The persistent idiopathic facial pain (PIFP) is characterized by a chronic intraoral pain located in the teeth and jaws without major pathology. It has been described as atypical odontalgia, atypical facial pain, persistent chronic facial pain, however it still has undefined criteria. The International Association for the Study of Pain (IASP) describes it as atypical odontalgia, and associates it with previous history of teeth extraction at the area of pain, in the absence of clinical and radiographic evidence of tooth pathology or other relevant orofacial hard or soft tissue lesion. However, there is no evidence in many patients of previous dental trauma and, although in some cases dental procedures are involved in its development, it still has an idiopathic unclear etiology. On the other hand, trigeminal traumatic neuropathic pain (TTN) is associated with major or minor nerve damage during oral surgery (for example, third molar extraction) with clear
etiological factor and evidence of abnormal sensory function. Many patients get complete recovery after oral nerve damage, but a few persist with pain associated with thermal hypoesthesia and warm allodynia.

The sensory findings in the scientific literature on these conditions remain controversial. PIFP does not differ from controls in quantitative sensory testing (QST), atypical facial pain showed to be a heterogeneous group, and atypical odontalgia that included only patients with previous history of dental procedures as etiological factors, showing abnormal sensory processing.

No studies had investigated separately patients with a clear history of trauma and those with idiopathic pain and spontaneous initial about their somatosensory impairment, and QST can help in the elucidation of mechanisms involved in sensory processing. Thus, the objective of this study was to investigate with a systematic protocol of QST patients with PIFP and TTN compared to controls.

MATERIAL AND METHODS
Subjects
Seventy-nine subjects were included in this study. Forty-nine consecutive patients (30 with PIFP and 19 with TTN) were evaluated between January 2007 and March 2009. They corresponded to patients diagnosed with PIFP and TTN that were referred to the Orofacial Pain Clinic of the Hospital das Clínicas, Medical School, University of São Paulo and that fulfilled the criteria of the International Headache Society (IHS). PIFP is defined as a persistent facial pain that does not have the classical characteristics of cranial neuralgias and is not attributed to another disorder. The pain is deep and well localized, typically reported as continuous with constant or fluctuating intensity and described as burning, aching, or cramping. In this study, only patients with no history of dental or facial trauma or any oral procedures within a period of six months before the evaluation were included. In the TTN Group, only patients with history of nerve damage after oral surgery (inferior alveolar or lingual nerve) and evidence of sensory loss and persistent pain within three months after surgery were included.

We enrolled 30 healthy subjects for the Control Group, with no fulfillment of diagnosis for any type of orofacial pain. No subject was excluded. These subjects were relatives and caregivers from patients and employees from the hospital, No subject was excluded by these criteria.

All patients and controls were informed about the purposes of the study, and signed the informed consent. The protocol had been approved by the local Ethics Committee (0751/10).

Subjective evaluation of sensitivity
All patients and controls were interviewed about their facial sensory perception including numbness and dysesthesia. The frequency of sensorial abnormalities (absent, eventual, frequent, or constant) and intensity of sensation (0 to 10 by the Visual Analogue Scale – VAS) were collected.

Quantitative sensory testing
All subjects underwent a standardized protocol of QST, which consisted of five tests grouped as follows: thermal detection (cold and warm perception); mechanical detection (touch perception and pinpricks for mechanical pain); and superficial pain thresholds.

The body regions evaluated were the three trigeminal branches: front, cheek, and chin. The mechanical pain perception with pinpricks was also performed intra-orally at the mandibular and maxillary branches (vestibular gingival tissue at the premolar area). The evaluation was performed bilaterally in all subjects.

All subjects were evaluated in the sitting position, with the head resting at a flat surface, and in a silent room with acoustic protection at the walls and the door closed. Only the patient and the researcher were in the room. All subjects were evaluated by the same researcher, who was a dentist trained in orofacial pain and trigeminal sensory testing. The patients and controls were oriented to keep their eyes closed during the exam and to be concentrated in the stimuli. Only the researcher knew the order of the stimuli, which was determined by randomization and was repeated in all subjects. There were no training sections but detailed explanations about the procedure of sensory testing in order to avoid expectation about the sequence of stimuli by the subjects. The interval between each type of stimuli was from two to five minutes.

Thermal detection
Thermal testing was performed using the Thermosensi II electric test device (Functional Neurosurgery Division – Hospital das Clínicas, College School, São Paulo University, Brazil). The baseline temperature was 32ºC, and the contact square area of the thermode was 10x10 mm. Cold and warm detection was tested with a ramped stimulus of 1ºC/s. For cold detection, the temperature tested was between 20 and 10ºC and, for the warm one, the temperature tested was between 40 and 45ºC. Three measurements were performed, and the means and standard deviations were considered for the analysis.
**Mechanical/tactile and pain perception**

Touch perception\(^1\) was assessed using a set of standardized vonFrey filaments with rounded tips of 0.5 mm diameter (g/mm\(^2\)) – IITC, Woodland Hills, USA. The mechanical pain detection was performed with standard pinpicks with 24 mm of length and 0.40 mm of diameter applied with an electronic device (g/mm\(^2\)) – Micromar®; Diadema, São Paulo, Brazil. The detection or not of the stimuli was considered in the evaluation. Three measurements were performed and the means and standard deviations were considered for the analysis.

**Superficial pain thresholds**

Superficial algometry\(^1\) was tested using disposable needles of 8x10x0.5 mm, which were applied with an electronic device with increasing force (Micromar®, Diadema, São Paulo, Brazil). Three measurements in g/mm\(^2\) were performed and the means and standard deviations were considered for the analysis.

**Corneal reflex**

Corneal reflex was tested using a vonFrey (IITC, Woodland Hills, EUA) filament with a rounded tip of 0.5 mm diameter in both eyes, and the presence or absence of reflex was noticed.

**Statistical analysis**

All data were tabled and the frequencies and percentages, means, standard deviations, and ranges were compared among the groups. After the initial descriptive evaluation, variables were tested about normal distribution with Shapiro-Wilk’s test and Q-Q plots. For the quantitative variables with normal distribution (cold, warm, tactile, pinprick, and pain detections), the ANOVA 1 factor was used. Post-hoc comparisons were calculated using Tukey’s test. Non-parametric test included Pearson’s \(\chi^2\) and Fisher’s exact tests. Correlations among the variables were tested with Pearson’s test. The analysis included the comparisons among the sites evaluated, and between the groups. The side affected was compared to the opposite one in patients with unilateral pain, rather than the comparison between right and left.

All statistical calculations were performed using SPSS 17.0 (SPSS Inc., Illinois, USA). The level of significance was 5%.

**RESULTS**

In the group of patients with PIFP, 29 (96.7%) were women and 1 (3.3%) was a man, being their mean age 43.80±17.46 years-old (mean±SD). In the group of patients with TTN, 14 (73.7%) were women and 5 (26.3%) men, and the mean age was 47.94±14.74 years-old (mean±SD). The Control Group had 19 (63.3%) women and 11 (36.7%) men, and the mean age was 45.82±16.24 years-old (mean±SD). Clinical characteristics of patients and controls can be observed in Table 1.

In this study, we observed that the patients had higher frequency of numbness and dysesthesia than the controls (Table 2).

The thermal testing presented no differences among the groups. Five (8.3%) patients with PIFP had low cold detection at all trigeminal branches, 4 (10.5%) with TTN had low cold detection at all trigeminal branches, and 1 (1.7%) control had low cold detection at the maxillary and mandibular trigeminal branches. Four (6.7%) patients with PIFP had low warm detection at the maxillary and mandibular branches, 5 (13.2%) with TTN had low warm detection at all trigeminal branches, and 1 (1.7%) control presented low warm detection at the mandibular branch.

There were also no differences in the tactile evaluation; 7 (11.7%) patients with PIFP had low tactile detection in all trigeminal branches, 7 (18.4%) with TTN had low tactile detection at the maxillary and mandibular branches, and 2 (3.3%) controls had low tactile detection at the maxillary branch.

The mechanical pain detection showed differences at the maxillary and mandibular branches. The extraoral evaluation showed eight (13.3%) patients with PIFP and eight (21.1%) with TTN including low detection at the maxillary and mandibular branches. At the intraoral exam, 12 (20.0%) patients with PIFP and 11 (28.9%) with TTN had low detection at the maxillary and mandibular branches.

**Table 1.** General characteristics of the patients and controls (means±standard deviation), n=79.

<table>
<thead>
<tr>
<th></th>
<th>Controls (n=30)</th>
<th>PIFP (n=30)</th>
<th>TTN (n=19)</th>
<th>p-value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>45.82±16.24</td>
<td>43.80±17.46</td>
<td>47.94±14.74</td>
<td>0.578</td>
</tr>
<tr>
<td>Gender (%)</td>
<td>19 (63.3) women</td>
<td>29 (96.7) women</td>
<td>14 (73.7) women</td>
<td>0.385</td>
</tr>
<tr>
<td>Duration (years)</td>
<td>6.5±1.2</td>
<td>6.3±1.2</td>
<td>4.3±2.5</td>
<td>0.125</td>
</tr>
<tr>
<td>Side affected (%)</td>
<td></td>
<td>16 (53.3) bilateral</td>
<td>3 (15.8) bilateral</td>
<td>0.276</td>
</tr>
<tr>
<td></td>
<td></td>
<td>7 (23.3) left</td>
<td>12 (63.2) left</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>7 (23.3) right</td>
<td>4 (21.1) right</td>
<td></td>
</tr>
<tr>
<td>Trigeminal branch affected (%)</td>
<td>16 (53.3) V2-3</td>
<td>9 (47.4) V2-3</td>
<td>6 (31.6) V3</td>
<td>0.356</td>
</tr>
<tr>
<td></td>
<td></td>
<td>7 (23.3) V3</td>
<td>6 (31.6) V3</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>7 (23.3) V2</td>
<td>4 (21.1) V2</td>
<td></td>
</tr>
</tbody>
</table>

*Pearson’s \(\chi^2\) test; PIFP: persistent idiopathic facial pain; TTN: trigeminal traumatic neuropathic pain; V2: maxillary branch; V3: mandibular branch; V2-3: maxillary and mandibular branches.
The superficial pain thresholds were similar among the groups and can be observed in Figure. Only two patients with TTN presented abnormal corneal reflex at the affected side, which was statistically different from the other groups (p=0.005, Pearson’s $\chi^2$ test).

There were positive correlations among the trigeminal branches in all sensorial modalities (p<0.005). The positive ones were found between tactile and warm detections (moderate Pearson’s correlation 0.532; p=0.003), tactile and cold detections (moderate Pearson’s correlation 0.472; p=0.008), pinprick and cold detections (moderate Pearson’s correlation 0.694; p<0.001), pinprick and warm detections (strong Pearson’s correlation 0.788; p=0.002). There were no associations of sensorial findings at the trigeminal area of pain.

**DISCUSSION**

In this study, both groups of patients had higher frequency of numbness and dysesthesia and lower mechanical pain perception than the controls, however there were no differences in thermal, superficial pain, and tactile evaluation. Only patients with TTN had abnormalities in corneal reflex. This appears to be the first study that investigated QST trigeminal neuropathic pain with or not previous history of oral trauma, and suggests that patients with PIFP and TTN have similar sensorial deficits and that, as in TTN, neuropathic pain mechanisms may be underlying PIFP.

**Sensorial abnormalities were similar in persistent idiopathic facial pain and trigeminal traumatic neuropathic pain**

PIFP, which corresponds to atypical facial pain and atypical odontalgia according to the classifications 2-5, can be associated with previous trauma history. Thus, several studies that had investigated somatosensory abnormalities in these patients had not separated them accordingly to the etiology of their pain. It is possible that the controversial results in different samples can be due to that aspect 9,11-13. In this paper, both patients’ groups (with or with no traumatic etiology) showed low mechanical pain detection at

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**Table 2. Subjective evaluation of sensitivity: patients had more numbness and dysesthesia than the controls (n=79).**

<table>
<thead>
<tr>
<th></th>
<th>Controls (n=30)</th>
<th>PIFP (n=30)</th>
<th>TTN (n=19)</th>
<th>p-value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Frequency of subjective numbness</td>
<td>1 (3.3%) constant</td>
<td>11 (36.7%) constant, 3 (10.0%) eventual, 1 (3.3%) frequent</td>
<td>14 (73.7%) constant, 2 (10.5%) eventual, 1 (5.3%) frequent</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Mean subjective numbness (VAS)</td>
<td>5.0</td>
<td>7.15±2.37 (2-10)</td>
<td>6.88±1.93 (4-10)</td>
<td>0.346</td>
</tr>
<tr>
<td>Dysesthesia (VAS)</td>
<td>0.0</td>
<td>7.92±1.73 (4-10)</td>
<td>7.81±1.68 (5-10)</td>
<td>0.003**</td>
</tr>
</tbody>
</table>

*Pearson’s $\chi^2$; Fisher’s exact test; Statistical differences are: PIFP versus controls and TTN versus controls (numbness and dysesthesia); PIFP: persistent idiopathic facial pain; TTN: trigeminal traumatic neuropathic pain; VAS: visual analogue scale; **F=26.801.

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PIFP: persistent idiopathic facial pain; TTN: trigeminal traumatic neuropathic pain.
the affected maxillary and mandibular branches, and the only difference between TTN and PIFP was that the corneal reflex was abnormal only in TTN. The corneal reflex had been reported as affected in other neuropathic conditions, such as burning mouth syndrome. These patients also have many abnormalities in somatosensory processing, and burning mouth is an idiopathic condition with no etiological factor that is currently been considered neuropathic due to the QST findings. Our results indicate that the criterion about absence of sensorial abnormality in PIFP should be revised.

Neuropathic mechanisms in idiopathic trigeminal pain
Abnormal somatosensory findings are considered in the current classification of neuropathic pain of the IASP as important for evaluation and diagnosis. In the current definition, neuropathic pain is diagnosed according to sensorial deficits, which were observed in both of our samples, and thus these results support neuropathic pathophysiology for both conditions. The structural integrity of the nervous system differentiates nociceptive pain from neuropathic pain, however, for idiopathic conditions, with no clear evidence of inflammatory/occiputive etiology, the absence of neurological abnormalities still makes them undefined. On the other hand, phenomena that are typical from neuropathic pain, such as allodynia, also occur in central sensitization of inflammatory conditions, and there is also peripheral and central hyperalgiesia in them.

For trigeminal neuropathic pain with traumatic origin, there are many evidences of central impairment of the somatosensory and motor processing involving deficits in the descending inhibition. Motor-sensory integration is evidenced by the recovery of abnormal thermal processing by the stimulation of motor areas. The neuroplastic phenomena involve the activation of glial cells surrounding affected neurons at the central nervous system, in many subtypes of trigeminal pain, including neuropathic pain and inflammatory etiologies, and thus their physiopathology share many similarities when gets chronic.

Correlations among variables
We did not find any association between the location of pain and the sensorial findings. However, there were several positive correlations among the different modalities (cold, tactile, warm, and pain); the mechanisms underlying it might involve central processing of sensorial modalities, discrete impairment or sensory losses can occur in association.

Limitations of the study
This study presented some limitations, including a great variability in sensorial detection that would make necessary a larger sample. On the other hand, these patients represent those looking for treatment in a specialized clinic and not the population, and thus the demographic data may not be generalized. However, they were carefully evaluated by an experienced dentist and their diagnosis was very accurate, with no concomitancy of other pain causes as temporomandibular disorders, which could compromise results.

All patients were evaluated in the same sites representing the trigeminal branches in order to standardize the studied groups and to allow comparison among them. It is possible that eventual abnormal sensory testing restricted to the site of the pain was missed in this evaluation. However, the objectives of this study were to investigate and to compare the abnormal sensations in the trigeminal territories, but not to verify the extension of sensorial findings in these patients. Besides, the qualitative evaluation of the corneal reflex did not allow the investigation of the part of the reflex that was found abnormal in TTN patients.

Another limitation of the study is the fact that patients were not investigated about their psychological characteristics and it is known that chronic pain is often associated with anxiety or depression. Both could interfere in the accuracy of answer during QST and must be considered in the interpretation of these results.

In conclusion, patients with PIFP and TTN had lower detection of mechanical pain stimuli (pinpricks) than the controls at the maxillary and mandibular trigeminal branches. These results support neuropathic mechanisms involving pain processing in PIFP and TTN.

References


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