Spread and Referral of Experimental Pain in Different Jaw Muscles

Peter Svensson, DDS, PhD, Dr Odont
Professor
Department of Clinical Oral Physiology
Royal Dental College
University of Aarhus
Aarhus, Denmark

Consultant
Department of Maxillofacial Surgery
Aarhus University Hospital
Aarhus, Denmark

Jesper Bak, DDS
Private Practice
Aarhus, Denmark

Thor Troest, DDS
Private Practice
Aarhus, Denmark

Correspondence to:
Prof Peter Svensson
Department of Clinical Oral Physiology
Royal Dental College
University of Aarhus
Vennelyst Boulevard 9
DK-8000 Aarhus C, Denmark
E-mail: psvensson@odont.au.dk

Aims: *To test the hypothesis that there would be no differences in perceived pain intensity and spread and referral of pain evoked by injection of a similar amount of hypertonic saline into 6 different jaw-muscle sites in healthy female subjects.* ***Methods:*** *A total of 15 healthy women participated in 3 experimental sessions separated by 1 week. In a randomized sequence, the deep layers of the masseter, superficial layers of the masseter, anterior temporalis, lateral pterygoid, medial pterygoid, and anterior digastric muscles were injected with 5.8% hypertonic saline (0.2 mL). The subjects rated the perceived intensity of pain on an electronic 0- to 10-cm visual analog scale (VAS). The distribution of pain was drawn by the subjects on anatomical maps of the face, and a Danish version of the McGill Pain Questionnaire (MPQ) was filled out.* ***Results:*** *All injections were associated with moderate to strong pain intensity (mean peak value: 5.6 to 6.4 cm) with no significant differences between muscle sites (analysis of variance [ANOVA]: P = .520). Pain rating indices derived from the MPQ did not suggest significant differences between muscle sites (ANOVA: P = .898). However, the area of perceived pain differed significantly between muscle sites (ANOVA: P = .038) with the greatest area following the injection into the anterior temporalis muscle (Tukey: P < .05). On direct inspection, the pain maps appeared quite similar, but a new analysis technique based on a center-of-gravity method revealed significantly different coordinates and length of vectors (ANOVA: P < .001) with longer vectors associated with the pain areas in the anterior temporalis muscle compared with the other muscle sites (Tukey: P < .05). All muscles were frequently associated with referral of pain to intraoral structures (40% to 87%), but only pain in the anterior digastric muscle was referred to the tip of the tongue (53%).* ***Conclusion:*** *The data suggest no major differences in pain sensitivity between the examined jaw-muscle sites, but pain in the anterior temporalis muscle spreads to a larger area independent of pain intensity. There are subtle but detectable differences in the location and referral of pain patterns between jaw muscles. This will be helpful in the differential diagnosis of myofascial temporomandibular disorder pain.*
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Key words: jaw-muscle physiology, pain assessment, referred pain, temporomandibular disorder

Knowledge of spread and referral of pain from deep craniofacial structures is a prerequisite for diagnosis of temporomandibular disorders (TMD) and craniofacial pain complaints.[1] The distinction between spread and referral of pain is rather arbitrary, but referred pain has been defined as pain felt at a site remote from the site of origin or stimulation.[2,3] Pain from deep tissues is classically described as diffuse and difficult to locate

precisely in contrast to superficial types of pain.[4] Travell and Simons[5] demonstrated the topographic distributions of craniofacial pain based on their own clinical observations with activation of trigger points. More recently, a comprehensive study in 196 TMD patients demonstrated similar overall patterns of spread and referral of pain following manual stimulation of trigger points[6] compared with the pain drawings from Travel and Simons.[5] Thus, there is clinical consensus that there appears to be consistent and reliable patterns of spread and referred pain from deep craniofacial tissues in TMD pain conditions.[7–10] However, no attempts have so far been made to quantify pain patterns in the craniofacial region under more controlled conditions.

Experimental jaw-muscle pain evoked by injection of hypertonic saline shares many of the clinical features of persistent TMD pain with a spread and referral of pain to the temporomandibular joint, mandible, and teeth.[2,11,12] Thus, human experimental pain models can be used to systematically study the spread and referral of pain following stimulation of different jaw-muscle sites. So far, only the pain patterns from the masseter and anterior temporalis muscles have been described but not quantified.[2,13]

The aim of the present study was to test the hypothesis that there would be no differences in perceived pain intensity and spread and referral of pain evoked by injection of a similar amount of hypertonic saline into 6 different jaw-muscle sites in healthy female subjects.

Materials and Methods

Subjects

A total of 15 healthy female volunteers without signs or symptoms of TMD according to the Research Diagnostic Criteria for Temporomandibular Disorders (RDC/TMD)[14] were recruited from university students. Only women were studied since there is a strong predominance of female TMD patients.[15,16] The age, weight, and height (mean ± SEM) of the women were 26.5 ± 0.9 years, 60 ± 2 kg and 168 ± 1 cm, respectively. Oral contraceptives were used by 9 women; all women except 1 reported regular menstrual cycles. The local ethics committee in Denmark (Aarhus County) approved the study protocol, and all individuals gave their informed consent in accordance with the Helsinki Declaration.

Intramuscular Injection Technique

Each injection was given manually over a 10-second period with a 27-gauge hypodermic needle and disposable syringe in accordance with previous descriptions.[17] A total of 0.2 mL of 5.8% hypertonic saline (pH 6.8 to 7.0) was injected. Injections were preceded by careful palpation of the muscles and their insertions and followed previous injection guidelines.[5] Six muscle sites were injected: *(1)* deep layers of the masseter muscle—injection two thirds of the distance between the lower border of the mandible and the temporomandibular joint and 1 cm anterior to the posterior border of the ramus to a depth of 1.5 to 2 cm; *(2)* superficial layers of the masseter muscle—injection midway between its superior and inferior borders and 1 cm posterior to its anterior border to a depth of approximately 1.5 to 2 cm; *(3)* anterior part of the temporalis muscle—injection at the most bulky part of the muscle, approximately 2 cm posterior to the eyebrow and to a depth of 1 cm; *(4)* lateral pterygoid muscle—injection through the mandibular notch while the volunteer was biting on a gag of approximately 2.5 cm, the needle was directed medially at a 45-degree angle to a depth of about 2.5 cm aiming for the inferior head of the muscle; *(5)* medial pterygoid muscle—injection medial to the pterygoid tuberosity about 2 cm anterior to the posterior border of the ramus and directed cranially to a depth of 2 cm; and *(6)* anterior digastric muscle—the muscle was palpated and the injection carried out midway between the fovea digastrica mandibulae and the hyoid bone to a depth of 1 cm.

The muscle sites were injected in a randomized but balanced manner. Each subject drew 1 card, which indicated the sequence and side of the injection. All subjects participated in 3 sessions separated by 1 week. In each session, 2 injections were given (1 on each side). Half of the subjects received the first injection on the right side, and vice versa. There was no a priori reason to believe that there would be systematic side-to-side differences. Furthermore, any such effects would have been minimized by the randomization procedure.

Pain Assessment

The subjects were instructed to continuously rate the pain intensity evoked by the injections of hypertonic saline on an electronic 10-cm visual analog scale (VAS) for 15 minutes with their jaw at rest. The lower endpoint of the VAS was labeled "no pain at all" and the upper endpoint labeled

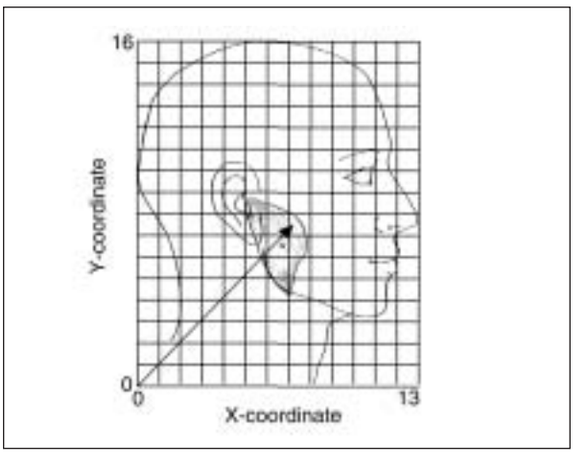

Fig 1 Schematic presentation of the center-of-gravity (COG) technique applied to a pain map from a single subject following injection of hypertonic saline into the superficial layers of the masseter muscle. The X- and Y-coordinates of the COG were calculated in a 13 × 16 grid system (see Materials and Methods), and the length of the pain vector *(arrow)* could be computed in arbitrary units.

"most pain imaginable." The VAS signals were sampled every 1 second and stored on a personal computer. The maximum pain was measured as the peak VAS score. The area under the VAS curve (VAS_{AUC}) was used to obtain a measure of the overall amount of pain, and the onset and offset of pain was determined from the VAS profiles. After the end of the infusion, the subjects described the quality of their pain on a validated Danish version of the McGill Pain Questionnaire (MPQ).[18] The pain rating indices (PRI) of the sensory, affective, evaluative, and miscellaneous dimensions of pain were calculated according to Melzack,[19] and the words chosen by at least 30% of the group were noted. The subjects drew the distribution of pain on a lateral or frontal projection of the face (dimension: 65 × 80 mm) (Fig 1). Moreover, drawings of the teeth and intraoral structures were also included. Specific information on possible referral patterns was avoided in order not to induce bias.[20] The pain maps were then digitized (ACECAD, model D9000+ digitizer, Taiwan) to calculate the area of perceived pain expressed in arbitrary units (au). Furthermore, in order to obtain a quantitative estimate of the localization of the perceived pain area, a new technique was introduced. The center-of-gravity (COG) analysis has been used as a measure of the spatial extent of physical events, such as motor-evoked potentials.[21] However, this technique so far has not been applied to pain maps. In the present study a grid outline with 5-mm resolutions (ie, a total of 13 × 16 = 208 grids) was superimposed on the lateral pain maps, and each grid in the coordinate system was assigned a value on a dichotomous basis (0 = no pain, 1 = pain) (Fig 1). The COG coordinates (X = anterior-posterior, Y = inferior-superior) in arbitrary units were calculated according to the formula:

$$X = \frac{\sum_{i=0}^{13}\sum_{j=0}^{16}(X_i \cdot gridvalue_{i,j})}{\sum_{i=0}^{13}\sum_{j=0}^{16}(gridvalue_{i,j})}$$

$$Y = \frac{\sum_{i=0}^{13}\sum_{j=0}^{16}(Y_i \cdot gridvalue_{i,j})}{\sum_{i=0}^{13}\sum_{j=0}^{16}(gridvalue_{i,j})}$$

Furthermore, the length of the pain vector (X, Y) was calculated as: $\sqrt{(X^2 + Y^2)}$.

Statistical Analyses

Mean (± SEM) values are reported in the text and figures. The VAS pain scores were analyzed with 2-way analysis of variance (ANOVA) with muscle sites (6 levels) and sequence (6 levels) as factors. Two-way ANOVA was also used to analyze the MPQ with the factors muscle sites (6 levels) and dimension of pain rating index (4 levels). The pain maps were analyzed with a 1-way ANOVA but only with 5 muscle levels since pain in the anterior digastric muscle only was drawn on the lateral map in 7 subjects. The ANOVAs were followed by post-hoc comparisons with the use of Tukey tests. A Pearson product moment correlation was used to examine the association between the area of the pain map (au) and the VAS pain scores. For all tests, the significance level was set at $P < .05$.

Results

In the initial examination, only 2 subjects reported slight pain upon palpation of 1 to 3 out of 20 muscle sites, and none of the subjects reported persistent pain in the craniofacial region, which is consistent with the absence of a myofascial TMD diagnosis according to the RDC/TMD. One subject had a soft reproducible click (disc displacement with reduction) in the temporomandibular joint without any pain. The maximum unassisted jaw-opening including the vertical overbite was 56 mm ± 4 mm, and the maximum assisted jaw-opening was 57 mm ± 4 mm. These findings clearly suggest that a non-TMD population was studied.

Perceived Pain Intensity

In all subjects and at all muscle sites the injection of hypertonic saline was reported to be overtly painful. No side effects were observed following any of the injections. ANOVAs did not indicate significant differences in any VAS pain parameters (VAS onset, offset, peak, and VAS_{AUC}) between the different muscle sites ($F < 0.850$; $P > .520$) or related to injection sequence ($F < 2.371$; $P > .051$) (Table 1). Thus, in the average subject the pain started about 11 seconds after the injection and lasted less than 300 seconds with a VAS_{peak} pain score around 6. An additional ANOVA tested the potential influence of oral contraceptives on VAS pain parameters but did not indicate consistent effects in this small sample ($F < 2.184$; $P > .143$).

Analysis of the PRI from the MPQ demonstrated no significant differences between muscle sites ($F = 0.323$; $P = .898$), but a significant effect on pain dimension ($F = 147.791$; $P < .001$). The sensory dimension was significantly higher compared to the evaluative, affective, and miscellaneous dimensions (Tukey: $P < .001$) (Fig 2). Both the affective and evaluative dimensions were smaller compared with the miscellaneous dimension (Tukey: $P < .05$). Words chosen by more than 30% of the subjects to describe the quality of the evoked pain sensation are shown in Table 2.

Pain Distribution

The distribution and extent of the perceived pain areas are shown in Fig 3. Similar to the VAS pain parameters, no significant effects of oral contraceptive use on pain areas could be detected in the group ($F = 0.016$; $P = .899$). Only 7 subjects marked pain on the lateral drawing of the face following injection into the anterior digastric muscle and this muscle was therefore not included in the statistical analysis. Quantification of the pain areas revealed significant differences in size ($F = 2.731$; $P = .038$) (Fig 4). The pain area associated with the injection into the anterior temporalis muscle was significantly larger compared to all other pain areas (Tukey: $P < .05$).

Direct inspection of the distribution of external pain following injection of hypertonic saline into the different muscles indicated subtle differences (Fig 3). Therefore, the COG was determined as an attempt to quantify the pain maps. The analysis demonstrated significant differences for the Y-coordinate ($F = 6.940$; $P < .001$), but not for the X-coordinate ($F = 2.477$; $P = .056$) (Table 3). Post-hoc tests showed that the Y-coordinate was placed significantly more superior following injection into the anterior temporalis muscle compared to all other muscles, and the Y-coordinate following injection into the medial pterygoid muscle was located significantly more inferior compared with the anterior temporalis muscle and deep masseter muscle (Tukey: $P < .05$). Also the length of the pain vector varied between muscle injections ($F = 10.594$; $P < .001$). The longest pain vector was associated with the injection into the anterior temporalis muscle (Tukey: $P < .05$) and the shortest with the injection into the medial pterygoid muscle (Tukey: $P < .05$) (Table 3).

In addition to the spread of pain to various extraoral areas (Fig 3), many subjects experienced referral of pain to intraoral structures (Table 4). Thus, referred pain in either the teeth or gingiva was reported by the subjects following injection into the deep masseter (40%), superficial masseter (80%), anterior temporalis (67%), lateral pterygoid (53%), medial pterygoid (87%), and anterior digastric (80%). The subjects could discriminate whether the pain was felt in the gingiva or teeth, but in the total group of subjects there was no clear pattern of referrals to either the gingiva or teeth in the maxilla or mandible except that pain from the anterior digastric predominantly was referred to the mandible (Table 4). Furthermore, in 53% of the subjects, pain in the anterior digastric caused referred pain to the tip of the tongue, which was not observed for any other muscles.

Table 1 Perceived Pain Intensity Following Injection of 0.2 mL Hypertonic Saline into 6 Jaw-Muscle Sites

	Pain onset (s)	Pain offset (s)	VAS peak (cm)	VAS_{AUC} (cm · s)
Deep masseter	11 ± 2	295 ± 30	6.2 ± 0.5	1111 ± 123
Superficial masseter	15 ± 2	267 ± 23	5.6 ± 0.6	938 ± 120
Anterior temporalis	11 ± 2	280 ± 24	6.1 ± 0.5	1065 ± 129
Lateral pterygoid	16 ± 2	292 ± 22	5.7 ± 0.5	1021 ± 111
Medial pterygoid	13 ± 2	300 ± 28	6.4 ± 0.5	980 ± 100
Anterior digastric	15 ± 1	248 ± 29	5.7 ± 0.5	848 ± 144
ANOVA	$P = .520$	$P = .667$	$P = .527$	$P = .677$

Mean values and SEM (n = 15) of VAS pain parameters.
ANOVAs did not indicate significant differences between muscle sites.

Correlation Between Pain Intensity Scores and Pain Areas

There were no significant relationships between the VAS_{peak} or VAS_{AUC} values and the perceived pain area for any of the injected muscles analyzed

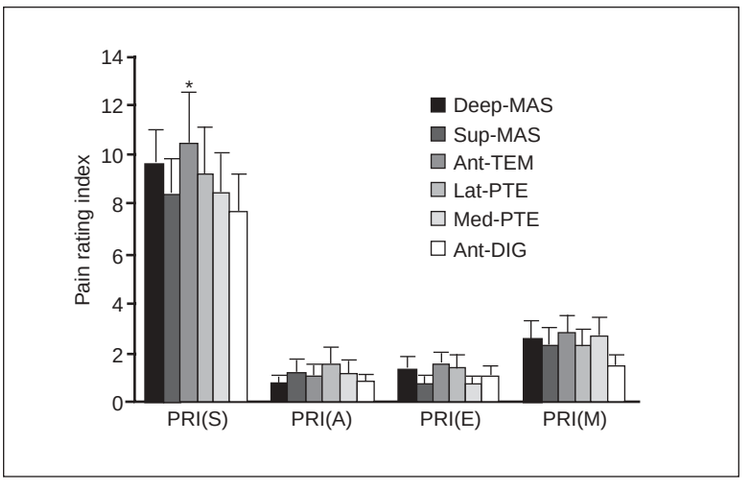

Fig 2 Pain rating indices (PRI) from the McGill Pain Questionnaire following injection of hypertonic saline into 6 jaw-muscle sites. Deep-MAS = deep layers of masseter, Sup-MAS = superficial layers of masseter, Ant-TEM = anterior temporalis, Lat-PTE = lateral pterygoid, Med-PTE = medial pterygoid, and Ant-DIG = anterior digastric muscle. S = sensory, A = affective, E = evaluative, and M = miscellaneous. Mean values ± SEM (n = 15). *Indicates significantly higher values for PRI(S) for all 6 muscles compared to the other dimensions (Tukey: $P < .001$).

Table 2 Percentage of Subjects (n = 15) Using Word Descriptors From the McGill Pain Questionnaire to Describe Their Pain in 6 Jaw-Muscle Sites

	Deep-MAS	Sup-MAS	Ant-TEM	Lat-PTE	Med-PTE	Ant-DIG
Sensory						
Shooting (%)	53	13	33	33	33	13
Boring (%)	47	33	33	33	40	33
Sharp (%)	40	27	33	13	13	33
Pressing (%)	33	27	27	27	13	13
Hot (%)	20	27	40	20	33	40
Aching (%)	20	27	53	60	33	40
Taut (%)	47	40	47	40	20	33
Evaluative						
Intense (%)	33	13	27	33	13	20
Miscellaneous						
Spreading (%)	20	13	47	33	27	27
Tight (%)	33	33	27	33	27	20

Deep-MAS = deep layers of masseter, Sup-MAS = superficial layers of masseter, Ant-TEM = anterior temporalis, Lat-PTE = lateral pterygoid, Med-PTE = medial pterygoid, and Ant-DIG = anterior digastric muscle.

separately (Pearson rank: $r < 0.276$; $P > .319$) or combined (Pearson product moment: n = 82; $r = 0.223$; $P = .423$).

Discussion

The present study demonstrated that the perceived pain intensity is similar between the 6 tested jaw-muscle sites whereas significant differences could be detected in the perceived area of pain and quantitative measures of pain localization.

Perceived Pain Intensity

The sensitivity of different jaw muscles to painful stimuli has not previously been reported. Injection of hypertonic saline causes VAS_{peak} pain scores around 5 to 6 on a 0 to 10 VAS,[2,17] with no differences between the masseter and anterior temporalis muscles.[9] Numerous studies have assessed pressure-pain thresholds in various craniofacial muscles,[22–24] but these muscle sites have not been systematically examined because of practical difficulties in applying a pressure algometer on, for example, the lateral pterygoid muscle or anterior digastric muscle. Some studies have reported higher sensitivity to pressure in the masseter muscle compared with the anterior temporalis muscles,[25,26] but other studies have found either no differences or even the reverse relationship.[27] It could be speculated that the lateral pterygoid muscle would be more sensitive than the other jaw muscles since this muscle in particular has attracted a lot of attention in the pathophysiologic mechanisms of TMD pain. However, there were

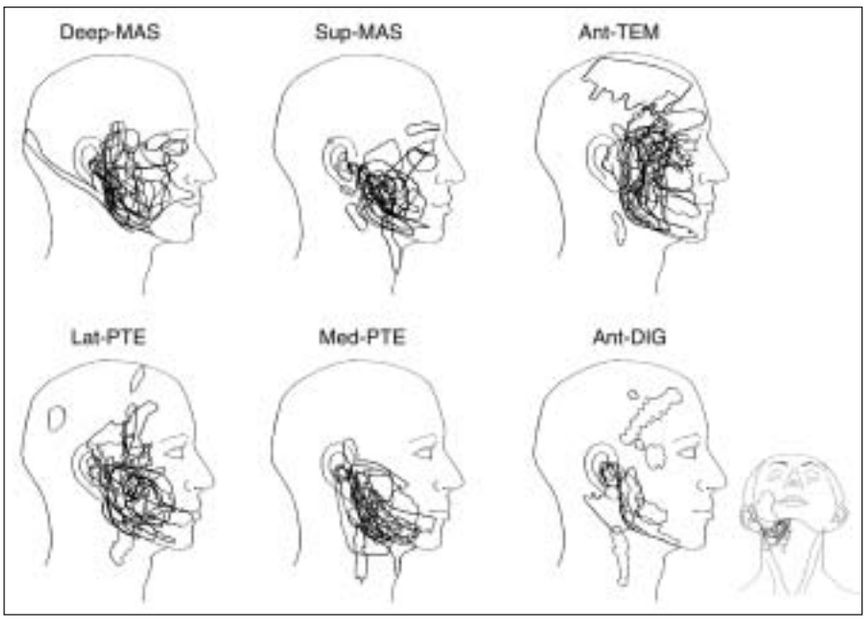

Fig 3 Subject-based, superimposed drawings (n = 15) of perceived pain in external areas following injection of hypertonic saline into 6 jaw-muscle sites. Deep-MAS = deep layers of masseter, Sup-MAS = superficial layers of masseter, Ant-TEM = anterior temporalis, Lat-PTE = lateral pterygoid, Med-PTE = medial pterygoid, and Ant-DIG = anterior digastric muscle. Only 7 subjects marked pain on the lateral face drawing following Ant-DIG injections, and the small insert illustrates the pain on the preferred anatomical map.

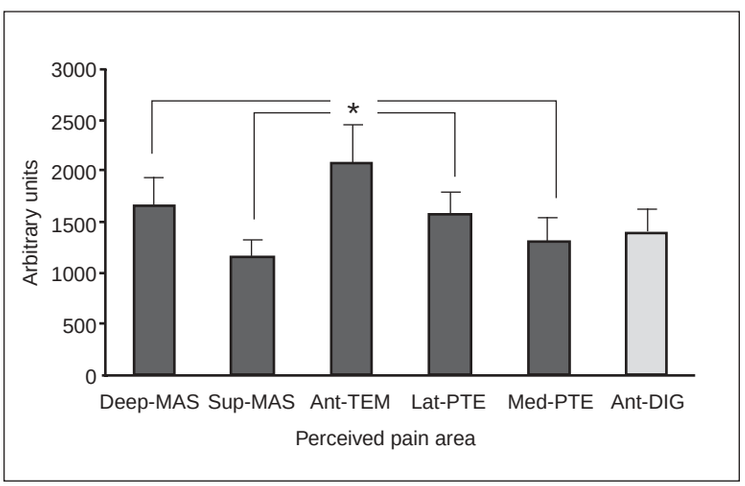

Fig 4 The pain drawings following injection of hypertonic saline into 6 jaw-muscle sites were digitized and the area calculated in arbitrary units. Deep-MAS = deep layers of masseter, Sup-MAS = superficial layers of masseter, Ant-TEM = anterior temporalis, Lat-PTE = lateral pterygoid, Med-PTE = medial pterygoid, and Ant-DIG = anterior digastric muscle. Mean values ± SEM (n = 15) except for Ant-DIG (n = 7). *Indicates significant difference between pain areas (Tukey: $P < .05$).

Table 3 Center-of-Gravity Measurements of the Pain Drawings from 15 Subjects (mean ± SEM)

	X-coordinate	Y-coordinate	Vector length
Deep masseter	7.4 ± 0.4	8.2 ± 0.1	11.1 ± 0.2
Superficial masseter	8.2 ± 0.2	7.7 ± 0.2	11.3 ± 0.3
Anterior temporalis	8.1 ± 0.2	9.5 ± 0.4	12.5 ± 0.3
Lateral pterygoid	8.1 ± 0.2	7.7 ± 0.6	11.3 ± 0.3
Medial pterygoid	7.4 ± 0.4	6.8 ± 0.4	10.2 ± 0.3
Anterior digastric*	7.3 ± 0.4	7.3 ± 0.5	10.4 ± 0.4
ANOVA	$P = .056$	$P < .001$	$P < .001$

*n = 7.

Table 4 Details on Referral of Pain to Intraoral Structures Following Injection of Hypertonic Saline into 6 Jaw-Muscle Sites in 15 Subjects. Frequencies (%) of Responses Where Pain was Indicated in the Teeth and Gingiva

	Deep-MAS	Sup-MAS	Ant-TEM	Lat-PTE	Med-PTE	Ant-DIG
Teeth						
Molar						
Maxilla	7	33	13	27	27	7
Mandible	0	27	20	20	33	33
Premolar						
Maxilla	0	13	7	0	0	7
Mandible	0	13	0	13	13	13
Front						
Maxilla	0	0	7	0	0	0
Mandible	0	0	0	0	0	7
Gingiva						
Molar						
Maxilla	33	27	33	33	27	7
Mandible	7	20	7	20	27	27
Premolar						
Maxilla	13	13	0	13	13	7
Mandible	0	7	7	13	20	13
Front						
Maxilla	0	0	0	0	7	7
Mandible	0	0	0	0	0	7

Deep-MAS = deep layers of masseter, Sup-MAS = superficial layers of masseter, Ant-TEM = anterior temporalis, Lat-PTE = lateral pterygoid, Med-PTE = medial pterygoid, and Ant-DIG = anterior digastric muscle.

no indications in the present study that painful injections of hypertonic saline into the lateral pterygoid muscle produced higher VAS pain scores or larger and more frequent areas of pain than similar injections into other jaw-muscle sites. A recent study suggested discarding palpation of the lateral pterygoid muscle due to lack of validity and reliability.[28] Thus, there appears to be little evidence to support the notion that the lateral pterygoid muscle should be more likely to become painful although the physiology and function of this heterogenous muscle remain intriguing and highly complex.[29] It is interesting to note that although there is no clear evidence to support a differential sensitivity of jaw muscles to painful stimuli, studies with intramuscular electrical stimulation[30] or with palpometers[31] may be useful quantitative techniques to further examine this question. Information on differential sensitivity of jaw muscles will be useful for guidelines related to palpation procedures.

In the present study only women were studied because the majority of patients in the TMD clinic are women.[15] It was not the purpose of the study to examine gender differences in deep pain sensitivity (this topic has recently been studied and discussed).[16,32,33] Women were not examined in a particular phase of their menstrual cycle and women taking/not taking oral contraceptives were included. Recent studies have indicated significant, although minor, differences in deep pain sensitivity across the menstrual cycle,[24,34–36] but there may

still be debate with respect to which specific phase is the most sensitive.[37] The authors cannot exclude the possibility that there might have been a fluctuation in deep pain sensitivity during the course of this 3-week study and that such differences could have cancelled out differences in pain sensitivity between the different jaw-muscle sites. However, additional analysis of the women on oral contraceptives and those who did not take oral contraceptives did not indicate significant effects in accordance with a recent study.[33] Furthermore, the sequence of injections was randomized and no significant effects could be detected. Thus, we do not believe that the lack of differences in VAS pain scores is due to confounding effects of menstrual cycle and oral contraceptive use.

The MPQ could not differentiate between pain in the different jaw-muscle sites, and there appeared to be no specific word for any of the jaw muscles (Table 2). The family of words used to describe the hypertonic saline-evoked pain sensation in the jaw muscles was in accordance with previous descriptions of both experimental and clinical jaw-muscle pain,[2,10,12,38,39] except that "cramping" pain seldom is chosen in our experience.[12] It is also noteworthy that the prevalence of the word "spreading" (13% to 47%) did not match the occurrence of referred pains (40% to 87%) well. However, the prevalence of words from the entire group 17 in the MPQ (spreading, radiating, penetrating, and piercing) ranged from 33% to 67%, and better indicated pain outside the site of injection, ie, referred pain.

Pain Distribution

Few studies have attempted to quantify the pain maps or drawings. Usually, pain maps are inspected visually and described qualitatively to report the frequency of patients or subjects with pain referred to different anatomical regions. Superimposition of pain drawings will help to visualize common and rare patterns of referral.[6] One study superimposed a 5 mm grid on lateral pain drawings and recorded the coordinates of the pain pattern. This was followed by construction of similarity matrices, which provided the degree of similarity of an individual pain distribution compared with all others. The groups of closely related individuals were extracted by a cluster analysis technique. With this technique, Gray et al[40] were able to discriminate 77.5% of patients with craniofacial pain complaints into 5 discrete groups based on their pain drawings. Türp et al[38] also applied a grid system to pain maps of the entire body and recorded the number of involved squares in relation to the maximum number of squares in different anatomical regions. These authors noted 3 clusters of patients with craniofacial pain complaints: 37/200 patients only marked pain in the trigeminal innervated regions; 32/200 reported pain in the trigeminal dermatomes and one or more of the spinal C2-C4 dermatomes; and finally 131/200 patients had pain involving other dermatomes in addition to the trigeminal or C2-C4 dermatomes. Thus, application of grids on pain drawings is a simple and useful technique to analyze the distribution and frequency of pain maps.

Another way to quantify pain maps has been to digitize the area with commercially available systems. With this technique, it has been possible to demonstrate a significant increase in the area of perceived pain during continued infusion of hypertonic saline.[41] Furthermore, myofascial TMD patients,[42] chronic whiplash patients,[43] and fibromyalgia patients[44] all have larger pain areas compared with matched control subjects in response to painful injections of hypertonic saline. Moreover, women have recently been demonstrated to have larger pain areas following injection of glutamate compared with men.[32] The present study showed that the perceived pain area differed between the 6 jaw-muscle sites. Pain in the anterior temporalis muscle was associated with significantly larger pain maps and this was unrelated to the perceived pain intensity. In fact, no significant relationship between perceived pain area and pain intensity was observed in the present study in contrast to a previous study performed on the leg where the intensity of electrically evoked muscle pain was significantly correlated with the areas of referred pain.[30] The reason for the lack of correlation between pain intensity and area of pain in the present trigeminal study is not known but could be due to a relatively small variation in VAS pain scores or differences between spinal and trigeminal processing of nociceptive information. Nevertheless, measurement of pain areas seems to be a sufficiently sensitive method to provide useful information on the characteristics of basic and clinical muscle pain.

No studies have so far employed a COG method to pain maps, which is a well–described technique to quantify cortical maps of motor-evoked potentials.[21] The advantage with the COG method is the localization of a characteristic point described by coordinates. In addition, the length of the vector can be used as a quantitative measure. This method is sensitive to detect subtle shifts in maps of motor-evoked potentials.[45] Also in the present study with pain maps, the COG method was sensitive enough

to discriminate between the spread of pain from different jaw-muscle sites. It can be seen that the calculated coordinates for the 2 masseter injections (Table 3) corresponded very closely to the actual sites of injections (Fig 1), whereas injection into the anterior temporalis muscle (approximate coordinates of the injection point: X = 9, Y = 11) was associated with pain maps in a more inferior region (Table 3). However, it is clear that there are inherent limitations with this 2-dimensional method since the location of deep pain is a 3-dimensional problem. In fact, this raises the fundamental question of how accurate surface pain maps can reflect projections of pain from deep structures and deeply located muscles, such as the lateral pterygoid muscle. Three-dimensional maps would probably be more correct but too complicated to use, and therefore there is no solution to this problem at the moment. However, pain maps still provide useful, although incomplete, information on the distribution of deep pain. The presented COG method is suggested to be an improvement on the existing techniques and could be used to obtain clinically meaningful information on the pain distribution in tension-type headache patients versus myofascial TMD patients.

Mechanisms Underlying Referral and Spread of Jaw-Muscle Pain

Referred pain is probably a combination of central processing and peripheral input as it is possible to induce referred pain to limbs with complete sensory loss due to an anesthetic block.[30] However, the importance of peripheral input from the referred pain area is not clear, as anesthetizing this area shows inhibitory or no effects on the referred pain intensity.[46] Central sensitization of wide-dynamic-range and nociceptive-specific neurons may be involved in the generation of referred pain.[47] Animal studies have clearly shown a development of new and/or expansion of existing receptive fields by a deep noxious stimulus.[48,49] For example, recordings from dorsal horn neurons with receptive fields located in the biceps femoris muscle show new receptive fields in the anterior tibialis muscle and on the foot after intramuscular injection of bradykinin into the anterior tibialis muscle.[48] Furthermore, unmasking of new receptive fields due to central sensitization could mediate referred pain.[50] This has been suggested to be the phenomenon of secondary hyperalgesia in deep tissue. Plasticity of the central nervous system may also alter somatosensory sensitivity and may contribute to deep tissue hyperalgesia, eg, increased responses to palpation of the muscle.

In conclusion, the present study has systematically examined the perceived pain intensity and pain maps following injection of hypertonic saline into 6 different jaw-muscle sites. No differences were observed for the VAS pain scores or the description of pain on MPQ, but the pain maps associated with pain in the anterior temporalis muscle were significantly larger compared with all other jaw muscles. Finally, a new COG analysis of the pain maps was able to quantify and discriminate the location of these maps. Knowledge of spread and referral patterns is useful in the clinic to diagnose TMD and craniofacial pain disorders.

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