average sleep duration

DMG :definite migraine group

NMG :non-migrainous headache group

HFG :headache free group

PSQI :Pittsburgh Sleep Quality Index

ESS :Epworth Sleepiness Scale

ISI :Insomnia Severity Index

1. Introduction

Headache and sleep disorders are common in the general population and often related to each other.(1, 2)The associations between headache, especially migraine, and sleep are complex. Headache has been regarded as either the cause or result of disrupted sleep.(3)Headache episodes are precipitated by sleep deprivation or excessive sleep.Clinical population based studies showed disrupted sleep pattern was one of migraine attack triggers.(2, 4)A case-control study in children with migraine without aura showed high prevalence of sleep disturbance compared with control group, and polysomnographic findings showed increased sleep latency, decreased total sleep time, and nocturnal awakenings, as well as sleep breathing disorders.(5, 6)Insomnia is the most common sleep disturbance in headache clinical population, observed in half to two thirds of migraine patients.(7)Recent prospective population-based cohort study showed insomnia at baseline was related with 40% increased risk for headache.Other sleep problems such as sleep apnea would be investigated via polysomnography to define the cause of morning headache. Headache can also be induced by restless legs syndrome or periodic leg movements of sleep (PLMS).(8)Other sleep disrupting medical or psychological condition such as chronic pain or depression should be considered as the cause of headache.On the contrary to relationships as above, chronic tension-type headache or migraine disorder with or without medication overuse or depression can induce sleep disturbance.(1)

Chronobiologicalaspects have been identified in migraine patients as well as general associations between sleep and headache.(5, 9, 10) Migraine attacks have been reported to occur more often in the morning, and the circadian preference of migraine attacks has been explained by the mechanism of periodic hypothalamic dysfunction.(11-13) However, the otherstudy showed the circadian preference of migraine attacks was just after noon, and altered sleep pattern and work-related stress were suggested as the important trigger factors.(3, 11)Besides to circadian rhythm pattern in migraine attack timing, there were other reports focusing on the association between sleep pattern and neuronal mechanism of migraine.(6)The associations between sleep and headache were stronger for chronic migraine than for chronic tension type headache, suggesting of impact of migraine pathology on sleep homeostasis.(14, 15)

The main goal of this study was to investigate the association between sleep quality, insomnia, daytime sleepiness and headache in a large non-clinical population. There was no study for a large non-clinical general population in previous reports. We focused on the differences of the sleep profiles between migrainous headache and non-migrainous headache. To clarify the role of sleep in headache patients in our study, the relationship between headache and individual chronotype, which is endogenous variation in circadian rhythm (16-18),was estimated as well as other sleep problems.

2. Methods

2.1. Subjects and procedures

Subjects were recruited from Korean Headache Survey, which wasa cross-sectional nation-wide population based interview survey for general population aged 19 years and over who resided in South Korea. The estimated population of Korea in 2009 was 49,759,000, of whom 37,782,000 were aged 19 years and older.The target population was 2,800 in our study. The survey was performed by Gallup Korea in 2010 using multistage clustered random sampling from 15 administrative districts. First, Gallup Korea allocated sample numbers to each administrative district according to population distribution, Subsequently, Gallup Korea approached 7615 individuals and a total of 2836 subjects (1412 men, 1424 women) completed the questionnaires. Seventy-six interviewers participated in this survey. Before the face-to-face interview, well trained interviewers explained the aim of the study to all individuals. The response rate was 37.2%. We excluded persons aged more than 70 years (n=141) orshift workers (n=145). An age exclusion criteria was set based on capacity to comprehend all questions in the questionnaires.Finally, 2550 subjects(1244 men, 1306 women), were analyzedin our study.

2.2. Ethical considerations

In this survey, the following ethical considerations were taken into account: (1) subjects' participation was voluntary, and their informed consent was required; (2) permission to conduct the study was obtained from all institutional review board associations.

2.3. Materials and definitions

All data were derived from self-report questionnaires with 60 questions. The following five domainswere included in the questionnaires used in these survey (1) General characteristics: the participants were required to put down the age, gender, height, weight, alcohol and smoking. (2) Headache status: The international classification of headache disorders second edition (ICHD-2) criteria was used to differentiate the definite migraine headache from non-migrainous headache. We diagnosed definite migraine headache of at least five attacks per one month fulfilling following headache characteristics: unilateral location, pulsating quality, moderate to severe intensity, lasting 4-72 hours and associated symptoms such as nausea and/or vomiting, photophobia and phonophobia. We classified the participants into headache group and headache free group, and then divided headache group into two groups as non-migrainous headache group (NMG) and definite migraine group (DMG).Also, we evaluated headache severity with scale of headache impact test-6 (HIT-6).More than 60 points on the HIT-6 scores were coded as severe impact. (3) Depression and anxiety: Personal health questionnaire depression scale (PHQ-9) and Goldberg anxiety scale were used to evaluate depression and anxiety. Subjects' scores on the PHQ-9 were coded as depression (10-27) and no depression (0-9). Scores on the Goldberg anxiety scale were coded as anxiety (5-9) and no anxiety (0-4). (4) Sleep time: bedtime onset, bedtime off and total sleep time on workdays (SD_W) and free days (SD_F) were measured. With measured sleep time, midpoint between bedtime onset and bedtime off was calculated and named as mid sleep time on workdays (MSW) and free days (MSF). Average sleep duration (SD_{Avg}) was calculated as follows: $(5*SD_W + 2*SD_F)/7$. In this study, mid sleep time based on Munich ChronoType Questionnaire (MCTQ) was used as index of participants' circadian preference. To minimize the confounding effect of work-week accumulated sleep debt, corrected mid sleep time on free days (MSF_{SC}) was calculated as follows:$MSF_{SC} = MSF - 0.5*(SD_F - SD_{Avg})$.We divided the chronotype distribution into three types groups based on MSF_{SC}. (5) Sleep problems questions: the Pittsburgh Sleep Quality Index (PSQI) was used to measure sleep quality of participants. The PSQI is a self-administered questionnaire, which is composed of seven components: sleep quality, sleep latency, sleep duration, sleep efficiency, and sleep disturbances, use of sleep medication and daytime dysfunction. The sum of each component's scores yields one total score. The higher total score, the sleep is considered to be more disturbed one. In this study, the PSQI scores cutoff point was set to 6 or higher as previous studies. To assess excessive daytime sleepiness and insomnia, the Epworth Sleepiness Scale (ESS) and Insomnia Severity Index (ISI) were used. The ESS scores more than 11 points were defined as daytime sleepiness and the ISI scores more than 8 points were considered as clinical insomnia in this study.Habitual snoring and observed apnea were estimated to evaluate sleep breathing disorder. Snoring more than three times per one week was set as habitual snoring and apnea more than three times per one week was defined as observed apnea.

2.4. Statistical analyses

Descriptive statistics were calculated to summarize demographic data, anxiety, depression, mid sleep time on weekdays (MSW) and free days (MSF), total sleep duration on weekdays (SD_W) and free days (SD_F), ESS, ISI, PSQI in patients classified into headache free group (HFG), non-migrainous headache group (NMG) and definite migraine group (DMG). Categorical variables were summarized as proportions (%) and normally distributed continuous variables were summarized as mean±standard deviation (SD). Unadjusted differences in categorical variables andcontinuous variables were assessed for statistical significance using the χ^2 test or the analysis of variance (ANOVA). Analyses of covariance (ANCOVA) were performed to investigate the effect of headache status or severity on sleep parameters such as total sleep time and mid sleep time. Logistic regression analyses were conducted to assess the association between headachestatusesor severity and daytime sleepiness, insomnia, sleep disturbance. In these analyses, we set age, gender and depression scale (PHQ-9) at the time of the baseline as covariates. An alpha of < 0.05 was considered statistically significant. SPSS 20.0 version for Windows was used for statistical analyses.

3. Results

3.1. Prevalence and characteristics of headache

For the 2550 subjects (1244 men, 1306 women), the mean age was 42.88 years (standard deviation [SD], 13.68; range 19-69 years). Subjects numbers of definite migraine group (DMG) and non-migrainous headache group (NMG) were 134 (5.3%) and 1081 (42.3%), respectively. The prevalence of definite migraine in our study is similar with one in other studies (5%). The remaining 1335 subjects (52.4%) were classified as headache free group (HFG). Comparing the gender distribution, there is a significant difference in the proportion between DMG (74.6% female) and NMG (59.2% female) ($p < 0.001$). In addition to the gender, age distribution between three groups showed significant differences between three groups (Summarized in Table 1). The frequency, duration, unilateral location, and pulsating quality of headache between DMG and NMG showed significant differences. In addition to characteristics as above mentioned, severity scores on HIT-6 test showed significant severity in definite migraine group ($p < 0.001$). Considering anxiety and depression, DMG showed significant differences compared with HFG and NMG ($p < 0.001$) (Table 1).

3.2. Sleep time

There was no significant difference about bedtime onset and bedtime off between three groups. Considering total sleep duration, DMG showed significantly shorter sleep duration on weekdays ($p = 0.011$), but no significant differences about sleep duration on free days and average sleep duration(Table 1). In order to control the confounding effect on group differences, GLM (General Linear Model) was conducted on sleep duration considering three headache groups as independent factors and age, gender, depression scale (PHQ-9) as covariates. There was no significant effect of migraine headache status on average sleep duration at the $p < 0.05$ level for the three conditions [$F (2, 2544) = 2.827$, $p = 0.059$] Even after conducting the linear trend analyses, there was no significant trend between groups on average sleep duration ($p = 0.232$) (Table 2). To analyze the effect of headache severity on sleep profiles, headache group (migrainous headache and non-migrainous headache) was reclassified into three groups based on headache impact test (HIT-6). Subjects numbers of no effect or mild effect group and moderate effect group were 1044 (85.9%) and 64 (5.3%), respectively. Numbers of severe effect group were 107 (8.8%). No significant effect of headache severity on total sleep duration of weekdays or weekend and average sleep duration was documented (Table 3).

3.3. Circadian preference

Mid sleep time on weekdays (MSW) or free days (MSF) and sleep-corrected mid sleep time on free days (MSF_{SC}) showed late circadian preference in definite migraine group. In order to control the confounding effects, General Linear Model was conducted on mid sleep time considering three headache groups as independent factors and age, gender, depression scale (PHQ-9) as covariates.Group differences on MSW and MSF were also confirmed in the analysis at the $p < 0.05$ level after controlling covariates [MSW, F (2, 2544) = 7.378, p = 0.001; MSF, F (2, 2544) = 4.575, p = 0.010]. About $MSF_{SC,}$ there was no significant group differences after controlling covariates [MSF_{SC}, F (2, 2544) = 2.633, p = 0.052]. With linear trend analyses, MSW, MSF and MSF_{SC} showed later circadian preferences in definite migraine group (Table 2). As well as on total sleep duration, the effect of headache severity on circadian preference was analyzed. No significant effect of headache severity on mid sleep time of weekdays (MSW) or free days (MSF) and sleep-corrected mid sleep time on free days (MSF_{SC}) was documented (Table 3).We divided the chronotype distribution into three types groups (early, intermediate and late type) based on MSF_{SC} (Table 1 and 4). Univariate analysis demonstrated definite migraine group showed late chronotype preference (25.4%, p = 0.004). Among three types of chronotype groups, definite migraine was most prevalent in late chronotype group among three types of chronotype groups (5.9%, p =0.004). Late chronotypes were significantly younger [F (2, 2547) = 483.908, $p < 0.001$; mean ages: early types 54.86 years ±0.50, intermediate types 42.28 years ±0.31, late types 33.05 years ± 0.49].Late chronotypes significantly showed male preferences (53.1% male, p = 0.05), and early chronotypes showed female preferences (53.9% female, p = 0.05). Depression, which was estimated with PHQ-9, was prevalent in late chronotype group (6.5%, p = 0.008). We therefore used age, gender and depression as covariates in the analysis. Group differences on MSW, MSF and MSF_{SC} were confirmed in the analysis at the $p < 0.05$ level after controlling covariates, but total sleep duration showed no differences between three groups (Table 4). There were significant correlations between three headache groups and three chronotype groups after controlling covariates (Table 2 and 4). Definite migraine group showed significant correlation with late type chronotype (OR = 2.17, p = 0.036) (Table 2).There was no significant association between three chronotype groups and headache severity.

3.4. Sleep disturbance, sleepiness and insomnia

Linear regression with three headache groups as an independent variable adjusting for age, gender, depression scale (PHQ-9) was conducted on excessive daytime sleepiness (Epworth

Sleepiness Scale), insomnia (Insomnia Severity Index) and poor sleep quality (Pittsburgh Sleep Quality Index). Definite migraine group (DMG) showed significant main effect on insomnia (OR = 4.14, $p < 0.001$), daytime sleepiness (OR = 1.70, $p = 0.028$) and poor sleep quality (OR = 2.32, $p < 0.001$), which was also confirmed by trend analyses (Table 2).Contrary to total sleep duration or circadian preference, headache severity showed significant effect on insomnia (OR = 1.12, $p < 0.001$), daytime sleepiness (OR = 1.10, $p < 0.001$) and poor sleep quality (OR = 1.18, $p < 0.001$) (Table 3).Chronotype grouping revealed insomnia was more prevalent in late type group ($p = 0.003$) by the result of univariate analysis. Daytime sleepiness was highest in early chronotype group ($p = 0.004$). Sleep quality was lowest in late chronotypes ($p < 0.001$). Multivariate analysis demonstrated that insomnia and sleep quality were statistically associated with late circadian preference (Table 4).

4. Discussion

While frequently commented upon the association between sleep and headache, sleep habits and sleep problems on headache status or severity in a large general population have rarely been studied.(2, 9, 19)Especially, the studies about circadian preference of headache patients have rarely been reported.(9, 18)A case-control study showed no differences were found regarding the distribution of chronotypes in patients with menstrual migraine and healthy controls.(9)The other case-control study reported morning preference and evening preference types were more represented in migraine group than in control group.(18)Previous other reports have evaluated circadian preference (chronotype) with MEQ (Morningness–Eveningness Questionnaire).(18) Several studies show that chronotype based on MCTQ(Munich ChronoType Questionnaire) strongly correlate with morningness-eveningness evaluated by MEQ.(20, 21) Furthermore, in comparison to MEQ, MCTQ can quantitatively assess sleep habits with time scale during work days or free days, separately. Light exposure time, self-assessed chronotype and familial tendency about chronotype can be also evaluated via MCTQ(17, 22). The midpoint between sleep onset and rise time is called “Mid sleep time“, which has been reported as the best phase reference point(23). Mid sleep time has been known to reflect individual’s circadian preference after validation with other indexes of circadian rhythm. We calculated mid sleep time from the data based on our questionnaire answers, and designated mid sleep time as the circadian preference of each person.

Our study is the first report on the associations between sleep time, circadian preference, sleep problems and headache of adults in a large non-clinical population with the use of multiple questionnaires.Especially, we focused migraine headache in study population due to headache severity and chronobiological aspects of migraine. We divided the study population into three groups as definite migraine group, non-migrainous headache group and headache free group. The most significant factor differentiating three headache groups is headache severity.(24)As well as headache status, we divided headache group into three groups based on headache severity. We also analyzed the relationship between headache severity and sleep profiles.(25)

We observed no significant association between headache statusand average sleep duration ($p = 0.059$, p for trend = 0.232). Migraine headache group significantly showed short sleep duration for weekdays ($p = 0.009$), but there were no significant differences about average sleep duration or sleep duration for free days between groups. No clear relationship between headache severity and total sleep duration was also documented. Even though individual's life was severely affected by headache, it made no differences about total sleep duration. These resultsarecontrast with other studies based on clinical population that have found that severe headache sufferers showed short sleep duration.(3)One previous report based on children and adolescents showed no significant relevance between headache status and total sleep time.(25)Headache attacks had been known to be provoked by too little sleep or prolonged sleep , but, we could notidentify headacheattacks frequency depending on the amount of sleep duration because of cross-sectional designed study. The chronotype depends on both genetic and environmental factors.(26, 27) Mid sleep time on free days (MSF) was known to reflect the chronotype more than one on work days (MSW), because sleep rhythm on weekend without social obligation depends on more natural and intrinsic circadian preference by genetic factor.(17)Most people accumulate sleep deficiency through all week days as 'sleep debt', and compensate for on free days.Therefore, MSF is needed to clean from the confounder sleep debt, and designated as $MSF_{SC.}$ (17, 28)Definite migraine group showed significant association with later circadian preference as shown with later mid sleep time was shown during weekdays or weekend. Corrected mid sleep time on free days (MSF_{SC})did not show statistically significant association at the $p < 0.05$ level after controlling covariates. But, linear trend analysesshowed significant association between definite migraine group and later circadian preference with later MSF_{SC}($p = 0.05$). Chronotype grouping based on MSF_{SC} demonstrated definite migraine was significantly related to 'late'chronotype compared with 'early' or 'intermediate' type. Headache severity was not associated with this correlation. This finding has never been reported in the cross-sectional study for non-clinical population except one report of children.(25)With the limitation of cross-sectional design, the causal relationship between late chronotype and migrainecould not be identified. We analyzed the relationship between mid-sleep time and headache severity, but there was no significant result. Therefore, late chronotype in migraine group could be explained by unique characteristics of migraine rather than headache impact related to severity. In multivariate analysis of total sleep time and mid sleep time in each headache group, we identified that total sleep duration and chronotype are controlled independently, and our results showed that migraine is associated withchronotype, not to the average sleep duration.

The association between late chronotype and migraine could be explained with the role of melatonin in headache patients.Because of tendency to occur in response to change in the internal or external environments, headache has been thought to be associated with melatonin which plays an important role in maintaining homeostasis against environmental changes(3). Plasma melatonin level has been described to have nocturnal peak at 2 to 3 a.m. and decrease upon waking. Delayed sleep phase syndrome patients have a phase delay in the melatonin peak, and melatonin has been known to be effective treatment of delayed sleep phase syndrome.(16, 29, 30)Furthermore, melatonin has been identified to play an analgesic role in headache.(31).There are several action mechanisms which account for analgesic role of melatonin in headache.(31) Melatonin enhances the inhibitory function of GABA neurotransmitter. Reduced level of melatonin might lower pain threshold. Melatonin modulates vessel tone reactivity of cerebral vessel via calcium ion action. Besides of two mechanisms above mentioned, serotonin or prostaglandin E2 are involved in the role of melatonin in headache.Melatonin levels showed abnormal curve pattern in the chronic migraine or chronic tension headache patients.(30) Chronic migraine group showed a lack of melatonin nocturnal peak and also prolonged peakeven on waking stage compared with control group.(30, 32)These findings were contrast with the findings of Peres et al.(29), whose chronic migraine group presented similar nocturnal melatonin level with control group.Despite of controversy, people with chronic migraine might have reduced level and delayed peak of melatonin. Therefore, delayed circadian preference and migraine attack could be explained with the role of melatonin related to hypothalamic dysfunction. Melatonin secretion is significantly reduced in chronic type headaches more than episodic headache.(30) Few articles demonstrated latechronotypes were related to pain such as fibromyalgia syndrome.(33, 34)Migraine itself or other pain syndrome could be suggested to be associated with late circadian preference, regardless of its severity.(34) Late chronotypes have already been shown to suffer more from bipolar disorders, headaches, seasonal depression and depression.(25, 35)

People suffering from insomnia were known to complain headache, and our study result showed that migraine headache was significantly associated with insomnia at the $p < 0.05$ level in multivariate analyses in each headache group. Sleep fragmentation and recurrent arousal might be related to this association. Anxiety or depression, which is frequent comorbid withinsomnia, should be considered as associative factor. Excessive daytime sleepiness was significantly determined to be associated withmigraine headache, although definite migraine group did not sleep significantly less than other groups as seen in multivariate analyses of total sleep duration in each group. Definite migraine group also showed significantly poor sleep quality, which might be related to daytime sleepiness. These associations of insomnia, daytime sleepiness, and poor sleep quality might be related to headache severity or chronic painful condition, not to unique feature of migraine. Allodynic feature of migraine could result in sleep disturbance.(36) In our study results, non-migrainous headache group showed also significant relation to insomnia, daytime sleepiness and poor sleep quality, as well as in definite migraine group. To clarify this confounding effect of painful condition, we did multivariate analyses of insomnia, daytime sleepiness, and sleep qualityin three groups based on headache impact test (Table 3). Weidentified significant associations between these sleep profiles and headache severity. It could be explained with the association between chronically painful conditions and sleep disturbance, which has long been recognized(37, 38) and known to be bidirectional.(39, 40) Clinically significant insomnia has been reported by 53% of chronic pain patients, relative to 3% of controls.(41) As well as insomnia, sleep discontinuity and disrupted sleep architectures are identified.(40).

Inversely, poor sleep quality could aggravate pain symptoms. How sleep deprivation, sleep fragmentation and recurrent arousal affect pain perception has been discussed.(39, 40)Sleep deprivation has been suggested to have hyperalgesic effect.(42) Analgesic action of endogenous opioid is dependent on undisrupted sleep continuity and sleep deprivation can induce change in the 5-HT system or other neurotransmitter systems involved in pain modulation.(39, 40)Several reports showed sequential relations of increased pain after sleep restriction.(43)

Chronotype grouping showed late circadian preference group showed significant association with insomnia and poor sleep quality as well as migraine. Late chronotypes frequently report lower sleep quality and daytime sleepiness.(44-46)Typical school or work schedule start early in the day, so late chronotypes combined early social arousals lead to substantial sleep debt and poor sleep quality in adolescents or socially active adult group.(45, 46) Daytime sleepiness and disturbed psychological wellbeing might be related to behavior, and it is called as 'social jetlag'.(44) Social jetlag can be calculated by the absolute difference between MSW and MSF(44), so our results identified a good correlation between social jetlag and late chronotypes[F (2, 2547) = 201.384, $p < 0.001$].

Our study has a number of limitations. First we used the cross-sectional design, so we cannot make assumptions about the cause and effect relationship of study results.Second our study questionnaire was not designed to involve all the questions in MCTQ, so we could not get the information about self-assessed chronotype. There were no identified factors that influence circadian preference in our study such as light exposure and daily activities. Finally, the time information on sleep habits was obtained via self-report, so it was not as accurate as one via polysomnography. However, self-report method is widely used in population-based studies, as it is fast and simple.

Taken together, these results suggest that migraineis really associated with late circadian preference and sleep problems. Late chronotypes are more affected by headache or pain itself, regardless of its severity.(34)Late circadian preference leads to more sleep debt during workweek, which is known to cause mood disturbance, decrease attention and social performance.(35) Mood disturbance might be related to severe headache, but the association between headache severity and chronotypes was not proved in our study. Themore severe headache is suffered from, sleep continuity is more disrupted and it would result in insomnia or poor sleep quality. Poor sleep quality would be reduced to daytime sleepiness.

Sleep and headache are unequivocally associated in non-clinical population. Sleep problems and sleep habits modification can be important modifiable factors to manage headache. Many researchers suggested treatment effect of sleep on headache.(47)Interventions that improve sleep hygiene and advance circadian rhythm could be helpful in ameliorating headache and vice versa. Future prospective study would be needed to prove these treatment effects of sleep on headache. Prospective studies are required to understand better the association between circadian rhythm and headache. More objective measures such as body temperature, cortisol or melatonin level and polysomnogrphic data to evaluate chronotypes would be needed.

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Table 1. Demographic characteristics of total study population and each headache group

	Total (n=2550)	Headache Free (n=1335, 52.4%)	Non-migrainous Headache (n=1081, 42.3%)	Definite Migraine (n=134, 5.3%)	p-value
Demographics					
AGE	42.88 ±13.68	43.49 ±14.11	42.29 ±13.28	41.63 ±12.27	0.056
Gender (men)	48.8	57.6	40.8	25.4	< 0.001
BMI	23.00 ±3.02	23.18 ±3.01	22.83 ±3.00	22.66 ±3.15	
Alcohol	23.0	26.7	19.1	17.2	< 0.001
Smoking	27.2	30.0	25.0	16.4	< 0.001
Anxiety	11.3	5.6	15.8	31.3	< 0.001
Depression	4.2	1.6	6.1	14.9	< 0.001
Headache					
Headache Intensity*			35.6	80.6	< 0.001
HIT-6§			6.0	31.3	< 0.001
Sleep profile					
Chronotype					0.004
Early	542	320 (24.0%)	205 (19.0%)	17 (12.7%)	
Intermediate	1435	731 (54.8%)	621 (57.4%)	83 (61.9%)	
Late	573	284 (21.2%)	255 (23.6%)	34 (25.4%)	
Mid sleep time					
Weekdays	3 : 18 ± 75	3 : 13 ± 73	3 : 23 ± 78	3 : 35 ± 72	< 0.001
Weekend	3 : 51 ± 90	3 : 45 ± 89	3 : 57 ± 91	4 : 07 ± 91	0.001
MSFsc	3 : 36 ± 84	3 : 32 ± 82	3 : 40 ± 84	3 : 51 ± 83	0.009
Total sleep time					
Weekdays	7.10 ± 1.26	7.17 ± 1.25	7.02 ± 1.27	7.00 ± 1.30	0.011
Weekend	7.79 ± 1.54	7.77 ± 1.49	7.80 ± 1.59	7.78 ± 1.60	0.892
Average	7.29 ± 1.23	7.34 ± 1.21	7.25 ± 1.24	7.22 ± 1.27	0.124
Poor sleep quality	18.1	12.9	22.6	34.3	< 0.001
Insomnia	16.2	8.9	22.7	36.6	< 0.001
Daytime sleepiness	11.4	9.4	13.0	17.9	0.001
Habitual snoring	2.4	2.7	2.3	0.7	0.356
Observed apnea	18.4	17.8	19.1	17.2	0.661

Results presented as mean ± SD (hh : mm ± m or hr ± hr) or %

* Headache intensity : moderate to severe, § Headache impact test : severe (≥60),

Table 2. Multivariate analysis of sleep profiles in total study population and each headache group

	Headache Free (n=1335, 52.4%)	Non-migrainous Headache (n=1081, 42.3%)	Definite Migraine (n=134, 5.3%)	p-value	Trend
Total sleep time					
Weekdays	7.17 ±0.03	7.02 ± 0.04	7.01 ±0.11	0.009	0.151
Weekend	7.80 ± 0.04	7.78 ± 0.05	7.74 ±0.13	0.919	0.702
Average	7.35 ± 0.03	7.24 ± 0.04	7.22 ± 0.11	0.059	0.232
Mid sleep time					
Weekdays	3 : 14 ±72	3 : 22 ± 78	3 : 33 ± 72	0.001	0.002
Weekend	3 : 47 ± 89	3 : 55 ± 91	4 : 02 ± 91	0.010	0.026
MSFsc	3 : 32± 82	3 : 40± 84	3 : 51± 83	0.052	0.039
Chronotype					
Late type	1.00 (Ref)	1.35 (1.00-1.80)	2.17 (1.05–4.49)	0.036	0.042
Sleep problems					
Insomnia*	1.00 (Ref)	2.58 (2.02-3.30)	4.14 (2.68-6.40)	< 0.001	< 0.001
Daytime sleepiness*	1.00 (Ref)	1.36 (1.04-1.78)	1.70 (1.02-2.86)	0.028	0.043
Poor sleep quality*	1.00 (Ref)	1.64 (1.31-2.06)	2.32 (1.50-3.59)	< 0.001	< 0.001

Results presented as mean ± SD (hh : mm ± m or hr ± hr) or number (%)

* Values are presented as Odds ratio

Table 3. Multivariate analysis of sleep profiles by headache impact test (headache severity)

	No effect or mild effect (n=1044, 85.9%)	Moderate effect (n=64, 5.3%)	Severe effect (n=107, 8.8%)	p-value
Total sleep time				
Weekdays	7.04 ± 1.24	7.06 ± 1.51	6.77 ± 1.38	0.356
Weekend	7.80 ± 1.53	7.84 ± 1.79	7.77 ± 1.97	0.903
Average	7.26 ± 1.21	7.28 ± 1.45	7.06 ± 1.42	0.484
Mid sleep time				
Weekdays	3 : 24 ±2	3 : 34 ± 8	3 : 18 ± 7	0.325
Weekend	3 : 56 ± 88	4 : 15 ± 99	4 : 07 ± 108	0.633
MSFsc	3 : 40 ± 81	3 : 58 ± 97	3 : 46 ± 100	0.402
Sleep problems				
Insomnia*	1.00 (Ref)	1.10 (1.05-1.15)	1.12 (1.08-1.16)	< 0.001
Daytime sleepiness*	1.00 (Ref)	1.16 (1.08-1.23)	1.10 (1.04-1.16)	< 0.001
Poor sleep quality*	1.00 (Ref)	1.17 (1.07-1.28)	1.18 (1.10-1.27)	< 0.001

Results presented as mean ± SD (hh : mm ± m or hr ± hr)

Results are adjusted for age, gender, depression scale (PHQ-9)

* Values are presented as Odds ratio

Table 4. Multivariate analysis of sleep profiles in each chronotype group

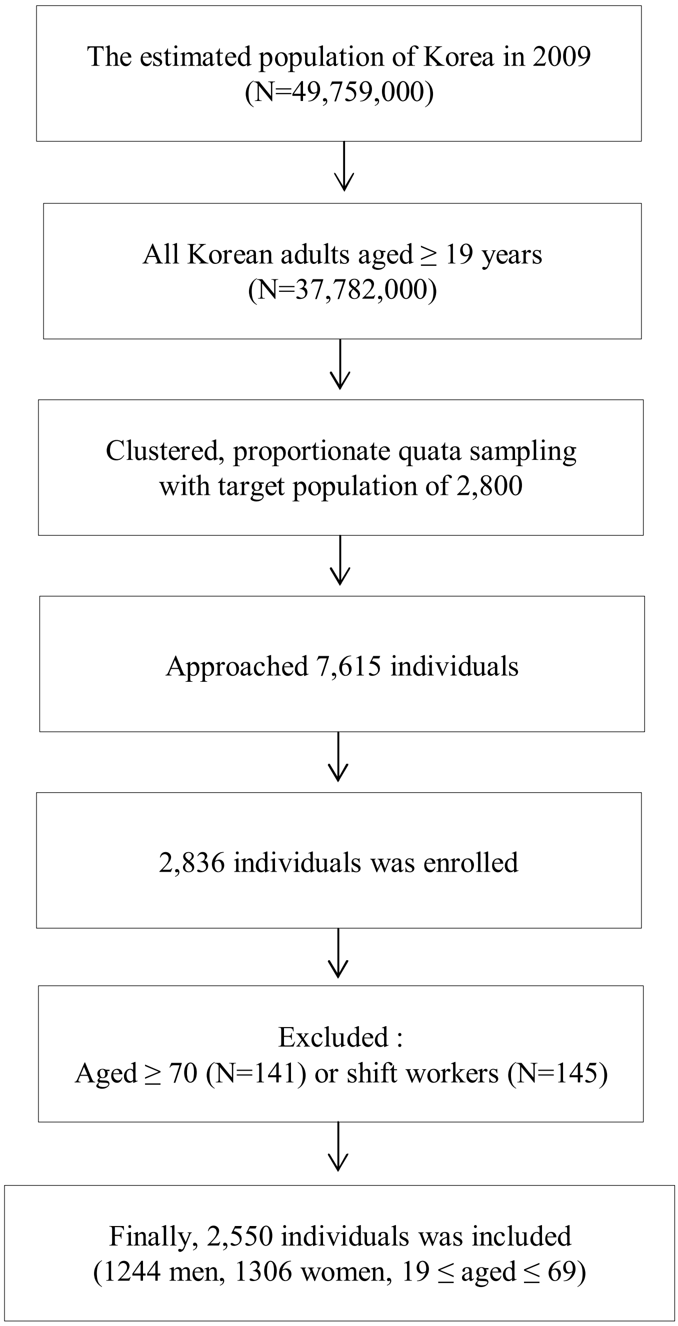
	Early Type (n=542, 20%)	Intermediate Type (n=1435, 60%)	Late Type (n=573, 20%)	p-value
Total sleep time				
Weekdays	7.05 ± 1.31	7.07 ± 1.15	7.22 ± 1.47	0.189
Weekend	7.42 ± 1.47	7.84 ± 1.43	8.00 ± 1.78	0.965
Average	7.16 ± 1.29	7.29 ± 1.12	7.44 ± 1.41	0.661
Mid sleep time				
Weekdays	1 : 54 ± 44	3 : 17 ± 38	4 : 41 ± 79	< 0.001
Weekend	1 : 59 ± 43	3 : 48 ± 40	5 : 45 ± 74	< 0.001
MSFsc	1 : 51 ± 38	3 : 31 ± 29	5 : 29 ± 67	< 0.001
Sleep problems				
Insomnia*	1.00 (Ref)	0.87 (0.63-1.19)	1.57 (1.17-2.09)	0.002
Daytime sleepiness*	1.00 (Ref)	0.70 (0.50-0.97)	0.83 (0.58-1.29)	0.304
Poor sleep quality*	1.00 (Ref)	0.63 (0.47-0.85)	2.18 (1.65-2.87)	< 0.001

Results presented as mean ± SD (hh : mm ± m or hr ± hr) or numbers (%)

Results are adjusted for age, gender, depression scale (PHQ-9)

* Values are presented as Odds ratio

Figure 1. Flow chart of the sampling procedure



국문초록

목적: 두통과 수면의 관계는 복잡하다. 편두통은 일상 생활에 상당한 영향을 미치는 두통으로, 이전에 있었던 소규모 임상 그룹을 대상으로한대부분의 단면 연구들은 불량한 수면 양상이 편두통과 연관성이 있다는 보고를 해왔다. 하지만 주기성 리듬과 두통의 연관관계에 대한 보고는 극히 드물다. 이번 연구에서는 일반인구를 대상으로 하여 편두통 혹은 다른 두통과 주기성 리듬과의 관계에 대해 보고자 하였다. 또한 추가적으로 불면증, 주간 과다졸림증, 수면의 질과 편두통과의 관계도 살펴보고자 하였다.

실험 방법: 총 2886명의 일반 인구를 모집하였고,면접관의 설명을 듣고 설문지를 작성하도록 하였다. 설문지에는 수면 시각, Pittsburgh Sleep Quality Index, Insomnia Severity Index 그리고 Epworth Sleepiness Scale 등의 지표와 관련한 질문들이 있다. 최종적으로 연구대상을 2550명으로 확정하였고 그들을 ICHD-2 기준에 따라, 편두통, 편두통 외 두통, 두통이 없는 사람 이렇게 세개의 군으로 나누어 분석하였다.

결과:ICHD-2 기준에 따라 나눈 결과 총 연구대상의 5.2%에서 편두통군으로 분류되었고, 편두통군일수록 수면 주기성 성향이 늦었고 ($p=0.039$), 수면의 질이 낮았으며($p < 0.001$) 불면증 ($p < 0.001$), 주간 과다졸림증 ($p=0.028$)과 의미있는 상관 관계를 보여주었다. 늦은 수면 주기성 성향과 두통의 중증도 자체와는 무관하였다.

결론: 우리는 이 연구에서 주기성 성향과 두통의 관계를 대규모 일반 인구를 대상으로 보고자 하였다. 편두통군일수록 늦은 시각대에 수면을 취하려고 하는 주기성 성향을 보였고, 불면증, 주간 졸림증과 상관 관계를 보였으며 수면의 질이 낮았다.

Keywords: 주기성 성향, 두통, 편두통, 불면증, 수면의 질,

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