Objective. The aim of this study was to examine atypical odontalgia (AO) patients with extraoral quantitative sensory testing (EQST) and an intraoral mucosal cold test.

Study design. Twenty-one subjects with AO and 18 control subjects underwent EQST for electrical and thermal pain and detection thresholds. Cold was applied to painful mucosal areas in AO patients and randomly in control subjects.

Results. Electrical pain thresholds were higher in AO patients than in control subjects in the same dermatome affected by the pain ($P = .03$), but no significant differences were observed in electrical detection thresholds and heat pain and detection thresholds at other sites. Cold application was painful in control and AO subjects, but duration of pain sensation was significantly longer in AO patients ($P = .019$ in contralateral side; $P = .029$ in affected side).

Conclusions. The finding of extended painful after-sensation following cold application in AO patients supports the involvement of central mechanisms. The cold test is clinically easy to apply and of clinically significant value. (Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2011;111:312-319)
Peripheral nerve injury in the orofacial region may cause neuropathic pain, which may occur as a result of loss of afferent nerve input to the central nervous system. Neuropathic pain is characterized by spontaneous pain often of burning quality, accompanied by hyperesthesia, hyperalgesia, allodynia, and/or paresthesia. Neuropathic pain and AO seem to be similar, but not identical, conditions. Although the etiology of AO is not clear, and an assumption of previous nerve damage is often made, traumatic neuropathic pain cases involve previous nerve damage by definition. However, there is overlap and some confusion in the literature between the 2 terms, largely due to the clinical similarity and the common features. Also, the lack of universally accepted criteria for trigeminal traumatic neuropathies offers no reasonable alternative.

Case descriptions reveal that AO presents as periods of continuous, or almost continuous, throbbing, burning, or aching pain, varying in intensity. There is a delay in onset of weeks to up to a year after a dental procedure such as endodontic treatment or extraction. Pain in AO can cross the midline, and the area affected may expand. The pain is sometimes difficult to localize by the patient because it can be in single or multiple sites, but it is usually worst at the site of the original trauma. Continuous pain is accompanied by hyperesthesia, hyperalgesia, or allodynia. Dysesthesia and sensory aberrations, such as the feeling that the area affected is enlarged, are often described by AO patients.

The prognosis is poor, and patients rarely obtain relief with analgesics, including narcotics. Local anesthetic blocks show ambiguous effectiveness, and the majority of patients do not have complete pain relief.

Based on the signs and symptoms the assumption remains that a neuropathic pain mechanism is involved in AO. If so, it is likely that AO patients would suffer somatosensory deficits (e.g., thermal and/or mechanical), and these can be assessed with quantitative sensory testing (QST). Recent studies that have used QST on AO patients have shown a number of sensory abnormalities. Increasing evidence thus supports the use of QST in the assessment of nerve damage, neural inflammatory processes, and central processing of neuropathic pain.

The aim of the present study was to complement earlier studies by using QST methodology intra- and extraorally. These tests assess the nerve terminal, which has demonstrated detectable changes as a result of inflammation or nerve damage along the axon. We assessed patients diagnosed with AO and control subjects by the following QST methodology: extraoral electrical and heat detection and pain thresholds and a novel intraoral cold test not previously performed in AO patients. This methodology was adopted after clinical observation by one of the authors (Y.S.) and a pilot study that demonstrated cold allodynia in the intraoral soft tissue in these patients.

**MATERIAL AND METHODS**

Patients were recruited from the orofacial pain clinic in the New Jersey Dental School, and each of the patients signed a consent form before participation in the study. The Institutional Review Board at the University of Medicine and Dentistry of New Jersey approved the study.

Information about the subjects’ medical history, current medications, age, gender, ethnicity, and current and past illnesses was gathered. Pain and inconvenience levels were assessed using the Gracely pain score and visual analog scale (VAS). Two groups of patients were included in the study: patients suffering from AO and healthy control subjects. One clinician performed all of the clinical examinations.

**Inclusion and exclusion criteria**

The AO group included patients suffering from continuous aching/pain present for >4 months, burning or throbbing pain in a tooth or tooth site, with a negative clinical examination, and no radiographic pathologies. Patients under pharmacologic treatment before enrollment were included in the study, and the type of treatment and duration were recorded. The control group included healthy volunteers with no dental pathologies and who had not undergone dental treatment <6 months before the examination with the exception of periodontal maintenance appointments. Patients were requested to maintain a pain diary for 2 weeks to assess pain fluctuation during the day.

Patients <21 years old, pregnant women, and patients suffering from other neurologic diseases or other chronic orofacial pain conditions were excluded from the study.

**Extraoral sensory testing**

Warm detection threshold and heat pain threshold were assessed by a 15 × 15-mm water-cooled Peltier probe (Model Tsa II 2001; Medoc, Ramat Yishai, Israel).

Detection threshold was assessed bilaterally at the areas above the upper lip and chin innervated by the infraorbital and mental nerves, respectively. The medial part of the arms, innervated by the medial antebrachial...
cutaneous nerve, served as the intrapatient control site. Pain threshold was determined at the same sites using an ascending (from 32°C to pain at a rate of 0.5°C/s, not surpassing a maximum temperature of 50°C) method of limits. The threshold was computed from the average of 3 trials. During the entire testing period, the computer monitor where the stimulus intensities were displayed was faced away from the subjects. Electrical detection and pain thresholds were assessed with transcutaneous electrical stimuli delivered by the Neumometer Nervscan NS3000 device (Neurotron, Baltimore, MD, USA). Electrodes used were 1 cm diameter gold-plated (Goldtrode; Neurotron, Baltimore, MD, USA). Large Nervscan NS3000 device (Neurotron, Baltimore, MD, USA). Electrodes used were 1 cm diameter gold-plated (Goldtrode; Neurotron, Baltimore, MD, USA) consistently placed in close proximity to each other to focus the stimuli. Stimuli were delivered in frequency of 250 Hz was used to assess A fibers.34-36 A small amount of hypoallergenic electrode gel was applied to the surface electrodes before placement, and a nonconductive soft white adhesive strip (Softape; Neurotron) was used to hold the electrodes in place during stimulation. The train of stimuli controlled by the device started with the lowest output intensity of 0.001 mA and did not surpass 9.99 mA. The subjects were instructed to release a control button upon the first sensation felt, such as tingling, burning, or pins and needles, for electrical detection threshold assessment or first pain sensation for electrical pain threshold assessment. Throughout the entire testing, both the operator and the patients were blinded to the output intensity provided.

**Intraoral sensory testing**

A cotton swab (5 mm in diameter) sprayed with Gebauer ethyl chloride was applied to the alveolar mucosa apical to the painful tooth in the AO group or a randomly selected tooth in the control group and its homologous contralateral tooth. The cooled cotton swab was immediately placed in contact with the alveolar mucosa for 3 seconds. The subject was asked to inform the investigator the type and intensity of sensation felt, if either painful or nonpainful. Pain and cold sensations were rated using a 10-cm VAS. The minimum and maximum possible sensations were defined as “no sensation” and “freezing cold” for cold and “no pain” and “worst possible pain” for pain. The duration of sensation (pain or cold) after the removal of the stimulus was recorded using a stopwatch.

**Effect of local anesthesia**

In AO cases where the clinician considered that the effect of local anesthesia may contribute to the diagnosis and the patient consented, a regional block and/or local infiltration anesthesia was administered. Response to local anesthesia in the AO patients was evaluated and categorized as responsive (no pain) or equivocal/nonresponsive. Equivocal response to local anesthetic block is considered to be a sign for the involvement of central processes.

**Nonlocalized versus localized pain**

During evaluation it was noticeable that some of the patients reported that the pain expanded beyond the original tooth area to a larger receptive field. The pain reported was considered to be nonlocalized when it involved a different dermatome from the primary area in pain.

**Statistics**

Statistical analyses were performed with StatView (1992-98; SAS Institute, Cary, NC, USA), with alpha for significance set at 5%. All data are presented as mean ± SD; for clarity, graphs show standard error of the mean.

Chi-square ($\chi^2$) analysis of the raw data were used to analyze the results between the presence of possible AO comorbidities, such as myalgia. An unpaired Student t test was used to analyze QST results between the AO and control groups. The electrical QST results were analyzed based on the raw data of each site, but also based on the ratio between the affected side and contralateral side to minimize the interpatient variability that is often observed in electrical QST. An analysis of variance (ANOVA) and Fisher partial least-squares difference were used to compare the QST results and pain diary profile with medication intake profile, local anesthetic effect, and nonlocalized pain. Bivariate regression analysis (with 95% confidence intervals) was used to analyze the correlation between quantitative sensory testing with duration of AO and pain intensity at the moment of testing.

**RESULTS**

A total of 39 subjects were included in the study: 21 subjects diagnosed with AO and 18 healthy control subjects recruited from staff and students who volunteered.

Women comprised 77% of the subjects in the AO group and 67% in the control group. The mean age was 57.23 ± 9.83 (range 42-71 years old) and 45.05 ± 16.55 (range 25-72 years old) years old, respectively. There was a marked prevalence of non-Hispanic white subjects in the AO (86%) and control groups (89%). There was no statistical difference in the level of pain between women (Gracely pain scale: 6.8 ± 1.13) and men (4.60 ± 1.50; $P > .05$). Fifty-nine percent of the AO cases involved molars, 22% premolars, 14% incisors, and 5% canines with no statistically significant difference between the affected jaws (50% maxillary and 50% mandibular teeth).

Fifty-five percent of the AO subjects were taking neuropathic pain medications, such as opioids, antide-
pressants (e.g., tricyclic antidepressants), anticonvulsants, or combinations. The difference of the level of pain on the affected side between AO subjects taking pain medications (7.40 ± 3.5 on the Gracely pain scale) and not taking pain medications (5.27 ± 4.9 on the Gracely pain scale) was not statistically significant ($P = .267$). The pain level among AO subjects varied from mild to moderate (2-14 on the Gracely pain scale). AO pain was present during most or all of the day and tended to increase in intensity from morning to bedtime, but the differences were not statistically significant (repeated-measures ANOVA: $P > .05$).

Myalgia, limited opening, disk displacement, arthralgia, arthrosis, vascular pain, neuropathic pain, burning mouth syndrome, and taste alterations were assessed in AO as possible comorbidities. Myalgia or positive tenderness to muscle palpation was present in 55% of the AO subjects and 3% of the control group ($\chi^2 = 4.915; P = .027$). There were no statistically significant differences between the AO and control groups for the remaining conditions.

**Extraoral quantitative sensory testing**

The site of pain is described as the “affected” site. The other, contralateral, side is referred to as “contralateral.” “Antagonist” refers to the same side as the pain but in the other dermatome (mental versus infraorbital). Contralateral antagonist thus refers to the contralateral site of the antagonist.

The raw electrical detection thresholds showed no statistically significant difference between the sites and between the AO and control groups. When the analyses were performed using the ratio of the affected side over the contralateral side, the same result was confirmed.

There was no statistically significant difference between electrical detection thresholds in subjects taking or not taking neuropathic pain medication and control subjects (Fig. 1). There was no significant correlation between the electrical detection threshold in AO subjects and duration in pain.

The electrical pain threshold was significantly elevated in AO patients compared with the control subjects in the affected side (AO $226 \pm 48$, control $109 \pm 17$; unpaired Student $t$ test: $P = .03$). The remaining sites of AO subjects demonstrated a trend to be elevated compared with controls, but this was not statistically significant (unpaired Student $t$ tests: $P < .05$). Electrical pain threshold on the affected and contralateral sides of subjects taking neuropathic pain medication was slightly elevated compared with those not taking medication (Fig. 2); however, this was not statistically significant. Bivariate regression showed no correlation

![Fig. 1. Evaluation of electrical detection threshold results between atypical odontalgia (AO) subjects on medication, AO subjects not on medication, and control subjects. No significant statistical differences were found (analysis of variance).](image1.png)

![Fig. 2. Electrical pain threshold comparison between atypical odontalgia (AO) subjects taking and not taking neuropathic pain medications. There was no statistical difference between the subjects taking and not taking pain medications, but there was a trend of increased electrical pain threshold in subjects on pain medications (analysis of variance).](image2.png)
between electrical pain threshold and duration of pain within the AO group.

The data from this study did not show significant differences in the warm detection and heat pain thresholds between sites and between the AO and control groups. There was no statistical difference between subjects on neuropathic pain medication, those not taking medications, and control subjects. No correlation was found between warm detection and heat pain thresholds to duration of painful condition.

**Intraoral quantitative sensory testing**

In response to cold stimulus (ethyl chloride), 34% of the control subjects and 47% of the AO subjects reported a painful sensation, such as sharp or burning pain, whereas the remaining described it as a mild cold sensation.

The level of pain to cold stimulus was not statistically different between the AO and control groups (Table I). Based on VAS adapted to perception assessment (0-10 scale), cold intensity was not statistically different in the affected side (unpaired Student t test: $P = .823$) or in the contralateral side (unpaired Student t test: $P = .827$). However, the duration of the painful sensation after removal of the cold stimulus lasted significantly longer in AO patients in both the affected (AO $65.72 \pm 15.6$ s, control $25.71 \pm 7.4$ s; unpaired Student t test: $P = .029$) and the contralateral sides (AO $57.83 \pm 12.8$ s, control $22.4 \pm 6.3$ s; unpaired Student t test: $P = .019$; Fig. 3; Table II).

The duration of the cold-pain aftersensation in AO subjects not taking medication (affected side: 69.50 ± 22.9; contralateral side: 74.50 ± 18.3) was significantly longer than that in control subjects (affected side: 23.87 ± 5.8 ($P = .02$); contralateral side: 21.33 ± 5.2 ($P = .002$); Fig. 4). Aftersensation in AO subjects taking medication (affected side: 49.67 ± 20.2; contralateral side: 46.11 ± 19.34) was not statistically different from those not taking neuropathic pain medications (affected side: $P = .52$; contralateral side: $P = .31$).

No correlation was found between time since the onset of pain and the duration of the aftersensation (bivariate regression: $r^2 = 0.33; P = .619$).

**Response to local anesthesia**

Of the AO patients, 17 underwent diagnostic anesthesia, with 59% reporting total pain relief and 41%

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**Table I.** Level of perception to cold stimulus in the atypical odontalgia (AO) and control groups based on the visual analog scale

<table>
<thead>
<tr>
<th></th>
<th>Maximum</th>
<th>Minimum</th>
<th>Mean ± SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>AO</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Affected side</td>
<td>7</td>
<td>0</td>
<td>2.15 ± .48</td>
</tr>
<tr>
<td>Contralateral side</td>
<td>4</td>
<td>0</td>
<td>2.32 ± .40</td>
</tr>
<tr>
<td>Control</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Affected side</td>
<td>4</td>
<td>0</td>
<td>2.02 ± .50</td>
</tr>
<tr>
<td>Contralateral side</td>
<td>4</td>
<td>0</td>
<td>2.45 ± .43</td>
</tr>
</tbody>
</table>

**Table II.** Duration (s) of cold pain sensation (aftersensation) following application of cold (ethyl chloride) to the gingiva

<table>
<thead>
<tr>
<th></th>
<th>Affected side</th>
<th>Contralateral side</th>
</tr>
</thead>
<tbody>
<tr>
<td>AO group</td>
<td>65.72 ± 15.6</td>
<td>57.83 ± 12.8</td>
</tr>
<tr>
<td>Control group</td>
<td>25.71 ± 7.4</td>
<td>22.4 ± 6.3</td>
</tr>
<tr>
<td>$P$ value</td>
<td>.029</td>
<td>.019</td>
</tr>
</tbody>
</table>

*AO, Atypical odontalgia.

Fig. 3. Aftersensation following cold stimulus lasted significantly longer in the atypical odontalgia (AO) group on the affected and contralateral sides compared with the control group. *Statistical significance (unpaired Student t test; affected side: $P = .029$; contralateral side: $P = .019$).

Fig. 4. Comparison of duration of cold aftersensation between atypical odontalgia (AO) subjects taking neuropathic pain medications (n = 9), AO subjects not taking medications (n = 8), and control subjects (n = 17). *Statistical significance (analysis of variance): affected side, $P = .02$; contralateral, $P = .002$. 
reporting equivocal results. Electrical detection threshold, electrical pain threshold, warm detection threshold, heat pain threshold, perception of cold stimulus, and the duration of the cold after sensation were not different in responders or nonresponders to local anesthesia.

Nonlocalized versus localized pain

Pain levels were not statistically significant between AO subjects with localized and nonlocalized pain (Gracely pain scale: nonlocalized pain 8.67 ± 1.2, localized pain 5.33 ± 1.1; unpaired Student t test: \( P = .109 \)).

Electrical detection thresholds, electrical pain threshold, warm detection threshold, heat pain threshold, and perception of cold stimulus were not different in patients with localized or nonlocalized pain. However, the after sensation duration following cold stimulus was significantly longer bilaterally in AO subjects with nonlocalized pain, when compared with controls (ANOVA: affected side \( P = .030 \); contralateral side, \( P = .002 \). *Statistical significance (analysis of variance).

Fig. 5. Comparison of duration of cold after sensation between atypical odontalgia (AO) subjects with nonlocalized pain or localized pain and control subjects. After sensation duration was significantly longer bilaterally in AO subjects with nonlocalized pain compared with controls; affected side, \( P = .030 \); contralateral side, \( P = .002 \). *Statistical significance (analysis of variance).

The cold test protocol applied to the alveolar mucosa (rather than the teeth) performed in this study has never been used in somatosensory assessment studies on AO patients. A lack of difference of cold sensitivity (pain intensity) between AO subjects and healthy control subjects has been reported in previous studies, but the duration of the after sensation was never assessed. This simple test demonstrated the most interesting findings of the present study. The results showed prolonged

DISCUSSION

In accordance with previous studies, there was a non-Hispanic white female predominance in the AO group (86%). This predominance has been suggested to be associated with the fact that women tend to seek care more often than men. The mean age of the AO group was 57 years old, similar to what has been reported previously. More than 50% of the AO subjects had pain in their molars; the premolars were

the second most affected, similar to previous studies, but we found no jaw predilection.

AO is believed to be a neuropathy, and patients are usually diagnosed after they undergo several dental procedures. In line with these data, in our group of subjects, the majority reported that the pain began after endodontic treatment. Chronic pain conditions, such as musculoskeletal pain, temporomandibular disorder, and headaches, have been reported as comorbidities of AO. In the present study, myalgia was the dominant comorbid condition affecting a significant number (55%) of subjects with AO. However, comorbid muscle pain is present in many orofacial pain conditions, including migraine, neurovascular orofacial pain, and others.

A confounder in this study is the fact that about one-half of the AO patients recruited were taking neuropathic pain medication. Interestingly, pain levels in AO subjects who were not taking medications were not significantly different from the subjects taking medication. AO patients are notoriously difficult to treat, which may reflect the poor therapeutic prognosis. Alternatively, the level of pain of those not taking medication may have been originally mild, whereas those on medication had severe pain before they started the pharmacologic treatment.

Extraoral electrical detection, warm detection, and heat pain thresholds were not different between the AO and control groups. Based on these results, extraoral psychophysical tests seem not to be able to assess differences of the peripheral nervous system function between AO patients and control subjects. Indeed, there may be no significant sensory changes in extraoral regions. List et al. and Baad-Hansen et al. reported that intraoral heat pain stimuli demonstrated hypersensitivity on the painful side compared with the nonpainful side, although Lang et al. could not replicate these findings. Nonetheless, the trend toward an elevated electrical pain threshold seen in all sites assessed in the AO patients is interesting. As already noted, in some cases it may be a result of the anticonvulsants and antidepressants intake, although there are no previous reports relating pain threshold increase to these groups of medications. The present study sample is too small, and further studies may elucidate this possible association.

The cold test protocol applied to the alveolar mucosa (rather than the teeth) performed in this study has never been used in somatosensory assessment studies on AO patients. A lack of difference of cold sensitivity (pain intensity) between AO subjects and healthy control subjects has been reported in previous studies, but the duration of the after sensation was never assessed. This simple test demonstrated the most interesting findings of the present study. The results showed prolonged
cold and pain aftersensations to cold stimuli in AO patients. Duration of the aftersensation in AO was more than twofold, which is clinically significant and easy to assess. In a study performed by Juhl et al. on central sensitization after third molar extraction, a significant prolonged aftersensation was reported after the application of cold (induced by ice cubes) and pinprick stimulation in the extraction site. However, there are no studies in the literature to our knowledge that have evaluated cold aftersensation in individuals with AO. In a recent study, healthy subjects surprisingly reported “heat” sensations after cold stimulation of the gingiva. The mechanism underlying this paradoxical effect, particularly in healthy subjects, is unclear. We did not investigate the quality of the pain in depth but did find a number of AO patients who reported burning pain after cold application. Plastic neuropathic changes may explain this in AO patients. In view of the present and earlier findings, it would be interesting to compare pain quality, severity, and duration (aftersensation) in control subjects and patients with intraoral neuropathies.

The fact that the contralateral side was also affected and subjects with nonlocalized pain were the ones that indeed had greater difference compared with control subjects reinforces the hypothesis that AO pain is at least partly mediated centrally. Further studies should be performed with a larger sample size to evaluate cold detection and pain thresholds and to possibly determine a normal range for cold aftersensation. Equivocal response to local anesthetic is also believed to be a sign of centrally maintained pain. List et al. showed in a randomized cross-over study that the majority of subjects with AO respond significantly to local anesthetic block, but not completely, whereas in this study 41% did not respond. We evaluated the effect of this response on the results of quantitative sensory testing, but there was no statistically significant differences between the AO subjects that responded completely to local anesthetic and those whose response was equivocal. The methodology in our study pertaining to the use of local anesthetic was weak, however, because no control subjects were used. The results should therefore be interpreted with caution.

CONCLUSIONS

Subjects with AO demonstrated sensory alterations for cold aftersensation, suggesting a neuropathic mechanism with involvement of central factors. The association of this response with other characteristics of central sensitization, such as pain extending to a larger area from the primary site and pain occurring on the contralateral side, reinforces the importance of these findings. Testing for soft tissue cold allosthesia is a simple test and may be a significant addition to the limited diagnostic tools we currently have to diagnose this condition.

Extraoral quantitative sensory testing seemed not to be able to detect alterations, such as inflammatory process or nerve damage of the nerve branches affected.

REFERENCES


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