Systematic Review

Associations Between Headache (Migraine and Tension-Type Headache) and Psychological Symptoms (Depression and Anxiety) in Pediatrics: A Systematic Review and Meta-analysis

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Background: There have been no recent meta-analysis studies on specific psychological symptoms (depression and anxiety) according to the type of primary headache disorder in children and adolescents.

Objectives: We performed a meta-analysis of various psychodiagnostic scales. Psychological symptoms of primary headache disorders have been reported in previous studies.

Study Design: A systematic review and meta-analysis.

Methods: We conducted systematic reviews using the PubMed, Embase, Cochrane Library, and Scopus databases up to October 19, 2022. Ten studies were selected by applying the inclusion criteria. The psychological symptoms (depression and anxiety) of children and adolescents with migraine and tension-type headache (TTH) were compared with those of healthy controls using scale scores. All statistical analyses of the pooled data were performed using RevMan 5.3 software.

Results: Psychodiagnostic tools to assess depression scored higher in patients with migraine than in healthy controls; however, most anxiety-related scores were not significantly different between the migraine and control groups. In contrast, anxiety-related scores were higher in patients with TTH than in healthy controls, but the score to measure the degree of depressive symptoms was not significantly different from the control group in patients with TTH.

Limitations: A limited number of studies for each scale were included. In addition, each scale has different sensitivities and specificities, which may have affected the results. In addition, we did not evaluate the differences in psychological symptoms according to the frequency and severity of headaches.

Conclusions: Depression is more associated with migraine; whereas, anxiety is more associated with TTH than healthy controls. Therefore, the screening and assessment of psychological symptoms should be performed in children and adolescents with primary headache disorders.

Key words: Headache, migraine, tension-type headache, depression, anxiety, children, adolescents

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Headache is a common neurological problem in children and adolescents that can lead to a decreased quality of life. The prevalence of headache increases throughout childhood, and peaks between the ages of 11 and 13 years in both genders (1,2). In Korea, the prevalence of headache among

elementary school students was 29.1%, although a significant difference exists in the prevalence of each study worldwide (3). Headaches are divided into 2 types, primary and secondary, depending on their etiology. Primary headaches do not occur due to other disorders and account for the majority of headaches (4-6). The 2 most common primary headache types are migraines and tension-type headaches (TTH) (7).

Primary headache disorders in children and adolescents generally have a good clinical progress; however, recurrent or chronic diseases can interfere with daily activities and lead to negative emotional states. Numerous studies (8-11) over the past decades have reported a relationship between headaches and psychopathology in children and adolescents. Longitudinal population-based studies (12-14) conducted in Norway using a questionnaire to evaluate psychopathological symptoms found that both depressive and anxiety symptoms were associated with recurrent headaches.

This study aimed to investigate the association between specific psychological symptoms, such as depression and anxiety, in pediatric patients with migraine and TTH. We reviewed studies using various psychodiagnostic tools in this meta-analysis for a detailed evaluation of depression and anxiety.

Methods

Search Strategy

This meta-analysis was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines. The protocol for this review was registered with the International Platform of Registered Systematic Review and Meta-analysis Protocols (INPLASY, registration number: INPLASY2022100078). Relevant articles, published by October 19, 2022, were systematically searched using the PubMed, Embase, Cochrane Library, and Scopus databases. The search terms were as follows: (headache OR migraine OR tension headache OR TTH) AND (depression OR anxiety) AND (children OR adolescents). A detailed search strategy is presented in Supplementary 1.

Description of Scales

Several psychodiagnostic scales have been used to assess the mental health of children and adolescents (particularly for depression and anxiety).

Children's Depression Inventory (CDI) is a self-report inventory devised by Kovacs (15-16)_and Beck et al (18) to measure children's level of depression. It is used in children and adolescents between the ages of 7 and 17 years.

Beck's Depression Inventory (BDI) is a 21-question multiple-choice self-report inventory measuring the severity of depression, which was developed by Upton (17) and Beck et al (18).

Multidimensional Anxiety Scale for Children (MASC) is a 39-item, 4-point Likert-style self-report scale completed by children to score symptoms of anxiety (19,20).

Screen for Child Anxiety-Related Disorders (SCARED) is a child and parent self-report instrument used to assess childhood anxiety (21,22).

State-Trait Anxiety Inventory (STAI), developed by Spielberger et al (24), is a 4-point Likert-type scale composed of a 40-item self-report questionnaire to assess the level of trait and state anxiety (23).

Beck Anxiety Inventory (BAI) consists of 21 self-reported questionnaire items and is a scale for measuring the severity and level of anxiety (25).

Study Selection

Studies that met the following criteria were included in this meta-analysis: (1) pediatric patients aged < 19 years, (2) patients with migraine and TTH diagnosed using the International Headache Society criteria, (3) evaluation of the association between headache (migraine or TTH) and psychological symptoms (depression and anxiety), (4) comparison between the group with headache (migraine or TTH) and control group, (5) use of tools to evaluate the degree of depression or anxiety, and (6) written in English. The exclusion criteria were as follows: (1) nonoriginal articles, such as review articles, case reports, letters, editorials, or conference presentations, and (2) studies with insufficient data or results. Two independent reviewers (HJL and MCC) excluded articles after reviewing their titles and abstracts, and full-text assessments were performed to exclude articles that did not fulfill the selection criteria. The 2 reviewers attempted to resolve any discrepancies through consensus. If necessary, a third reviewer (SYK) was considered to resolve the disagreement.

Data Extraction

All data were independently extracted by 2 reviewers (HJL and MCC). The data were acquired using a standard data collection format. The following data were recorded from eligible studies: (1) name of the first author, (2) publication year, (3) type of study, (4) number of patients, (5) patient age, (6) type of headache, (7) clinical evaluation tools, and (8) results of the

selected studies. For depression, the CDI and BDI results were extracted for the meta-analysis. For anxiety, the MASC, SCARED, STAI, and BAI scores were extracted.

Quality Assessment

The methodological quality of the selected studies was assessed using the Newcastle–Ottawa Scale (NOS). The NOS comprises 3 assessment categories: patient selection, group comparability, and outcome or exposure assessment. The quality of each study was graded as low (0-3 points), moderate (4-6 points), or high (7-9 points). All disagreements were resolved by a consensus.

Statistical Analyses

All statistical analyses of the pooled data were performed using Review Manager software (Version 5.3; http://tech.cochrane.org/revman). I^2 statistics were used to measure the extent of inconsistency among the meta-analysis results and assess the heterogeneity between studies. The I^2 percentages of approximately 25% indicate low heterogeneity, 50% indicate moderate heterogeneity, and 75% indicate high heterogeneity. Pooled data were considered homogeneous if I^2 was < 50%, and a fixed-effects model was used for data analysis. Conversely, if I^2 was 50% or more, significant heterogeneity exists, and a random-effects model was used. The results of the meta-analysis were considered to be statistically significant at $P < 0.05$.

Funnel plots were used to determine the publication bias of individual studies in this meta-analysis based on pooled estimates. Egger's test was performed to ensure symmetry of the funnel plot. Possible publication bias was considered when the result of Egger's test was $P < 0.05$. Publication bias analysis was performed using R version 4.1.2.

Results

Study Selection

A total of 13,290 studies were identified using the designated search terms, and 1,994 duplicate studies were removed. After confirming the titles and abstracts of 11,296 initially identified studies, 11,240 that did not meet the inclusion criteria were excluded. The remaining 50 studies were evaluated for eligibility, and 40 were excluded for the following reasons: (1) 20 had no control group, (2) 3 did not classify the headache types, (3) 3 did not use psychodiagnostic tools, (4) 4 used psychodiagnostics tools that were not available for meta-analysis, (5) 7 did not diagnose headache according to the diagnostic criteria, and (6) 3 were excluded because they could not be used for analysis owing to insufficient data (no mean values = 1, no SD values =1, neither mean nor SD values =1). Finally, 10 studies were selected for this meta-analysis (Fig. 1) (26-35). The characteristics of the selected studies are presented in Table 1.

Results of the Meta-analysis Evaluating the Association Between Migraine and Psychological Symptoms (Depression and Anxiety)

In the meta-analysis of the differences in the results of CDI between the migraine and control groups, the random-effect model was used because the I^2 value was 71%. The CDI scores were significantly higher in the migraine group than in the control group (degrees of freedom [df] = 6; standardized mean difference [SMD], 0.46; 95% CI, 0.16-1.76; $P = 0.003$) (Fig. 2A). In the meta-analysis of the

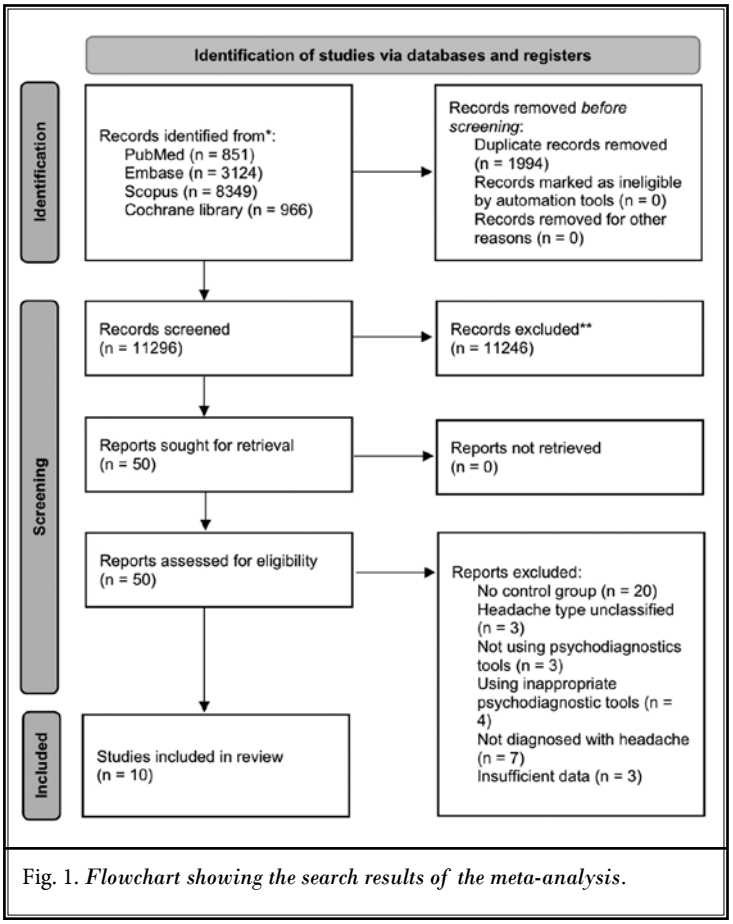

Fig. 1. *Flowchart showing the search results of the meta-analysis.*

Table 1. *Summary of the included studies.*

First Author	Year of Publication	Patients (n, mean age ± SD (y), M:W)	Headache Type	Headache Fiagnosis	Psychodiagnostic tools
Mazzone et al[26]	2006	Migraine: 67, 11.13 ± 1.90, 33:34 TTH: 47, 11.11 ± 1.59, 28:19 Control: 36, 10.35 ± 2.35, 20:16	Migraine, TTH	ICHD II	CDI, MASC
Vannatta et al[27]	2008	Migraine: 47, 11.82 ± 1.80, 26:42 Control: 46, 12.01 ± 1.85, 25:42	Migraine, TTH	ICHD II	CDI
Anttila et al[28]	2004	Migraine: 59, 13.5 ± 0.3, 27:32 TTH: 65, 13.6 ± 0.4, 44:21 Control: 59, 13.5 ± 0.3, 22:37	Migraine, TTH	IHS criteria (ICHD I)	CDI
Reale et al[29]	2011	BPVC: 21, 10.52 ± 3.14, 9:12 Migraine: 20, 10.70 ± 2.00, 10:10 Control: 19, 10.50 ± 2.28, 7:12	Migraine	ICHD II	CDI, MASC
Kandemir et al[30]	2018	Migraine: 50, 14.6 ± 2.62, 14:36 Control: 50, 13.46 ± 2.77, 13:37	Migraine	ICHD III beta	CDI, SCARED
Smith et al[31]	2003	Migraine: 179, 13.6 ± 2.0, 72:107 Chronic fatigue: 97, 15.0 ± 1.8, 29:68 Control: 32, 13.5 ± 1.0, 14:18	Migraine	IHS criteria (ICHD I)	CDI, STAI
Öztop et al[32]	2016	Migraine: 35, 12.2 ± 1.95, 9:26 Control: 35, 12.2 ± 1.95, 9:26	Migraine	ICHD II	CDI, STAI
Arita et al.[33]	2013	Episodic migraine: 44, 15.6 ± 2.2, N/A Chronic migraine: 46, 15.4 ± 2.3, N/A Control: 47, 16.1 ± 1.8, N/A	Migraine	ICHD II	BDI
Uçar et al[34]	2020	Migraine: 71, 14.45 ± 2.48, 16:55 Control: 41, 15.24 ± 1.67, 15:26	Migraine	ICHD III beta	SCARED
Bektaş et al[35]	2015	Migraine: 550, 14.2 ± 2.59, 235:315 Probable migraine: 523, 13.8 ± 2.64, 225:298 TTH: 883, 14.0 ± 2.59, 421:462 Other headaches: 157, 14.2 ± 2.55, 70:87 Control: 3242, 13.0 ± 2.65, 1696:1546	Migraine, TTH	ICHD II	BAI

Abbreviations: TTH, tension-type headache; BPVC, benign paroxysmal vertigo of childhood.

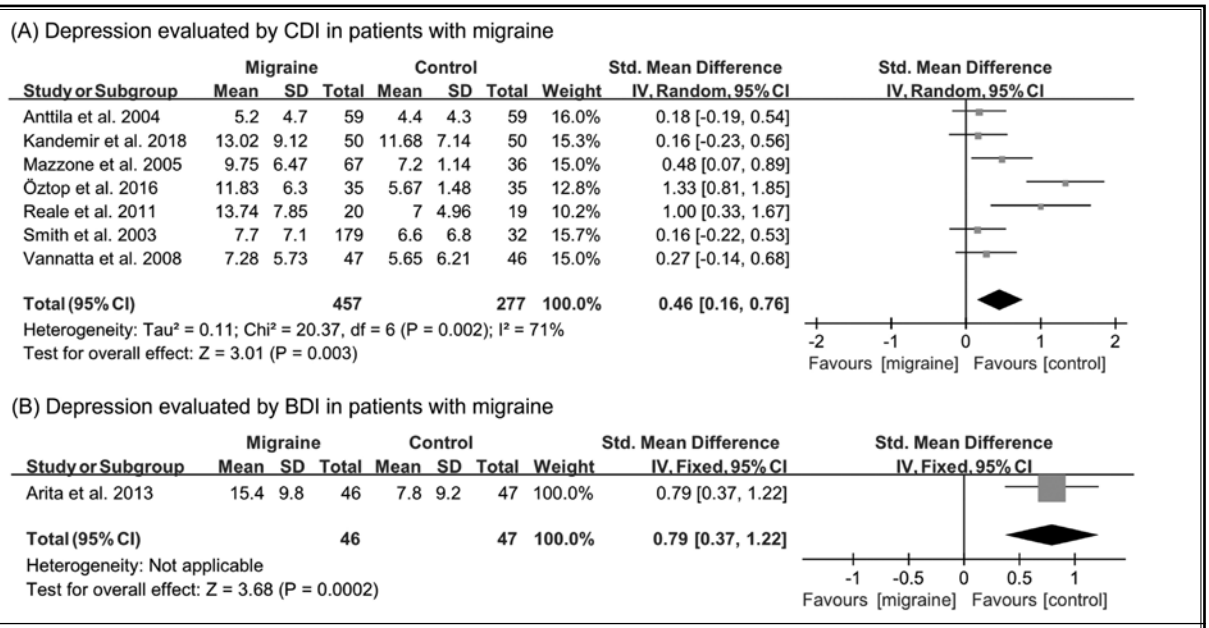

Fig. 2. *Forest plot showing the results of the correlation between migraine and depression.*

differences in the results of the BDI between the migraine and control groups, the BDI scores were significantly higher in the migraine group than in the control group (SMD, 0.79; 95% CI, 0.37-1.22; $P < 0.001$) (Fig. 2B).

In the meta-analysis of the differences in the results of the MASC between the migraine and control groups, the random-effect model was used because the I^2 value was 90%. The MASC scores were not significantly different between the migraine and control groups (df = 1; SMD, 1.14; 95% CI, -0.22 to 2.51; $P = 0.01$) (Fig. 3A). In the meta-analysis of the differences in the results of SCARED between the migraine and control groups, the random-effect model was used because the I^2 value was 87%. The SCARED scores were not significantly different between the migraine and control groups (df = 1; SMD, 0.45; 95% CI, -0.33 to 1.24; $P = 0.26$) (Fig. 3B). In the meta-analysis of the differences in the results of the STAI between the migraine and control groups, the random-effect model was used because the I^2 value was 60%, and a significant difference in the STAI scores was not observed (df = 2; SMD, 0.42; 95% CI, -0.05 to 0.89; $P = 0.08$) (Fig. 3C). Regarding the meta-analysis of the differences in the results of the BAI, the scores in the migraine group were significantly higher than those in the control group (SMD, 0.39; 95% CI, 0.30-0.49; $P < 0.001$) (Fig. 3D).

Results of the Meta-analysis Evaluating the Association Between TTH and Psychological Symptoms (Depression and Anxiety)

In the meta-analysis of the differences in the re-

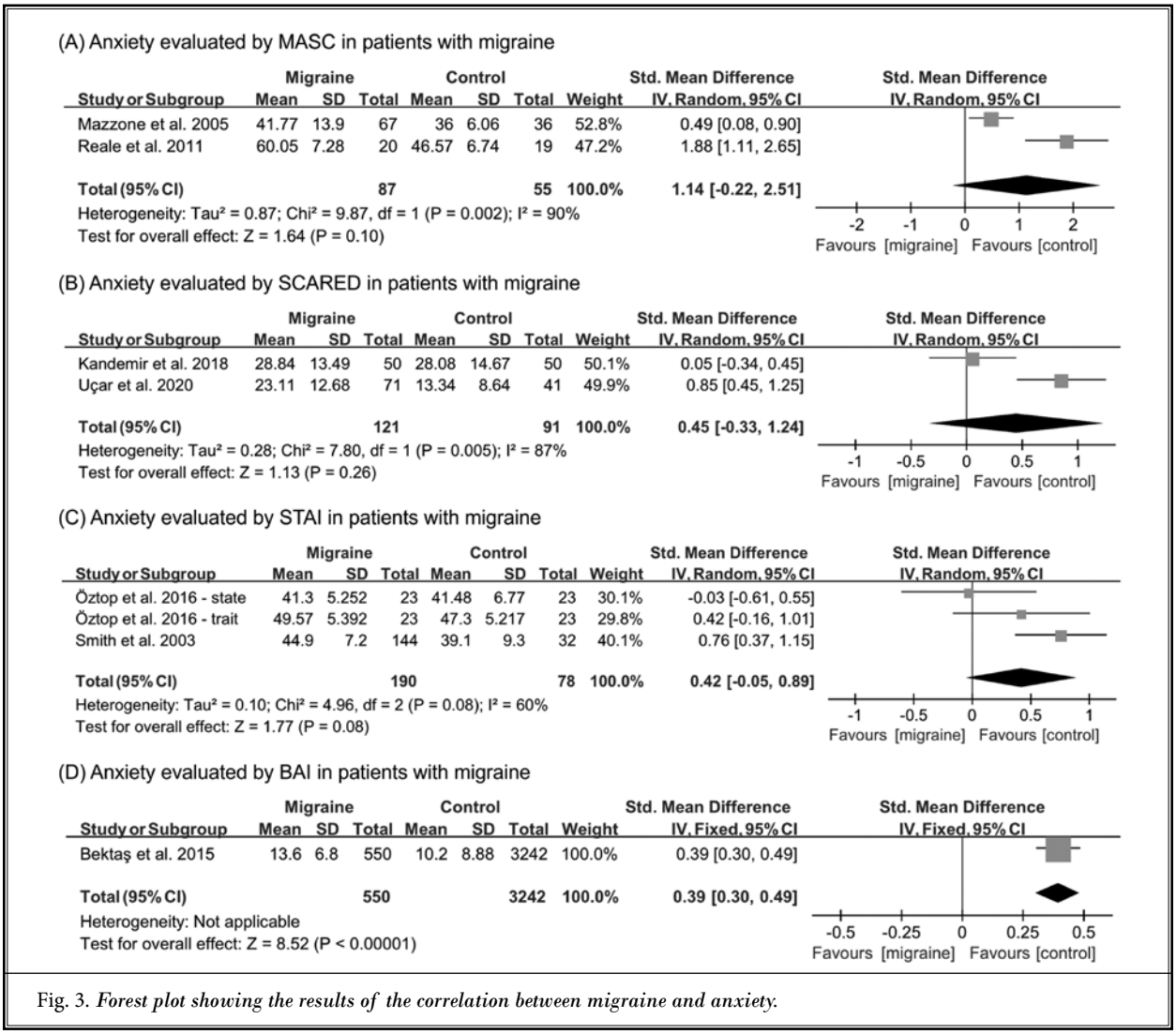

Fig. 3. *Forest plot showing the results of the correlation between migraine and anxiety.*

sults of CDI between the migraine and control groups, the random-effect model was used because the I^2 value was 79%, and the CDI scores were not significantly different between the TTH and control groups (df = 1; SMD, 0.40; 95% CI, -0.22 to 1.03; *P* = 0.21) (Fig. 4A).

In the meta-analysis of the differences in the results of the MASC and BAI between the TTH and control groups, the scores of the MASC and BAI were significantly higher in the TTH group than those in the control group (MASC, SMD, 0.71; 95% CI, 0.26-1.16; *P* = 0.002; BAI, SMD, 0.86; 95% CI, 0.79-0.94) (Figs. 5A and 5B).

Assessment of the Study Quality

For each evaluation item of the NOS, one point was given to each asterisk to calculate the summed score. Of the 10 included studies, one was of low quality (33), 8 (26-29,31,32,34,35) were of moderate quality, and one was of high quality (30). In the domain of patient selection, case definition (26,27,29-35) and control selection (26-33,35) were reported in 9 studies. However, it has been poorly reported in the domain of case representativeness and control definition. In the domain of comparability of the groups, 5 studies (27,29,30,32,34) were evaluated to have well controlled for confounding variables. Although the method of measuring the outcomes of the cases and controls in all studies was the same, there was a risk of potential bias because most studies used self-report questionnaires only. In addition, only 3 studies (30,32,34) properly accounted for the nonresponse rates (or explanations for dropouts). The quality assessment results are presented in Table 2.

Publication Bias

The funnel plots did not show significant asymme-

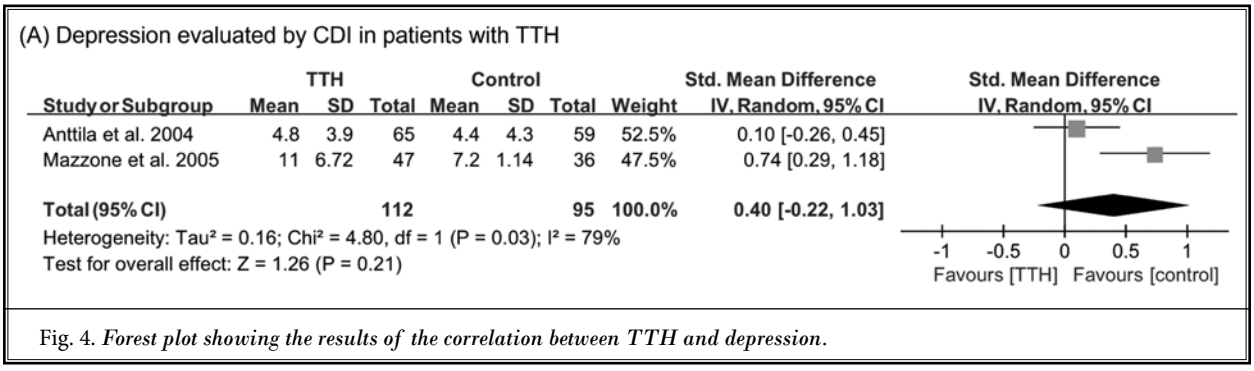

Fig. 4. *Forest plot showing the results of the correlation between TTH and depression.*

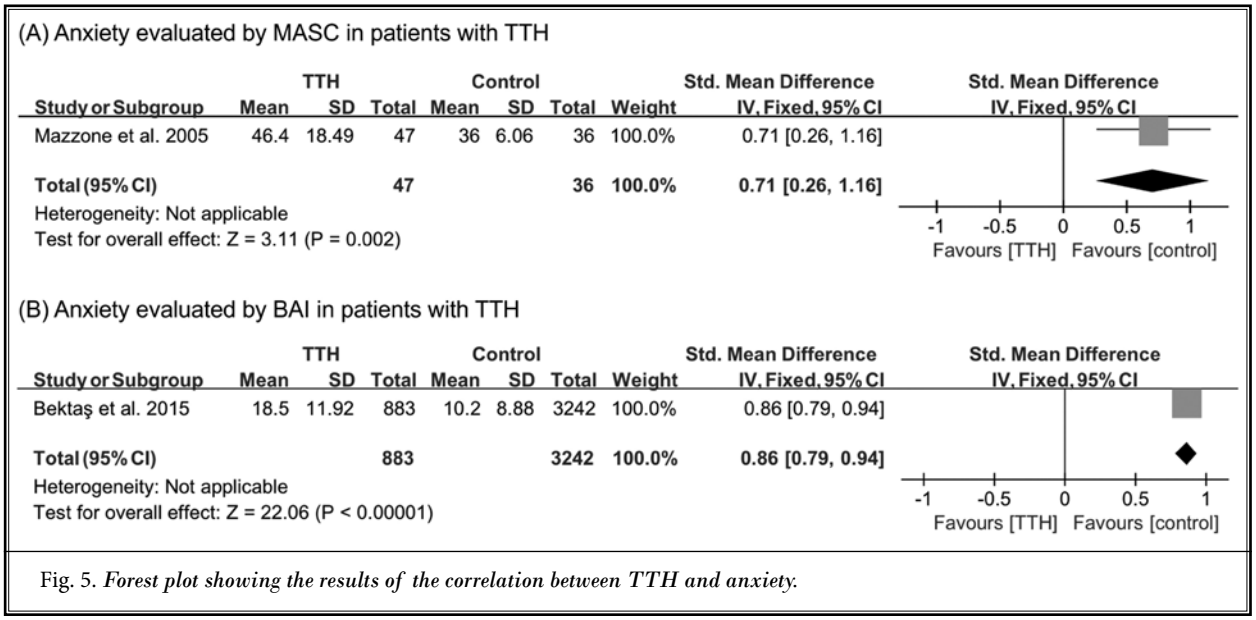

Fig. 5. *Forest plot showing the results of the correlation between TTH and anxiety.*

Table 2. *Risk of bias in case-control studies included in this study evaluated using the NOS.*

Study	Selection				Comparability	Exposure		
	Is the Case Definition Adequate?	Representativeness of the Cases	Selection of Controls	Definition of Controls	Comparability of Cases and Controls on the Basis of the Design or Analysis	Ascertainment of Exposure	Same Method of Ascertainment for Cases and Controls	Nonresponse Rate
Mazzone et al 2006[26]	*	-	*	-	*	-	*	-
Vannatta et al 2008[27]	*	-	*	*	**	-	*	-
Anttila et al 2004[28]	-	*	*	-	*	*	*	-
Reale et al 2011[29]	*	-	*	-	**	*	*	-
Kandemir et al 2018[30]	*	-	*	*	**	-	*	*
Smith et al 2003[31]	*	-	*	-	*	-	*	-
Öztop et al 2016[32]	*	-	*	-	**	-	*	*
Arita et al 2013[33]	*	-	*	-	-	-	*	-
Uçar et al 2020[34]	*	*	-	-	**	-	*	*
Bektaş et al 2015[35]	*	*	*	-	*	-	*	-

Abbreviation: NOS, Newcastle-Ottawa Scale.

try in the intergroup comparisons of anxiety evaluated by the STAI in patients with migraine and depression evaluated by CDI in patients with migraine (Fig. 6). Moreover, the P value of Egger's test was > 0.05, indicating an insignificant publication bias (anxiety evaluated by the STAI in patients with migraine, 0.3357; depression evaluated by the CDI in patients with migraine, 0.0210).

Discussion

We found that the psychodiagnostic tools to assess depression (CDI and BDI) scored higher in patients with migraine than in healthy controls. However, most anxiety-related scores, including the MASC, SCARED, and STAI scores, were not significantly different between the migraine and control groups. Only the BAI scores were higher in the migraine group than in the control group, and only one study was included. In contrast, for TTH, the anxiety-related scores (MASC and BAI) were higher in the healthy controls. However, the CDI score, measuring the degree of depressive symptoms in patients with TTH, did not differ significantly from that of the control groups.

Headache disorders in childhood carry significant physical, psychological, and economic burdens (36). Due to interrelated physical, psychological, and social developmental challenges, childhood is a stage of life that is particularly susceptible to the onset of health issues, such as headache disorders (11). Unexpected recurrent headaches can frighten children and adolescents, interfere with daily activities, reduce their quality of life, and make patients feel unprotected. In addition, negative emotions, such as depression and anxiety, can induce psychological distress and behavioral reactions (11,37).

Some previously published systematic reviews or meta-analyses have assessed psychopathological symptoms in children and adolescents with headaches.

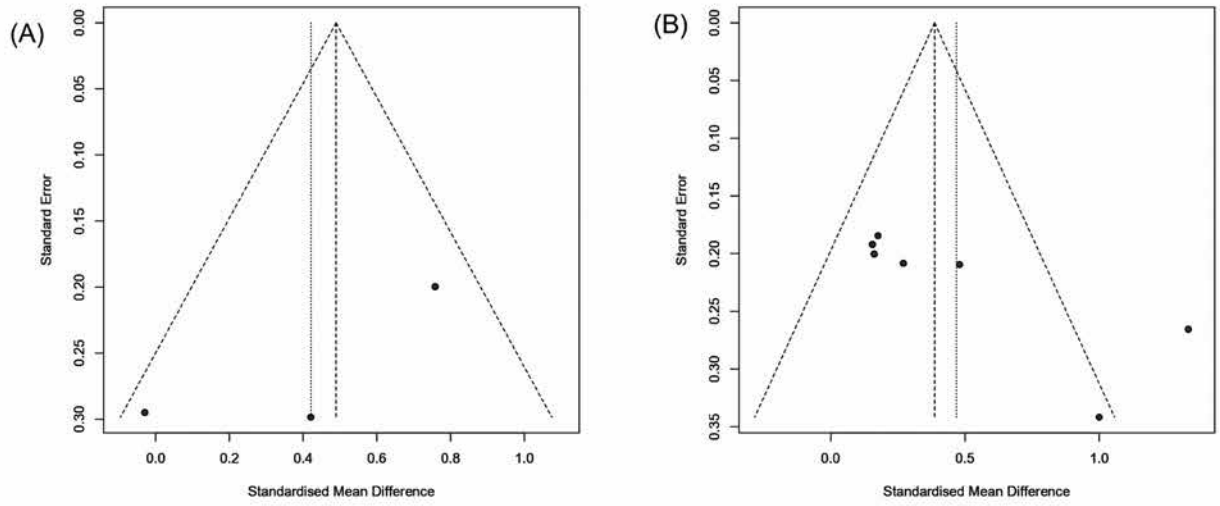

Fig. 6. *Graphic funnel plots of the included studies. (A) Anxiety evaluated by the STAI in patients with migraine. (B) Depression evaluated by the CDI in patients with migraine*

In 2010, Bruijn et al (38) assessed the prevalence and manifestations of psychological functioning and psychological comorbidity of migraine in children and concluded that patients did not exhibit more psychological comorbidities than healthy controls. In 2013, Balottin et al (39) reviewed 10 studies using the Child Behavior Checklist as a psychodiagnostic tool and assessed the externalizing symptom scale (delinquent behavior and aggressive behavior) and internalizing symptom scale (withdrawn, somatic complaints, and anxious/depressed). They found that patients with both migraine and TTH showed more internalizing symptoms than healthy controls; however, the externalizing symptom scale scores were higher only in patients with migraine than in healthy controls(39).

In our meta-analysis, we assessed psychological symptoms in children and adolescents affected by migraine and TTH. Although the previous meta-analyses did not divide the primary headache into different subtypes and only analyzed the overall broad psychological symptoms of the primary headache, our study divided the headache type into migraine and TTH and analyzed them separately. In addition, for a detailed study of psychological symptoms, we specified symptoms, such as depression or anxiety, and reviewed articles using various specific rating scales. Our study showed that migraine is associated with depression rather than anxiety; whereas, TTH is associated with anxiety rather than depression.

Numerous studies (40-43) suggested that hypothalamic-pituitary-adrenocortical (HPA) axis has been implicated in the pathophysiology of psychological symptoms. The HPA axis is a hormone response system that responds to stressful stimuli and returns to normal condition (homeostasis) (44). Due to the continued maturation of the stress-sensitive limbic and cortical brain regions during adolescence, adolescents may be especially susceptible to these changes in responsiveness (45). Headaches are stressful not only in the pain itself, but also in the unpredictability of the onset of headache attacks. Therefore, prolonged repetitive headaches in children and adolescents may lead to psychological symptoms, such as depression and anxiety. However, more research is needed on the reasons for the different psychological symptoms, depending on the type of headache. Migraines are characterized by moderate to severe pain, worsening with daily activities, and sensitivity to light and noise (46). The quality of life is also affected by migraine attacks, such as absence from school. In our opinion, these features make patients more prone to depression. In the case of TTH, TTH is a mild pain intensity and is associated with physical fatigue and mental stress (47). Anxiety can cause TTH through muscle contractions; whereas, repetition of TTH can be associated with anxiety.

Psychological problems in headache patients are associated with poorer prognosis, higher medical expenses, chronification of disease, and poorer response to treatment (48-50). In addition to psychological disorders, suicidal risk has also been reported in ado-

lescents with chronic daily headaches (51). However, the diagnosis of childhood psychological disorders is complex and difficult because mental illness in childhood often presents with atypical symptoms, such as irritability, school refusal, and somatic symptoms (52,53). In addition, the symptoms of pediatric patients are limited because children rarely report themselves, and their guardians are often unaware of the potential mental health problems of children and adolescents. In addition, there is a risk of misdiagnosis owing to the overlap of symptoms with various psychological conditions and other emotional, behavioral, and developmental disorders (54-56). Furthermore, adolescence is a period in which many psychological and physiological changes occur along with the maturation of stress-sensitive limbic and cortical brain regions; therefore, exposure to repetitive stress may result in maladaptive neurobehavioral development (45). Therefore, children and adolescents with primary headache disorders and their caregivers should be informed of their developmental features and possible psychological comorbidities, and various psychodiagnostic tools should be used to screen and detect these mental problems.

Limitation

Our meta-analysis has some limitations. As there is no unified scale for mental health screening for children and adolescents, we decided to select studies using various scales; therefore, a limited number of studies for each scale were included. In addition, each scale has different sensitivities and specificities, which may have affected the results. Also, it was found that the authors of previous studies had not considered prior mental issues. Our results may, accordingly, have been affected by the presence of previous psychological symptoms. Furthermore, we performed our meta-analysis without considering factors, such as the duration of symptoms, frequency and severity of headaches, and treatment status. Therefore, further research is needed.

Conclusions

In conclusion, our study found that migraine was associated with depression and TTH was associated with anxiety. When pediatric patients are diagnosed with primary headaches, physicians should evaluate their mental health. Also, periodic screening for depression and anxiety should be performed for early treatment of primary headache disorders.

References

1. Onofri A, Pensato U, Rosignoli C, et al. Primary headache epidemiology in children and adolescents: A systematic review and meta-analysis. *J Headache Pain* 2023; 24:8.
2. Abu-Arafehi I, Razak S, Sivaraman B, Graham C. Prevalence of headache and migraine in children and adolescents: A systematic review of population-based studies. *Dev Med Child Neurol* 2010; 52:1088-1097.
3. Rho YI. Prevalence of headache and headache-related disability in children and adolescents. *J Korean Med Assoc* 2017; 60:112-117.
4. Kelly M, Strelzik J, Langdon R, DiSabella M. Pediatric headache: Overview. *Curr Opin Pediatr* 2018; 30:748-754.
5. Benoliel R, Eliav E. Primary headache disorders. *Dent Clin North Am* 2013; 57:513-539.
6. Roser T, Bonfert M, Ebinger F, et al. Primary versus secondary headache in children: A frequent diagnostic challenge in clinical routine. *Neuropediatrics* 2013; 44:34-39.
7. Gupta R, Bhatia MS. Comparison of clinical characteristics of migraine and tension type headache. *Indian J Psychiatry* 2011; 53:134.
8. Shimomura H. Emotional problems in pediatric headache patients. *Curr Pain Headache Rep* 2022; 26:469-474.
9. Polese D, Belli A, Esposito D, et al. Psychological disorders, adverse childhood experiences and parental psychiatric disorders in children affected by headache: A systematic review. *Neurosci Biobehav Rev* 2022; 140:104798.
10. Larsson B, Sigurdson JF, Sund AM. Long-Term follow-up of a community sample of adolescents with frequent headaches. *J Headache Pain* 2018; 19:1-8.
11. Dyb G, Stensland S, Zwart JA. Psychiatric comorbidity in childhood and adolescence headache. *Curr Pain Headache Rep* 2015; 19:1-8.
12. Blaauw BA, Dyb G, Hagen K, et al. Anxiety, depression and behavioral problems among adolescents with recurrent headache: The Young-HUNT study. *J Headache Pain* 2014; 15:38.
13. Holmen TL, Bratberg G, Krokstad S, et al. Cohort profile of the Young-HUNT study, Norway: A population-based study of adolescents. *Int J Epidemiol* 2014; 43:536-544.
14. Blaauw BA, Dyb G, Hagen K, et al. The relationship of anxiety, depression and behavioral problems with recurrent headache in late adolescence – a Young-HUNT follow-up study. *J Headache Pain* 2015; 16:10.
15. Kovacs M. *Childen's Depression Inventory*. Second Edition. WPS, Torrance, CA 2019.
16. Kovacs M. Children's depression inventory. *Acta Paedopsychiatr Int J Child Adolesc Psychiatry* 1992.
17. Upton J. Beck depression inventory (BDI). *Encycl Behav Med* 2020; 202-203.
18. Beck AT, Ward CH, Mendelson M, et al. An inventory for measuring depression. *Arch Gen Psychiatry* 1961; 4:561-571.
19. Spence SH. Assessing anxiety disorders in children and adolescents. *Child Adolesc Ment Health* 2018; 23:266-282.
20. March JS, Parker JD, Sullivan K, Stallings P, Conners CK. The multidimensional anxiety scale for children (MASC): Factor structure, reliability, and validity. *J Am Acad Child Adolesc Psychiatry* 1997;

36:554-565.

21. Behrens B, Swetlitz C, Pine DS, Pagliaccio D. The screen for child anxiety related emotional disorders (SCARED): Informant discrepancy, measurement invariance, and test–retest reliability. *Child Psychiatry Hum Dev* 2019; 50:473-482.
22. Birmaher B, Khetarpal S, Brent D, et al. The screen for child anxiety related emotional disorders (SCARED): Scale construction and psychometric characteristics. *J Am Acad Child Adolesc Psychiatry* 1997; 36:545-553.
23. Zsido AN, Teleki SA, Csokasi K, et al. Development of the short version of the spielberger state—trait anxiety inventory. *Psychiatry Res* 2020; 91:113223.
24. Spielberger CD. *State-Trait Anxiety Inventory for Adults*, Palo Alto, CA 1983.
25. Bardhoshi G, Duncan K, Erford BT. Psychometric meta-analysis of the English version of the Beck Anxiety Inventory. *J Couns Dev* 2016; 94:356-373.
26. Mazzone L, Vitiello B, Incorpora G, Mazzone D. Behavioural and temperamental characteristics of children and adolescents suffering from primary headache. *Cephalalgia* 2006; 26:194-201.
27. Vannatta K, Getzoff EA, Powers SW, Noll RB, Gerhardt CA, Hershey AD. Multiple perspectives on the psychological functioning of children with and without migraine. *Headache* 2008; 48:994-1004.
28. Anttila P, Sourander A, Metsähonkala L, Aromaa M, Helenius H, Sillanpää M. Psychiatric symptoms in children with primary headache. *J Am Acad Child Adolesc Psychiatry*. 2004; 43:412-419.
29. Reale L, Guarnera M, Grillo C, et al. Psychological assessment in children and adolescents with benign paroxysmal vertigo. *Brain Dev* 2011; 33:125-130.
30. Kandemir G, Hesapcioglu ST, Kurt NC. What are the psychosocial factors associated with migraine in the child? Comorbid psychiatric disorders, family functioning, parenting style, or mom's psychiatric symptoms?. *J Child Neurol* 2018; 33:174-181.
31. Smith MS, Martin-Herz SP, Womack WM, Marsigan JL. Comparative study of anxiety, depression, somatization, functional disability, and illness attribution in adolescents with chronic fatigue or migraine. *Pediatrics* 2003; 111:e376-e381.
32. Öztop DB, Taşdelen Bİ, Poyrazoğlu HG, et al. Assessment of psychopathology and quality of life in children and adolescents with migraine. *J Child Neurol* 2016; 31:837-842.
33. Arita JH, Lin J, Pinho RS, et al. Adolescents with chronic migraine commonly exhibit depressive symptoms. *Acta Neurol Belg* 2013; 113:61-65.
34. Uçar HN, Tekin U, Tekin E. Irritability and its relationships with psychological symptoms in adolescents with migraine: A case-control study. *Neurol Sci* 2020; 41:2461-2470.
35. Bektaş Ö, Uğur C, Gençtürk ZB, et al. Relationship of childhood headaches with preferences in leisure time activities, depression, anxiety and eating habits: A population-based, cross-sectional study. *Cephalalgia* 2015; 35:527-537.
36. O'Donnell DM, Agin A. Management of headaches in children and adolescents. *Curr Probl Pediatr Adolesc Health Care* 2021; 51:101034.
37. Simonton KL, Garn AC. Negative emotions as predictors of behavioral outcomes in middle school physical education. *Eur Phys Educ Rev* 2020; 26:764-781.
38. Bruijn J, Locher H, Passchier J, et al. Psychopathology in children and adolescents with migraine in clinical studies: A systematic review. *Pediatrics* 2010; 126:323-332.
39. Balottin U, Poli PF, Termine C, Molteni S, Galli F. Psychopathological symptoms in child and adolescent migraine and tension-type headache: A meta-analysis. *Cephalalgia* 2013; 33:112-122.
40. Keller J, Gomez R, Williams G, et al. HPA axis in major depression: Cortisol, clinical symptomatology and genetic variation predict cognition. *Mol Psychiatry* 2017; 22:527-536.
41. Mikulska J, Juszczyk G, Gawrońska-Grzywacz M, Herbet M. HPA axis in the pathomechanism of depression and schizophrenia: New therapeutic strategies based on its participation. *Brain Sci* 2021; 11:1298.
42. Misiak B, Łoniewski I, Marlicz W, et al. The HPA axis dysregulation in severe mental illness: Can we shift the blame to gut microbiota? Prog Neuro-Psychopharmacology *Biol Psychiatry* 2020; 102:109951.
43. Iob E, Kirschbaum C, Steptoe A. Persistent depressive symptoms, HPA-axis hyperactivity, and inflammation: The role of cognitive-affective and somatic symptoms. *Mol Psychiatry* 2020; 25:1130-1140.
44. Joseph DN, Whirledge S. Stress and the HPA axis: Balancing homeostasis and fertility. *Int J Mol Sci* 2017; 18:2224.
45. Romeo RD. The impact of stress on the structure of the adolescent brain: Implications for adolescent mental health. *Brain Res* 2017; 1654:185-191.
46. Bohm PE, Stancampiano FF, Rozen TD. Migraine headache: Updates and future developments. *Mayo Clin Proc* 2018; 93:1648-1653.
47. Ashina S, Mitsikostas DD, Lee MJ, et al. Tension-Type headache. *Nat Rev Dis Prim* 2021; 7:24.
48. Minen MT, De Dhaem OB, Van Diest AK, et al. Migraine and its psychiatric comorbidities. *J Neurol Neurosurg Psychiatry* 2016; 87:741-749.
49. Blumenfeld AM, Bloudek LM, Becker WJ, et al. Patterns of use and reasons for discontinuation of prophylactic medications for episodic migraine and chronic migraine: Results from the second international burden of migraine study (IBMS-II). *Headache J Head Face Pain* 2013; 53:644-655.
50. Dresler T, Caratozzolo S, Guldolf K, et al. Understanding the nature of psychiatric comorbidity in migraine: A systematic review focused on interactions and treatment implications. *J Headache Pain* 2019; 20:1-17.
51. Romano C, Cho SY, Marino S, et al. Primary headache in childhood associated with psychiatric disturbances: An update. *Eur Rev Med Pharmacol Sci* 2020; 24:6893-6898.
52. Kawsar MDS, Yilanli M, Marwaha R. School refusal. In: *StatPearls [Internet]*. StatPearls Publishing, Treasure Island, FL 2022.
53. Costello EJ, Mustillo S, Erkanli A, et al. Prevalence and development of psychiatric disorders in childhood and adolescence. *Arch Gen Psychiatry* 2003; 60:837-844.
54. Patra S. Assessment and management of pediatric depression. *Indian J Psychiatry* 2019; 61:300.
55. Freidl EK, Stroeh OM, Elkins RM, et al. Assessment and treatment of anxiety among children and adolescents. *Focus (Madison)* 2017; 15:144-156.
56. Reimherr JP, McClellan JM. Diagnostic challenges in children and adolescents with psychotic disorders. *J Clin Psychiatry* 2004; 65:5-11.

Supplementary 1. *Search Strategy*

A search strategy was developed to identify studies that reported the associations between headache (migraine and tension-type headache {AU: Global to "[TTH]"?}) and psychotic symptoms (depression and anxiety) in pediatrics.

The search keywords were combined as follows:

"headache," "migraine," "tension headache," "tension type headache"

AND

"depression," "anxiety"

AND

"children," "adolescents"

The search keywords were devised using a combination of subject indexing terms in the titles and abstracts. For the index related to headache was referenced [Probyn K, Bowers H, Mistry D On behalf of the CHESS team., et al. Non-pharmacological self-management for people living with migraine or tension-type headache: a systematic review including analysis of intervention components BMJ Open 2017;7:e016670. Supplementary 13] and [Lu L, Wen Q, Hao X, Zheng Q, Li Y, Li N. Acupoints for Tension-Type Headache: A Literature Study Based on Data Mining Technology. Evid Based Complement Alternat Med. 2021 Mar 12;2021:5567697. Table 1. Search strategy of the literature study]. For the index related to symptoms was referenced [CCDAN's core search strategies in Cochrane Common Mental Disorders. Available from: https://cmd.cochrane.org/search-strategies-identification-studies]. For the index related to child was referenced [Leclercq E, Leeflang MM, van Dalen EC, Kremer LC. Validation of search filters for identifying pediatric studies in PubMed. J Pediatr. 2013 Mar;162(3):629-634.e2. Appendix 3. Child search filters for PubMed].

Search strategy for: Probyn K, Bowers H, Mistry D. On behalf of the CHESS team, et al. Non-pharmacological self-management for people living with migraine or tension-type headache: A systematic review including analysis of intervention components. BMJ Open 2017; 7:e016670.

Embase search strategy

1 exp episodic cluster headache/ or exp cluster headache/ or exp episodic tension headache/ or exp headache/ or exp chronic tension headache/ or exp new daily persistent headache/ or exp secondary headache/ or exp tension headache/ or exp chronic daily headache/ or exp chronic cluster headache/ or exp primary headache/

2 exp migraine aura/ or exp migraine/ or exp migraine with aura/ or exp migraine without aura/

3 (headache* or migraine*).mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword]

4 1 or 2 or 3

5 exp psychosocial disorder/ or exp psychosocial rehabilitation/

6 psychosocial.ti,ab.

7 exp mindfulness/

8 mindfulness.ti,ab.

9 exp cognitive therapy/

10 (cognitive therapy or CBT).ti,ab.

11 exp group therapy/

12 group therapy.ti,ab.

13 exp self care/

14 (self-management or self management or self-care).ti,ab.

15 (training adj5 program*).ti,ab.

16 (behavioral or behavioural).ti,ab.

17 pain treatment*.ti,ab.

18 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17

19 4 and 18

Search strategy for: Lu L, Wen Q, Hao X, Zheng Q, Li Y, Li N. Acupoints for Tension-Type Headache: A Literature Study Based on Data Mining Technology. Evid Based Complement Alternat Med. 2021 Mar 12; 2021:5567697.

Search strategy of the literature study.

A. Search strategy to locate "tension-type headache"
#1. tension-type headache [MeSH]
#2. TTH [tw]
#3. primary headache [MeSH]
#4. or/#1-#3
B. Search strategy to locate acupuncture interventions
#5. acupuncture [MeSH]
#6. acupuncture therapy [MeSH]
#7. acupuncture points [MeSH]
#8. body acupuncture [tw]
#9. electroacupuncture [MeSH]
#10. electro-acupuncture [tw]
#11. electrical acupuncture [tw]
#12. scalp acupuncture
#13. dry needling
#14. triggers point [tw]
#15. moxibustion [MeSH]
#16. acupoint [tw]
#17. or/#5-#16
C. Search strategy to locate literature studies for this study
#4 and #17

Search strategy for: CCDAN's core search strategies in Cochrane Common Mental Disorders.

OVID MEDLINE is searched as follows (1950 to date):

1. EATING DISORDERS/ or ANOREXIA NERVOSA/ or BINGE-EATING DISORDER/ or BULIMIA NERVOSA/ or FEMALE ATHLETE TRIAD SYNDROME/ or PICA/

2. HYPERPHAGIA/ or BULIMIA/

3. SELF-INJURIOUS BEHAVIOR/ or SELF MUTILATION/ or SUICIDE/ or SUICIDAL IDEATION/ or SUICIDE, ATTEMPTED/

4. MOOD DISORDERS/ or AFFECTIVE DISORDERS, PSYCHOTIC/ or BIPOLAR DISORDER/ or CYCLOTHYMIC DISORDER/ or DEPRESSIVE DISORDER/ or DEPRESSION, POSTPARTUM/ or DEPRESSIVE DISORDER, MAJOR/ or DEPRESSIVE DISORDER, TREATMENT-RESISTANT/ or DYSTHYMIC DISORDER/ or SEASONAL AFFECTIVE DISORDER/

5. NEUROTIC DISORDERS/

6. DEPRESSION/

7. ADJUSTMENT DISORDERS/

8. exp ANTIDEPRESSIVE AGENTS/

9. ANXIETY DISORDERS/ or AGORAPHOBIA/ or NEUROCIRCULATORY ASTHENIA/ or OBSESSIVE-COMPULSIVE DISORDER/ or OBSESSIVE HOARDING/ or PANIC DISORDER/ or PHOBIC DISORDERS/ or STRESS DISORDERS, TRAUMATIC/ or COMBAT DISORDERS/ or STRESS DISORDERS, POST-TRAUMATIC/ or STRESS DISORDERS, TRAUMATIC, ACUTE/

10. ANXIETY/ or ANXIETY, CASTRATION/ or KORO/

11. ANXIETY, SEPARATION/

12. PANIC/

13. exp ANTI-ANXIETY AGENTS/

14. SOMATOFORM DISORDERS/ or BODY DYSMORPHIC DISORDERS/ or CONVERSION DISORDER/ or HYPOCHONDRIASIS/ or NEURASTHENIA/

15. HYSTERIA/

16. MUNCHAUSEN SYNDROME BY PROXY/ or MUNCHAUSEN SYNDROME/

17. FATIGUE SYNDROME, CHRONIC/

18. OBSESSIVE BEHAVIOR/

19. COMPULSIVE BEHAVIOR/ or BEHAVIOR, ADDICTIVE/

20. IMPULSE CONTROL DISORDERS/ or FIRESETTING BEHAVIOR/ or GAMBLING/ or TRICHOTILLOMANIA/

21. STRESS, PSYCHOLOGICAL/ or BURNOUT, PROFESSIONAL/

22. SEXUAL DYSFUNCTIONS, PSYCHOLOGICAL/ or VAGINISMUS/

23. ANHEDONIA/

24. AFFECTIVE SYMPTOMS/

25. *MENTAL DISORDERS/

26. (eating disorder* or anorexia nervosa or bulimi* or binge eat* or (self adj (injur* or mutilat*)) or suicide* or suicidal or parasuicid* or mood disorder* or affective

disorder* or bipolar i or bipolar ii or (bipolar and (affective or disorder*)) or mania or manic or cyclothymic* or depression or depressive or dysthymi* or neurotic or neurosis or adjustment disorder* or antidepress* or anxiety disorder* or agoraphobia or obsess* or compulsi* or panic or phobi* or ptsd or posttrauma* or post trauma* or combat or somatoform or somati#ation or medical* unexplained or body dysmorphi* or conversion disorder or hypochondria* or neurastheni* or hysteria or munchausen or chronic fatigue* or gambling or trichotillomania or vaginismus or anhedoni* or affective symptoms or mental disorder* or mental health).ti.

27. or/1-26

28. controlled clinical trial.pt.

29. randomized controlled trial.pt.

30. (randomi#ed or randomi#ation).ab,ti.

31. randomly.ab.

32. (random* adj3 (administ* or allocat* or assign* or class* or control* or determine* or divide* or distribut* or expose* or fashion or number* or place* or recruit* or subsitut* or treat*)).ab.

33. placebo*.ab,ti.

34. drug therapy.fs.

35. trial.ab,ti.

36. groups.ab.

37. (control* adj3 (trial* or study or studies)).ab,ti.

38. ((singl* or doubl* or tripl* or trebl*) adj3 (blind* or mask* or dummy*)).mp.

39. clinical trial, phase ii/ or clinical trial, phase iii/ or clinical trial, phase iv/ or randomized controlled trial/ or pragmatic clinical trial/

40. (quasi adj (experimental or random$)).ti,ab.

41. ((waitlist* or wait* list* or treatment as usual or TAU) adj3 (control or group)).ab.

42. or/28-41

43. 27 and 42

[pt=publication type; ab=abstract; ti=title; fs=floating subheading; sh=subject heading; mp=title, original title, abstract, name of substance word, subject heading word, unique identifier]

Search strategy for: Leclercq E, Leeflang MM, van Dalen EC, Kremer LC. Validation of search filters for identifying pediatric studies in PubMed. J Pediatr 2013; 162:629-634.e2.

Appendix 3. Child search filters for PubMed

CCG7:

Infant OR infan* OR newborn OR newborn* OR new-born* OR baby OR baby* OR babies OR neonat* OR perinat* OR postnat* OR child OR child* OR schoolchild* OR schoolchild OR school child OR school child* OR kid OR kids OR toddler* OR adolescent OR adoles* OR teen* OR boy*

OR girl* OR minors OR minors* OR underag* OR under ag* OR juvenil* OR youth* OR kindergar*

OR puberty OR puber* OR pubescen* OR prepubescen* OR prepuberty* OR pediatrics OR pediatric* OR paediatric* OR peadiatric* OR schools OR nursery school* OR preschool* OR pre school* OR primary school* OR secondary school* OR elementary school* OR elementary school OR high school* OR highschool* OR school age OR schoolage OR school age* OR schoolage* OR infancy OR schools, nursery OR infant, newborn

CHF3:

Infant[MeSH] OR Infant* OR infancy OR Newborn* OR Baby* OR Babies OR Neonat* OR Preterm* OR Prematur* OR Postmatur* OR Child[MeSH] OR Child* OR Schoolchild* OR School age* OR Preschool* OR Kid OR kids OR Toddler* OR Adolescent[MeSH] OR Adoles* OR Teen* OR Boy* OR Girl* OR Minors[MeSH] OR Minors* OR Puberty[MeSH] OR Pubert* OR Pubescen* OR Prepubescen* OR Pediatrics[MeSH] OR Pediatric* OR Paediatric* OR Peadiatric* OR Schools[MeSH] OR Nursery school* OR Kindergar* OR Primary school* OR Secondary school* OR Elementary school* OR High school* OR Highschool*

Best Bets1 (without journals names) adapted for PubMed:

Perinat* OR neonat* OR newborn* OR infan* OR bab* OR toddler* OR boy* OR girl* OR kid* OR school*age OR juvenil* OR under*age* OR teen* OR minor* OR pubescen* OR adolescen* OR child[mh] OR child* OR pediatrics[mh] OR pediatric* OR paediatric*

Kastner2 pediatric 1 (best sensitivity), adapted for PubMed:

Child OR infan* OR adolescent.

Kastner2 pediatric 2 (best optimization of sensitivity and specificity),

adapted for PubMed:

Adolescent[tiab] OR children[tiab] OR child, preschool[mh]

Kastner2 pediatric 3 (best specificity), adapted for PubMed:

Children[tiab]

PubMed4 Limit All Child: 0-18

years OR "child"[MeSH Terms] OR "Infant"[MeSH Terms] "adolescent"[MeSHTerms]

Selection of eligible studies

Trial registers and databases including PubMed, Embase, Scopus, and Cochrane were searched for studies published up to October 19, 2022. The results of the database searches were exported to an EndNote X9 library. Duplicates were deleted using the EndNote X9 deduplication function. Two reviewers (HJL and MCC) removed irrelevant records based on the titles and abstracts. Subsequently, the reviewers examined the full text to select articles that meet the selection criteria.

Each database was searched with the following criteria:

1. PubMEd (851)
- Language: English
2. Embase (3,124)
- Publication types: article
- Language: English
3. Scopus (8,349)
- Open access: all open access
- Document types: article
- Publication stage: final
- Source types: journal
- Language: English
- Keyword: Headache, Child, Children, Adolescent, Depression, Anxiety, Migraine
4. Cochrane library (966)
- trials

Eligibility criteria.

Population	Studies that reported the associations between headache (migraine and tension-type headache) and psychotic symptoms (depression and anxiety) in pediatrics.
Intervention	pediatric patients with migraine and tension-type headache.
Comparison	pediatric patients without migraine and tension-type headache.
Outcome	Studies were eligible for inclusion in this review if they report on the results of Children's Depression Inventory (CDI), Beck's Depression Inventory (BDI), Multidimensional Anxiety Scale for Children (MASC), Screen for Child Anxiety Related Disorders (SCARED), State-Trait Anxiety Inventory (STAI), and Beck Anxiety Inventory (BAI).
Study design	Clinical trials in humans were included in this review.
Limitation	Studies published as case reports, reviews, letters, or other undistinctive forms were excluded. Studies from all years were considered.