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INTRODUCTION

Headache is defined as pain located in the head, above the orbitomeatal line and or the nuchal crest(1). The primary classifications of headaches encompass primary headaches (PH), secondary headaches, painful neuropathy, other facial pain, and additional headache types(1). PH are not caused by or associated with an underlying disease. They can be differentiated from secondary headaches, which may exhibit similar phenotypic characteristics but fulfill the causal criteria of another disorder(1). PH, including migraine headache (MH), tension-type headache (TTH), and cluster headache (CH), are among the most common and disabling neurological disorders(2). Their pathophysiology is complex and multifactorial, involving genetic predisposition(3), central and peripheral nervous system dysfunction(3, 4), neurovascular interactions(5), and neuroinflammatory processes(4, 6). Each type of PH has distinct features, but there are overlaps that complicate diagnosis and treatment. A deeper understanding of these mechanisms is essential to guide more targeted and effective therapeutic strategies(7).

Temporomandibular disorders (TMD), in contrast, are a group of neuromuscular conditions related to the temporomandibular joint and all associated tissues(8). These disorders have a complex pathophysiology influenced by multiple risk factors(8). Although PH and TMD differ in classification, with PH considered primary pain disorders and TMD often categorized as secondary, both represent highly prevalent chronic pain conditions that significantly impact quality of life and healthcare systems(2, 9). Emerging evidence suggests that they may share overlapping pathophysiological mechanisms, including peripheral and central sensitization, altered pain modulation, and involvement of common trigeminal pathways(10). This shared neurobiological substrate may explain the frequent clinical comorbidity observed between TMD and PH(11).

Related to PH, reviews have explored peripheral sensitization in TTH and MH. Castien et al. (2021)(12) reported that individuals with PH show greater pericranial tenderness than healthy controls, measured by the Total tenderness score (TTS). Findings from quantitative sensory testing (QST) studies, including the systematic review by van Welie et al. (2024)(13), show reduced pressure pain thresholds (PPT) in both trigeminal and extra-trigeminal sites, suggesting generalized hypersensitivity consistent with central sensitization. These findings emphasize the need to evaluate local and distant pain thresholds to distinguish between peripheral and central sensitization mechanisms in headache disorders(13).

Similar to PH, TMD are associated with peripheral sensitization related to tenderness in the masticatory system(14), and studies show pericranial tenderness increases with TMD severity(15). Meng et al. (2021)(16) reported evidence of decreased local and peripheral PPT sites related to TMD, supporting widespread mechanical hypersensitivity and central sensitization in these patients. Almoznino et al. (2019)(14) evaluated muscle tenderness in TMD patients using the TTS and examined whether comorbid PH affected tenderness severity. They found that patients with TMD and MH showed the highest pericranial and cervical tenderness, followed by those with TTH, suggesting a gradient of musculoskeletal hypersensitivity by headache type. However, the study did not assess extra-trigeminal regions, limiting conclusions about whether increased TTS reflects local peripheral mechanisms or broader central sensitization. In addition, because participants were recruited based on TMD and PH was treated as a comorbidity, the diagnostic interpretation is unclear: the subgroup with highest tenderness may represent individuals whose primary disorder is PH who happened to meet RDC/TMD criteria at evaluation, rather than patients with "TMD plus PH." These limitations emphasize the need for studies that recruit patients based on PH diagnosis, assess TMD with DC/TMD, and characterize somatosensory phenotypes to clarify the bidirectional relationship.

Beyond the overlap between PH and TMD, some patients present an even broader pattern of pain susceptibility. Individuals with TMD who exhibit widespread tenderness frequently show multiple chronic overlapping pain conditions (COPC), such as PH, low back pain, irritable bowel syndrome, chronic fatigue syndrome, and fibromyalgia(17, 18). Chen et al. (2012)(17) reported that TMD patients with widespread pain are significantly more likely to present several COPC compared to those without widespread pain or to non-TMD controls. Other studies have linked these comorbid conditions to greater TMD severity, longer pain duration, and poorer treatment response(19-21). This broader comorbidity profile suggests that widespread tenderness may reflect a systemic sensitization process rather than isolated regional dysfunction, underscoring the clinical relevance of routinely assessing COPC in patients with TMD.

Both in TMD and PH, recent systematic reviews have identified similar methodological limitations that hinder clear interpretation and comparison across studies. In MH research, Welie et al. (2024)(13) noted considerable heterogeneity in QST protocols, with differences in stimulation modalities, anatomical test sites, and testing phases (ictal versus interictal) often poorly described. Similarly, Meng et al. (2021)(16) reported substantial variability in QST procedures for TMD, including inconsistent pressure rates, probe sizes, and selection of local or

extra-trigeminal sites. In both conditions, many studies relied on small samples and lacked appropriate stratification by migraine subtype (episodic versus chronic) or TMD subtype (myofascial versus arthralgia), as well as inadequate control of comorbid pain conditions or medication use, which may have biased results(16). Collectively, these methodological limitations highlight the need for standardized, adequately powered, and integrative studies assessing both local and widespread sensitivity to better delineate peripheral and central sensitization processes.

Research has indicated that individuals with myofascial TMD are more prone to chronic daily headaches, MH, and episodic TTH(22). This suggests common underlying mechanisms, such as nociceptive pathway sensitization and dysfunction of endogenous pain modulation systems(23) To accurately investigate this overlap, a multidisciplinary approach integrating orofacial pain specialists and headache physicians is essential(24). In line with these recommendations, the present study will include patients with PH clinically diagnosed according to the ICHD-3 criteria, while TMD will be assessed, at the same time, using the standardized DC/TMD protocol. Cranial, facial, and cervical tenderness will be quantified through the TTS, and PPT will be measured at extratrigeminal sites to capture potential central sensitization phenomena. In addition, the number of COPC will be recorded, as a higher burden of comorbid pain conditions has been associated with increased headache frequency, greater TMD severity, and enhanced pain sensitivity.

This integrative approach aims to clarify how peripheral factors reflected in orofacial and cervical tenderness, central mechanisms reflected in extratrigeminal hypersensitivity, and the presence of multiple COPC contribute to the clinical expression and overlap between TMD and headache. Furthermore, the concurrent assessment of both conditions will allow exploration of whether current DC/TMD criteria under-identify headache components when applied in isolation, highlighting the importance of adopting a multidisciplinary perspective in both diagnosis and treatment.

Taken together, these considerations define a clear research gap: despite strong evidence of shared pathophysiological pathways between PH and TMD, no multicentric study has yet simultaneously assessed pericranial tenderness, extra-trigeminal hypersensitivity, and comorbid pain conditions under standardized protocols. Addressing this gap is essential to better understand the spectrum of sensitization and comorbidity in PH and their relationship with TMD.

OBJECTIVES

- To determine whether subjects with PH, both acute and chronic, have higher scores of pericranial and neck tenderness (local sensitivity), measured using the TTS, than healthy subjects.
- To determine whether subjects with PH, both acute and chronic, have lower extra-trigeminal PPT (generalized sensitivity), measured using an algometer, than healthy subjects.
- To examine the association between the number of COPC and local sensitization processes, as reflected by increased pericranial tenderness measured with the TTS.
- To examine the association between the number of COPC and peripheral sensitization processes, as reflected by reduced PPT at extra-trigeminal sites.
- To explore the coexistence and overlap between TMD and PH, and to determine whether the presence of TMD is associated with greater local or generalized tenderness and a higher comorbidity burden.

a. Hypothesis

1. Hypothesis 1: It is hypothesized that patients with PH, especially those with chronic forms, will exhibit higher severity of pericranial and general tenderness compared to healthy subjects.
2. Hypothesis 2: It is hypothesized that there is a positive correlation between the number of associated COPC and measures of central sensitization in relation to pericranial and peripheral sensitivity levels in patients with primary headaches.
3. Hypothesis 3: It is hypothesized that there is a significant overlap in the diagnosis of myofascial TMD among patients with PH. Should this association be substantiated, it would be essential to document it, as it should be incorporated into the screening process for TMD, particularly within the PH anamnesis, to facilitate a more comprehensive and precise diagnostic evaluation.~~.~~.

METHODS

A cross-sectional study will be conducted comparing two groups: i) PH group ii) Control group with no headaches, or with infrequent episodic headaches. Within the PH group,

if feasible, participants will be further classified into two subgroups: one with frequent episodic headaches (FEH) and one with chronic headaches (CH). Recruitment and observations will be carried out in a multicenter fashion, both in Spain and Germany. They will take place at the University of Manresa, the International University of Catalonia in Spain and at the University of Applied Sciences Osnabrück in Germany. The study protocol will be evaluated by the respective Ethics Committee (XX) and registered in ClinicalTrials.gov (XX). All participants will be informed about the aim of the study and sign an informed consent. The trial will follow the STROBE statement guidelines for reporting observational studies(25).

a. Participants

Participants will be recruited by convenience sampling by neurologists at the Barcelona Headache Unit of the Hospital Sant Joan de Deu de Manresa - Fundació Althaia, by Orofacial pain specialists at the University Clinic of the International University of Catalonia in Spain and by Pain/Orofacial pain specialists at a German Pain Center.

Eligible participants must have a confirmed diagnosis of primary migraine or tension-type headache or other PH, established by a headache specialist according to the International Classification of Headache 3 (ICHD-3)(1) and be under medical treatment for at least 6 months. All patients referred for evaluation will complete a self-assessment questionnaire, specially designed for this cross-sectional study and based on the ICHD-3 criteria(1). It will be used to confirm the referred patient's diagnosis and classify the patient into episodic or chronic PH (see Appendix_1). It includes screening for migraine (codes 1.1, 1.2) and tension headache (codes 2.1, 2.2), as well as alert criteria for secondary headaches, such as thunderclap headache (code 4.6), post-traumatic headache (codes 5.1, 5.2), infection-related headache (code 9.1), intracranial pressure-related headache (code 7.1.1) and headache with neurological deficit (code 6.2.2). The exclusion criteria will be the following: i) not understanding Spanish, English, or German; iii) severe dermatological problems or intraoral, head or neck injuries; iv) recent fractures; v) previous diagnosis of uncontrolled psychiatric disorder or neurodegenerative diseases; vi) recent onset of undiagnosed headache or unilateral

neck pain with associated neuropathic symptoms; and vii) pregnancy. Inclusion and exclusion criteria will be the same in all three recruitment centers. The person responsible for ensuring that all study participants meet the criteria will not be the same person responsible for evaluating the headache screening and self-assessment questionnaire.

b. Factors of interest

The principal investigator, a physiotherapist specialized in orofacial pain (Cristian Justribó-Manion), will be responsible for performing all assessments at the Spanish centers, including the pericranial and general sensitivity evaluation and the orofacial examination to identify pain-related TMD using the Spanish version of the DC/TMD(26). In the German center, the assessments will be conducted by a specialist in head and orofacial pain, who will apply the same procedures using the German version of the DC/TMD(27). At the same time, participants will use self-report scales to indicate the number of pain-associated comorbidities diagnosed by a physician, as well as the duration of their comorbid pain since diagnosis. The questionnaires will be administered by a person outside of the diagnostic process and assessment of the variables of interest. Self-reported questionnaires will be sent to participants via a secure web platform and data collection tool REDCAP.

c. Control

Healthy controls will be recruited by snowball sampling among students, university members, and related communities. Hypothetical controls will also complete the self-assessment questionnaire based on the ICHD-3 criteria(1) to rule out that they do not meet a headache criterion. Volunteers who meet the criteria for a possible headache disorder will be advised to see a specialist, and those who qualify as cases will be invited to participate. This process ensures the selection of truly headache-free individuals for the control group and will blind the evaluators as any subject can be considered a case.

The physiotherapist responsible for assessing the eligibility of both the interest group and the control group will not participate in the evaluation of sensitivity or any of the

variables assessed. The physiotherapist responsible (Jordi Padrós-Augé) is an expert in the clinical management of headaches, in the use of the ICDH-3 criteria(1) and is a professor at the University of Manresa and Director of the University Postgraduate Course "Expert in headaches and vestibular syndromes" taught at the University. Therefore, screening of participants recruited in all participating centers in Spain will be performed at the University of Manresa. In the German center, a specialist in head and orofacial pain will perform the screening of the subjects, will perform the DC/TMD, and classify participants to keep the blinding.

d. Primary variables (sensitivity assessment)

The primary dependent variable for this analysis will be the total pericranial tenderness score, secondary variable will be the overall PPT.

For the assessment of the pericranial tenderness, the TTS protocol(12), in which pericranial muscle tenderness is assessed by palpation of specific cranial and facial points, will be performed. This method has been widely used in previous studies to detect muscle tenderness and pain sensitivity in patients with TMD and headaches(12, 14). Bilateral manual palpation of 8 pairs of muscle bodies and insertions (masseter, temporal, frontal, coronoid process, upper trapezius, sternocleidomastoid, suboccipital muscles and mastoid process). The second and third fingertips will be rotated for 4-5 seconds(28). In accordance with validation guidelines(29) and previous clinical trial protocols(14, 30), muscle palpation shall be performed with approximately 1 kg of pressure. Prior to each assessment, assessors will calibrate using a digital algometer. The examiner will assess participants' reactions using a 4-point scale: 0 indicated no observable response or reported discomfort; 1 signified a mild facial reaction with no verbal indication of discomfort; 2 denoted both verbal and facial expressions of painful tenderness and discomfort; and 3 represented pronounced grimacing or withdrawal, accompanied by verbal reports of significant painful tenderness and pain[22]. The maximum possible TTS was calculated as 48, derived by multiplying 8 painful points by 2 (for the right and left sides) and then by 3 (the maximum score for each painful point).

TTS has been shown to be effective in assessing peri-cranial muscle tenderness in a variety of headaches. Studies have consistently shown that patients with TMD and headache, particularly those with tension headache and migraine, have higher TTS compared to healthy controls(14, 31). Research results have consistently shown that TTS is higher in subjects with chronic TTH than in healthy controls. The pooled estimated mean difference was 1.57 (95% confidence interval 1.24 to 1.91)(12). For patients with migraine, the pooled estimated mean difference was 1.27 [95% confidence interval 0.91 to 1.63](12). In the same direction, individuals with TMD-related myalgia showed a higher mean difference of 2.22 points and a standard error of 0.31 compared to healthy persons.

In addition, overall pain sensitivity will be assessed using PPT measurements obtained with a portable digital algometry device (NOD A, OT Bioelettronica, Torino, Italy), equipped with a 1 cm^2 contact probe composed of biocompatible materials suitable for temporary skin contact.The NOD device incorporates a calibrated force sensor and provides real time visual biofeedback through a dedicated mobile application, allowing standardized control of the rate of pressure application. During the clinical assessment, the probe of the device will be positioned perpendicular to the participant's skin at the selected anatomical sites. Pressure will be progressively applied while the examiner follows the visual guideline displayed by the application in order to maintain a constant rate of force increase. PPT measurements have been validated to assess general tenderness in both orofacial pain and generalized pain conditions, including TMDs and headaches(32). The NOD device has demonstrated good measurement reliability and validity when compared with established dynamometry systems used in clinical research. Validation studies have reported high levels of agreement with reference instruments such as the Jamar dynamometer, with intraclass correlation coefficients around 0.90, supporting its use as a reliable tool for force measurement in clinical and research settings(33).

Participants will be notified of the gradual increase in pressure and instructed to raise their right index finger when they begin to perceive the pressure as uncomfortable.

Measurements were taken at three commonly used anatomical sites(28, 34) following a randomization:

- Tibialis anterior muscle (Evaluated in the central region of the muscle, with the participant supine).
- Radial carpal extensor (Measured at the dorsal aspect of the wrist joint line, with the participant in the supine position).
- Low back (Examined in the interspinous space between L5 and S1, with the participant lying face down).

The assessor will apply pressure consecutively in each zone. After applying pressure to the three zones, the subjects will be allowed to rest for 5 min. This procedure will be repeated a total of 3 times. The mean of the three assessments will be recorded. This approach helps to avoid possible hypervigilance of the individual during the first assessment, which increases reliability(35) (Cronbach's alpha: 0.94-0.98). In previous research, a minimal detectable difference in the tibialis anterior of 1.24 kg/cm2 (CI: 0.76-2.03) was observed. The mean for each body zone and the overall mean extra trigeminal sensitivity will be calculated.

e. Secondary variables

The key covariates to be examined will cover the occurrence of TMD according to the Spanish/German version of the DC/TMD(26, 27), the total central sensitization score and the number of coexisting conditions identified using the Central Sensitization Inventory (CSI) (Spanish/German versions)(36, 37), a pain body drawing(38) and the intensity of pain using the Brief pain inventory short form (BPI-SF) (Spanish/German versions)(39, 40).

Individuals with a positive diagnosis of pain-related TMD will be classified as: i) Arthralgia: Joint pain as the only pain symptom ii) Myalgia: Muscle pain as the only pain symptom iii) Myalgia and Arthralgia (mixed pain) iv) Headache attributed to TMD: Patients with arthralgia or myalgia and headache attributed to TMD. The Diagnostic

Criteria for Temporomandibular Disorders (DC/TMD) have demonstrated a sensitivity of ≥0.86 and specificity of ≥0.98 for the most common pain-related TMD(38).

The initial section of the CSI, Part A, will be used to assess overall sensitization scores. This part examines 25 health-related symptoms commonly associated with central sensitization, with scores ranging from 0 to 100. A score of 40 or higher suggests central sensitization. A score of 40 or higher suggests central sensitization. Part B, which is not scored, inquires about previous diagnoses of specific disorders, including seven distinct central sensitization syndromes. The researchers incorporated chronic low back pain as an additional syndrome. This addition is consistent with their previous research, which demonstrated a strong correlation between low back pain and these syndromes(18, 41). The Spanish/ German adaptation of the CSI has demonstrated a satisfactory threshold of 75% for both sensitivity and specificity in the identification of centrally sensitive syndromes. In addition, it has shown strong internal consistency ($\alpha = 0.872$) and excellent test-retest reliability ($r = 0.91$) (36, 37).

The BPI-SF will be used to quantify pain intensity and pain-related interference. It provides two summary scores ranging from 0 to 10, where higher values indicate greater pain burden. The instrument shows good measurement reliability(39, 40), with a standard error of measurement of approximately 1.6 points and a minimal detectable change of about 2 points, indicating that reductions of this magnitude in pain severity and approximately 1 point in pain interference represent clinically meaningful improvement(42). In addition, a pain body drawing will be used to document the distribution of pain, allowing the identification of widespread pain patterns and facilitating the classification of participants according to the presence or absence of multisite pain.

Cervical motor and sensorimotor variables will also be assessed using the NeckCare System (NeckCare, Reykjavík, Iceland), a wearable sensor-based platform designed to provide objective assessment of cervical spine function. The system uses a lightweight head mounted sensor connected via Bluetooth to a computer platform that records cervical kinematics in real time and generates automated reports of cervical

performance. It allows clinicians to objectively evaluate cervical range of motion, proprioception, and sensorimotor control during standardized clinical tests. Active cervical range of motion (ROM) will be recorded for flexion, extension, right and left rotation, and right and left lateral flexion. The system quantifies cervical motion in degrees while tracking movement patterns and symmetry across planes. Cervical proprioception will be assessed using the Joint Position Error (JPE) test. In this procedure, the participant performs active cervical movements and subsequently attempts to relocate the head to the initial neutral position without visual feedback. The system automatically calculates the repositioning error in degrees, providing an objective measure of cervical joint position sense. Sensorimotor control will be further evaluated using the Butterfly Test®. In this test, the participant attempts to follow a moving visual target on a computer screen using head movements tracked by the sensor. The platform compares the trajectory of the head movement with the target path and quantifies movement accuracy, smoothness, and coordination between the visual, vestibular, and cervical motor systems.

Finally, the Maximum voluntary contraction and endurance of the cervical flexor muscles will be assessed using a portable digital dynamometry and biofeedback device (NOD A, OT Bioelettronica, Torino, Italy). The device incorporates a calibrated force sensor and provides real time visual feedback through a dedicated mobile application, allowing participants to monitor the target force during testing.

All measurements will be performed with the participant in a supine position on an examination table. A support cushion will be placed under the occipital region to maintain a standardized head position. The force sensor of the NOD device will be positioned on the participant's forehead and secured with a fixation strap to ensure stable contact during the test.

Participants will first perform two maximal voluntary contractions (MVC) of the cervical flexor muscles by pressing the forehead against the device while maintaining the head supported on the examination table. The mean value of the two maximal force recordings will be calculated and used as the reference MVC.

Subsequently, a cervical flexor endurance test will be conducted. Participants will be instructed to maintain a contraction corresponding to 25 percent of their previously determined MVC for as long as possible. Real time visual biofeedback will be provided by the device, allowing participants to monitor the percentage of force produced and maintain the target contraction level within a tolerance margin of ±5 percent of the prescribed force. Endurance time will be recorded as the duration for which the participant is able to maintain the required force within the predefined target range.

Figure 1 shows the flow chart of the study, which summarizes the main phases of the process: selection of participants, random assignment to a diagnostic group and evaluation.

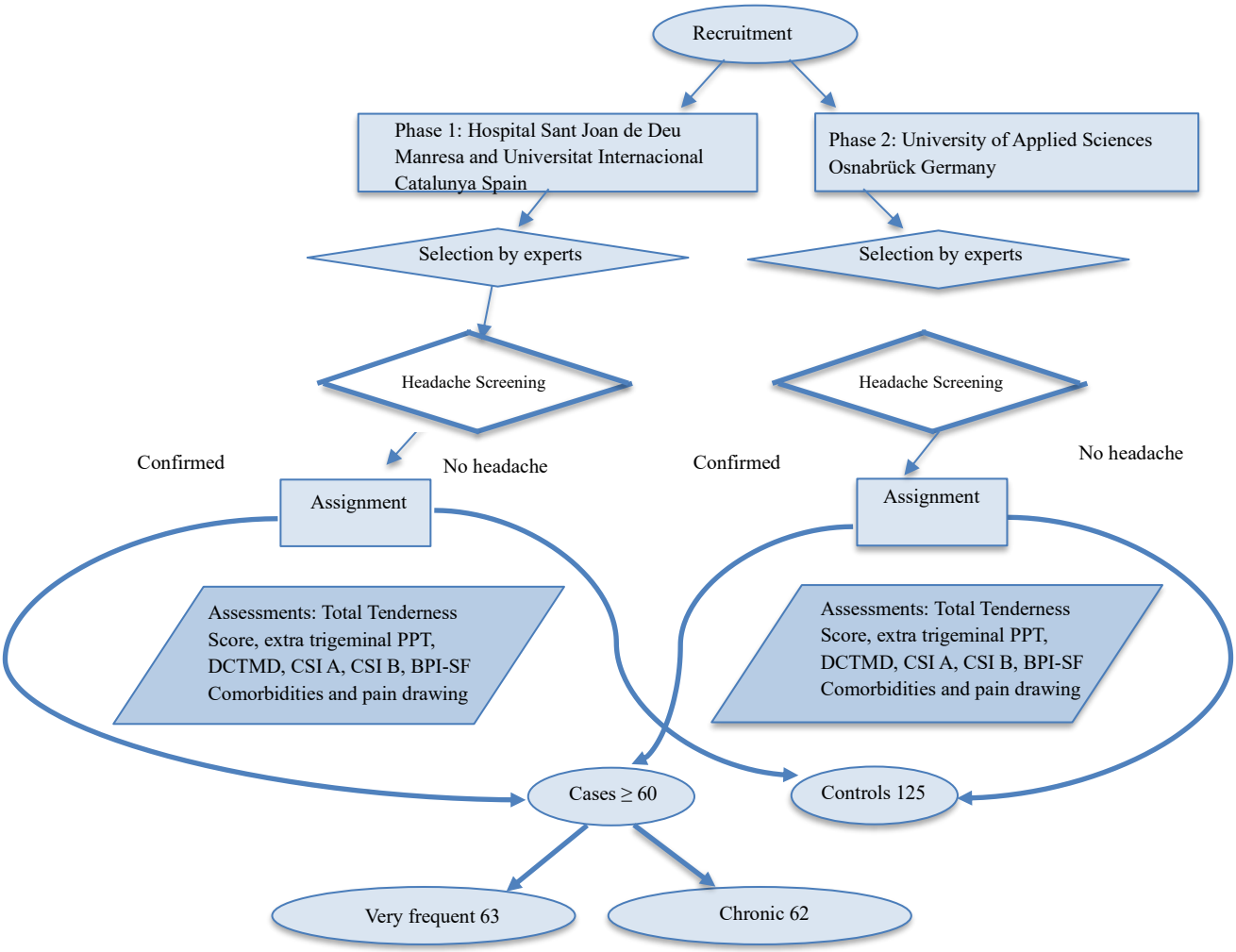

Figure 1. Diagram of the study flowchart. Abbreviations: Central Sensitization Inventory CSI, Pain Pressure Threshold PPT, DCTMD Diagnostic Criteria for Temporomandibular Disorders.

Statistical analysis

All statistical analyses will be performed with R version 4.4.2. The pwr(43) package was used to calculate the sample size. In a previous study, Almoznino et al.(14) analyzed the differences in pericranial sensitivity between 44 subjects with myalgia-associated TMD and 99 healthy controls. They reported a mean difference of -2.22 with a standard error of 0.31, measured using the TTS. Using the formula (Standard deviation = Standard error we calculated a standard deviation of 3.71. For our study, we considered a one-to-one ratio between the groups and a one-sided contrast, as we expect the effect to be biased toward the group of patients with headache. The sample size was determined using an alpha level of 0.05 and a statistical power of 0.90. Since this study has no follow-up, we assumed no loss of participants. The calculation determined that each group should have a minimum of 60 subjects to detect a clinically significant difference. To further strengthen the study, we intend to recruit a larger sample for the development of prediction models using all subjects evaluated. The sample size calculation for prediction modeling was based on an expected R^2 of 0.6, a maximum of 10 parameters, an alpha level of 0.05 and a power of 0.8. As no participant losses are expected, we set the reduction factor to 0%. According to these parameters, the total sample size needed for the prediction model is 250 participants in total. We estimate to recruit 80 cases and 80 controls at the Barcelona Headache Unit of the Hospital Sant Joan de Deu de Manresa, 25 cases and 25 controls at the dental clinic of the UIC and 20 cases and 20 controls at the Osnabrück University of Applied Sciences.

Descriptive statistics will be used to summarize the data. Continuous variables will be expressed as mean ± standard deviation (SD) if normally distributed, or as median and interquartile range (IQR) if non-normally distributed. Categorical variables will be presented as absolute and relative frequencies. Comparisons between groups will be made using independent t-tests for normally distributed continuous variables or Mann-Whitney U-tests for non-normally distributed data. The presence of TMD will be compared by Chi-square tests, or Fisher's exact test when the expected frequencies are low. Correlation between pericranial sensitivity and severity of general sensitivity with

other factors will be assessed by Pearson's correlation for normally distributed data or Spearman's correlation otherwise.

To assess the levels of pericranial and general sensitivity in patients with primary headaches and to compare individuals with acute and chronic conditions with healthy controls (Objective 1), descriptive statistics and group comparisons will be performed. Mean values and standard deviations of sensitivity measures between groups will be calculated, and appropriate statistical tests, such as ANOVA or Kruskal-Wallis, will be used to detect significant differences. Pairwise comparisons will be adjusted for multiple testing when necessary.

To examine the association between the total number of comorbidities and central sensitization with pericranial sensitivity (Objective 2), multivariable regression models will be used to determine prognostic relationships. Pericranial and overall sensitivity will be set as dependent variables in separate models, whereas total number of comorbidities, central sensitization score, and up to 10 relevant cofactors will be included as independent variables. Collinearity between exposure factors will be tested using the variance inflation factor (VIF) to exclude confounders, where a VIF of 1 indicates no collinearity(44). The adjusted R^2, the statistical significance of the final model, the B coefficient, the standard error (SE), the standardized B coefficient and the significance for each factor will be reported. The p-value will be interpreted according to Sterne and Smith(45) , where *$p \leq .001$ indicates strong evidence, p between .001 and .05 indicates good evidence, p between .05 and .10 indicates moderate evidence, and $p > .10$ indicates weak evidence. The R^2 effect size will be interpreted following Cohen(46) as 0.02 (small), 0.15 (medium), and 0.35 (large).

To examine the overlap between temporomandibular disorders (TMD) and primary headaches (Objective 3), the presence of TMD will be assessed using the Diagnostic Criteria for Temporomandibular Disorders (DC/TMD). Chi-square tests or logistic regression models will be used to identify significant patterns of coexistence between these conditions. The strength of associations will be quantified using odds ratios (ORs)

and confidence intervals (CIs) to determine whether individuals with primary headaches are at significantly increased risk for TMD compared to healthy controls.

4. PLANNING

Phase 1: The study protocol was approved by the Ethics Committee (CEIm) of the International University of Catalonia, Spain, on June 4, 2025. Subsequently, the protocol will be submitted for approval to the CEIm IRIS-CC of the University of Manresa, Spain, and to the Ethics Committee of the University of Applied Sciences Osnabrück, Germany.

Phase 2: Recruitment and evaluation at the International University of Catalonia, Spain , and at the Osnabrück University of Applied Sciences, Germany. March 1 to December 7, 2026. Data analysis and manuscript writing, with a deadline of early March 2027.

Phase 4: Publication, with a deadline of December 2028.

5. LINK BETWEEN MOBILITY AND THE LINE OF RESEARCH

The international mobility aspect of the project plays a key role in enhancing the research line by providing access to specialized resources, expertise and methodologies. The collaboration between the University of Manresa and the Osnabrück University of Applied Sciences fosters the intercultural exchange of knowledge, especially in the field of orofacial pain. Through the mobility, the researcher will come into contact with advanced research in orofacial physiotherapy, led by Dr. Susan Armijo-Olivo, and will be able to integrate this knowledge into research. This movement between institutions will contribute to the improvement of research methods and facilitate a comprehensive approach to understanding and addressing orofacial pain.

Principal Investigator

s/he is Dr./Dr.

Appendix_1 Screening for Headaches

Self-Assessment Form for Screening Healthy Participants and Headaches.

Instructions: Answer the following questions honestly. If you answer "Yes" in certain sections, you may not meet the criteria to participate in the study.

I. General Information.

- **Patient Code: _____**
- **Age: _____**
- **Sex:**☐ Male☐ Female☐ Other
- **Date of birth:** //____
- **Height (cm): _____**
- **Weight (kg): _____**
- **Do you currently smoke?** ☐ Yes☐ No
- **Do you consume alcohol regularly?** ☐ Yes☐ No

II. History of Headache

1. **Have you had a headache in the last 3 months?** ☐ Yes☐ No
    - If NO, go to section IV.
2. **If yes, how often do you usually have a headache?**

    Average number of days with headache per month: _____

Minimum number of headache days per month: _____

Maximum number of headache days per month: _____

3. **From what age do you experience headaches?** _____

4. **Have you been diagnosed with any type of headache (migraine, tension headache, etc.) by a physician?** ☐ Yes☐ No

    - If "Yes", please indicate diagnosis: (select from the list) List: migraine, migraine with aura, tension type headache, cluster headache, SUNCT/SUNA, hemicrania continua, paroxysmal hemicrania, primary cough headache, primary exercise headache, primary headache associated with sexual activity, primary thunderclap headache, nummular headache, hypnic headache, new daily persistent headache, other headache.)

5. **Do you take medication regularly for headaches?** ☐ Yes☐ No

Category	Medications	Duration (months) / Frequency (days/month)
Analgesics	Paracetamol, Acetylsalicylic acid, Naproxen	
Triptans	Sumatriptan, Rizatriptan, Zolmitriptan, Almotriptan, Eletriptan, Naratriptan, Frovatriptan	
Opioids	Tramadol, Codeine, Morphine, Fentanyl, Oxycodone, Hydromorphone	
Ergot derivatives	Dihydroergotamine	
Beta-blockers	Propranolol, Metoprolol	
Antiepileptics	Topiramate, Sodium valproate	
Antidepressants	Amitriptyline	
Migraine preventive	Botulinum toxin, Anti-CGRP monoclonal antibodies (Erenumab, Fremanezumab, Galcanezumab, Eptinezumab)	
Oxygen therapy	Oxygen	

Indomethacin	Indomethacin
Gepants	Ubrogepant, Rimegepant, Atogepant
Ditans	Lasmiditan

6. **How long have you been taking medication to treat your headache?**

_____

III. Characteristics of Headache

How long does a typical episode of your headache last? (choose the answer that fits better for your headache attacks)

☐ Seconds

☐ 2-10 minutes

☐ 10-30 minutes

☐ Hours to 3 days (when untreated)

☐ More than 3 days

When you have a headache, is it usually...?

☐ Unilateral (affects only one side of the head)

☐ Bilateral (affects both sides of the head)

Is the pain usually...?

☐ Throbbing (like a heartbeat)

☐ Oppressive (like a band around the head)

☐ Other: _____

Does the pain get worse with physical activity? ☐ Yes☐ No

Is the headache accompanied by one of the following? (Check all that apply)

☐ Nausea

☐ Vomiting

☐ Sensitivity to light (photophobia)

☐ Sensitivity to noise (phonophobia)

☐ Visual or sensory aura before headache

☐ None of the above

IV. Evaluation of Possible Secondary Headaches

10. **Has the pain changed in intensity, frequency or pattern in the last month?**

    ☐ Yes ☐ No

11. **Is your headache accompanied by fever, unexplained weight loss, or night sweats?**

    ☐ Yes ☐ No

12. **Have you suffered a head injury or traffic accident that initiated or worsened your headache?**

    ☐ Yes ☐ No

13. **The headache is preceded in the previous minutes by:**

    Double vision ☐ Yes ☐ No

    Difficulty in speaking ☐ Yes ☐ No

    Weakness or numbness ☐ Yes ☐ No

14. **Is the pain made worsened or triggered by coughing, sneezing, or changing position?**

☐ Yes ☐ No

Participant's Signature

I declare that the information provided is true and complete.

Signature: _____

Date: //____

Healthy Subject Inclusion Criteria

✓ **You are considered "healthy" if:**

- Answers "NO" to all questions in **section IV** (rule out secondary headache).
- You do not have a medical diagnosis of primary headache or take medication for it.
- If you have had headaches, they are occasional and without symptoms indicative of ✖ migraine or tension headache.

Will be excluded if:

- You answer "Yes" to any question in **section IV**.
- Frequent use of headache medication.

The answers will be evaluated by a Headache Physiotherapist to categorize the patient into Primary, Episodic, Chronic or other Secondary Headache.

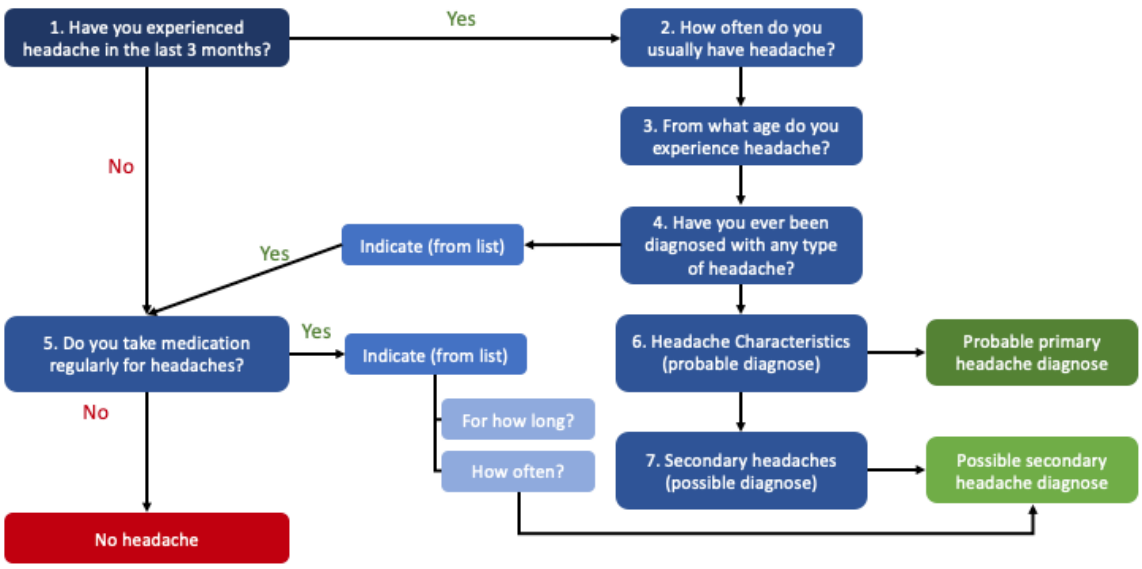

Figure XX. Screening diagram for headaches

Appendix 2_ICHD-3 Glossary of Headache Terms

1.1 Migraine without aura

Recurrent headache of moderate or severe intensity, unilateral localization, throbbing, worse with physical activity and may be accompanied by nausea, vomiting, photophobia or phonophobia.

1.2 Migraine with aura

A form of migraine preceded or accompanied by reversible neurological symptoms, typically visual (such as flashes of light or partial loss of vision), but may also include sensory or speech disturbances.

2.1 Infrequent episodic episodic tension headache

Mild to moderate, oppressive or band-like, bilateral headache that does not worsen with physical activity and is not usually associated with nausea. Occurs less than once a month.

2.2 Frequent episodic tension headaches

Similar to the previous one, but with a higher frequency (1-14 days per month), which may affect quality of life.

4.6 Thunderclap headache

Headache with abrupt onset and maximum intensity in less than one minute. May be a sign of serious pathologies such as subarachnoid hemorrhage and requires urgent evaluation.

5.1 Acute post-traumatic headache

Headache that appears within 7 days of a head injury and lasts less than 3 months.

5.2 Persistent post-traumatic headache

Headache that persists beyond 3 months after a head injury.

6.2.2 Headache attributed to ischemic or hemorrhagic stroke

Headache associated with stroke (cerebral infarction or hemorrhage), with focal neurological symptoms.

7.1.1 Headache attributed to idiopathic intracranial hypertension (pseudotumor cerebri)

Headache caused by increased intracranial pressure with no identifiable cause on neuroimaging. May be associated with blurred vision, tinnitus and pain that worsens on lying down.

9.1 Headache attributed to intracranial or systemic infection

Headache secondary to infections such as meningitis, encephalitis or severe systemic infections, often accompanied by fever and other general or neurological symptoms.

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