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Research paper

Heart rate variability and tension-type headache: A population-based cross-sectional study

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ABSTRACT

Background: The relationship between tension-type headache (TTH) and autonomic functions is poorly understood, although TTH is one of the most prevalent disorders in the general population. The aim of this study was to investigate the direct and indirect effects of TTH on the autonomic functions measured by heart rate variability (HRV).

Methods: This population-based cross-sectional study was carried out in the general population of Ulaanbaatar between July and September in 2020. After physical examination, trained researchers applied structured interviews to examine the remote history of TTH and mental distress, followed by a recording of HRV to detect autonomic activity. Psychological factors and the quality of life were measured using Hospital Anxiety Depression Scale (HADS), Pittsburgh Sleep Quality Index (PSQI), and the World Health Organization Quality of Life–Brief (WHOQOL-BREF). Binary logistic regression and GLM mediation model analysis were used to examine the effects of risk factors on the associations between TTH and autonomic functions.

Results: Among participants ($n = 217$, mean age=41.8 ± 11.5 years), a total of 117 (53.9%) participants had a remote history of TTH. The age and sex-adjusted prevalence was 43%. Groups did not differ statistically in the HRV indices. LF/HF (ratio of low-frequency to high frequency), the index of sympathovagal balance, was correlated with the HADS anxiety. TTH was associated with mental distress. Binary logistic regression analysis confirms the relationship suggesting that TTH was associated with increased likelihood of mental distress, and decreasing RMSSD (root mean square of the sum of the squares of differences between adjacent NN intervals) and pNN50 (NN50 divided by the total number of NN intervals) were the independent predictors of TTH. GLM mediation model indicated that the relationship between TTH and RMSSD was mediated by mental distress.

Conclusions: The present study suggests that mental distress is a critical factor in the association between TTH and autonomic dysfunction. Additionally, our findings demonstrate the influence of age and gender on TTH. These results highlight the need to understand the mechanisms underlying pathophysiology to facilitate targeted and efficacious prevention and management approaches for TTH.

Abbreviations: CI, Confidence interval; DBP, Diastolic blood pressure; GLM, Generalized linear models; HADS, Hospital Anxiety and Depression Scale; HF, High-frequency; HRV, Heart Rate Variability; LF, Low-frequency; LF/HF, Ratio of low-frequency to high frequency; NN50, Number of consecutive NN intervals that varied by more than 50 ms; pNN50, NN50 divided by the total number of NN intervals; PSQI, Pittsburgh Sleep Quality Index; QOL, Quality of life; RMSSD, Root mean square of the sum of the squares of differences between adjacent NN intervals; SD, Standard deviation; SBP, Systolic blood pressure; SDDN, Standard deviation of the normalized R-to-R (NN) intervals; TP, Total power; TTH, Tension-type headache; VLF, Very low-frequency; WHOQOL-BREF, World Health Organization Quality of Life–Brief Questionnaire.

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1. Introduction

Tension-type headache (TTH) is one of the most common disorders of the nervous system. According to the World Health Organization (WHO) reports, headaches cause a recognizable burden on sufferers including psychiatric manifestations, impaired quality of life, disability, and financial cost (Ashina et al., 2021a, 2021b;GBD, 2016 Headache Collaborators, 2018; GBD, 2019 Diseases and Injuries Collaborators, 2020). Recent data show that 44% of the adult population worldwide suffer from TTH and it is the third most prevalent disorder in the world, following dental caries and age-related hearing loss (GBD 2019 Diseases and Injuries Collaborators). Despite the relatively lower prevalence of TTH in the Asia-Pacific region (17.5%) (GBD, 2016 Headache Collaborators, 2018;Ge and Chang, 2023), a study conducted in Mongolia reported a notably higher prevalence of 29.1% (Luvsannorov et al., 2019). To improve the health service and prevention of headaches, it's important to determine possible causes and risk factors to avoid associated burdens of disease both in personal suffering and economic loss (Gustavsson et al., 2011; Pesa and Lage, 2004). However, little is known about the exact cause of TTH and most studies were hospital-based which is not adequate to project in the general population. Several contributing risk factors for TTH seem to be mental distress, anxiety, depression, sleep problems, and substance use (Ashina et al., 2021a, 2021b; Fumal and Schoenen, 2008). Of note, consisting evidence suggested that early life stress including childhood abuse/maltreatment may be one of the potential etiological factors for the development of headaches strongly associated with decreased quality of life (QOL) and suicidality (Anto et al., 2021; Elbers et al., 2017; Serafini et al., 2017; Stensland et al., 2014). Therefore, TTH was previously called stress headache, psychogenic headache, and muscle contraction headache pointing out its uncertain cause.

Mental distress can be measured more objectively and specifically than self-report questionnaires by analyzing changes in sympathetic and parasympathetic nervous system activities extrapolated through heart rate variability (HRV) analysis (Laborde S et al., 2017; Lkhagvasuren B et al., 2023). HRV measures the variation in time between successive heartbeats, reflecting the balance between the sympathetic and parasympathetic branches of the autonomic nervous system. The most frequently employed HRV indices include the standard deviation of NN intervals (SDNN), the root mean square of successive differences (RMSSD), and the ratio of low-frequency (LF) to high-frequency (HF) components (LF/HF). Higher SDNN values indicate a healthier autonomic function, and RMSSD indicates increased parasympathetic activity and better stress resilience, whereas LF/HF is utilized as an index of sympathovagal balance (Shaffer and Ginsberg, 2017). However, the relationship between HRV indices and TTH is poorly understood.

We hypothesized that mental distress contributes to the effect of TTH on HRV. The aim of this study was to investigate the direct and indirect effects of TTH on autonomic functions as measured by HRV in the general population.

2. Materials and methods

2.1. Study population and data collection

This population-based cross-sectional study was conducted between July and September in 2020 as a part of a nationwide multicenter, interdisciplinary, prospective, population-based cohort study to investigate brain-related disorders in the general population of Mongolia. The population of Mongolia was 3296,866 in 2019 based on data from the National Statistical Office of Mongolia. Approximately half the population lives in Ulaanbaatar, the capital city, and the remaining population lives in 4 rural regions (National Statistical Office of Mongolia, 2019). The cohort was chosen using multi-stage cluster sampling. In the first stage, we randomly selected primary sampling units within capital city. Geopolitical units studied were the following 8 districts of capital city Ulaanbaatar: Baganuur, Bayangol, Bayanzürkh, Chingeltei, Khan Uul, Nalaikh, Songino Khairkhan and Sukhbaatar. In the second stage, we chose 38 primary health centers of 8 districts in Ulaanbaatar. Primary health centers provide health care services to all individuals within certain geopolitical units where the entire population is registered by name, age, gender, education, employment, and household income.

The target population consisted of all individuals aged 18 or older living in Ulaanbaatar. The sampling size was calculated to be 384 using a confidence level (CI) of 95%, margin of error of 5%, design effect of 1.50, assumed prevalence of 5%, attrition rate of 20% for the population size of 1,024,632 individuals aged between 18 and 65 years in Ulaanbaatar. Among the invited individuals, 79 did not attend the procedure at a given date and time. A total of 305 participants were approached for eligibility after the aims and objectives of the study had been explained. Participants were excluded according to the following criteria: (i) who had an established diagnosis with severe diseases by physicians that occurred within 6 months; (ii) who had history of a traumatic brain injury; (iii) who had clinical symptoms of autonomic dysfunctions; (iv) who cannot maintain daily living regardless of employment. Participants were asked to undergo vital function tests and HRV recording followed by structured interviews by trained facilities. The study was administered in the official language Mongolian Cyrillic. A total of 45 were excluded and 43 had missing data on self-report questionnaires or inadequate HRV data recordings. The remaining 217 participants were included in the final analysis (Appendix 1). The institutional review board and Ethics committee of the Mongolian National University of Medical Sciences approved the study protocol and procedures for informed consent on 2020/03–05.

2.2. Questionnaires

The World Health Organization Quality of Life – Brief (WHOQOL-BREF) questionnaire is a 26-item self-report questionnaire that evaluated physical, mental, social, and environmental health functioning in the past 2 weeks prior to the questionnaire administration. It is one of the most commonly used health-related QOL questionnaires developed by the WHOQOL group in 1996 (World Health Organization DoMH, 1996). The WHOQOL-BREF questionnaire has been validated in Ulaanbaatar adult population using Mongolian version (Bat-Erdene et al., 2023). It is designed to measure an individual's QOL across four domains: physical health, psychological health, social relationships, and environment. The first two items represent the perception of overall quality of life and general health. Each item on the WHOQOL-BREF is rated on a 5-point Likert scale, with responses ranging from 1 to 5. The resulting domain scores will range from 4 (lowest QOL) to 20 (highest QOL), which can be transformed into a 0–100 scale. After transforming the domain scores, the endpoints range from 0 (lowest QOL) to 100 (highest QOL). There are no universally accepted cut-off values for the WHOQOL-BREF, as the instrument is designed to measure quality of life on a continuous scale rather than to categorize individuals into specific groups.

The Hospital Anxiety and Depression Scale (HADS) is a 14-item self-report questionnaire widely used to evaluate the severity of anxiety and depression symptoms in the past week. It has been developed by Zigmond and Snaith to identify cases of mental disorders such as anxiety and depression among patients in a nonpsychiatric hospital clinic. The questionnaire consists of 14 items, seven of them are for anxiety (HADS-A) and the remaining seven are for depression (HADS-D). Each item is rated on 4-point scale, with responses ranging from 0 to 3. To calculate the scores for the anxiety and depression subscales, the item scores will be summed within each subscale. The endpoints for each subscale score range from 0 (no symptoms) to 21 (maximum symptom severity). The ranges of cut-off scores for cases on each subscale are 0–7 or normal, 8–10 or mild disorder, 11–14 or moderate disorder, and 15–21 or severe disorder (Zigmond and Snaith, 1983). With a sample of Mongolian general population, Mongolian version of the HADS found to be valid and reliable (Tumurbaatar et al., 2021).

The Pittsburgh Sleep Quality Index (PSQI) is a 19-item self-report questionnaire designed to measure sleep quality and sleep disturbance over the past month in both clinical and non-clinical populations (Buysse et al., 1989). The 19 items are grouped into 7 components, including 1) sleep duration, 2) sleep disturbance, 3) sleep latency, 4) daytime dysfunction due to sleepiness, 5) sleep efficiency, 6) overall sleep quality, and 7) sleep medication use. Each of the sleep components yields a score ranging from 0 to 3, with 3 indicating the greatest dysfunction. The global score is calculated by summing the seven component scores. The endpoints for the global PSQI score range from 0 (good sleep quality) to 21 (poor sleep quality). In distinguishing good and poor sleepers, a global PSQI score > 5 yields a sensitivity of 89.6% and a specificity of 86.5%. We used a validated Mongolian version of PSQI (Tumurbaatar et al., 2023).

2.3. Physician Examination

Vital signs were determined as a physical health status and potential associations with mental health characteristics, as follows: 1) body temperature 2) systolic blood pressure (SBP) and diastolic blood pressure (DBP) 3) heart rate, and 4) arterial oxygen saturation. Temperature was measured at the forehead or wrist via an electric infrared thermometer gun (the Tida, TD-133, Guangzhou Feng Lei Electronic Technology, China). Blood pressure and heart rate were measured by an advanced blood pressure monitor (BP A6 PC, Microlife, Switzerland). Oxygen saturation was measured by pulse oximetry (PO40, Beurer, Germany). The measurement tools, except the thermometer, were produced by well-accepted companies, which follow international standards to ensure their accuracy and reliability. All procedures were non-invasive and were taken by trained personnel. Furthermore, body weight (kg) and height (cm) were measured. The body mass index (BMI) was calculated as the ratio of body weight to squared height, according to the WHO guidelines (WHO, 2023).

2.4. Structured interviews

2.4.1. A 17-item structured interview for a remote history of TTH

As shown in Appendix 2, the 17-item structured interview was developed using the operational diagnostic criteria of the International Classification of Headache Disorders-3 (ICHD-III) developed by the International Headache Society to identify a lifetime TTH in participants (Headache Classification Committee of the International Headache Society (IHS), 2018). The validity and reliability of ICHD-III criteria have been previously established through a multicenter clinical study, which provided evidence supporting the use of ICHD-III criteria for accurate and consistent diagnosis of tension-type headaches in diverse populations (Kong et al., 2018). Participants were considered to have TTH if they fulfilled criteria B through E (B: lasting from 30 min to 7 days; C: at least two of the four typical headache characteristics: bilateral pain, non-pulsating quality, mild-to-moderate pain intensity, and no aggravation by routine physical activity; D: not associated with nausea or vomiting, not associated with no more than one of photophobia and phonophobia, and E: not better accounted for by another ICHD-III diagnosis). We did not apply the frequency criterion A in the diagnosis of a remote history of TTH. Thus, patients with TTH evaluated in this study included those with infrequent TTH, frequent TTH, and chronic TTH. According to ICHD-III, if a participant's headache fulfilling the criteria for both TTH and probable migraine, the participant was considered to have TTH (Headache Classification Committee of the International Headache Society (IHS), 2018). Selected researchers completed a training program on conducting the interview and measuring the vital function indices. The average time for each interview was 21.2 ± 6.3 min.

2.4.2. A 13-item structured interview for identifying mental distress

We also measured mental distress using a structured interview by licensed psychiatrists, in addition to HRV recording. As shown in Appendix 3, the structured interview consisted of three sections. At first, the interviewer collected detailed life history, including family history, relationship history, developmental history, educational history, legal history, work history, lifestyle, circadian rhythms, and distressful incidences such as grief, violence, traumas, and other psychosocial factors. Second, medical history was collected including presenting problems, history of presenting problems (onset, severity, and stressor), information about any chronic medical condition, mental health problems or illnesses, suicide attempts, alcohol and substance abuse, psychotic episodes, and previous counseling. Every mentioned medical condition was double-checked with the participant's medical registration card, which stores all medical services received. Finally, a mental status examination was performed with a specially developed checklist. Major components assessed were: appearance, speech, eye contact, motor activity, emotion, mood, orientation impairment, memory impairment, attention, perception, suicidality, homicidality, delusions, behavior, insight, and judgment. Selected researchers were licensed psychiatrists and they were trained in the structured interview before the field study began. The interview was conducted in a separate room to protect individual`s privacy. All participants were informed about the confidentiality and anonymity of their participation. All interviews were noted. The average time for each interview was 36 ± 6.5 min. Although the structured interview has been tailored to the study population and offers a comprehensive assessment by licensed psychiatrists, the accuracy and reliability of the mental distress assessments cannot be generalizable due to the lack of prior validation.

2.5. Heart rate variability - short term recording

A short-term (5-minute) HRV analysis was completed according to the standard method described in detail in the literature (Force, 1996). The assessment was performed in the daytime to prevent the possible influence of circadian rhythm. During assessment, participants were instructed to sit calmly and to breathe in a normal rhythm. They were asked not to fall asleep, fidget, or make a special effort to notice any stimuli. We used an HRV analyzer (Dailycare Biomedical Inc, Taiwan) for the acquisition, storage, and processing of signals. The dataset was stored for further examination. A fast Fourier transformation was automatically performed. It extracts the data by the standard time-domain and frequency-domain parameters. Time-domain parameters include SDNN, RMSSD, and the proportion of adjacent sinus RR intervals differing by more than 50 ms (pNN50). SDNN is an overall indicator of HRV and reflects both sympathetic and parasympathetic activities, whereas RMSSD and pNN50 are related to parasympathetic activity. Frequency-domain parameters include the total power (TP), very low frequency (VLF), LF, HF, and LF/HF. TP indicates the overall HRV. VLF (0.0033–0.04 Hz) is proposed to sympathetic activity; LF (0.04–0.15 Hz) indicates sympathetic activity; HF (0.15–0.4 Hz) reflects parasympathetic activity; LF/HF measures the balance between sympathetic and parasympathetic activity. A higher LF/HF ratio indicates greater sympathetic activity, while a lower ratio suggests increased parasympathetic (Sammito and Bockelmann, 2016; Shaffer and Ginsberg, 2017). SDNN, RMSSD, pNN50, and the LF/HF ratio are widely recognized as the most frequently employed HRV indices for evaluating autonomic functions. Other HRV indices provide additional insights or subsidiary findings in relation to the primary outcomes.

2.6. Statistical analysis

Data were presented as mean $\pm$ standard deviation. The distributions of continuous variables were evaluated by the Kolmogorov-Smirnoff test. Differences between the groups in categorical variables were tested by the χ^2 test. Differences in continuous variables were assessed by the Student's t-test or Mann-Whitney u-test as appropriate. The correlation analyses between continuous variables were performed using Spearman's bivariate test, whereas between categorical variables were by Cramer's V coefficient. A binary logistic regression test was used to examine the relations of the factors with TTH. Statistical significance was set at $p < 0.05$, and all tests were two-tailed. Data were analyzed using SPSS v26.0 and JAMOVI v2.2.5.

3. Results

3.1. Demographic characteristics and TTH

This study included participants aged between 18 and 65 years (n = 217, mean age = 41.8 ± 11.5, 79.7% women). 37.8% of the participants held a bachelor's degree or above, 75.5% had income lower than $350, whereas 77.4% were married and 57.6% employed. Age group, gender, and living condition differences between TTH groups were occurred. Moreover, there were significant differences between DBP and BMI of the participants (Table 1).

3.2. HRV characteristics and TTH

Table 2 shows the HRV indices in total participants and both groups according to the remote history of TTH.

As shown in Table 2, participants with and without a remote history of TTH did not differ in HRV indices.

3.3. Relationship between TTH and HRV

Table 3 displays the results of Spearman's correlation analysis between HRV indices and main characteristics of interest.

LF/HF, the index of sympathovagal balance, was correlated with the HADS anxiety score.

Furthermore, as shown in Fig. 1, Cramer's V coefficient indicated that there was a direct relationship between TTH and mental distress.

Binary logistic regression was performed to elucidate the effects of factors independently affecting TTH (Table 4).

Binary logistic regression analysis suggested that TTH was associated with increased likelihood of mental distress, and decreasing RMSSD and pNN50 were the independent predictors of TTH.

Table 1
Prevalence of tension-type headache by demographic characteristics and vital function indices.

Characteristics		Total, n (%)		Tension-type headache				p value
				Yes		No		
Total, n (%)		217	(100.0)	117	(53.9)	100	(46.1)	
Gender, n (%)	Male	44	(20.3)	14	(31.8)	30	(68.2)	0.001
	Female	173	(79.7)	103	(59.5)	70	(40.5)	
Age-group, n (%)	18–25	18	(8.3)	3	(16.7)	15	(83.3)	0.007
	26–35	48	(22.1)	24	(50.0)	24	(50.0)	
	36–45	72	(33.2)	39	(54.2)	33	(45.8)	
	46–55	43	(19.8)	28	(65.1)	15	(34.9)	
	56 <	36	(16.6)	23	(63.9)	13	(36.1)	
Marital status, n (%)	Never-married	168	(77.4)	93	(55.4)	75	(44.6)	0.432
	Others[#]	15	(6.9)	9	(60)	6	(40)	
	Married	34	(15.7)	15	(44.1)	19	(55.9)	
Education, n (%)	Below bachelor's degree	135	(62.2)	78	(57.8)	57	(42.2)	0.187
	Bachelor's degree	69	(31.8)	31	(44.9)	38	(55.1)	
	Above bachelor's degree	13	(6.0)	8	(61.5)	5	(38.5)	
Employment, n (%)	Unemployed	92	(42.4)	54	(58.7)	38	(41.3)	0.226
	Employed	125	(57.6)	63	(50.4)	62	(49.6)	
Income, n (%)	< 175$	73	(33.6)	42	(57.5)	31	(42.5)	0.742
	175$– 350$	91	(41.9)	47	(51.6)	44	(48.4)	
	> 350$	53	(24.4)	28	(52.8)	25	(47.2)	
Living condition, n (%)	Ger horoolol*	112	(51.6)	68	(60.7)	44	(39.3)	0.038
	Apartment	105	(48.4)	49	(46.7)	56	(53.3)	
Physical examination, mean ± SD	Body temperature	36.5	± 0.3	36.5	0.3	36.6	± 0.3	0.330
	Heart rate	78.4	± 13.8	79.4	± 15.5	77.3	± 11.5	0.278
	Systolic Blood Pressure	127.8	± 20.1	128.9	± 21.2	126.6	± 18.7	0.413
	Diastolic Blood Pressure	80.6	± 13.0	82.3	± 13.2	78.6	± 12.5	0.036
	Oxygen saturation	94.7	± 2.4	94.6	± 2.6	94.9	± 2.2	0.373
	Body mass index	27.4	± 6.1	28.3	± 6.2	26.4	± 5.8	0.018
HADS, mean ± SD	Anxiety score	6.3	± 3.1	5.9	± 3.0	6.7	± 3.3	0.056
	Depression score	5.8	± 2.8	5.7	± 2.6	6.0	± 3.0	0.459
WHOQOL-BREF, mean ± SD	Physical	64.6	± 12.8	65.7	± 11.6	63.3	± 14.1	0.182
	Psychological	74.8	± 11.8	75.5	± 10.1	73.9	± 13.5	0.301
	Social	72.0	± 13.7	72.4	± 13.0	71.7	± 14.4	0.708
	Environmental	69.6	± 12.9	70.5	± 11.6	68.6	± 14.3	0.306
PSQI, mean ± SD	Sleep duration	0.80	± 0.99	0.94	± 1.00	0.65	± 0.96	0.034
	Sleep disturbance	1.00	± 0.55	1.02	± 0.55	0.99	± 0.54	0.712
	Sleep latency	1.21	± 0.89	1.18	± 0.89	1.25	± 0.90	0.553
	Sleepiness	1.11	± 0.60	1.16	± 0.56	1.05	± 0.64	0.186
	Sleep efficiency	0.93	± 1.08	0.98	± 1.09	0.88	± 1.07	0.491
	Overall sleep quality	0.17	± 0.56	0.17	± 0.55	0.17	± 0.57	0.981
	Sleep medication use	0.40	± 0.73	0.37	± 0.66	0.43	± 0.81	0.562
	Total score	5.63	± 3.09	5.81	± 3.04	5.42	± 3.15	0.354

p-values were analyzed with the Mann-Whitney or the Kruskal-Wallis tests, and independent t samples test.
[#] Others included re-married, co-habiting, separated, divorced, and widowed. * a community with no public water and sewer system. HADS: Hospital Anxiety and Depression Scale. PSQI: Pittsburgh Sleep Quality Index. SD: standard deviation. WHOQOL-BREF: World Health Organization Quality of Life – Brief Version.

Table 2
Heart rate variability indices among participants by tension-type headache, n = 217.

Components, mean ± SD	Total	Tension-type headache		p value
		Yes	No	
SDNN	33.4 ± 15.2	33.33 ± 16.55	33.57 ± 13.65	0.416
RMSSD	24.7 ± 13.4	24.05 ± 13.30	25.52 ± 13.55	0.285
NN50	23.7 ± 34.7	24.01 ± 36.50	23.36 ± 32.65	0.297
pNN50	7.33 ± 11.4	7.41 ± 11.83	7.25 ± 10.98	0.317
VLF	315.0 ± 449.0	347.89 ± 554.35	277.28 ± 282.65	0.955
LF	224.0 ± 326.0	235.98 ± 382.25	209.41 ± 219.89	0.440
HF	166.0 ± 286.0	174.28 ± 277.96	157.17 ± 296.33	0.777
TP	706.0 ± 828.0	759.19 ± 966.92	645.02 ± 632.83	0.701
LF/HF	2.09 ± 1.87	2.05 ± 1.92	2.13 ± 1.82	0.907

p-values were analyzed with the Student's *t*-test. HF: High-frequency. LF: Low-frequency. LF/HF: Ratio of low-frequency to high frequency. NN50: Number of consecutive NN intervals that varied by more than 50 ms. pNN50: NN50 divided by the total number of NN intervals. RMSSD: Root mean square of the sum of the squares of differences between adjacent NN intervals. SD: standard deviation. SDDN: Standard deviation of the normalized R-to-R (NN) intervals. TP: Total power. VLF: Very low-frequency.

GLM mediation model was used to analyze whether TTH alters RMSSD and pNN50 directly or through mental distress. As shown in Fig. 2, it indicated that the relationship between TTH and RMSSD was mediated by mental distress, whereas there was no significant direct relationship.

4. Discussion

The current study aimed to explore the relationship between TTH and HRV indices in a population-based sample. The results suggest that the effect of TTH on autonomic functions might be limited and mediated by mental distress. The demographic characteristics showed a diverse representation of participants with varying levels of education, income, marital status, and employment. Significant differences in age group, gender, and living conditions were found between TTH groups, as well as differences in diastolic blood pressure DBP and body mass index BMI.

In examining HRV indices, no significant differences were found between participants with and without a remote history of TTH. However, we found that TTH was associated with an increased likelihood of mental distress, and that decreasing RMSSD and pNN50 were independent predictors of TTH. This finding supports our hypothesis that TTH might be linked to altered autonomic nervous system function, as reflected by HRV indices. This result is consistent with a few studies that have found that individuals with headaches might have altered HRV, indicating an imbalance in autonomic nervous system function. Lower HRV has been reported in some individuals with tension-type headaches, suggesting that they may have reduced parasympathetic activity, increased sympathetic activity, or both. This imbalance in the autonomic nervous system could contribute to the development or exacerbation of tension-type headaches (Koenig et al., 2016). Earlier research has identified decreased parasympathetic activity in migraine patients, but not in TTH patients (Tabata et al., 2000). Specifically, the impact of

Table 3
Correlation analysis between the heart rate variability indices and risk factors, n = 217.

Characteristics	HRV indices								
	SDNN	RMSSD	NN50	pNN50	VLF	LF	HF	TP	LF/HF
Demographic characteristics									
Age	-0.011	-0.068	-0.122	**-0.141***	0.019	0.080	-0.033	0.021	-0.016
Physical examination									
Body temperature	0.006	0.023	0.025	0.050	-0.003	0.004	0.092	0.041	-0.100
Heart rate	0.054	0.052	0.064	0.075	-0.020	-0.040	-0.059	-0.048	-0.003
Systolic Blood Pressure	**0.153***	0.092	-0.055	0.003	0.172*	0.185**	0.177**	0.206**	-0.053
Diastolic Blood Pressure	0.075	0.024	-0.080	-0.027	0.111	0.107	0.084	0.115	-0.090
Oxygen saturation	-0.018	-0.020	-0.064	-0.060	0.022	0.044	0.007	0.027	0.153*
Hospital Anxiety and Depression Scale (HADS)									
Anxiety score	0.082	0.089	0.125	0.104	-0.005	-0.004	-0.056	-0.028	0.136*
Depression score	-0.096	-0.020	0.107	0.066	-0.172*	-0.150*	-0.164*	-0.187**	0.082
World Health Organization Quality of Life – Brief Version (WHOQOL-BREF)									
Physical	0.089	0.067	0.130	0.090	0.039	0.058	0.038	0.052	-0.039
Psychological	0.021	-0.026	-0.005	-0.039	0.022	0.080	0.016	0.044	0.038
Social	0.053	0.025	0.064	0.036	-0.011	0.009	0.007	0.003	0.006
Environmental	0.094	0.103	**0.134***	0.080	0.064	0.175**	0.079	0.122	-0.050
Pittsburgh Sleep Quality Index (PSQI)									
Sleep duration	-0.095	-0.052	0.015	0.008	-0.111	-0.084	-0.101	-0.110	0.002
Sleep disturbance	0.153*	0.076	0.119	0.113	0.130	0.074	0.031	0.080	0.081
Sleep latency	0.066	0.059	0.103	0.072	0.038	-0.013	0.002	0.007	-0.079
Sleepiness	0.061	0.077	0.092	0.055	0.038	0.112	0.103	0.100	-0.035
Sleep efficiency	0.006	0.045	0.074	0.084	-0.031	0.021	0.001	-0.001	-0.054
Overall sleep quality	-0.094	-0.047	-0.055	-0.062	-0.067	0.005	-0.025	-0.029	-0.037
Sleep medication use	0.174*	0.133	0.113	0.118	0.214**	0.116	0.095	0.149*	-0.011
Global score	0.054	0.068	0.116	0.100	0.033	0.040	0.012	0.030	-0.043

p-values were calculated using the Spearman's rank order correlation.
*$p < 0.05$, **$p < 0.01$. HF: High-frequency. LF: Low-frequency. LF/HF: Ratio of low-frequency to high frequency. NN50: Number of consecutive NN intervals that varied by more than 50 ms. pNN50: NN50 divided by the total number of NN intervals. RMSSD: Root mean square of the sum of the squares of differences between adjacent NN intervals. SDDN: Standard deviation of the normalized R-to-R (NN) intervals. TP: Total power. VLF: Very low-frequency.

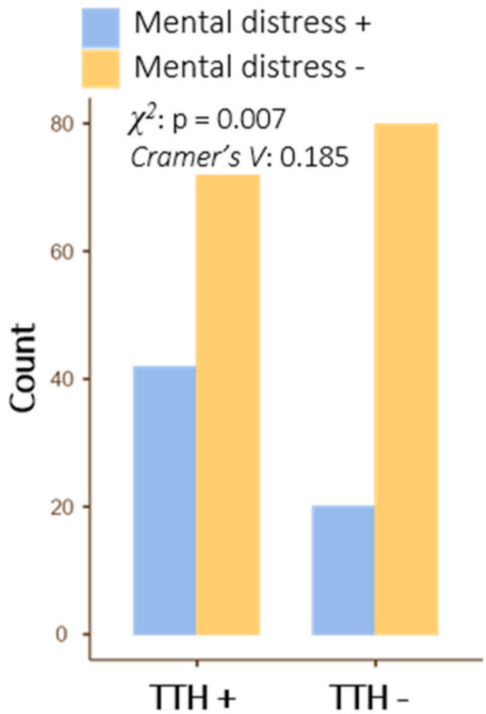

Fig. 1. Relationship between TTH and mental distress. The chi-square test indicated that TTH is associated with mental distress (Cramer's V = 0.185, p = 0.007).

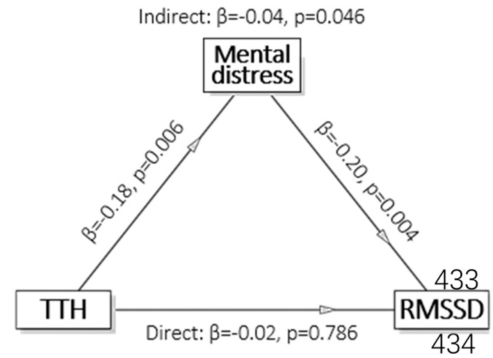

Fig. 2. GLM mediation model for the relationship between TTH and RMSSD by mediation of mental distress The mediation model indicated that the indirect pathway from TTH to RMSSD through mental health showed a significant relationship (p = 0.046).

TTH on parasympathetic activity was mediated by mental distress; however, TTH did not mediate the effect of mental distress on autonomic functions. Intriguingly, sympathovagal imbalance, as indicated by the LF/HF ratio, correlated with anxiety, in line with recent studies (Cheng et al., 2022). In detail, the effect of TTH on parasympathetic activity was mediated by mental distress, however, TTH was not mediating the effect of mental distress on autonomic functions. Interestingly, the sympathovagal imbalance, indicated by LF/HF, was correlated with anxiety in line with previous studies (Agelink et al., 2002). Further analysis using a GLM mediation model showed that the relationship between TTH and RMSSD was mediated by mental distress, while no significant direct relationship was found. This suggests that mental distress might play a key role in the association between TTH and HRV indices, potentially highlighting the importance of addressing mental health factors in the prevention and management of tension-type headaches.

In our study, age and gender significantly affected TTH which was consistent with previous studies suggesting that increased parasympathetic activity measures caused by the low sympathetic tone in middle-aged women compared to men (Bonnemeier et al., 2003; Fuensalida-Novo et al., 2020). It is also reported that females show greater parasympathetic activity compared to males due to the effects of estrogen (Du et al., 2006; Koenig et al., 2016). In contrast to previous reports, sleep quality showed no effect on autonomic functions in participants with a remote history of TTH (Gass and Glaros, 2013).

We found that anxiety, depression, sleep quality, and quality of life measured by the HADS, PSQI, and WHOQOL-BREF, did not differ between the groups. This finding contrasts with previous hospital-based studies, which reported higher levels of anxiety, depression, impaired sleep quality, and reduced quality of life in TTH patients compared to controls (Balottin et al., 2013; Sullivan et al., 2019; Wang et al., 2001). The discrepancy in findings may be attributed to the difference in study populations, as hospital-based studies typically involve more severe TTH cases requiring hospitalization, whereas our population-based study

Table 4
Binary logistic regression analysis on risk factors associated with tension-type headache, n = 217.

						95% CI	
Predictor	Estimate	SE	Z	p value	OR	Lower	Upper
Intercept	-11.515	21.134	-0.545	0.586			
Age	-0.052	0.016	-3.339	< .001	0.950	0.921	0.979
Gender	-0.999	0.421	-2.374	0.018	0.368	0.161	0.840
Heart rate	-0.021	0.013	-1.638	0.101	0.979	0.955	1.004
Systolic Blood Pressure	0.002	0.013	0.143	0.886	1.002	0.977	1.027
Diastolic Blood Pressure	-0.026	0.020	-1.330	0.184	0.974	0.937	1.013
Oxygen saturation	0.025	0.065	0.389	0.697	1.026	0.903	1.165
Mental_distress	0.754	0.378	1.996	0.046	2.126	1.014	4.457
Depression score (HADS)	0.002	0.064	0.024	0.981	1.002	0.884	1.134
Sleep quality (PSQI)	0.059	0.053	1.122	0.262	1.061	0.957	1.177
Physical (WHOQOL-BREF)	-0.015	0.017	-0.874	0.382	0.986	0.954	1.018
Psychological (WHOQOL-BREF)	0.006	0.021	0.300	0.764	1.006	0.966	1.048
Social (WHOQOL-BREF)	0.018	0.018	1.003	0.316	1.018	0.983	1.053
Environmental (WHOQOL-BREF)	-0.020	0.019	-1.050	0.294	0.981	0.946	1.017
SDNN	-0.012	0.018	-0.692	0.489	0.988	0.954	1.023
RMSSD	-0.075	0.038	-2.001	0.045	1.078	1.002	1.161
pNN50	-0.084	0.036	-2.365	0.018	0.919	0.857	0.986

p-values were tested using the binary logistic regression. CI: confidence interval. HADS: Hospital Anxiety and Depression Scale. OR: odds ratio. PSQI: Pittsburgh Sleep Quality Index. SE: standard error. pNN50: NN50 divided by the total number of NN intervals. RMSSD: Root mean square of the sum of the squares of differences between adjacent NN intervals. SDDN: Standard deviation of the normalized R-to-R (NN) intervals. WHOQOL-BREF: World Health Organization Quality of Life – Brief Version. Z: regression coefficient.

likely captured a more diverse and potentially milder range of TTH patients.

There were several limitations to this study. First, we did not gather comprehensive data on factors such as medication use, alcohol consumption, smoking, and physical activity before conducting the HRV recordings, which could potentially affect HRV measurements. Second, due to time constraints and the need to account for circadian rhythm influences, we employed short-term HRV recordings at rest. A more rigorous evaluation of autonomic activity could be achieved using extended data collection periods, such as 3-day Holter monitoring. Third, the absence of headache frequency data raises the possibility that our study population may have predominantly included individuals with infrequent TTH, thereby influencing the results. Moreover, the cross-sectional design of this study limits the ability to infer causal relationships between TTH and HRV indices.

Future research should aim to elucidate the underlying mechanisms linking stress-induced autonomic dysfunction and TTH, as this understanding could help identify potential targets for intervention and treatment strategies. Evaluating the effectiveness of mental health interventions in alleviating TTH symptoms and restoring autonomic balance is another important area of exploration. Longitudinal studies that assess the temporal relationship between changes in HRV indices, mental distress, and TTH symptomatology may provide valuable insights into potential causal pathways. Comparisons between population-based and hospital-based studies could also contribute to a deeper understanding of how TTH severity impacts HRV indices and mental health outcomes. Pursuing these research directions may inform the development of more effective prevention and management strategies for TTH patients, potentially improving their QOL and overall well-being.

5. Conclusions

The present study suggests that mental distress is a critical factor in the association between TTH and autonomic dysfunction. Additionally, our findings demonstrate the influence of age and gender on TTH. These results highlight the need to understand the mechanisms underlying pathophysiology to facilitate targeted and efficacious prevention and management approaches for TTH.

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CRediT authorship contribution statement

B.L. conceived and designed the study; E.T., T.A., M.D., and G.T. performed and collected data; E.T., E.B., G.G., and G.T. analyzed the data; T.J and D.B. contributed reagents and materials; B.L., T.J., T.O. and C.E. reviewed and edited the paper; B.L. and E.T. wrote the paper.

Declaration of Competing Interest

The authors declare no conflict of interest.

Data Availability

Data sharing is not applicable.

Acknowledgments

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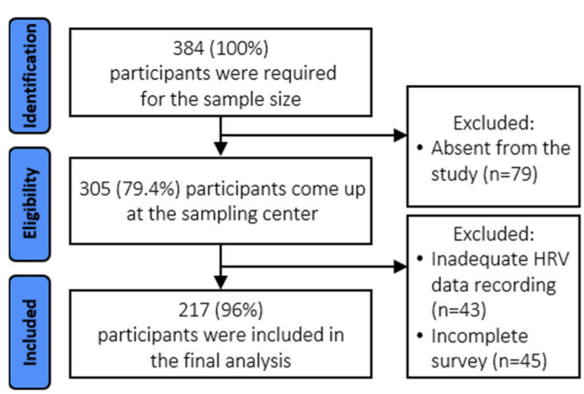
Compliance with ethical standards

The institutional review board and Ethics committee of the Mongolian National University of Medical Sciences approved the study protocol and procedures for informed consent on 2020/03–05.

Informed consent statement

Written informed consent was obtained from all participants.

Appendix 1. Study flowchart



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HRV: heart rate variability.

Appendix 2. A 17-item structured interview for a remote history of tension-type headache

Question	Answer		
I. Identifying Information			
1.	Name of interviewer		
2.	Code of participant		
II. Screening question for tension-type headache			
1.	Have you ever been diagnosed with tension-type headache by physicians?	Yes	○
		No	○
III. Clinical features of tension-type headache			
A.	Frequency of headache (at least one of the three characteristics):	Yes	○
	• At least 10 episodes of headache occurring on $<$ 1 day per month on average ($<$12 days per year);	No	○
	• At least 10 episodes of headache occurring on 1–14 days per month on average for $>$ 3 months ($\geq$12 and $<$180 days per year);		
	• Headache occurring on $\geq$ 15 days per month on average for $>$ 3 months ($\geq$180 days per year)		
B.	The pain is lasting from 30 min to 7 days.	Yes	○
		No	○
C.	Quality of pain (at least two of the four characteristics):		○
1.	The pain is typically bilateral.	Yes	○
		No	○
2.	The pain is pressing or tightening in quality (non-pulsating).	Yes	○
		No	○
3.	The pain is mild to moderate intensity.	Yes	○
		No	○
4.	The pain does not worsen with routine physical activity.	Yes	○
		No	○
D.	Association of pain attacks (yes to both)		○
1	The pain is not associated with nausea or vomiting.	Yes	○
		No	○
2.	The pain is not associated with more than one of photophobia and phonophobia.	Yes	○
		No	○
E.	The pain is not better accounted for by another ICHD-III diagnosis.	Yes	○
		No	○
*	The pain is associated with increased pericranial tenderness on manual palpation.	Yes	○
		No	○
IV. Diagnostic Criteria			
If answered YES to question A, B, C (2 out of 4), D, and E is considered as tension-type headache.			
V. Diagnosis			
1.	Tension-type headache G44.2 (ICD-10)		○
2.	Other (write down)		○
Comment: What is the participant`s insight of the illness?			
Signature: Date:			

* This item is not included in the diagnosis of tension-type headache. ICHD-III: International Classification of Headache Disorders-3. ICD-10: International Classification of Diseases-10.

Appendix 3. A 13-item structured psychiatric interview for mental distress

Name:		Interviewer:				
Stage I. Life history:						
Stage II. Medical history:						
Stage III. Mental status examination:						
1.	Appearance	o Neat	o Inappropriate	o Dirty	o Unusual	o Other
2.	Speech	o Normal	o Pressured	o Slow	o Irrational	o Other…
3.	Eye Contact	o Direct	o Avoidant	o Other…		
4.	Motor Activity	o Normal	o Restless	o Tic	o Slowed	o Other
5.	Mood	o Euthymic	o Anxious	o Depressed	o Angry	o Euphoric
6.	Orientation impairment	o None	o Place	o Object	o Person	o Time
7.	Memory impairment	o None	o Short-term	o Long-term	o Other…	
8.	Attention	o Good	o Distracted	o Other…		
9.	Perception change	o Hallucination	o Derealization	o Depersonalization	o Illusion	o Metamorphopsia
10.	Thought change	o Suicidal	o Homicidal	o Delusional	o Paranoia ideation	
11.	Behavior	o Normal	o Agitated	o Hyperactive	o Aggressive	o Withdrawn
12.	Insight	o Good	o Fair	o Poor		
13.	Judgement	o Good	o Fair	o Poor		

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