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*Published in:*  
Pain Practice

*DOI (link to publication from Publisher):*  
[10.1111/papr.12565](https://doi.org/10.1111/papr.12565)

*Publication date:*  
2017

*Document Version*  
Accepted author manuscript, peer reviewed version

[Link to publication from Aalborg University](#)

### *Citation for published version (APA):*

Palacios Ceña, M., Castaldo, M., Wang, K., Madeleine, P., Guerrero, Á. L., Arendt-Nielsen, L., & Fernández-de-Las-Peñas, C. (2017). Topographical pressure pain sensitivity maps of the temporalis muscle in people with frequent episodic and chronic tension-type headache. *Pain Practice*, 17(8), 1050-1057.  
<https://doi.org/10.1111/papr.12565>

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Received Date : 28-Nov-2016  
Revised Date : 10-Jan-2017  
Accepted Date : 17-Jan-2017  
Article type : Original Manuscript

# Topographical Pressure Pain Sensitivity Maps of the Temporalis Muscle in People with Frequent Episodic and Chronic Tension-Type Headache

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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: 10.1111/papr.12565

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Article Type: ORIGINAL ARTICLE

Key Words: tension-type headache, pressure pain, temporalis

Running Head: Topographical Maps in Tension-Type Headache

Submitted: November 28, 2016; Revision accepted: January 17, 2017

## ABSTRACT

### Background

Previous pilot studies suggest the presence of heterogeneous sensitivity to pressure in primary headaches without considering the frequency of headache episodes.

### Objective

To investigate the differences in topographical pressure pain sensitivity maps in the temporalis muscle between individuals with frequent episodic (FETTH) and chronic (CTTH) tension-type headache by controlling the presence of anxiety and depression.

### Methods

Pressure pain thresholds (PPTs) were assessed bilaterally from 9 points distributed over the temporalis muscle (3 points in the anterior portion, 3 in the middle portion, and the remaining 3 in the posterior portion of the muscle belly) in 113 patients with FETTH and 91 with CTTH in a blinded design. Topographical pressure pain sensitivity maps based on interpolation of the PPTs were constructed. Clinical features of headache were collected in a 4-week headache diary. Anxiety and depression (Hospital Anxiety and Depression Scale) were also assessed.

## Results

The multilevel analysis of covariance found significant difference in PPT levels between points ( $F = 47.649$ ;  $P < 0.001$ ), but not between groups ( $F = 0.801$ ;  $P = 0.602$ ) or sides ( $F = 0.331$ ;  $P = 0.565$ ). No significant effect of gender ( $F = 0.785$ ;  $P = 0.667$ ), depression ( $F = 0.515$ ;  $P = 0.846$ ), or anxiety ( $F = 0.639$ ;  $P = 0.745$ ) was observed. Post hoc comparisons revealed: (1) no differences between FETTH or CTTH; (2) no side-to-side differences; and (3) anterior-to-posterior gradient with the most sensitive points located in the anterior column, followed by those located in the central column and the posterior column of the muscle (all,  $P < 0.001$ ).

## Conclusions

This study confirmed an anterior-to-posterior gradient of sensitivity to pressure in both groups, with the highest sensitivity at the anterior part of the muscle. Further, we found similar pressure pain sensitivity in the trigeminal area in people with FETTH or CTTH with no association to depressive or anxiety levels.

## INTRODUCTION

Tension-type headache constitutes a major, but generally unrecognized, health problem for society.<sup>1</sup> It can affect up to 80% of the general population at sometime during their lives,<sup>2</sup> but its global prevalence in adults is around 42%.<sup>3</sup> The general costs in Europe in 2010 were €13.8 billion for headaches, including migraine and tension-type headache.<sup>4</sup> In the Global Burden of Disease Study, tension-type headache has been found to be the second most prevalent disorder in the world leading to high chronic sequelae.<sup>5</sup>

Although the mechanisms underlying the transition from episodic to chronic are not fully understood, the existing literature supports that sensitization mechanisms play an important role in the transition from acute to chronic tension-type headache.<sup>6</sup> In fact, the most

accepted theory is that frequent episodic tension-type headache (FETTH) is more peripherally dominant, whereas chronic tension-type headache (CTTH) is centrally dominant, although both mechanisms are interconnected.<sup>7</sup> Subjects with CTTH exhibit mechanical hypersensitivity, that is, lower pressure pain thresholds (PPTs), as compared to asymptomatic people, particularly in the trigeminocervical area, as a manifestation of altered nociceptive processing.<sup>8</sup> A recent systematic review concluded that PPTs are consistently lower in subjects with tension-type headache than in healthy people, the temporalis area being the most sensitive to pressure pain.<sup>9</sup> However, all studies included in this review analyzed PPTs over a single standardized point in the temporalis muscle.

It is currently known that mechanical pain sensitivity is not uniformly distributed within the same muscle or across muscles<sup>10</sup> since spatial changes in pressure sensitivity exist in different chronic pain conditions such as shoulder pain,<sup>11</sup> elbow pain,<sup>12</sup> carpal tunnel syndrome<sup>13</sup> or low back pain.<sup>14</sup> In fact, 2 studies have investigated topographical pressure pain sensitivity maps in subjects with tension-type headache. Both studies found heterogeneous distribution of pressure sensitivity in the temporalis<sup>15</sup> and trapezius<sup>16</sup> muscles. Interestingly, the anterior column of the temporalis muscle has been reported to be the most sensitive part of the muscle in subjects with CTTH, but not in healthy controls, where the center of the muscle belly was the most sensitive part.<sup>15</sup> These findings give a potential explanation for discrepancies between studies investigating differences in pressure pain sensitivity between subjects with headaches and healthy controls. However, previous studies included small sample sizes, did not differentiate between FETTH and CTTH, and did not control the presence of mood disorders (eg, anxiety or depression), which may affect the pressure pain sensitivity.<sup>9</sup>

The application of topographical pressure pain sensitivity maps on the temporalis muscle may contribute to a better understanding of manifestations of pain processing in tension-type headache. Therefore, the aim of our study was to evaluate differences in topographical pressure pain sensitivity maps of the temporalis muscle between subjects with FETTH and CTTH by controlling the role of anxiety and depression on PPTs. We hypothesized that subjects with CTTH would exhibit lower PPTs than those with FETTH, but similar distribution of topographical pressure sensitivity maps of the temporalis muscle.

## **METHODS**

### **Participants**

Subjects with headache were recruited from 4 different university-based hospitals between January 2015 and October 2016. All diagnoses were performed following the criteria of the International Classification of Headache Disorders, third edition (ICHD3 beta, 2013) down to third-digit level (codes 2.2, 2.3) by neurologists who were experts in headaches.<sup>17</sup> They had to describe all pain features typical of tension-type headache: bilateral location, pressing or tightening pain, moderate intensity ( $\leq 6.5$  on an 11-point numerical pain rating scale [NPRS] anchored with 0 = no pain and 10 = maximum pain), and no aggravation of pain during physical activity. Subjects needed to report no more than 1 of the symptoms photophobia, phonophobia, or mild nausea, and no moderate or severe nausea or vomiting as requested by the ICHD-III diagnostic criteria.<sup>17</sup> Patients were classified with FETTH when they suffered from at least 10 episodes of headache occurring on 1 to 14 days per month on average for more than 3 months ( $\geq 12$  and  $< 180$  days per year) or CTTH when they had headache occurring on  $\geq 15$  days per month on average for more than 3 months ( $\geq 180$  days per year).<sup>17</sup>

A 4-week headache diary was used to substantiate the diagnosis and to obtain consistent headache features.<sup>18</sup> In this diary, participants registered the number of days with

headache (days/month), the duration of each headache attack (hours/day), and the intensity of the pain during the headache attack on an 11-point NPRS.<sup>19</sup> Preventive medication intake was also recorded. Subjects were excluded if they presented (1) any other primary or secondary headache, including medication overuse headache as defined by the ICHD-III; (2) previous neck or head trauma; (3) cervical herniated disc or cervical osteoarthritis on medical records; (4) any systemic medical disease; (5) fibromyalgia syndrome; (6) a history of physical therapy treatment or anesthetic blocks in the head or neck within the previous 6 months; or (7) pregnancy. All subjects read and signed a written consent form prior to their participation in the study. The study design was approved by local ethics committees (URJC 23/2014, HRJ 07/14, Aalborg N20140063, CESU 5/2015) and was conducted following the Helsinki Declaration.

Evaluations were conducted when patients were headache free or, in those with a high frequency of headaches, when the intensity of pain was graded as  $\leq 3$  points. Participants were asked to avoid any analgesic or muscle relaxant 24 hours prior to the examination. No change was made on their regular prophylactic treatment.

### **Pressure Pain Thresholds**

An electronic pressure algometer (Somedic<sup>®</sup> Algometer type 2, Sollentuna, Sweden) with a 1-cm<sup>2</sup> rubber-tipped plunger mounted on a force transducer was used to measure the PPTs. PPT is defined as the minimal amount of pressure where a sense of pressure first changes to pain. Participants were instructed to press the “stop” button of the algometer as soon as the pressure resulted in the first sensation of pain. Pressure was increased at a rate of approximately 30 kPa/s. The mean of 3 trials on each point, with a 30-second resting period for avoiding temporal summation of pain,<sup>20</sup> was calculated and used for analyses. The order of assessment was randomized between participants, and the experimenters were blinded with



respect to the subtype of headache. Participants practiced first on the wrist extensors of the right forearm. The reliability of pressure algometry has been found to be high.<sup>21,22</sup>

### **Topographical Pressure Pain Sensitivity Maps**

PPTs were measured over the temporalis muscle following previous guidelines as follows.<sup>15</sup> Nine points over the temporalis muscle were marked with a wax pencil. The ear of each subject was taken as the anatomical reference point for the mapping of the PPT grid. The vertical line of the ear defined the center of the muscle belly and, therefore, central column of the mapping. Over this line, 3 vertical points separated by 1.5 cm were marked. These points (labeled 2, 5, and 8) were used to define the anterior and posterior columns. The points located in the anterior part of the muscle (labeled 3, 6, and 9) were located 1 cm anterior to each respective vertical point, whereas the points located in the posterior part (labeled 1, 4, and 7) were located 1 cm posterior to each respective vertical point (Figure 1). With these points, the 3 portions of the temporalis muscle (anterior, middle, and posterior) were covered.

Topographical pressure pain sensitivity maps were generated using the averaged PPT of each point. An inverse distance-weighted interpolation was used to generate the maps.<sup>23</sup> The inverse distance-weighted interpolation consists of computing PPT values of unknown locations by using mean values from the known PPTs and their topographical locations.<sup>10,15</sup>

### **Hospital Anxiety and Depression Scale (HADS)**

The HADS questionnaire consists of 14 items scored on a 4-point scale ranging from 0 to 3 points to assess anxiety (HADS-A) and depressive (HADS-D) symptoms during the preceding week.<sup>24</sup> This questionnaire is considered reliable and valid for assessing anxiety

and depressive symptoms.<sup>25</sup> In individuals with headache, the HADS has also shown good internal consistency.<sup>26</sup>

### **Sample Size Calculation**

Sample size determination and calculations were based on detecting a moderate effect size of 0.55 between individuals with FETTH and CTTH, a 2-tailed test, with an alpha level ( $\alpha$ ) of 0.05, and a desired power ( $\beta$ ) of 90%. This generated a sample size of 71 participants per group.

### **Statistical Analysis**

Data were analyzed with the SPSS statistical package (version 22.0; IBM Corp., Armonk, NY, U.S.A.). Results are expressed as means and 95% confidence intervals (95% CI). The Kolmogorov-Smirnov test revealed a normal distribution of the data. A multilevel (mixed-effect) analysis of covariance (ANCOVA) was applied to detect differences in PPT with point (from 1 to 9) and side (left, right) as within-subjects factors, group (FETTH or CTTH) as a between-subjects factor, and depression or anxiety scores and gender as main covariates. Post-hoc comparisons were conducted with Student-Newman-Keuls analysis. Finally, Spearman's rho test was used to analyze the association between clinical variables relating to headache and PPTs. The statistical analysis was conducted at a 95% confidence level. A  $P$  value  $< 0.05$  was considered statistically significant.

## **RESULTS**

### **Clinical Features of the Sample**

From the 250 individuals with headache screened for possible eligibility criteria, 46 were excluded for the following reasons: comorbid migraine pain ( $n = 34$ ), medication overuse headache ( $n = 6$ ), fibromyalgia ( $n = 4$ ), or previous whiplash ( $n = 2$ ). Finally, 204 subjects

(72% women) satisfied all eligibility criteria, agreed to participate, and read and signed the informed consent. One hundred and thirteen individuals (55%) were classified as FETTH, whereas 91 (45%) were classified as CTTH accordingly to the ICHD-III beta 2013 diagnostic criteria. Sixty (30%) were taking prophylactic drugs (ie, amitriptyline) on a regular basis. A significantly higher proportion ( $P < 0.001$ ) of subjects with CTTH (43%) were taking preventive medication as compared to those with FETTH (19%).

Subjects with CTTH exhibited higher frequency and longer duration ( $P < 0.001$ ), but similar intensity, of headache pain than did those with FETTH. Further, subjects with CTTH also showed higher depressive levels than did those with FETTH (all,  $P < 0.001$ ). No significant differences in anxiety were observed ( $P = 0.866$ ). Table 1 summarizes the demographic and clinical data of each group.

### **Topographical Pressure Pain Sensitivity Maps**

The mixed-model ANCOVA revealed significant differences in PPTs between points ( $F = 47.649$ ;  $P < 0.001$ ), but not between groups ( $F = 0.801$ ;  $P = 0.602$ ) or between sides ( $F = 0.331$ ;  $P = 0.565$ ). No significant Group\*Side\*Points interaction was observed ( $F = 0.686$ ;  $P = 0.705$ ). No significant effects of gender ( $F = 0.785$ ;  $P = 0.667$ ), depression ( $F = 0.515$ ;  $P = 0.846$ ), or anxiety ( $F = 0.639$ ;  $P = 0.745$ ) on pressure sensitivity maps were found. Table 2 summarizes mean PPTs of each point for both sides in either the FETTH or CTTH group.

The post hoc analysis revealed (1) no significant differences between FETTH or CTTH ( $P = 0.708$ ); (2) no side-to-side differences in either group ( $P = 0.55$ ); and (3) an anterior-to-posterior gradient bilaterally with the most sensitive points located in the anterior column (points 3, 6, and 9), followed by those located in the central column (points 2, 5, and 8) and the posterior column of the muscle (points 1, 4, and 7; all,  $P < 0.001$ ). Figure 2 graphs

topographical pressure pain sensitivity maps in both dominant and nondominant sides of subjects with FETTH and CTTH.

### **Associations**

No significant associations between topographical pressure pain sensitivity maps and any of the headache pain features were observed in either group (all,  $P > 0.109$ ).

## **DISCUSSION**

The current study revealed similar pressure pain sensitivity in the temporalis area in subjects with FETTH or CTTH with no association to depressive or anxiety levels. Further, topographical pressure pain sensitivity maps confirmed an anterior-to-posterior gradient of sensitivity to pressure in both groups, with the highest sensitivity within the anterior part of the temporalis muscle for both groups.

The utility of multiple site recordings for PPT mapping leading to a new imaging modality of sensitivity to pain has been previously documented as the technique to detect and visualize nonuniformity in pressure pain sensitivity and as an important development as compared with the traditional single-site assessment.<sup>27</sup> In fact, the analysis of topographical pressure pain sensitivity maps in subjects with tension-type headache has been previously assessed in pilot studies<sup>15,16</sup>; but the current study is the first one including a large sample size, differentiating between FETTH and CTTH and controlling the presence of mood disorders such as depressive and anxiety levels. This study confirms previous indications that the temporalis muscle shows an anterior-to-posterior sensitivity to pressure, and this gradient is not associated to the frequency of the headache episodes. The fact that topographical pressure sensitivity maps revealed an anterior-to-posterior gradient can be related to potential different distribution of muscle nociceptors between the different parts of the temporalis muscle, but

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this cannot so far be confirmed by any histological study. It is also possible that sensitization of central pathways lead to a bilateral posterior-to-anterior distribution of sensitivity to pressure in the temporalis muscle in tension-type headache. In fact, the latter hypothesis agrees with a previous study showing similar pressure pain sensitivity maps in the nonsymptomatic side in patients with strictly unilateral migraine.<sup>28</sup> In such a scenario, central sensitization may account for bilateral and generalized pressure pain hyperalgesia as previously suggested.<sup>29</sup> Therefore, it would be possible that topographical pressure pain sensitivity maps can provide information related to potential underlying mechanisms in primary headaches and, hence, can also be related to different therapeutic approaches.

We did not find significant differences in topographical pressure sensitivity maps between subjects with FETTH or CTTH, suggesting similar sensitization mechanisms. The hypothesis that subjects with FETTH also exhibit generalized pain hypersensitivity is also supported by previous experimental pain models.<sup>30,31</sup> Additionally, a population-based study also did not observe significant differences in PPTs over the temporalis area between FETTH and CTTH.<sup>32</sup> Subjects with FETTH included in our study suffered from 10 headache episodes per month, which could explain why these patients also exhibited pressure pain hypersensitivity similar to those with CTTH (as per definition more than 15 episodes per month). It is possible that a higher number of headache attacks may sensitize the central nervous system, supporting the concept that both FETTH and CTTH are part of a continuum. Nevertheless, it is possible that some individual differences can be observed between patients with lower frequency of headaches (1–2 attacks/month) as compared to those with higher frequency of headaches (20–25 attacks/months).

Although the strengths of this study are the large sample size, the inclusion of both FETTH and CTTH patients accordingly the most updated diagnostic criteria, and the inclusion of mood disorders as covariates, we should recognize some limitations. First,

patients were recruited from tertiary care hospitals; therefore, it may be possible that they represent a specific subgroup of the general population with tension-type headache. Second, we did not include a control group without headache since our aim was to confirm topographical distribution of pressure pain sensitivity in this primary headache. Third, depression and anxiety levels in our sample were low. Therefore, the role of these mood factors in topographical pressure pain maps should be considered with caution at this stage. Fourth, the sample of this study was calculated for detecting clinical differences between groups. It is possible that small differences between some patients were not detected. Finally, the cross-sectional nature of the study design does not permit determination of a cause-and-effect relationship between topographical pressure pain sensitivity maps and tension-type headache. Nevertheless, a longitudinal study showed that increased pain sensitivity was a consequence of tension-type headache, and not a risk factor,<sup>33</sup> supporting the hypothesis that maybe sensitization mechanisms are responsible for this topographical distribution of sensitivity to pressure in the trigeminal area in tension-type headache.

### *Conclusions*

The current study confirms that topographical pressure pain sensitivity maps of the temporalis muscle exhibit an anterior-to-posterior gradient of sensitivity to pressure, with the anterior part of the muscle belly being the most sensitive. Further, similar pressure pain sensitivity was observed in the temporalis area in individuals with FETTH and CTTH with no association to depressive or anxiety levels.

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Figure 1. Reference points for pressure pain threshold measurements over the temporalis muscle.

Figure 2. Topographical pressure pain sensitivity maps of the temporalis muscle for the group of patients with frequent episodic tension-type headache (FETTH) (left) and chronic tension-type headache (CTTH) (right). “X” represents the location of the points where the pressure pain threshold (PPT) was measured.

Table 1. Clinical and Demographic Characteristics of Patients with Frequent Episodic and Chronic Tension-Type Headache

	Frequent Episodic Tension-Type Headache ( <i>n</i> = 113)		Chronic Tension-Type Headache ( <i>n</i> = 91)	
	Mean	95% CI	Mean	95% CI
Demographic Data				
Gender (male/female)	28/85		29/62	
Age (years)	44	41–47	45	42–48
Headache Pain Characteristics				
Time of onset (years)	11.0	8.5–13.5	9.5	7.0–12.0
Frequency (days/month)*	9.0	8.4–9.6	26.0	25.2–26.8
Pain intensity (0-10)	5.8	5.0–6.6	6.0	5.5–6.5
Pain duration (hours/day)*	6.4	5.1–7.7	8.4	7.4–9.4
Preventive medication (yes/no)*	21/92		39/52	
Psychological Outcomes				
HADS-D (depression, 0–21)*	6.7	5.8–7.6	9.5	8.4–10.7
HADS-A (anxiety, 0–21)	9.9	8.8–11.0	9.8	8.6–11.0

\*Significant differences between patients with frequent episodic and chronic tension-type headache ( $P < 0.001$ ).

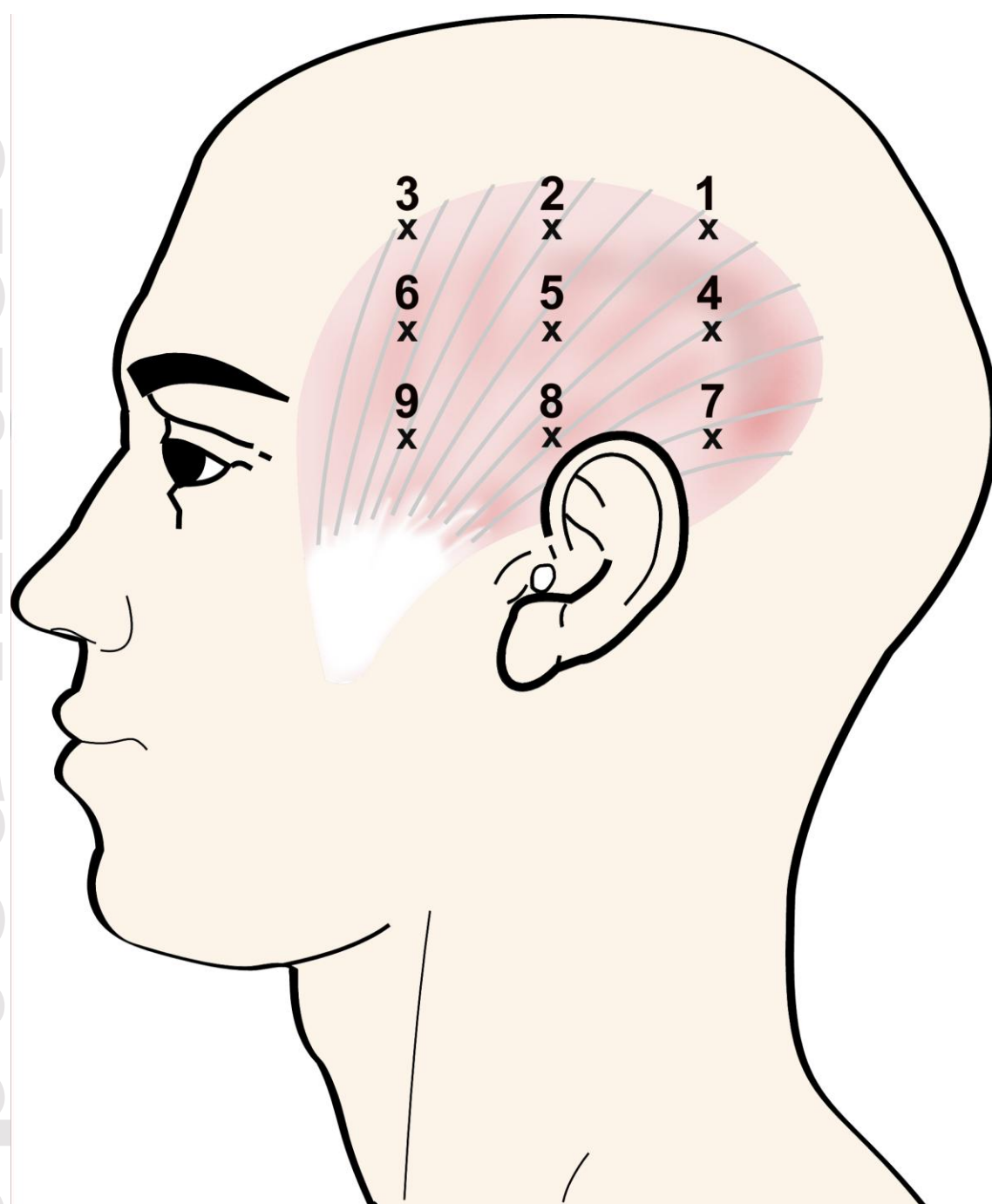
CI, confidence interval; HADS, Hospital Anxiety and Depression Scale.

Table 2. Pressure Pain Thresholds (PPT, kPa) of Each Point in Either Right or Left Side in Subjects with Tension-Type Headache

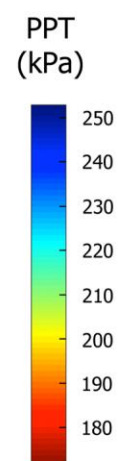
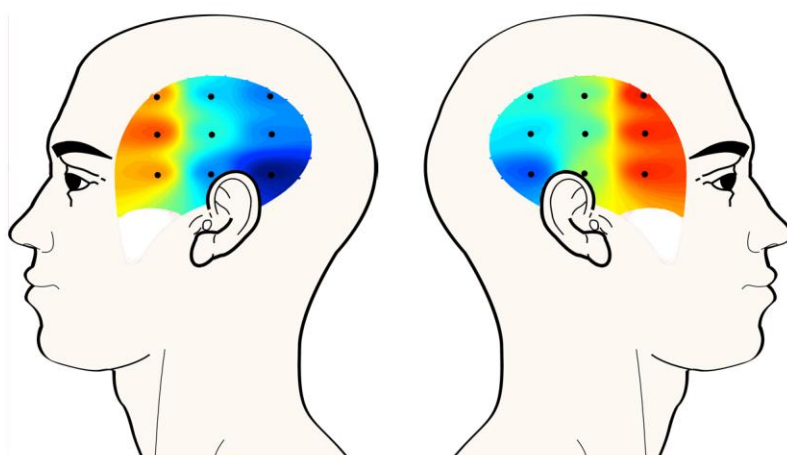
	Frequent Episodic Tension-Type Headache ( <i>n</i> = 113)		Chronic Tension-Type Headache ( <i>n</i> = 91)	
Point 1	Left side	225.1 (207.3, 243.0)	Left side	219.8 (199.9, 239.8)
	Right side	233.5 (215.6, 251.4)	Right side	232.3 (212.4, 252.2)
Point 2	Left side	203.8 (186.2, 221.5)	Left side	212.6 (196.0, 235.3)
	Right side	220.2 (202.6, 237.9)	Right side	225.6 (206.0, 245.3)
Point 3 <sup>*</sup>	Left side	171.0 (154.6, 187.5)	Left side	179.0 (160.6, 197.4)
	Right side	182.9 (166.4, 199.3)	Right side	191.4 (173.0, 209.8)
Point 4	Left side	230.6 (210.8, 250.4)	Left side	223.8 (201.8, 245.9)
	Right side	233.4 (213.6, 253.2)	Right side	231.6 (209.6, 253.7)
Point 5	Left side	206.8 (188.6, 225.0)	Left side	214.9 (194.6, 235.1)
	Right side	208.5 (190.3, 226.7)	Right side	219.3 (199.1, 239.6)
Point 6 <sup>*</sup>	Left side	179.7 (163.4, 195.9)	Left side	183.5 (165.4, 201.6)
	Right side	182.9 (166.7, 199.2)	Right side	187.0 (168.9, 205.1)
Point 7	Left side	240.7 (209.3, 272.0)	Left side	236.0 (201.1, 271.0)
	Right side	239.3 (208.0, 270.7)	Right side	252.9 (218.0, 287.9)
Point 8	Left side	201.9 (184.5, 219.4)	Left side	209.0 (189.6, 228.5)
	Right side	214.6 (197.2, 232.0)	Right side	230.8 (211.7, 250.2)
Point 9 <sup>*</sup>	Left side	179.7 (163.7, 195.8)	Left side	183.4 (165.5, 201.3)
	Right side	190.2 (174.1, 206.2)	Right side	192.7 (174.8, 210.6)

Pressure pain thresholds are expressed as means (95% confidence interval).

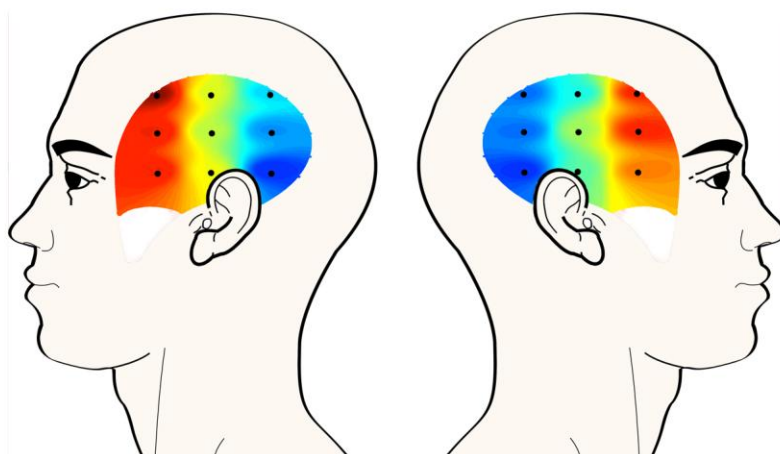
<sup>\*</sup>Significant differences between points (multi-effect, ANCOVA, *P*<0.001)



FETTH  
Patients



CTTH  
Patients



Left side

Right side