Experimental Jaw-Muscle Pain Has a Differential Effect on Different Jaw Movement Tasks

Daraporn Sae-Lee, DDS, PhD, MSc
Postgraduate Student

Terry Whittle, BSocSci
Research and Education Officer

Chris C. Peck, PhD, MSc, BDS
Associate Professor

Anna R. C. Forte, BSc
Research Assistant

Iven J. Klineberg, PhD, MDS, BDS
Professor of Prosthodontics

Greg M. Murray, PhD, MDS, BDS
Professor

Jaw Function and Orofacial Pain Research Unit
Faculty of Dentistry, University of Sydney
Westmead Hospital Centre for Oral Health
Westmead, Australia

Correspondence to:
Dr Greg M. Murray
Jaw Function and Orofacial Pain Research Unit
Faculty of Dentistry, University of Sydney
Professorial Unit, Level 3
Westmead Hospital Centre for Oral Health
Westmead NSW 2145
Australia
Fax: +61 2 9633 2893
E-mail: gregm@usyd.edu.au

Aims: *To determine the effects of experimental jaw-muscle pain on jaw movements.* ***Methods:*** *Mandibular mid-incisor point was tracked in 22 asymptomatic subjects during standardized (at 2.2 mm/s) protrusion, contralateral excursion, and open jaw movements, as well as free, right-sided chewing and chewing standardized for timing (900 ms/cycle). Tonic infusion of 4.5% hypertonic saline into the right masseter muscle maintained pain intensity between 30 and 60 mm on a 100-mm visual analog scale. Subjects performed tasks in 3 sessions on the same experimental day: control condition (baseline trials), test condition 1 (during hypertonic or 0.9% isotonic saline infusion), and test condition 2 (during isotonic or hypertonic saline infusion).* ***Results:*** *In comparison with control, there were no significant effects of hypertonic saline infusion on amplitude or velocity for protrusion or contralateral jaw movements or on velocity for jaw opening. Jaw-opening amplitude was significantly smaller in comparison with control during hypertonic, but not isotonic, saline infusion. During free but not standardized chewing, subjects chewed faster and exhibited larger amplitude gapes during hypertonic and isotonic infusion in comparison with control. Therefore, it was unlikely that pain had an effect on the kinematic parameters of jaw movement during free chewing. Qualitatively, individual subject data revealed considerable variability in the effects of hypertonic saline on movement parameters, which suggests that the effect of pain on jaw movement may not be uniform between individuals.* ***Conclusions:*** *The data indicate that the effect of pain on jaw movement may vary with the task performed.* J OROFAC PAIN 2008;22:15–29

Key words: chewing, experimental pain, hypertonic saline, jaw movement, Pain Adaptation Model

Temporomandibular disorders (TMD) are the most prominent chronic pain condition in the orofacial area.[1–3] Although a common symptom of TMD is limitation of jaw movement, the precise relationship between orofacial pain and jaw motor behavior is unclear. The Pain Adaptation Model is generally considered the most appropriate explanation of this relationship. As applied to the jaw motor system, the model proposes that pain leads to alterations in jaw-muscle activity that lead to a reduction in the amplitude and velocity of jaw movement, and that these changes represent a functional, adaptive response to protect the jaw system from further injury and thereby promote healing.[4–6]

In general, the findings from many human experimental and clinical muscle pain studies lend support to the Pain Adaptation Model.[4,5,7–13] For example, reductions in the amplitude and veloc-

ity of movement in comparison with pain-free individuals have been observed in several chronic musculoskeletal pain conditions, including chronic low-back pain patients[11,14] and TMD patients,[15,16] as well as in several human experimental pain studies of gait,[14,17] trunk movement,[18] and mastication.[4,19] These findings are also in agreement with the findings of some animal studies of the effects of noxious stimuli on rhythmic masticatory movements.[20,21]

However, the effects reported in some of these studies of the relationship between pain and jaw motor behavior do not always appear consistent with some aspects of motor behavior suggested by the model.[6,9,22–25] For example, in well-studied experimental rat models of temporomandibular joint (TMJ) pain, short-duration, robust and simultaneous increases in electromyographic (EMG) activity in *both* jaw-opening and jaw-closing muscles are routinely observed following injection of algesic chemicals, eg, mustard oil or glutamate, into the TMJ[26–29] or jaw muscles.[30] These changes in EMG activity do not appear entirely consistent with the Pain Adaptation Model. Further, Svensson et al[9] did not find a significant effect of experimental jaw-muscle pain on the maximum amplitudes of jaw movements during mastication, while Madeleine et al[24] found that the amplitude of arm and trunk movements tended to increase after hypertonic saline infusion. One explanation for this lack of consistency between studies is that the Pain Adaptation Model may not be generally applicable to all types of movements. Indeed, there is some suggestive evidence in the literature that the nature of the task being performed influences the effects of pain on the motor system.[8,11] Studies have identified reductions in protrusive and lateral excursion with hypertonic saline injections[31] or changes in lateral excursions but not speech and masticatory movements in TMD patients.[32] However, while Dworkin et al[15] identified clear changes in the maximum voluntary jaw opening in TMD patients, changes that were significantly smaller than those observed for control subjects, pain had no effect on maximum lateral and protrusive movements. Despite this variability between studies, it is possible that the effect of pain on movement may be influenced by the nature of the task being performed. A recent comprehensive review of chronic lower back pain and trunk motor activity[11] identified changes in EMG activity that appeared tuned to the mechanical circumstances, or in other words, to the task at hand.

Another reason for the lack of consistency between studies as to the effects of pain on motor activity may relate to the variability between humans in the experience of, and the response to, noxious stimuli. Standardized noxious stimuli are associated with considerable interindividual variability in the subjectively described pain boundaries (ie, pain maps), visual analog scale (VAS) scores, affective qualities, sensitivity to analgesics, pain thresholds, pain tolerance levels, and placebo effects.[33–37] Given the close interrelationships between the sensory, motor, and limbic systems (affective and cognitive influences),[38,39] it is likely that individuals will vary considerably in the reaction of their motor systems to pain. This has been raised as a possible reason for the variability in the motor response to experimental trunk muscle pain[40] and to clinical low back pain.[11]

There is only limited data of the effects of orofacial pain on jaw movements in humans, and this information has been obtained in subjects/patients performing only a few jaw movement tasks. It is proposed that an analysis of the effects of orofacial pain on a broader range of tasks would provide greater insight into the effects of pain on the motor system. It is not known, for example, how the jaw motor system functions under pain where the subject is motivated to achieve the same jaw kinematic parameters during pain as during the pain-free condition, eg, to produce clearly articulated speech in demanding work situations. Therefore, the general aim of the present study was to determine the effects of experimental jaw-muscle pain on jaw movements. It was hypothesized that the effects of pain on jaw movement vary with the task performed. To address this hypothesis, the specific aim was to determine whether experimental pain in the right masseter muscle changes the ability to move the jaw to perform standardized jaw tasks in terms of amplitude and velocity.

Materials and Methods

Twenty-two subjects without signs or symptoms of TMD were recruited for this study (age, 22 to 42 years; 13 male, 9 female). All subjects gave their informed consent. Experimental procedures were approved by the Western Sydney Area Health Service Human Ethics Committee of Westmead Hospital and the Human Ethics Committee of the University of Sydney. Some of the procedures have been described in detail previously.[41–43]

Jaw Movement Recording and Visual Feedback

An optoelectronic jaw-tracking system (JAWS3D, Metropoly, Switzerland) recorded the movement of

the mandible in 6 degrees of freedom (sampling rate: 67 Hz).[44] The movement of the mid-incisor point, ie, the point between the incisal edges of the mandibular central incisors, was displayed as a moving dot on a video screen in front of the subject and provided visual feedback for the subject in tracking a computer-controlled target. This target consisted of a linear bank of light-emitting diodes (LEDs) that was placed to the side of the trajectory of mid-incisor point movement in the axis in which the jaw predominantly moved. These LEDs were illuminated in sequence and were the target for jaw tracking. Custom-made metal clutches, temporarily attached to 2 to 3 maxillary and mandibular anterior teeth, supported the target frames of the tracking system. EMG electrodes also recorded from selected jaw muscles; the data will be reported in a separate paper.

Standardized Jaw Tasks

Recordings of jaw movement were made during each of the following jaw tasks, which were performed by each subject in the following sequence:

1. Postural jaw position (2 recordings of ~15 seconds each).
2. Horizontal jaw movement and vertical jaw movement tasks, ie, protrusion, contralateral (ie, in a direction opposite to the side of the JAWS3D target frames and therefore in a leftward direction), and open/close jaw movements. Each of these 3 tasks was repeated 5 times, with a rest period of 30 seconds between each trial, and the tasks were performed in the following sequence: contralateral, protrusion, open/close.
3. Unilateral chewing of gum, which involved keeping the softened gum on the side ipsilateral to the infused masseter muscle during natural chewing (nonstandardized chewing) or during chewing in time with a computer-controlled target (standardized chewing). Three trials of nonstandardized chewing and 3 trials of standardized chewing were performed. The duration for each chewing trial was approximately 15 seconds and consisted of a sequence of 10 to 15 chewing cycles.
4. A maximum jaw clench (3 trials of 3 seconds separated by 2- to 3-second rest periods) in intercuspal position by biting on cotton rolls between molars bilaterally.

Standardization of horizontal and vertical jaw movements was achieved by having the subject move the position of the mid-incisor point marker on the screen to track the target LEDs as closely and smoothly as possible. After a period of 2 seconds at postural jaw position, each subject moved the mandible outward at 2.2 mm/s (ie, anteriorly for protrusion, left laterally for contralateral movement, downward during opening) following the sequentially illuminated LEDs (outgoing phase). The subject held the jaw steadily at the specified target position for 3 to 5 seconds (holding phase) before returning to postural jaw position (returning phase). The subject was required to track the target by moving the dot within the boundary of the LED, corresponding to the required displacement.

For the chewing tasks, the subject softened chewing gum (0.14 g) for 30 seconds by chewing on the left side. During the recordings, the subject was asked to chew only on the right side as naturally as possible and, in another sequence, to follow the time and speed of the target LED, which was adjusted to 900 ms/chewing cycle. The task was standardized for timing but not amplitude.[45]

Induction and Assessment of Jaw-Muscle Pain

Experimental jaw-muscle pain was induced by tonic infusion of 4.5% hypertonic saline (Pharmalab, Lane Cove, NSW, Australia) into the right masseter. A bolus infusion of 0.2 mL hypertonic saline (or isotonic saline, 0.9% NaCl; solution was randomly assigned) was infused over 20 seconds in most subjects to rapidly achieve the target pain intensity of between 30 to 60 mm as measured on a VAS. A continuous infusion was maintained by an infusion pump (IVAC Model P2000, UK) with a steady infusion rate of 6 to 9 mL/h[9] for ~ 20 minutes. Pain intensity was quantified, prior to the experiment and after each jaw task trial, with a 100-mm VAS with anchors of zero denoting "no pain at all" and 100 mm denoting "the worst imaginable pain." Manual changes in infusion rate were made in steps of 3 mL/h to maintain pain intensity at a constant level of 30 to 60 mm on the VAS.[9] In some subjects, it was necessary to change the infusion rate to > 9 mL/h or < 6 mL/h to achieve this pain range. After each trial, each subject mapped the pain location and perceived distribution on lateral-profile outline pictures of the head and neck. Pain affect was quantified with the McGill Pain Questionnaire (MPQ) after each infusion was terminated.

Jaw movement trajectories and EMG activity were recorded during all of the aforementioned tasks in a repeated-measures design as follows:

1. Control (without any infusion, defined as a baseline trial)
2. Test 1 (during hypertonic or isotonic saline infusion)
3. Test 2 (during isotonic or hypertonic saline infusion)

All trials were performed on a single experimental day in a single sitting. The infusion of isotonic saline was used as a control in 17 of the 22 subjects. The data from only 16 were analyzed for possible EMG and/or jaw-movement effects from volumetric change within the muscle. The rate was set between 6 and 9 mL/h as previously discussed; this rate was modified to match the rate of a previous hypertonic infusion in that subject. The mean total infused solution (ie, 0.2 mL bolus volume plus continuous infusion volume) was not significantly different for hypertonic versus isotonic saline (2.3 ± 0.9 mL versus 2.5 ± 0.5 mL; paired *t* test, $P = .128$). The total amount of infused hypertonic saline used to achieve a constant pain intensity of 30 to 60 mm on a 100-mm VAS varied widely (0.4 mL to 4.2 mL). There was no significant difference (*t* test, $P > .05$) between the volume of hypertonic saline infused in the male subjects (2.5 ± 0.9 mL, n = 9) and the volume infused in the female subjects (2.0 ± 0.8, n = 8); only some tasks were performed in the remaining 5 of the 22 subjects. Consistent with previous reports,[10,46,47] no complications were reported, and the pain usually subsided within a few minutes after the infusion was terminated.

Data Analysis

For each jaw task in each subject, the mid-incisor point trajectories in the axis in which the jaw predominantly moved were plotted as time-displacement plots, and 5 trials of data were superimposed. The axis chosen varied with the individual jaw task, ie, x-axis (anterior-posterior) for protrusion, y-axis (mediolateral) for contralateral movement, and z-axis (superior-inferior) for open/close movement and chewing cycles. The trajectories of mid-incisor-point jaw movements for protrusion, contralateral, and open/close movements were superimposed for each jaw task for control and experimental conditions in each subject for qualitative analyses. The kinematic parameters, ie, amplitude and velocity of each jaw movement trial, were calculated for the entire outgoing phase in each subject performing the different standardized jaw tasks during control and during infusion of hypertonic and isotonic saline trials.

A customized computer program identified, for the outgoing phase of each trial of movement, the onset of mid-incisor point movement as the time at which the mid-incisor point had displaced 0.5 mm from the postural jaw position. This software also identified the offset of jaw movement as the last 0.5 mm of movement before the subject held the jaw steady at the holding phase (for the horizontal and jaw-opening tasks), or the last 0.5 mm of opening movement before jaw closing (for the chewing tasks). The amplitude of movement was calculated as the maximum displacement of the jaw between the onset and offset of jaw movement along the x-axis (anterior-posterior) for protrusion, y-axis (mediolateral) for the contralateral task, and along the z-axis (superior-inferior) for jaw opening and chewing tasks. The velocity was then calculated by dividing the amplitude by the time between onset and offset. The effect of hypertonic saline or isotonic saline infusion on the mean amplitude and velocity of each jaw movement was statistically compared with the control baseline trials across all subjects with a repeated-measures analysis of variance (ANOVA); as the data were not complete for all subjects, the repeated-measures ANOVA tests were done on fewer than 22 subjects.

For analysis of chewing cycles, unwanted chewing strokes, identified as those displaying highly irregular jaw trajectories during jaw opening and closing, were rejected, as were the first and the last strokes of each chewing sequence. The amplitude and velocity for the opening phase of each chewing cycle were calculated as for the other jaw tasks. The period between each onset of jaw opening within a chewing sequence was defined as a masticatory cycle. The duration of each masticatory cycle and the duration of the opening phase of each cycle were then recorded. Statistical tests for pain intensity involved paired-samples *t* tests, and univariate ANOVA using mean scores across all trials within a movement; statistical significance was established at $P < .05$. For the horizontal and vertical jaw movement tasks and for chewing, analyses of possible differences in parameters between male and female subjects were evaluated with *t* tests.

Results

Subjective Description of Experimental Jaw-Muscle Pain

Infused Volumes and Pain Intensity. The 16 subjects who had been infused with both solutions and accomplished all jaw tasks experienced signifi-

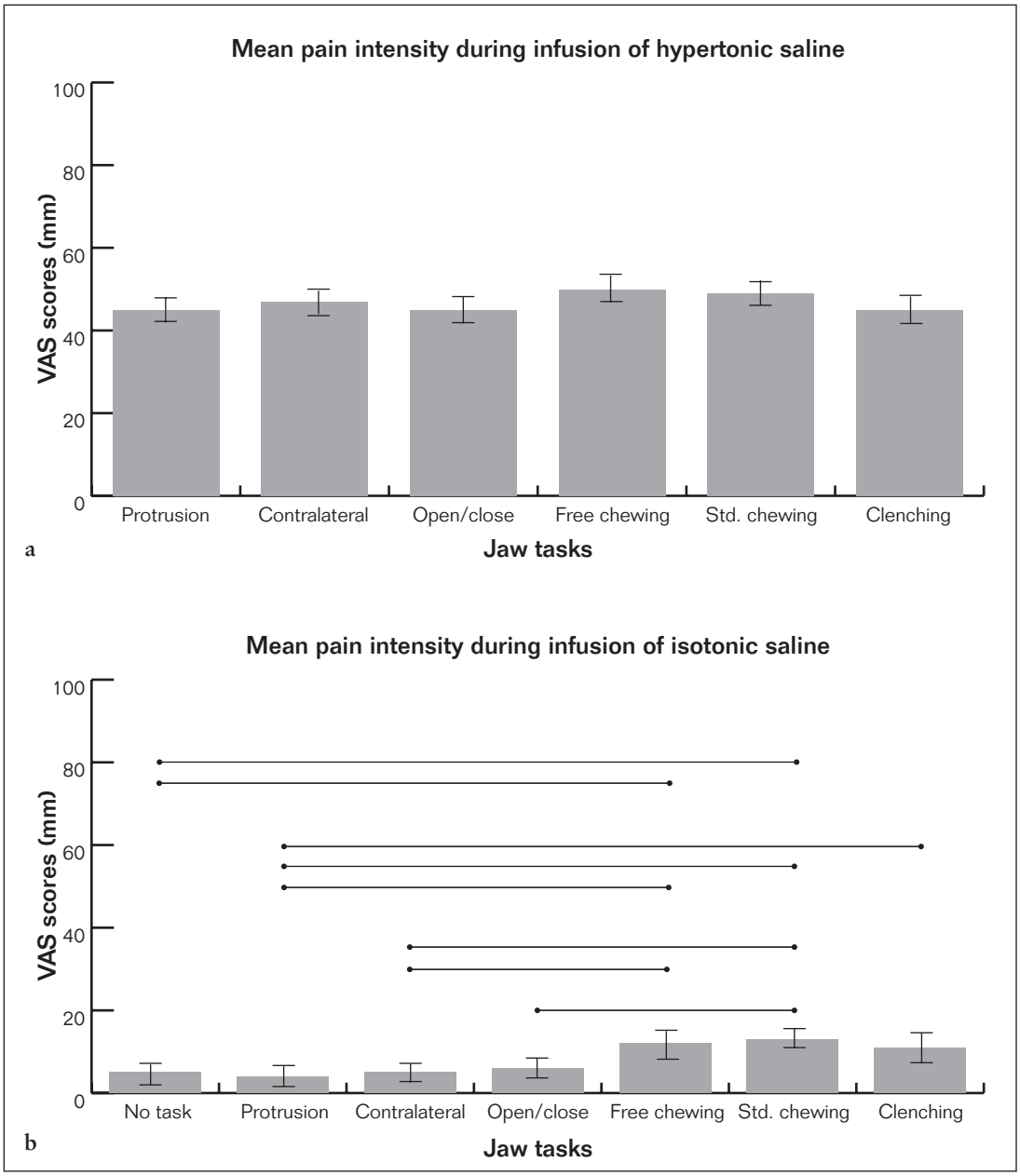

Fig 1 VAS scores across all subjects during infusion of *(a)* hypertonic saline and *(b)* isotonic saline, estimated after each subject performed each jaw task. Error bars indicate SEM. The dots and continuous lines *(b)* indicate significant differences for the mean VAS values between tasks. The data for 1 subject (S7) were excluded from this analysis because of the great variation of the subject's VAS scores. Std. = standardized.

cantly more pain (paired-samples *t* test, t(15) = 9.094, $P < .001$) during infusion of hypertonic saline (mean ± SD, VAS 47.3 ± 14.3 mm; SEM: 3.6) than during infusion of isotonic saline (12.2 ± 17.3 mm; SEM: 4.3).There was no significant main effect for the jaw tasks performed on the mean VAS scores during hypertonic saline infusion (univariate analysis of variance, F[5,115] = 0.486, $P = .786$; Fig 1). During isotonic saline infusion, there was a significant main effect for the tasks on the mean VAS scores (F[6,106] = 2.704, $P < .05$), with the VAS scores under no task (jaw was in the rest or postural jaw position), protrusion, or contralateral task being significantly lower than those under free chewing and standardized chewing, as examples of high levels of jaw-closing activity (Fig 1). Clench was also associated with high jaw-closing activity, but the VAS scores during protrusion were the only scores to be significantly different from those during clench.

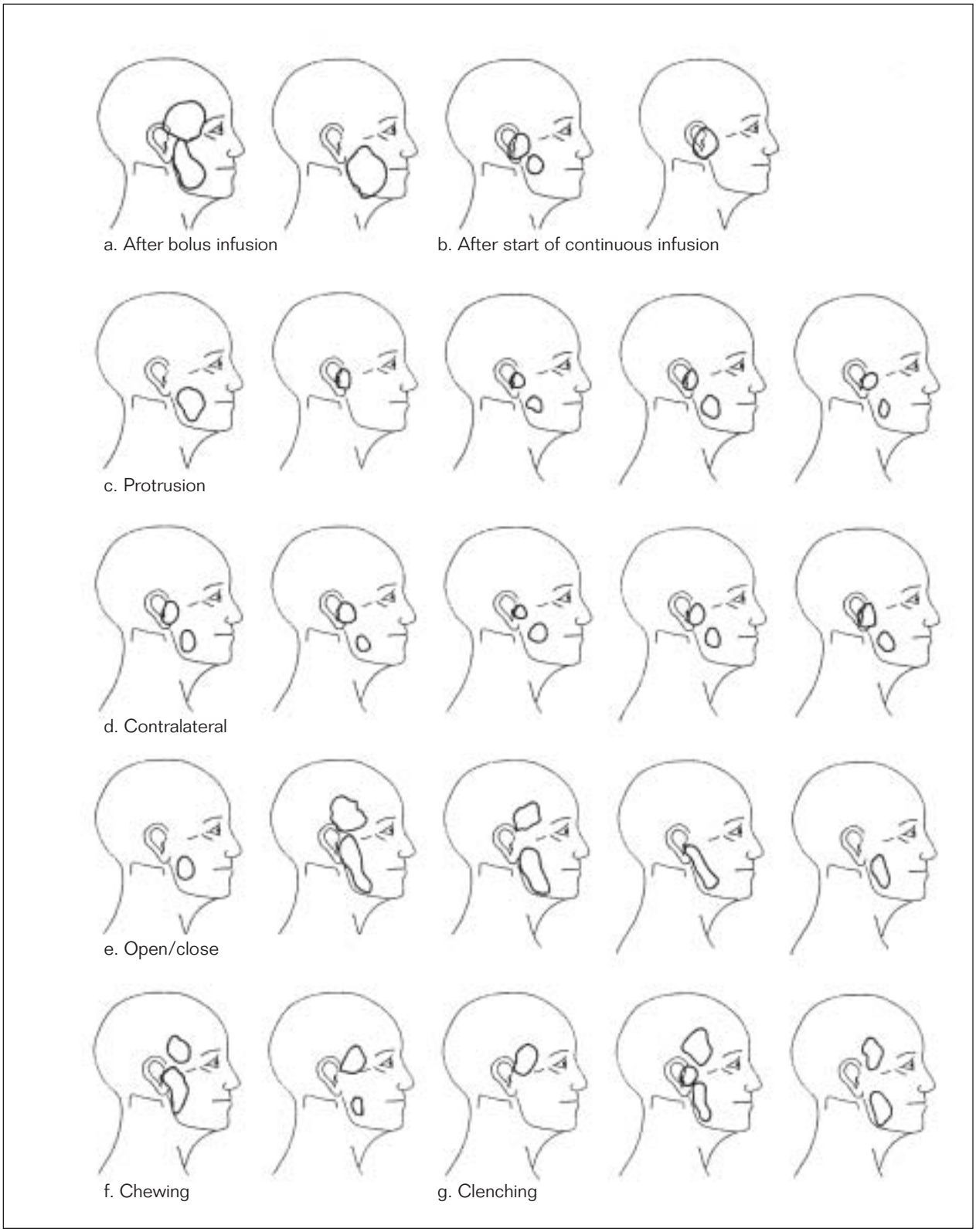

Fig 2 Representative data from 1 subject (S3) showing the original pain mappings after this subject performed each jaw task trial *(a through g)* during hypertonic saline infusion. A pain map was recorded at 30 seconds and 1 minute after *(a)* commencement of bolus infusion and *(b)* continuous infusion.

Table 1 The Mean PRI, Present Pain Intensity (PPI), and Number of Words Chosen on the MPQ During Infusion of Hypertonic and Isotonic Saline

McGill Pain	Hypertonic saline (n = 22)		Isotonic saline (n = 17)		
	Rank score	Weight-rank score	Rank score	Weight-rank score	*P*
PRI-Sensory	8.68	7.98	4.71	4.51	< .05
PRI-Affective	1.55	2.68	0.29	0.52	< .05
PRI-Evaluative	1.55	1.47	0.71	0.71	NS
PRI-Miscellaneous	3.50	3.81	1.24	1.33	< .05
PRI-Total	15.28	15.94	6.95	7.07	< .05
PPI	3		1.41		< .05
No. of words chosen	5.95		3.18		< .05

NS = no significant difference between hypertonic saline and isotonic saline.

Table 2 Mean (± SD) Amplitude (mm) and Velocity (mm/s) Under Control Conditions and During Infusion of Hypertonic or Isotonic Saline for Standardized Protrusion, Contralateral, and Open/Close Jaw Movements

	Amplitude (mm)			Velocity (mm/s)		
	Control	Hypertonic	Isotonic	Control	Hypertonic	Isotonic
Protrusion (n = 17)	5.2 ± 1.5	5.1 ± 1.6	5.2 ± 1.6	3.1 ± 1.6	2.8 ± 1.1	2.8 ± 0.8
Contralateral (n = 16)	6.7 ± 2.4	6.6 ± 2.4	6.6 ± 2.0	2.1 ± 0.6	2.3 ± 0.7	2.3 ± 0.7
Open/close (n = 17)	21.9 ± 11.0	17.9 ± 8.9*	19.6 ± 8.6	4.2 ± 2.0	4.3 ± 2.5	4.3 ± 2.1

* $P < .05$ (significant difference between hypertonic and control).

Distribution of Jaw-Muscle Pain. Despite the standardized noxious stimulus, there was considerable variability between some subjects in the sensory-discriminative aspects of the pain experience. In all subjects, tonic infusion of hypertonic saline into the deep central region of the masseter caused localized pain, usually in the region of the right masseter muscle. In 7 subjects, this local pain was associated with a spread and/or referral of pain (eg, Fig 2) to the right TMJ (n = 5), along the lower border of the mandible (n = 3), or to more distant regions, including the right orbital (n = 2), submandibular (n = 1), temporal (n = 4), neck (n = 1), or intraoral regions (n = 1; eg, Fig 2). The spread and referral pattern of pain was usually quite consistent from task to task within a subject; however, 4 of the 7 subjects recorded larger pain areas, with some referred pain to the temporal region during jaw opening, chewing, and clenching, in comparison to that in protrusion and contralateral movements, eg, compare Figs 2e, 2f, and 2g with Figs 2c and 2d.

Description of Jaw Muscle Pain by MPQ. Significant pain rating index (PRI) differences between hypertonic saline and isotonic saline were detected for all the MPQ features but 1 (Table 1). During hypertonic saline infusion, "sharp" and "aching" were the most frequent sensory word descriptors; they were chosen by 36% and 32% of subjects, respectively. "Exhausting" and "fearful" were the most frequent affective word descriptors; they were chosen by 18% and 14% of subjects, respectively.

Jaw-Muscle Pain and Jaw Movements

Contralateral, Protrusion, and Open/Close Jaw Movements. Figure 3 demonstrates that there was qualitatively no effect of hypertonic or isotonic saline infusion on the mid-incisor point trajectories in representative subjects during protrusion (Fig 3a), contralateral jaw movement (Fig 3c), or open/close jaw movement (Fig 3e). The left-hand traces (Figs 3b, 3d, and 3f) show that the trajectories during hypertonic saline did not closely match those during control trials. Usually, isotonic saline did not have a marked effect on the mid-incisor point trajectories, eg, Figs 3c and 3d (right), and there were no obvious effects when all subjects were grouped, although effects during protrusion and open/close are shown in Figs 3b and 3f (right side).

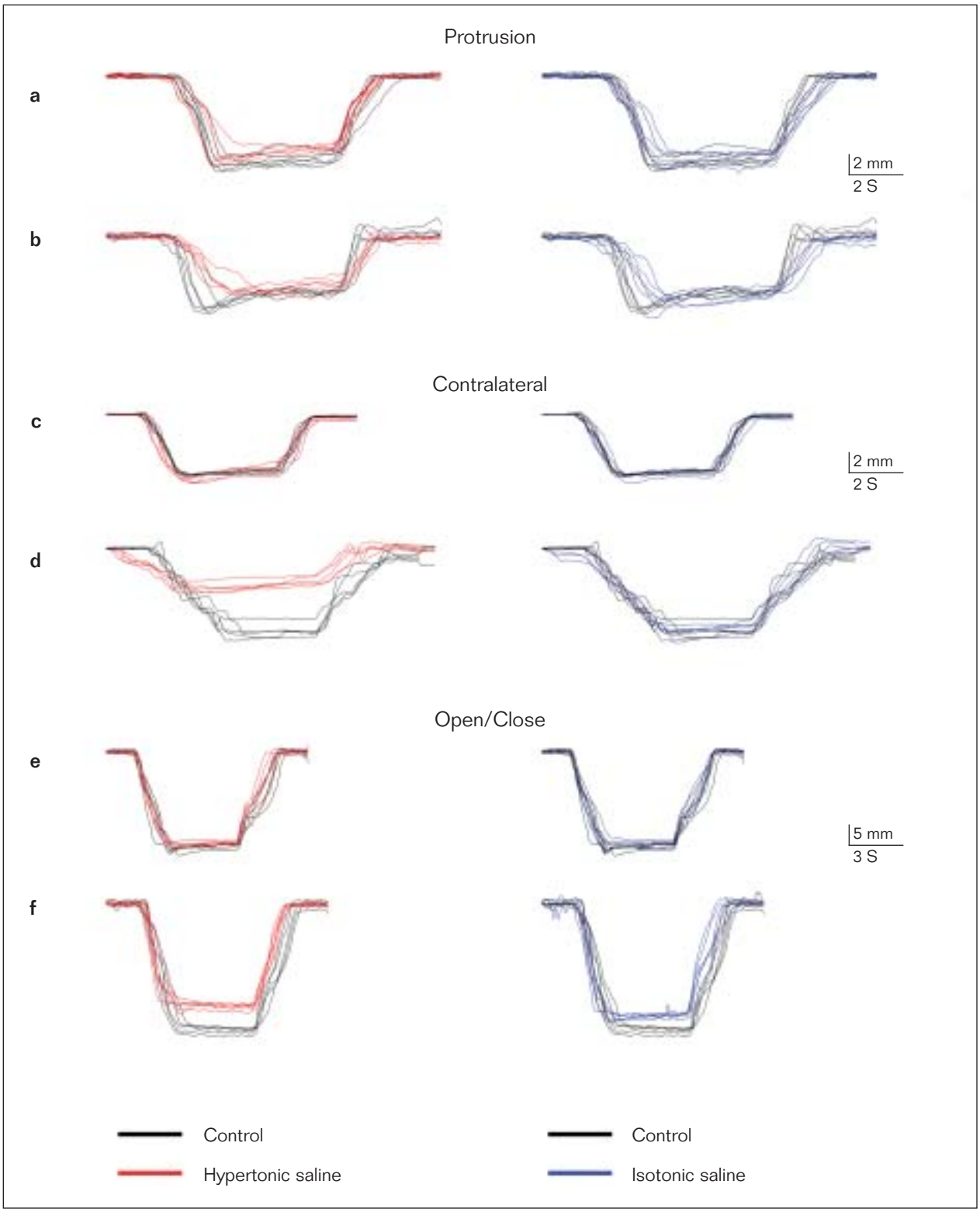

Fig 3 Examples of mid-incisor point displacement data for standardized protrusion *(a and b, plotted along the x-axis (anterior-posterior))*, for standardized contralateral movement *(c and d, y-axis (mediolateral))*, and for standardized open/close movement *(e and f, z-axis (superior-inferior))*. Five trials were superimposed from each experimental condition. Subjects a (S15), c (S16), and e (S18) showed similar jaw movements during control trials (black lines) as for trials during hypertonic saline infusion (red lines) and isotonic saline infusion (blue lines). The mid-incisor point displacement data from subjects b (S5), d (S5), and f (S10) did not show a close match between control and hypertonic or isotonic trials.

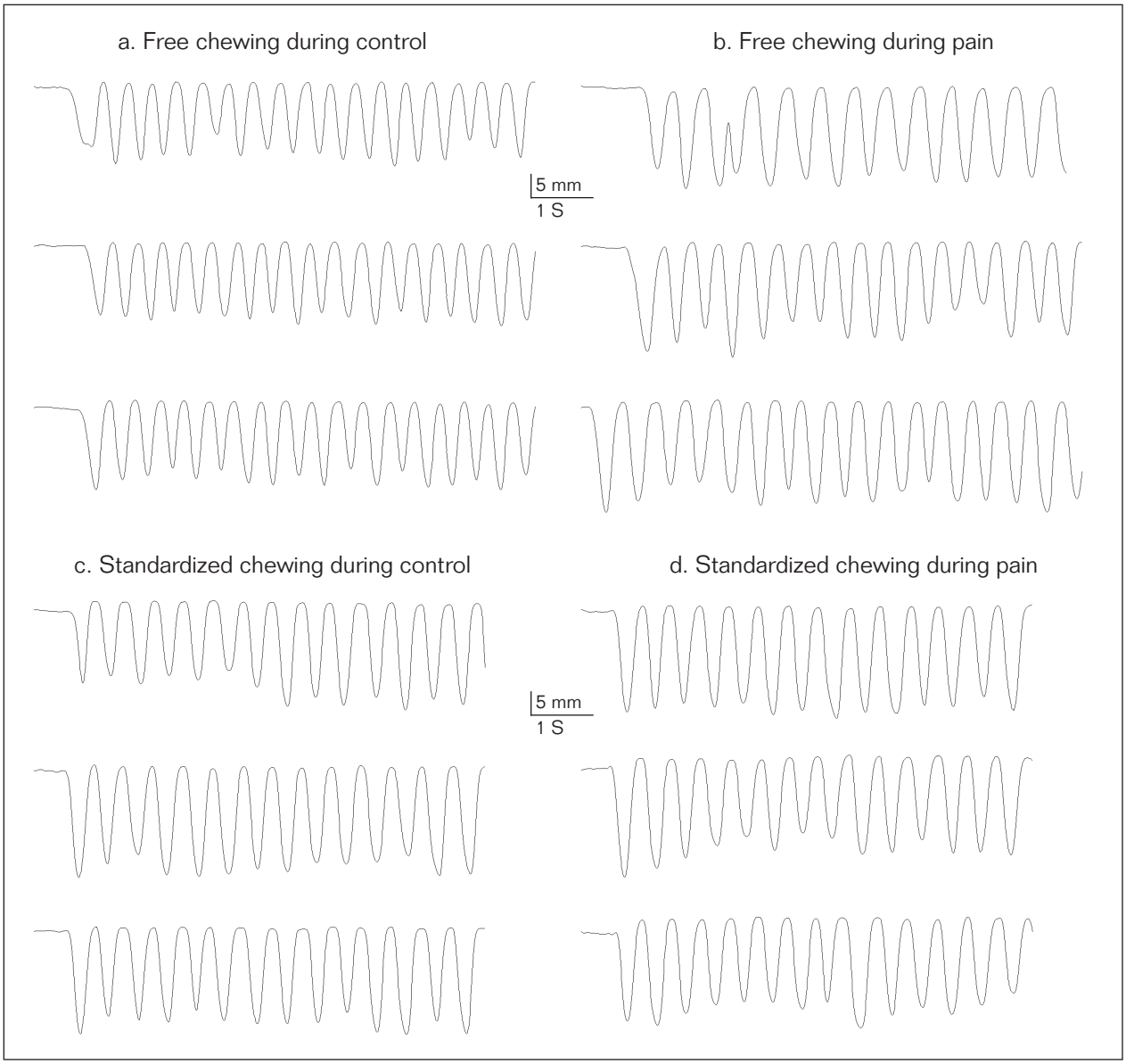

Fig 4 Example from 1 subject (S8) showing 3 trials of consecutive chewing cycles for free chewing during *(a)* control and *(b)* hypertonic-saline-induced pain trials. *(c and d)* Comparable data for standardized chewing.

There were no significant differences between hypertonic or isotonic saline infusion and the control trials for amplitude or velocity for protrusion or contralateral jaw movements or for velocity for open/close movement ($P > .05$, repeated-measures ANOVA; Table 2). However, the amplitude of the open/close jaw movement was significantly smaller during infusion of hypertonic saline ($F[2,16] = 5.477$, $P = .033$) in comparison with the control trials. Isotonic saline trials did not differ significantly from control or hypertonic trials.

There were no significant differences (*t* tests, $P > .05$) between male and female subjects for velocity or amplitude of contralateral, protrusion, or open/close jaw movements under control, isotonic, or hypertonic saline infusion conditions. For example, raw mean ± SD values for opening amplitude during control, isotonic, or hypertonic saline infusion conditions for all male subjects and all female subjects, respectively, were 25.0 ± 12.0 mm (n = 11) and 18.1 ± 8.7 mm (n = 9) under control conditions, 21.2 ± 8.9 mm (n = 8) and 18.2 ± 8.6 mm (n = 9) with isotonic saline, and 18.9 ± 9.3 mm (n = 11) and 16.6 ± 8.7 mm (n = 9) with hypertonic saline.

Table 3 The Mean (± SD) for the Kinematic Parameters During Free and Standardized Chewing Under Control, Hypertonic Saline–induced Pain, and Isotonic Saline Infusion for 16 Subjects

Parameter/condition	Free chewing			Standardized chewing		
	Mean ± SD	*P**	Pairwise	Mean ± SD	*P*	Pairwise
Amplitude (mm)						
Control	10.9 ± 2.5	< .001		14.4 ± 4.1	.297	A
Hypertonic	13.7 ± 3.3		A	15.0 ± 4.4		A
Isotonic	14.0 ± 3.6		A	15.5 ± 4.2		A
Duration open (ms)						
Control	456 ± 94	.06	A	482 ± 72	.240	A
Hypertonic	433 ± 84		AB	465 ± 88		AB
Isotonic	406 ± 70		B	459 ± 71		B
Velocity open (mm/s)						
Control	25.7 ± 9.2	< .001		31.4 ± 11.5	.124	A
Hypertonic	33.5 ± 11.3		A	33.6 ± 11.3		A
Isotonic	35.8 ± 10.8		A	35.4 ± 12.2		A
Duration total (ms)						
Control	887± 119	.002	B	944 ± 177	.442	A
Pain	852 ± 134		AB	923 ± 190		A
Isotonic	793 ± 107		A	924 ± 170		A

*ANOVA.
For each kinematic parameter (ie, amplitude, duration, velocity), values labeled with the same uppercase letter are not significantly different ($P > .05$, pairwise comparisons).

Standardized and Nonstandardized Chewing. Representative examples of 3 trials of consecutive free chewing cycles and standardized chewing cycles during control and hypertonic saline infusion trials in 1 subject are shown in Fig 4. The amplitude of the free chewing cycles under control conditions was smaller and appeared to be more consistent than during hypertonic saline infusion, while the amplitude of the standardized chewing cycles appeared comparable between control and hypertonic saline infusion trials. Average kinematic parameters from all chewing cycles in the 16 subjects for control and hypertonic saline or isotonic saline infusion trials show that subjects were likely to chew faster (shorter cycle durations, faster velocities during opening) and exhibit bigger gapes during hypertonic saline or isotonic saline (Table 3) infusion under free chewing in comparison with the control trial. There were no significant differences ($P > .05$) between any of the conditions for the kinematic parameters during standardized chewing (Table 3).

There were no significant differences (*t* tests, $P > .05$) between males and females for chewing cycle amplitude, duration of opening phase, or velocity of opening phase for free or standardized chewing under control, isotonic, or hypertonic saline infusion conditions, nor for total cycle duration under control or hypertonic saline conditions. The total cycle duration for free chewing (but not standardized chewing) under isotonic saline conditions was significantly lower ($P < .05$) in male subjects (737.3 ± 103.0 ms, n = 8) than in female subjects (848.3 ± 83.7 ms, n = 8).

Discussion

The findings of the present study show that experimentally induced pain rated at 30 to 60 mm on a 100-mm VAS scale through continuous infusion of 4.5% hypertonic saline into the right masseter muscle was not associated with a significant change in amplitude or velocity of jaw movement during standardized horizontal jaw movement tasks (ie, lateral excursion, protrusion). However, the pain was associated with a significant reduction in the amplitude of a voluntary jaw-opening movement, with no significant difference between control conditions and isotonic saline infusion. Although a significant increase in the amplitude and velocity of jaw opening during free chewing and a significant decrease in individual cycle duration and total duration of a free chewing sequence occurred during hypertonic saline infusion, the same significant effects were also observed during isotonic saline infusion, making it unlikely that pain had any effect on the kinematic parameters of

jaw movement during free chewing. During standardized chewing, no significant effects were observed. Qualitative analyses of individual subject data revealed considerable variability in the effects of pain on movement parameters.

Experimental Jaw-Muscle Pain Model

Pain Intensity. This standardized infusion paradigm provoked moderate pain intensity at an approximately steady level for about 20 minutes during the performance of the various tasks. The results of the present study were generally consistent with previous findings.[33,48–51] The wide range of infused volumes used to achieve a standard pain intensity range of 30 to 60 mm on a 100-mm VAS suggests that a standard noxious stimulus at the same muscle location will result in different pain intensities in different subjects.[34,52] The overall mean pain intensity across all subjects and jaw tasks (47.3) was slightly higher than that reported by Svensson et al[51] (mean ± SEM 33.5 ± 3.7) at 12 minutes after infusion commencement and was lower than that reported by Wang et al[50] (mean ± SEM 65 ± 5 mm). However, it was comparable with that reported by Stohler and Lund[48] (scores of about 40 mm). The variability of the VAS scores reported in the present study (ie, SEM: 3.6; SD: 14.3) was comparable to previous studies.[48,50,51] Infusion of isotonic saline (0.9% NaCl) caused little or no pain in most individuals, and this is also consistent with previous reports.[33,49,51]

The significantly higher VAS scores during chewing compared to scores during rest and horizontal jaw tasks probably reflects the higher intramuscular pressures during chewing than at rest, which may directly activate sensitized nociceptors[29,53] from the intramuscular electrode and catheter placements and isotonic saline infusion.[54] This most likely explains the higher pain scores during clenching, although these scores were significantly higher only than the protrusion VAS scores. Given that infusion rates were controlled to maintain pain levels, no significant task effect was noted on the VAS scores during hypertonic saline infusion.

Pain Maps and Qualitative Descriptors. The pain mappings showed a wide distribution of pain areas and referral patterns from an injection into the same general region of the masseter muscle across subjects. This variability is consistent in general terms with previous reports following hypertonic saline or glutamate injections into the jaw muscles[34,48,52,55] or limb muscles[46,49] and may contribute to the variability in the response of motor systems to pain.[11,40]

The significant effect of experimental condition (hypertonic or isotonic saline injection) on the total PRI from the MPQ is in agreement with Svensson et al.[51] In addition, the similarity in the frequency of sensory, affective, evaluative, and miscellaneous word descriptors,[48] as well as the pain maps, are all consistent with the conclusion that, in terms of the sensory-discriminative and motivational-affective dimensions of pain, the tonic experimental pain model is comparable to the chronic muscle pain state.[56,57]

Effect of Experimental Jaw-Muscle Pain on Jaw Motor Behavior

Standardized Protrusive, Contralateral, and Open/Close Jaw Movement. During pain, subjects were usually able to perform the horizontal goal-directed jaw movement tasks (ie, protrusion and contralateral movement) as well as during the pain-free condition, as indicated by the absence of a significant difference in amplitude or velocity of jaw movements for all subjects grouped together during pain trials in comparison with control trials. Under non–goal-directed conditions, pain decreased the orientation and magnitude of the mandibular lateral border movements[31] and the amplitude and velocity of symmetric and empty open/close jaw movements.[4] When standardized jaw movements in the vertical plane (ie, open/close movement of mandible) were observed under the painful condition, however, there was a significant decrease in the vertical range of movement despite the goal-directed nature of the task. This latter finding is consistent with the subjective reports and objective findings of changes in motor behavior (eg, reductions in amplitude and velocity of movement) caused by muscle pain reported for low-back pain, fibromyalgia, and TMD patients. These changes have been regarded as normal protective adaptations rather than the cause of the pain.[4,10–12,15] The absence of a significant overall effect on the horizontal-movement tasks during pain in comparison with the presence of a significant effect on the open/close movements may reflect the presence of a noxious stimulus in one of the principal agonists or antagonists for the latter task but not the former. It may be that when a principal agonist is in pain then the achievement of a goal-directed task becomes more difficult than when the painful muscle is not the principal agonist of a movement.

The amplitude of the opening movement, but not the velocity, during painful open/close movements was decreased in comparison to control conditions. However, Lund et al[4] reported a velocity

decrease. This difference from Lund et al[4] may reflect the standardized nature of the goal-directed open/close task, where subjects were aiming to track a target at constant velocity. The present data suggest that under goal-directed conditions, pain has a differential effect on kinematic parameters, ie, it affects amplitude but not velocity. Given that, in comparison with control, there was no significant overall effect of isotonic saline on amplitude or velocity of the vertical jaw movement task, the decrease in the amplitude of the jaw opening movement is attributed to a net effect of pain and not to volumetric change associated with the injected volume of solution within the muscle. Therefore, although isotonic saline could evoke a low level of pain in some subjects, there appears to be no effect of this low level of pain on movement trajectories, which is consistent with previous reports.[8,49,54,58]

Effect of Pain on Masticatory Movement. During painful free chewing, in comparison with pain-free chewing, jaw-opening movements in each cycle were larger, faster, and of shorter duration, and the total duration of all chewing cycles was shorter. However, the same pattern of differences was seen during isotonic saline infusion. There are 2 possible interpretations of these data. First, given the close similarities in the statistical analyses of the kinematic parameters under hypertonic and isotonic saline conditions, it is possible that pain has no effect on any of the kinematic parameters of free chewing under the experimental paradigm employed in this study. This interpretation attributes the effects observed to non-pain effects, eg, volume change of the injected solution, or nonspecific motivational or other effects, such as desire to complete the task, that are overriding any possible pain effect.

A second possible interpretation of the data is that pain is having an effect but that the intensity of the pain is not a factor in determining whether an effect is observed. Figure 1 shows that during isotonic saline infusion, free and standardized chewing were associated with significantly higher VAS scores than during no-task conditions. It is therefore possible that the low level of pain generated by the isotonic saline during the chewing sequence might be sufficient to produce significant effects on the kinematic parameters observed in the present study. If this interpretation is correct, then the observation that few significant effects were observed during standardized chewing suggests that the goal-directed nature of the standardized task can override pain effects. This interpretation suggests that isotonic saline may be an imperfect control for the volume of solution, given that it can evoke a low level of pain.

The vertical displacement of the mid-incisor point during control trials of unilateral free chewing (mean ± SD: 10.9 ± 2.5 mm) was lower than some previous reports (13.7 ± 2.4 mm),[44,45] but the vertical displacement during standardized chewing (14.4 ± 4.1 mm) was comparable with that reported by Howell et al.[45] The mean velocity during the jaw-opening phase in pain-free trials (25.7 ± 9.2 mm/s, free chewing; 31.4 ± 11.5 mm/s, standardized chewing) was also lower than in previous reports (58.9 ± 10.3 mm/s).[55] However, the mean masticatory cycle duration in pain-free trials (887 ± 119 ms, free chewing; 944 ± 177 ms, standardized chewing) was comparable with the findings of Howell et al[45] (920 ± 200 ms). The lack of agreement with regard to the amplitude and velocity with earlier studies may be due to the large variations in amplitude, duration, and velocity profiles of the human chewing cycle both within and between subjects.[59,60] Another factor is the unique methodological setup in the present study, ie, the presence of an intramuscular EMG electrode, the JAW3D target frames, the requirement for unilateral chewing, and the anticipation of a subsequent 15 minutes of noxious stimulation. The setup may have influenced the chewing-cycle parameters both under control conditions and during pain.

If the effects observed during hypertonic saline infusion were indeed related to the pain, the findings of an increase in jaw-opening amplitude during free chewing are in contrast to previous findings of significantly smaller jaw movements during painful mastication (VAS: 7.0 ± 1.0 on a 0-to-10 scale) induced by a single bolus injection of hypertonic saline.[55] The differences in affective and sensory scores that have been described arising from acute pain (lasting ~100 seconds) in comparison with tonic pain (lasting ~18 minutes)[57] may help explain the difference between a previous study[55] that used a bolus infusion and the present study, which employed continuous infusion. However, this explanation may not be valid if the low-level and short-duration pain evoked by chewing during isotonic saline infusion is indeed the reason for the effect on chewing-cycle parameters (see second interpretation of data). Further, other studies[8,9,59] did not reveal a significant effect of unilateral or bilateral jaw-muscle pain on maximum or peak displacement during mastication, although in the study by Stohler et al,[59] the variability in maximum gape (ie, amplitude of the jaw-opening movement) was greater than in pain-free function. It is possible that pain would have caused significant effects on jaw movement in these studies and in the present study if the pain-free chewing was initially performed

with larger amplitudes. Faster and larger jaw movements during pain may also be related to a possible practice effect.[9,61] Studies of the effects of pain on the limb motor system are also not always consistent with each other (eg, Madeleine et al,[24] Ervilha et al[25]). Another variable could relate to the possibility, suggested by Mohri et al,[62] that rhythmic behavior of chewing (at least 5 minutes of chewing) may suppress nociceptive responses in the human by enhancing the serotonergic descending inhibitory pathway. Individuals may differ in the degree of suppression of these nociceptive responses.

Analysis for Possible Sex Differences. TMD are more prevalent in women than men,[63] and there is a rapidly emerging human and experimental animal literature of the presence of sex differences in the discrimination and perception of nociceptive stimuli.[64–66] The present study consisted of an approximately equal number of male and female subjects. Therefore, although analysis of sex differences was not a primary aim of the study, an analysis was performed for possible differences between males and females in the effects of pain on movement. No significant differences were identified, except during isotonic saline infusion under free chewing, where the total cycle duration was longer in women than in men. However, no adjustment was made for multiple comparisons, and given the small sample size, further definitive comment on possible differences between males and females in the effects of pain on movement features is an avenue for further investigation.

Role of Suprabulbar Influences in the Inter-relationship Between Pain and Motor Behavior. The influence of higher-order brain centers may also play a role in the effects of pain on jaw movements, as illustrated in a study by Stohler et al.[7] Significant increases were observed in EMG activity in the temporalis and masseter muscles during hypertonic saline injection into masseter muscles, but these increases in activity were no different from the increases that occurred with sham pain, ie, recalling an experience of past pain. The motivational-affective and cognitive-evaluative dimensions of the pain experience[36,67] may well influence the motor reaction to pain.

The findings of the present study indicate that, except for jaw opening, individuals can "drive" their motor systems to perform a goal-directed task while in pain. Therefore, motivation to achieve the target kinematic parameters clearly plays an important role. Analogous results have been reported for the forelimb motor system.[68] This is relevant in orofacial pain patients who still need to perform a precise task, for example, produce clearly articulated speech in demanding work situations or chew unexpectedly hard foods in particular social situations. The aforementioned factors may also contribute to the variability observed between individuals in the performance of the jaw-opening tasks during pain. There was considerable evidence for variability between subjects in the sensory manifestations of the noxious stimulus, and this interindividual variability was evident in pain referral patterns, sizes of pain areas, and volumes of solution to achieve VAS target levels. In addition, some pain patterns changed to referral in some individuals during the chewing tasks in comparison to the horizontal or vertical jaw tasks. Given the close interrelationships between sensory, motor, and limbic systems,[38,39] together with the individual variability in sensory manifestation of the noxious masseter stimulus, it is proposed that individuals will vary in the reaction of their motor systems to pain, and this has been considered a possible reason for the variability in the motor response to experimental trunk-muscle pain.[40]

Finally, the applicability of the Pain Adaptation Model to the motor effects of orofacial pain has recently been reviewed and discussed.[69–72] The present findings suggest that the manifestation of the Pain Adaptation Model may be modified when the motor system is driven to perform a task. Therefore, although the potential protective mechanism through the Pain Adaptation Model may be present when nonstandardized or non–goal-directed jaw tasks are performed, the decrease of movement amplitude and velocity due to the pain (as suggested by the Pain Adaptation Model) may not occur under conditions where the subject is driving his or her motor system to achieve the same kinematic parameters as in the absence of pain.

Acknowledgments

The research was supported by the National Health and Medical Research Council of Australia (grant no. 302005) and the Australian Dental Research Foundation. Dr Daraporn Sae-Lee was the recipient of an International Postgraduate Research Scholarship (IPRS) sponsored by the Australian government. Some of the data in this paper forms part of her PhD thesis. Dr Sae-Lee is currently with the Department of Prosthodontics, Faculty of Dentistry, Khon Kaen University, Khon Kaen 400002, Thailand.

References

1. von Korff M, Dworkin SF, LeResche L, Kruger A. An epidemiologic comparison of pain complaints. Pain 1988;32:173–183.
2. LeResche L. Epidemiology of orofacial pain. In: Lund JP, Lavigne G, Dubner R, et al (eds). Orofacial Pain: From Basic Science to Clinical Management. Chicago: Quintessence, 2001:15–25.
3. Bakke M. Jaw muscle disorders. In: Klineberg IJ, Jagger R (eds). Occlusion and Clinical Practice: An Evidence-based Approach. Edinburgh: Wright, 2004:75–82.
4. Lund JP, Donga R, Widmer CG, Stohler CS. The pain-adaptation model: A discussion of the relationship between chronic musculoskeletal pain and motor activity. Can J Physiol Pharmacol 1991;69:683–694.
5. Lund JP. Pain and movement. In: Lund JP, Lavigne G, Dubner R et al (eds). Orofacial Pain: From Basic Science to Clinical Management. Chicago: Quintessence, 2001:151–163.
6. Murray GM, Peck CC. Orofacial pain and jaw muscle activity: A new model. J Orofac Pain 2007;21:263–278.
7. Stohler CS, Zhang X, Lund JP. The effect of experimental jaw muscle pain on postural muscle activity. Pain 1996;66:215–221.
8. Svensson P, Houe L, Arendt-Nielsen L. Bilateral experimental muscle pain changes electromyographic activity of human jaw-closing muscles during mastication. Exp Brain Res 1997;116:182–185.
9. Svensson P, Arendt-Nielsen L, Houe L. Muscle pain modulates mastication: An experimental study in humans. J Orofac Pain 1998;12:7–16.
10. Svensson P, Graven-Nielsen T. Craniofacial muscle pain: Review of mechanisms and clinical manifestations. J Orofac Pain 2001;15:117–145.
11. van Dieën J, Selen LPJ, Cholewicki J. Trunk muscle activation in low-back pain patients, an analysis of the literature. J Electromyogr Kines 2003;13:333–351.
12. Stohler CS. Craniofacial pain and motor function: Pathogenesis, clinical correlates, and implications. Crit Rev Oral Biol Med 1999;10:504–518.
13. Graven-Nielsen T, Svensson P, Arendt-Nielsen L. Interaction between muscle pain and motor control. In: Johansson H, Windhorst U, Djupsjöbacka M et al (eds). Chronic Work-Related Myalgia: Neuromuscular Mechanisms Behind Work-Related Chronic Muscle Pain Syndromes. Umeå, Sweden: Gävle University Press, 2003:141–154.
14. Arendt-Nielsen L, Graven-Nielsen T, Svarrer H, Svensson P. The influence of low back pain on muscle activity and coordination during gait: A clinical and experimental study. Pain 1996;64:231–240.
15. Dworkin SF, Huggins KH, LeResche L, et al. Epidemiology of signs and symptoms in temporomandibular disorders: Clinical signs in cases and controls. J Am Dent Assoc 1990;120:273–281.
16. Tsolka P, Fenlon MR, McCullock AJ, Prieskel HW. A controlled clinical, electromyographic, and kinesiographic assessment of craniomandibular disorders in women. J Orofac Pain 1994;8:80–89.
17. Graven-Nielsen T, Svensson P, Arendt-Nielsen L. Effects of experimental muscle pain on muscle activity and co-ordination during static and dynamic motor function. Electroencephalogr Clin Neurophysiol 1997;105:156–164.
18. Zedka M, Prochazka A, Knight B, Gillard D, Gauthier M. Voluntary and reflex control of human back muscles during induced pain. J Physiol 1999;520.2:591–604.
19. Svensson P, Arendt-Nielsen L, Houe L. Sensory-motor interactions of human experimental unilateral jaw muscle pain: A quantitative analysis. Pain 1995;64:241–249.
20. Schwartz G, Lund JP. Modification of rhythmical movements by noxious pressure applied to the periosteum of the zygoma in decerebrate rabbits. Pain 1995;63:153–161.
21. Westberg K-G, Clavelou P, Schwartz G, Lund JP. Effects of chemical modulation of masseter muscle nociceptors on trigeminal motoneuron and interneuron activities during fictive mastication in the rabbit. Pain 1997;73:295–308.
22. Birch L, Christensen H, Arendt-Nielsen L, Graven-Nielsen T, Søgaard K. The influence of experimental muscle pain on motor unit activity during low-level contraction. Eur J Appl Physiol 2000;83:200–206.
23. Schulte E, Ciubotariu A, Arendt-Nielsen L, Disselhorst-Klug C, Rau G, Graven-Nielsen T. Experimental muscle pain increases trapezius muscle activity during sustained isometric contractions of arm muscles. Clin Neurophysiol 2004;115:1767–1778.
24. Madeleine P, Lundager B, Voigt M, Arendt-Nielsen L. Shoulder muscle co-ordination during chronic and acute experimental neck-shoulder pain. An occupational study. Eur J Appl Physiol 1999;79:127–140.
25. Ervilha UF, Arendt-Nielsen L, Duarte M, Graven-Nielsen T. Effect of load level and muscle pain intensity on the motor control of elbow-flexion movements. Eur J Appl Physiol 2004;92:168–175.
26. Yu X-M, Sessle BJ, Vernon H, Hu JW. Effects of inflammatory irritant application to the rat temporomandibular joint on jaw and neck muscle activity. Pain 1995;60:143–149.
27. Hu JW, Tsai C-M, Bakke M, et al. Deep craniofacial pain: Involvement of trigeminal subnucleus caudalis and its modulation. In: Jensen TS, Turner JA, Wiesenfeld-Hallin Z (eds). Proceedings of the 8th World Congress on Pain, Progress in Pain Research and Management, vol 8. Seattle: IASP Press, 1997:497–506.
28. Cairns BE, Sessle BJ, Hu JW. Evidence that excitatory amino acid receptors within the temporomandibular joint are involved in the reflex activation of the jaw muscles. J Neurosci 1998;18:8056–8064.
29. Sessle BJ. Acute and chronic craniofacial pain: Brainstem mechanisms of nociceptive transmission and neuroplasticity, and their clinical correlates. Crit Rev Oral Biol Med 2000;11:57–91.
30. Ro JY, Svensson P, Capra NF. Effects of experimental muscle pain on electromyographic activity of masticatory muscles in the rat. Muscle Nerve 2002;25:576–584.
31. Obrez A, Stohler CS. Jaw muscle pain and its effect on gothic arch tracings. J Prosthet Dent 1996;75:393–398.
32. Nielsen IL, Marcel T, Chun D, Miller AJ. Patterns of mandibular movements in subjects with craniomandibular disorders. J Prosthet Dent 1990;63:202–217.
33. Graven-Nielsen T, McArdle A, Phoenix J, et al. In vivo model of muscle pain: Quantification of intramuscular chemical, electrical, and pressure changes associated with saline-induced muscle pain in humans. Pain 1997;69:137–143.
34. Svensson P, Wang K, Arendt-Nielsen L, Cairns BE, Sessle BJ. Pain effects of glutamate injections into human jaw or neck muscles. J Orofac Pain 2005;19:109–118.

35. Zubieta J-K, Heitzeg MM, Smith YR, et al. COMT val158met genotype affects m-opioid neurotransmitter responses to a pain stressor. Science 2003;299:1240–1243.
36. Melzack R. From the gate to the neuromatrix. Pain 1999;6(suppl):121–126.
37. Mogil JS. The genetic mediation of individual differences in sensitivity to pain and its inhibition. Proc Natl Acad Sci USA 1999;96:7744–7751.
38. Price DD. Psychological and neural mechanisms of the affective dimension of pain. Science 2000;288:1769–1772.
39. Morgane PJ, Galler JR, Mokler DJ. A review of systems and networks of the limbic forebrain/limbic midbrain. Prog Neurobiol 2005;75:143–160.
40. Hodges PW, Moseley GL, Gabrielsson A, Gandevia SC. Experimental muscle pain changes feedforward postural responses of the trunk muscles. Exp Brain Res 2003;151:262–271.
41. Murray GM, Phanachet I, Hupalo M, Wanigaratne K. Simultaneous recording of mandibular condylar movement and single motor-unit activity at verified sites in the human lateral pterygoid muscle. Arch Oral Biol 1999;44:671–682.
42. Phanachet I, Whittle T, Wanigaratne K, Murray GM. Functional properties of single motor units in inferior head of human lateral pterygoid muscle: Task relations and thresholds. J Neurophysiol 2001;86:2204–2218.
43. Sae-Lee D, Wanigaratne K, Whittle T, Peck CC, Murray GM. A method for studying jaw muscle activity during standardized jaw movements under experimental jaw muscle pain. J Neurosci Methods 2006;157:285–293.
44. Mesqui F, Palla S. Real-time non-inversion recording and display of functional movements. J Oral Rehabil 1985;12:541–550.
45. Howell PGT, Ellis S, Johnson CWL, Watson IB, Klineberg IJ. The recording and analysis of EMG and jaw tracking. II. Reproducibility of jaw tracking. J Oral Rehabil 1993;20:33–43.
46. Kellgren JH. Observations on referred pain arising from muscle. Clin Sciences 1938;3:175–190.
47. Capra NF, Ro JY. Human and animal experimental models of acute and chronic muscle pain: Intramuscular algesic injection. Pain 2004;110:3–7.
48. Stohler CS, Lund JP. Psychophysical and orofacial motor response to muscle pain: Validation and utility of an experimental model. In: Morimoto T, Matsuya T, Takada K (eds). Brain and Oral Function. Amsterdam: Elsevier, 1995:227–237.
49. Graven-Nielsen T, Arendt-Nielsen L, Svensson P, Jensen TS. Experimental muscle pain: A quantitative study of local and referred pain in humans following injection of hypertonic saline. J Musculoskel Pain 1997;5:49–69.
50. Wang K, Arima T, Arendt-Nielsen L, Svensson P. EMG-force relationships are influenced by experimental jaw-muscle pain. J Oral Rehabil 2000;27:394–402.
51. Svensson P, Graven-Nielsen T, Arendt-Nielsen L. Mechanical hyperalgesia of human facial skin induced by tonic painful stimulation of jaw muscles. Pain 1998;74:93–100.
52. Cairns BE, Hu JW, Arendt-Nielsen L, Sessle BJ, Svensson P. Sex-related differences in human pain and rat afferent discharge evoked by injection of glutamate into the masseter muscle. J Neurophysiol 2001;86:782–791.
53. Sessle BJ. Mechanisms of oral somatosensory and motor functions and their clinical correlates. J Oral Rehabil 2006;33:243–261.
54. Türp JC, Schindler HJ, Pritsch M, Rong Q. Antero-posterior activity changes in the superficial masseter muscle after exposure to experimental pain. Eur J Orthod 2002;110:83–91.
55. Svensson P, Arendt-Nielsen L, Houe L. Sensory-motor interactions of human experimental unilateral jaw muscle pain: A quantitative analysis. Pain 1996;64:241–249.
56. Dao TTT, Lund JP, Lavigne G. Pain responses to experimental chewing in myofascial pain patients. J Dent Res 1994;73:1163–1167.
57. Stohler CS, Kowalski CJ. Spatial and temporal summation of sensory and affective dimensions of deep somatic pain. Pain 1999;79:165–173.
58. Ernberg M, Lundeberg T, Kopp S. Pain and allodynia/hyperalgesia induced by intramuscular injection of serotonin in patients with fibromyalgia and healthy individuals. Pain 2000;85:31–39.
59. Stohler CS, Ashton-Miller JA, Carlson DS. The effects of pain from the mandibular joint and muscles on masticatory behaviour in man. Arch Oral Biol 1988;33:175–182.
60. Theusner J, Plesh O, Curtis DA, Hutton JE. Axiographic tracings of temporomandibular joint movements. J Prosthet Dent 1993;69:209–215.
61. Svensson P, Arendt-Nielsen L, Bjerring P, Bak P, Hjorth T, Troest T. Human mastication modulated by experimental trigeminal and extra-trigeminal painful stimuli. J Oral Rehabil 1996;23:838–848.
62. Mohri Y, Fumoto M, Sato-Suzuki I, Umino M, Arita H. Prolonged rhythmic gum chewing suppresses nociceptive response via serotonergic descending inhibitory pathway in humans. Pain 2005;118:35–42.
63. LeResche L. Epidemiology of temporomandibular disorders: Implications for the investigation of etiologic factors. Crit Rev Oral Biol Med 1997;8:291–305.
64. Aloisi AM, Bonifazi M. Sex hormones, central nervous system and pain. Horm Behav 2006;50:1–7.
65. Kuba T, Quinones-Jenab V. The role of female gonadal hormones in behavioral sex differences in persistent and chronic pain: Clinical versus preclinical studies. Brain Res Bull 2005;66:179–188.
66. Craft RM, Mogil JS, Aloisi AM. Sex differences in pain and analgesia: The role of gonadal hormones. Eur J Pain 2004;8:397-411.
67. Keefe FJ, Dixon KE, Pryor RW. Psychological contributions to the understanding and treatment of pain. In: Merskey H, Loeser JD, Dubner R (eds). The Paths of Pain 1975–2005. Seattle: IASP Press, 2005:403–420.
68. Birch L, Graven-Nielsen T, Christensen H, Arendt-Nielsen L. Experimental muscle pain modulates muscle activity and work performance differently during high and low precision use of a computer mouse. Eur J Appl Physiol 2000;83:492–498.
69. Murray GM, Peck CC. Orofacial pain and jaw muscle activity: A new model. J Orofac Pain 2007;21:263–278.
70. Mense S. Critical commentary 1. Orofacial pain and jaw muscle activity: A new model. J Orofac Pain 2007;21:279–281.
71. Lund JP, Stohler C. Critical commentary 2. Orofacial pain and jaw muscle activity: A new model. J Orofac Pain 2007;21:282–283.
72. Svensson P. Critical commentary 3. Orofacial pain and jaw muscle activity: A new model. J Orofac Pain 2007;21:284–286.