Pain from Dental Implant Placement, Inflammatory Pulpitis Pain, and Neuropathic Pain Present Different Somatosensory Profiles

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Aims: To address the two following questions: *(1)* What kind of somatosensory abnormalities may be characterized in patients receiving dental implants (IMP), in ongoing inflammatory dental pulpitis (IP) patients, and in neuropathic pain (atypical odontalgia [AO]) patients? and *(2)* What sort of sensory and neural changes may result from dental implant placement surgery and pulpectomy? **Methods:** A total of 60 subjects were divided into three groups: the IMP (n = 20), IP (n = 20), and AO groups (n = 20). Quantitative sensory testing (QST) was performed preoperatively (baseline) for all three groups and postoperatively at 1 month and 3 months after dental implant placement or pulpectomy (in the IMP group and IP group, respectively). Statistical analyses were completed with one-way and two-way analysis of variance and *z* score transformations (α = 5%). **Results:** The main findings of this study indicated that: *(1)* Elevations in mechanical detection threshold (MDT) and in current perception threshold (CPT) related to C-fiber activation, indicating a loss of function, were found at baseline in IP patients; *(2)* Somatosensory abnormalities such as allodynia, reduced MDT and mechanical pain threshold (MPT), and impaired pain modulation were found in AO patients; *(3)* No somatosensory alterations after implant placement were found in the IMP group; and *(4)* Somatosensory alterations in the form of reduction in the CPT related to C-fiber activation were reported 3 months after pulpectomy in the IP group. **Conclusion:** This study showed that somatosensory abnormalities were evident in AO and IP patients, and somatosensory alterations were seen in IP patients even 3 months after pulpectomy. However, no somatosensory alterations were seen after implant placement. *J Oral Facial Pain Headache 2017;31:19–29. doi: 10.11607/ofph.1680*

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Dental pain or pain in the dentoalveolar region is regarded as the most common orofacial pain disorder.[1] Orofacial pain conditions can be classified into different categories.[2–4] Pain from dental implant placement may be classified as a somatic pain triggered by a noxious stimulus, generally induced by peripheral trauma. Somatic pain is generally pinpointed by the patient and described as aching, gnawing, throbbing, or cramping.[2–4] Inflammatory dental pulpitis (IP) is triggered by inflammation and is associated with diffuse discomfort and possibly swelling.[2–4] Another orofacial pain condition is neuropathic pain, which may arise from injury to peripheral nerves or have an idiopathic etiology.[5–7] Atypical odontalgia (AO) is a continuous neuropathic pain diagnosed by exclusion of other possible diseases and is identified through clinical, dental, neurologic, and imaging examinations.[8] AO is usually described as diffuse, throbbing, and burning.[9]

Quantitative sensory testing (QST) is a standardized method used to assess the clinical manifestations and somatosensory abnormalities of the peripheral and central nervous systems.[10–12] QST assesses the functionality of somatosensory afferent nerve fibers and their associated circuits in the brain that receive and process QST-evoked activity conducted by myelinated A fibers (A-beta and A-delta fibers) and unmyelinated C fibers.[12–14]

Sensory sensitization processes have been reported in patients with AO; eg, allodynia, hyperalgesia, and pain exacerbation by thermal, mechanical, and/or chemical stimuli.[6,10,15] However, QST has not been fully utilized in assessing pain from dental implant placement and IP. In addition, the effect of tissue and nerve damage on the somatosensory system after trauma from dental treatment warrants further investigation. Therefore, this study aimed to address the two following questions: *(1)* What kind of somatosensory abnormalities may be characterized in patients receiving dental implants (IMP group), in patients with ongoing IP (IP group), and in patients with neuropathic pain (AO group)?; and *(2)* What sort of sensory and neural changes may result from dental implant placement and pulpectomy?

Materials and Methods

This study was supported by the São Paulo research foundation – FAPESP (no. 2013/15496-1). There were no conflicts of interest in the performance of this study. The study was conducted in accordance with Helsinki guidelines and was approved by the local ethics committee (certificate of presentation for ethical consideration #19840113.2.0000.5417). Written informed consent was obtained from all participants.

Subjects

Subjects were recruited at the Bauru School of Dentistry, University of São Paulo, São Paulo, Brazil, from December 2013 to January 2015. In total, 469 subjects were eligible, and 409 of those subjects were excluded. Exclusion criteria were diverse and included uncontrolled diabetes, uncontrolled hypertension, no indication for dental implant surgery or pulpectomy, avulsed tooth, < 19 years old, dental difficulties on approach (ie, subjects with psychological complications leading to difficulties in the research evaluation), temporomandibular disorders, and other criteria, which can be seen in Fig 1. Potential sources of bias were managed individually for each group and explained below. The 60 subjects who were eligible agreed to participate and were allocated into one of the three groups, as follows:

IMP Group

The IMP group included 20 healthy subjects who were to undergo dental implant placement.

The healthy adults could not have previously received a neuropathy diagnosis and needed to be free from any type of pain and dental pathology for at least 6 months.[3] This group was to undergo delayed implant placement into nongrafted areas and also a delayed loading protocol (3 months) based on general clinical indications, including sufficient and adequate bone quantity and quality; single or multiple partial units (fixed dental prostheses) or full-arch supported prostheses; or single-tooth replacement or replacement of two or three teeth.[3,16]

Local anesthesia (articaine 4% and epinephrine 1:100.000) was used during standardized surgery procedures. At 1 hour after implant placement, a medication protocol was started and standardized regarding drug class and dosage. The protocol followed the same guidelines for all subjects and consisted of an antibiotic (amoxicillin 500 mg every 8 hours for 7 days) and an anti-inflammatory drug (nimesulide 100 mg every 12 hours for 3 days). The diameter and length of dental implants were individualized for each case based on the patient`s bone dimensions.

IP Group

The IP group included 20 subjects with acute pulpitis who were to undergo pulpectomy.

Individuals were diagnosed following the mandatory criteria of acute toothache related to an inflamed dental pulp with moderate or severe pain intensity, which could vary over time and go through asymptomatic periods. Pain could be provoked by a stimulus or occur spontaneously. It could also be intermittent or continuous and affected by body position.[5] Periapical radiography was always used for differential diagnosis, and cases with apical periodontitis were excluded.

Individuals with ongoing use of analgesics and/or anti-inflammatory drugs were included in the study, if moderate to severe pain still remained. Subjects were excluded if they had no pain at the time of evaluation, or if after taking analgesics they had pain rated at an intensity lower than 50 mm on a visual analog scale (VAS). The VAS consisted of a horizontal line, 100 mm long, anchored by word descriptors at each end: the far left end read “no pain” and the right end read “worst pain imaginable.” The subjects were requested to make a vertical mark on the VAS line at the point that they felt represented the intensity of their current pain state.[17]

The dental implant placement and pulpectomy procedures were performed and supervised by experienced faculty from the Bauru School of Dentistry at the University of São Paulo.

AO Group

The AO group included 20 subjects diagnosed with neuropathic pain classified as AO.

Prior to the patients’ enrollment in the study, orofacial pain specialists (A.L.P., Y.M.C., J.S.B.) diagnosed AO based on the currently published and accepted criteria for this condition: persistent pain present at least 8 hours per day for 15 days or more per month for at least 3 months; localized in the dentoalveolar area within a defined anatomical area; and

not caused by another disease or disorder excluded by dental and neurologic examination and imaging.[2,5,8] Panoramic or periapical radiography was requested for all patients, and a cone beam computed tomography (CBCT) scan was performed in patients when any diagnostic uncertainty remained after the complementary examinations and radiographs.[18] Patients taking pain medications when pain persisted were also included in this group.

Study Design

A sequence of five different QST measurements and the conditioned pain modulation (CPM) test were performed in all subjects comfortably seated in a quiet room with an ambient temperature of 22°C to 25°C. The total duration of all tests was approximately 45 minutes. An experienced researcher (A.L.P.) performed all procedures and oriented participants throughout the entire process to ensure accuracy. Tests were applied over the dentoalveolar-attached mucosa, the closest region to the tooth, within an area of approximately 10 mm^2.[12,19] The region was group dependent and comprised the area where the implant was placed (in the IMP group), the toothache area (in the IP group), or the painful region (in the AO group). Pain intensity reports, as well as QST, were performed preoperatively (at baseline) and postoperatively 1 month and 3 months after tissue trauma following implant placement or pulpectomy (in the IMP group and IP group, respectively). The AO group was examined only once, at baseline. A diagram with the follow-up of the experimental protocol is depicted in Fig 2.

Variables

Mechanical Detection Threshold

The mechanical detection threshold (MDT) test was performed to estimate the least amount of force at which subjects recognized the sensation of a light, nonpainful touch.[20] This test was executed with a kit of 20 von Frey nylon monofilaments with different diameters, calibrated to exert specific forces when bending, ranging from 0.008 g/mm^2 to 300 g/mm^2.[20] The monofilament was applied perpendicularly and maintained over the dentoalveolar region with the monofilament bent for 1 to 1.5 seconds.[21] The method of limits was used, in which approximately 6 to 8 ascending and descending monofilament stimuli were applied, and the average force that elicited the measured response was calculated.[21]

Mechanical Pain Threshold

The same protocol for MDT was executed for mechanical pain threshold (MPT); however, in this case, the lowest von Frey monofilament stimulus that was recognized by the subject as a painful sensation was calculated.[12]

Dynamic Mechanical Allodynia[22]

To measure dynamic allodynia, the slight vibration of a cotton swab was applied for 10 seconds to the dentoalveolar mucosa (estimated area of 2 mm^2) and, immediately after, pain intensity was recorded on a VAS.[12]

Current Perception Threshold

Current perception threshold (CPT) was performed with the aid of painless electrodiagnostic sensory nerve testing equipment (Neurometer) and is defined as the mean of all the minimum intensities consistently detected by patients from an electrical stimulus. The CPT device is a transcutaneous electrical stimulator that uses an automated procedure to quantitatively measure the conduction and functional integrity of three main somatosensory fibers and their associated somatosensory circuits in the brain. It does this by using three different electrical frequencies to selectively activate the three main fibers and then measures the velocity of response to the threshold of each CPT test. Three different electrical frequencies were used: 2,000 Hz (A-beta fibers), 250 Hz (A-delta fibers), and 5 Hz (C fibers). For each frequency, the current intensity was slowly increased from 0.01 mA (output intensity range of 0.01 to 9.99 mA) until the patient just perceived an electrically evoked sensation, but not pain.[23–26]

Two small gold-plated electrodes (10 mm each) coated with 0.3 mL of electroconductive gel were placed on the dentoalveolar region, and during the three different frequencies the subjects held a remote control that they could use to stop the electrical stimulus.[25,26]

Temporal Summation

For temporal summation (TS), a repeated painful stimulus of 26 g/mm^2 during a continuous 30-second sequence using one von Frey monofilament (approximately one stimulus per second, frequency of 1 Hz) was applied to the mucosa. At the 1st second, 10th second, 20th second, and 30th second, subjects rated their pain intensity on a 0–10 numeric rating scale (NRS), where 0 indicated "no pain" and 10 indicated the "worst pain imaginable."[27,28] For statistical analysis, a single value for TS ratio was determined by using subtraction calculations (pain intensity after 30 seconds of pinprick stimulations minus the pain intensity at the first second of pinprick).

Conditioned Pain Modulation

At 5 minutes after TS, subjects were submitted to a conditioned stimulus (CS) for 30 seconds, in which the nondominant hand was immersed, up to the wrist with fingers apart, in a container of water at 47°C. With the hand still immersed in the container, TS was applied a second time and pain was rated again within the 30-second sequence.[12] The immersion of the nondominant hand in a container with water at

Table 1 Characteristics of Groups at Baseline

	IMP group	IP group	AO group
Age (SD)	50.22 (6.66)	35.1 (8.68)	57.84 (13.42)
Gender	14 F 6 M	14 F 6 M	15 F 5 M
Evaluated region	2 incisor 2 canine 10 premolar 6 molar	0 incisor 2 canine 4 premolar 14 molar	2 incisor 3 canine 7 premolar 8 molar
Pain intensity (SD) on VAS	0 (0)	68.6 (22.99)	62.5 (23.47)
Systemic conditions	None	1 controlled hypertension	3 cholesterol problems 8 controlled hypertension 2 controlled type 2 diabetes mellitus 1 hypothyroidism
Previous medications	None	3 analgesic and muscle relaxant formulation 2 Dipyrone	1 Amitriptyline (25 mg) 6 Gabapentin (300 mg) 3 Carbamazepine (200 mg) 2 Duloxetine (30 mg) 1 Topiramate (25 mg)

IMP group = implant patient group; IP group = inflammatory pulpitis group; AO group = atypical odontalgia; SD: standard deviation; F = female; M = male; VAS = visual analog scale.

47°C was used to elicit a painful thermal conditioned stimulus.

For statistical analysis, a single value for condition pain modulation (CPM) ratio was determined by using subtraction calculations (pain intensity of 30 seconds of pinprick stimulations after CS minus pain intensity of the first second of pinprick stimulations before CS). Also, the CPM degree (percent of reduction in pain in the span of 30 seconds) in pain rating after CS compared to before CS was evaluated.

Data Reduction and Analysis

All analyses were performed by using Statistica for Windows version 10.0 (StatSoft) and MedCalc (MedCalc Software). Between-group characteristics, pain intensity, baseline QST values, CPM ratio, and CPM degree were analyzed by using one-way analysis of variance (ANOVA). Analyses of QST and CPM data over time (1 and 3 months) were performed with repeated-measures two-way ANOVA, in which group and time were the two factors. When appropriate, Tukey's post hoc analysis was used to determine significant differences between groups. In addition, QST data correlation at baseline for all groups was performed with Spearman correlation. The results were considered significant at a level of 5%. Furthermore, raw QST values from each patient were transformed to *z* scores to obtain a single value for each test for comparison[13]:

$$z \text{ score calculation index} = (X_{\text{single patient}} - \text{mean}_{\text{reference}}) / \text{standard deviation}_{\text{reference}}$$

Three *z* score transformations were performed: *(1)* the X value was used for the IP and AO groups at baseline, and the references were the values of the IMP group at baseline; *(2)* the X value was the IMP and IP groups' values 1 month after the procedure, and the references were the IMP and IP groups' values at baseline, respectively; and *(3)* the X value was the IMP and IP groups' values 3 months after the procedure, and the references were the values of the IMP and IP groups at baseline, respectively.

z scores above 1.96 or below –1.96 fell outside the 95% confidence interval (CI) of the mean and therefore were considered sensory abnormalities. Abnormalities were subsequently categorized as a gain (above 1.96) or a loss (below –1.96) of sensory function.

Results

Group Characteristics

Sample characteristics such as age, gender, evaluated regions, pain intensity, systemic conditions, and previous medications are presented in Table 1. Mean pain levels of the IP and AO groups did not show a significant difference at baseline. There were no complications during or after the procedures for the IMP and IP groups. In the IMP group, there were no reports of adverse events or need for extra intake of medication. Average implant diameter was 3.75 mm (3.25–5.00 mm) and length was 10 mm (8.50–13.50 mm). All implants were external hexagon, 10 from Neodent and 10 from SIN. There were also no reports of adverse events in the IP group, and intake of painkiller after pulpectomy was reported by only three subjects, once on the first day for each.

All 60 eligible subjects who met the inclusion criteria agreed to participate. However, 18 subjects were considered withdrawn from the study because

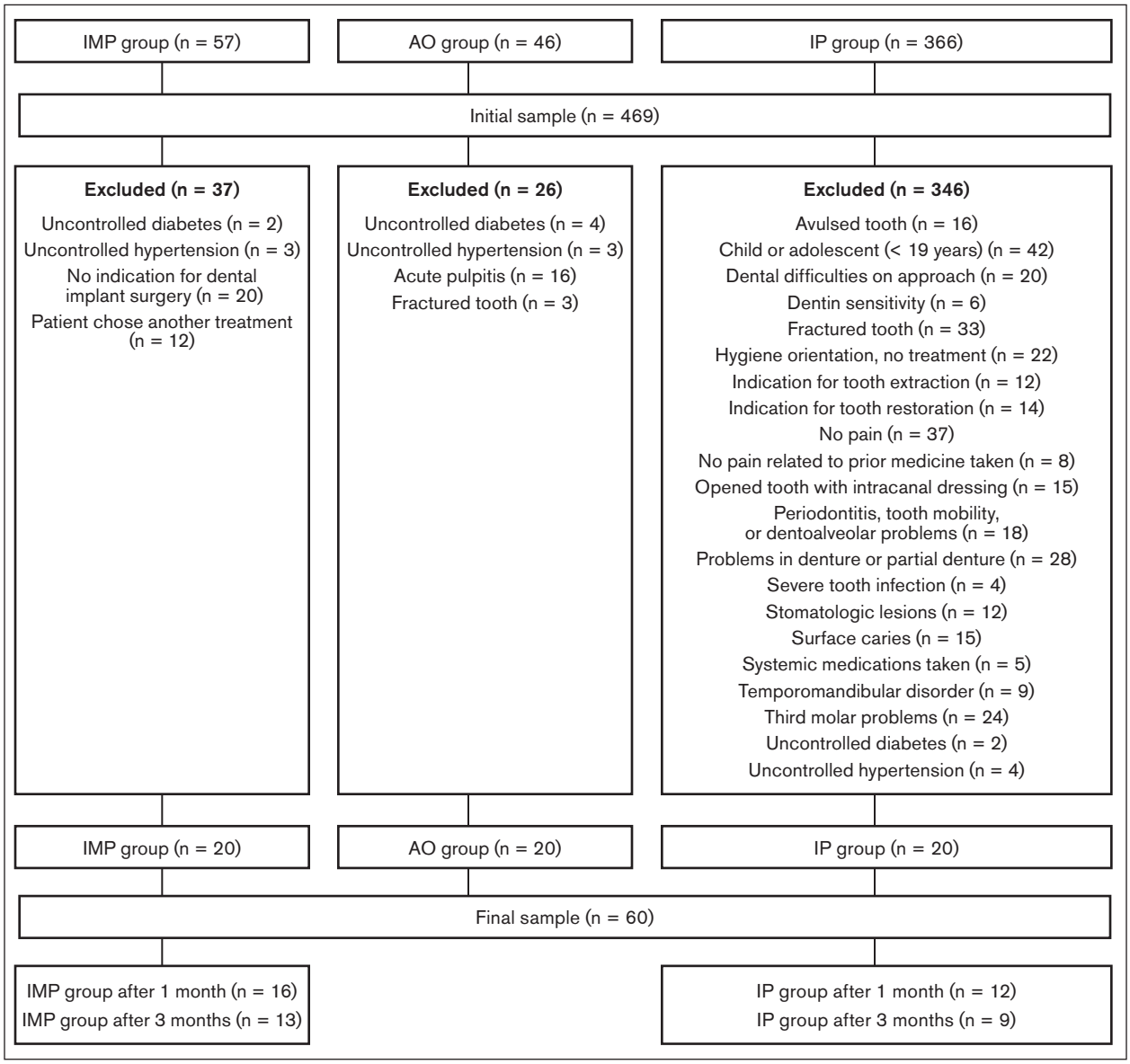

Fig 1 Flowchart of exclusion criteria for the selected subjects. IMP = implant group; IP = inflammatory pulpitis group; AO = atypical odontalgia group.

they did not attend the appointments after recurrent calls. In the IMP group, 16 subjects completed the first appointment (1 month) and 13 completed the second appointment (3 months). In the IP group, 12 and 9 subjects completed the first and second appointments, respectively (Fig 1).

In 13 AO subjects, CBCT was performed to assist in differential diagnosis due to the visualization difficulty with conventional and panoramic radiographs of possible dental or bone alterations.

Baseline Analyses

The study protocol for each group is shown in Fig 2, and all QST values are shown in Fig 3.

IMP and IP groups presented higher MDT ($F = 24.44$, $P < .001$; post hoc test = 0.0001; error between mean square [MS] = 5.09; df = 98.00) and MPT ($F = 16.88$, $P < .001$; post hoc test = 0.0001; error between MS = 334.68; df = 98.00) than the AO group. Only subjects with AO reported pain (33.9 mm on a VAS) after vibration of a cotton swab. No differences in CPT related to activation of any type of fiber (A-beta, A-delta, and C fibers), nor in TS, were found between or among the groups.

After *z* score transformation, elevations in MDT and CPT related to C-fiber activation (indicating a loss of function) were found in patients with IP, as well as reduced MPT and CPT related to A-delta

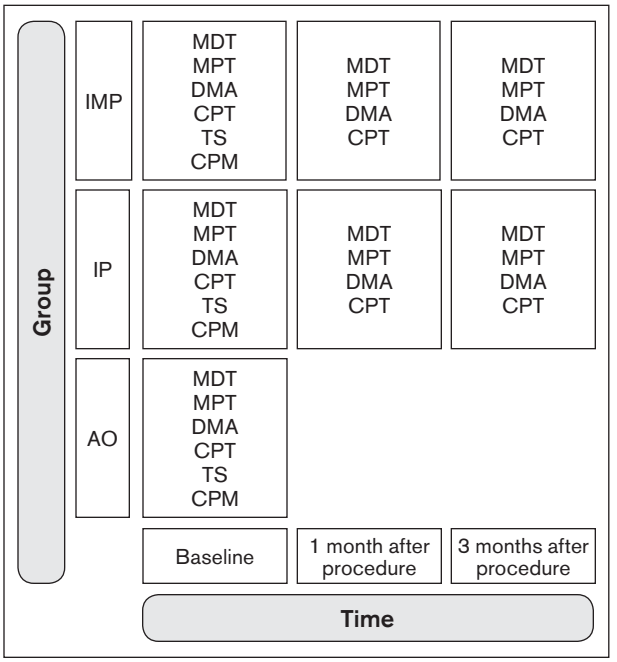

Fig 2 IMP = implant group; IP = inflammatory pulpitis group; AO = atypical odontalgia group; MDT = mechanical detection threshold; MPT = mechanical pain threshold; DMA = dynamic mechanical allodynia; CPT = current perception threshold; TS = temporal summation; CPM = conditioned pain modulation.

fiber activation in AO subjects. Also, a gain of function was observed for the allodynia test in AO subjects (Fig 4).

AO subjects presented ineffective endogenous pain modulation measured through the CPM test. IMP and IP subjects showed higher CPM degrees and lower CPM ratios than AO patients, suggesting an undamaged intrinsic modulatory system ($F = 17.88$, $P < .001$; post hoc test = 0.03; error between MS = 4.35; df = 50.00) (Fig 5). The overall pain amelioration after CS in the AO group was only 7.84% (standard deviation [SD] ± 30.56%), whereas the IMP and IP groups' values were 19.86% (± 37.96%) and 48.76% (± 41.54%), respectively ($F = 5.27$, $P = .006$).

QST Data Correlation at Baseline

The IMP and IP groups showed strong correlations among the CPTs related to activation of A-beta and A-delta fibers ($\rho = 0.72$ and $\rho = 0.82$, respectively). The CPT related to C-fiber activation had a moderate correlation with the stimulation of A-delta fibers in the IMP group ($\rho = 0.47$) and with the stimulation of A-beta fibers in the IP group ($\rho = 0.44$). For the IP group, the greater the MDT, the greater the MPT ($\rho = 0.60$). For the AO group, the greater the MDT, the greater the MPT ($\rho = 0.53$); and the greater the dynamic allodynia, the lower the MDT ($\rho = -0.55$) and MPT ($\rho = -0.60$).

Between-time Analyses

For the IMP group, a slight pain started during implant placement for some subjects (mean VAS: 8.5 mm), even though they were under local anesthesia. This was reported by some of the subjects after the procedure. Pain increased in intensity 1 hour after the procedure (VAS: 23.4 mm; $F = 13.00$; $P = .003$; post hoc test = 0.0002; error between MS = 210.74; df = 176.00) (Fig 3). Two hours later, pain reduced (VAS: 12.4 mm) and was no different from baseline ($F = 76.19$, $P < .001$). For the IP group, pain was moderate at baseline (VAS: 68.6 mm) and decreased immediately after pulpectomy (VAS: 19.5 mm), with progressive pain relief until 4 hours after pulpectomy ($F = 76.19$, $P < .001$; post hoc test = 0.000; error between MS = 213.73; df = 176.00). After 5 hours, no pain was observed in any of the IP patients. After 1 and 3 months, both IMP and IP groups were free of pain.

No somatosensory alterations at 1 month after implant surgery for the IMP group or 1 month after pulpectomy for the IP group were found for MDT, MPT, dynamic allodynia, or CPTs related to activation of A-beta, A-delta, or C fibers ($F = 6.29$, $P = .99$). At 3 months after implant surgery, no somatosensory alterations were observed for the IMP group ($F = 6.29$, $P = .99$); however, at 3 months after pulpectomy, an increased MDT for the IP group was observed, and this threshold was significantly higher than those of the IMP and AO groups ($F = 6.29$, $P < .001$, post hoc test = 0.0001; error between MS = 5.09; df = 98.00). At this follow-up, the IP group also expressed significant reduction in CPT related to C-fiber activation compared to the IMP and AO groups ($F = 6.30$, $P < .001$, post hoc test = 0.04; error between MS = 1040.90; df = 98.00). The IMP and IP groups showed no differences in MPT or CPT related to activation of A-beta and A-delta fibers ($F = 1.17$, $P = .32$; post hoc test = 0.0001; error between MS = 334.68, df = 98.00).

Furthermore, *z* scores indicated no loss or gain of function at 1 or 3 months after implant placement (Fig 4b), and for only four subjects with IP was a loss of function seen in CPT related to C-fiber activation at 1 month and in three subjects 3 months after pulpectomy (Fig 4c).

Discussion

The present study was one of a relatively small number of QST studies that have examined and compared somatosensory features in pain from dental implant placement, IP pain, and neuropathic pain. Evaluation of somatosensory function is a field that is exponentially growing in research and clinical practice, and QST may provide a better understanding

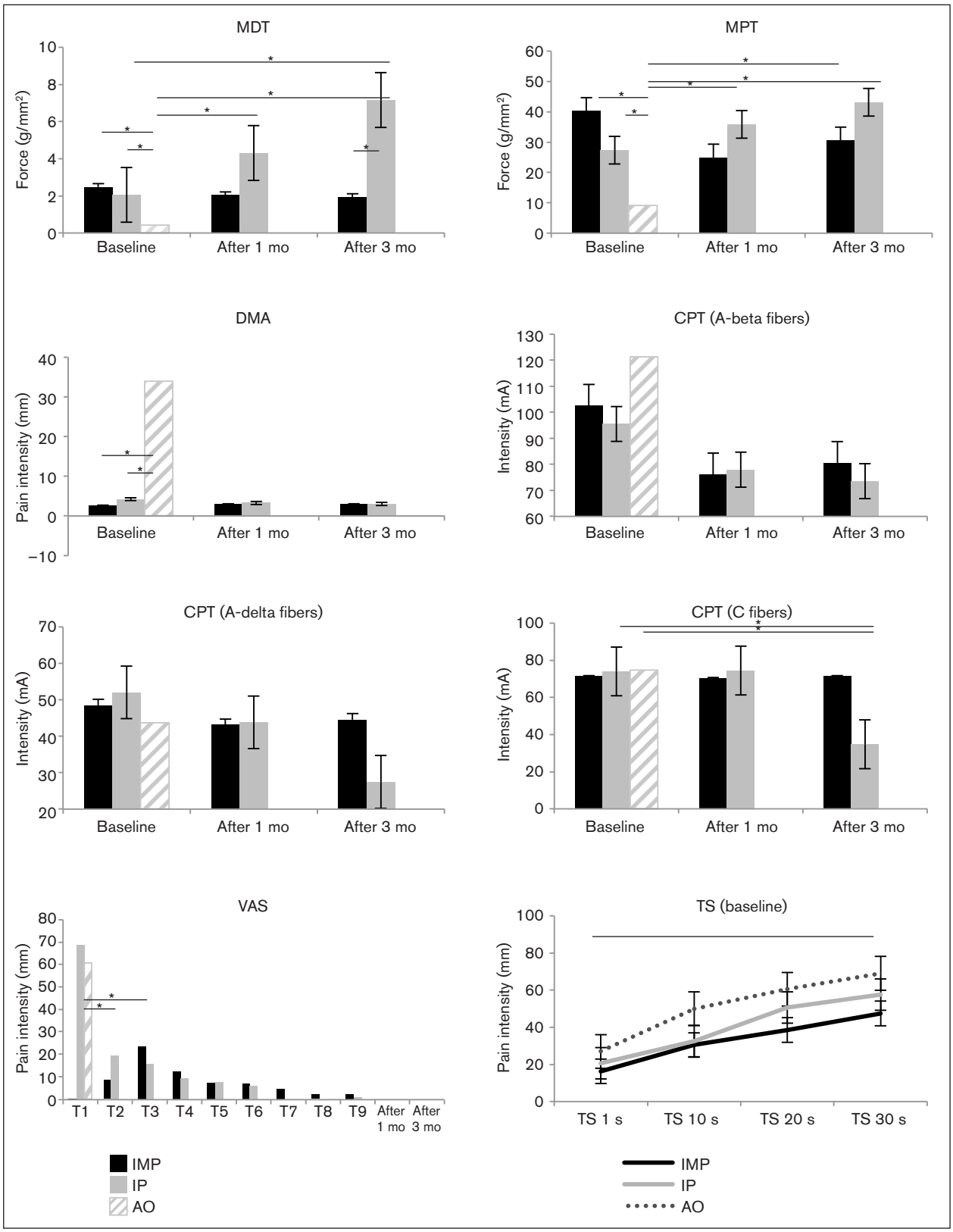

Fig 3 Differences between groups by time and group differences in pain intensity evaluated by a visual analog scale (except for TS, which was evaluated by a numeric rating scale) at different intervals. IMP = implant group; IP = inflammatory pulpitis group; AO = atypical odontalgia group; MDT = mechanical detection threshold; MPT = mechanical pain threshold; DMA = dynamic mechanical allodynia; CPT = current perception threshold; TS = temporal summation; VAS = visual analog scale; T1 = baseline; T2 = during procedure (implant installation or pulpectomy); T3 = 1 hour after procedure; T4 = 2 hours after procedure; T5 = 3 hours after procedure; T6 = 4 hours after procedure; T7 = 5 hours after procedure; T8 = 1 day after procedure; T9 = 1 week after procedure. *$P < .05$.

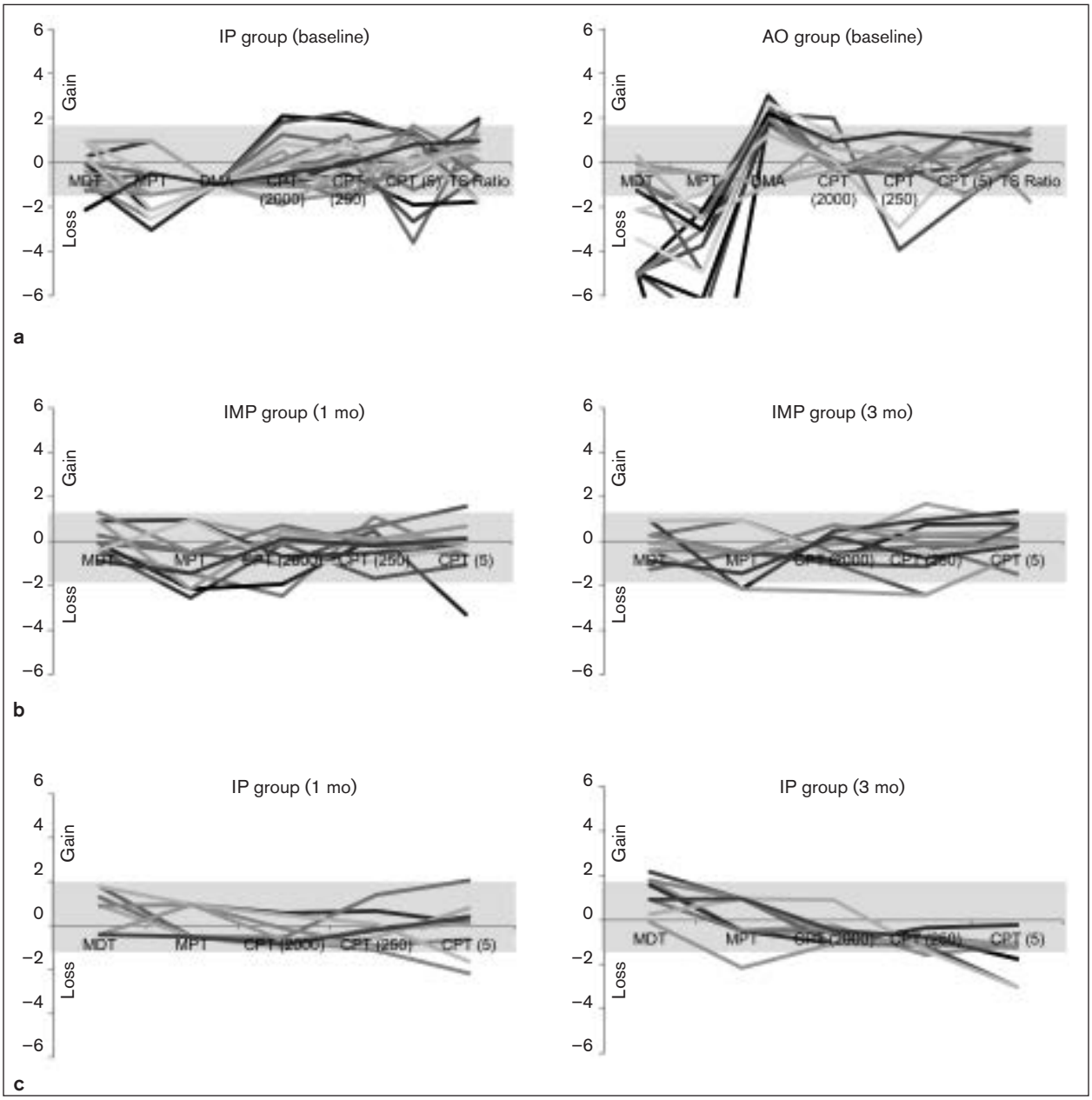

Fig 4 **(a)** *z* score sensory profiles at baseline for IP and AO groups compared to the IMP group; **(b)** *z* score sensory profiles for IMP group at 1 month and 3 months compared to baseline profile; **(c)** *z* score sensory profiles for IP group at 1 month and 3 months compared to baseline profile. IMP = implant group; IP = inflammatory pulpitis group; MDT = mechanical detection threshold; MPT = mechanical pain threshold; CPT = current pain threshold; TS = temporal summation; DMA = dynamic mechanical allodynia.

of sensory mechanisms underlying a variety of pain conditions.[29,30] Studies have shown that after intraoral damage involving neural tissues, three situations can follow: the first and most common situation is that after the healing process, the peripheral inflammation and pain cease and the sensory system may function as it formerly did[22]; in the second situation, pain may be evoked by an innocuous or nociceptive stimulus; and the third condition is the manifestation of hypoesthesia, hypoalgesia, paresthesia, or analgesia.[12,31] In the present study, no differences at baseline were observed between the mean pain levels of the IP and AO groups despite the different pain types, and this similarity may have resulted from the fact that certain groups had the same pain intensity at the time of evaluation.

Epidemiologic studies have provided evidence that after endodontic procedures, the nerve damage caused by the procedure may persist in 3% to 6% of patients, leading to an intraoral neuropathic pain.[9] Cases of post–implant placement neuropathic pain are less explored and seem to be around 13%.[32] In the

present study, no patient developed persistent pain or paresthesia after implant surgery or pulpectomy. This is in contrast to other studies in which 7% to 39% of patients receiving dental implants have been reported to experience some sensory disturbances such as paresthesia, allodynia, or even hyperesthesia.[33,34]

Allodynia, hyperalgesia, and decreased MDT and MPT (representing a gain of function) were seen in the present study for patients with AO. In addition, no somatosensory abnormalities were found in IMP patients at baseline. Since this group was free of pain at baseline and not yet exposed to implant placement, the findings are in accordance with the current literature.[11,32,35]

An important result of this study was the possible impaired pain modulation in AO patients. A recent study had similar results in patients with persistent postendodontic pain (PPEP) that suggested a reduced function of the endogenous pain inhibitory systems for PPEP patients.[36] However, the present results were also contradictory to a previously published study in which the effect of pain modulation was tested by using the nociceptive blink reflex as the TS protocol and capsaicin application as the CS.[37] The authors concluded that no signs of disturbances in endogenous pain inhibitory systems were found for AO or healthy participants.[37] Also, to the authors' knowledge, the present study is the first to assess CPM in IMP and IP patients, and the findings suggest that the endogenous pain modulation system is working efficiently in these individuals.

This study found no somatosensory alterations and no changes to CPT after implant placement, suggesting the absence of persistent damage to sensory nerve fibers or reformulation of the sensory innervation around the implant. The present study's CPT values also revealed alterations in C fibers or their associated somatosensory circuits in the brain 3 months after pulpectomy in patients with IP. One possible explanation for this finding could be related to sprouting of C fibers after pulp extirpation. Studies have shown that C fibers are located in the pulp itself, while A fibers are mainly located at the pulp-dentin boundaries at the coronal portion of the pulp and concentrated at the pulp horns.[14,38] The location of C fibers in the central region of the pulp may lead to reduced excitability and a higher threshold, which would require more intense stimulation for their activation.[39,40] Since the QST electrical stimuli were applied to the oral mucosa and not to the dental pulp itself, this could provide evidence of possible changes in the apical area of the tooth. Moreover, in this apical area, after pulpectomy, evidence of formation of a disorganized group of sprouting and branching axons from the alveolar nerve has been reported in the literature; this suggests some features in common with neuromas.[38]

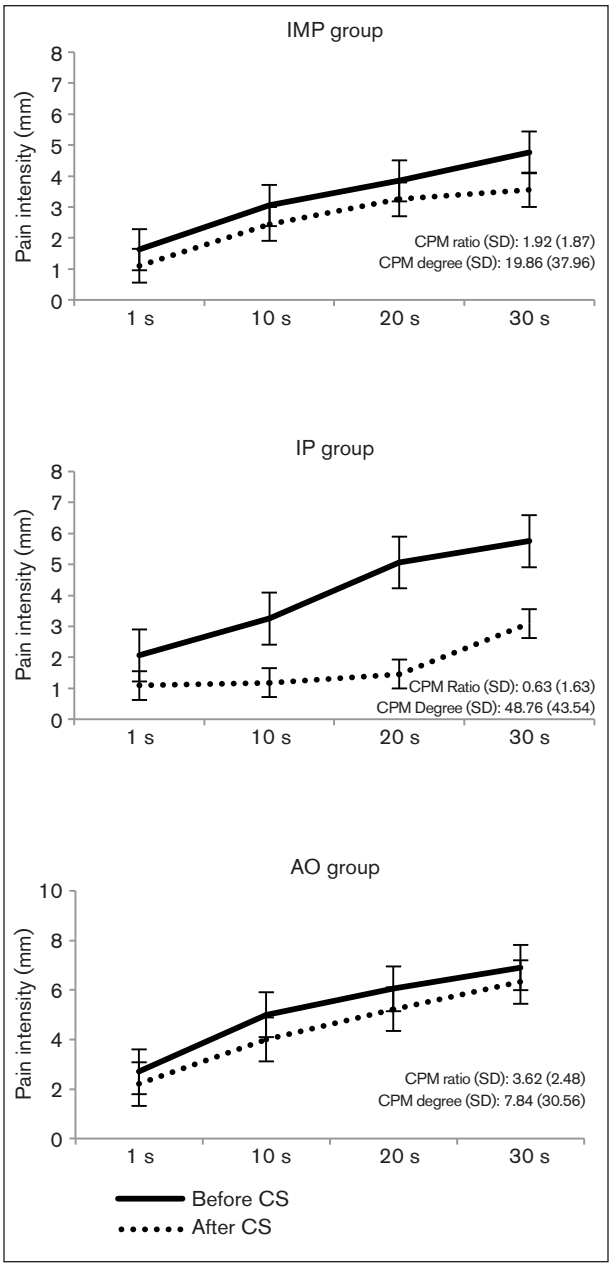

Fig 5 Conditioned pain modulation (CPM) protocol showing pain intensity evoked by a pinprick stimulus before and after a conditioned stimulus (immersion of the hand in a container of water at 47°C). CS = conditioned stimulus; SD = standard deviation.

The concept of neurogenic inflammation after pulpectomy is well established and refers to inflammatory vascular changes that may occur with the release of substance P and calcitonin gene-related peptide (CGRP), and consequently the activation of afferent nerves. A study in the canine of ferrets provided considerable histologic evidence of periapical inflammation, sprouting, and expression of CGRP in injured tissues that were still present 3 months after endodontic treatment.[38,41]

Furthermore, the differences in somatosensory thresholds may be a result of neuronal changes resulting from pain persistence—ie, the chronic nature of AO in comparison with the short-lasting nature of IP and implant placement—rather than a difference in the location of the pain. For instance, one study with subjects presenting acute and chronic lower back pain showed significantly higher pain sensitivity only in chronic lower back pain patients when compared to controls.[42]

CPT is a component of QST and has been proposed based on its noninvasiveness and selectiveness for certain types of nerve fibers.[43] However, there is no validation or estimation of normal values for CPT in intraoral conditions. Studies on diabetic neuropathy have shown that CPT might be a useful screening instrument to comprehensively assess the functional integrity of different nerve fiber populations and their associated brain circuits.[26,44] These studies have been based primarily on findings correlated with other examination techniques, such as thermal and vibration threshold tests. However, it is likely that more than one type of sensory fiber is being stimulated simultaneously with CPT, and that different somatosensory circuits are involved in the brain that receive and process the QST-evoked activity conducted into the brain by these fibers. Further studies should focus on the sensitivity and specificity of CPT testing to establish and compare it to an appropriate standard test—for instance, microneurography.[45,46]

Some limitations in this study should be highlighted, including the absence of somatosensory evaluation immediately after implant surgery or pulpectomy. However, some difficulties were observed when this approach was attempted in a pilot study; subjects reported pain after surgery or they were uncooperative after pulpectomy, which lead to suspension of the research tests. Another limitation is that although the IMP group at baseline was used as a control, a QST comparison for time duration was not performed in healthy subjects that had not been exposed to any procedure, which could limit the extrapolation of the present results. Another limitation was the possible influence of the age of subjects on the QST results. Even though there were no differences in subject age between IMP and AO groups, the IP group was composed of younger subjects (mean 35.1 years old). One study has already demonstrated in healthy subjects that a younger group (age 24–40 years old) was more sensitive compared to an older group (age 41–69 years old) in MDT tests.[47]

The considerable dropout during the experimental period should also be noted. More than half of the subjects dropped out from the IP group, and there were unsuccessful attempts at calling them back to the study. This may be due to the fact that the subjects were painless after receiving the pulpectomy, and also because the ethical committee did not approve of offers of financial incentives for those who did not return.

Conclusions

The present study showed two main results: *(1)* Somatosensory abnormalities in the form of elevated MDT and CPT related to activation of C fibers (indicating a loss of function) were present in IP patients, while allodynia, hyperalgesia, and reduced MDT and MPT (indicating a gain of function) associated with impaired pain modulation were detected in AO subjects; and *(2)* No somatosensory modification was seen after implant surgery, in contrast to the reduced CPT related to activation of C fibers in IP patients at 3 months after pulpectomy.

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