BrJP. 2025, v.8:e20250011 • https://doi.org/10.63231/2595-0118.20250011-en

BrJP
Brazilian Journal of Pain

ORIGINAL ARTICLE

Temporal summation, conditioned pain modulation, pressure pain threshold and central sensitization symptoms in individuals with chronic migraine: cross sectional observational study

Somação temporal, modulação condicionada da dor, limiar de dor à pressão e sintomas de sensibilização em indivíduos com migrânea crônica: estudo observacional transversal

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Submitted on:
February 2, 2024.

Accepted for publication on:
December 2, 2024.

Conflict of interests:
none.

Sponsoring sources:
The authors received the following financial support for the research, authorship and/or publication of this article: Foundation for the Support of Research and Technological Innovation of the State of Sergipe (FAPITEC/SE); National Council for Scientific and Technological Development (CNPq); Coordination for the Improvement of Higher Education Personnel, Brazil (CAPES), Financial Code 001.

Associate editor in charge:
Renato Leonardo de Freitas

ABSTRACT

BACKGROUND AND OBJECTIVES: Chronic migraine is defined by attacks on 15 or more days per month, with at least eight of them presenting typical migraine characteristics, and is recognized as a central sensitization syndrome marked by somatosensory alterations and a pathophysiology that remains not fully understood. This study investigates the clinical presentation of somatosensory aspects in individuals with chronic migraine during the interictal phase compared to healthy individuals.

METHODS: This is a cross-sectional observational study conducted in individuals with chronic migraine and healthy individuals aged between 18 and 55 years. Measures**:** temporal summation (temporal summation test), conditioned pain modulation (conditioned pain modulation test), pressure pain threshold (algometer), central sensitization (Central Sensitization Inventory) and allodynia (12-item checklist of allodynia symptoms).

RESULTS: 32 migraine individuals (MG) and 22 from the health control group (CG) were included in this study. In the temporal sum test, pain amplification showed a significant difference between groups MG and CG in all seconds analyzed. Pressure pain thresholds were significantly lower in the moments of three measurements in the MG compared to the CG in the conditioned pain modulation test. Pressure pain thresholds in the head, neck and right tibialis anterior muscles were significantly lower in the MG compared to the CG. Central Sensitization Inventory scores were equivalent to an average of 56/100 points, representing a severe level of these central sensitization symptoms with chronic migraine. Severe symptoms of allodynia were present in 52% of participants with chronic migraine.

CONCLUSION: When assessed in the interictal period, individuals with chronic migraine showed alterations in somatosensory aspects related to pain, identified by amplification of the magnitude of the pain response, deficits in endogenous pain inhibition mechanisms, profound mechanical hyperalgesia and allodynia.

KEYWORDS: Central nervous system sensitization, Chronic pain, Headache disorders, Migraine disorders, Pain measurement.

RESUMO

JUSTIFICATIVA E OBJETIVOS: A migrânea crônica é definida por ataques em 15 ou mais dias por mês, com pelo menos oito deles apresentando características típicas de migrânea, sendo reconhecida como uma síndrome de sensibilização central marcada por alterações somatossensoriais e uma fisiopatologia que permanece não totalmente compreendida. Este estudo investiga a apresentação clínica dos aspectos somatossensoriais em indivíduos com migrânea crônica durante a fase interictal em comparação com indivíduos saudáveis.

MÉTODOS: Trata-se de um estudo transversal observacional conduzido em indivíduos com migrânea crônica e indivíduos saudáveis com idade entre 18 e 55 anos. Medidas**:** somação temporal (teste de somação temporal), modulação condicionada da dor (teste de modulação condicionada da dor), limiar de dor à pressão (algômetro), sensibilização central (Central Sensitization Inventory) e alodínia (lista de verificação de 12 itens de sintomas de alodínia).

RESULTADOS: Foram incluídos neste estudo 32 indivíduos com migrânea crônica (GM) e 22 no grupo controle (GC). No teste de somação temporal, a amplificação da dor apresentou diferença significativa entre os grupos GM e GC em todos os segundos analisados. Os limiares de dor à pressão foram significativamente menores nos momentos das três medidas no GM em comparação ao GC no teste de modulação condicionada da dor. Os limiares de dor à pressão nos músculos da cabeça, pescoço e tibial anterior direito foram significativamente menores no GM em comparação ao GC. Os escores do Inventário de Sensibilização Central foram equivalentes à média de 56/100 pontos, representando um nível grave desses sintomas de sensibilização central nos participantes com migrânea crônica. Sintomas graves de alodínia estavam presentes em 52% dos participantes com migrânea crônica.

CONCLUSÃO: Quando avaliados no período intericta, os indivíduos com migrânea crônica apresentaram alterações nos aspectos somatossensoriais relacionados à dor identificados por meio da amplificação da magnitude da resposta dolorosa, déficits nos mecanismos endógenos de inibição da dor, hiperalgesia mecânica profunda e alodínia.

DESCRITORES: Dor crônica, Medição da dor, Sensibilização do sistema nervoso central, Transtornos de cefaleia, Transtornos de migrânea.

HIGHLIGHTS

- Chronic migraines are characterized by an amplification of the pain response, deficits in endogenous pain inhibition and mechanical hyperalgesia, with a high prevalence of symptoms of central sensitization and allodynia
- Tools such as quantitative sensory tests map the somatosensory profile, deepening the understanding of the mechanisms underlying pain and aiding in the personalization of therapeutic strategies
- Reduced efficiency in conditioned pain modulation, associated with cutaneous allodynia, demonstrates dysregulation in pain modulation mechanisms

INTRODUCTION

Primary headache is a type of headache whose etiology is unknown, it is characterized by hypersensitivity to stimuli and was considered the second leading cause of disability in 2016 by the Global Burden of Disease Study[1,2]. According to the International Classification of Headaches, migraine consists of a chronic condition when it recurs on 15 days a month, of which at least 8 days have migraine characteristics, such as pain with moderate to severe intensity, pulsatile, unilateral and phobia of smells, sounds and lights[1].

The clinical presentation of migraine is complex and multifaceted, with four phases: premonitory, aura, headache and postdrome, which can be linear, overlapping or cyclical[3]. Furthermore, the period between attacks known as interictal, which is related to the absence of migraine symptoms[4].

Despite the exponential growth of studies about migraine in recent years, its pathophysiology is still not fully understood, but some mechanisms identified as likely responsible for the development and management of migraine crises[5]. For a long time, changes in the vascular system justified the existence of crises, but recently other currents have come to consider migraine as a central sensitization syndrome, with the involvement and impairment of several body systems[3,5].

From the activation and involvement of several brain areas, whether triggering a migraine crisis, causing pain, or even in the presence of associated symptoms that occur during the duration of the crisis, given the inherent complexity of cases of chronic migraine, it is worth highlighting the aspects somatosensory factors involved in its pathophysiology and in the chronification process: temporal summation, conditioned pain modulation, pressure pain threshold, allodynic and central sensitization symptoms[3,5].

However, despite extensive research efforts, controversies persist regarding the alterations in parameters associated with the perception of both nociceptive and non-nociceptive stimuli throughout the cyclic phases of migraine. Notably, existing literature has primarily focused on the somatosensory aspects during the ictal and perictal phases, leaving gaps in our understanding of the interictal phase of chronic migraine[6].

Recent studies have contributed valuable insights in this area. An observational study explored profiles of patients with episodic migraine during the ictal/perictal phase, revealing distinct groups based on clinical and psychophysical variables[6]. Similarly, another observational study investigated these profiles during the interictal phase, identifying heterogeneous patterns of pain sensitivity and functional impairment among patients with episodic and chronic migraine[7]. Additionally, another observational study examined the intricate relationship between clinical and psychophysical characteristics across different phases of the episodic and chronic migraine cycle[7].

Despite this progress, further investigations are needed to elucidate the underlying mechanisms driving these observed variations and their implications for personalized strategies in an attempt to managing chronic migraine. Therefore, the aim of this study was to investigate the clinical presentation of somatosensory aspects in subjects with chronic migraine during the interictal phase compared to healthy subjects.

METHODS

Study design

This is an epidemiological, observational, comparative and cross-sectional study, in which individuals with a clinical diagnosis of chronic migraine were considered as the target population and compared with healthy individuals. This study considered and met the requirements of the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE)[8].

This study included individuals of both genders aged between 18 and 55 years, with a history of chronic migraine diagnosed by a qualified neurologist according to the criteria of the International Headache Society[1].

In addition, individuals with other types of associated secondary headache, history of head and/or neck trauma, neurological diseases, psychiatric diseases, inability to understand instructions or consent for the study, severe respiratory diseases, and pregnancy were not included in the study, and with comorbidities that present symptoms of headache, such as uncontrolled high blood pressure and fibromyalgia.

Control group consisted of participants with a maximum of two episodes of headache in the last year who did not meet the criteria for migraine or any other type of chronic headache. Exclusion criteria for the control group were the same as those used for the migraine group. Additionally, individuals did not have any other type of pain in other body regions.

Procedures

The recruitment of participants was carried out through social networks (official website of the University, official laboratory

pages on Instagram and Facebook, as well as by referral, from January 2019 to February 2020.

People who met the inclusion criteria and who did not have a clinical diagnosis were referred to a neurologist experienced in headache. After diagnostic consolidation, the volunteers were evaluated individually, as well as the individuals in the control group.

Two investigators underwent training and conducted a pilot study to standardize the evaluation using the instruments established for the research methodology. The evaluation proceeded as follows:

- Migraine group: temporal summation tests, conditioned pain modulation test, pressure pain threshold, central sensitization inventory and 12-item checklist of allodynia symptoms were performed.
- Control group: the evaluation was equivalent to that performed in the migraine group; however, the following variables were not applied: central sensitization inventory, and the 12-item checklist of allodynia symptoms.

It is worth mentioning that, in all evaluations carried out in the group of patients with migraine, they were in the interictal phase without headache or other symptoms. The assessment form consisted of sociodemographic data such as age, height, weight, body mass index, age at which migraine attacks began, history of the current illness, family history, the drugs used, associated illnesses and social history.

- Temporal summation (TS): consists of a quantitative sensory test, which seeks to verify the mechanism of constant and repetitive nociceptive nerve stimulation (wind-up) that results in an exacerbated response in the central nervous system, with an increase in the magnitude and frequency of this response[9]. For this test, a digital pressure algometer (Impac™, Paulínia, SP, Brazil; with an area of 1 cm^2) was used with a pressure of 2.5 kg applied on the anterior surface of the patient's dominant forearm, 7.5 cm proximally to the distal crease of the wrist. After that, this continuous pressure was applied for 30 seconds, with four measurements related to pain intensity through an 11-point numerical scale, at the 1st second, 10th second, 20th second and 30th second[10,11]. The pressure of 2.5 kg was chosen based on specific protocols to evaluate sensitivity to mechanical stimulus and pain response. To ensure pressure adequacy and avoid excessive discomfort, the protocol was monitored and adjusted as necessary. Participants were instructed about the procedure and the pain scale, and adjustments were made so that the pressure was not enough to cause pain or was uncomfortable, always within ethical and safety limits[12].
- Conditioned pain modulation (CPM): corresponds to the phenomenon in which the perception of pain at a site is inhibited in the face of a conditioned painful stimulus, based on the descending noxious inhibitory control mechanism or "pain inhibiting pain"[13]. The initial pressure pain threshold (PPT) was measured using a digital pressure algometer (Impac™, Paulínia, SP, Brazil; with an area of 1 cm^2), positioned on the anterior surface of the dominant forearm, 7.5 cm proximally to the distal crease of the wrist. Then, an ischemic compression was performed on the individual's contralateral upper limb, using a sphygmomanometer (Mikatos™, Embu, SP, Brazil) positioned with the lower edge of the device 3 cm proximal to the cubital fossa and a pressure of 270 mmHg maintained. Then, the individual was asked about the intensity of pain from the numerical scale of 11 points, after reporting pain 4, a new measurement of the PPT was performed in the dominant forearm simultaneously with the ischemic compression. Then, five minutes after the end of the procedure, the PPT was measured again.
- Pressure pain threshold (PPT): represents the initial pain sensitivity reported by the patient and can be measured using a mechanical or electronic pressure algometer[14]. The thresholds were evaluated using a previously calibrated digital pressure algometer (Impac™, Paulínia, SP, Brazil; with an area of 1 cm^2). Participants were instructed to report when the pressure sensation became painful. With the patient in the supine position, three bilateral measurements evaluated in the muscle bellies of the following muscles (primary PPT): A – temporal (muscle belly), B – frontal (2 cm above the midpoint of the supraorbital arch), C – masseter (1 cm superior and 2 cm anterior to the mandibular angle), D – sternocleidomastoid (SCOM) and E – upper trapezius muscle. The secondary PPT evaluated in the right anterior tibial muscle[15,16].
- Central sensitization: described as a phenomenon involving hypersensitivity of the central nervous system[17]. The Central Sensitization Inventory (CSI) was validated for Portuguese in 2017; this instrument evaluates the presence of central sensitization in patients with chronic pain in clinical practice and scientific research[18]. It consists of two parts, the first part consists of 25 items that generate a final score from 0 to 100 points, while the second part is related to diagnoses already closed, the higher the scores, the more likely the involvement of mechanisms consistent with the diagnosis.
- Allodynia symptom: presents itself from a stimulus that normally does not cause pain, generating a painful sensation; this symptom can be pointed out as a predictive factor of migraine chronification. The 12-item Allodynia Symptom Checklist (ASC-12) is a quick and easy-to-administer questionnaire, validated for the Brazilian version in individuals with migraine[19]. It assesses symptoms of cutaneous allodynia and categorizes them into severity levels. It consists of 12 questions and their sum provides a score from 0 to 24, where each question is scored as follows: "this situation does not apply to me", "rarely", or "no, never" = 0; "sometimes yes, sometimes no" = 1; "most of the time" = 2. Thus, it is classified according to severity, where: no allodynia (0-2 points); mild allodynia (3-5 points); moderate allodynia (6-8 points); severe allodynia (9 or more points).

Bias

To minimize the biases involved in this type of study, the following precautions were considered:

- Observer/interviewer bias: the same observer assessed all individuals included in the study using validated tools and questionnaires; however, there was no blinding regarding exposure and outcome.
- Recall bias: participants were blinded to the study hypothesis, in addition, cases and controls were equally encouraged to

recall past events, and both assessments/interviews of cases and controls were carried out in the same room and with the same controlled environment.
- Performance bias: in both groups the interviewer/evaluator maintained the standard posture during the study stages.
- Detection bias: in both groups the same assessment instruments and questionnaires were used, except those tools and questionnaires that were specific for the assessment of individuals with chronic migraine.
- Confusion bias: to avoid this type of bias the study design outlined the eligibility criteria, pairing and stratification of the sample.

Sample size

Sample size was determined based on the mean and standard deviation (SD) taken from a study that compared PPTs in the trapezius muscle between individuals with migraine and healthy participants[20]. *PEPI-for-Windows™ (WinPEPI)* software was used in the *Sample Size* domain, comparing two groups (radius B:A=1), using mean (SD), SD migraine group (A)=2.5; SD healthy individuals (B)=2.8, of the variable PPT, assuming a clinically significant difference of 20% in the PPT. The alpha domain was 5%, assuming a significance of 0.05 and the beta domain 80%. The required sample was 56 subjects (28 in group A and 28 in group B), with an expected accuracy of approximately 95% confidence interval for mean difference (D)= D - 1.405 to D + 1.405.

Ethical aspects

This project was approved by the Ethics Committee for Research with Human Beings of the Federal University of Sergipe, CAEE: 08310319.1.0000.5546, under opinion number 3.303.828. All subjects included in this study signed the Free and Informed Consent Term (FICT) prior to the evaluation, in compliance with Resolution 466/12 of the Brazilian Health Council (*Conselho Nacional de Saúde* - CNS).

Statistical analysis

The collected data was transferred to Microsoft® Office Excel, 2018 data sheets. The software used to perform the statistical analyzes was GraphPad Prism version 6.0 (San Diego, CA, USA). Values were expressed as mean, standard error of mean and frequency. All variables were tested for normality using the Shapiro-Wilk test. Data that followed a normal distribution were analyzed using the t test for independent measures, whereas non-parametric data were compared using the Mann-Whitney test. Categorical variables were evaluated using Fisher's Exact test and the Chi-square test, according to their specificities.

For variables with several measures within the same group over a previously stipulated period (temporal summation and conditioned pain modulation), ANOVA test was also used for repeated measures followed by Bonferroni *post hoc* when the data were parametric (conditioned modulation of pain; pain strata mild pain and moderate pain) and Friedman followed by Tukey's *post hoc* for those non-parametric data. In all comparisons, statistically significant differences were considered when the p value in the analysis was less than 0.05 ($p<0.05$), indicating a minimal chance of the event occurring due to chance.

RESULTS

A total of 69 eligible volunteers were recruited through phone screening, of whom thirty-five were excluded based on pre-established criteria. This resulted in the recruitment of 34 volunteers, but two did not attend the assessments. Consequently, 32 individuals with migraines were evaluated. Therefore, total sample for this study consisted of 32 migraine patients (MG) and 32 healthy control volunteers (CG). Sociodemographic characteristics of participants from both groups are described in Table 1.

Variables

In the temporal summation test, pain amplification showed a significant difference between the migraine group compared to the control group in all analyzed timepoints, being in normal patterns in the control group and exacerbated in the migraine group. The following values were found: in the first second, MG 3.25±0.42 and CG 1.59±0.35 with p=0.009; in the twelfth, MG 4.65±0.52 and CG 2.18±0.38 with p=0.002; in the twenty second, MG 5.15±0.53 and CG 3.09±0.47 with p=0.009; and in the thirty second, MG 5.84±0.53 and CG 3.40 ±0.50 with p=0.003 (Figure 1).

In the conditioned pain modulation test, PPTs were significantly lower at all three measurement times in the migraine group compared to the control group. Before ischemic compression, the GM subjects had 3.59±0.31 kgf, while CG had 5.91±0.51 kgf, with p= 0.003; during ischemic compression, GM had 4.59±0.32 kgf and CG 7.44±0.54 kgf, with p= 0.001; after five minutes of ischemic compression, GM had 3.86±0.33 kgf) and CG had 5.68±0.44 kgf, with p=0.001 (Figure 2).

Pressure pain thresholds in the muscles of the head, neck and right tibialis anterior muscle were significantly lower in the migraine group compared to the control group (Figure 3).

Scores found through the Central Sensitization Inventory were equivalent to 56 points on a score from 0 to 100. Allodynia verified by the 12-item list of allodynia symptoms was applied only to 25 patients out of 32 patients with chronic migraine and demonstrated that 52% had severe allodynic symptoms, 24% moderate allodynic symptoms, 4% mild allodynic symptoms and only 20% had no allodynic symptoms.

DISCUSSION

The main findings of this study can be summarized as follows: people with chronic migraine exhibited amplification of the magnitude of pain response, deficits in endogenous pain inhibition mechanisms and decreased pressure pain thresholds or mechanical hyperalgesia when compared to control individuals. In addition,

Table 1. Sociodemographic characterization of the sample.

Variables	Migraine Group (n=32)	Control Group (n=22)	p-value
Gender			
Female	28 (87.5%)	18 (81.8%)	0.701[c]
Male	4 (12.5%)	4 (18.2%)	
Age (years)	33.84±1.47	29.27±0.93	0.047[b]
Weight (kg)	64.64±2.94	66.19±2.13	0.514b
Height (m)	1.64±0.01	1.63±0.01	0.713[a]
BMI (kg/m^2)	23.73±0.77	24.73±0.73	0.279b

Data presented as mean, standard error of mean and percentage. kg: kilogram; m: meters; kg/m^2: kilogram divided by meter squared; n: number of individuals per group; BMI = body mass index; [a]t test for independent measures; [b]Mann-Whitney test for independent measures; [c]Chi-square test.

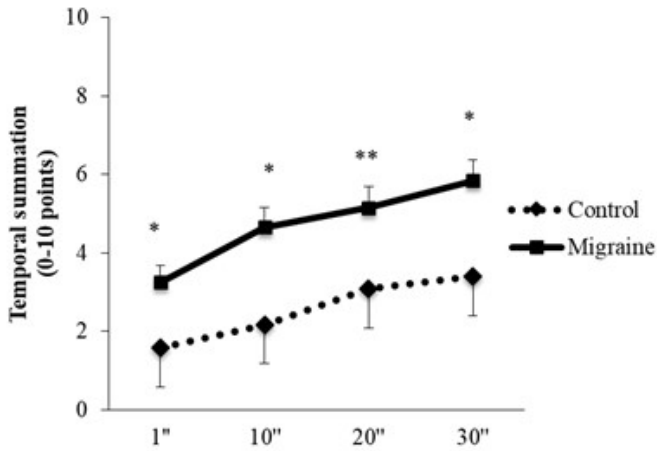

Figure 1. Temporal summation test through pain intensity at sequential times (1st second, 10th second, 20th second and 30th second) between control group and migraine group. Data expressed as mean and standard error of the mean. *Different from the control group, Mann-Whitney test for independent samples (p<0.05). **Different from the control group, t-test for independent samples (p=0.009).

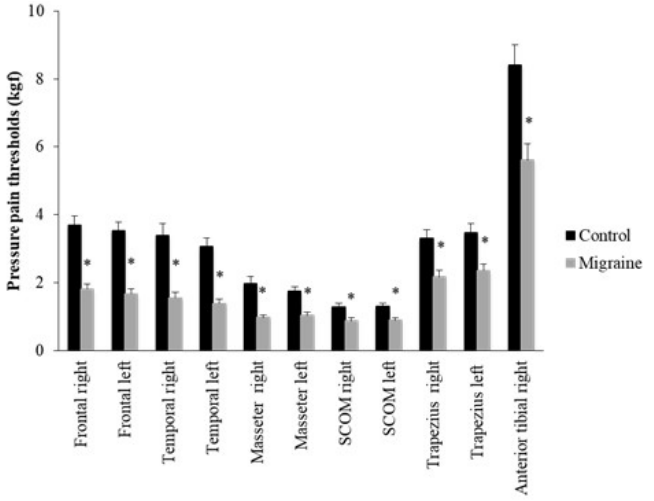

Figure 3. Pressure pain threshold in kgf in the head and neck muscles and in the tibialis anterior muscle between the control group and the migraine group. SCOM = sternocleidomastoid. Data expressed as mean and standard error of the mean. *Different from the control group for all assessed muscles, Mann-Whitney test (p<0.05).

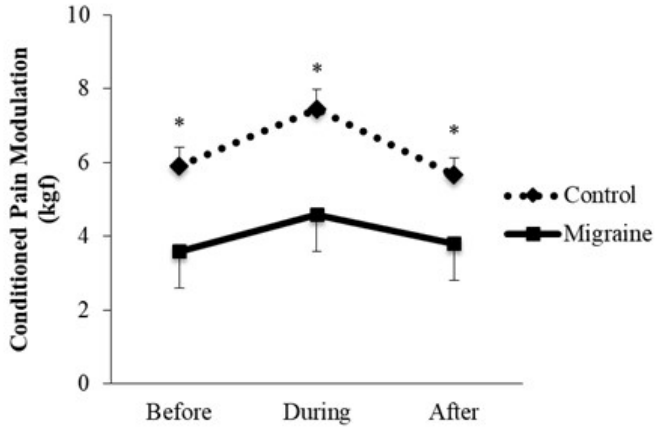

Figure 2. Conditioned pain modulation measured using pressure pain threshold (kgf) between control and migraine groups. Data expressed as mean and standard error of the mean. *Mann-Whitney test for independent samples, different from the control group assuming the highest p value, in this case p=0.003.

it was possible to identify severe levels of central sensitization and severe allodynic conditions in people with chronic migraine.

Quantitative sensory tests are used to assess somatosensory functions and help to understand the clinical neurophysiology of pain[5,21]. In this study, three quantitative sensory tests were used, namely, temporal summation, conditioned pain modulation and pressure pain thresholds, these contribute to the mapping of the somatosensory profile in people with chronic migraine in the interictal phase and control subjects.

This study observed that people with chronic migraine presented an amplification of the painful response to a repetitive stimulus through the pain temporal summation mechanism. In agreement with previous studies with experimental and daily stimuli[22], which presented similar results, however using different protocols, such as the use of von Frey filaments and the visual analog pain scale.

Persons with chronic migraine exhibited less efficient conditioned pain modulation mechanism than healthy controls

in this research. These findings are suggestive of the presence of deregulation of pain modulatory mechanisms. In this context, pain descending inhibitory pathways may be deficient in these people, leading to increased pain perception with a subsequent process of hyperactivation of pain facilitation pathways, in line with data highlighted in reviews previously found in the literature[5,21,23].

Furthermore, the individuals with chronic migraine showed increased mechanical hyperalgesia compared to control subjects in the sample of this research. Commonly, this assessment of the mechanical pain threshold has been performed in the head and neck muscles, representing primary and secondary hyperalgesia and consequent peripheral sensitization process. However, few studies, like the present study, have evaluated the pressure pain threshold in regions distal to the main pain area, representing tertiary hyperalgesia, reaffirming the presence of the central sensitization process[24].

In this study, people with migraine had an average score above 40 points, indicating moderate levels of severity for central sensitization symptoms[25]. So far, this study observed the need for more studies that assess the presence of central sensitization symptoms through CSI in chronic migraine patients in order to carry out compilations of future results in scientific research with high methodological rigor.

This study noticed a high prevalence of allodynic symptoms, especially in individuals with moderate to severe levels of severity. Clinically, it is important to recognize this symptom of cutaneous allodynia, as it is a known factor in the chronification process and can influence the poor response to some therapeutic modalities, such as neuromodulation, electrical stimulation, and manual therapies due to contact in the region[26].

Some limitations can be listed in this study, first care must be taken when extrapolating these data to the male population, since this population corresponded to the minority of the sample. Likewise, migraine is associated with alterations in the female hormonal cycle, and this study did not record the phase of the menstrual cycle at the time of evaluation. Another point to consider is the format of the study itself since it makes it impossible to establish a cause and consequence relationship between the results found due to the cross-sectional nature of this study. Finally, although two trained assessors performed assessments, they not blinded to the chronic migraine diagnosis and control subjects.

Strengths of this study include the population of people with chronic migraine well established and provided through a clinical diagnosis. In this study, all description and design followed the recommendations of STROBE tool[8]. Furthermore, a clinical neurophysiological approach to pain was used through quantitative sensory tests described in the literature[21]. Clinically, the responses observed in the sample of this study reinforce that people with chronic migraine present somatosensory disorders even in the absence of crises, implying central and peripheral symptomatology.

The findings of this study provide valuable information for clinicians in the management of chronic migraine. The identification of amplification of the pain response, deficits in endogenous pain inhibition, and mechanical hyperalgesia highlights the need for comprehensive therapeutic approaches. Quantitative sensory testing offers a useful tool for mapping the somatosensory profile, allowing for a more in-depth understanding of the clinical physiology of pain. The observation of reduced efficiency in conditioned pain modulation suggests possible dysregulations in pain modulating mechanisms, indicating specific therapeutic pathways. The high prevalence of symptoms of central sensitization and allodynia highlights the need to consider these aspects when formulating treatment strategies. Recognizing the presence of cutaneous allodynia is crucial for appropriate therapy selection as it may influence the response to specific therapeutic modalities.

Future studies may consider the presence of a greater description of migraine-related characteristics, such as intensity, frequency, duration, and associated symptoms. In addition, this study can support future intervention studies focused on the aspects addressed.

CONCLUSION

Individuals with chronic migraine have increased pain response magnitude, deficits in endogenous pain inhibition mechanisms and decreased pressure pain thresholds when compared to control individuals. In addition, it was possible to identify severe levels of central sensitization and severe allodynic conditions in people with chronic migraine.

REFERENCES

1. International Headache Society. Headache Classification Committee. The International Classification of Headache Disorders, 3rd ed. (beta version). Cephalalgia. 2013;33(9):629-808. http://doi.org/10.1177/0333102413485658. PMid:23771276.

2. Vos T, Abajobir AA, Abate KH, Abbafati C, Abbas KM, Abd-Allah F, Abdulkader RS, Abdulle AM, Abebo TA, Abera SF, Aboyans V, Abu-Raddad LJ, Ackerman IN, Adamu AA, Adetokunboh O, Afarideh M, Afshin A, Agarwal SK, Aggarwal R, Agrawal A, Agrawal S, Ahmadieh H, Ahmed MB, Aichour MTE, Aichour AN, Aichour I, Aiyar S, Akinyemi RO, Akseer N, Al Lami FH, Alahdab F, Al-Aly Z, Alam K, Alam N, Alam T, Alasfoor D, Alene KA, Ali R, Alizadeh-Navaei R, Alkerwi A, Alla F, Allebeck P, Allen C, Al-Maskari F, Al-Raddadi R, Alsharif U, Alsowaidi S, Altirkawi KA, Amare AT, Amini E, Ammar W, Amoako YA, Andersen HH, Antonio CAT, Anwari P, Ärnlöv J, Artaman A, Aryal KK, Asayesh H, Asgedom SW, Assadi R, Atey TM, Atnafu NT, Atre SR, Avila-Burgos L, Avokphako EFGA, Awasthi A, Bacha U, Badawi A, Balakrishnan K, Banerjee A, Bannick MS, Barac A, Barber RM, Barker-Collo SL, Bärnighausen T, Barquera S, Barregard L, Barrero LH, Basu S, Battista B, Battle KE, Baune BT, Bazargan-Hejazi S, Beardsley J, Bedi N, Beghi E, Béjot Y, Bekele BB, Bell ML, Bennett DA, Bensenor IM, Benson J, Berhane A, Berhe DF, Bernabé E, Betsu BD, Beuran M, Beyene AS, Bhala N, Bhansali A, Bhatt S, Bhutta ZA, Biadgilign S, Bicer BK, Bienhoff K, Bikbov B, Birungi C, Biryukov S, Bisanzio D, Bizuayehu HM, Boneya DJ, Boufous S, Bourne RRA, Brazinova A, Brugha TS, Buchbinder R, Bulto LNB, Bumgarner BR, Butt ZA, Cahuana-Hurtado L, Cameron E, Car M, Carabin H, Carapetis JR, Cárdenas R, Carpenter DO, Carrero JJ, Carter A, Carvalho F, Casey DC, Caso V, Castañeda-Orjuela CA, Castle CD, Catalá-López F, Chang H-Y, Chang J-C, Charlson FJ, Chen H, Chibalabala M, Chibueze CE, Chisumpa VH, Chitheer AA, Christopher DJ, Ciobanu LG, Cirillo M, Colombara D, Cooper C, Cortesi PA, Criqui MH, Crump JA, Dadi AF, Dalal K, Dandona L, Dandona R, das Neves J, Davitoiu DV, de Courten B, De Leo DD, Defo BK, Degenhardt L, Deiparine S, Dellavalle RP, Deribe K, Des Jarlais DC, Dey S, Dharmaratne SD, Dhillon PK, Dicker D, Ding EL, Djalalinia S, Do HP, Dorsey ER, dos Santos KPB, Douwes-Schultz D, Doyle KE, Driscoll TR, Dubey M, Duncan BB, El-Khatib ZZ, Ellerstrand J, Enayati A, Endries AY, Ermakov SP, Erskine HE, Eshrati B, Eskandarieh S, Esteghamati A, Estep K, Fanuel FBB, Farinha CSES, Faro A, Farzadfar F, Fazeli MS, Feigin VL, Fereshtehnejad S-M, Fernandes JC, Ferrari AJ, Feyissa TR, Filip I, Fischer F, Fitzmaurice C, Flaxman AD, Flor LS, Foigt N, Foreman KJ,

Franklin RC, Fullman N, Fürst T, Furtado JM, Futran ND, Gakidou E, Ganji M, Garcia-Basteiro AL, Gebre T, Gebrehiwot TT, Geleto A, Gemechu BL, Gesesew HA, Gething PW, Ghajar A, Gibney KB, Gill PS, Gillum RF, Ginawi IAM, Giref AZ, Gishu MD, Giussani G, Godwin WW, Gold AL, Goldberg EM, Gona PN, Goodridge A, Gopalani SV, Goto A, Goulart AC, Griswold M, Gugnani HC, Gupta R, Gupta R, Gupta T, Gupta V, Hafezi-Nejad N, Hailu GB, Hailu AD, Hamadeh RR, Hamidi S, Handal AJ, Hankey GJ, Hanson SW, Hao Y, Harb HL, Hareri HA, Haro JM, Harvey J, Hassanvand MS, Havmoeller R, Hawley C, Hay SI, Hay RJ, Henry NJ, Heredia-Pi IB, Hernandez JM, Heydarpour P, Hoek HW, Hoffman HJ, Horita N, Hosgood HD, Hostiuc S, Hotez PJ, Hoy DG, Htet AS, Hu G, Huang H, Huynh C, Iburg KM, Igumbor EU, Ikeda C, Irvine CMS, Jacobsen KH, Jahanmehr N, Jakovljevic MB, Jassal SK, Javanbakht M, Jayaraman SP, Jeemon P, Jensen PN, Jha V, Jiang G, John D, Johnson SC, Johnson CO, Jonas JB, Jürisson M, Kabir Z, Kadel R, Kahsay A, Kamal R, Kan H, Karam NE, Karch A, Karema CK, Kasaeian A, Kassa GM, Kassaw NA, Kassebaum NJ, Kastor A, Katikireddi SV, Kaul A, Kawakami N, Keiyoro PN, Kengne AP, Keren A, Khader YS, Khalil IA, Khan EA, Khang Y-H, Khosravi A, Khubchandani J, Kiadaliri AA, Kieling C, Kim YJ, Kim D, Kim P, Kimokoti RW, Kinfu Y, Kisa A, Kissimova-Skarbek KA, Kivimaki M, Knudsen AK, Kokubo Y, Kolte D, Kopec JA, Kosen S, Koul PA, Koyanagi A, Kravchenko M, Krishnaswami S, Krohn KJ, Kumar GA, Kumar P, Kumar S, Kyu HH, Lal DK, Lalloo R, Lambert N, Lan Q, Larsson A, Lavados PM, Leasher JL, Lee PH, Lee J-T, Leigh J, Leshargie CT, Leung J, Leung R, Levi M, Li Y, Li Y, Li Kappe D, Liang X, Liben ML, Lim SS, Linn S, Liu PY, Liu A, Liu S, Liu Y, Lodha R, Logroscino G, London SJ, Looker KJ, Lopez AD, Lorkowski S, Lotufo PA, Low N, Lozano R, Lucas TCD, Macarayan ERK, Magdy Abd El Razek H, Magdy Abd El Razek M, Mahdavi M, Majdan M, Majdzadeh R, Majeed A, Malekzadeh R, Malhotra R, Malta DC, Mamun AA, Manguerra H, Manhertz T, Mantilla A, Mantovani LG, Mapoma CC, Marczak LB, Martinez-Raga J, Martins-Melo FR, Martopullo I, März W, Mathur MR, Mazidi M, McAlinden C, McGaughey M, McGrath JJ, McKee M, McNellan C, Mehata S, Mehndiratta MM, Mekonnen TC, Memiah P, Memish ZA, Mendoza W, Mengistie MA, Mengistu DT, Mensah GA, Meretoja TJ, Meretoja A, Mezgebe HB, Micha R, Millear A, Miller TR, Mills EJ, Mirarefin M, Mirrakhimov EM, Misganaw A, Mishra SR, Mitchell PB, Mohammad KA, Mohammadi A, Mohammed KE, Mohammed S, Mohanty SK, Mokdad AH, Mollenkopf SK, Monasta L, Montico M, Moradi-Lakeh M, Moraga P, Mori R, Morozoff C, Morrison SD, Moses M, Mountjoy-Venning C, Mruts KB, Mueller UO, Muller K, Murdoch ME, Murthy GVS, Musa KI, Nachega JB, Nagel G, Naghavi M, Naheed A, Naidoo KS, Naldi L, Nangia V, Natarajan G, Negasa DE, Negoi RI, Negoi I, Newton CR, Ngunjiri JW, Nguyen TH, Nguyen QL, Nguyen CT, Nguyen G, Nguyen M, Nichols E, Ningrum DNA, Nolte S, Nong VM, Norrving B, Noubiap JJN, O'Donnell MJ, Ogbo FA, Oh I-H, Okoro A, Oladimeji O, Olagunju TO, Olagunju AT, Olsen HE, Olusanya BO, Olusanya JO, Ong K, Opio JN, Oren E, Ortiz A, Osgood-Zimmerman A, Osman M, Owolabi MO, Pa M, Pacella RE, Pana A, Panda BK, Papachristou C, Park E-K, Parry CD, Parsaeian M, Patten SB, Patton GC, Paulson K, Pearce N, Pereira DM, Perico N, Pesudovs K, Peterson CB, Petzold M, Phillips MR, Pigott DM, Pillay JD, Pinho C, Plass D, Pletcher MA, Popova S, Poulton RG, Pourmalek F, Prabhakaran D, Prasad NM, Prasad N, Purcell C, Qorbani M, Quansah R, Quintanilla BPA, Rabiee RHS, Radfar A, Rafay A, Rahimi K, Rahimi-Movaghar A, Rahimi-Movaghar V, Rahman MHU, Rahman M, Rai RK, Rajsic S, Ram U, Ranabhat CL, Rankin Z, Rao PC, Rao PV, Rawaf S, Ray SE, Reiner RC, Reinig N, Reitsma MB, Remuzzi G, Renzaho AMN, Resnikoff S, Rezaei S, Ribeiro AL, Ronfani L, Roshandel G, Roth GA, Roy A, Rubagotti E, Ruhago GM, Saadat S, Sadat N, Safdarian M, Safi S, Safiri S, Sagar R, Sahathevan R, Salama J, Saleem HOB, Salomon JA, Salvi SS, Samy AM, Sanabria JR, Santomauro D, Santos IS, Santos JV, Santric Milicevic MM, Sartorius B, Satpathy M, Sawhney M, Saxena S, Schmidt MI, Schneider IJC, Schöttker B, Schwebel DC, Schwendicke F, Seedat S, Sepanlou SG, Servan-Mori EE, Setegn T, Shackelford KA, Shaheen A, Shaikh MA, Shamsipour M, Shariful Islam SM, Sharma J, Sharma R, She J, Shi P, Shields C, Shifa GT, Shigematsu M, Shinohara Y, Shiri R, Shirkoohi R, Shirude S, Shishani K, Shrime MG, Sibai AM, Sigfusdottir ID, Silva DAS, Silva JP, Silveira DGA, Singh JA, Singh NP, Sinha DN, Skiadaresi E, Skirbekk V, Slepak EL, Sligar A, Smith DL, Smith M, Sobaih BHA, Sobngwi E, Sorensen RJD, Sousa TCM, Sposato LA, Sreeramareddy CT, Srinivasan V, Stanaway JD, Stathopoulou V, Steel N, Stein MB, Stein DJ, Steiner TJ, Steiner C, Steinke S, Stokes MA, Stovner LJ, Strub B, Subart M, Sufiyan MB, Sunguya BF, Sur PJ, Swaminathan S, Sykes BL, Sylte DO, Tabarés-Seisdedos R, Taffere GR, Takala JS, Tandon N, Tavakkoli M, Taveira N, Taylor HR, Tehrani-Banihashemi A, Tekelab T, Terkawi AS, Tesfaye DJ, Tesssema B, Thamsuwan O, Thomas KE, Thrift AG, Tiruye TY, Tobe-Gai R, Tollanes MC, Tonelli M, Topor-Madry R, Tortajada M, Touvier M, Tran BX, Tripathi S, Troeger C, Truelsen T, Tsoi D, Tuem KB, Tuzcu EM, Tyrovolas S, Ukwaja KN, Undurraga EA, Uneke CJ, Updike R, Uthman OA, Uzochukwu BSC, van Boven JFM, Varughese S, Vasankari T, Venkatesh S, Venketasubramanian N, Vidavalur R, Violante FS, Vladimirov SK, Vlassov VV, Vollset SE, Wadilo F, Wakayo T, Wang Y-P, Weaver M, Weichenthal S, Weiderpass E, Weintraub RG, Werdecker A, Westerman R, Whiteford HA, Wijeratne T, Wiysonge CS, Wolfe CDA, Woodbrook R, Woolf AD, Workicho A, Xavier D, Xu G, Yadgir S, Yaghoubi M, Yakob B, Yan LL, Yano Y, Ye P, Yimam HH, Yip P, Yonemoto N, Yoon S-J, Yotebieng M, Younis MZ, Zaidi Z, Zaki MES, Zegeye EA, Zenebe ZM, Zhang X, Zhou M, Zipkin B, Zodpey S, Zuhlke LJ, Murray CJL. Global, regional, and national incidence, prevalence, and years lived with disability for 328 diseases and injuries for 195 countries, 1990–2016: a systematic analysis for the Global Burden of Disease Study 2016. Lancet. 2017;390(10100):1211-59. http://doi.org/10.1016/S0140-6736(17)32154-2. PMid:28919117.

3. Charles A. The pathophysiology of migraine: implications for clinical management. Lancet Neurol. 2018;17(2):174-82. http://doi.org/10.1016/S1474-4422(17)30435-0. PMid:29229375.

4. Conforto AB, Chaim KT, Peres MFP, Gonçalves AL, Siqueira IL, Barreiros MAM, Amaro E Jr. Interictal abnormal fMRI activation of visual areas during a motor task cued by visual stimuli in migraine. Einstein. 2017;15(1):17-23. http://doi.org/10.1590/s1679-45082017ao3719. PMid:28444083.

5. Goadsby PJ, Holland PR, Martins-Oliveira M, Hoffmann J, Schankin C, Akerman S. Pathophysiology of migraine: a disorder of sensory processing. Physiol Rev. 2017;97(2):553-622. http://doi.org/10.1152/physrev.00034.2015. PMid:28179394.

6. Helfenstein C, Strupf M, Stefke A, Fraunberger B, Renner B, Suchantke I, Rothermel M, Messlinger K, DeCol R, Namer B. Cyclic changes of sensory parameters in migraine patients. Cephalalgia. 2022;42(11-12):1148-59. http://doi.org/10.1177/03331024221097932. PMid:35514204.

7. Di Antonio S, Arendt-Nielsen L, Ponzano M, Bovis F, Torelli P, Finocchi C, Castaldo M. Profiling migraine patients according to clinical and psychophysical characteristics: a cluster analysis approach. Pain Med. 2023;24(9):1046-57. http://doi.org/10.1093/pm/pnad048. PMid:37137231.

8. Malta M, Cardoso LO, Bastos FI, Magnanini MM, Silva CM. STROBE initiative: guidelines on reporting observational studies. Rev Public Health. 2010;44(3):559-65. http://doi.org/10.1590/S0034-89102010000300021. PMid:20549022.

9. Starkweather AR, Heineman A, Storey S, Rubia G, Lyon DE, Greenspan J, Dorsey SG. Methods to measure peripheral and central sensitization using quantitative sensory testing: a focus on individuals with low back pain. Appl Nurs Res. 2016;29:237-41. http://doi.org/10.1016/j.apnr.2015.03.013. PMid:26856520.

10. Jensen MP, Karoly P, Braver S. The measurement of clinical pain intensity: a comparison of six methods. Pain. 1986;27(1):117-26. http://doi.org/10.1016/0304-3959(86)90228-9. PMid:3785962.

11. Vase L, Nikolajsen L, Christensen B, Egsgaard LL, Arendt-Nielsen L, Svensson P, Jensen TS. Cognitive-emotional sensitization contributes to wind-up-like pain in phantom limb pain patients. Pain. 2011;152(1):157-62. http://doi.org/10.1016/j.pain.2010.10.013. PMid:21067864.

12. Mailloux C, Beaulieu LD, Wideman TH, Massé-Alarie H. Within-session test-retest reliability of pressure pain threshold and mechanical temporal summation in healthy subjects. PLoS One. 2021;16(1):e0245278. http://doi.org/10.1371/journal.pone.0245278. PMid:33434233.

13. Kennedy DL, Kemp HI, Ridout D, Yarnitsky D, Rice ASC. Reliability of conditioned pain modulation: a systematic review. Pain. 2016;157(11):2410-9. http://doi.org/10.1097/j.pain.0000000000000689. PMid:27559835.

14. Hale N, Paauw DS. Diagnosis and treatment of headache in the ambulatory care setting. Med Clin North Am. 2014;98(3):505-27. http://doi.org/10.1016/j.mcna.2014.01.006. PMid:24758958.

15. Andersen S, Petersen MW, Svendsen AS, Gazerani P. Pressure pain thresholds assessed over temporalis, masseter, and frontalis muscles in healthy individuals, patients with tension-type headache, and those with migraine: a systematic review. Pain. 2015;156(8):1409-23. http://doi.org/10.1097/j.pain.0000000000000219. PMid:25955963.

16. Garrigós-Pedrón M, La Touche R, Navarro-Desentre P, Gracia-Naya M, Segura-Ortí E. Effects of a physical therapy protocol in patients with chronic migraine and temporomandibular disorders: a randomized, single-blinded, clinical trial. J Oral Facial Pain Headache. 2018;32(2):137-50. http://doi.org/10.11607/ofph.1912. PMid:29694464.

17. Scerbo T, Colasurdo J, Dunn S, Unger J, Nijs J, Cook C. Measurement properties of the central sensitization inventory: a systematic review. Pain Pract. 2018;18(4):544-54. http://doi.org/10.1111/papr.12636. PMid:28851012.

18. Caumo W, Antunes LC, Elkfury JL, Herbstrith EG, Busanello Sipmann R, Souza A, Torres IL, Santos VS, Neblett R. The Central Sensitization Inventory validated and adapted for a Brazilian population: psychometric properties and its relationship with brain-derived neurotrophic factor. J Pain Res. 2017;10:2109-22. http://doi.org/10.2147/JPR.S131479. PMid:28979158.

19. Florencio LL, Chaves TC, Branisso LB, Gonçalves MC, Dach F, Speciali JG, Bigal ME, Bevilaqua-Grossi D. 12 item Allodynia Symptom Checklist/Brasil: cross-cultural adaptation, internal consistency and reproducibility. Arq Neuropsiquiatr. 2012;70(11):852-6. http://doi.org/10.1590/S0004-282X2012001100006. PMid:23175197.

20. 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(8):1629-34. http://doi.org/10.1111/pme.12767. PMid:25929269.

21. Nahman-Averbuch H, Shefi T, Schneider VJ 2nd, Li D, Ding L, King CD, Coghill RC. Quantitative sensory testing in patients with migraine: a systematic review and meta-analysis. Pain. 2018;159(7):1202-23. http://doi.org/10.1097/j.pain.0000000000001231. PMid:29781957.

22. Granovsky Y, Shor M, Shifrin A, Sprecher E, Yarnitsky D, Bar-Shalita T. Assessment of responsiveness to everyday non-noxious stimuli in pain-free migraineurs with versus without aura. J Pain. 2018;19(8):943-51. http://doi.org/10.1016/j.jpain.2018.03.008. PMid:29597079.

23. Aguggia M, Saracco MG, Cavallini M, Bussone G, Cortelli P. Sensitization and pain. Neurol Sci. 2013;34(1, Suppl 1):S37-40. http://doi.org/10.1007/s10072-013-1382-0. PMid:23695043.

24. Castien RF, Coppieters MW, Durge TSC, Scholten-Peeters GGM. High concurrent validity between digital and analogue algometers to measure pressure pain thresholds in healthy participants and people with migraine: a cross-sectional study. J Headache Pain. 2021;22(1):69. http://doi.org/10.1186/s10194-021-01278-8. PMid:34253164.

25. Neblett R, Cohen H, Choi Y, Hartzell MM, Williams M, Mayer TG, Gatchel RJ. The Central Sensitization Inventory (CSI): establishing clinically significant values for identifying central sensitivity syndromes in an outpatient chronic pain sample. J Pain. 2013;14(5):438-45. http://doi.org/10.1016/j.jpain.2012.11.012. PMid:23490634.

26. Han SM, Kim KM, Cho SJ, Yang KI, Kim D, Yun CH, Chu MK. Prevalence and characteristics of cutaneous allodynia in probable migraine. Sci Rep. 2021;11(1):2467. http://doi.org/10.1038/s41598-021-82080-z. PMid:33510340.

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