Running title

Widespread Pain in Chronic Pain Patients.

Title

Patients with Concomitant Chronic Neck Pain and Myofascial Pain in Masticatory Muscles Have More Widespread Pain and Distal Hyperalgesia than Patients with Only Chronic Neck Pain.

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ABSTRACT

Objective: Insufficient evidence exists to compare widespread pain (WP), pain sensibility, and psychological factors that occur in patients presenting with chronic neck pain (CNP) or a combination of temporomandibular disorder (TMD) and other complaints. The present study compared the pain sensibility and psychological factors of subjects with CNP with those with TMD+CNP.

Design: Cross-sectional study.

Setting: Local community.

Subjects: A nonprobabilistic convenience sample of 86 persons with CNP or TMD was recruited into three groups: CNP, TMD with myofascial pain in masticatory muscles with cocomitant CNP (TMD+CNP), and asymptomatic control groups consisted of 27, 29, and 30 participants, respectively.

Methods: Participants underwent a clinical examination to evaluate WP with computerized assessment based on the pain drawing, pressure pain thresholds (PPT), and psychological factors, which were evaluated using the pain catastrophizing scale (PCS) and the state-trait anxiety inventory (STAI).

Results: Statistically significant differences were observed between participants with CNP and TMD+CNP for WP (t 5 -2.80, P<0.01, d 5-1.06). Post hoc analyses only revealed significant differences between TMD+CNP participants and asymptomatic controls for PPT at extratrigeminal areas. Pearson correlation analyses showed a moderate positive association between symptomatic groups within the WP and STAI (P<0.05) and a moderate negative association between PCS and PPT (P < 0.05) at the right tibialis muscle.

Conclusions: TMD+CNP participants had more areas of pain and also showed widespread pain hyperalgesia. Both groups of participants had psychological factors

positively associated with STAI and WP; further, PCS and the PPT at the extratrigeminal region were negatively associated with each other in both groups, except for the left tibialis in the TMD+CNP group.

Key words: Neck Pain, Orofacial Pain, Widespread Pain, Pain Catastrophizing, Anxiety.

INTRODUCTION

Idiopathic chronic neck pain (CNP) is a frequent health problem encountered worldwide. Currently, this condition is considered one of the primary causes of disability (1). Previous research has shown that recovery from idiopathic CNP is poor, with at least half of patients suffering neck pain (NP) involving chronification of pain and disability (2). There are numerous causes and predictors for long-term symptoms of idiopathic CNP, including psychological factors and reported levels of perceived pain (3).

All of these factors presented together frequently sur- pass trigeminal innervations to the back of the head, which is innervated by the greater occipital nerve (4). This can lead to orofacial pain. These clinical features suggest an overlap between trigeminal and cervical sensory afferent projections in the central nervous system. This overlap likely occurs in the upper cervical segments, such as the trigeminal nucleus caudalis. Several clinical studies have demonstrated trigger points in the neck muscles that are linked to the orofacial region (5,6), as well as the zygapophysial joints of C3–C4 (7). Moreover, in addition to disability, recent studies have noted a significant association between cervical spine impairment and temporomandibular disorders (TMD) (8,9). The severity of TMD increases with NP severity (10). The number of patients suffering from TMD is also increasing (11). However, the prevalence of patients with impairments in the masticatory musculature, temporomandibular joints, or both is very heterogeneous (12).

These clinical manifestations have been diagnosed frequently as central sensitization. This occurs when there is an expansion of deep neural and cutaneous receptive fields

beyond the trigeminal areas. There are also alterations in neuronal properties and spinal nociceptive pathways (13,14) that lead to an expansion of pain in the trigeminal and cervical regions, poor localization of pain, hyperalgesia, mechanical allodynia (15,16), and dysfunction of the descending inhibitory system (17). These symptoms are all strongly influenced by supraspinal processes (18) such as general psychological distress, anxiety, and catastrophizing.

Recent studies have mapped the spatial extent of body pain drawings associated with alterations in pressure pain thresholds (PPTs) (19). Widespread pain (WP) can be associated with health status (20,21). Moreover, WP and psychosocial issues, such as anxiety and depression, have been reported in pain clinics (22,23).

Additionally, psychosocial factors are related to the presence of neck and orofacial pain (24). Psychosocial factors play an important role in chronic pain patients. For example, it was shown in a cohort study that stress, negative affect, and coping strategies for pain had a significant impact on TMD patients (25). Similarly, Kindler and colleagues (26) found that anxiety was strongly associated with muscle pain in TMD patients. Psychological characteristics, including somatization, depression, and anxiety, appear to have a significant impact on the prevalence of this impairment (27).
Nevertheless, there is insufficient evidence to compare pain sensibility, psychological factors, and WP between patients presenting only with CNP and those with TMD and additional mixed complaints. Having this data could provide relevant information to rehabilitators in clinical settings, which could improve the care of patients with chronic pain. Therefore, our hypothesis is that psychosocial factors and WP are higher in participants with concomitant CNP and myofascial pain in masticatory muscles than in

participants with only CNP.

This study accordingly addressed these two questions: 1) Are there differences in the pain sensibility and psychosocial factors of participants with CNP and those with TMD+CNP? 2) Is widespread pain correlated with psychological state in CNP and TMD+CNP participants?

METHODS

We developed a cross-sectional study. This study was conducted as a single-blind experiment. Further, we adhered to the International Recommendations for Reporting Observational Studies in Epidemiology (STROBE) (28) in order to strengthen our study. The protocol was conducted in accordance with the Helsinki Declaration and was approved by the local ethics committee (CSEULS-PI-004/2013).

The research team was composed of two clinical examiners with over seven years of experience in clinical assessment: One researcher conducted participant group allocation, and the other was a single-blinded evaluator who proceeded with the experiment measurements without knowing the group allocation.

Subjects

We recruited a consecutive, nonprobabilistic convenience sample of participants from a local community with CNP and TMD between November 2015 and February 2016; we also recruited asymptomatic sub- jects for the control group. All participants were be- tween the ages of 18 and 40 years; were recruited from the local community using flyers, posters, and social media (e.g., Facebook); and were encouraged to withdraw

from all dietary sources of caffeine and alcohol 48hours prior to the evaluation. Participants with infrequent episodes of tension-type headaches were permitted.

Symptomatic subjects were selected if they fulfilled the following inclusion criteria: They had experienced pain in the neck region for at least 12 weeks (e.g., neck and/or shoulder pain with symptoms provoked by changes in neck posture or neck movement or palpation of the cervical musculature). Once these criteria were screened, the clinical examiner proceeded with recognition of cervical spinal pain based on the procedures described by Visscher et al. (2000) (29), a Neck Disability Index (NDI) score of at least 5 (30), and if they had a pain rating of at least 3 on the numerical pain rating scale (NPRS) over the course of the last three months (31). Subjects were assigned to the TMD+CNP group if they re- ported orofacial pain diagnosed with myofascial pain following Axis 1 (myofascial pain) of the Research Diagnostic Criteria for TMD (32) and bilateral pain of the temporal and masseter muscles as their primary pain complaint for at least three months.

Subjects were excluded from the study for any of the following reasons: previous surgery for treatment of TMD pain; history of rheumatoid disease or whiplash trauma; extensive anatomical destruction or deterioration of the temporomandibular joint; diagnosis of pain caused by neuropathic or odontogenic factors; diagnosis of psychosis; or current use of antidepressants or anxiolytics and current use of narcotic pain medication or pregnancy.

Finally, asymptomatic subjects were excluded if they were taking any medication; they had a history of neck, facial, or head pain; or they had a diagnosis of any systemic disease.

Outcomes measured

A validated Spanish version of the Neck Disability Index (NDI) (30), a reliable self-assessment tool consisting of 10 questions for measuring disability in CNP patients on a six-point scale (0 = no disability, 5 = full disability), was completed by all participants.

Pain Drawings

To measure the extent of ongoing pain spatially, each participant was asked to fill in a body pain diagram. This exercise, which made use of a diagram printed on a sheet of A4 paper, asked participants to mark all areas in which they experienced pain. To ensure that the participants did not focus only on their most painful areas, the instructions stated, “Indicate all locations in which you feel pain, even if the area is not the location of your most intense pain.” Next, the researcher jointly discussed the pain diagram with each participant to prevent representation errors.

Later, using an electronically scanned version of the body diagram, we used open-source software (33) to calculate the total body area in each pain diagram, which is highly reliable according to Dos Reis et al. (34). This measurement was obtained by shading the figure systematically from the cranial to caudal sections and from the left to right side of the figure, as described elsewhere in the literature (35). The computerized assessment for measuring the pain areas was easy and did not require significant training. Nevertheless, the first assessments were measured twice to compare the results.

Based on the literature, we decided to calculate the percentage pain surface area (PPSA) (36). The data were measured in pixels, transformed to centimeters, and finally represented as a percentage of the shaded body area.

Additionally, we also analyzed the pain drawing using a quantitative scoring system that assessed the total area shaded as previously described (37). This allowed us to count the number of pain sites in order to evaluate WP (36,38,39). Further, it enabled participants to show us where they had experienced pain during the past week. The pain diagrams were scored manually by attributing one point to each square that contained any marking.

Psychological Assessment

To evaluate the participants' propensity to catastrophize about their pain, we used the validated Spanish version (40) of the pain catastrophizing scale (PCS) (41). Participants also completed the State-Trait Anxiety Inventory (STAI), a self-reported assessment with good internal consistency (a = 0.90) that includes separate measurements of state (A-state) and trait anxiety (A-trait) (42) and is validated for Spanish participants (43). Participants use a four-point response scale ranging from ''almost never'' to ''almost always'' to indicate the extent to which they experience each emotion; higher scores indicate greater anxiety.

Pressure-Pain Threshold (PPT)

We assessed PPTs using the minimal amount of pressure that corresponds to a feeling of pain (44). We used a digital algometer (Model FDX 100, Wagner Instruments, Greenwich, CT, USA) to measure pressure point threshold (PPT; kg/cm^2). The pressure

was applied at a rate of 0.31 kg/second (45). All of the assessments were carried out in a quiet room. In order to familiarize the participants with the test procedure, pressure was first applied to an area that would not be tested during the study.

The PPTs were measured bilaterally at the trigeminal and extratrigeminal regions. The order of assessments was randomized between the participants. The masseter point (located 2.5 cm anterior to the tragus and 1.5 cm inferior to the tragus) and temporalis muscles point (located 3 cm above the line between the lateral edge of the eye and the anterior part of the helix on the anterior fibers) were chosen as trigeminal areas (46). The upper trapezius muscle was chosen because it is the most common site of pain for participants with idiopathic CNP. The tibialis anterior point was chosen as a remote distant site. Each location was tested three times; each trial was separated by 30 seconds. The mean of the three trials was calculated and used for the analysis. The reliability of pressure algometry is high (intraclass correlation = .91, 95% confidence interval [CI] = 0.82–0.97) (47).

Procedure

The study protocol was the same for the CNP subjects, the TMD+CNP subjects, and the asymptomatic control group. All of the participants signed a consent form prior to participating. The examinations were conducted in a quiet, draft-free, temperature-regulated, and humidity-controlled laboratory (24 ± 1ºC, relative humidity 25–35%). This protocol was performed by a single blind evaluator who had not participated in the selection process, administration of the questionnaire, or any of the data-collecting procedures.

In order to assess if participants met the inclusion criteria, CNP-related disabilities were first evaluated using the Spanish version of the NDI (30). Next, we evaluated the pain drawings in the different participant groups (Figure 1). Then the PPTs were taken, and finally a battery of questionnaires was completed on the day of the evaluation by each participant. These questionnaires included various questions to self-report demographic data and pain-related disability variables. The sociodemographic questionnaire collected information regarding the following variables: sex, age, and duration of pain. Once the participants had completed all demographic data, they completed the psychological questionnaires of the PCS (40) and STAI (43).

Sample size

We conducted a pilot study to determine the effect size between CNP and TMD+CNP participants using pain drawing because previous studies have not investigated this topic. This pilot study included 14 CNP participants and 14 TMD+CNP participants and obtained an effect size (Cohen's d) of 0.93.

We used the statistical software G*Power 3.1.7 (University of Düsseldorf, Germany) (48) to calculate the sample size needed to complete this study. We opted to use an independent t test in order to detect differences between both symptomatic groups for WP. Moreover, we used an alpha error level of 0.05, a statistical power of 80% (1-β error), and a large effect size of 0.93 (based on the aforementioned pilot study). A total sample size of 52 participants (26 CNP and 26 TMD+CNP) was estimated to ensure reliability.

Statistical analysis

All of the data analyses were performed using SPSS for Windows, version 21.0 (SPSS Inc., Chicago, IL, USA). The statistical analyses were conducted at a 95% confidence level; a P value of less than 0.05 was considered statistically significant. We generated descriptive statistics for the sociodemographic, psychosocial, and pain-related disability variables and physical measures. We expressed our results as means and standard deviations (SD) with 95% confidence intervals. We confirmed the normality of the data using the Kolmogorov-Smirnov test.

To compare the primary outcomes (widespread pain and PPSA) between the two symptomatic groups, we used a Student's t test for independent samples. We calculated effect sizes (Cohen's d) for the outcome variables. According to Cohen's method, the magnitude of the effect was classified as small (0.20–0.49), medium (0.50–0.79), or large (≥0.8) (49).

We used a one-way analysis of variance (ANOVA) to analyze the groups' PPTs and psychosocial variables. Significant ANOVA findings were followed up using a post hoc test and a Bonferroni correction. We calculated the partial eta-squared (η^2_p) as a measurement of the effect size (strength of association) for each main effect and interaction in the ANOVAs. For this analysis, 0.010–0.059, 0.060–0.139, and >0.14 represented small, medium, and large effects, respectively (50).

We examined the relationships among pain sensibility, widespread pain, and psychosocial measures using Pearson correlation coefficients. A Pearson correlation

coefficient >0.60, between 0.30 and 0.60, and <0.30 indicated high, medium, and low correlations, respectively (51).

RESULTS

The study involved 86 participants (27 with CNP, 29 with TMD+CNP, and 30 asymptomatic controls). Both symptomatic groups exhibited similar outcomes for cervical pain duration, pain intensity, and neck disability (P>0.05). The duration of orofacial pain observed in participants with TMD+CNP was 3.32±4.03 years. The sociodemographic and clinical characteristics of the participants are presented in Table 1.

Comparisons between groups

There were no statistically significant differences between the symptomatic groups in terms of PPSA (P>0.05), except for widespread pain in the body pain diagram ($t = -2.80$, $P < 0.01$, $d = -1.06$) (Table 2).

One-way ANOVA revealed significant differences for all the psychosocial measurements (PCS: $F = 4.17$, $P = 0.019$, $g2P = 0.10$; A-state: $F = 9.04$, $P < 0.001$, $g2P = 0.19$; and A-trait: $F = 6.02$, $P = 0.004$, $g2P = 0.14$). However, the post hoc analysis revealed only statistically significant differences when comparing the TMD+CNP group with the control group for all of these variables; there was a large effect size ($d \geq 0.9$) for the anxiety variables and a medium effect size for PCS ($d \geq 0.7$) (Table 2).

The results pertaining to the PPT data are presented in Table 3. We observed statistical differences between the symptomatics groups and asymptomatic individuals for all of

the variables ($P<0.05$), except for the distant area (tibialis muscle) in the CNP group ($P > 0.05$). Furthermore, we noted differences within the CNP and TMD+CNP groups when the masseter muscle ($d \geq 0.8$, $P < 0.05$), the left trapezius muscle ($d \geq 0.7$, $P < 0.05$), and the tibialis muscle ($d \geq 0.9$, $P < 0.05$) data were examined.

Correlations analysis

Pearson correlation analysis revealed a moderate positive association between WP and the A-STAI in the CNP group ($r = 0.448$, $P = 0.04$) and with the A-trait in the TMD+CNP group ($r = 0.417$, $P = 0.03$). Participants with a higher anxiety score displayed a greater extent of pain.

Additionally, the TMD+CNP group exhibited an association between WP and orofacial pain chronicity ($r = 0.552$, $P<0.01$). Finally, PCS was associated with the NDI in the CNP and TMD+CNP groups ($r = 0.494$, $P = 0.01$, and $r = 0.404$, $P = 0.04$, respectively). The other correlations are listed in Table 4.

DISCUSSION

Our primary objective was to analyze the pain sensibility and psychosocial factors associated with different symptomatic groups. Our results revealed statistical differences among symptomatic groups when the PPTs at extratrigeminal sites, the left trapezius, and bilateral masseters were measured. When we examined the data obtained at the distant point (tibialis muscle), we noted large effect size differences that exceeded the minimum detectable change (52). This central and peripheral sensitization was noted previously by a few research studies as a potential mechanism to explain the pain in patients with neck pain (53) and other chronic pain (54); it may represent altered

processing within descending pathways from the brain (e.g., descending facilitation or loss of descending inhibition) (55). Moreover, a recent systematic review presented a lack of central sensitization in idiopathic neck pain conditions (56), which is consistent with our results. Nevertheless, TMD patients frequently report central sensitization, which manifests clinically as increased pain in the trigeminal and cervical areas, poor localization of pain and hyperalgesia, and descending inhibitory system dysfunction (57–59). These findings are consistent with our results. Furthermore, the authors found statistical differences between the TMD+CNP group and the asymptomatic subjects when examining all of the psychosocial variables. These medium-to-large effect sizes maybe clinically relevant (60).

When comparing the pain drawings among participants, we did not observe any statistically significant differences in the PPSAs of each group. Nevertheless, widespread pain persisted in more areas in participants in the TMD+CNP group; this difference was significant and had a large effect size. Although the PPSAs of both groups were similar, the number of pain sites could be a key factor that contributes to sensitization differences between the groups. However, the present study is a cross-sectional study, so the results may not provide information about cause-and-effect relationships.

The secondary objective of this study was to analyze the associations between widespread pain and the physiological state of participants suffering from CNP and TMD. In the CNP group, WP was associated with the A- state variable. Anxious individuals may perceive more situations, such as interpersonal situations involving a threat to one’s self-esteem or new or difficult tasks, as threatening, which may result in

421 a corresponding increase in their anxiety state. Furthermore, the group of participants
422 with TMD+CNP had associated WP with trait anxiety, which is most likely influenced
423 by past experiences and a propensity to respond with anxiety in the anticipation of a
424 challenging situation. In contrast to these results, a systematic review by Carnes et al.
425 (2006) (61) concluded that the available data did not support the hypothesis that pain
426 drawings were associated with the psychological state. This finding is inconsistent with
427 more recent studies such as Visser et al. (36), who found that patients with WP reported
428 "severe" or "extremely severe" levels of anxiety. These findings are largely consistent
429 with epidemiological studies reporting associations between the extent of bodily pain
430 (typically the number of body sites affected) and anxiety, depression, and insomnia
431 (20,39,62). Furthermore, these data were similar in WP patients suffering from stressful
432 events and trauma (63,64). Stress causes psychosocial alterations that are associated
433 with the experience of pain, which could lead to a "pain-tension cycle"; widespread
434 body pain may lead to enhanced central sensitization, not just nociceptive pain (65–67).
435 Finally, we did not find a relationship between WP and sensitization when comparing
436 PPT measurements; other researchers have noted an association with higher
437 hypersensitivity that may be explained by the fact that they explored other chronic
438 conditions like fibromyalgia (68). These data may be of interest to the clinical setting,
439 such as rehabilitators working with TMD+CNP patients. Our results may help
440 practitioners to develop better health care strategies (69).
441
442 Moreover, chronic pain data, which were associated previously with WP (39,70,71), are
443 often collected during clinical interviews to ensure better diagnoses and the best
444 treatment option. These data agree with the moderate associations that we found in our
445 TMD+CNP participants, in whom more areas of pain were associated with increased

orofacial chronification. The mechanisms underlying WP are likely complex and are currently poorly understood; there is also growing evidence that genetic factors (72,73) contribute to this condition.

When examining psychosocial associations, we found that the PCS increased with increased disability due to neck pain. This finding corresponds with previous literature and with the fear avoidance model proposed by Vlaeyen and Linton (3). Cognitive processes, such as pain catastrophizing, are an important variable to consider within the disability and the clinical signs presented by various patients with chronic pain (74,75). A scale of jaw disability would likely provide additional information.

PCS was related to more pain sensibility in the extratrigeminal areas. This relationship may be due to the central sensitization process in these participants, which was discussed earlier in this section.

Future research and clinical treatment of this group of subjects should carefully identify patients with WP based on pain drawing analysis and psychosocial factors for specific clinical treatment. Also, future studies should consider the classification of these chronic pain patients with the recent criteria for TMD assessment (DC/TMD) including Axis II.

It is likely that patient-centered approaches based on the specific needs, values, and beliefs of chronic pain patients could be implemented. Physical assessment and psychosocial functioning can guide a practitioner’s approach to empower a patient and boost their self-confidence regarding their decision-making during everyday activities.

This type of intervention is successful for reducing anxiety in chronic pain patients (76). Such personalized approaches are not yet discussed in the current treatment guidelines for patients with either neck conditions (77) or TMD (78).

Limitations

The samples that we investigated differed regarding sex and age. Recent studies have confirmed that women report more frequent and severe signs of TMD and CNP than men (79,80). The age difference between our sample groups (approximately six years) was not likely to be clinically relevant. Furthermore, we did not assess the contribution of the participants' socioeconomic status. Some studies have found that a lower socioeconomic status modifies the probability of WP in chronic conditions (38).

We did not control for the recent hypothesis that reduced quantity of vitamin D and physical inactivity are associated with extended body pain (81). We also did not obtain pain drawings at multiple time points throughout the evaluation process, which was recently recommended (82). Nevertheless, we followed other proposed recommendations. Finally, we did not use a specific test to measure the craniofacial disability, which is desirable for future studies.

CONCLUSION

Clinicians should be aware that subjects presenting with TMD+CNP likely have differences in pain hyperalgesia at extratrigeminal regions and in psychosocial factors. STAI and widespread pain were positively associated with psychosocial factors in both groups of symptomatic subjects; moreover, PCS and the PPT at the extratrigeminal regions were negatively associated in these groups of subjects, except for the left tibialis

in the TMD+CNP group.

REFERENCES

[1]. Vos T, Flaxman AD, Naghavi M, et al. Years lived with disability (YLDs) for 1160 sequelae of 289 diseases and injuries 1990-2010: A systematic analysis for the Global Burden of Disease Study 2010. Lancet 2012;380:2163–96.

[2]. Carroll LJ, Hogg-Johnson S, Côté P, et al. Course and prognostic factors for neck pain in workers: Results of the Bone and Joint Decade 2000-2010 task force on neck pain and its associated disorders. J Manipulative Physiol Ther 2009;32:S108–16.

[3]. Vlaeyen JWS, Linton SJ. Fear-avoidance model of chronic musculoskeletal pain: 12 years on. Pain 2012;153:1144–7.

[4]. Piovesan EJ, Kowacs PA, Tatsui CE, et al. Referred pain after painful stimulation of the greater occipital nerve in humans: Evidence of convergence of cervical afferences on trigeminal nuclei. Cephalalgia 2001;21:107–9.

[5]. Wright EF. Referred craniofacial pain patterns in patients with temporomandibular disorder. J Am Dent Assoc 2000;131:1307–15.

[6]. Fernández-de-Las-Peñas C, Galán-Del-Río F, Alonso-Blanco C, et al. Referred pain from muscle trigger points in the masticatory and neck-shoulder musculature in women with temporomandibular disoders. J Pain 2010;11:1295–304.

[7]. Cooper G, Bailey B, Bogduk N. Cervical zygapophysial joint pain maps. Pain Med 2007;8:344–53.

[8]. Armijo-Olivo S, Silvestre RA, Fuentes JP, et al. Patients with temporomandibular disorders have increased fatigability of the cervical extensor muscles. Clin J Pain 2012;28:55–64.

[9]. Muñoz-García D, Gil-Martínez A, López-López A, et al. Chronic neck pain and cervico-craniofacial pain patients express similar levels of neck pain- related disability, pain catastrophizing, and cervical range of motion. Pain Res Treat 2016; in press.

[10]. Wiesinger B, Malker H, Englund E, Wänman A. Does a dose-response relation exist between spinal pain and temporomandibular disorders? BMC Musculoskelet Disord 2009;10:28.

[11]. Resende CM, Alves AC, Coelho LT, et al. Quality of life and general health in patients with temporomandibular disorders. Braz Oral Res 2013;27:116–21.

[12]. Okeson JP, de Leeuw R. Differential diagnosis of temporomandibular disorders and other orofacial pain disorders. Dent Clin North Am 2011;55 :105–20.

[13]. Lam DK, Sessle BJ, Hu JW. Glutamate and capsaicin effects on trigeminal nociception II: Activation and central sensitization in brainstem neurons with deep craniofacial afferent input. Brain Res 2009; 1253:48–59.

[14]. Vernon H, Sun K, Zhang Y, Yu X-M, Sessle BJ. Central sensitization induced in trigeminal and upper cervical dorsal horn neurons by noxious stimulation of deep cervical paraspinal tissues in rats with minimal surgical trauma. J Manipulative Physiol Ther 2009;32:506–14.

[15]. Sessle BJ. Peripheral and central mechanisms of orofacial inflammatory pain. Int Rev Neurobiol 2011; 97:179–206.

[16]. Sessle BJ. Recent insights into brainstem mechanisms underlying craniofacial pain. J Dent Educ 2002;66:108–12.

[17]. Sarlani E, Grace EG, Reynolds MA, Greenspan JD. Evidence for up-regulated central nociceptive processing in patients with masticatory myofascial pain. J Orofac Pain 2004;18:41–55.

[18]. Gatchel RJ, Peng YB, Peters ML, Fuchs PN, Turk DC. The biopsychosocial approach to chronic pain: Scientific advances and future directions. Psychol Bull 2007;133:581–624.

[19]. Gerhardt A, Eich W, Janke S, et al. Chronic widespread back pain is distinct from chronic local back pain: Evidence from quantitative sensory testing, pain drawings, and psychometrics. Clin J Pain 2015;32(7):568–79.

[20]. Ektor-Andersen J, Isacsson SO, Lindgren A, Orbaek P. The experience of pain from the shoulder-neck area related to the total body pain, self-experienced health and mental distress. The Malmö Shoulder-Neck Study group. Pain 1999;82:289–95.

[21]. Kamaleri Y, Natvig B, Ihlebaek CM, Benth JS, Bruusgaard D. Number of pain sites is associated with demographic, lifestyle, and health-related factors in the general population. Eur J Pain 2008;12:742–8.

[22]. Gerrits MMJG, van Oppen P, van Marwijk HWJ, Penninx BWJH, van der Horst HE. Pain and the onset of depressive and anxiety disorders. Pain 2014;155:53–9.

[23]. Gupta A, Silman AJ, Ray D, et al. The role of psychosocial factors in predicting the onset of chronic widespread pain: Results from a prospective population-based study. Rheumatology 2007;46 :666–71.

[24]. Rantala MA, Ahlberg J, Suvinen TI, et al. Temporomandibular joint related painless symptoms, orofacial pain, neck pain, headache, and psychosocial factors among non-patients. Acta Odontol Scand 2003;61:217–22.

[25]. Fillingim RB, Ohrbach R, Greenspan JD, et al. Potential psychosocial risk factors for chronic TMD: Descriptive data and empirically identified domains from the OPPERA case-control study. J Pain 2011; 12:T46–60.

[26]. Kindler S, Samietz S, Houshmand M, et al. Depressive and anxiety symptoms as risk factors for temporomandibular joint pain: A prospective cohort study in the general population. J Pain. 2012;13 :1188–97.

[27]. Licini F, Nojelli A, Segù M, Collesano V. Role of psychosocial factors in the

etiology of temporomandibular disorders: Relevance of a biaxial diagnosis. Minerva Stomatol 2009;58:557–66.

[28]. von Elm E, Altman DG, Egger M, et al. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: Guidelines for reporting observational studies. J Clin Epidemiol 2008;61.

[29]. Visscher CM, Lobbezoo F, de Boer W, et al. Clinical tests in distinguishing between persons with or without craniomandibular or cervical spinal pain complaints. Eur J Oral Sci 2000;108:475–83.

[30]. Andrade Ortega JA, Delgado Martínez AD, Almécija Ruiz R. Validation of the Spanish version of the neck disability index. Spine (Phila Pa 1976) 2010;35:E114–8.

[31]. Jensen MP, Turner JA, Romano JM, Fisher LD. Comparative reliability and validity of chronic pain intensity measures. Pain 1999;83:157–62.

[32]. Dworkin SF, LeResche L. Research diagnostic criteria for temporomandibular disorders: Review, criteria, examinations and specifications, critique. J Craniomandib Disord 1992;6:301–55.

[33]. GIMP Team. GIMP User Manual; 2009. http://docs.gimp.org/2.8/en/ (accessed July 1, 2016).

[34]. Dos Reis FJJ, de Barros E Silva V, de Lucena RN, Mendes Cardoso BA, Nogueira LC. Measuring the pain area: An intra- and inter-rater reliability study using image analysis software. Pain Pract 2016;16:24–30.

[35]. Persson AL, Garametsos S, Pedersen J. Computeraided surface estimation of pain drawings - intra- and inter-rater reliability. J Pain Res 2011;4:135–41.

[36]. Visser EJ, Ramachenderan J, Davies SJ, Parsons R. Chronic widespread pain drawn on a body diagram is a screening tool for increased pain sensitization, psycho-social load, and utilization of pain management strategies. Pain Pract 2014;16:31–7.

[37]. Hägg O, Fritzell P, Hedlund R, et al. Pain-drawing does not predict the outcome of fusion surgery for chronic low-back pain: A report from the Swedish Lumbar Spine Study. Eur Spine J 2003;12:2–11.

[38]. Rannestad T, Skjeldestad F. Socioeconomic conditions and number of pain sites in women. BMC Womens Health 2012;12: 7.

[39]. Andersson HI. The course of non-malignant chronic pain: A 12-year follow-up of a cohort from the general population. Eur J Pain 2004;8:47–53.

[40]. Garcia Campayo J, Rodero B, Alda M, et al. [Validation of the Spanish version of the pain catastrophizing scale in fibromyalgia]. Med Clin 2008; 131:487–92.

[41]. Sullivan MJL, Bishop SR, Pivik J. The pain catastrophizing scale: Development and validation. Psychol Assess 1995;7:524–32.

616 [42]. Spielberger CD, Gorsuch RL, LRE. Manual for the State-Trait Anxiety
617 Inventory. Palo Alto, CA; Consulting Psychologists Press 1970.

618 [43]. Spielberger CD, Gorsuch RL LR. STAI, Cuestionario de Ansiedad
619 Estado/Rasgo. TEA ediciones SA, 2001.

620 [44]. Vanderweeën L, Oostendorp RAB, Vaes P, Duquet W. Pressure algometry in
621 manual therapy. Man Ther 1996;1:258–65.

622 [45]. Chesterton LS, Sim J, Wright CC, Foster NE. Interrater reliability of algometry
623 in measuring pressure pain thresholds in healthy humans, using multiple raters.
624 Clin J Pain 23:760–6.

625 [46]. Linari-Melfi M, Cantarero-Villanueva I, Fernández-Lao C, et al. Analysis of
626 deep tissue hypersensitivity to pressure pain in professional pianists with
627 insidious mechanical neck pain. BMC Musculoskelet Disord 2011;12:268.

628 [47]. Fernández-de-las-Peñas C, Galán-del-Río F, Fernández-Carnero J, et al.
629 Bilateral widespread mechanical pain sensitivity in women with myofascial
630 temporomandibular disorder: Evidence of impairment in central nociceptive
631 processing. J Pain 2009;10:1170–8.

632 [48]. Faul F, Erdfelder E, Lang A-G, Buchner A. G*Power 3: A flexible statistical
633 power analysis program for the social, behavioral, and biomedical sciences.
634 Behav Res Methods 2007;39:175–91.

635 [49]. Cohen J. Statistical Power Analysis for the Behavioral Sciences. Lawrence
636 Erlbaum Associates, Hillsdale, MI; 1988.

637 [50]. Cohen J. Eta-squared and partial eta-squared in fixed factor ANOVA designs.
638 Educ Psychol Meas 1973;33:107–12.

639 [51]. Hinkle D, Jurs S, Wiersma W. Applied statistics for the behavioral sciences. 2nd
640 ed. Boston, MA: Houghton Mifflin; 1988.

641 [52]. Walton DM, Macdermid JC, Nielson W, et al. Reliability, standard error, and
642 minimum detectable change of clinical pressure pain threshold testing in people
643 with and without acute neck pain. J Orthop Sports Phys Ther 2011;41:644–50.

644 [53]. La Touche R, Fernández-de-Las-Peñas C, Fernández-Carnero J, et al. Bilateral
645 mechanical-pain sensitivity over the trigeminal region in patients with chronic
646 mechanical neck pain. J Pain 2010;11:256–63.

647 [54]. Blumenstiel K, Gerhardt A, Rolke R, et al. Quantitative sensory testing profiles
648 in chronic back pain are distinct from those in fibromyalgia. Clin J Pain
649 2011;27:682–90.

650 [55]. Porreca F, Ossipov MH, Gebhart GF. Chronic pain and medullary descending
651 facilitation. Trends Neurosci 2002;25:319–25.

652 [56]. Malfliet A, Kregel J, Cagnie B, et al. Lack of evidence for central sensitization
653 in idiopathic, non-traumatic neck pain: A systematic review. Pain Physician

654 18:223–36.

655 [57]. Park JW, Clark GT, Kim YK, Chung JW. Analysis of thermal pain sensitivity
656 and psychological profiles in different subgroups of TMD patients. Int J Oral
657 Maxillofac Surg 2010;39:968–74.

658 [58]. Lorduy KM, Liegey-Dougall A, Haggard R, Sanders CN, Gatchel RJ. The
659 prevalence of comorbid symptoms of central sensitization syndrome among
660 three different groups of temporomandibular disorder patients. Pain Pract
661 2013;13:604–13.

662 [59]. Carvalho GF, Chaves TC, Florencio LL, et al. Reduced thermal threshold in
663 patients with temporomandibular disorders. J Oral Rehabil 2016;43(6):401–8.

664 [60]. Tingey R, Lambert M, Burlingame G, Hansen N. Assessing clinical
665 significance: Proposed extensions to method. Psychother Res 1996;6:109–23.

666 [61]. Carnes D, Ashby D, Underwood M. A systematic review of pain drawing
667 literature: Should pain drawings be used for psychologic screening? Clin J Pain
668 2006;22:449–57.

669 [62]. Tait RC, Chibnall JT, Margolis RB. Pain extent: Relations with psychological
670 state, pain severity, pain history, and disability. Pain 1990;41:295–301.

671 [63]. Jones GT, Power C, Macfarlane GJ. Adverse events in childhood and chronic
672 widespread pain in adult life: Results from the 1958 British Birth Cohort Study.
673 Pain 2009;143:92–6.

674 [64]. Wynne-Jones G, Jones GT, Wiles NJ, Silman AJ, Macfarlane GJ. Predicting
675 new onset of widespread pain following a motor vehicle collision. J Rheumatol
676 2006;33:968–74.

677 [65]. Rehm SE, Koroschetz J, Gockel U, et al. A cross-sectional survey of 3035
678 patients with fibromyalgia: Subgroups of patients with typical comorbidities and
679 sensory symptom profiles. Rheumatology 2010;49:1146–52.

680 [66]. Koroschetz J, Rehm SE, Gockel U, et al. Fibromyalgia and neuropathic pain–
681 differences and similarities. A comparison of 3057 patients with diabetic painful
682 neuropathy and fibromyalgia. BMC Neurol 2011;11:55.

683 [67]. Amris K, Jespersen A, Bliddal H. Self-reported somatosensory symptoms of
684 neuropathic pain in fibromyalgia and chronic widespread pain correlate with
685 tender point count and pressure-pain thresholds. Pain 2010;151:664–9.

686 [68]. Carli G, Suman AL, Biasi G, Marcolongo R. Reactivity to superficial and deep
687 stimuli in patients with chronic musculoskeletal pain. Pain 2002;100:259–69.

688 [69]. Pain Australia. National Pain Strategy. Available at:
689 http://www.painaustralia.org.au/the-national-pain-strategy/national-pain-
690 strategy.html; 2011 (accessed June 2016).

691 [70]. Staud R, Price DD, Robinson ME, Vierck CJ. Body pain area and pain-related

692 negative affect predict clinical pain intensity in patients with fibromyalgia. J
693 Pain 2004;5:338–43.

694 [71]. Krause SJ, Tait RC, Margolis RB. Pain distribution, intensity, and duration in
695 patients with chronic pain. J Pain Symptom Manage 1989;4:67–71.

696 [72]. Arnold LM, Hudson JI, Hess EV, et al. Family study of fibromyalgia. Arthritis
697 Rheum 2004;50:944–52.

698 [73]. Holliday KL, Nicholl BI, Macfarlane GJ, et al. Genetic variation in the
699 hypothalamic-pituitary-adrenal stress axis influences susceptibility to
700 musculoskeletal pain: Results from the EPIFUND study. Ann Rheum Dis
701 2010;69:556–60.

702 [74]. Picavet HSJ, Vlaeyen JWS, Schouten JSAG. Pain catastrophizing and
703 kinesiophobia: Predictors of chronic low back pain. Am J Epidemiol
704 2002;156:1028–34.

705 [75]. Somers TJ, Keefe FJ, Pells JJ, et al. Pain catastrophizing and pain-related fear in
706 osteoarthritis patients: Relationships to pain and disability. J Pain Symptom
707 Manage 2009;37:863–72.

708 [76]. Alamo MM, Moral RR, Pérula de Torres LA. Evaluation of a patient-centred
709 approach in generalized musculoskeletal chronic pain/fibromyalgia patients in
710 primary care. Patient Educ Couns 2002;48:23–31.

711 [77]. Childs JD, Cleland JA, Elliott JM, et al. Neck pain: Clinical practice guidelines
712 linked to the international classification of functioning, disability, and health
713 from the orthopedic section of the American Physical Therapy Association. J
714 Orthop Sports Phys Ther 2008;38:A1–34.

715 [78]. Durham J. Summary of Royal College of Surgeons' (England) clinical
716 guidelines on management of temporomandibular disorders in primary care. Br
717 Dent J 2015;218:355–6.

718 [79]. Adèrn B, Stenvinkel C, Sahlqvist L, Tegelberg A. Prevalence of
719 temporomandibular dysfunction and pain in adult general practice patients. Acta
720 Odontol Scand 2014;72:585–90.

721 [80]. Schmid-Schwap M, Bristela M, Kundi M, Piehslinger E. Sex-specific
722 differences in patients with temporomandibular disorders. J Orofac Pain
723 2013;27:42–50.

724 [81]. McBeth J, Pye SR, O'Neill TW, et al. Musculoskeletal pain is associated with
725 very low levels of vitamin D in men: Results from the European Male Ageing
726 Study. Ann Rheum Dis 2010;69:1448–52.

727 [82]. Hawkins JM, Schmidt JE, Hargitai IA, et al. Multimodal assessment of body
728 pain in orofacial pain patients. Pain Med 2016; in press.

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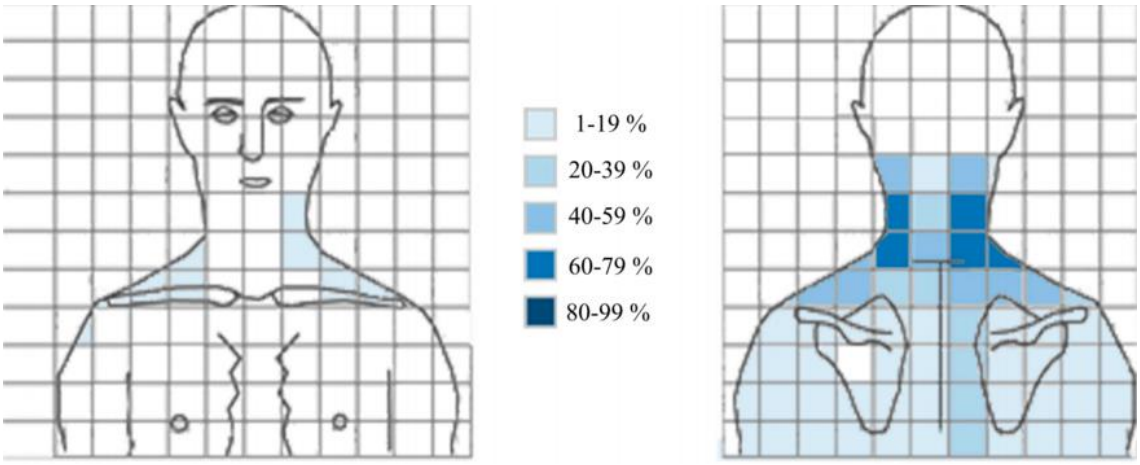
Figure 1. Pain drawing.

A) Chronic neck pain group pain drawing group



B) Temporomandibular disorder with chronic neck pain group pain drawing

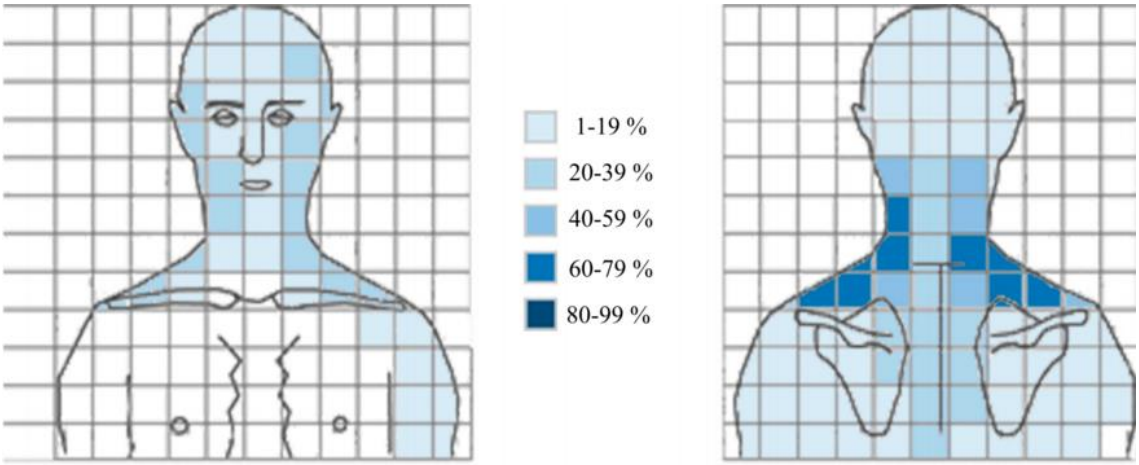


Table 1. Descriptive data of participants and clinical characteristics of patient groups.

	Mean ± SD			P
	CNP (N= 27)	TMD+CNP (N= 29)	Asymptomatic (N=30)	
Age, mean SD, y	27.52 ± 4.82	33.21 ± 6.69	26.51 ± 4.51	<0.001*
Gender, female:male	17:10	26:3	17:13	0.014†
NPRS	5.67 ± 1.89	6.02 ± 3.22	–	0.635‡
NDI	23.11 ± 7.69	26.41 ± 10.03	–	0.171‡
Pain duration, y	2.84 ± 3.03	1.75 ± 2.08	–	0.278‡

CNP, chronic neck pain; NPRS, numerical pain rating scale; NDI, Neck Disability Index; TMD, temporomandibular disorder.
*One-way analysis of variance.
†Chi-square tests.
‡Independent Student's test.

Table 2. Descriptive data and multiple comparisons of pain drawings and psychological.

	Mean ± SD			**Mean difference (95% CI), effect size (*d*)**
	CNP	**TMD+CNP**	**Asymptomatic**	**a) CNP vs TMD+CNP** **b) CNP vs asymptomatic** **c) TMD+CNP vs asymptomatic**
Widespread pain UB	12.69 ± 6.90	26.41 ± 16.88	–	a) -13.72 (-20.70– -6.74), -1.06**
				b) –
				c) –
PPSA UB, %	12.47 ± 10.05	14.08 ± 10.19	–	a) -1.62 (-6.95– -3.72), -0.16
				b) –
				c) –
PCS	13.37 ± 9.97	20.33 ± 12.50	12.65 ± 9.50	a) -6.96 (-14.13– -0.20), -0.62
				b) 0.72 (-6.51– -7.95), 0.07
				c) -7.68 (0.45– 14.91), 0.69*
A-state	16.38 ± 9.56	20.55 ± 9.94	10.30 ± 8.45	a) -4.17 (-10.70– 2.36), -0.43
				b) 6.08 (-0.40– 12.56), 0.67
				c) 10.25 (4.32– 16.18), 1.11**
A-trait	17.40 ± 8.82	22.52 ± 9.29	14.43 ± 7.94	a) -5.12 (-11.47– 1.23), -0.56
				b) 2.97 (-3.15– 9.08), 0.35
				c) 8.09 (2.35– 13.82), 0.94*

A-state, state anxiety; A-trait, trait anxiety; CI, confidence interval; CNP, chronic neck pain; PCS, pain catastrophizing scale; PPSA, percentage pain surface area; TMD, temporomandibular disorder; UB, upper body.
*P<0.05
**P <0.01

Table 3. Descriptive data and multiple comparisons of the pressure-pain threshold variable.

	Mean ± SD			ANOVA inter-groups η^2_p	Mean difference (95% CI), effect size (*d*) **a) CNP vs TMD+CNP** **b) CNP vs asymptomatic** **c) TMD+CNP vs asymptomatic**
	CNP	**TMD+CNP**	**Asymptomatic**		
C2, kg/cm^2	1.60 ± 0.68	1.34 ± 0.75	2.29 ± 0.99	F = 17.28, P < 0.01 η^2_p = 0.29	a) 0.26 (-0.27– 0.80), 0.36 b) -0.69 (-1.22– -0.16), -0.81** c) -0.96 (-1.47– -0.43), -1.08**
Right masseter, kg/cm^2	1.16 ± 0.44	0.79 ± 0.48	1.51 ± 0.49	F = 17.28, P < 0.01 η^2_p = 0.29	a) 0.37 (0.06– 0.68), 0.80* b) -0.35 (-0.66– -0.04), -0.75* c) -0.72 (-1.02– -0.42), -1.48**
Left masseter, kg/cm^2	1.10 ± 0.48	0.71 ± 0.39	1.47 ± 0.62	F = 16.49, P < 0.01 η^2_p = 0.28	a) 0.38 (0.52– 0.71), 0.89* b) -0.38 (-0.70– -0.05), -0.67* c) -0.76 (-1.08– -0.44), -1.47**
Right temporal, kg/cm^2	1.44 ± 0.67	1.05 ± 0.59	1.97 ± 0.91	F = 11.39, P < 0.01 η^2_p = 0.21	a) 0.39 (-0.09– 0.87), 0.62 b) -0.53 (-1.01– -0.05), 0.66* c) -0.92 (-1.39– -0.45), -1.20**
Left temporal, kg/cm^2	1.30 ± 0.57	0.99 ± 0.59	1.87 ± 0.82	F = 12.92, P < 0.01 η^2_p = 0.24	a) 0.32 (-0.13– 0.76), 0.53 b) -0.57 (-1.00– -0.13), -0.81** c) -0.88 (-1.31– -0.45), -1.23**
Right trapezius, kg/cm^2	1.77 ± 0.76	1.34 ± 0.61	2.24 ± 0.77	F = 11.71, P < 0.01 η^2_p = 0.22	a) 0.44 (-0.32– 0.91), 0.62 b) -0.47 (-0.93– -0.00), -0.61* c) -0.91 (-1.36– -0.45), -1.30**
Left trapezius, kg/cm^2	1.72 ± 0.67	1.29 ± 0.60	2.35 ± 0.97	F = 14.17, P < 0.01 η^2_p = 0.25	a) 0.43 (-0.07– 0.94), 0.68** b) -0.63 (-1.13– -0.13), -0.76** c) -1.06 (-1.55– -0.57), -1.31**
Right tibialis, kg/cm^2	4.51 ± 1.65	3.04 ± 1.32	5.70 ± 2.54	F = 14.19, P < 0.01 η^2_p = 0.25	a) 1.47 (0.22– 2.72), 0.98* b) -1.19 (-2.43– -0.06), -0.56 c) -2.66 (-3.88– -1.44), -1.31**
Left tibialis, kg/cm^2	4.36 ± 1.52	3.02 ± 1.31	5.19 ± 2.72	F = 9.01, P < 0.01 η^2_p = 0.18	a) 1.34 (0.05– 2.63), 0.94* b) -0.82 (-2.10– -0.45), -0.38 c) -2.16 (-3.42– -0.91), -1.02**

C2, spinous process of the second cervical vertebra; CI, confidence interval; CNP, chronic neck pain; TMD, temporomandibular disorder; UB, upper body.
*P<0.05
**P <0.01

Table 4. Pearson correlation coefficient for all outcomes in patient groups.

	Chronicity	Age	NPRS	PCS	A-state	A-trait	Group
Widespread pain UB	–	0.056	0.394	0.260	0.448*	0.058	CNP
	0.552**	0.446*	0.226	0.134	0.245	0.417*	TMD+CNP
NDI	–	-0.321	0.204	0.494**	0.466*	0.547*	CNP
	0.337*	0.182	0.107	0.404*	0.222	0.555**	TMD+CNP
C2	–	0.389*	-0.494*	-0.169	-0.292	0.011	CNP
	0.036	-0.110	0.141	-0.281	-0.043	0.138	TMD+CNP
Left masseter	–	0.406*	-0.468*	-0.251	-0.171	-0.064	CNP
	0.026	-0.148	-0.048	-0.171	-0.107	-0.199	TMD+CNP
Right masseter	–	0.363	-0.446*	-0.316	-0.236	-0.136	CNP
	-0.019	-0.111	0.113	-0.329	-0.175	-0.094	TMD+CNP
Left temporal	–	0.403*	-0.295	-0.199	-0.100	-0.019	CNP
	-0.023	-0.187	-0.072	-0.361	-0.185	-0.171	TMD+CNP
Right temporal	–	0.396*	-0.447*	-0.202	-0.215	-0.070	CNP
	-0.131	-0.223	0.057	-0.336	-0.101	-0.035	TMD+CNP
Left trapezius	–	0.334	-0.355	-0.187	-0.257	-0.014	CNP
	-0.126	-0.060	-0.275	-0.336	-0.011	-0.105	TMD+CNP
Right trapezius	–	0.230	-0.416	-0.183	0.232	0.064	CNP
	-0.104	-0.027	-0.222	-0.318	-0.063	-0.128	TMD+CNP
Left tibialis	–	0.480*	-0.378	-0.636**	-0.232	-0.238	CNP
	0.00	-0.091	-0.137	-0.318	-0.261	-0.037	TMD+CNP
Right tibialis	–	0.452*	-0.431	-0.592**	-0.288	-0.207	CNP
	0.125	-0.058	-0.176	-0.422*	-0.219	0.076	TMD+CNP

A-state, state anxiety; A-trait, trait anxiety; C2, spinous process of the second cervical vertebra; CNP, chronic neck pain; NDI, Neck Disability Index; NPRS, numerical pain rating scale; PCS, Pain Catastrophizing Scale; temporomandibular disorder; UB, upper body.

*P<0.05

**P <0.01