**Preclinical signs of a temporomandibular disorder in females with episodic cervicogenic
headache vs asymptomatic controls: A cross-sectional study**

Temporomandibular disorder in episodic headache

Sarah Mingels, M PT^{1,2†}, Wim Dankaerts, PhD² and Marita Granitzer, PhD¹

1. REVAL Rehabilitation Research Centre, Biomedical Research Institute, Faculty of
Rehabilitation Sciences, Hasselt University, 3500, Hasselt, Belgium

2. Musculoskeletal Research Unit, Department of Rehabilitation Sciences, Faculty of
Kinesiology and Rehabilitation Sciences, Leuven University, 3001, Belgium

[†]Corresponding author: Hasselt University, Faculty of Rehabilitation Sciences, Agoralaan,
3590, Diepenbeek, Belgium.

Tel.: +32-11-268509

Email: sarah.mingels@uhasselt.be

Disclosure for all authors

Nothing to disclose

Acknowledgements

The authors would like to thank Dr. Bart Craane, Stephanie Vriens and Elien Schoofs for their
scientific contribution and assistance in the data collection.

This article has been accepted for publication and undergone full peer review but has not
been through the copyediting, typesetting, pagination and proofreading process, which
may lead to differences between this version and the Version of Record. Please cite this
article as doi: 10.1002/pmrj.12156

List of abbreviations

CeH: Cervicogenic Headache

CI: Confidence Interval

DC/TMD: Diagnostic Criteria for Temporomandibular Disorders

ES: Effect Size

ICHD: International Classification of Headache Disorders

mm: millimetre

n: number of participants

N/A: Not Applicable

OR: Odds Ratio

PPT(s): Pressure Pain Threshold(s)

PSS: Perceived Stress Scale

ROM: Range Of Motion

TMD: Temporomandibular Dysfunction

TMJ: Temporomandibular Joint

VAS: Visual Analogue Scale

y: years

Introduction

The International Classification of Headache Disorders-3 accepted ‘headache attributed to temporomandibular disorder (TMD)’ as a valid headache-type.¹ Such a headache can be explained by common neuronal pathways and central sensitization processes.² Migraine, tension-type and secondary cervicogenic headache (CeH) are frequently associated with TMD.³⁻⁵ CeH and TMD are even hypothesised to share an identical pathophysiology, in which the upper-cervical spine is an important processing station for noxious signals.^{6,7} TMD can be associated with an upper-cervical dysfunction and cervical pain. Both of which are diagnostic criteria of CeH.^{1,8,9} Further, neurophysiological processes seem to interconnect the cervical spine and temporomandibular joint (TMJ).^{7,10} Headache attributed to a TMD can be explained by convergence between stimulated cervical C1-C3 afferents, mandibular, ophthalmic and maxillary branches of the trigeminal nerve at the trigeminal nucleus caudalis. The convergence mechanism may provide an explanation for the relationship between fascial pain (TMD) and headache.⁴ Such relationship can however be bidirectional, leading to a new hypothesis in which CeH might facilitate pain in the TMJ region¹¹⁻¹³ Afferent inputs from the C1-C3 spinal nerves can also converge to trigeminal motor neurons at the trigeminocervical nucleus caudalis. Excitement of such motor neurons could result in contractions of the masticatory muscles.¹¹ The latter may also be disproportionally activated via synergistic co-contractions as a response to contractions of the cervical muscles.^{14,15} Several authors hypothesize that painful conditions such as primary and secondary headaches have a negative impact on the course of a clinical TMD.^{4,16,17} The neurophysiologic interplay between cervical structures and the TMJ suggests a new hypothesis, in which patients with headache are susceptible to develop a TMD.^{4,7,16,17} This hypothesis could be supported by the ‘sliding cranium theory’ in which a forward head posture creates biomechanical compressive forces on the TMJ. Such posture is already common in patients with CeH or

TTH.¹⁸

The interplay between the TMJ and cervical structures should be placed within a biopsychosocial context. According to the OPPERA-study, TMD is a heterogeneous condition that consists of complex biopsychosocial phenotypes.¹⁹ Psychosocial variables might be predisposing risk factors for the development of chronic pain. Stress for instance predicted a first onset of TMD in a cohort of healthy females²⁰ and lowered the nociceptive threshold in patients with headache.^{21,22} Preexisting anxiety, for instance, was an indicator to develop chronic orofacial pain.²³ Similar findings support psychosocial variables as premorbid risk factors to develop numerous chronic pain conditions.²⁴

The goal of the current cross-sectional study was to screen patients with episodic CeH compared to a Control group for preclinical signs of TMD within a biopsychosocial context.²⁵ The following hypotheses were formulated: there are no differences in range of motion (ROM) of the TMJ, (extra)trigeminal pressure pain thresholds (PPTs), painful palpation and perceived stress between participants with episodic CeH and a Control group.

Method

Design

A case-controlled cross-sectional design was used to compare the TMJ ROM, PPTs, painful palpations, and level of perceived stress between women with episodic CeH and a matched asymptomatic control group.

Participants

Eighty potential candidates (40 episodic CeH, 40 Control) responded to a general call launched at -. Inclusion criteria for the episodic CeH group were: females, --, between 18 and 30 years, fulfilling the International Classification of Headache Disorders-3 (2018) (ICHD-3)¹

diagnostic criteria of episodic CeH, no diagnosis or history indicative for TMD or headache attributed to TMD based on the ICHD-3 (ICHD-3 2018)¹ and the TMD Pain Screener.²⁵

Diagnosis of CeH was based on the diagnostic criteria of the ICHD-3 (2018)¹ rather than the criteria of the ‘The Cervicogenic Headache International Study Group’. The latter includes ‘ipsilateral neck, shoulder, or arm pain of a rather vague non-radicular nature or, occasionally, arm pain of a radicular nature’ as a criterion. In the current study, diagnosis of CeH was based on upper-cervical dysfunctions (confirmed by a neurologist). Radiculitis and/or radiculopathy from upper-cervical spinal abnormalities were however exclusion criteria (ICHHD, 2018).¹ Exclusion criteria were: pregnancy, physiotherapy for head-or neck-related disorders four weeks before the start of the study, serious pathology (musculoskeletal, neurological, endocrine, cardiovascular, psychiatric), pain radiation to the arm(s), medication overuse, history of neck/head trauma, orthodontics. Inclusion criteria for the Control group were: asymptomatic females, --, between 18 and 30 years, no diagnosis or history indicative for a TMD based on the TMD Pain Screener.²⁵ Exclusion criteria were: headache, pregnancy, physiotherapy for head-or neck-related disorders four weeks before the start of the study, serious pathology (musculoskeletal, neurological, endocrine, cardiovascular, psychiatric), pain radiation to the arm(s), medication overuse, history of neck/head trauma, orthodontics. Eighteen participants with headache were excluded from the study after applying the in- and exclusion criteria. Reasons for exclusion were: migraine (n = 1), gender (n = 2), trauma (n = 1), co-morbidity (n = 2), braces (n = 2), temporomandibular surgery (n = 1), excessive medication-use (n = 4) and recent treatment for headache (n = 5). In the end, 22 participants met the criteria for the episodic CeH group. Twenty-two asymptomatic female participants were matched for age and socio-economic background (level of education and occupation) to compose the Control group through purposive sampling.

The study was registered as an ‘Observational Study’ at ‘ClinicalTrials.gov (ID --)’ and the Medical Ethical Committee of the ‘--’ granted approval (ref--). All participants signed the written informed consent in which information was given concerning the confidentiality of the data. The protection of personal data is legally determined by the law of December 8th 1992 on the protection of privacy according to the -- law.

Outcomes, measurements and instruments

Primary outcomes were (1) maximal (un)assisted temporomandibular ROM, (2) temporomandibular palpation pain, (3) PPT and, (4) level of perceived stress.

(1) *Temporomandibular ROM*. Maximal unassisted and assisted temporomandibular ROM (millimetre) were determined via opening of the mouth. Vertical mouth-opening is a valid test to differentiate between participants with and without TMD.²⁶ The unassisted and assisted temporomandibular ROM have a good reliability (ICC .89 – .91).^{27,28} Pain (binary response; yes/no) and pain location during opening of the mouth were questioned according to the Diagnostic Criteria for TMD (DC/TMD).

(2) *Temporomandibular palpation pain*. Palpation pain of the lateral TMJ and m. masseter (binary response; yes/no) were questioned. Pain responses could be further subdivided in: (a) local myalgia: pain at the site of palpation, (b) myofascial pain: pain spreading beyond the site of palpation, within the boundary of the muscle being palpated, and (c) myofascial pain with referral. Intra-tester reliability for palpation pain of the TMJ and the m. masseter amount respectively .29 and .31-.45.²⁹

(3) *PPT*. An electronic pressure algometer (Somedic Sales AB, Stockholm, Sweden) was used to determine the bilateral trigeminal (anterior, central and posterior m. temporal) and extra-trigeminal (m. anterior tibial) PPT (kPa/cm²).³⁰ The PPT was defined as the minimal amount

of pressure where a sense of pressure first changed into pain. Overall reliability of the Somic algometer amounts .89-.92.³¹

(4) *Level of perceived stress*. The perception of stress was analysed with the Dutch 'Perceived Stress Scale (PSS)'.^{32,33} This 10-item scale is a measure of the degree to which extent situations are considered as stressful and the extent to which individuals perceive themselves as capable of coping with such situations. Cronbach's alfa (.84 -.86), test-retest reliability (.85) and validity (.52 -.76) are good.³² The PSS is scored on a five-point scale ranging from 0 (never) to 4 (very often). The maximum individual score is 40, with scores ranging from 0-13 considered as low, 14-26 moderate, and 27-40 as high levels of perceived stress.³²

Secondary outcomes were (1) headache intensity (10 cm Visual Analogue Scale (VAS) for pain intensity per attack)³⁴, (2) duration (hours per attack), (3) frequency (days per month), and (4) referred pain from the neck (yes or no) extracted from a headache diary which had to be completed four weeks before the start of the study.³⁵

Procedure

The VAS for headache intensity had to be < 3 cm on the test day to limit the effect of pain on the measurements. Next, the PSS was completed, followed by two attempts to provoke pain through bilateral palpation on the origin, body, and insertion of the masseter muscle, and palpation of the lateral TMJ. The palpation pressure was set at one kilogram.²⁵ Then, the maximal unassisted and assisted vertical ROM of the TMJ were measured. The intercal distance was determined at the end-range of the unassisted and assisted movement by placing one end of a ruler against the incisal edge of one of the central incisors, and the other end against the incisal edge of the opposing maxillary incisor.²⁶ Two trials were executed before the final measurement. The ROM and the presence of pain were determined during two

unassisted and two assisted movements. Results of each of the two measurements were averaged.

The bilateral PPTs of the m. temporalis and anterior tibial were determined at the muscle belly with an electronic algometer.³⁶ Pressure was applied perpendicular using a one cm² probe with a slope of 30kPa/sec.³⁷ Participants were instructed to push the stop-button when the sensation of pressure first changed into pain. A trial was performed on the right arm before actually starting. Measurements were executed twice (intra-tester ICC .86-.99)³⁸ in a standardised order to avoid temporal summation³⁹: (1) left m. temporal (posterior, anterior, central), (2) left m. anterior tibial, (3) right m. anterior tibial, and (4) right m. temporal (posterior, anterior, central).^{40,41} Averages of two measurements on each point were calculated and used for further analysis. After testing the 10 cm VAS-headache intensity was questioned.

Statistics

Analysis was done via SAS JMP Pro 13. Two-tailed *P*-values were reported with a 95% confidence level ($P < .05$). Parametric or non-parametric statistics were applied based on the assumptions: sample size, normality (QQ-plot, Shapiro-Wilk) and equivalence of variance (Brown-Forsythe).

Based on the assumptions (linearity, equal variances and normal distribution) correlations between variables were estimated. A logistic regression model was built to calculate associations between stress and the PPTs of the (1) m. temporal and (2) m. anterior tibial. Spearman's rho was used to calculate possible associations between the ROM of the TMJ and headache characteristics from the headache diary. Power analysis was based on previous data indicating the standard deviation and mean of 'jaw pain', 'face pain' and 'head pain' measured with the Numeric Rating Scale (0–10).⁴²

Nineteen participants per group were needed to obtain a power of 80%. Effect sizes (ES) were calculated based on the parametric (Cohen's *d*) or non-parametric (*r*-value, odds ratio (OR)) statistics (Table 2).

Results

Characteristics of the participants

Table 1 summarizes the characteristics of the participants.

[Table 1]

Temporomandibular characteristics

Maximal unassisted (*P* .003; ES -.45) and assisted (*P* .002; ES -.34) ROM of the opening of the mouth differed significantly between the groups with consistently smaller openings in the episodic CeH group. No pain during or after opening was reported.

Palpations of the m. masseter showed significantly more positive local pain-responses in the episodic CeH group at the left (*P* .009; ES ∞) and right (*P* .002; ES 17.5) origo, left (*P* .004; ES 14.54) and right (*P* .03; ES 5.71) body and left (*P* < .001; ES 12) insertion compared to the Control group. The OR indicate higher risks of positive pain responses in the episodic CeH group (Table 2).

Pressure pain threshold

PPTs on the left and right m. temporalis were significantly lower (*P* .009; ES -.48) respectively (*P* .01; ES -.32) in the episodic CeH group.

Significantly lower PPTs for the left and right anterior (*P* .03; ES -.33 respectively *P* .02; ES -.35) and central (*P* .003; ES 1.02 respectively *P* .02; ES .79), and right posterior m. temporal (*P* .03; ES .62) were found in the episodic CeH group (Table 2).

The PPT of the right anterior tibial muscle was significantly lower (*P* .03; ES -.33) in the

episodic CeH group. No significant differences were seen for the left anterior tibial muscle (Table 2).

Stress

The level of perceived stress was low in 13.6%, moderate in 81.8%, and high in 4.6% of the participants in the episodic CeH group which differed significantly ($P .02$) from respectively 50%, 50% and 0% in the Control group.

Significant different answers were reported on questions ‘2. *In the last month, how often have you felt that you were unable to control the important things in your life?*’ And question ‘3. *In the last month, how often have you felt nervous and “stressed”?*’ In the episodic CeH group, 36.4% answered ‘Fairly often’ to question 2 compared to 0% in the Control group ($P .01$; ES ∞). Concerning question 3, 63.6% of participants in the episodic CeH group were ‘Fairly often’ and 13.6% ‘Very often’ nervous and stressed compared to 32.8% ‘Fairly often’ in the Control group ($P .007$; ES 3.75). The OR indicate higher risks of perceiving stress in the episodic CeH group (Table 2).

Associations

Unassisted and assisted opening of the mouth were significantly negatively associated with headache frequency (ρ -.55 respectively ρ -.64) in the episodic CeH group, meaning that the higher the headache frequency, the smaller the ROM of the TMJ. There were no associations between the level of perceived stress and the PPTs of the (1) m. temporal ($P .45$), and (2) m. anterior tibial ($P .54$).

[Table 2]

[Figure 1]

Discussion

Preclinical signs of a TMD are present in patients with episodic CeH. Moderate to large clinically significant differences between the episodic CeH group and Control group were found for the unassisted and assisted ROM of the TMJ and the PPTs of the temporal muscle. In addition, the episodic CeH group showed a higher risk of positive responses to pain provocation on the TMJ and m. masseter.

Participants

Targeting females in our study limits the generalisability, although this choice was supported by epidemiological studies indicating that CeH and TMD are common conditions with a female preponderance.^{43,44} In addition, nociceptive thresholds for mechanical stimuli are generally lower, and joint mobility generally higher in females.⁴⁶⁻⁴⁸

We focussed on a young population to minimize the risk that participants in the current study were already suffering from TMD since TMD has a peak prevalence around the age of 30 (30.2-39.4 years).^{43,45}

Preclinical signs of TMD in patients with episodic cervicogenic headache

The magnitude of the opening of the mouth is a reliable measure to discriminate between participants with TMD and healthy controls.²⁶ The unassisted (61.7 (1.4) mm vs. 68.2 (1.4) mm) and assisted (66 (1.5) mm vs. 75 (1.5) mm) ROM in the TMJ were significantly smaller in the episodic CeH group. The difference in maximal unassisted mouth opening between the episodic CeH group and Control group was larger than the smallest detectable difference (5 mm).⁴⁹ Such results, together with the higher positive pain-response on palpation, might be early signs of a preclinical TMD.

The cervical spine and TMJ are described as a functional compound, where movements of the atlanto-occipital joint and cervical vertebrae co-occur with activation of the masticatory muscles.⁵⁰ The pathophysiological and functional relations between the cervical spine and stomatognathic system could support an association between cervical dysfunctions and TMD.^{6,51,52}

Although there are no direct anatomical connections between the cervical spine and the trigeminal nerve, nociceptive information from the trigeminal and cervical regions activates neurons in the trigeminal nucleus caudalis. This overlap between the trigeminal and cervical nerve is known as the convergence mechanism. Stimulated cervical C1-C3 afferents and trigeminal afferents that converge at the trigeminal nucleus caudalis could be responsible for pain in the fascial and/or cranial region originating from cervical noxious input.⁵³ Such mechanism is mooted to be responsible for headache attributed to TMD.⁵⁴ However, the cluster of signs in the episodic CeH group namely, local pain response on palpation of the m. masseter, smaller ROM of the TMJ and absence of temporal headache are not part of the diagnostic criteria for CeH (ICHD-3, 2018). We might conclude that episodic CeH in our participants does not primary originate from the TMJ. TMD is however more prevalent in patients with headache. Although the exact nature of such association is unclear, CeH and TMD are hypothesised to share a common pathophysiology given that both disorders are related to the convergence mechanism.^{4,54} Clinical awareness of a multidimensional association between CeH and TMD could influence future treatment.⁵⁵ Detecting signs of a preclinical TMD is crucial to identify patients at risk for a clinically-manifest TMD.⁵⁶ In such a situation, TMD can exacerbate already existing headache via an overlap of innervation involving the trigeminal nerve.⁵⁷ We therefore agree with authors that advise clinicians to look for preclinical signs of TMD when examining patients with headache, particularly if

treatment directed exclusively to the cervical spine failed.⁵⁸ Longitudinal research is however needed to further support a new hypothesis in which CeH could facilitate TMD-related pain.

Lower pressure pain thresholds in patients with episodic cervicogenic headache

The significantly lower trigeminal and extra-trigeminal PPTs in patients with episodic CeH are features of sensitization of the trigeminocervical nucleus.⁵⁹ Although cephalic and extra-cephalic sensitization are features of chronic headache, a more recent study mooted central sensitization in episodic headache.³⁰ The lower extra-trigeminal PPTs in our study suggest involvement of central mechanisms in episodic headache.³⁰ An ongoing sensitization process might facilitate the development of preclinical temporomandibular signs via activation of trigeminal motor neurons. Such activation results in contractions of the masticatory muscles.¹¹

Higher levels of perceived stress in patients with episodic cervicogenic headache

A merely biomedical approach seems too restricted for managing both episodic CeH and TMD.^{60,61} An appropriate treatment should therefore be based on a biopsychosocial model.⁶² Negative emotions and stress can amplify and prolong pain via neurophysiological processes between the brain, spinothalamic tracts, dorsal horn, and peripheral nerves.⁶³ Stress can be a provocative factor for CeH⁶⁴, a predictor for the first-onset of TMD^{65,66} and a contributor to hyperalgesia.^{21,22}

Noxious input to the trigeminocervical nucleus in combination with stress may facilitate peripheral sensitization and influence the descending pain modulatory pathways at the trigeminal dorsal horn.^{21,67} Such processes can induce supra-spinal sensitization.⁶⁸ The higher level of perceived stress and the lack of perceived control in the episodic CeH group might facilitate a chronification process for both CeH and TMD.^{22,66} Additionally, psychosocial factors such as stress may contribute to an upregulation of the hypothalamic-pituitary-adrenal

axis.⁶⁹ Such upregulation could contribute to a maladaptive stress response and lower nociceptive thresholds which facilitates the progression from acute to chronic pain.⁷⁰

Limitations and Future research

The authors acknowledge that case-controlled studies are sensitive to selection bias. Generalisation of the results is therefore limited to females with episodic CeH between 18 and 30 years. Longitudinal and multimodal research is needed to examine causal relationships between CeH and TMD and to understand the contribution of psychosocial and lifestyle factors. Further, fundamental research is needed to map the areas involved in central sensitization and the related pathways in patients with CeH.⁵⁹ Haggman-Hendrikson et al (2013)⁷¹ described a functional sensorimotor integration between the jaw and neck region in patients with chronic whiplash associated disorders. The relationship between an increased headache frequency and a smaller opening of the mouth should be examined since reducing the headache frequency predicts an improvement in psychosocial wellbeing.⁷²

Clinical relevant outcomes should be further explored for the measurements (i.e. assisted ROM, PPT and PSS) and the target population in the current study. Such information might improve clinical decision making in patients CeH and TMD. Finally, no Bonferroni corrections were applied given the explorative nature of the study. The authors realize the consequence (Type I (α) error).

Conclusion

Patients with episodic CeH clearly present with signs of a preclinical TMD. Knowledge of a possible multidimensional association between CeH and TMD could influence the treatment. The added value of a (preclinical) TMJ examination in patients with episodic CeH should therefore be further explored. CeH might create a context in which the development of TMD

is facilitated. Future research should analyse if episodic CeH is a catalyst for TMD since the current study cannot support or refute such a hypothesis.

The clinically relevant smaller ROM, lower trigeminal and extra-trigeminal PPTs and higher levels of perceived stress further accentuate the multidimensional character of the problem.

References

1. Headache Classification Committee of the International Headache Society. The International Classification of Headache Disorders, 3rd edition. *Cephalalgia*. 2018;38(1):1-211.
2. Speciali JG, Dach F. Temporomandibular dysfunction and headache disorder. *Headache*. 2015;55:72-83.
3. Ballegaard V, Thede-Schmidt-Hansen P, Svensson P, Jensen R. Are headache and temporomandibular disorders related? A blinded study. *Cephalalgia*. 2008;28(8):832-841.
4. Goncalves DAG, Bigal ME, Jales LCF, Camparis CM, Speciali JG. Headache and Symptoms of Temporomandibular Disorder: An Epidemiological Study. *Headache*. 2010;50(2):231-241.
5. Di Paolo C, D'Urso A, Papi P, Di Sabato F, Rosella D, Pompa G, Polimeni A. Temporomandibular Disorders and Headache: A Retrospective Analysis of 1198 Patients. *Pain Res Manag*. 2017. doi: 10.1155/2017/3203027.
6. Bogduk N. The neck and headaches. *Neurol Clin*. 2014;32(2):471-487.
7. Conti PC, Costa YM, Gonçalves DA, Svensson P. Headaches and myofascial temporomandibular disorders: overlapping entities, separate managements? *J Oral Rehabil*. 2016;43(9):702-715.
8. Visscher CM, Lobbezoo F, De Boer W, Van Der Zaag J, Naeije M. Prevalence of cervical spinal pain in craniomandibular pain patients. *Eur J Oral Sci*. 2001;109(2):76-80.
9. Grondin F, Hall T, Laurentjoye M, Ella B. Upper cervical range of motion is impaired in patients with temporomandibular disorders. *Cranio*. 2015;33(2):91-99.
10. Armijo-Olivo S, Magee D. Cervical musculoskeletal impairments and temporomandibular disorders. *J Oral Maxillofac Res*. 2012;3(4). doi: 10.5037/jomr.2012.3404.

11. Svensson S, Arendt-Nielsen L. Muscle pain modulates mastication: an experimental study in humans. *J Orofac Pain*. 1998;12:7-16.
12. Almoznino G, Zini A, Zakuto A, Zlutzky H, Bekker S, Shay B, Haviv Y, Sharav Y, Benoliel R. Muscle tenderness score in temporomandibular disorders patients: A case-control study. *J Oral Rehabil*. 2018;10.1111/joor.12743. [Epub ahead of print]
13. Silveira A, Armijo-Olivo S, Gadotti IC, Magee D. Masticatory and cervical muscle tenderness and pain sensitivity in a remote area in subjects with a temporomandibular disorder and neck disability. *J Oral Facial Pain Headache*. 2014;28(2):138-146.
14. Clark GT, Browne PA, Nakano M, Yang Q. Co-activation of sternocleidomastoid muscles during maximum clenching. *J Dent Res*. 1993;72:1499-1502.
15. Kraus S. Temporomandibular Disorders, Head and Orofacial Pain: Cervical Spine Considerations. *Dent Clin North Am*. 2007;51(1):161-193.
16. Lim PF, Smith S, Bhalang K, Slade GD, Maixner W. Development of temporomandibular disorders is associated with greater bodily pain experience. *Clin J Pain*. 2010;26:116-120.
17. Ohrbach R, Fillingim RB, Mulkey F, Gonzalez Y, Gordon S, Gremillion H, Lim PF, Ribeiro-Dasilva M, Greenspan JD, Knott C, Maixner W, Slade G. Clinical findings and pain symptoms as potential risk factors for chronic TMD: descriptive data and empirically identified domains from the OPPERA case-control study. *J Pain*. 2011;12:27-45.
18. Makofsky H. The effect of head posture on muscle contact position: the sliding cranium theory. *Cranium*. 1989;7:286-292.
19. Bair E, Gaynor S, Slade GD, Ohrbach R, Fillingim RB, Greenspan JD, Dubner R, Smith SB, Diatchenko L, Maixner W. Identification of clusters of individuals relevant to temporomandibular disorders and other chronic pain conditions: the OPPERA study. *Pain*. 2016;157(6):1266-1278.

20. Slade GD, Diatchenko L, Bhalang K, Sigurdsson A, Fillingim RB, Belfer I, Max MB, Goldman D, Maixner W. Influence of psychological factors on risk of temporomandibular disorders. *J Dent Res*. 2007;86:1120–1125.
21. Chen Y. Advances in the pathophysiology of tension-type headache: from stress to central sensitization. *Curr Pain Headache Rep*. 2009;13(6):484-494.
22. Cathcart S, Bhullar N, Immink M, Della Vedova C, Hayball J. Pain sensitivity mediates the relationship between stress and headache intensity in chronic tension-type headache. *Pain Res Manag*. 2012;17(6):377-380.
23. Aggarwal VR, Macfarlane GJ, Farragher TM, McBeth J. Risk factors for onset of chronic oro-facial pain--results of the North Cheshire oro-facial pain prospective population study. *Pain*. 2010;149:354–359.
24. Nahit ES, Pritchard CM, Cherry NM, Silman AJ, Macfarlane GJ. The influence of work related psychosocial factors and psychological distress on regional musculoskeletal pain: a study of newly employed workers. *J Rheumatol*. 2001;28(6):1378-1384.
25. Schiffman E, Ohrbach R, Truelove E, Look J, Anderson G, Goulet JP, List T, Svensson P, Gonzalez Y, Lobbezoo F, Michelotti A, Brooks SL, Ceusters W, Drangsholt M, Ettlin D, Gaul C, Goldberg LJ, Haythornthwaite JA, Hollender L, Jensen R, John MT, De Laat A, de Leeuw R, Maixner W, van der Meulen M, Murray GM, Nixdorf DR, Palla S, Petersson A, Pionchon P, Smith B, Visscher CM, Zakrzewska J, Dworkin SF. Diagnostic criteria for temporomandibular disorders (DC/TMD) for clinical research applications: Recommendations of the International RDC/TMD consortium network and orofacial pain special interest group. *J Oral Facial Pain Headache*. 2014;28:1-27.
26. Walker N, Bohannon RW, Cameron D. Discriminant validity of temporomandibular joint range of motion measurements obtained with a ruler. *J Orthop Sports Phys Ther*. 2000;30(8):484-492.

27. Schmitter M, Ohlmann B, John MT, Hirsch C, Rammelsberg P. Research diagnostic criteria for temporomandibular disorders: a calibration and reliability study. *Cranio*. 2005;23(3):212-218.
28. John MT, Dworkin SF, Mancl LA. Reliability of clinical temporomandibular disorder diagnoses. *Pain*. 2005;118(1-2):61-69.
29. Osiewicz MA, Manfredini D, Loster BW, Selms MKA, Lobbezoo F. Comparison of the outcomes of dynamic/static tests and palpation tests in TMD-pain patients. *J Oral Rehabil*. 2018;45(3):185-190.
30. Palacios Ceña M, Castaldo M, Kelun Wang, Torelli P, Pillastrini P, Fernández-de-Las-Peñas C, Arendt-Nielsen L. Widespread pressure pain hypersensitivity is similar in women with frequent episodic and chronic tension-type headache: A blinded case-control study. *Headache*. 2017;57(2):217-225.
31. Martínez-Segura R, De-la-Llave-Rincón AI, Ortega-Santiago R, Cleland JA, Fernández-de-Las-Peñas. Immediate changes in widespread pressure pain sensitivity, neck pain, and cervical range of motion after cervical or thoracic thrust manipulation in patients with bilateral chronic mechanical neck pain: a randomized clinical trial. *J Orthop Sports Phys Ther*. 2012;42(9):806-814.
32. Cohen S, Kamarck T, Mermelstein R. A global measure of perceived stress. *J Health Soc Behav*. 1983;24:385-396.
33. Cohen S, Williamson G. Perceived stress in a probability sample of the U.S. In S. Spacapan & S. Oskamp (Eds.), *The social psychology of health: Claremont Symposium on Applied Social Psychology*. 1988. Newbury Park, CA: Sage.
34. Hjerstad MJ, Fayers PM, Haugen DF, Caraceni A, Hanks GW, Loge JH, Fainsinger R, Aass N, Kaasa S. Studies comparing numerical rating scales, verbal rating scales, and visual

analogue scales for assessment of pain intensity in adults: a systematic literature review. *J Pain Symptom Manage*. 2011;41:1073–1093.

35. Universitair Ziekenhuis Brussel. Hoofdpijndagboek. www.uzbrussel.be/u/download/nl/5898918. Accessed November 15, 2017

36. Albuquerque-Sendín F, Madeleine P, Fernández-de-las-Peñas C, Rezende Camargo P, Salvini TF. Spotlight on topographical pressure pain sensitivity maps: a review. *J Pain Res*. 2018;11:215–225.

37. O'Sullivan P, Waller R, Wright A, Gardner J, Johnston R, Payne C, Shannon A, Ware B, Smith A. Sensory characteristics of chronic non-specific low back pain: a subgroup investigation. *Man Ther*. 2014;19(4):311-318.

38. Balaguier R, Madeleine P, Vuillerme N. Is one trial sufficient to obtain excellent pressure pain threshold reliability in the low back of asymptomatic individuals? A test-retest study. *PLoS One*. 2016;11:e0160866. doi: 10.1371/journal.pone.0160866.

39. Finocchietti S, Nielsen M, Mørch CD, Arendt-Nielsen L, Graven-Nielsen T. Pressure-induced muscle pain and tissue biomechanics: a computational and experimental study. *Eur J Pain*. 2011;15(1):36-44.

40. Kim HS, Chung SC, Kim YK, Lee SW. Pain-pressure threshold in the head and neck region of episodic tension-type headache patients. *J Orofac Pain*. 1995;9(4):357-364.

41. Walton DM, Macdermid JC, Nielson W, Teasell RW, Chiasson M, Brown L. Reliability, standard error, and minimum detectable change of clinical pressure pain threshold testing in people with and without acute neck pain. *J Orthop Sports Phys Ther*. 2011;41(9): 644-650.

42. Glaros AG, Urban D, Locke J. Headache and temporomandibular disorders: evidence for diagnostic and behavioural overlap. *Cephalalgia*. 2007;27:542–549.

43. Manfredini D, Guarda-Nardini L, Winocur E, Piccotti F, Ahlberg J, Lobbezoo F. Research diagnostic criteria for temporomandibular disorders: a systematic review of axis 1

epidemiological findings. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod.* 2011;112(4):453-462.

44. Hagen K, Asberg AN, Uhlig BL, Tronvik E, Brenner E, Stjern M, Helde G, Gravdahl GD, Sand T. The epidemiology of headache disorders: a face-to-face interview of participants in HUNT4. *J Headache Pain.* 2018;19(25). doi: 10.1186/s10194-018-0854-2.

45. Ferreira CL, Silva MA, Felicio CM. Signs and symptoms of temporomandibular disorders in women and men. *Codas.* 2016;28(1):17-21.

46. Kroner-Herwig B, Gassmann J, Tromsdorf M, Zahrend E. The effects of sex and gender role on responses to pressure pain. *Psychosoc Med.* 2012;9:1-10.

47. Melo CE, Oliveira JL, Jesus AC, Maia ML, de Santana JC, Andrade LS, Quintans JD, Quintans-Junior LJ, Conti PC, Bonjardim LR. Temporomandibular disorders dysfunction in headache patients. *Med Oral Patol Oral Cir Bucal.* 2012;17(6):e1042-6.

48. Schmid-Schwab M, Bristela M, Kundi M, Piehslinger E. Sex-specific differences in patients with temporomandibular disorders. *J Orofac Pain.* 2013;27(1):42-50.

49. Kropmans T, Dijkstra P, Stegenga B, Stewart R. Smallest detectable difference in outcome variables related to painful restriction of the temporomandibular joint. *J Dent Res.* 1999;78(3):784-789.

50. Kitsoulis P, Marini A, Iliou K, Galani V, Zimpis A, Kanavaros P, Paraskevas G. Signs and symptoms of temporomandibular joint disorders related to the degree of mouth opening and hearing loss. *BMC Ear Nose Throat Disord.* 2011;11:5. doi: 10.1186/1472-6815-11-5.

51. Eriksson P, Haggman-Henrikson B, Nordh E, Zafar H. Coordinated mandibular and head-neck movements during rhythmic jaw activities in man. *J Dent Res.* 2000;79:1378–1384.

52. Olivo SA, Bravo J, Magee DJ, Thie NM, Major PW, Flores-Mir C. The association between head and cervical posture and temporomandibular disorders: a systematic review. *J Orofac Pain.* 2006;20(1):9-23.

53. Johnston MM, Jordan SE, Charles AC. Pain referral patterns of the C1 to C3 nerves: implications for headache disorders. *Ann Neurol*. 2013;74(1):145-148.
54. Svensson P. Muscle pain in the head: overlap between temporomandibular disorders and tension-type headaches. *Curr Opin Neurol*. 2007; 20:320–325.
55. Costa YM, Conti PCR, de Faria FAC, Bonjardim LR. Temporomandibular disorders and painful comorbidities: clinical association and underlying mechanisms. *Oral Surg Oral Med Oral Pathol Oral Radiol*. 2017;123(3):288-297.
56. Jensen U, Ruf S. Longitudinal changes in temporomandibular disorders in young adults: Indication for systematic temporomandibular joint screening. *J Orofac Orthop*. 2007;68(6):501–509.
57. Graff-Radford SB. Temporomandibular disorders and headache. *Dent Clin North Am*. 2007;51:129–144.
58. von Piekartz H, Hall T. Orofacial manual therapy improves cervical movement impairment associated with headache and features of temporomandibular dysfunction: a randomized controlled trial. *Man Ther*. 2013;18(4):345-350.
59. Chua NH, van Suijlekom HA, Vissers KC, Arendt-Nielsen L, Wilder-Smith OH. Differences in sensory processing between chronic cervical zygapophysial joint pain patients with and without cervicogenic headache. *Cephalalgia*. 2011;31(8):953-963.
60. Slade GD, Fillingim RB, Sanders AE, Bair E, Greenspan JD, Ohrbach R, Dubner R, Diatchenko L, Smith SB, Knott C, Maixner W. Summary of findings from the OPPERA prospective cohort study of incidence of first-onset temporomandibular disorder: implications and future directions. *J Pain*. 2013;14(12 Suppl):116-124.
61. Martin PR. Classification of Headache Disorders: Extending to a Multiaxial System. *Headache*. 2016;56(10):1649-1652.

62. Rosen NL. Psychological issues in the evaluation and treatment of tension-type headache. *Curr Pain Headache Rep.* 2012;16(6):545-553.
63. Garland EL. Pain processing in the human nervous system: a selective review of nociceptive and biobehavioral pathways. *Prim Care.* 2012;39(3):561-571.
64. Kaur J, Malik M, Rani M. Efficacy of Neural Mobilization and Advice on Postural Correction in Cervicogenic Headache: A Case Report. *Int J Physiother.* 2016;13(6):726-730.
65. Fillingim RB, Ohrbach R, Greenspan JD, Knott C, Diatchenko L, Dubner R, Bair E, Baraian C, Mack N, Slade GD, Maixner W. Psychological factors associated with development of TMD: the OPPERA prospective cohort study. *J Pain.* 2013;(12 Suppl):75-90.
66. Lei J, Fu J, Yap AU, Fu KY. Temporomandibular disorders symptoms in Asian adolescents and their association with sleep quality and psychological distress. *Cranio.* 2016;34(4):242-249.
67. Olesen J. Clinical and pathophysiological observations in migraine and tension-type headache explained by integration of vascular, supra-spinal and myofascial inputs. *Pain.* 1991;46:125-132.
68. Ashina S, Bendtsen L, Ashina M, Magerl W, Jensen R. Generalized hyperalgesia in patients with chronic tension-type headache. 2006. *Cephalalgia*;26:940-948.
69. Staniszewski K, Lygre H, Bifulco E, Kvinnsland S, Willassen L, Helgeland E, Berge T, Rosen A. Temporomandibular Disorders Related to Stress and HPA-Axis Regulation. *Pain Res Manag.* 2018. doi: 10.1155/2018/7020751.
70. Borsook D, Maleki N, Becerra L, McEwen B. Understanding migraine through the lens of maladaptive stress responses: a model disease of allostatic load. *Neuron.* 2012;73(2):219–234.
71. Häggman-Henrikson B, Lampa E, Nordh E. Altered thermal sensitivity in facial skin in chronic whiplash-associated disorders. *Int J Oral Sci.* 2013;5(3):150–154.

72. Kristoffersen ES, Aaseth K, Grande RB, C Lundqvist, MB Russell. Psychological distress, neuroticism and disability associated with secondary chronic headache in the general population - the Akershus study of chronic headache. *J Headache Pain*. 2018;19:62. doi: 10.1186/s10194-018-0894-7.

Tables

Table 1. Summary of the group characteristics

	episodic CeH (n = 22)	Control (n = 22)	P value
Age, mean (SD), y	20.7 (2.5)	21 (2.3)	.39 [†]
Socio-economic background			.41 [‡]
Student, n (%)	17 (77)	20 (91)	
Working, n (%)	5 (23)	2 (9)	
Headache duration, mean hours per attack (SD)	4.6 (3.3)	N/A	N/A
CI	(2.9 - 6.3)		
Headache intensity, mean 10 cm VAS per attack (SD)	4.2 (2.2)	N/A	N/A
CI	(3 - 5.4)		
Headache frequency, mean days per month (SD)	8.6 (6.7)	N/A	N/A
CI	(5 - 12.2)		
Referred pain from the neck, n (%)	17 (77)	N/A	N/A

CeH, cervicogenic headache; y, years; n, number of participants; VAS, Visual Analogue Scale; N/A, not applicable; [†], unpaired t-test; [‡], Fisher's exact test; CI, 95% confidence interval range. Results concerning the headache characteristics for the episodic CeH group were retrieved from the headache diary

Table 2. Summary of the results

Variable	episodic CeH (n = 22)	Control (n = 22)	P value	ES
Temporomandibular characteristics				
Unassisted ROM, mm (<i>SD</i>) [†]	61.7 (1.4)	68.2 (1.4)	.003*	-.45
<i>CI</i>	(57.9 - 65.5)	(66.4 - 67)		
Assisted ROM, mm (<i>SD</i>) [†]	66 (1.5)	75 (1.5)	.002*	-.34
<i>CI</i>	(62 - 69.7)	(69.5 - 73.5)		
Palpation lateral TMJ, n (%) local pain				
Left [§]	4 (18)	4 (18)	1	1
Right [§]	6 (27)	2 (9)	.24	3.75
Palpation m. masseter, n (%) local pain				
<i>Origo</i>				
Left [§]	7 (32)	0 (0)	.009*	∞
Right [§]	10 (45)	1 (5)	.002*	17.5
<i>Body</i>				
Left [§]	9 (41)	1 (5)	.004*	14.54
Right [§]	8 (36)	2 (9)	.03*	5.71
<i>Insertion</i>				
Left [§]	16 (73)	4 (18)	< .001*	12
Right [§]	11 (20)	5 (23)	.06	3.4
Pressure pain threshold				
m. temporal left, kPa/cm ² (<i>SD</i>) [†]	395.3 (97.3)	520.2 (163.4)	.009*	-.48
<i>CI</i>	(352.1 - 438.4)	(447.8 - 592.7)		
- anterior, kPa/cm ² (<i>SD</i>) [†]	323.1 (87.9)	409.1 (127.3)	.03*	-.33
<i>CI</i>	(284.2 - 362.1)	(352.7 - 465.6)		
- central, kPa/cm ² (<i>SD</i>) [‡]	388.9 (102.6)	543.2 (186.9)	.03*	1.02
<i>CI</i>	(343.4 - 434.4)	(460.4 - 626.1)		
- posterior, kPa/cm ² (<i>SD</i>) [‡]	473.7 (123.4)	608.3 (209.4)	.05	.78
<i>CI</i>	(419. - 528.4)	(515.5 - 701.1)		
m. temporal right, kPa/cm ² (<i>SD</i>) [†]	384.9 (116.5)	484.5 (157.9)	.01*	-.32
<i>CI</i>	(333.3 - 436.6)	(414.5 - 554.5)		
- anterior, kPa/cm ² (<i>SD</i>) [†]	290 (82)	386.6 (124.1)	.02*	-.35
<i>CI</i>	(253.6 - 326.3)	(331.6 - 441.7)		
- central, kPa/cm ² (<i>SD</i>) [‡]	413.8 (134.3)	520 (181.6)	.02*	.79
<i>CI</i>	(354.2 - 473.3)	(439.5 - 600.5)		
- posterior, kPa/cm ² (<i>SD</i>) [‡]	451.1 (153.5)	546.8 (183.3)	.03*	.62
<i>CI</i>	(383.1 - 519.1)	(465.5 - 628.0)		
m. anterior tibial left (<i>SD</i>) [†]	623.6 (333.2)	780.7 (309.4)	.07	-.28
<i>CI</i>	(475.9 - 771.3)	(643.5 - 917.9)		
m. anterior tibial right (<i>SD</i>) [†]	613.7 (273.9)	834.4 (346.1)	.03*	-.33
<i>CI</i>	(492.3 - 735.1)	(680.9 - 987.9)		
Perceived Stress Scale				
Total score [§]			.02*	
- Low level perceived stress, n (%)	3 (14)	11 (50)		.16
- Moderate level perceived stress, n (%)	18 (82)	11 (50)		4.5
- High level perceived stress, n (%)	1 (4)	0 (0)		∞

Question 2: 'In the last month, how often have you felt that you were unable to control the important things in your life?'			.01*
- Fairly often, n (%)	8 (36)	0 (0)	∞
Question 3: 'In the last month, how often have you felt nervous and "stressed"?'			.007*
- Fairly often, n (%)	14 (64)	7 (32)	3.75

CeH, cervicogenic headache; n, number of participants; TMJ, temporomandibular joint; CI, 95% confidence interval; ES, effect size; *, $P < .05$; †, Wilcoxon Signed Ranked Test (ES: r ; .1 = small, .3 = moderate and .5 = large effect); ‡, unpaired t-test (ES: Cohen's d ; .2 = small, .5 = moderate and .8 = large effect); §, Fisher's exact test (ES: odds ratio); only positive pain responses were considered for the pain palpation.

Figure legend

Figure 1. Hypothesized interaction between episodic CeH and TMD within the neuromatrix (CeH, episodic cervicogenic headache; TMD, temporomandibular disorder)