# Blink Reflexes in Patients with Atypical Odontalgia

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***Aims:*** *To use the human blink reflex (BR) to explore possible neuropathic pain mechanisms in patients with atypical odontalgia (AO).* ***Methods:*** *In 13 AO patients, the BR was elicited using a concentric electrode and recorded bilaterally with surface electromyographic (EMG) electrodes on both orbicularis oculi muscles. Electrical stimuli were applied to the skin above branches of the V1, V2, and V3 nerves and to the V branch contralateral to the painful branch. Sensory and pain thresholds were determined. The BR examination of the painful V branch was repeated during a capsaicin pain-provocation test. The data were analyzed with nonparametric statistics.* ***Results:*** *The BR responses (R2 and R3) evoked by stimulation of V3 were significantly smaller than the BR responses evoked by stimulation of V1 and V2 (*$P < .004$*). There were no differences in BR (R2 or R3) between the painful and nonpainful sides (*$P > .569$*), and the BR (R2 and R3) was not significantly modulated by experimental pain (*$P > .080$*). The sensory thresholds were significantly lower on the painful side compared to the nonpainful side (*$P = .014$*). The pain thresholds were not different between sides (*$P > .910$*).* ***Conclusion:*** *No major differences between the V nociceptive pathways on the right and left sides were found in a relatively small group of AO patients. Future studies that compare BRs in AO patients and healthy volunteers are needed to provide further knowledge on the pain mechanisms in AO.* J OROFAC PAIN 2005;19:239–247

**Key words:** atypical odontalgia, blink reflex, capsaicin, pain, trigeminal nociception

The human blink reflex (BR) can be evoked by mechanical or electrical stimulation of the facial skin and recorded by surface electromyographic (EMG) electrodes on the orbicularis oculi muscles. The afferent part of the BR arc is mediated by the trigeminal afferent fibers connected to the trigeminal and facial brainstem nuclei in the lower pons and medulla oblongata. Efferent fibers of the facial nerve on both sides serve as the efferent arc.[1] Reflex tests can be useful in diagnosing lesions along the afferent, central, or efferent pathways of the reflex.[2] Lesions along these pathways will cause either suppression or facilitation of the reflex response.[2]

The BR can be elicited by electrical stimulation of sites supplied by branches of the ophthalmic (V1), maxillary (V2), and mandibular (V3) divisions of the trigeminal nerve: the supraorbital nerve (V1); the infraorbital nerve (V2); and the mental nerve (V3). The BR consists of an early ipsilateral response (R1) with an onset latency of 11 ms and 2 bilateral components (R2 and R3) with onset latencies of around 33 ms (R2) and 84 ms (R3).[1] R1 and R2

are evoked by painful and nonpainful mechanical or electrical stimuli, whereas the R3 component of the BR is seen mostly after strong unexpected stimuli; it is not seen when the stimulus is announced.[3,4]

It has been proposed that trigeminal nociception can be tested with the use of the BR, because it may be either facilitated or inhibited by acute and chronic pain conditions in the trigeminal area.[5] For example, the BR elicited by a so-called "nociceptive-specific" electrode is facilitated in patients during migraine attacks,[6,7] but not in patients with acute unilateral painful frontal sinusitis.[8] One such chronic pain condition is atypical odontalgia (AO). It is sometimes referred to as "phantom tooth pain." AO pain is located in a former or present permanent tooth. It must be present for at least 6 months to be considered AO. The symptoms often begin after deafferentiation of primary afferent trigeminal nerve fibers, for example, after root canal treatment, tooth extraction, or apicectomy.[9] AO pain is present during most of the day and is not paroxysmal. Clinical and radiologic examinations reveal no signs of tissue pathology.[10,11] Typically, these patients have seen 5 to 6 different specialists before being referred to a specialized pain clinic,[12] and they have received multiple and often invasive treatments without a lasting effect. AO is currently a diagnosis of exclusion, because no specific diagnostic test is available. Recently, the BR has been tested in patients with atypical facial pain (AFP),[13] an enigmatic condition like AO, although AO is confined to the oral cavity, while AFP involves an area of the face. Twelve of 17 AFP patients had an abnormal BR in terms of either prolonged latencies or abnormal habituation patterns, ie, amplitude attenuation of consecutive R2 components in a series of responses.[13] The underlying pain mechanisms of AO and AFP are currently unknown, but it has been proposed that they may represent neuropathic pain conditions.[14] This hypothesis has not yet been confirmed.

Experimental pain models can be used to examine the influence of nociceptive afferent inputs on, for example, reflex pathways in a highly standardized manner. The cutaneous application of capsaicin, the burning ingredient in chili peppers, is widely used as a pain model in the study of neuropathic pain mechanisms,[15–17] but only a few studies have used capsaicin applied to the oral mucosa as a pain model.[18,19] Capsaicin causes moderate levels of pain and a robust increase in thermal sensitivity when applied to the alveolar mucosa.[19]

The present investigators wanted to compare the quality of AO pain with experimentally evoked capsaicin pain in an attempt to develop a model for AO pain in healthy subjects for future studies. They also wanted to know whether the experimentally evoked pain would influence the BR by either facilitating or inhibiting the response. Therefore, the aim of this study was to use the BR to explore possible neuropathic pain mechanisms in AO patients by comparing *(1)* the BR elicited by the stimulation of the 3 branches of the trigeminal nerve in patients with AO; *(2)* the BR evoked on the same side as the painful trigeminal branch before and during a pain provocation test with capsaicin on the painful area of the patient; and *(3)* the BR evoked on the same side as the painful branch with the contralateral BR evoked from the corresponding contralateral branch.

## Materials and Methods

### Patients

Fifteen patients with a clinical diagnosis of AO (4 men and 11 women, mean age 58 years, range 31 to 76 years) were recruited at the Orofacial Pain Unit in Malmö. Inclusion criteria were ongoing pain (> 6 months) perceived in a missing or existing permanent tooth, pain that was present during most of the day and nonparoxysmal in character, and the absence of tissue pathology upon clinical or radiologic examination. The patients were carefully examined by a dentist and a neurologist to avoid the inclusion of patients with other craniofacial pain conditions, such as odontogenic pain, trigeminal neuralgia, or cluster headache. Two patients (1 man and 1 woman) were excluded from the study, 1 because he was diagnosed with depression shortly after the examination and the other because she did not understand the difference between spontaneous and evoked pain. Spontaneous pain on the day of the test was determined on a visual analog scale (VAS), and the duration of pain was reported by the patients. The location of the pain was noted. The patients were examined for somatosensory disturbances, which will be the subject of a separate report. Informed consent was obtained from all patients before testing. The study was performed in accordance with the Declaration of Helsinki, and it was approved by the research ethics committee at Lund University.

### Blink Reflex

The study was performed in a quiet room with a temperature of about 20°C. Each study session

lasted approximately 1.5 hours. Before testing, all patients filled out the McGill Pain Questionnaire (MPQ)[20] to describe the quality of their spontaneous pain, and pain rating indices (PRIs) were calculated from this according to the method described by Melzack.[20] The BR was recorded with surface EMG electrodes placed bilaterally on in the infraorbital region of the face and at the corner of the eye. The Nicolet Viking EMG apparatus was used for sampling and analysis (2,000 Hz sampling, filter 20 to 1,000 Hz). The BR was elicited with the use of a concentric electrode with a central metal cathode with a diameter of 1 mm and an external circular anode with a diameter of 9 mm. Stimuli were applied to the skin directly above the entry zones of V1, V2, and V3 in a random manner in all patients on the painful side of the face. In order to keep the sessions short (< 1.5 hours), only the branch corresponding to the painful branch of the patient (V2 or V3) was stimulated on the contralateral side of the face. The individual sensory and pain thresholds to electrical stimuli were determined by at least 2 series of ascending and descending stimuli at each stimulus site. The sensory threshold was defined as the lowest stimulus intensity required to evoke a sensation, and the pain threshold was defined as the lowest stimulus intensity required to elicit a sensation that was just barely painful. Repeated stimuli (n = 9) with durations of 0.2 ms were applied at each stimulus site, with an interstimulus interval of approximately 15 seconds and a stimulus intensity of approximately 2 times the individual pain threshold. The first sweep was excluded in every series of 9 stimuli, and the remaining 8 sweeps were rectified and averaged. The degree of habituation of the BR at the level of the infraorbital branch, that is, the amplitude attenuation of the ipsilateral R2 component, was tested with a train of 8 repeated stimuli with a frequency of 1 Hz, all with the same individual stimulus intensity (1.5 to 2 times the individual pain threshold) that was used during reflex testing.[21]

### Pain-Provocation Test

After these 4 sites were tested (painful side: V1, V2, and V3; nonpainful side: V2 or V3), 30 μL of 5 mg/mL capsaicin was applied under a Urihesive (ConvaTec) bandage to the painful intraoral site for 15 minutes.[19] Two minutes after capsaicin application, the series of 9 electrical stimuli was repeated at the capsaicin-treated site, with the same stimulus intensity as before capsaicin application. The patients filled out the MPQ again during capsaicin stimulation to describe the quality of the capsaicin-evoked pain, and PRIs were calculated. The patients continuously rated the capsaicin-evoked pain on a 0-to-10 electronic VAS. The subjects were asked whether the experimental capsaicin pain was similar to their spontaneous pain. They had the option of responding *(1)* "Not at all"; *(2)* "A little"; *(3)* "Very much"; or *(4)* "Completely."

### EMG Analysis

The EMG response was quantified as the root mean square (RMS) of the rectified and averaged EMG signals in the following time intervals: 27 to 87 ms for R2 and 90 to 130 ms for R3.[22] The R1 response was not analyzed because of contamination by the stimulus artifact. Onset latencies of the R2 response were assessed for the averaged signals by an investigator blinded to the specific conditions (trigeminal branch, painful versus nonpainful, capsaicin versus no capsaicin) under study. In contrast, no attempts to determine onset latencies of the R3 response were made, because of inconsistency in its occurrence. The patients rated the stimulus-evoked pain on a 0-to-10 VAS. Habituation was considered normal when the RMS value of R2 to the fifth stimulus attenuated to less than 50% of R2 to the first stimulus.[13]

### Statistics

The results are presented as median values and interquartile ranges. Friedman repeated measures analysis of variance on ranks was used to compare the data for the 3 trigeminal branches. The Wilcoxon signed rank test was used to compare data on the painful side with data on the nonpainful side and to compare data on the conditions before and during capsaicin application. Results were considered significant if $P$ was found to be less than .05.

## Results

### Patient Characteristics

On the day of testing, the patients experienced spontaneous pain with a median intensity of 2.8 (1 to 6.5) on a 0-to-10 VAS. The median pain duration was 5 years (4 to 12 years). Nine patients experienced intraoral pain in the maxilla (V2) and 4 experienced it in the mandible (V3).

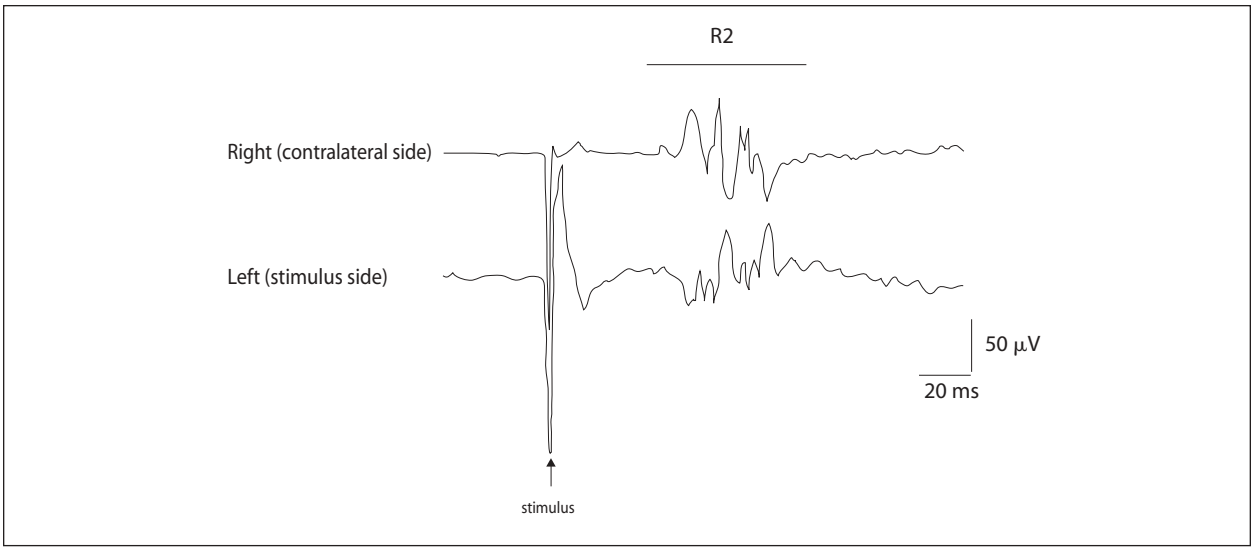


**Fig 1** Rectified and averaged EMG signals (n = 8 sweeps) during stimulation of the left V1 region in 1 patient. Clear bilateral R2 components of the blink reflex can be seen.

### Blink Reflex

In all but 3 patients, clear R2 responses (Fig 1) were evoked by stimulation of skin innervated by all 3 nerve branches. In 2 patients, electrical stimulation of V3 evoked no BR. One patient exhibited only an ipsilateral R2 to stimulation of the painful branch, but stimulation of the contralateral branch evoked a bilateral R2. These 3 patients were excluded from the analysis of onset latencies because of the lack of R2. R1 was only seen ipsilaterally; it was often contaminated by the stimulus artifact. R2 and R3 were both observed bilaterally, in accordance with previous findings,[1] although R3 occurred inconsistently.

The median onset latency of the ipsilateral R2 component upon stimulation of the painful nerve branch was 41.2 ms (33.0 to 45.0 ms). For the contralateral branch, median onset latency was 44.8 ms (34.1 to 45.4 ms). This was not a significant difference ($P$ = .734). Likewise, the median onset latency of the contralateral R2 component upon stimulation of the painful branch, 41.6 ms (35.1 to 44.5 ms), was not different from that of the contralateral branch, 45.2 ms (39.4 to 46.6 ms) ($P$ = .734). The onset latencies of the ipsilateral R2 response evoked by stimulation of the painful branch were not significantly influenced by the application of capsaicin (median, 34.4 ms; 31.0 to 39.3 ms) (P = .250). This was also true for the latencies of the contralateral R2 response (median, 32.4 ms; 30.6 to 41.9 ms) ($P$ = .297).

Bilateral R2 and R3 responses to electrical stimulation were significantly different from the pre-stimulus EMG activity ($P$ < .05). The prestimulus activity did not differ between sides ($P$ = .635). Prestimulus activity also did not differ from activity before or during capsaicin application ($P$ = .787). No differences were detected in responses (R2-ipsilateral, R2-contralateral, R3-ipsilateral, and R3-contralateral) between the painful and nonpainful sides (Figs 2a and 2b; $P$ > .569) or between responses before and during capsaicin application (Figs 2c and 2d; $P$ > .080). The ipsilateral and contralateral R2 and R3 components of the BR following stimulation of V3 were significantly smaller than the R2 and R3 to stimulation of the V1 and V2 (ipsilateral: R2, $P$ = .004; R3, $P$ = .006 (Fig 2e); contralateral: R2, $P$ = .002; R3, $P$ = .001 (Fig 2f), in accordance with previous findings.[21]

Two patients were excluded from the analysis of habituation because they did not relax during the habituation test. They statically contracted the orbicularis oculi muscles during the habituation test. Three patients showed attenuation to less than 50%, which is the normal habituation pattern.[13] The habituation patterns of 8 patients were abnormal, with only minor attenuation or an increase in the response from the first to the fifth stimulus of the 8 stimuli. The median reduction in the RMS of the ipsilateral R2 component of the BR from the first to the fifth stimulus was 22% (–27% to 65%).

**Table 1** The Stimulus Intensity ($I_{stim}$) to Evoke BR, the Stimulus -Evoked Pain on a 0–10 VAS, and Individual Sensory and Pain Thresholds Evoked by Electrical Stimulation of the 3 Nerve Branches

| | $I_{stim}$ (mA) | Stimulus evoked pain (VAS score) | Sensory threshold (mA) | Pain threshold (mA) |
|---|---|---|---|---|
| V1 | *7.1 (4.9–12.0) | 5.0 (3.2–6.3) | 1.4 (1.0–1.6) | 2.6 (1.6–4.0) |
| V2 | *6.9 (5.1–12.4) | 4.5 (3.1–6.6) | 1.4 (1.4–1.6) | 2.8 (2.5–4.3) |
| V3 | 14.5 (7.9–15.3) | 3.7 (2.7–5.9) | 1.4 (1.2–1.6) | 5.1 (2.5–7.4) |

Medians with quantiles shown for 13 subjects. Note the significantly higher stimulus intensities used at V3 compared to V1 and V2, indicated by * ($P$ = .001).

**Table 2** The Electrical Sensory and Pain Thresholds and Stimulus-Evoked Pain Between the Painful and Nonpainful Sides Before and During Capsaicin Application

| | Sensory threshold (mA) | Pain threshold (mA) | Stimulus-evoked pain (VAS score) |
|---|---|---|---|
| Painful side | | | |
| Before capsaicin | *1.4 (1.2–1.5) | 3.0 (2.0–6.8) | 4.7 (3.0–6.8) |
| During capsaicin | †1.6 (1.6–1.9) | 3.3 (2.7–7.7) | 3.3 (2.5–5.6) |
| Nonpainful side | 1.6 (1.4–2.1) | 3.5 (2.7–6.5) | 5.1 (2.9–6.9) |

Medians with quantiles shown for 13 subjects. Stimulus-evoked pain measured using a 0–10 VAS. *Indicates a significant difference between sides ($P$ = .014). † Indicates a significant difference between measurements made before and during capsaicin ($P$ = .016).

### Psychophysical Characteristics

The stimulus intensity used to evoke BR in this study was 2 to 3 times the individual pain threshold, (Table 1). A comparison of stimulus intensities, stimulus-evoked pain, and individual sensory and pain thresholds in the 3 nerve branches is presented in Table 1. The stimulus intensities used in V3 were significantly higher than in V1 and V2 ($P$ = .001). There were no differences in stimulus intensities between V1 and V2 ($P$ > .05). No differences were found in stimulus-evoked pain, individual sensory thresholds, or pain thresholds between branches (Table 1). Stimulus-evoked pain and the individual sensory and pain thresholds are compared between the painful and nonpainful sides before and during capsaicin application capsaicin application to the painful side in Table 2. The individual sensory thresholds were significantly lower on the painful side compared to the nonpainful side ($P$ = .014), and the sensory thresholds of the painful side were significantly increased during capsaicin application ($P$ = .016). No differences between sides were found in comparisons of pain thresholds and stimulus-evoked pain ($P$ > .910), nor between "before" and "during" capsaicin application on the painful side ($P$ > .244).

### Capsaicin-Evoked Pain

The mean peak VAS pain rating during capsaicin application was 8.2 ± 1.6 (Fig 3). The most frequently used words on the MPQ are listed in Table 3. Several words were used by more than 30% of the patients to describe both their spontaneous (AO) and the capsaicin evoked-pain. These words were: "throbbing," "pounding," "pressing," "burning," "aching," "tender," "tiring," "sickening," "intense," "troublesome," and "discomforting." On the other hand, some of the words frequently used to describe AO pain were not frequently used in the description of capsaicin pain: "dull," "sore," "hurting," "fearful," "wretched," "annoying," "stabbing," "sharp," "cutting," "radiating," "gnawing," and "horrible." No differences in PRIs were found between spontaneous and capsaicin-evoked pain ($P$ > .271). When asked about the resemblance of the capsaicin-evoked pain to the spontaneous pain, 4 patients answered "a little," 4 answered "very much," and 2 felt that the capsaicin-evoked pain was identical to their everyday pain in character. Three patients were not asked this question.

There were no dropouts in the study, and no adverse effects were reported besides transient increased pain.

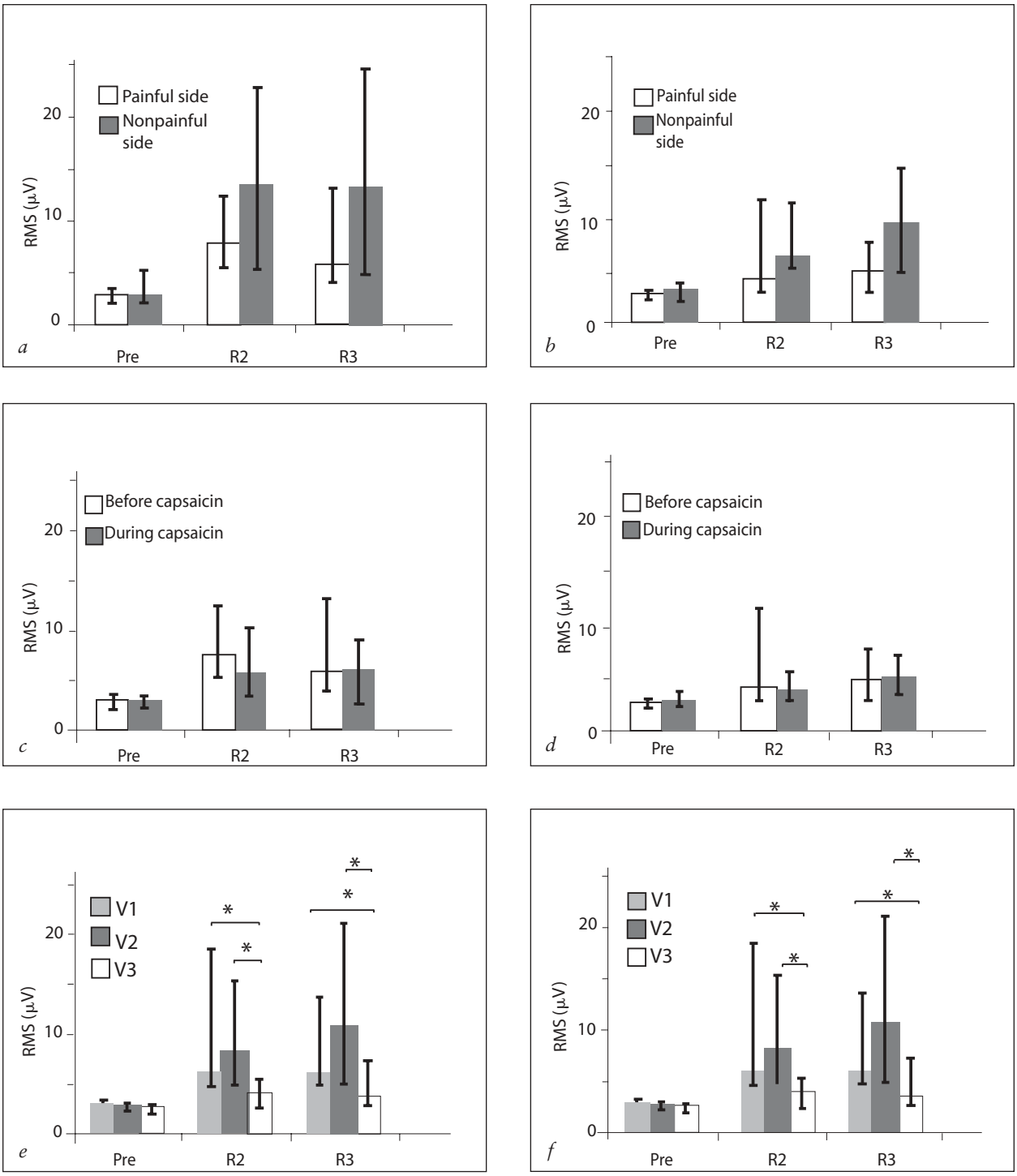


**Fig 2** The median RMS with interquartile ranges of the BR in 3 time windows: Pre (prestimulus) (–40 to 0 ms), R2 (27 to 87 ms), and R3 (90 to 130 ms). *(a)* Ipsilateral responses to stimulation of the painful VI, V2, or V3 branch (painful side) and the corresponding contralateral branch (nonpainful side). *(b)* Contralateral responses to stimulation of the painful and nonpainful sides. *(c)* Ipsilateral responses to stimulation of the painful branch before and during application of capsaicin. *(d)* Contralateral responses to stimulation of the painful branch before and during application of capsaicin. *(e)* Ipsilateral responses to stimulation of the 3 branches. *(f)* Contralateral responses to stimulation of the 3 branches. * Indicates a significant difference between the branches ($P < .006$).

**Table 3** The Most Frequently Used Words on the McGill Pain Questionnaire

| Pain word | Spontaneous pain | Capsaicin-evoked pain |
|---|---|---|
| Throbbing | **6** | **4** |
| Pounding | **4** | **4** |
| Pricking | 2 | **7** |
| Stabbing | **4** | 1 |
| Sharp | **4** | 3 |
| Cutting | **4** | 3 |
| Pressing | **5** | **4** |
| Gnawing | **4** | 3 |
| Burning | **4** | **9** |
| Smarting | 1 | **8** |
| Dull | **5** | 3 |
| Sore | **6** | 2 |
| Hurting | **4** | 2 |
| Aching | **10** | **7** |
| Tender | **5** | **5** |
| Tiring | **10** | **5** |
| Sickening | **4** | **4** |
| Fearful | **4** | 2 |
| Troublesome | **8** | **8** |
| Wretched | **4** | 1 |
| Annoying | **4** | 0 |
| Intense | **5** | **7** |
| Radiating | **7** | 3 |
| Discomforting | **11** | **7** |
| Distressing | 3 | **6** |
| Horrible | **4** | 2 |

The "spontaneous pain" column shows the number of AO patients who used each term to describe their everyday pain; the "capsaicin-evoked pain" column shows the number of AO patients who used each term to describe their capsaicin-evoked pain. Data for 13 patients are shown. Numbers shown in bold represent usage of the term by more than 30% of the 13 patients.

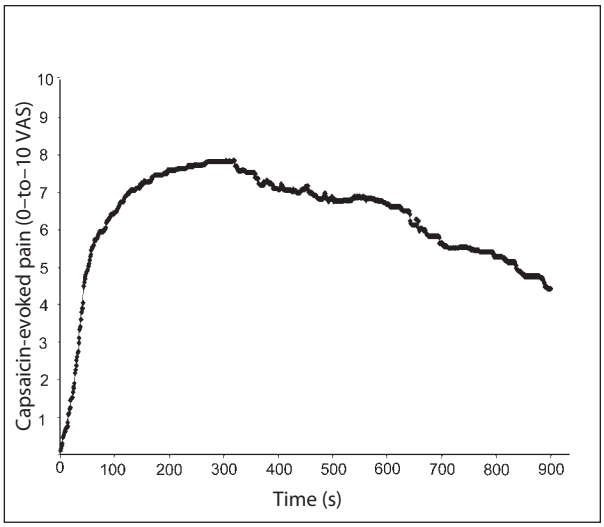


**Fig 3** Mean VAS scores of the pain evoked by topical application of capsaicin to the painful intraoral site during 900 seconds. The patients scored their pain continuously on a 0-to-10 electronic VAS. Note the high level of pain (mean $VAS_{peak}$ = 8.2 ± 1.6) produced by topical application of capsaicin to the mucosa.

## Discussion

### Blink Reflex

There was a significantly smaller BR response during stimulation of the skin innervated by the V3 branch in comparison to responses elicited by V1 and V2 stimulations in AO patients. This was found despite higher stimulus intensities being used to elicit a reproducible R2 with V3 stimulation. In fact, in some patients, V3 stimulation failed to evoke an R2 response in accordance with the notion that BR evoked by stimulation of the the mental nerve may be too inconsistent to be useful in clinical practice.[21] The difference in BR evoked by stimulation of the 3 trigeminal branches has been studied before, and the BR evoked by stimulation of the V3 shows poorer excitability and a different recovery cycle when compared to V1 and V2 stimulations in healthy subjects.[21] The V3 was included in the present study because the pain in 4 of the patients involved the V3.

The BR was not significantly modulated by the addition of an experimental pain to the painful area of patients suffering from AO in this study. However, this may potentially be due to the limited size of the study population, since a tendency toward a lowered R2 response in the stimulus side was found during capsaicin application ($P$ = .080). This could also be explained by a ceiling effect, because the high stimulus intensities resulted in close to maximal BR responses, as the Aβ, the Aδ, and the C fibers in the skin were likely all stimulated. Recently, the effect on the BR of painful stimuli to the temple and hand has been examined,[23] and it was found that the R2 component of the BR was suppressed during these painful stimuli. Further studies with larger groups of participants and nociceptive-specific stimulation, eg, laser stimulation[24] or the so-called nociceptive-specific electrode,[6] will be necessary to explore this observation.

Comparisons of responses from the painful trigeminal branch with the corresponding contralateral branch revealed no difference in RMS or R2 onset latencies. It can be speculated that heterogeneity in the present sample of patients in terms of differences in pain intensity, location, and

character may explain the failure to find a difference in BR measures between the painful and the nonpainful sides. Alternatively, it is possible that central connections between the right and left trigeminal nociceptive pathways are a factor.[25] Another limitation of the present study is that the electrical stimulation was carried out on the skin above the entry zones of the V1, V2, and V3 branches, and not at the actual painful sites of the patients. Also, a finding of an altered BR response on the painful side compared with the nonpainful side could have indicated neural changes proximal to the site of possible nerve damage, eg, central sensitization.[26] In addition, the location of the stimulation sites proximal to the painful sites of the patients made it difficult for any pure peripheral changes in the nociceptive pathways to be detected. Further studies will be needed to examine clinical and neurophysiological signs of peripheral and central sensitization.

The habituation pattern was abnormal in 8 of 11 patients, according to the criterion for normality, in that the response to the fifth stimulus was less than 50% of the first response.[13] The RMS of the ipsilateral R2 was used in a predefined time interval in the analysis, because this, in the opinion of the authors, is a more reliable measure than the amplitude of a single response. The present findings regarding habituation patterns in patients with AO, however, are similar to the abnormal habituation reported for patients with atypical facial pain.[13]

### Psychophysical Characteristics

The electrical sensory thresholds were lower in the area of the painful trigeminal branch compared with the area of the contralateral branch. Changes in somatosensory sensitivity can be due to central or peripheral sensitization or both.[26] Electrical stimulation at the low intensities used to determine sensory thresholds activates mostly large-diameter Aβ low-threshold mechanosensitive afferents by directly stimulating the primary afferent axons and bypassing the receptors.[27] In patients with pain in the temporomandibular joint (TMJ), the use of electrical stimuli has revealed that Aβ-fiber hypersensitivity is found in the overlying skin, whereas in patients with temporomandibular disorder muscle pain, hyposensitivity in the Aβ-fibers is found in the overlying skin.[27] Hypersensitivity in patients with arthralgia may be caused by local inflammatory changes in the skin overlying the TMJ, whereas hyposensitivity in patients with muscle pain may reflect changes in central processing.[27] The pain thresholds in this study, on the other hand, were not different between sides. The electrode used in this study was nonspecific, in the sense that it may have stimulated Aβ, Aδ, and C fibers at the stimulus site when stimulus intensities well above the sensory threshold were used. Detection of pain thresholds with reliable nociceptive-specific stimulation may be a better approach in the future.

### Capsaicin-Evoked Pain

The topical application of capsaicin on the painful intraoral areas of the patients caused high levels of pain (mean $VAS_{peak}$ scores 8.2 ± 1.6) in this study. In a previous study with healthy young volunteers, only moderate levels of pain (mean $VAS_{peak}$ scores 5.0 ± 1.9) were obtained during capsaicin application.[19] Because the same method of application and volume and concentration of capsaicin was used in both studies, this difference in mean $VAS_{peak}$ suggests that AO patients could be more sensitive to capsaicin than healthy subjects are. Further investigation of this relationship is required, because the 2 study populations were not age matched. Capsaicin stimulates the TRPV1 receptor,[28] which is also involved in the peripheral transmission of nociceptive impulses.[29,30] Central or peripheral sensitization in patients with AO is therefore a plausible explanation for the high mean $VAS_{peak}$ scores given in response to capsaicin in these patients. Changes in somatosensory sensitivity are often found in neuropathic pain conditions,[31,32] and therefore the present investigators agree with, for example, Marbach,[14] who suggested that the pain in patients with AO could be neuropathic.

Pain-provocation tests and pain models (eg, with capsaicin) have proven useful in the study of pain mechanisms in other chronic pain conditions.[33,34] In this study, the patients were asked whether the capsaicin-evoked pain mimicked the spontaneous pain of AO. No patients answered "not at all," but the other options were almost equally used. No differences in MPQ pain rating indices were found between spontaneous pain and capsaicin-evoked pain. It can therefore be argued that capsaicin evokes sensations similar to the spontaneous pain experienced by AO patients and that the application of capsaicin to the oral mucosa of healthy subjects is a suitable pain model for controls in studies on AO pain.

## Conclusions

The R2 and R3 components of the BR did not differ between the painful and the nonpainful sides,

and the BR was not significantly modulated by capsaicin application to the painful area. A future study comparing AO patients with age- and sex-matched healthy volunteers with respect to capsaicin-evoked pain, nociceptive-specific BR responses and BR modulation by experimental pain could provide us with further knowledge about the pain mechanisms of AO.

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