Bilateral Mechanical-Pain Sensitivity Over the Trigeminal Region in Patients With Chronic Mechanical Neck Pain

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Abstract: The aim of this study was to investigate bilateral pressure-pain sensitivity over the trigeminal region, the cervical spine, and the tibialis anterior muscle in patients with mechanical chronic neck pain. Twenty-three patients with neck pain (56% women), aged 20 to 37 years old, and 23 matched controls (aged 20 to 38 years) were included. Pressure pain thresholds (PPTs) were bilaterally assessed over masseter, temporalis, and upper trapezius muscles, the C5-C6 zygapophyseal joint, and the tibialis anterior muscle in a blinded design. The results showed that PPT levels were significantly decreased bilaterally over the masseter, temporalis, and upper trapezius muscles, and also the C5-C6 zygapophyseal joint (P < .001), but not over the tibialis anterior muscle (P = .4) in patients with mechanical chronic neck pain when compared to controls. The magnitude of PPT decreases was greater in the cervical region as compared to the trigeminal region (P < .01). PPTs over the masseter muscles were negatively correlated to both duration of pain symptoms and neck-pain intensity (P < .001). Our findings revealed pressure-pain hyperalgesia in the trigeminal region in patients with mechanical chronic neck pain, suggesting spreading of sensitization to the trigeminal region in this patient population.

Perspective: This article reveals the presence of bilateral pressure-pain hypersensitivity in the trigeminal region in patients with idiopathic neck pain, suggesting a sensitization process of the trigemino-cervical nucleus caudalis in this population. This finding has implications for development of management strategies.

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Key words: Neck pain, trigeminal sensitization, pressure pain threshold.

Chronic mechanical neck pain is a significant clinical problem. It seems that the prevalence of neck pain is as high as the prevalence of low back pain. A systematic review reported a 1-year prevalence for neck pain ranging from 16.7 to 75.1%, with a mean of 37.2%. A best-evidence synthesis showed an incidence rate for self-reported neck pain in the general population between 146 and 213 per 1,000 patients per year. Nearly half of neck-pain patients develop chronic symp-

toms, and many will continue to exhibit moderate disability at long-term follow-up. The economic burden associated with the management of neck pain is second only to low back pain in annual workers’ compensation costs in the United States.

Although the aetiology of insidious mechanical neck pain is under debate, it is clear that neck pain is multifactorial in nature, with both physical and psychosocial contributors. In recent years, there has been an increasing interest in the study of nociceptive-pain processing in different musculoskeletal-pain conditions. For instance, pressure pain thresholds have been extensively used for investigating mechanical pain hypersensitivity in several chronic pain conditions, eg, whiplash, fibromyalgia, unilateral migraine, repetitive strain injury, tension-type headache, osteoarthritis, low back
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region, 7, 8, 23 and headaches. 29 The expansion of symp-
pain also suffered from symptoms in the orofacial
neck pain.
spread central sensitization, in patients with idiopathic
ence of hypersensitivity restricted to the neck region
fined to the neck area with little evidence of spread to
more remote body regions, eg, the tibialis anterior mus-
cle, as opposite happens in chronic whiplash. The pres-
ence of hypersensitivity restricted to the neck region
may reflect segmental local sensitization, but not wide-
spread central sensitization, in patients with idiopathic
neck pain.

Several studies have reported that patients with neck
pain also suffered from symptoms in the orofacial
region, 7, 8, 23 and headaches. 29 The expansion of sympt-
oms from the neck area to the trigeminal region may
be related to the convergence of the nociceptive sec-
cond-order neurons receiving both trigeminal and cervi-
ical inputs into the trigemino-cervical nucleus caudalis
in the spinal gray matter of the spinal cord. 25 To the
best of our knowledge, no previous study has investi-
gated the pressure hypersensitivity over the trigeminal
region in chronic mechanical neck pain. Further, Rhudy
and Meagher 31 demonstrated that psychological states,
particularly anxiety and depression, induce an increased
effect on pressure-pain sensitivity. Therefore, the aim of
the present study was to investigate trigeminal sensitiza-
tion in patients with chronic mechanical neck pain con-
trolling psychological aspects, such as depression and
anxiety.

Methods

Subjects

Patients presenting with mechanical insidious neck
pain referred by their primary-care physicians to a spe-
cialized physical-therapy clinic between September
2007 and February 2008 were screened for possible eligi-
bility criteria. Mechanical neck pain was defined as gen-
eralized neck and/or shoulder pain with symptoms
provoked by neck postures, neck movement, or palpa-
tion of the cervical musculature. Symptoms had to be bi-
lateral and present for at least 6 months. Patients were
excluded if they exhibited any of the following: 1) unilat-
eral neck pain; 2) diagnosis of fibromyalgia; 43 3) previous
whiplash; 4) cervical spine surgery; 5) clinical diagnosis of
cervical radiculopathy or myelopathy; 6) history of previ-
ous physical-therapy intervention for the cervical region;
7) presence of severe degenerative arthritis (confirmed by
cervical radiography taken for all patients over the
age of 30 years); 8) less than 18 years; 9) diagnosis of
any TMD, according to the Research Diagnostic Criteria
for TMD (RDC/TMD) 10; or 10) concomitant diagnosis of
primary headache.

Demographic and Clinical Data

Demographic data including age, gender, height, weight, location, and nature of the symptoms was col-
lected. An 11-point numerical point rate scale 22 (NPRS;
0 = no pain, 10 = maximum pain) was used to assess cur-
rent level of neck pain. Patients also completed the Neck
Disability Index (NDI) to measure perceived disability, 42
the Beck Depression Inventory (BDI-II) to assess symp-
toms of depression, 2 and the State-Trait Anxiety Inven-
tory (STAI) for assessing state and trait anxiety. 34

The NDI consist of 10 questions measured on a 6-point
scale (0 = no disability, 5 = full disability). 42 The numeric
score for each item is summed for a score varying from
0 to 50, where higher scores reflect greater disability.
The NDI has demonstrated to be a reliable (intraclass cor-
relation coefficients ranging from .50 to .98) 24 and valid
self-assessment of disability in chronic neck pain. 19, 39

The BDI-II is a 21-item self-report measure assessing
affective, cognitive, and somatic symptoms of depres-
sion. 2 Patients choose from a group of sentences that
best describe how they have been feeling in the past 2
weeks. Higher scores indicate higher levels of depressive
symptoms. 2 The BDI-II showed good internal consistency
(alpha coefficient .90) and adequate divergent validity. 41

The STAI is a self-report assessment device which
includes separate measures of state and trait anxiety. 34
In the present study, the trait-anxiety subscale which
denotes relatively stable anxiety proneness and refers to
a general tendency to respond with anxiety to per-
ceived threats in the environment was used. Participants
use a 4-point response scale ranging from “almost never”
to “almost always”, indicating the extent to which they
experience each emotion. The State-Trait questionnaire
has shown good internal consistency (x = .83). Higher
scores indicate greater trait anxiety. 34

Finally, healthy controls were recruited from volunteer
who responded to a local announcement and were ex-
cluded if they exhibited a history of neck, facial, or
head pain (infrequent episodic tension-type headache
was permitted), any systemic disease or any history of
traumatic event (whiplash).

The study was conducted in accordance with the Hel-
sinki Declaration, and all subjects provided informed con-
sent which was approved by the local ethics committee.

Sample Size Determination

The sample-size determination and power calculations
were performed with an appropriate software (Tamaño
de la Muestra, v.1.1, Universidad de Medicina, Madrid,
Spain). The calculations were based on detecting, at
the least, significant clinical differences of 20% on pres-
sure pain threshold (PPT) between both groups, 28 with
an alpha level of .05 and a desired power of 80%, and
an estimated interindivudual coefficient of variation for
PPT measures of 20%. This generated a sample size of
at least 16 participants per group.

PPT Assessment

PPT is defined as the minimal amount of pressure
where a sensation of pressure first changes to pain. 40 A
mechanical pressure algometer (Pain Diagnosis and
Treatment Inc, Great Neck, NY) was used in this study.
The device consists of a round rubber disk (1 cm2)
atached to a pressure gauge. The gauge displays values
in kg/cm², ranging from 0 to 10 kg. The mean of 3 trials (intraexaminer reliability) was calculated and used for the main analysis. A 30-second resting period was allowed between each trial. The reliability of pressure algometry has been found to be high in both asymptomatic subjects (ICC .78–.93; 95% CI .53–.97) and neck pain patients (ICC .78–.93; 95% CI .53–.97).

**Study Protocol**

The study protocol was the same for neck-pain patients and healthy controls. All examinations were done in a quiet, draught-free, temperature- and humidity-controlled laboratory (24°C ± 1°C, relative humidity 25–35%). All participants were restricted from vigorous exercise from the day prior to the examination. None of the patients were taking any preventive drug at the time the study was performed. Participants were not allowed to take analgesics or muscle relaxants through the 72 hours prior to the examination. PPTs were measured bilaterally over masseter and temporalis muscles, the articular pillar of C5-C6 zygapophyseal joint (based on palpation of C6-C7 spinous processes), the upper trapezius muscle (midway between C7 and acromion), and tibialis anterior muscle (upper one-third of the muscle belly) by an assessor blinded to the subject’s condition. The masseter and temporalis muscles were chosen as trigeminal areas, the articular pillar of C5-C6 and the upper trapezius muscle were chosen as the most common sites of involvement in idiopathic neck pain, and the tibialis anterior was chosen as a remote distant site. The order of assessment was randomized between the participants.

**Pressure Pain Threshold Data Management**

In the current study, the magnitude of sensitization was investigated by assessing the differences of absolute and relative PPT values between both groups. For relative values, we calculated a “PPT Index,” dividing the PPT of each patient at each point by the mean of PPT score of the control group at the same point. PPT indices were only calculated in those PPT levels significantly different between patients and controls. A greater PPT Index (%) indicates lower degree of sensitization.

**Statistical Analysis**

Data were analysed with the SPSS statistical package (SPSS v.16.0; SPSS, Inc, Chicago, IL). Results are expressed as mean, standard deviation (SD), and 95% confidence interval (95% CI). The Kolmogorov-Smirnov test was used to analyze the normal distribution of the variables (P > .05). Quantitative data without a normal distribution (ie, pain history, current level of pain, and NDI) were analyzed with nonparametric tests, whereas data with a normal distribution (PPT levels, BDII, and STAI) were analyzed with parametric tests. The intraclass correlation coefficient (ICC) was used to evaluate the intraexaminer reliability of PPT data. A 2-way ANCOVA was used to investigate the differences in PPT assessed over each point (masseter, temporalis, upper trapezius, tibialis anterior muscles, and the C5-C6 zygapophyseal joint) with side (dominant or nondominant) as within-subject factor and group (patients or controls) as the between-subject factor. A 2-way ANCOVA test was used for assessing the differences in PPT index with side (dominant, nondominant) as within-patient factor, point (masseter, temporalis, upper trapezius, tibialis anterior muscles, and the C5-C6 joint) as between-patient factor, and age, sex, BDII, and STAI scores as covariates. Post hoc comparisons were conducted with the Bonferroni test. Finally, the Spearman’s rho (r) test was used to analyze the association between PPTs and the clinical variables relating to symptoms, disability, anxiety, and depression. The statistical analysis was conducted at a 95% confidence level and a P value less than .05 was considered statistically significant.

**Results**

**Demographic and Clinical Data of the Patients**

Forty consecutive patients presenting with neck pain between January and May 2009 were screened for possible eligibility criteria. Seventeen patients were excluded: concomitant diagnosis RDC/TMD (n = 8), migraine (n = 5), and previous whiplash (n = 4). Finally, 23 patients (10 men and 13 women) with mechanical neck pain, aged 20 to 37 years (mean, 28 ± 5 years; mean weight, 70 ± 10 kg; mean height, 168 ± 10 cm), and 23 matched controls, aged 20 to 38 years old (mean, 28 ± 6 years; mean weight, 66 ± 11 kg; mean height, 168 ± 9 cm) were included. No significant differences between both groups for age (P = .9), weight (P = .3) and height (P = .8) were found. Patients with neck pain showed greater levels (P < .001) of depression (BDI-II, 7.5 ± 3) and anxiety (STAI, 22.4 ± 3.2) as compared to controls (BDI-II, 3 ± 3; STAI, 10 ± 8, respectively).

Within the patient group, mean duration of neck pain history was 10 ± 4.6 months (95% CI 7.8–11.7 months), the mean intensity (NPRS) of neck pain was 3.6 ± 1.5 (95% CI 3.2–4.8), the mean NDI was 18.5 ± 3.3 (95% CI 17–20), the mean BDII was 7.5 ± 1.6 (95% CI 6–9), and the STAI was 22 ± 3 (95% CI 21–24). Furthermore, positive correlations between duration of pain history with current level of pain (r = .55, P = .007 [Fig 1A]) and BDII (r = .58, P = .004 [Fig 1B]) were found: the longer the duration of the symptoms, the greater the intensity of the perceived pain and the greater the self-reported depression. Further, current level of pain was also positively correlated to disability (r = .57, P = .004 [Fig 2A]) and to BDII (r = .64; P = .001, [Fig 2B]): the greater the intensity of the perceived pain, the greater the self-reported disability and the greater the self-reported depression.

**Pressure Pain Sensitivity Over the Trigeminal Region**

The intraexaminer repeatability of PPT readings for the masseter and temporalis muscle was .9 and .92 for the most painful side and .91 for the contralateral side. The standard error of measurement (SEM) was .14 kg/cm².
for the most painful side and .11 kg/cm² for the contralateral side.

The ANOVA revealed significant differences between both groups, but not between sides, for PPT levels over the masseter (group: \(F = 257.3, \ P < .001\); side: \(F = .58, \ P = .447\)) and temporalis (group: \(F = 124.8, \ P < .001\); side: \(F = .06, \ P = .803\)) muscles. Over both muscles, patients showed bilateral lower PPT levels than healthy controls (\(P < .001\)). Table 1 summarizes PPT assessed over the masseter and temporalis muscles for both sides within each study group.

**Pressure Pain Sensitivity Over the Cervical Region**

The intraexaminer repeatability of PPT over the C5-C6 joint and the upper trapezius muscle was .91 for the most painful side and .89 for the contralateral side, respectively. The SEM was .11 and .13 kg/cm² for the most painful side and .15 kg/cm² for the contralateral side.

The ANOVA revealed significant differences between both groups, but not between sides, for PPT levels over the upper trapezius muscle (group: \(F = 355.9, \ P < .001\); side: \(F = .03, \ P = .851\)), and the C5-C6 zygapophyseal joint (group: \(F = 291.5, \ P < .001\); side: \(F = .08, \ P = .776\)). Again, patients showed bilateral lower PPT levels in both points as compared to healthy controls (\(P < .001\)). Table 1 shows PPT over the upper trapezius muscle and the C5-C6 zygapophyseal joint for both sides within each group.

**Pressure Pain Sensitivity Over the Tibialis Anterior Muscle**

The intraexaminer repeatability of PPT over tibialis anterior muscle was .93 for the most painful side and .91 for the contralateral side, whereas the SEM was .18 and .2 kg/cm², respectively.

The ANOVA did not find significant differences between groups and sides for PPT levels over the tibialis anterior muscle (group: \(F = 1.49, \ P = .461\); side: \(F = .05, \ P = .824\)). Table 1 shows PPT over the tibialis anterior muscle for both sides within each group.

There was no effect of age, BDI-II, or STAI score on PPT levels (\(P > .2\)), although there was an effect of sex at the tibialis anterior with females having lower PPTs (\(F = 8.8, \ P = .005\)) than males.

**Pressure Pain Threshold Indices**

The ANOVA revealed significant differences for PPT indices between sites (\(F = 8.7, \ P < .001\)), but not between
sides (F = .03, P = .859). The post hoc analysis showed significant differences between both masseter and temporalis muscles with the upper trapezius muscle (P < .001) and between the temporalis muscles with the C5–C6 joint (P = .02). In such a way, the cervical region (upper trapezius muscle and C5–C6 joint) showed lower PPT indices (greater degree of sensitization) compared to the trigeminal region (masseter and temporalis muscles) for both sides (Fig 3).

**Pressure Sensitivity and Clinical Features in Patients with Mechanical Neck Pain**

Finally, a significant negative correlation between history of symptoms and PPT levels over both masseter muscles (dominant side: r_s = −.64, P < .001 [Fig 4A]; nondominant side: r_s = −.42, P = .04 [Fig 4B]) was found: the longer the duration of the symptoms, the lower the PPT levels over both masseter muscles. In addition, current level of pain intensity was also negatively correlated with bilateral PPT levels over the masseter muscles (dominant side: r_s = −.62, P < .001 [Fig 5A]; nondominant side: r_s = −.51, P = .02 [Fig 5B]): the greater the pain intensity, the lower the bilateral PPT levels. No significant correlations between NDI, BDI-II, and PPT levels were found.

### Discussion

This study showed bilateral pressure-pain hyperalgesia in both the trigeminal and cervical region, but not over the tibialis anterior muscle, in patients with mechanical chronic neck pain as compared to healthy controls. The decrease in PPT levels over the trigeminal region was associated with the intensity and duration of pain symptoms, supporting a role of the peripheral nociceptive input as an important factor driving the development of spreading sensitization.

Current results of cervical, but not widespread, pressure-pain hypersensitivity in patients with idiopathic neck pain are very similar to those previously found by Scott et al. The findings from both studies support the idea that mechanical nontraumatic neck pain is characterized by pressure-pain hyperalgesia in the cervical spine, probably reflecting peripheral nociceptor sensitization. Furthermore, our study increases evidence that pressure-pain hyperalgesia is not only restricted to cervical joints (C5–C6 or C2–C3 as previously reported) but also to cervical muscles (upper trapezius). This is expected since the upper trapezius muscle receives nerve innervation from the C2–C4 level. Nevertheless, lower PPT levels over the upper trapezius may also be related to muscle spasm residing in the neck muscles in this patient population.

The present study demonstrated that patients with mechanical chronic neck pain also have pressure-pain hyperalgesia in the trigeminal region. This finding may reflect a sensitization process of the trigemino-cervical nucleus caudalis due to the convergence of inputs from

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**Table 1. Pressure Pain Thresholds (PPTs) in Patients With Mechanical Neck Pain (n = 23) and Matched Control Subjects (n = 23). Mean Values ± Standard Deviation and 95% Confidence Intervals in Parenthesis (kg/cm²)**

<table>
<thead>
<tr>
<th></th>
<th>MECHANICAL NECK PAIN</th>
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<th>HEALTHY CONTROLS</th>
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<tr>
<td></td>
<td>DOMINANT SIDE</td>
<td>NON-DOMINANT SIDE</td>
<td>DOMINANT SIDE</td>
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<td></td>
<td></td>
<td></td>
<td>NON-DOMINANT SIDE</td>
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<tr>
<td>Trigeminal Area</td>
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<tr>
<td>Masseter</td>
<td>2 ± .4 (1.8–2.2)</td>
<td>2 ± .5 (1.8–2.2)</td>
<td>3.4 ± .5 (3.2–3.6)</td>
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<tr>
<td>Temporalis</td>
<td>2.2 ± .5 (1.9–2.5)</td>
<td>2.1 ± .5 (1.9–2.4)</td>
<td>3.7 ± .6 (3.4–3.9)</td>
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<tr>
<td>Joint</td>
<td></td>
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<tr>
<td>C5–C6</td>
<td>1.7 ± .4 (1.5–1.9)</td>
<td>1.6 ± .3 (1.4–1.8)</td>
<td>3.2 ± .4 (3.1–3.4)</td>
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<tr>
<td>Muscle</td>
<td></td>
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<tr>
<td>Upper trapezius</td>
<td>1.8 ± .4 (1.6–2)</td>
<td>1.8 ± .3 (1.6–2)</td>
<td>3.8 ± .7 (3.6–4)</td>
</tr>
<tr>
<td>Tibialis anterior</td>
<td>5.0 ± .8 (4.6–5.3)</td>
<td>5 ± .9 (4.6–5.4)</td>
<td>5.2 ± .7 (4.9–5.6)</td>
</tr>
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</table>

*Indicates significant difference between neck pain and control subjects (ANOVA, P < .001).
the trigeminal and cervical regions. In fact, neck-pain patients included in the current study were completely asymptomatic in the orofacial region, which supports that the pressure-pain hyperalgesia found over masseter and temporalis muscles reflects a sensitization process. Nevertheless, it seems that there is a greater sensitization degree in the cervical spine. This is supported by the fact that the magnitude of PPT changes was higher over the upper trapezius muscle (48–49%) and C5-C6 zygapophyseal joint (51–53%) when compared to the magnitude of PPT changes over the masseter (57–58%) and temporalis (60%) muscles. Nevertheless, there is no consensus about the PPT that are needed to consider differences as real changes. Different studies have suggested that differences ranging from 123 kPa to 200 kPa (1.2–2 kg) are needed to consider real differences. In the current study, differences between trigeminal (1.4–1.5 kg) and cervical regions (1.5–2 kg) were placed within this interval, so differences between both groups can be considered as real.

Our results increase the evidence that nontraumatic neck pain is characterized by segmental, but not widespread, sensitization mechanisms that are mostly restricted to the trigemino-cervical region. The involvement of segmental sensitization mechanisms has been reported in several local pain syndromes, eg, repetitive strain injury, chronic tension-type headache, low back pain, osteoarthritis, carpal tunnel syndrome, and unilateral shoulder pain. The existence of sensitization mechanisms in local pain syndromes suggests that sustained peripheral noxious input to the central nervous system plays a role in the initiation and maintenance of sensitization process. This is supported by the fact that central sensitization is a dynamic condition influenced by multiple factors, including activity of peripheral nociceptive inputs. For instance, in insidious mechanical neck pain, where there is no sudden nociceptive barrage to the central nervous system as in patients with whiplash syndrome, a prolonged, continued nociceptive barrage from different cervical structures, eg, muscles or facet joints, may be capable of leading to impairment in the nociceptive processing of the trigemino-cervical nucleus caudalis. This was supported by the fact that duration of symptoms was positively related to current level of pain and PPT levels over the masseter muscle. On the contrary, Scott et al found that duration of pain symptoms was not related to PPT levels over the cervical spine. It should be considered that patients included in the study by Scott et al have a greater duration of symptoms (mean: 51.5 ± 40 months), were more disabled (NDI: 29 ± 16), and had greater levels of anxiety (STAI: 40.6 ± 11) than patients included in the present study (duration of symptoms: 10 ± 4.6 months; NDI, 18.5 ± 3.3; STAI, 22.4 ± 3.2), which may explain...
differences between both studies. Finally, we do not know if sensitization mechanisms found in this study are mediated via a deregulation of second-order neurons in a segmental fashion or via glia and other immune cells that reside in the trigeminal-cervical region. Future studies are needed to further elucidate the mechanisms involved in trigemino-cervical sensitization in neck pain.

It has been suggested that anxiety and depression may influence pressure-pain hypersensitivity. Our results were independent of levels of depression (BDI-II) and the state anxiety (STAI). Additionally, patients included in the present study showed scores < 8 points in the BDI-II, which are considered normal. Our results agree with those previously reported by Scott et al in which anxiety appears not to influence pressure-pain sensitivity in patients with insidious mechanical neck pain. Nevertheless, further studies investigating the influence of psychological factors are required.

### Conclusion

Bilateral pressure-pain hyperalgesia was detected in both trigeminal and cervical regions in patients with mechanical chronic neck pain. The decrease in pressure pain thresholds in the trigeminal region was associated with the intensity and duration of the neck-pain symptoms, supporting a role of the peripheral nociceptive input as a driving factor for inducing sensitization. Our study further supports that nontraumatic neck pain shows sensitization in the trigemino cervical region, which has clinical implications in terms of spreading symptomatology to this body area.

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