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Published in:
Acta Neurologica Belgica

DOI (link to publication from Publisher):
10.1007/s13760-020-01450-y

Publication date:
2020

Document Version
Accepted author manuscript, peer reviewed version

Title Page

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Association of Dynamic and Widespread Mechanical Sensitivity in Cluster Headache

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Abstract

Objective: To investigate if dynamic pressure pain sensitivity in the symptomatic area is associated with pressure sensitivity in local and distant pain-free areas in cluster headache (CH).

Methods: A pressure algometry set consisting of 8 rollers with fixed pressure levels ranging from 500g to 5300g was used to assess dynamic pressure pain sensitivity in men with episodic CH. Each roller was moved from an anterior-to-posterior direction over the temporalis muscle. The load level of the first painful roller was considered the dynamic pain threshold (DPT). Further, pain elicited during DPT (roller evoked pain) was also assessed. We used a pressure algometer to determine pressure pain thresholds (PPTs) over the temporalis muscle, C5/C6 joint, second metacarpal, and tibialis anterior. Patients were assessed in an asymptomatic (remission) phase, at least 6 months after their last cluster period and without taking pharmacological treatment.

Results: Forty men with episodic CH (mean age 42 years) were included. Both outcomes, DPTs ($r=0.781$, $P<0.001$) and roller-evoked pain ($r=0.586$; $P<0.001$) were bilaterally correlated. Further, DPT, but not roller-evoked pain, was moderately associated with PPTs measured at the symptomatic (temporalis: $r=0.665$, $P<0.001$) and distant pain-free (C5-C6 joint: $r=0.389$, $P=0.013$; second metacarpal: $r=0.551$, $P<0.001$; and, tibialis anterior: $r=0.308$, $P=0.035$) points.

Conclusions: Dynamic pressure sensitivity in the trigeminal area was correlated to pressure pain sensitivity at both symptomatic and distant pain-free areas in men with CH supporting the use of roller pressure algometry. Dynamic pressure algometry may be a new tool for assessing the status of sensitization in primary headaches.

Key words: Cluster headache, dynamic pressure pain, pressure pain threshold.

Association of Dynamic and Widespread Mechanical Sensitivity in Cluster Headache

Introduction

Cluster headache (CH) is a trigeminal autonomic cephalalgia showing a one-year and lifetime prevalence of 53/100,000 and 124/100,000 respectively [1]. Current pathogenic theories for CH hypothesize a role of the posterior hypothalamus, the activation of the trigemino-vascular system, and the presence of sensitization mechanisms [2]. A common clinical manifestation of sensitization is the presence of hyperalgesic and allodynic responses to pressure pain.

The most common tool for determining pressure pain sensitivity of deep tissues is pressure algometry. Some studies suggest the presence of pressure pain hypersensitivity at both symptomatic and distant pain-free areas as a clinical manifestation of widespread sensitization of nociceptive pathways in CH by using static pressure algometry [3,4]. Yet, it should be considered that pressure algometry is statically applied to a particular point and, therefore, it represents a static outcome of nociception in a particular point. Another feature of central sensitization is the presence of dynamic mechanical pain sensitivity. The quantitative sensory testing protocol proposed by the German Research Network includes both static and dynamic assessment of cutaneous mechanical pain sensitivity [5]. However, until recently there was no method of quantifying this dynamic pressure pain sensitivity over deep tissues. The dynamic pressure algometer was developed to quantify dynamic pressure to deep musculoskeletal tissues [6]. These authors found that the roller algometer was a potentially tool for quantitative assessing of dynamic pain sensitivity [6].

The roller pressure algometer has already been used in individuals with primary headaches, specifically migraine [7] and tension type headache [8]. These studies reported that dynamic pressure pain sensitivity over the temporalis muscle, main symptomatic area in primary headaches, was correlated with static widespread pressure pain sensitivity [7, 8]. In addition, dynamic, but not static, pressure pain sensitivity revealed differences between the episodic or chronic form of migraine [8], supporting its potential use. No previous study has used the dynamic algometer in patients with CH. The main objective of the current study was to investigate if dynamic pressure pain sensitivity over the symptomatic area (roller pressure algometer), was associated to widespread pressure pain sensitivity (static pressure algometry) in a sample of men with episodic CH.

Methods

Participants

Consecutive patients with CH attending two specialized headache units between July 2018 and March 2019 were screened for their inclusion in the study. Patients had to meet the diagnostic criteria of episodic CH according to the third edition of International Classification of Headache Disorders [9]. Clinical features (i.e., time from the onset of CH, number of cluster periods per year, symptomatic side during cluster periods, intensity and duration of headache episodes, time from the last cluster period and medication intake) were obtained through a personal interview. All participants exhibited normal neurologic and ophthalmologic examinations as well as a normal brain MRI.

Participants were excluded if: 1, were younger than 18 or older than 65 years old; 2, concomitant primary and/or secondary headaches; 3, peripheral neuropathy or another neurological disease; 4, any medical systemic disease (e.g., systemic lupus erythematosus or rheumatoid arthritis); 5, history of head or neck trauma (whiplash); or 6, previous head or neck surgery. A written consent form was signed by all participants prior participation in the study. The study design was approved by local Ethics Committees (Hospital Clínico San Carlos, code 17/513-E; Hospital Clínico Universitario Valladolid, code PI 17-875).

The evaluation was conducted in an asymptomatic/remission phase, defined when no headache attack had occurred for at least 3 months and at least 2 months after treatment discontinuation. Participants were asked for not intaking analgesic or muscle relaxation drugs from at least 48 hours before testing.

Dynamic Pressure Algometry

Dynamic pressure pain sensitivity was evaluated with a roller pressure algometer (Aalborg University®, Denmark) consisting of 11 different rollers, each one with a fixed load level from 500g, 700g, 850g, 1350g, 1550g, 2200g, 2500g, 3100g, 3500g, 3850g, to 5300g. The diameter of the hard-plastic wheel was 35mm, and the width was 10mm (**Fig. 1A**). The wheel was rolled in an anterior to posterior direction over the temporalis muscle belly for about 60mm as described (**Fig. 1B**) [7,8]. The pressure was maintained constant while the hard-plastic roller was moving at a speed of approximately 0.5 cm/sec. The measurement was repeated twice on each temporalis, once the pain provoked by the first assessment has disappeared.

The load level of the roller where the dynamic assessment was first perceived as painful was defined as the dynamic pressure threshold (DPT), whereas the roller-evoked pain was defined as the pain intensity perceived by the patient while the DPT roller was moving over the temporalis muscle. The roller evoked pain was assessed with a numerical pain rating scale (NPRS) ranging from 0 (no pain) to 10 (maximum pain) points. This procedure has shown good reliability (ICC from 0.75 to 0.88) [6].

Static Pressure Algometry

An electronic pressure algometer (Somedic AB®, Farsta, Sweden) was used to assess pressure pain thresholds (PPTs) bilaterally over a trigeminal point (temporalis muscle), and extra-trigeminal point (the C5/C6 zygapophyseal joint), and two distant pain-free points (second metacarpal and tibialis anterior) in a randomized order. Patients should press the "stop-button" as soon as they perceived the first pain sensation during pressure assessment. The assessor increased the pressure approximately at a rate of 30kPa/s. Pressure was assessed 3 times on each point, 30sec apart each one, for avoiding temporal summation of pain [10]. The main of the 3 trials was calculated and used for main analyses. Static pressure algometry has also shown high reliability [11,12].

Sample size calculation

The Ene 3.0® software (Autonomic University of Barcelona, Spain) was used to calculate the sample size. Sample size calculation was calculated on detecting moderate to large correlations (r=0.75) between dynamic and widespread static algometry, with an alpha level (α) of 0.05, and a desired power (β) of 90%. This calculation generated a size of the sample of at least 30 patients with CH.

Statistical analysis

The statistical analysis was conducted with the SPSS statistical package (22.0V). All quantitative data exhibited a normal distribution as assessed with the Kolmogorov-Smirnov test (P>0.05). Since no side-to-side differences in PPTs and DPT were found (see table 2), the mean of both sides was calculated used in the correlational analysis. The associations between clinical variables relating to CH, DPT, roller evoked pain, and PPTs were determined with Pearson correlation tests (r). A correlation r<0.3 was considered weak; moderate when 0.3<r<0.7, and strong when r>0.7 [13]. The statistical analysis was conducted at a 95% confidence level and P-values less than 0.05 were considered significant.

Results

Clinical Data of the Sample

Fifty individuals with CH were screened for eligible criteria. Ten (20%) subjects were excluded: chronic form of CH (n=4), concomitant migraine (n=3) and being with an active cluster period (n=3). A total of 40 men diagnosed with episodic CH (mean age: 42±10 years) were finally included in this study. **Table 1** shows clinical features of the total sample. All participants were analyzed in a late remission phase with 9.9 months (95%CI 7.2, 11.6) from the last cluster period and 9.0 months (95%CI 7.0, 11.0) without taking medication. **Table 2** summarizes the values of DPT and roller-evoked pain of both symptomatic and non-symptomatic sides in men with episodic CH.

Consistency of Dynamic Pressure Algometer in Cluster Headache

A strong association between symptomatic-non/symptomatic side DPT (r=0.781, P<0.001) and a moderate side-to-side correlation roller-evoked pain (r=0.586; P<0.001) was observed, supporting side-to-side consistency of roller algometry in CH.

Dynamic Pressure Threshold and Cluster Headache Features

No significant associations between DPT or roller evoked pain with the clinical features of headache were observed (all, P>0.165).

Association between Dynamic and Static Mechanical Thresholds

The DPT over the temporalis muscle showed moderate and positive associations with PPTs over the C5-C6 zygapophyseal joint (r=0.389, P=0.013, **Fig. 2A**), temporalis muscle (r=0.665, P<0.001, **Fig. 2B**), second metacarpal (r=0.551, P<0.001, **Fig. 2C**) and tibialis anterior (r=0.308, P=0.035, **Fig. 2D**): the lower the DPT over the temporalis, the lower the PPTs in all points.

In contrast, the roller evoked pain did not show any significant association with PPTs over the temporalis muscle (r=-0.144, P=0.375), C5-C6 joint (r=-0.212; P=0.190), second metacarpal (r=-0.083, P=0.612), or tibialis anterior (r=-0.093, P=0.570).

Discussion

We found that dynamic pain thresholds (DPT) over the trigeminal area were associated with pressure pain thresholds (PPTs) within the trigeminal, extra-trigeminal and distant pain-free points in men with episodic CH in a late remission phase. On the contrary, roller evoked pain during DPT was not associated with widespread PPT. No association of dynamic pain sensitivity and clinical features was observed.

The dynamic pressure algometer was developed for assessing dynamic deep tissue sensitivity in a similar way that dynamic cutaneous pain sensitivity is assessed [6]. Previous studies have observed an internal (side-to-side) consistency for dynamic roller algometer in patients with migraine [7] or tension-type headache [8]. In this study, we also found side-to-side correlations for both dynamic sensitivity outcomes (DPTs and roller evoked pain) supporting that dynamic algometry is also consistent in men with CH. Current and previous findings would support the consistency of this new tool, at least for its use in primary headaches.

Our findings observed that dynamic pressure algometry (DPT) over the symptomatic (trigeminal) area was positive associated with static widespread PPTs in trigeminal, extra-trigeminal and distant pain-free areas in men with episodic CH in a late remission phase and with a long history of headache. Since CH is also associated with widespread pain hypersensitivity [3,4], its association with trigeminal dynamic pain sensitivity suggests that both outcomes are intrinsically related. These findings would further support the use of the roller algometer for evaluating dynamic deep tissue pain sensitivity in headaches and its use as a future outcome for assessing impaired nociceptive processing. It should be noted that PPT is a static outcome of pain hypersensitivity on a particular point, whereas DPT is a dynamic outcome of pain sensitivity stimulating larger areas. It would be possible that dynamic pain sensitivity provides complementary information to static pain sensitivity by stimulating dynamic nociceptors or by activating different neural networks. It should be noted that patients with CH included in the current study reported long history of headaches (mean 13 years) with could lead to the presence of potential sensitization. Nevertheless, it is also important to note that patients were evaluated in a remission period (i.e., at least 6 months after the last headache attack and free of any medication intake) suggesting that the association between static and dynamic pressure pain sensitivity can be a stable phenomenon non-related to the presence of headache. In addition, dynamic algometry can be also used as a potential quantitative tool in treatment profiling studies since it is less time consuming. It would be interesting to determine if dynamic algometry can be a predictive value for treatment outcomes in clinical trials.

We did not find significant associations between roller evoked-pain during DPT with widespread pressure pain sensitivity or headache clinical features supporting that each outcome can represent different aspects of the pain spectrum. For instance, it seems that association of physiological outcomes (e.g., PPT) with clinical outcomes (e.g., pain or related-disability) is conflicting since no clear association exists, at least, in spinal pain disorders [14]. Different pain outcomes could be used for better characterization of the pain spectrum.

Finally, this study has some potential limitations. First, we only included subjects with episodic CH; therefore, we do not know if individuals with chronic CH will exhibit similar results. Similarly, only men were included in our study. Since women have greater susceptibility to pressure excitability than males [15], it is possible that our results would be different in women with CH. Second, we cannot determine a cause and effect relationship of the observed associations because the cross-sectional design of the study. The potential clinical relevance of dynamic algometry in primary headaches, including CH, should be assessed in future studies.

Conclusions

This study reported that dynamic pressure pain sensitivity over the trigeminal area was positively associated with widespread static pressure pain sensitivity in men with episodic CH in a late remission phase. On the contrary, roller evoked pain during DPT was not associated with widespread PPT. No association of dynamic pain sensitivity and headache clinical feature was either found. Assessing static and dynamic pressure pain sensitivity may provide complementary information about underlying mechanisms in headaches.

Author contribution

All authors contributed to the study concept and design. MLC and CFdlP did the statistical analysis and interpretation of data. AGP, VGM and DGA contributed to draft the paper. All authors provided administrative, technical, and material support. LAN and MLC supervised the study. All authors have read, revised and approved the final version of the manuscript.

Acknowledgement

The Shionogi Science Program

Legend of Figures

Figure 1: (A) Dynamic pressure algometry set (Aalborg University, Denmark®), (B) Assessment of dynamic pain sensitivity over the temporalis muscle in a patient with cluster headache.

Figure 2: Scatter plots of correlations between dynamic pressure threshold (DPT, mean score of both sides) and pressure pain thresholds (PPTs, mean score of both sides) over C5-C6 zygapophyseal joint (A), temporalis muscle (B), second metacarpal (C) and tibialis anterior (D) in men with episodic cluster headache (n=40). Note that several points are overlapping. A positive linear regression line is fitted to the data.

Compliance with Ethical Standards

Funds: No funds were obtained for this study.

Conflict of Interest: Ángel Guerrero-Peral declares that he has no conflict of interest; Víctor Gómez-Mayordomo declares that he has no conflict of interest; David García-Azorín declares that he has no conflict of interest; Nuria González-García declares that she has no conflict of interest.; César Fernández-de-las-Peñas declares that he has no conflict of interest; Lars Arendt-Nielsen declares that he has no conflict of interest; María L. Cuadrado declares that she has no conflict of interest.

Ethical approval: All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent: Informed consent was obtained from all individual participants included in the study.

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