Gender differences in clinical and psychological variables associated with the burden of headache in tension-type headache

Fuensalida-Novo, Stella; Parás-Bravo, Paula; Jiménez-Antona, Carmen; Castaldo, Matteo; Wang, Kelun; Benito-González, Elena; Arendt-Nielsen, Lars; Fernández-De-Las-Peñas, César

Published in:
Women & Health

DOI (link to publication from Publisher):
10.1080/03630242.2019.1696440

Publication date:
2020

Document Version
Accepted author manuscript, peer reviewed version

Gender Differences in Clinical and Psychological Variables Associated with the Burden of Headache in Tension Type Headache

Authors

Stella Fuensalida-Novo[1] PT, MSc; Paula Parás-Bravo[2,3] PT, PhD; Carmen Jiménez-Antona[1] PT, PhD; Matteo Castaldo[4,5,6] PT, PhD; Kelun Wang[4] DDS, PhD; Elena Benito-González[1] PT, MSc; Lars Arendt-Nielsen[4] PhD, Dr.Med.Sci.; César Fernández-de-las-Peñas[1,4] PT, PhD, Dr.Med.Sci.

Affiliations

(1)Department of Physical Therapy, Occupational Therapy, Rehabilitation and Physical Medicine, Universidad Rey Juan Carlos, Alcorcón, Spain

(2)Department of Nursing, Universidad de Cantabria, Spain

(3)Nursing Group IDIVAL, Santander, Cantabria, Spain

(4)CNAP, Center for Sensory-Motor Interaction (SMI), Department of Health Science and Technology, Faculty of Medicine, Aalborg University, Aalborg, Denmark

(5)Master in Sport Physiotherapy, University of Siena, Italy

(6)Poliambulatorio Fisiocenter, Collecchio (Parma), Italy

Address for reprint requests / corresponding author.

César Fernández de las Peñas
Facultad de Ciencias de la Salud
Universidad Rey Juan Carlos
Avenida de Atenas s/n
28922 Alcorcón, Madrid
SPAIN
E-mail address: cesar.fernandez@urjc.es

Telephone number: + 34 91 488 88 84
Fax number: + 34 91 488 89 57

The study protocol was approved by the ethics board of the Universidad Rey Juan Carlos.

The authors declare no conflicts of interest with the content of this article.

Short title: Gender differences in burden in tension type headache

Gender Differences in Clinical and Psychological Variables Associated with the Burden of Headache in Tension Type Headache

Abstract

Our aim was to assess gender differences in variables associated with the emotional and physical burdens of tension type headache (TTH). Participants with TTH diagnosed according to the ICHD-III were recruited from three university-based hospitals (in Spain, Italy, Denmark) between January 2015 and June 2017. The physical/emotional headache burden was assessed with the Headache Disability Inventory (HDI-P/HDI-E, respectively). Headache features were collected with a four-week diary. Sleep quality was assessed with Pittsburgh Sleep Quality Index. The Hospital Anxiety and Depression Scale evaluated anxiety and depressive symptom levels. Trait and state anxiety levels were evaluated with State-Trait Anxiety Inventory. Two hundred and twelve (28% men) participants (aged 41-48 years old) participated. Multiple regression models revealed that sleep quality explained 36.7% of the variance of HDI-E and 31.1% of the variance of HDI-P in men; whereas headache intensity, depressive levels and younger age explained 37.5% of the variance of HDI-E and 32.8% of the variance of HDI-P in women (all $p<0.001$). This study observed gender differences in variables associated with headache burden in TTH. Management of men with TTH should focus on interventions targeting sleep quality, whereas management of women with TTH should combine psychological approaches and interventions targeting pain mechanisms.

Keywords: Gender, tension type headache, sleep quality, pain, depression, burden.

Gender Differences in Clinical and Psychological Variables Associated with the Burden of Headache in Tension Type Headache

Introduction

Tension type headache (TTH) is the most frequently occurring headache disorder with a general prevalence of 42% (Ferrante et al. 2013) and an important socio-economic impact (Dowson 2015). In the Global Burden of Disease Study 2015, headache was the second most prevalent disorder in the world (GBD 2016). The Eurolight project observed that the burden associated with primary headaches, such as TTH, was substantial and involved professional, personal, and social aspects (Steiner et al. 2014). In fact, indirect costs, e.g., missed working days, associated to headache burden accounted for the 92% of the financial costs of TTH (Linde et al. 2012).

Our group has previously described a mediation interaction between depressive symptom levels and pain interference with headache burden in individuals with chronic TTH, suggesting a complex interaction between these factors (Fuensalida-Novo et al. 2017). It is important to consider that TTH is more prevalent in women than men (female: male ratio 3:1) (Manzoni and Stovner 2010). It has been previously suggested that headache relationships could differ according to gender because of the potential gender influence on primary headache phenotype, which is a complex process and needs further examination (Fumal and Schoenen 2008). For instance, although emotional stress and sleep disturbances are the most frequent trigger factors for headaches in both men and women with TTH (Wang et al. 2013), women with headaches are 1.3 to 2.0 times more likely to exhibit poor sleep (Reyner et al. 1995) and depressive/anxiety symptom levels (Lampl et al. 2016) than men with headaches. Further, evidence also supports gender differences in pain perception (Maurer et al. 2016), brain structural development and function (Ingalhalikar et al. 2014), life experiences and cultural expectations (Springer et al. 2012), and biopsychosocial factors associated with the pain experience (Racine et al. 2012).

A better understanding of gender differences in the relationships among headache features, sleep quality, mood disorders (i.e., anxiety and depressive levels) and headache burden in individuals suffering from TTH could assist clinicians in determining better interventional strategies according to gender. This is highly relevant because the impact of headache is higher in females, regardless of the headache diagnosis (Linde et al. 2012); however, we do not know if gender could also influence the variables associated with headache burden because no studies of which we are aware have previously investigated the role of gender on headache burden. Therefore, the purpose of the current study was to evaluate gender differences in the relationship between headache burden with headache pain features, sleep quality, anxiety, and depressive levels in men and women with TTH in a longitudinal design (one-year follow-up).

Methods

Study Design

The current analyses were included as part of a multicenter international headache study. Some participants from the current study were also included in a previous part of the study which has been already previously published (Fuensalida-Novo et al. 2017; Palacios-Ceña et al. 2017). This report presents new data by including new participants, different outcomes, and different analysis.

Participants

Participants with a diagnosis of TTH were recruited from three different university-based hospitals in Europe (Spain, Italy, Denmark) between January 2015 and June 2017.

Participants were recruited from those attending routine medical appointments during the study period. Diagnosis was conducted according to the International Classification of Headache Disorders criteria, third edition, beta version, by a neurologist who was expert in headaches (ICHD-III 2013). To be included in this study, participants had to describe typical pain features of TTH, including bilateral location, pressing and tightening pain, moderate intensity (≤7/10-points numerical pain rate scale, NPRS) and no aggravation of headache during physical activity. Additionally, participants with a high frequency of attacks should report no more than one of the following: photophobia, phonophobia or nausea and neither moderate nor severe nausea nor vomiting as recommended by the ICHD-III beta (ICHD-III 2013). They were excluded if they presented with any of the following: other primary and/or secondary concomitant headache, including medication overuse headache as defined by the ICHD-III; history of cervical and/or head trauma (i.e., whiplash); any systemic degenerative disease, e.g., rheumatoid arthritis, or lupus erythematous; diagnosis of fibromyalgia syndrome; receiving anesthetic block or physical therapy in the previous six months; or pregnancy. From a total of 250 participants screened for eligibility, 38 were excluded for: co-morbid migraine (n=26), previous cervical trauma (n=4), fibromyalgia diagnosis (n=4), and medication overuse headache (n=4). All participants read and signed a consent form prior to their inclusion. The local Ethics Committees approved the study (URJC 23/2014, HUFA 14/104, Region Nordjylland of Denmark N20140063, HRJ 07/14).

Burden of Headache

The main outcome of this study was the burden of headache at one year which was assessed with the Headache Disability Inventory (HDI) (Jacobson et al. 1994). This questionnaire consists of 25 items that inquire about the perceived impact of headache on emotional functioning (13 items, HDI-E) and physical daily life activities (12 items, HDI-

P). Each item can be answered YES (4 points), SOMETIMES (2 points) or NO (0 points). The HDI-E has a maximum score of 52 points, whereas the HDI-P has a maximum score of 48 points, with greater scores suggesting a greater headache burden. This questionnaire showed good stability at short and long-term in individuals with headache (Jacobson et al. 1995). The HDI was assessed at baseline and at one-year follow-up.

Clinical Outcomes - Headache Diary

A headache diary maintained by participants for four weeks at baseline was used to record the headache clinical features (Phillip et al. 2007). Participants registered the number of days with headache (days per week), the intensity of headache attacks on a 0-10 points numerical pain rate scale (Jensen et al. 1999) (NPRS; 0: no pain, 10: the maximum pain), and the duration of each headache attack (hours per day).

Sleep Quality

The Pittsburgh Sleep Quality Index (PSQI) was used to assess quality of sleep at baseline (Cole et al. 2007). This questionnaire consists of 19 self-rated questions and five questions answered by bed- or room-mates assessing the quality of sleep over the previous month period. The PSQI assesses usual bed time, usual wake time, number of actual hours slept, and number of minutes to fall asleep. Questions are answered on a 4-point (0-3) Likert-type scale. Answers from questions are summed giving a global total score ranging 0 to 21 points in which higher scores indicate worse quality of sleep (Buysse et al. 1989). The PSQI questionnaire has shown good internal consistency and test-retest reliability (Carpenter and Andrykowski 1998).

Psychological Variables

Anxiety and depressive symptoms were assessed at baseline with the self-rated Hospital Anxiety and Depression Scale (HADS). It consists of 14 items indicating the presence of potential anxiety (7 items, HADS-A) and depressive (7 items, HADS-D) symptoms (Zigmond and Snaiyh 1983). Each item is scored on a 4-point Likert scale (0-3), giving a maximum score of 21 points for each subscale (Herrmann-Lingen et al. 2011). The HADS has shown good validity and internal consistency for being used in headaches (Juang et al. 1999).

State and trait levels of anxiety were assessed at baseline with the State-Trait Anxiety Inventory (STAI). The STAI is a 40-item scale assessing the state (items 1-20, STAI-S) and trait (items 21-40, STAI-T) level of anxiety (Spielberger 1983; Spielberger 1989). The STAI-S includes items such as "I am worried" and "I am jittery". Participants use a 4-point response scale ranging from "not at all" to "very much" to indicate the extent to which they experience each emotion. The STAI-T consists of 20 statements requiring individuals to rate how they generally feel on a 4-point scale. In both scales, higher scores indicate greater state or trait anxiety levels. Both scales have shown a good internal consistency and test-retest reliability (Barnes et al. 2002).

Statistical analysis

Data was analyzed with the SPSS software version 22.0. Means and confidence intervals were calculated for variables by gender. The Kolmogorov-Smirnov test revealed that all data exhibited normal distributions ($p>0.05$). To assess the relationships between the dependent measure (headache burden at one year; HDI-E or HDI-P) and independent baseline variables, Pearson product-moment correlation coefficients were calculated by gender. The independent variables included in the current analyses included age, years with headache, headache intensity, headache frequency, headache duration, depressive (HADS-D) and anxiety (HADS-A) symptoms, sleep quality (PSQI), and trait (STAI-T) and state (STAI-S) anxiety levels at baseline. Statistical analyses were also used to check for multicollinearity and shared variance between all the outcomes. All correlation analyses were conducted in men and women, separately.

Hierarchical regression models were conducted to determine those variables that contributed significantly to the variance in the emotional (HDI-E) and physical (HDI-P) burden of headache, separately in either men or women. The baseline variables included on each hierarchical regression model were those showing significant correlations ($p<0.05$) with headache burden at one year. Changes in R^2 were reported after each step of the regression model to determine the contribution of the association of each additional variable to the regression model. Last, those baseline variables that significantly contributed to the score on the emotional or physical burden of headache were selected for inclusion into a parsimonious final regression model. All analyses were conducted in men and women, separately. The significance criterion of the critical F value for entry into the regression equation was set at $p<0.05$.

Results

Two hundred twelve, 59 men (28%) and 153 (72%) women satisfied inclusion criteria, agreed to participate and signed the informed consent. No significant differences were observed between men and women with TTH for all outcomes registered at baseline (all $p>0.166$) except for trait level of anxiety ($t=2.419$; $p=0.017$) and depressive symptoms ($t=2.503$; $p=0.013$): women had higher trait levels of anxiety and depressive symptoms than men (**Table 1**).

Emotional Burden of Headache

Within men with TTH, in unadjusted analyses, significant positive correlations were observed between HDI-E and the frequency of headaches ($r=0.392$; $p=0.007$), PSQI ($r=0.541$; $p<0.001$) and HADS-D ($r=0.565$; $p<0.001$): the higher the emotional burden, the higher the frequency of attacks, the worse the sleep quality, and the higher the level of depressive symptoms (**Table 2**). Further, a significant negative correlation between the HDI-E and age (r=-0.464; p=0.001) was also found: the younger the men with TTH, the higher the emotional burden.

Within women with TTH, in unadjusted analyses, significant positive correlations between HDI-E and headache intensity (r=0.314; p<0.001), headache frequency (r=0.361; p<0.001), PSQI (r=0.264; p=0.005), and HADS-D (r=0.515; p<0.001): the higher the emotional headache burden, the higher the headache intensity, the higher the frequency of attacks, the worse the sleep quality, and the higher the level of depressive symptoms in women with TTH. Age was also significantly and negatively associated (r=-0.424; p=0.008) with the emotional burden of headache: the younger the women, the higher the emotional burden of the headache

Significant correlations also existed among the independent variables (0.276 < r < 0.565; **Table 2**), with no multicollinearity (defined as r>0.80); therefore, each variable was included in multiple regression analyses.

Within men in adjusted analyses, baseline quality of sleep contributed approximately 34.2% (p<0.001), whereas age contributed an additional 12% (p<0.001) of the variance of the emotional burden of headache (HDI-E) at one year (**Table 3**). When combined, these variables explained 44.1% of the variance in emotional burden of headache in men (p<0.001). In women with TTH, baseline depressive symptom levels contributed 22.1% (p<0.001); baseline headache intensity contributed an additional 8% (p<0.001), and age contributed an additional 8% (p<0.001) of the variance in emotional burden of headache (HDI-E) at one year (**Table 3**). When combined, these variables explained 37.5% of the variance in emotional burden of headache in women (p<0.001).

Physical Burden of Headache

Within men with TTH, significant unadjusted positive correlations were observed between HDI-P with the PSQI ($r=0.487$; $p<0.001$) and the HADS-D ($r=0.488$; $p<0.001$): the higher the physical burden of headache, the worse the sleep quality and the higher the depressive symptoms (**Table 2**).

Within women with TTH, significant unadjusted positive correlations were observed between HDI-P with headache intensity ($r=0.270$; $p=0.003$), headache frequency ($r=0.254$; $p=0.005$) and the HADS-D ($r=0.366$; $p<0.001$): the higher the physical headache burden, the higher the headache intensity, the higher the frequency of headaches, and the higher the depressive symptom levels in women with TTH. Age was also significantly and negatively associated ($r=-0.407$; $p<0.001$) with the physical burden of headache: the younger the women, the higher the physical burden of the headache (**Table 2**).

Significant correlations also existed among the independent variables ($0.276 < r < 0.565$; **Table 2**), with no multicollinearity (defined as $r>0.80$); therefore, each variable was included into regression analyses.

Within men with TTH, adjusted analyses revealed that baseline quality of sleep was contributing 31.1% ($p<0.001$) of the variance of the physical burden of headache (HDI-P) at one year (**Table 4**). In women with TTH, headache intensity contributed to 12.8% ($p<0.001$), younger age contributed an additional 10% ($p<0.001$), and depressive symptoms contributed an additional 10% ($p<0.001$) of the variance in the physical burden of headache (HDI-P) at one year (**Table 4**). When combined, outcomes explained 32.8% of variance in physical burden of headache ($p<0.001$).

Discussion

This study showed gender differences in the variables associated with headache burden in people with TTH at one-year follow-up. Sleep quality was most associated with headache burden in men, and depressive levels and headache intensity were associated with headache burden in women with TTH.

Prior evidence supports that people with TTH exhibit co-morbid depression (Beghi et al. 2010; Lampl et al. 2016) and sleep disturbances (Uhlig et al. 2014); however, no previous studies of which we are aware have investigated the relation of these factors in headache burden by gender. Our study identified that sleep quality was most relevant to men with TTH, whereas depressive symptom levels were more relevant for women with TTH. Although depression is known to be associated with sleep quality, interestingly the association with headache burden was different in men and women with TTH. Biological, cultural, and experiential factors may underlie these gender differences (Altemus et al. 2014). For instance, it seems that depression has a marked impact on the burden in individuals with headache because it increases the risk of feeling less understood by the family and friends as well as increases risk of avoiding to tell other people about the headache (Zebenholzer et al. 2016). Because women are more likely to seek support from others, including family and friends, than men it is expected that emotional mood factors, e.g., depressive symptom levels, could lead to higher influence in the perceived burden (Taylor et al. 2000). Nevertheless, we should also recognize that higher depressive symptom levels observed in our sample of women with TTH could also be the responsible for this association. Similarly, the association of sleep quality with the burden of headache in men could be related to associated manifestations, such as tiredness or lack of energy, associated with poor sleep quality.

The multiple regression analyses also showed that headache intensity explained 10% of the variance of perceived burden in women, but not in men, with TTH. Gender differences in nociceptive pain processing could explain these results. Strong evidence supports that women exhibit significantly greater pain sensitivity than men (Racine et al. 2012) and also lower activation of conditioned pain modulation analgesia (Arendt-Nielsen et al. 2008). Therefore, it is possible that gender differences in the pain experience could explain our results.

Uncertainty over biological mechanisms in gender differences remain, but our results have potential implications for clinical practice because depressive symptoms, sleep quality and pain represent modifiable risk factors implicated in the chronicity of headaches (Rains 2008). Our results indicated that depressive symptoms were the outcome most related to headache burden in women with TTH, whereas sleep quality was the outcome most related in men with TTH Similarly, the intensity of headache was only associated with the burden of headache in women, but not in men, with TTH. Therefore, management of individuals with TTH should consider gender differences identified in the current study. For instance, management of men with TTH should mainly focus on interventions targeting to improve the quality of sleep (copying strategies, relaxation techniques, physical activity), whereas management of women with TTH should combine psychological approaches (copying and cognitive strategies) (Lee et al. 2019) and interventions targeting pain mechanisms related to headache intensity. These approaches are supported by studies suggesting that women tend to cope better with pain when employing pain attention focus or reinterpreting pain sensation strategies (Keogh and Herdenfeldt 2002).

Although the strengths of this study include a large sample size, the use of headache diary and standardized instruments, and a longitudinal design, some limitations should be recognized. First, we included a sample that consisted mainly of participants referred to tertiary headache centers and thus not representative of the general headache population. In addition, we only included patients with TTH, we do not know if similar differences would be observed in people with migraine or other headaches. Second, it should be noted that the HADS is more a screening rather than a diagnostic tool for depressive and anxiety symptoms with a tendency to underestimate prevalence of both disorders (Steel et al. 2014). Third, it was surprising that anxiety and depressive symptom levels observed in our sample were low because the female to male ratio was high; the chronic nature of the headache symptoms, and the population being drawn from a general neurology clinic may have increased the frequency of co-morbid mood disorders in our sample. Nevertheless, the prevalence of depressive symptoms in our sample was similar to that previously found in migraine sufferers (Zhu et al. 2003). It is possible that the inclusion of individuals with higher levels of depressive or anxiety symptoms can yield different results, although this is unlikely. Fourth, we did not evaluate the influence of socioeconomic status and cultural level which are factors associated with TTH in women, because women are more susceptible to socioeconomic influences (Chu et al. 2013). Finally, we did not include a headache-free control group, so we do not currently know if these gender differences would be related to the presence of TTH or are also present in healthy people.

Conclusions

In this study, sleep quality explained 36.7% of the emotional aspect of headache burden and 31.1% of the physical aspect of headache burden in men with TTH, whereas headache intensity and depressive levels explained 37.5% and 32.8% of emotional and physical aspects of headache burden, respectively, in women with TTH. The current findings identified some gender differences in those variables associated with headache burden in individuals with TTH. Future longitudinal studies will help to determine the clinical implications of these findings for the management and counselling of patients with TTH.

References

- Altemus, M., N. Sarvaiya and C. Neill Epperson. 2014. Sex differences in anxiety and depression clinical perspectives. *Frontiers in Neuroendocrinology* 35: 320-30.
- Arendt-Nielsen, L., KA. Sluka, and HL. Nie. 2008. Experimental muscle pain impairs descending inhibition. *Pain* 140: 465-71.
- Barnes, LLB., D. Harp, and WS. Jung. 2002. Reliability generalization of scores on the Spielberger State-Trait Anxiety Inventory. *Educational and Psychological Measurement* 62: 603-618.
- Beghi, E., G. Bussone, D. D'Amico, P. Cortelli, S. Cevoli, GC. Manzoni, P. Torelli, MC. Tonini, G. Allais, R. De Simone R, et al. 2010. Headache, anxiety and depressive disorders: the HADAS study. *The journal of headache and pain* 11: 141-50.
- Buysse, DJ., CF. Reynolds, TH. Monk, SR. Berman and DJ. Kupfer. 1989. The Pittsburgh Sleep Quality Index: a new instrument for psychiatric practice and research. *Psychiatry Research* 28: 193-213.
- Carpenter, JS. and MA. Andrykowski. 1998. Psychometric evaluation of the Pittsburgh Sleep Quality Index. *Journal of Psychosomatic Research* 45: 5-13.
- Chu, MK., DW. Kim, BK. Kim, JM. Kim, TW. Jang, JW. Park, KS. Lee, and SJ Cho. 2013. Gender-specific influence of socioeconomic status on the prevalence of migraine and tension-type headache: the results from the Korean Headache Survey. The *Journal of Headache and Pain* 14: 82.
- Cole, JC., D. Dubois, and M. Kosinski. 2007. Use of patient-reported sleep measures in clinical trials of pain treatment: a literature review and synthesis of

current sleep measures and a conceptual model of sleep disturbance in pain. *Clinical Therapeutics* 29: 2580-2588.

- Dowson, A. 2015. The burden of headache: global and regional prevalence of headache and its impact. *International Journal of Clinical Practice, Supplement* 182: 3-7.
- Ferrante, T., GC. Manzoni, M. Russo, C. Camarda, A. Taga, L. Veronesi, C. Pasquarella, G. Sansebastiano, and P. Torelli.2 013. Prevalence of tension-type headache in adult general population: the PACE study and review of the literature. *Neurological Sciences* 34: S137-8.
- Fuensalida-Novo, S., M. Palacios-Ceña, JJ. Fernández-Muñoz, M. Castaldo, K. Wang, A. Catena, L. Arendt-Nielsen, and C.Fernández-de-Las-Peñas. 2017. The burden of headache is associated to pain interference, depression and headache duration in chronic tension type headache: a 1-year longitudinal study. *The Journal of Headache and Pain* 18: 119.
- Fumal, A., and J. Schoenen. 2008. Tension-type headache: Current research and clinical management. *Lancet Neurology* 7: 70-83.
- GBD Disease and Injury Incidence and Prevalence Collaborators. 2016. Global, regional, and national incidence, prevalence, and years lived with disability for 310 diseases and injuries, 1990-2015: a systematic analysis for the Global Burden of Disease Study 2015. *Lancet* 388: 1545-602.
- Herrmann-Lingen, C., U. Buss, and RP. Snaith. 2013. *Hospital Anxiety and Depression Scale – Deutsche Version (HADS-D).* Bern: Verlag Hans Huber.
- ICHD-III International Classification of Headache Disorder. 2013. Headache Classification Subcommittee of the International Headache Society, 3nd edition. *Cephalalgia* 33: 629-808.

- Ingalhalikar, M., A. Smith, D. Parker, T. Satterthwaite, M. Elliot, K. Ruparel, H. Hakonarson, RE. Gur, RC. Gur, and R. Verma R. 2014. Sex differences in the structural connectome of the human brain. *Proceedings of the National Academy of Sciences* 111: 823-828.
- Jacobson, GP., NM. Ramadan, L. Norris and CW. Newman. 1995. Headache disability inventory (HDI): short-term test-retest reliability and spouse perceptions. *Headache* 35: 534-9.
- Jacobson, GP., NM. Ramadan, L. Norris, and CW. Newman. 1994. The Henry Ford Hospital Headache Disability Inventory. *Neurology* 44: 837-42.
- Jensen, MP., JA. Turner, JM. Romano, and L. Fisher. 1999. Comparative reliability and validity of chronic pain intensity measures. *Pain* 83: 157-162.
- Juang, KD., SJ. Wang, CH. Lin, and JL. Fuh. 1999. Use of the Hospital Anxiety and Depression Scale as a screening tool for patients with headache. *Zhonghua yi xue za zhi* 62: 749-55.
- Keogh, E., and M. Herdenfeldt. 2002. Gender, coping and the perception of pain. *Pain* 97: 195-201.
- Lampl, C., H. Thomas, C. Tassorelli, Z. Katsarava, JM. Laínez, M Lantéri-Minet, D. Rastenyte, E. Ruiz de la Torre, LJ. Stovner, C. Andrée. 2016. Headache, depression and anxiety: association in the Eurolight project. *The Journal of Headache and Pain* 17: 59.
- Lampl, C., H. Thomas, C. Tassorelli, Z. Katsarava, JL. Laínez, M. Lantéri-Minet, D. Rastenyte, E. Ruiz de la Torre, LJ. Stovner, and C. Andrée. 2016. Headache, depression and anxiety: associations in the Eurolight project. *The Journal of Headache and Pain* 17: 59.

- Lee, HJ., JH. Lee, EY. Cho, SM. Kim, and S. Yoon. 2019. Efficacy of psychological treatment for headache disorder: a systematic review and meta-analysis. *The Journal of Headache and Pain* 20: 17.
- Linde, M., A.Gustavsson, LJ. Stovner, TJ. Steiner, J. Barré, Z. Katsarava, JM. Lainez, C. Lampl, M. Lantéri-Minet, and D. Rastenyte. The cost of headache disorders in Europe: the Eurolight project. *European journal of neurology* 19: 703-711.
- Manzoni, GC., and LJ. Stovner. 2010. Epidemiology of headache. *Handbook of clinical neurology* 97: 3-22.
- Maurer, AJ., A. Lissounov, I. Knezevic, KD. Candido, and NN. Knezevic. 2016. Pain and sex hormones: a review of current understanding. *Pain management* 6: 285-96.
- Palacios-Ceña, M., JJ. Fernández-Muñoz, M. Castaldo, K. Wang, A. Guerrero-Peral, L. Arendt-Nielsen, and C. Fernández-de-Las-Peñas. 2017. The association of headache frequency with pain interference and the burden of disease is mediated by depression and sleep quality, but not anxiety, in chronic tension type headache. *The Journal of Headache and Pain* 18: 19.
- Phillip, D., AC. Lyngberg, and R. Jensen. 2007. Assessment of headache diagnosis: A comparative population study of a clinical interview with a diagnostic headache diary. *Cephalalgia.* 27: 1-8.
- Racine, M., Y. Tousignant-Laflamme, LA Kloda, D. Dion, G. Dupuis, and M. Choinière. 2012. A systematic literature review of 10 years of research on sex/gender and pain perception-Part 2: Do biopsychosocial factors alter pain sensitivity differently in women and men? *Pain* 153: 619-635.

- Racine, M., Y. Tousignant-Laflamme, LA. Kloda, D. Dion, G. Dupuis, and M. Choinière. 2012. A systematic literature review of 10 years of research on sex/gender and experimental pain perception-Part 1: Are there really differences between women and men? *Pain* 153: 602-618.
- Rains, JC. 2008. Chronic headache and potentially modifiable risk factors: screening and behavioral management of sleep disorders. *Headache* 48: 32-39.
- Reyner, L., J. Horne and, A. Reyner. 1995. Gender- and age-related differences in sleep determined by home-recorded sleep logs and actimetry from 400 adults. *Sleep* 18: 127-134.
- Spielberge,r CD. 1989. *State-Trait Anxiety Inventory: a comprehensive bibliography.* Palo Alto, CA: Consulting Psychologists Press.
- Spielberger, CD. 1983. *Manual for the State-Trait Anxiety Inventory STAI (Form Y).* Palo Alto, CA: Mind Garden.
- Springer, K., J. Stellman and, R. Jordan-Young. 2012. Beyond a catalogue of differences: a theoretical frame and good practice guidelines for researching sex/gender in human health. *Social science & medicine* 74: 1817-1824.
- Steel, Z., C. Marnane, C. Iranpour, T. Chey, JW. Jackson, V. Patel, D. Silove. 2014. The global prevalence of common mental disorders: a systematic review and meta-analysis 1980-2013. *International Journal of Epidemiology* 43: 476-493.
- Steiner, TJ., LJ. Stovner, Z. Katsarava, JM. Lainez, C. Lampl, M. Lantéri-Minet, D. Rastenyte, E. Ruiz de la Torre, C. Tassorelli, J. Barré, et al. 2014. The impact of headache in Europe: principal results of the Eurolight project. *The Journal of Headache and Pain* 15: 31.

- Taylor, S., L. Klein, B. Lewis, T. Gruenewald, R. Gurung, and J. Updegraff. 2000. Biochemical responses to stress in females: tend-and-befriend, not fight-or fight. *Psychological Review* 107: 411-429.
- Uhlig, BL., M. Engstrøm, SS. Ødegård, KK. Hagen, and T Sand. 2014. Headache and insomnia in population-based epidemiological studies. *Cephalalgia* 34:745-51.
- Wang, J., Q. Huang, N. Li, G. Tan, L. Chen, and J. Zhou. 2013. Triggers of migraine and tension-type headache in China: a clinic-based survey. *European Journal of Neurology* 20: 689-96.
- Zebenholzer, K., A. Lechner, G. Broessner, C. Lampl, G. Luthringshausen, A. Wuschitz, SM. Obmann, K. Berek, and C. Wöber. 2016. Impact of depression and anxiety on burden and management of episodic and chronic headaches - a cross-sectional multicentre study in eight Austrian headache centres. *The Journal of Headache and Pain* 17: 15.
- Zhu, Z., X. Fan, X. Li, G. Tan, L. Chen, and J. Zhou. 2013. Prevalence and predictive factors for poor sleep quality among migraineurs in a tertiary hospital headache clinic. *Acta Neurologica Belgica* 113: 229-35.
- Zigmond, AS, and RP. Snaith. 1983. The hospital anxiety and depression scale. *Acta Psychiatrica Scandinavica* 67: 361-70.