Perceived pain extent is not associated with widespread pressure pain sensitivity, clinical features, related-disability, anxiety, or depression in women with episodic migraine

Fernández-de-las-Peñas, Cesar; Falla, Deborah; Palacios-Ceña, María; Fuensalidad-Novo, Stella; Arias-Buría, Jose L.; Schneebeli, Alessandro; Arendt-Nielsen, Lars; Barbero, Marco

Published in:
Clinical Journal of Pain

DOI (link to publication from Publisher):
10.1097/AJP.0000000000000537

Publication date:
2018

Document Version
Accepted author manuscript, peer reviewed version

The Clinical Journal of Pain Publish Ahead of Print
DOI:10.1097/AJP.0000000000000537

Perceived Pain Extent is not associated with Widespread Pressure Pain Sensitivity, Clinical Features, Related-Disability, Anxiety, or Depression in Women with Episodic Migraine

Cesar Fernández-de-las-Peñas[1,2,3]; Deborah Falla[4]; María Palacios-Ceña[1,2,3]; Stella Fuensalidad-Novo[1,2]; Jose L Arias-Buría[2,5]; Alessandro Schneebeli[6]; Lars Arend-Nielsen[3]; Marco Barbero[6]

Institutional Information

[1] Department of Physical Therapy, Occupational Therapy, Physical Medicine and Rehabilitation, Universidad Rey Juan Carlos, Alcorcón, Spain.

[2] Cátedra de Investigación y Docencia en Fisioterapia: Terapia Manual y Punción Seca, Universidad Rey Juan Carlos, Alcorcón, Madrid, Spain.

[3] Center for Sensory-Motor Interaction (SMI), Department of Health Science and Technology, School of Medicine, Aalborg University, Aalborg, Denmark

[4] Centre of Precision Rehabilitation for Spinal Pain (CPR Spine), School of Sport, Exercise and Rehabilitation Sciences, College of Life and Environmental Sciences, University of Birmingham, Birmingham, United Kingdom

[5] Department of Physical Therapy, Universidad Francisco de Vitoria, Madrid, Spain

[6] Rehabilitation Research Laboratory 2rLab, Department of Business Economics, Health and Social Care, University of Applied Sciences and Arts of Southern Switzerland, Manno, Switzerland

Corresponding / reprint requests 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
Email: cesarfdlp@yahoo.es / cesar.fernandez@urjc.es

Abstract word account: 248 words

Text word account: 2,755 words

Disclosures: Financial disclosure statements have been obtained and no conflicts of interest have been reported by the authors or by any individuals in control of the content of this article.
No conflicts of interest

Abstract

Objective: People with migraine present with varying pain extent and an expanded distribution of perceived pain may reflect central sensitization. The relationship between pain extent and clinical features, psychological outcomes, related-disability and pressure pain sensitivity in migraine has been poorly investigated. Our aim was to investigate whether the perceived pain extent, assessed from pain drawings, relates to measures of pressure pain sensitivity, clinical, psychological outcomes, and related-disability in women with episodic migraine. **Methods**: Seventy-two women with episodic migraine completed pain drawings which were subsequently digitized allowing pain extent to be calculated utilising novel software. Pressure pain thresholds (PPT) were assessed bilaterally over the temporalis muscle (trigeminal area), the cervical spine (extra-trigeminal area) and tibialis anterior muscle (distant pain-free area). Clinical features of migraine, migraine related-disability (migraine disability assessment questionnaire, MIDAS), anxiety and depression (Hospital Anxiety-Depression Scale, HADS) were also assessed. Spearman rho correlation coefficients were computed to reveal correlations between pain extent and the remaining outcomes. **Results**: No significant associations were observed between pain extent and PPTs in trigeminal, extra-trigeminal or distant pain-free areas, migraine pain features, or psychological variables including anxiety or depression and migraine related-disability. **Conclusions**: Pain extent within the trigemino-cervical area was not associated with any of the measured clinical outcomes and not related to the degree of pressure pain sensitization in women with episodic migraine. Further research is needed to determine if the presence of expanded pain areas outside of the trigeminal area can play a relevant role in the sensitization processes in migraine.

Key words: migraine, pain area, pressure pain, anxiety, depression, sensitization

Introduction

Migraine is a primary headache disorder with a worldwide prevalence of 5 to 12%[1]. It is well accepted that migraine is associated with a deficient regulation of excitatory-inhibitory balance leading to facilitation of nociceptive gain and sensitization of the trigemino-cervical nucleus caudalis and third-order neurons[2,3]. Several studies have reported that people with migraine may exhibit pressure pain hyperalgesia within the trigemino-cervical area as a clinical manifestation of central nervous system hyper-excitability[4-7]. A recent study has also confirmed the presence of widespread pressure pain hypersensitivity over trigeminal and extra-trigeminal areas in individuals with episodic and chronic migraine suggesting that the sensitization process is present from the onset of the condition[8].

Pain drawings are used to obtain a graphic representation of pain location and distribution in individuals with musculoskeletal pain, e.g., low back pain[9]. It is accepted that larger pain extent represents a clinical sign of central sensitization[10,11] and enlarged areas of pain have been associated with more severe pain[12] and greater pressure-pain hypersensitivity[13] in individuals with painful knee osteoarthritis. Similarly, larger pain extent has been associated with higher disability and depression in people with chronic whiplash-associated disorders[14]. These results suggest that the pain drawing, and quantification of pain extent, can assist clinicians to identify individuals with facilitated central nociceptive gain or worse clinical features. Nevertheless, these findings have only been evaluated in people suffering with musculoskeletal pain disorders[12-14].

Since migraine is mainly attributed to a deficient regulation of excitatory-inhibitory balance, the relation between pain extent, central sensitization, and clinical features may be less obvious. Nevertheless, it is relevant to evaluate these associations to better understand the usefulness of the pain drawing for detecting signs of central sensitization in this patient group. Therefore, it would be interesting to determine these potential associations in people with episodic migraine to identify factors for preventing the evolution to the chronic form of the condition. Accordingly, the aims of the current study were to examine: 1) whether pain extent is related to widespread pressure pain

sensitivity in women with episodic migraine; and, 2) to investigate associations between pain extent and clinical variables, psychological variables and related-disability parameters. We hypothesized that larger pain extent is associated with greater widespread pressure pain sensitivity and worse clinical and psychological features in women with episodic migraine.

Methods

Participants

Patients with episodic migraine without aura were recruited from a tertiary university-based hospital from March 2015 to March 2016. Migraine was diagnosed according to the International Classification of Headache Disorders criteria, third edition (ICHD3 beta 2013) down to the third-digit level (code 1.1) by a neurologist with expertise in headache[15]. Migraine features including location, onset of migraine (years), frequency (days/month), duration (hours/attack), and intensity of migraine attacks (numerical pain rating scale, 0-10), headache-family history and medication intake were recorded. A neuro-imaging examination of the head was performed in all patients in order to exclude other disorders. They were excluded if presented any of the following criteria: 1, other primary or secondary headaches, including medication overuse headache according to the ICHD3 beta 2013 criteria[15]; 2, history of neck or head trauma; 3, pregnancy; 4, systemic medical disease, e.g., rheumatoid arthritis, lupus erythematous; 5, diagnosis of fibromyalgia syndrome; or, 6, positive-response to anesthetic blocks in the cervical spine within the past 6 months. All subjects signed an informed consent form before their inclusion in the study. The local Ethics Committee of Hospital Rey Juan Carlos (HRJ 07/14) approved the study design and the study was conducted according to the Declaration of Helsinki.

The evaluation was conducted when all patients were headache-free, and when at least one week had elapsed since the last migraine attack to avoid migraine related allodynia. Participants were asked to avoid any analgesic or muscle relaxant 24 hours prior to the examination. No change was made to their prophylactic treatment.

Pain drawings

All patients were requested to draw their pain on four different paper body charts of the head: ventral view, dorsal view, and two representing a lateral view (left and right). All body charts were printed on A4 sheets and patients were asked to shade their pain using a pencil. Standard instructions were provided to ensure that patients reported both the pain extent during their migraine attacks, independently from the type and severity of pain.

All the A4 sheets including the body chart and the pain drawing were digitized using a commercially available scanner. Two trained operators then reproduced the pain drawings on the scanned body charts on a blank digital body chart using an image analysis software (Inkscape version 0.48). The reliability of the described procedure has been previously confirmed[16,17]. Finally, pain extent was computed using custom made software presented and evaluated in previous work[17,18]. The software calculates the number of pixels included within each pain drawing. Any shading outside of the body chart borders were not included in the analysis. Pain extent for each patient was reported as the sum of the pixels in the ventral and dorsal views of the head, and expressed as a percentage of total dorsal and ventral body chart area (i.e. 507778 pixels, frontal: 252617 pixels, dorsal: 255166 pixels). Pain frequency maps were generated for the four different body charts of the head to illustrate where pain was most frequently perceived by the patients. Pain frequency maps were obtained by overlying all of the pain drawings performed on the same body chart. A colour scale was applied to highlight the percentage of patients that reported pain in a specific region.

Pressure Pain Thresholds (PPT)

The PPT, i.e., the amount of pressure where a sensation of pressure first changes to pain, was recorded with an electronic algometer (Somedic AB®, Farsta, Sweden). Pressure was applied using a $1cm^2$ probe at a rate of approximately 30kPa/s. Participants were instructed to press the "stop-button" of the algometer as soon as the pressure resulted in the first sensation of pain. They were trained with a first trial over the wrist extensor muscles of their right forearm. PPT was then

assessed bilaterally over the temporalis muscle (trigeminal area), C5/C6 zygapophyseal joint (extra-trigeminal area) and the tibialis anterior muscle (pain-free distant site). A mean PPT widespread score was obtained from the mean of the 3 body regions. The order of assessment was randomized between participants. A 30 s resting period was allowed between each trial (within and between body regions) to prevent over sensitization[19]. The mean of three trials on each point was calculated and used for the analysis. Since no side-to-side differences in PPTs were found, the mean of both sides on each point was used for the correlation analysis with pain extent. The reliability of algometry following this procedure is high[20].

Hospital Anxiety and Depression Scale (HADS)

The HADS was used to determine the presence of anxiety and depressive symptoms. This questionnaire consists of 7-items scored on a 4-points scale ranging from 0 to 3 points to assess anxiety (HADS-A) and other 7-items for depressive (HADS-D) symptoms[21]. Each subscale ranges from 0 to 21 points where higher scores represent higher levels of anxiety or depression symptoms[21]. This questionnaire is considered reliable and valid for assessing anxiety (Cronbach's α: 0.83) and depression (Cronbach's α: 0.82) separately[22]. In headache patients, the HADS has shown good internal consistency[23].

State-Trait Anxiety Inventory (STAI)

The STAI is a 40-item scale assessing separate dimensions of state anxiety (items l-20, STAI-S) and trait anxiety (items 21-40, STAI-T)[24]. The STAI-S assesses relatively enduring symptoms of anxiety. Participants use a 4-point response scale ranging from “not at all” to “very much”, to indicate the extent to which they experience each particular emotion. The STAI-T scale measures a stable propensity to experience anxiety, and tendencies of the subject to perceive stressful situations as threatening. It consists of 20 statements requiring individuals to rate how they generally feel on a 4-point scale. In both scales, total score ranges from 0 to 60 points where higher scores indicate greater state or trait anxiety levels. Both subscales have shown high internal consistency and test-retest reliability[25].

Migraine-related disability (MIDAS)

The Migraine Disability Assessment Scale (MIDAS) questionnaire was used to assess the related-disability in daily activities (work or school, family and social) caused by migraine[26]. This questionnaire consists of five questions related to days of partial or total loss within the last three months with respect to three main activities: 1, paid work or school; 2, household chores; 3, family, social and leisure activities. The questions ask about the number of days of missed activity or days in which productivity was reduced by at least half due to migraine. The final score corresponds to the sum of missed days for these three activities[27].

Sample size calculation

The sample size was calculated using Ene 3.0 software (Autonomic University of Barcelona, Spain) and based on detecting significant moderate correlations ($r=0.4$)[12,14] between the variables with an alpha level (α) of 0.05, and a desired power (β) of 95%. This generated a sample size of 71 participants.

Statistical analysis

The Shapiro-Wilk Normality Test revealed that the distribution of data for pain extent and 6 of the clinical parameters (years with migraine, migraine intensity, migraine frequency, migraine duration, HADS-A, MIDAS) significantly deviated from normality. Therefore, non-parametric tests were used in the correlational analysis. Spearman's rho rank-order correlation coefficients (r_s) were used to reveal possible associations between pain extent and self-rated outcomes, i.e., clinical migraine pain features, anxiety, depression, related-disability, and widespread pressure pain sensitivity. Correlations were considered weak when $r<0.3$; moderate when $0.3<r<0.7$, and strong when $r>0.7$[28]. A multivariate regression model including those variables significantly associated with pain extent was conducted to assess the variables that contributed significantly to the variance in the dependent variable i.e., pain extent. Statistical analysis was performed using R version 3.2.2. Significance was set to $\alpha=0.05$ and the Bonferroni correction was applied (α-adjusted=0.0036) to account for multiple testing[29].

Results

From 105 eligible subjects with migraine who accepted to participate, 33 were excluded for the following reasons: co-morbid headache (n=20); previous head/neck trauma (n=7); or pregnancy (n=6). Finally, a total of 72 patients with migraine were included. **Table 1** summarizes clinical and PPT data of the entire sample. Pain extent was 13.4 ± 9.4% across the entire group of women with migraine. Pain frequency maps for the entire sample are illustrated in **Figure 1**.

The mean time elapsed from the last migraine attack in the current patient sample was 10 days (95%CI 9.2, 10.8). All patients were taking prophylactic medication intake, i.e., amitriptyline, on a regular basis. Correlations between the area of pain, clinical symptoms and related-disability are reported in **Table 1**. No significant associations were observed between pain extent and clinical features, psychological variables including anxiety (HADS-A) or depressive (HADS-D) symptoms or with anxiety trait (STAI-T) or anxiety state (STAIT-S) levels. Finally, no significant associations were found between pain extent and PPT scores in either trigeminal, extra-trigeminal, distant pain-free areas or mean PPT score (**Table 1**).

Discussion

The degree of pain extent was not associated with clinical, psychological or disability variables nor with widespread pressure pain sensitivity in women with episodic migraine rejecting the initial hypothesis of the study.

Although it is accepted that people with migraine exhibit pain in the trigeminal area, mostly concentrated on the orbicular and temporalis areas, the evaluation of pain drawings in people with migraine is scarce. In fact, only two studies have evaluated the location of pain during migraine attacks in adults[30] and children[31] with migraine. The first showed that, from a total sample of 1283 patients with migraine, around 60%-65% reported pain in the fronto-orbital and temporal areas, whereas occipital and neck pain were present in almost 40% of the sample[30]. The second study observed that 66% of 200 children with migraine reported frontal pain, but the presence of occipital

pain was only 12%[31]. However, neither study included an actual evaluation of pain drawings but rather documented pain location based on questions asked to the patients[30,31]. The pain frequency maps generated from the current study, further supports the observations above since 60% of the patients exhibited pain in the fronto-orbital and/or temporalis areas during their migraine pain attacks. Further, the pain frequency maps also revealed that around 30% of the patient's exhibit pain in the occipital and neck area. Thus, both the current and previous findings confirm the high prevalence of concomitant neck pain in migraine sufferers[32].

Larger pain extent and widespread pressure hypersensitivity have been associated with stronger sensitization[8,10,11]; however, in the current study we did not observe any association between pain extent in the trigemino-cervical area and widespread pressure sensitivity. This is in contrast with the results observed in other painful conditions such as knee osteoarthritis where larger pain extent was associated with higher pressure hypersensitivity[13]. Similarly, the present study did not find associations between pain extent and clinical, psychological and related-disability outcomes in our sample of women with episodic migraine which is in disagreement with previous findings reported for other pain conditions, e.g. knee osteoarthritis[12] or chronic whiplash-associated disorders[14]. Our results support the findings of Kelman et al[30] which showed that headache location was not correlated with lifetime duration of migraine, intensity, time to peak of headache, recurrence frequency, and time to recurrence.

One possible explanation for the discrepancy between the current results and those observed in people with whiplash associated disorders or osteoarthritis, could be related to the fact that both osteoarthritis and whiplash are musculoskeletal disorders whereas migraine is attributed to deficient regulation of excitatory-inhibitory balance. Therefore, the potential relationship between pain extent, clinical, psychological and sensitization outcomes may be less clear. It is also possible that the presence of more widespread symptoms extending beyond the head and neck area[33] is more related to sensitization outcomes. Finally, it is also plausible that the inclusion of episodic, not chronic, migraine explains the lack of associations. In fact, all patients in our sample were taking

prophylactic treatment on a regular basis, which could have influenced the results. Nevertheless, the lack of association between pain extent and psychological outcomes, including anxiety and depression, confirms that expanded pain drawings are not always associated with psychological state[34].

This is the first study utilizing a novel software for extracting pain extent from pain drawings in a sample of women with migraine. This is a strength of the study since pain extent could be analyzed without any subjective influence from an operator and thus the software used to estimate pain extent eliminates estimation errors. However, we should recognize that the pain drawings were first drawn on paper body charts, and later scanned. It would be relevant to determine if pain drawings using electronics devices, e.g., on a tablet, instead of paper body charts would lead similar results. In addition, some potential methodological considerations should be mentioned. First, we collected data from a sample of women with episodic migraine; therefore current results should not be extrapolated to chronic migraine or to men. It would be interesting to determine if any association is observed in people with chronic migraine and this should be explored in future studies. Second, although the reliability of the assessment method has been shown to be high in people with musculoskeletal pain[18], we did not evaluate the reliability of pain location over time in our sample of patients with migraine. This might be relevant in individuals with migraine since pain drawings were obtained when patients were headache-free and when at least one week had elapsed since the last migraine attack and, therefore, a potential recall of bias can be present. Nevertheless, since patients in our sample suffered from migraine for more than 15 years, this seems unlikely. It would be relevant to determine longitudinal changes in pain extent in people with migraine and to see if differences are observed between the episodic and chronic forms of the condition. Third, we collected static outcomes of sensitization and only from one stimuli, pressure thresholds. We do not know if pain extent is associated with other manifestations of sensitization such as wind-up, spatial or temporal summation, or conditioned pain modulation. Finally, we did not ask the participants to report pain in other locations of their body and perhaps

widespread pain across the entire body is associated with psychological factors or sensitization in migraine sufferers.

Conclusions

This study utilised a reliable procedure to quantify pain extent in women with migraine. Pain extent within the trigemino-cervical area did not correlate with the degree of sensitization or any other clinical features in women with episodic migraine. Further research is needed to determine if the presence of expanded pain areas outside of the trigeminal-cervical area can play a relevant role in the sensitization processes in migraine.

Conflict of Interest Statement: The Author(s) declare(s) that there is no conflict of interest.

Legend of Figure

Figure 1: Pain frequency maps generated by superimposing the pain drawings of all women with episodic migraine (n=72). The colour bar represents the frequency of coloured areas. Dark red indicates the most frequently reported area of pain

References

1. Stovner LJ, Hoff JM, Svalheim S, Gilhus NE. Neurological disorders in the Global Burden of Disease 2010 study. *Acta Neurol Scand Suppl* 2014; 198: 1-6
2. Vecchia D, Pietrobon D. Migraine: a disorder of brain excitatory-inhibitory balance? *Trends Neurosci* 2012; 35: 507-520
3. de Tommaso M, Sciruicchio V. Migraine and central sensitization: Clinical features, main comorbidities and therapeutic perspectives. Curr Rheumatol Rev 2016; 12: 113-126.
4. Kitaj MB, Klink M. Pain thresholds in daily transformed migraine versus episodic migraine headache patients. *Headache* 2005; 45: 992-998.
5. Fernández-de-las-Peñas C, Madeleine P, Caminero A, Cuadrado ML, Arendt-Nielsen L, Pareja JA. Generalized neck-shoulder hyperalgesia in chronic tension-type headache and unilateral migraine assessed by pressure pain sensitivity topographical maps of the trapezius muscle. *Cephalalgia* 2010; 30: 77-86
6. Fernández-de-las-Peñas C, Madeleine P, Cuadrado ML, Ge HY, Arendt-Nielsen L, Pareja JA. Pressure pain sensitivity mapping of the temporalis muscle revealed bilateral pressure hyperalgesia in patients with strictly unilateral migraine. *Cephalalgia* 2009; 29: 670-676.
7. Florencio LL, Giantomassi MC, Carvalho GF, Gonçalves MC, Dach F, Fernández-de-las-Peñas C, Bevilaqua-Grossi D. Generalized pressure pain hypersensitivity in the cervical muscles in women with migraine. *Pain Med* 2015; 16: 1629-1634.
8. Palacios-Ceña M, Lima Florencio L, Natália Ferracini G, Barón J, Guerrero ÁL, Ordás-Bandera C, Arendt-Nielsen L, Fernández-de-Las-Peñas C. Women with chronic and episodic migraine exhibit similar widespread pressure pain sensitivity. *Pain Med*. 2016; 17: 2127-2133.
9. Hüllemann P, Keller T, Kabelitz M, Freynhagen R, Tölle T, Baron R. Pain drawings improve subgrouping of low back pain patients. *Pain Pract* 2017; 17: 293-304.

10. Graven-Nielsen T, Arendt-Nielsen L. Assessment of mechanisms in localized and widespread musculoskeletal pain. *Nat Rev Rheumatol* 2010; 6: 599-606.
11. Arendt-Nielsen L, Graven-Nielsen T. Translational musculoskeletal pain research. *Best Pract Res Clin Rheumatol* 2011; 25: 209-226.
12. Wood L, Peat G, Thomas E, Duncan R. Knee osteoarthritis in community-dwelling older adults: are there characteristic patterns of pain location? *Osteoarthritis Cartilage* 2007; 15: 615-623.
13. Lluch Girbés E, Dueñas L, Barbero M, Falla D, Baert IA, Meeus M, Sánchez-Frutos J, Aguilella L, Nijs J. Expanded distribution of pain as a sign of central sensitization in individuals with symptomatic knee osteoarthritis. *Phys Ther* 2016; 96: 1196-1207.
14. Falla D, Peolsson A, Peterson G, Ludvigsson ML, Soldini E, Schneebeli A, Barbero M. Perceived pain extent is associated with disability, depression and self-efficacy in individuals with whiplash-associated disorders. *Eur J Pain* 2016; 20: 1490-1501.
15. ICHD-III: International Classification of Headache Disorders: Headache Classification Subcommittee of the International Headache Society, 3nd edition. *Cephalalgia* 2013; 33: 629-808.
16. Dos Reis FJ, de Barros E Silva V, de Lucena RN, Mendes Cardoso BA, Nogueira LC. Measuring the pain area: An intra- and inter-rater reliability study using image analysis software *Pain Pract* 2016; 16: 24-30
17. Persson AL, Garametsos S, Pedersen J. Computer-aided surface estimation of pain drawings - intra- and inter-rater reliability. *J Pain Res* 2011; 4: 135-141.
18. Barbero M, Moresi F, Leoni D, Gatti R, Egloff M, Falla D. Test-retest reliability of pain extent and pain location using a novel method for pain drawing analysis. *Eur J Pain* 2015; 19: 1129-1138.
19. Nie H, Arendt-Nielsen L, Andersen H, Graven-Nielsen T. Temporal summation of pain evoked by mechanical stimulation in deep and superficial tissue. *J Pain* 2005; 6: 348-355

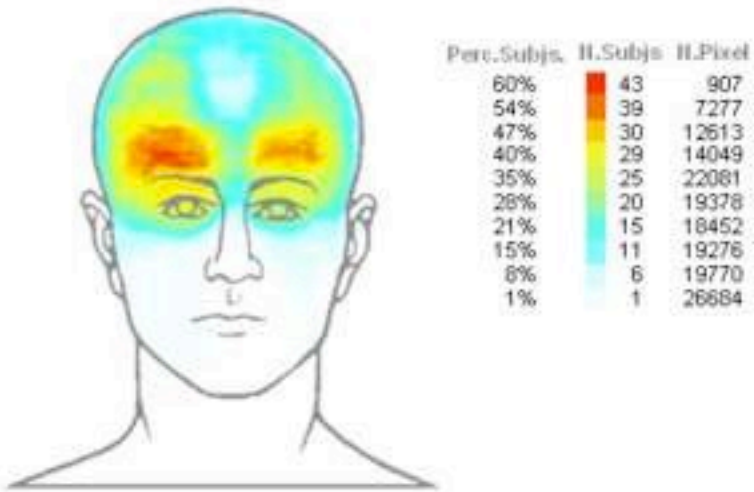
20. Walton DM, Macdermid JC, Nielson W, Teasell RW, Chiasson M, Brown L. Reliability, standard error, and minimum detectable change of clinical pressure pain threshold testing in people with and without acute neck pain. *J Orthop Sports Phys Ther* 2011; 41: 644-650
21. Zigmond AS, Snaith RP. The Hospital Anxiety and Depression Scale. *Acta Psychiatr Scand*1983; 67: 361-370.
22. Bjelland I, Dahl AA, Tangen Haug T, Neckelmann D. The validity of The Hospital Anxiety and Depression Scale: an updated literature review. *J Psychosom Res* 2002; 52: 69-77.
23. Juang KD, Wang SJ, Lin CH, Fuh JL. Use of the Hospital Anxiety and Depression Scale as a screening tool for patients with headache. *Zhonghua Yi Xue Za Zhi (Taipei)* 1999; 62: 749-755
24. Spielberger CD. State-Trait Anxiety Inventory: a comprehensive bibliography. Palo Alto, CA: Consulting Psychologists Press; 1989.
25. Barnes LLB, Harp D, Jung WS. Reliability generalization of scores on the Spielberger State-Trait Anxiety Inventory *Educ Psychol Meas* 2002; 62: 603-618
26. Stewart WF, Lipton RB, Kolodner K, Sawyer J, Lee C, Liberman JN. Validity of the Migraine Disability Assessment (MIDAS) score in com- parison to a diary-based measure in a population sample of migraine sufferers. *Pain* 2000; 88: 41-52.
27. Stewart WF, Lipton RB, Dowson AJ, Sawyer J. Development and testing of the Migraine Disability Assessment (MIDAS) questionnaire to assess headache-related disability. *Neurology* 2001; 56: S20-S28.
28. Dancey CP, Reidy J. Statistics without maths for psychology: Using SPSS for Windows. New York: Prentice Hall. 2004.
29. Shaffer JP. Multiple hypothesis testing. *Annu Rev Psychol* 1995; 46: 561-584

30. Kelman L. Migraine pain location: a tertiary care study of 1283 migraineurs. *Headache* 2005; 45: 1038-1047.
31. Chakravarty A, Mukherjee A, Roy D. Migraine pain location at onset and during established headaches in children and adolescents: a clinic-based study from eastern India. *Cephalalgia* 2007; 27: 1109-1114.
32. Ashina S, Bendtsen L, Lyngberg AC, Lipton RB, Hajiyeva N, Jensen R. Prevalence of neck pain in migraine and tension-type headache: A population study. *Cephalalgia* 2015; 35: 211-219.
33. Cuadrado ML, Young W, Fernández-de-las-Peñas C, Arias JA, Pareja JA. Migrainous corpalgia: body pain and allodynia associated with migraine attacks. *Cephalalgia* 2008; 28: 87-91.
34. Carnes D, Ashby D, Underwood M. A systematic review of pain drawing literature: should pain drawings be used for psychologic screening? *Clin J Pain* 2006; 22: 449-457.

Table 1: Spearman's rho coefficients between pain extent computed using pain drawings and clinical variables and psychological variables and pressure pain sensitivity in women with migraine (n=72).

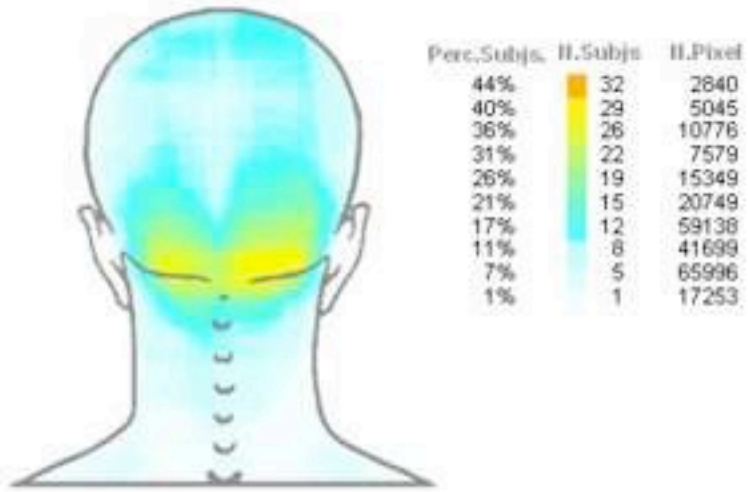
		Mean (95%CI)	rho value	P value
	Age (years)	42 (39-45)	-.046	.706
	History of migraine (years)	19.6 (16.3-22.8)	-.099	.412
	Pain extent (percentage)	13.4 (11.1-15.6)	-----	-----
	Related-disability (MIDAS)	44.1 (27.4-60.8)	.004	.977
Clinical Features	Migraine intensity (NPRS, 0-10)	8.1 (7.7-8.6)	-.026	.832
	Migraine duration (hours/attack)	23.7 (18.9-28.1)	-.110	.361
	Migraine frequency (days/month)	9.6 (8.1-11.1)	-.001	.990
Psychological variables	HADS-A (0-21)	12.3 (11.7-12.8)	-.076	.528
	HADS-D (0-21)	10.4 (9.7-11.1)	.045	.710
	STAI-trait (0-60)	25.3 (23.7-26.9)	.087	.467
	STAI-state (0-60)	21.8 (20.5-22.5)	.045	.710
PPT (kPa)	Temporalis muscle	161.5 (145.7-177.3)	.111	.354
	C5-C6 zygapophyseal joint	135.1 (124.7-145.6)	.069	.566
	Tibialis anterior muscle	333.2 (303.5-362.9)	.141	.238
	Widespread PPT mean value	210.5 (194.1-226.9)	.122	.309

NPRS: Numerical Pain Rate Scale; MIDAS: Migraine Disability Assessment Scale; PPT: Pressure Pain Threshold; HADS-A: Hospital Anxiety and Depression Scale - Anxiety Subscale; HADS-D: Hospital Anxiety and Depression Scale - Depression Subscale; STAI: State-Trait Anxiety Inventory; r: Pearson correlation test



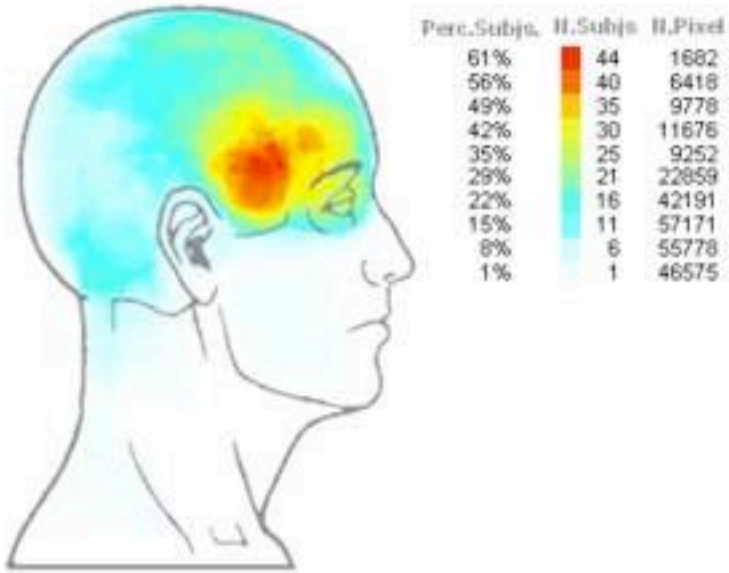
Perc.Subjs.	N.Subjs	N.Pixel
60%	43	907
54%	39	7277
47%	30	12613
40%	29	14049
35%	25	22081
28%	20	19378
21%	15	18452
15%	11	19276
8%	6	19770
1%	1	26684

Frontal view



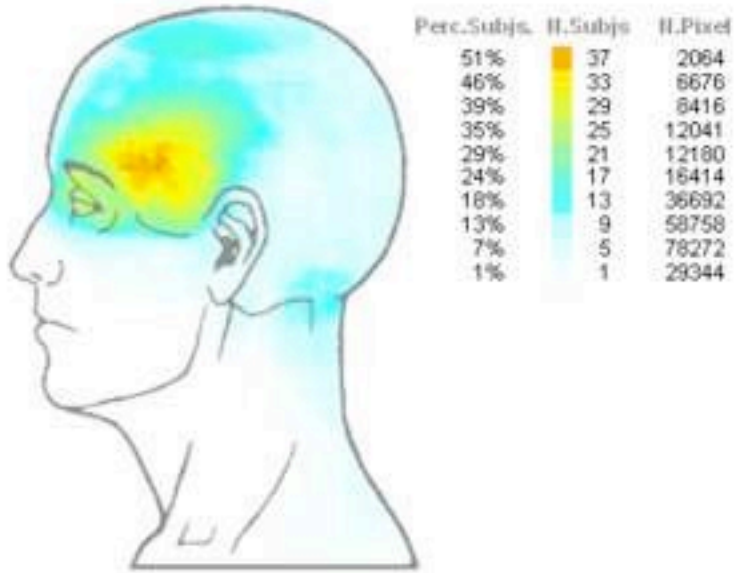
Perc.Subjs.	N.Subjs	N.Pixel
44%	32	2840
40%	29	5045
36%	26	10776
31%	22	7579
26%	19	15349
21%	15	20749
17%	12	59138
11%	8	41699
7%	5	65996
1%	1	17253

Dorsal view



Perc.Subjs.	N.Subjs	N.Pixel
61%	44	1682
56%	40	6418
49%	35	9778
42%	30	11676
35%	25	9252
29%	21	22859
22%	16	42191
15%	11	57171
8%	6	55778
1%	1	46575

Right side view



Perc.Subjs.	N.Subjs	N.Pixel
51%	37	2064
46%	33	6676
39%	29	8416
35%	25	12041
29%	21	12180
24%	17	16414
18%	13	36692
13%	9	58758
7%	5	78272
1%	1	29344

Left side view