Simultaneous Noxious Stimulation of the Human Anterior Temporalis and Masseter Muscles. Part II: Effects on Jaw Muscle Electromyographic Activity

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Aims: To test the hypotheses that, in comparison to control, the effects of simultaneous noxious stimulation of the right masseter and anterior temporalis muscles on jaw muscle activity *(1)* vary with the task; *(2)* are different between different agonist or antagonist muscles involved in a task; and *(3)* are correlated with mood or pain-related cognition scores. **Methods:** In 15 asymptomatic participants, recordings were made of jaw movement and electromyographic (EMG) activity of the right digastric and bilateral masseter and anterior temporalis muscles during standardized open/close and free and standardized chewing tasks. The tasks were repeated in three blocks: block 1 (baseline), block 2 (during simultaneous infusion of 5% hypertonic or 0.9% isotonic saline infusion into the right masseter and anterior temporalis muscles), and block 3 (infusion sequence reversed). The Depression, Anxiety and Stress Scales questionnaire was completed prior to the experiment, and the Pain Catastrophizing Scale was completed before and after the experiment. Linear mixed-effects model analysis compared root mean square (RMS) EMG activity under baseline, hypertonic saline, and isotonic saline (control), and Spearman correlations between RMS and psychologic scores were calculated. $P < .05$ was considered significant. **Results:** The significant effects of pain on the activity of a jaw muscle varied with the task, were different between different agonist and antagonist muscles in a task, and were significantly correlated with some of the psychologic scores. Qualitatively, the effects noted in a particular muscle could be different between different participants. **Conclusion:** Simultaneous noxious masseter and anterior temporalis stimulation results in changes in jaw muscle activity that can vary with the task, the muscle, the participant, and some psychologic variables. *J Oral Facial Pain Headache 2019;33:426–439. doi: 10.11607/ofph.2300*

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The interaction between pain and motor control is not fully understood, but the Vicious Cycle Theory (VCT)[1] and the Pain Adaptation Model (PAM)[2] have both been widely considered to explain this interaction. The VCT proposes a self-perpetuating cycle of muscle hyperactivity and pain.[1] The PAM predicts that existing pain results in an inhibition of agonist muscle activity and an excitation of antagonist muscle activity and that these effects generate smaller and slower movements so as to alleviate the pain and minimize further injury.[2] While there are some datasets consistent with both these theories, neither appears capable of explaining the range of possible motor effects that have been observed in the adaptation to pain.[3–7] Further, the neural basis of both theories resides within brainstem or spinal cord reflex circuits that generate the changes in motor activity in response to pain.[6] However, this neural framework does not readily accommodate the role of psychologic factors in the pain-motor interaction. These limitations have led to the development of newer theories.[3,4,6]

Most experimental studies of the effects of pain on the jaw motor system have focused on the effects of experimental pain induced in one muscle (typically, the masseter muscle[8–16]). Detailed studies on the effects of noxious stimulation of the masseter on jaw kinematics have reported significant reductions in jaw amplitude or velocity during opening

and closing jaw movements,[13,16] but no significant effects on free or standardized chewing.[13] In separate studies, noxious stimulation of the anterior temporalis muscle did not result in any significant effects on jaw amplitude or velocity during opening and closing jaw movements or during free or standardized chewing.[17] Despite the absence of effects or only minimal effects of masseter or anterior temporalis noxious stimulation on jaw movements, masseter noxious stimulation—and, in separate experiments, anterior temporalis noxious stimulation—did indeed result in significant changes in jaw muscle EMG activity,[14,18] even in tasks whose kinematic parameters were unaffected by the noxious stimulation.[13,17] One of these previous studies[18] also reported associations between some psychologic constructs and jaw closing EMG activity during pain, and these observations are in line with previous reports of similar associations.[16,18–23] In summary, some of these studies concluded that EMG changes during noxious jaw muscle stimulation could vary with the task performed, the participant being studied, the muscle, the magnitude of jaw displacement, and some psychologic scores (ie, the Depression, Anxiety and Stress Scales [DASS-21] or the Pain Catastrophizing Scale [PCS]).

Patients with temporomandibular disorders (TMD) may exhibit pain in muscles other than the masseter, such as the temporalis.[24] However, as outlined in the companion paper (Amhamed et al[25]), there is only one study that appears to examine the effect on jaw muscle activity of experimental pain in more than one muscle.[9] This companion paper[25] demonstrated that simultaneous hypertonic saline infusion into both the masseter and anterior temporalis muscles resulted in a significantly smaller opening and closing amplitude and a significantly lower velocity during free chewing in comparison with isotonic saline infusion into the same muscles, but there were, remarkably, no significant effects on kinematic parameters during standardized open/close jaw movements or standardized chewing. It is surprising that simultaneous noxious stimulation of two muscle sites producing moderate pain intensity at both sites either had no effect on jaw movement amplitude or velocity or only resulted in effects that could be considered mild; that is, only small reductions in amplitude and velocity were noted in relation to the mean values under control infusion.

The present study employed an experimental pain model involving simultaneous infusion of hypertonic saline into the right masseter and anterior temporalis muscles. In contrast to single muscle site infusion models, an infusion model involving two muscle sites may be a more clinically relevant model of myofascial TMD pain for some TMD patients who report pain in more than one muscle; for example, not only in the masseter but also in the temporalis. The aim was to test the hypotheses that, in comparison to control, the effects of simultaneous noxious stimulation of the right masseter and anterior temporalis muscles on jaw muscle activity *(1)* would vary with the task; *(2)* are different between different agonist or antagonist muscles involved in a task; and *(3)* are correlated with mood or pain-related cognition scores.

Materials and Methods

The accompanying paper[25] documented kinematic data from 15 asymptomatic participant volunteers (age: 29 to 55 years; 14 men and 1 woman), and the present paper documents the associated EMG data that were recorded in the same experimental sessions. Exclusion criteria are listed in the accompanying paper.[25] Many of the approaches used for jaw tracking, EMG recording, and experimental pain are similar to those detailed in previous publications by this group.[13,14,16–18,25] The following will briefly review the previously described experimental methodology[25] and provide detailed information about the EMG recordings and analysis procedures. Ethical approval was obtained from the Western Sydney Area Health Service Human Ethics Committee of Westmead Hospital and The Human Ethics Committee of the University of Sydney, and all participants gave written informed consent prior to enrolling in the study.

In brief, this was a repeated-measures design in which recordings of jaw movement and jaw muscle activity were made during jaw movement tasks that were repeated in three blocks: block 1 was the baseline block prior to any infusion; block 2 involved infusion of 5% hypertonic or 0.9% isotonic saline into the right masseter and anterior temporalis muscles simultaneously (duration: ~10 minutes); and block 3 (duration: ~10 minutes) was the reverse infusion sequence from that in block 2. The DASS-21[26] was completed prior to the experiment, and the PCS[27] prior to and after the experiment by all participants.

Jaw Movement Recording, EMG Electrode Placement, and Recording

Jaw movement was tracked with an optoelectronic jaw tracking system (JAWS3D or JAWS2K, Metropoly; sampling rate 67 samples/second or 200 samples/second, respectively; resolution: ~0.1 mm). Target frames containing light-emitting diodes were secured to the maxillary and mandibular teeth, and the displacement of these target frames was recorded by cameras and saved to a personal computer. An output from the jaw tracking system provided the position of the mid-incisor point of the mandible, and this point was displayed on a screen to assist in standardizing some of the jaw tasks (see below). Disposable bipolar

surface EMG electrodes (4 mm × 7 mm recording area, 12.5 mm in diameter and spaced 19 mm between centers; Duo-Trode, Myotronics) were used to record EMG activity from the right anterior temporalis (RAT), the left anterior temporalis (LAT), the right masseter (RMAS), the left masseter (LMAS), and the right digastric (RDIG) muscles. An electrode was placed over the RDIG only (not over the left digastric muscle) to minimize possible effects on chewing from the electrodes and the tape beneath the chin. The skin overlying the relevant muscle was initially cleansed with 70% isopropyl alcohol (Alcowipe, Promedica), and some additional electrode gel (Sigma Gel, Medtronic Denmark) was added to the electrode-conducting foam before placement on the skin. The electrodes were positioned parallel to the main fibers of the underlying muscle, ~2 cm posterior to the eyebrow for the RAT and LAT. For the RMAS and LMAS, the electrodes were placed halfway between the anterior and posterior borders and the superior and inferior borders. A ground electrode was placed on the wrist. The EMG signals were amplified by an isolated amplifier (1,000× – 10,000×; SA Instrumentation), filtered (100 Hz to 5 kHz), and digitized (5,000 samples/s) using data acquisition equipment from Cambridge Electronic Design (CED model micro1401) for offline analysis. Brief clenches and opening against resistance confirmed EMG activity in the jaw closing muscles and the RDIG, respectively.

Jaw Tasks

The jaw tasks are described fully in the accompanying paper[25] and, briefly, were:

- *Postural jaw position (15 seconds; one trial):* The postural jaw position task was not analyzed offline, but was used to confirm an EMG recording with low noise from all channels.
- *Standardized open/close jaw movement:* Consisted of five trials of opening and closing the jaw to match a visual target that was positioned to the side of the mid-incisor point dot on the screen positioned in front of the participant. This visual target displaced at a speed of 2.2 mm/second and to an opening displacement of 20 mm from the postural position.
- *Free chewing (~15 seconds; two trials):* Participants initially softened a piece of sugar-free chewing gum (0.14 g) (EXTRA, Wrigley), and then ~1 second after commencement of the trial, chewed the gum on the right side.
- *Standardized chewing (~15 seconds; two trials):* Participants softened a new piece of chewing gum and then chewed on the right side at a chewing rate of ~900 milliseconds/chewing cycle. The chewing rate was standardized by the participant matching the timing of their opening and closing during the chewing with the timing of a visual target.

Experimental Jaw Muscle Pain Induction

After the block 1 trials had been completed, an intravenous (IV) catheter (JELCO, 22 G × 1 inch, Smiths Medical Australasia) was placed into the RAT, and another IV catheter was also placed in the RMAS. The insertion site was initially swabbed with an alcohol wipe. After confirmation of negative aspiration, a polyethylene extension set (75 cm length, 0.7 mL, Medical Australia) was attached to the IV catheter in the RAT, and another extension set was attached to the IV catheter in the RMAS. Each extension set led to a 10-mL syringe (Becton Dickinson, North Ryde, Australia) driven by separate syringe pumps (IVAC Model P2000, Alaris Medical Systems). Experimental pain was induced in both the RAT and the RMAS simultaneously by the infusion of 5% sterile hypertonic saline (Phebra Pty) (3 to 6 mL/hour for the masseter infusion and 1 to 3 mL/hour for the temporalis infusion) into each muscle. The objective of each infusion was to achieve an intensity of 40–60/100 mm on separate visual analog scales (VAS) for the temporalis and masseter. Sterile isotonic saline (0.9%) was infused simultaneously into both muscles at similar infusion rates for block 2 or block 3; the sequence of infusion (ie, hypertonic saline or isotonic saline in block 2) was alternated between participants. As indicated in the accompanying manuscript, hypertonic saline at ~5% is a frequently used algesic chemical.[28–31] Pain maps, VAS scores, and the McGill Pain Questionnaire[32] (MPQ) were completed for each muscle after the end of each infusion block, and these data have been reported in the accompanying manuscript.[25]

Data Analyses

The statistical analysis involved six stages. In brief, the stages are as follows:

1. All cycles of chewing, as well as the opening and closing phases of the standardized open/close task, were segmented into opening and closing phases, as described in the accompanying paper.[25]
2. The root mean square (RMS) of the EMG activity was calculated at 0.5-mm increments in the opening and closing phases.
3. The RMS EMG data were log-transformed to stabilize the variance, and a linear mixed-effects model analysis was used to explore the effect of block on the EMG of each muscle.
4. A ratio of difference in the logRMS EMG activity between blocks was calculated.

5. An assessment was made as to whether the observed effects of pain on the activity of a muscle were consistent with the PAM and/or the VCT.
6. A Spearman correlation analysis was used to explore the association between the psychologic variable scores and the change in EMG from 0 to 15 mm displacement.

The following describes these analyses in detail.

Each trial of the standardized open/close jaw movement and each cycle of free and standardized chewing were segmented into an opening phase and a closing phase and analyzed as described in the accompanying paper.[25] Briefly, for the standardized open/close jaw movement, opening onset was defined as 0.5 mm displacement from the postural jaw position of the mandibular mid-incisor point along the *z* axis (inferior-superior axis). The end of opening was 0.5 mm from maximum opening displacement. The onset of the closing phase was from the end of the holding phase to within 0.5 mm of the postural position. All cycles of each chewing trial were also analyzed by determining the onset of each opening phase as 0.5-mm displacement of the mid-incisor point from the maximum closure of the previous chewing cycle (or from the postural jaw position for the first cycle of a chewing trial). The offset of the opening phase was defined as the maximum opening displacement. The onset of the closing phase was the maximum opening of a cycle, and the offset of closing was 0.5 mm from maximum closure for that chewing cycle.

Starting at the onset of opening or the offset of closing, the root mean square (RMS) of the EMG activity at each 0.5-mm increment of jaw displacement was calculated for each jaw muscle (ie, RMAS, LMAS, RAT, LAT, RDIG) during each opening and closing phase of all tasks and during all three blocks. The onset of opening or the offset of closing was taken as 0 mm of displacement for the purposes of this analysis. The RMS values at each 0.5 mm of displacement for each muscle were averaged across all repetitions of the opening and closing phases of the standardized open/close cycles, across all repetitions of the free chewing cycles, and across all repetitions of the standardized chewing cycles within each participant. The RMS values were log-transformed to resolve variability within trials and between participants, and variations in displacement were taken into account through a linear mixed-effects model analysis, with displacement as a covariate. This statistical analysis explored the effect of block (ie, baseline block, hypertonic saline infusion block, and isotonic saline infusion block) on the EMG activity of each muscle. This was done by using 0 mm of displacement (EMG intercept) and the rate of change in the EMG activity across the displacement (EMG slope). The 0 mm of displacement was the onset of opening or the offset of closing in the tasks. Plots were created of the logRMS of the EMG activity of the recorded muscles at 0 mm of displacement, together with the logRMS EMG activity after 20 mm of displacement for the standardized open/close task or after 10 mm of displacement for the free and standardized chewing tasks across all participants.

For each muscle and each task, a ratio of difference in the logRMS EMG activity for EMG intercept and EMG slope was calculated by comparing the activity obtained during one block from that of another block, namely hypertonic saline infusion or isotonic saline infusion from baseline, and isotonic saline infusion from hypertonic saline infusion. If the ratio of difference in EMG activity in terms of the RMS values was less than 1, this indicated that the EMG activity of the numerator was less than its comparator.

The PAM predicts that pain results in decreased activity when the muscle is an agonist in a task, but increased activity when a muscle is an antagonist in a task. The VCT proposes generalized increases in muscle activity during pain. To assess whether observed effects of experimental jaw muscle pain on the activity of a muscle were consistent with the PAM and/or the VCT, the RAT, LAT, RMAS, and LMAS were classified as agonists during the closing phases of all tasks and antagonists during the opening phases, while RDIG was classified as an antagonist during the closing phases and an agonist during the opening phases. This analysis involved comparing the hypertonic saline infusion block to the isotonic saline infusion block for the statistically significant comparisons. For example, for the agonists in a task, if the direction of change in EMG activity at the start of movement (EMG intercept) or the logRMS EMG slope was greater during hypertonic saline infusion than isotonic saline infusion, then this was taken as being consistent with the VCT; if the direction of change was less during hypertonic saline infusion than isotonic saline infusion, then this was taken as being consistent with the PAM.

For all muscles, the PCS and DASS-21 scores from each participant were correlated with EMG change scores. The DASS-21 was completed prior to the experiment, and the PCS prior to and after the experiment by all participants. The EMG change scores for each muscle in the opening and closing phases of each task for each block were obtained by subtracting the RMS values at 15 mm of displacement from those at 0 mm of displacement. A Spearman correlation analysis explored the association between the psychologic variable scores and the change in EMG from 0 to 15 mm displacement. For all statistical tests, statistical significance was accepted at $P < .05$. All statistical analyses used SPSS version 21 software (IBM).

Table 1 Results of Linear Mixed-Effects Model Analysis at the Start of the Opening and End of the Closing Phases

		Comparisons of EMG activity			
Jaw task	Muscle	Hypertonic/ baseline	Isotonic/ baseline	Isotonic/ hypertonic	Direction of effect on EMG
Open/close (opening)	RAT	.508	.169	.309	o
	LAT	**.000**	**.000**	.463	o
	RMAS	**.000**	.911	**.000**	H > I
	LMAS	**.000**	**.001**	**.001**	I > H
	RDIG	**.000**	**.000**	.886	o
Open/close (closing)	RAT	.748	.275	.425	o
	LAT	**.000**	**.000**	**.027**	I > H
	RMAS	**.000**	**.000**	**.007**	I > H
	LMAS	**.000**	**.000**	.275	o
	RDIG	**.001**	**.001**	.845	o
Free chewing (opening)	RAT	**.007**	**.000**	**.038**	I > H
	LAT	.675	.769	.893	o
	RMAS	.892	.387	.313	o
	LMAS	**.000**	**.000**	.369	o
	RDIG	**.000**	**.000**	.264	o
Free chewing (closing)	RAT	**.000**	**.000**	.981	o
	LAT	**.000**	**.000**	.667	o
	RMAS	.118	**.000**	**.000**	I > H
	LMAS	**.000**	**.000**	.121	o
	RDIG	.226	**.000**	**.001**	I > H
Standardized chewing (opening)	RAT	**.020**	**.000**	.096	o
	LAT	.395	.787	.257	o
	RMAS	.062	.502	**.010**	I > H
	LMAS	**.000**	**.000**	.447	o
	RDIG	**.000**	**.000**	.129	o
Standardized chewing (closing)	RAT	.183	.515	.487	o
	LAT	**.000**	**.000**	.258	o
	RMAS	**.000**	.802	**.000**	I > H
	LMAS	**.000**	**.001**	**.000**	H > I
	RDIG	.180	**.001**	**.040**	I > H

For the standardized open/close, free chewing, and standardized chewing tasks, *P* values are listed from the statistical analysis (linear mixed-effects model analysis) of the differences in EMG activity of each muscle at the start of the opening and the end of the closing phases of the different jaw tasks between baseline and hypertonic saline (HS) infusion, between baseline and isotonic saline (IS) infusion, and between HS and IS infusion. Bolded values indicate significant differences between pairs ($P < .05$). RAT = right anterior temporalis; LAT = left anterior temporalis, RMAS = right masseter; LMAS = left masseter; RDIG = right digastric muscles. Direction of effect: HS > IS = RMS EMG activity during HS is greater than during IS infusion; IS > HS = RMS EMG activity during HS is less than during IS infusion; o = no significant difference between HS and IS.

Results

The volumes infused have been summarized in the accompanying paper. In brief, the total amount of hypertonic saline infused into the RAT was 0.61 (standard deviation [SD] 0.46) mL, and the total amount of isotonic saline infused was 0.48 (0.23) mL. The total amount of hypertonic saline infused into the RMAS was 1.10 (0.43) mL, and the total amount of isotonic saline was 0.86 (0.34) mL.

Quantitative Analysis of Grouped Jaw Muscle EMG Data

Table 1 shows the results of the linear mixed-effects model analysis of the differences in EMG activity between blocks at the start of the opening and the end of the closing phases of the standardized open/close, free chewing, and standardized chewing tasks. Table 2 shows the results of the differences in logRMS EM slopes for the same comparisons. The remaining descriptions of these tables will be of the comparison between the hypertonic saline infusion block and the isotonic saline infusion block, as this comparison establishes the net effect of pain on motor activity (see Discussion). The isotonic saline infusion block will act as the control. Plots of the grouped data for the closing phases of standardized open/close and free and standardized chewing are shown for RAT and LMAS in Fig 1.

Effect of Task

For the comparison of isotonic saline to hypertonic saline at the start of the opening and the end of the closing phases (Table 1), the occurrence of significant differences for the opening or closing phases varied with the task. For example, at the onset of movement for the opening phases, RMAS was significantly increased during the standardized open/close task, was unaffected in free chewing, and was significantly decreased in standardized chewing (Table 1). The presence or not of a significant difference between isotonic saline and hypertonic saline blocks was not determined by whether the muscle was an agonist or an antagonist in the task—for example, at the end of the closing phases, while RMAS activity was significantly decreased for all three tasks, the RAT was unaffected (Table 1). Both muscles are agonists for this task and were the muscles receiving the infusions. In addition, LAT was significantly decreased only for the standardized open/close task, while LMAS was significantly increased only for standardized chewing (Table 1).

The logRMS EMG slopes (ie, the change in EMG activity across the displacement) were also compared between blocks (Table 2, representative plotted data in Fig 1), and there were no significant differences in slopes for any of the muscles during the opening phases of any task. However, the occurrence of significant differences varied with the task during the closing phases and was not determined by whether the muscle was an agonist in the task. For example, while significant

differences in the EMG slopes for the RAT and LAT were noted in the closing phases of all tasks, a decrease in slope was noted in the standardized open/close task (consistent with the predictions of the Pain Adaptation Model; see also Fig 1a for RAT), and an EMG slope increase was noted for free and standardized chewing (consistent with the predictions of the VCT; see also Figs 1b and 1c). In addition, for the LMAS, a significant decrease in slope was noted in the closing phase of the standardized open/close task (Fig 1a), a slope increase was noted in free chewing (Fig 1b), and no significant change in slope was noted for standardized chewing (Fig 1c). There were no significant differences in slope noted for the RMAS in any of the tasks.

Table 2 Results of Linear Mixed-Effects Model Analysis for EMG Slope

		Differences in EMG slope			
Jaw task	Muscle	Hypertonic/ baseline	Isotonic/ baseline	Isotonic/ hypertonic	Direction of effect on EMG
Open/close (opening)	RAT	**.008**	.103	.309	o
	LAT	**.000**	**.000**	.337	o
	RMAS	.930	.594	.639	o
	LMAS	.622	.796	.414	o
	RDIG	**.020**	.135	.410	o
Open/close (closing)	RAT	**.000**	**.042**	**.043**	I > H
	LAT	**.000**	**.000**	**.000**	I > H
	RMAS	**.007**	**.000**	.062	o
	LMAS	**.006**	**.000**	**.038**	I > H
	RDIG	.903	.903	.623	o
Free chewing (opening)	RAT	.535	.463	.930	o
	LAT	.156	.440	.454	o
	RMAS	.965	.340	.305	o
	LMAS	.969	.146	.125	o
	RDIG	**.000**	**.000**	.758	o
Free chewing (closing)	RAT	**.002**	.092	**.000**	H > I
	LAT	**.000**	**.002**	**.003**	H > I
	RMAS	**.003**	**.002**	.991	o
	LMAS	**.000**	.573	**.000**	H > I
	RDIG	.167	**.000**	**.036**	I > H
Standardized chewing (opening)	RAT	.587	.622	.942	o
	LAT	**.059**	**.036**	.897	o
	RMAS	.798	**.031**	.052	o
	LMAS	.659	.458	.775	o
	RDIG	**.000**	**.000**	.273	o
Standardized chewing (closing)	RAT	.677	**.007**	**.002**	H > I
	LAT	**.000**	**.039**	**.000**	H > I
	RMAS	.789	**.035**	.062	o
	LMAS	.002	.181	.067	o
	RDIG	**.031**	.161	.394	o

For the standardized open/close, free chewing, and standardized chewing tasks, *P* values of the differences in log-transformed root mean square [RMS] data of EMG slope (rate of change in EMG activity across the displacement) from the linear mixed-effects model analysis are listed for each muscle comparison between hypertonic saline (HS) and baseline, isotonic saline (IS) and baseline, and between HS and IS infusions. Bolded values indicate significant differences between pairs ($P < .05$). RAT = right anterior temporalis; LAT = left anterior temporalis, RMAS = right masseter; LMAS = left masseter.
Direction of effect: HS > IS = RMS EMG activity during HS is greater than during IS infusion; IS > HS = RMS EMG activity during HS is less than during IS infusion; o = no sngificant difference between HS and IS.

Effect of Jaw Displacement

Figure 2 shows the ratios of the differences in EMG activity between the isotonic saline infusion and the hypertonic saline infusion blocks for the muscles showing significant EMG slope differences (Table 2) during the closing phases of each task. Figure 2a shows, for the standardized open/close task, that the RAT, LAT, and LMAS EMG activity during isotonic saline infusion was mostly higher than during hypertonic saline infusion, and the ratio decreased with each decrease of displacement (Fig 1a). In contrast, Fig 2b shows that the EMG activity ratios for the RAT, LAT, and LMAS increased with each decrease of displacement for free chewing during isotonic saline infusion compared to hypertonic saline infusion (Fig 1b). The EMG activity ratios decreased for the RDIG. Figure 2c shows that the EMG activity ratios of the RAT and LAT increased with each decrease of displacement for standardized chewing (Fig 1c).

Correlations Between Psychologic Measures and RMS Change Scores

Table 3 lists the significant correlations between the psychologic variable scores and the EMG change scores for each of the opening and closing phases in each task for each block. Most of the correlations are noted during the hypertonic saline infusion (22 out of 31 correlations), and most are positive. For example, during the closing phases of standardized chewing during hypertonic saline infusion, individuals with higher PCS scores tended to exhibit higher levels of EMG activity for the RAT and RMAS (the infusion muscles). Significant positive correlations were also noted among depression, anxiety, and stress scores with the change scores from all jaw muscles in the opening and/or closing phases of free and/or standardized chewing during hypertonic saline infusion.

Qualitative Observations on Individual Participants' EMG Data

There was variation between participants as to the effect of hypertonic saline on the activity of the same muscle. Figure 3 shows that the average RMS values of the LMAS during hypertonic saline infusion

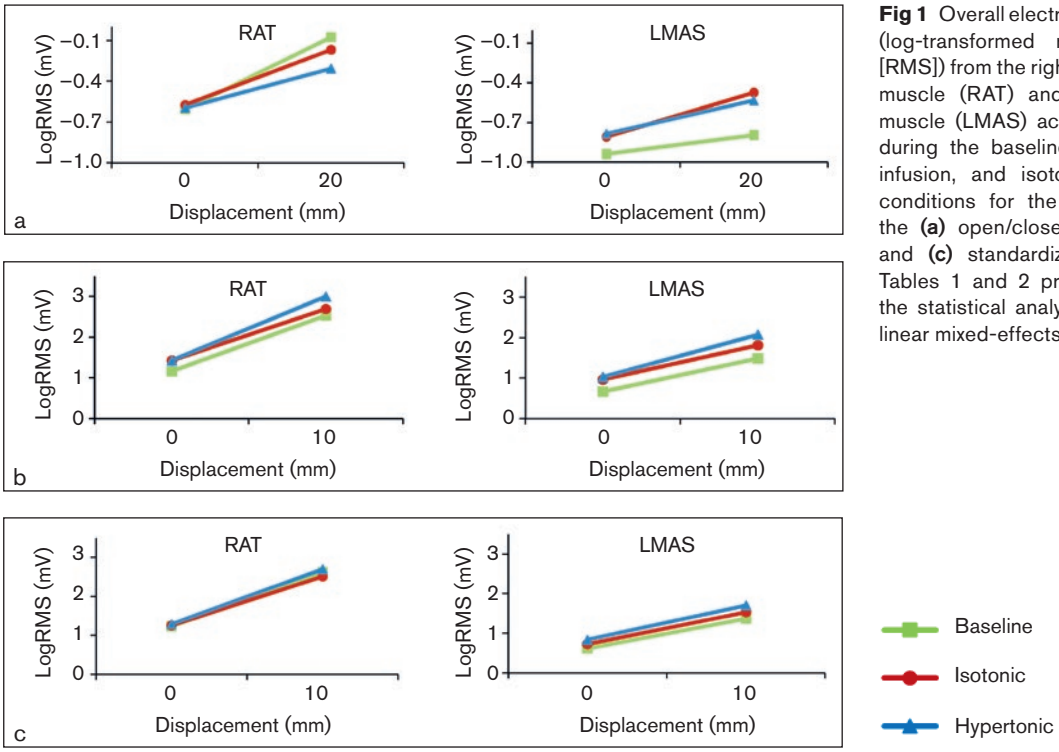

Fig 1 Overall electromyographic activity (log-transformed root mean square [RMS]) from the right anterior temporalis muscle (RAT) and the left masseter muscle (LMAS) across all participants during the baseline, hypertonic saline infusion, and isotonic saline infusion conditions for the closing phases of the **(a)** open/close, **(b)** free chewing, and **(c)** standardized chewing tasks. Tables 1 and 2 provide the results of the statistical analyses, which involved linear mixed-effects model analysis.

were less than the values during isotonic saline infusion in participant 4, but greater for participants 6 and 8. The RMS values for the LMAS in participant 14 during hypertonic saline infusion were lower than the values during isotonic saline infusion at small displacements, but were greater at larger displacements.

Discussion

Studies of the EMG effects of moderate pain, which has been experimentally induced simultaneously in both the RAT and RMAS, have not been previously reported. The effects noted on the activity of the jaw muscles were generally consistent with the hypotheses of the study; that is, the significant effects of pain on the activity of a jaw muscle varied with the task performed (Tables 1 and 2; Fig 1). Second, the significant effects of pain were different between different agonist and antagonist muscles involved in a task (Tables 1 and 2; Fig 1 and 2). Third, the significant effects of pain on the activity of a jaw muscle were correlated with some of the psychologic scores (Table 3). In addition, qualitatively, the effects noted on a particular muscle could be different between different individuals (Fig 3).

The fact that the present sample was almost all men is worthy of comment. It is well known that there is a predominance of women in comparison to men in TMD cohorts. Further, significant differences have been noted between healthy men and women in a number of pain-related measures; for example, pain scores following algesic chemical injections (for review[53]). The current sample employed a mostly male group of participants, and therefore the present findings cannot be used to conclude that TMD patients would exhibit similar changes in EMG activity, nor can it be concluded that simultaneous experimental pain induction in the masseter and anterior temporalis muscles of a healthy, mostly female sample would show comparable changes in EMG activity as in the present study.

The significant differences noted in jaw muscle EMG activity between hypertonic and isotonic saline infusions into the RAT and RMAS are considered to be due to pain and not to the physical presence of the catheter nor to mechanical effects related to the infused volume, as there were no significant differences in infused volumes between hypertonic and isotonic saline. The possible effects from other nonspecific effects, such as sequence effects, were minimized because the infusion sequence was alternated between participants. The isotonic saline infusion was not painless in all participants of the present study, consistent with previous reports.[10,17,33–35] Some significant motor effects were noted during the isotonic saline infusion (Tables 1 and 2) in comparison to baseline, and isotonic saline motor effects have been reported in previous studies.[10,14,34,36] These effects are attributed to the activation of nonnociceptive mechanosensitive af-

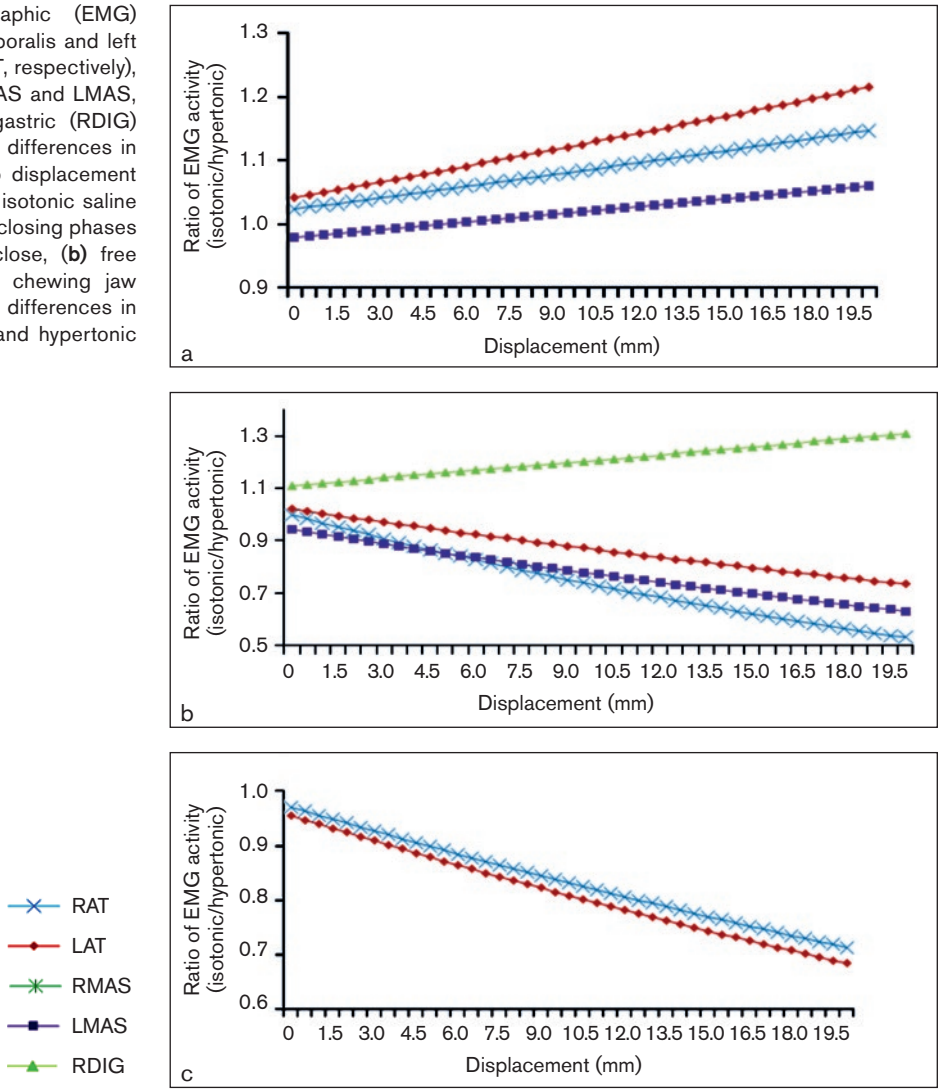

Fig 2 Ratios of electromyographic (EMG) activity of the right anterior temporalis and left anterior temporalis (RAT and LAT, respectively), the right and left masseter (RMAS and LMAS, respectively), and the right digastric (RDIG) muscles that showed significant differences in their EMG activity in relation to displacement for the statistical comparison of isotonic saline and hypertonic saline during the closing phases of the **(a)** standardized open/close, **(b)** free chewing, and **(c)** standardized chewing jaw tasks. Table 2 shows significant differences in EMG slopes between isotonic and hypertonic saline.

ferents and/or the effect of a low level of pain on EMG activity in some participants. The remaining discussion refers to the differences in EMG activity noted between the hypertonic and isotonic saline infusions; that is, the net effect of pain on motor activity. The isotonic saline infusion is taken as the control.

Effect of Pain on Jaw Muscle Activity

The effect of pain on jaw muscle activity varies with the task and between agonists or antagonists in a task.

Table 2 shows that there were significant differences in EMG slope between hypertonic saline and isotonic saline infusion for the agonist muscles, RAT and LAT, during the closing phases of all three tasks. However, although the EMG slopes for the RAT and LAT were decreased during the closing phase of the open/close task (Fig 1a), the slopes were increased during the closing phases of free chewing (Fig 1b) and standardized chewing (Fig 1c, Table 2). As another example, pain was associated with an increased slope for LMAS activity in the closing phase of free chewing (Fig 1b), as noted for RAT and LAT, but a decreased slope in standardized open/close, as also noted for RAT and LAT (Fig 1a).

The task performed appears to be an important factor in determining whether an agonist or an antagonist muscle is affected by pain, and the effect of pain on different agonists and antagonists within the same task can be different. Other studies have provided evidence for variations in pain effects in muscles depending on the level of activation in a task or the demands of a task.[9,14,18,37,38] The decreased slopes of the RAT, LAT, and LMAS during pain compared to the isotonic saline infusion control in the standardized open/close task, in the absence of significant effects on opening or closing amplitude or velocity,[25] suggest that rapid neuroplastic changes result in a reorganization of jaw muscle activity

Table 3 Significant Correlations Between Psychologic Scores and Electromyographic Change Scores During Isotonic or Hypertonic Saline

Psychological variable	Muscle	Mean RMS change scores	Movement task	Condition	Rank correlation	*P* value
PCS	RAT	–1.974917	Closing, standardized chewing	Hypertonic	0.460	.042
	LAT	–0.362196;	Closing, open/close;	Isotonic;	0.508;	.027
		–1.967519	Closing, free chewing	Hypertonic	–0.483	.034
	RMAS	–1.494327	Closing, standardized chewing	Hypertonic	0.475	.037
	LMAS	–0.255477	Closing, open/close	Isotonic	–0.464	.041
	RDIG	–	–	–	–	–
Depression	RAT	–0.9374087;	Opening, free chewing;	Hypertonic;	0.489;	.032
		–1.0370980	Opening, standardized chewing	Hypertonic	0.537	.020
	LAT	–1.14381860;	Opening, standardized chewing;	Hypertonic;	0.528;	.022
		–1.2087442	Opening, standardized chewing	Isotonic	0.492	.031
	RMAS	–0.8547373;	Opening, free chewing;	Hypertonic;	0.693;	.002
		–0.79809803	Opening, standardized chewing	Hypertonic	0.694	.002
	LMAS	–0.54657013;	Opening, free chewing;	Hypertonic;	0.451;	.046
		–0.5978240;	Opening, standardized chewing;	Hypertonic;	0.505;	.028
		–0.63743209	Opening, standardized chewing	Isotonic	0.489	.032
	RDIG	–	–	–	–	–
Anxiety	RAT	–0.9374087;	Opening, free chewing;	Hypertonic;	0.471;	.038
		–1.1610967	Opening, standardized chewing	Isotonic	0.580	.012
	LAT	–	–	–	–	–
	RMAS	–0.8547373;	Opening, free chewing;	Hypertonic;	0.740;	.001
		–0.79809803	Opening, standardized chewing	Hypertonic	0.471	.038
	LMAS	–1.2071931;	Closing, free chewing;	Hypertonic;	0.486;	.033
		–0.63743209	Opening, standardized chewing	Isotonic	0.454	.045
	RDIG	–	–	–	–	–
Stress	RAT	–0.9374087;	Opening, free chewing;	Hypertonic;	0.461;	.042
		–1.0370980;	Opening, standardized chewing;	Hypertonic;	0.539;	.019
		–1.9749173;	Closing, standardized chewing;	Hypertonic;	0.471;	.038
		–1.1610967	Opening, standardized chewing	Isotonic	0.532	.021
	LAT	–	–	–	–	–
	RMAS	–0.8547373	Opening, free chewing	Hypertonic;	0.450;	.046
	LMAS	–1.1051033;	Closing, free chewing;	Isotonic;	0.457;	.043
		–1.2071931	Closing, standardized chewing	Hypertonic	0.493	.031
	RDIG	0.4685180;	Opening, free chewing;	Hypertonic;	0.461;	.042
		–0.0216322;	Closing, free chewing;	Hypertonic;	0.512;	.025
		0.4665346;	Opening, standardized chewing;	Hypertonic;	0.448;	.047
		–0.0545638	Closing, standardized chewing	Isotonic	0.466	.040

Spearman correlation analysis. PCS = Pain Catastrophizing Scale; DASS-21 = Depression, Anxiety and Stress Scales; RAT = right anterior temporalis; LAT = left anterior temporalis; RMAS = right masseter; LMAS = left masseter; RDIG = right digastric muscle; RMS = root mean square.

to allow the task to be performed. The face area of the primary motor cortex (face M1) is likely to play a dominant role in driving the motor units involved in the standardized open/close task,[39] and there is good evidence for changes in face M1 activity during pain,[40–43] as has been noted in the limb.[44] Therefore, at least some of the neuroplastic changes responsible for the reorganization of jaw muscle motor unit activity may be occurring within the face M1.

While a decreased slope was noted in the agonist muscles RAT, LAT, and LMAS during pain in the closing phase of the open/close task, these same agonist muscles exhibited increased EMG slopes during pain in the closing phases of free chewing. The antagonist RDIG exhibited a decreased EMG slope in comparison with isotonic saline. The increased EMG activity in the agonists during the closing phases of the chewing tasks occurred in the presence of slight but significant decreases in the amplitude and velocity of free chewing (Amhamed et al[25]). Given the necessity to generate sufficient force to crush the chewing gum food bolus, the masticatory central pattern generator and/or the face M1 may be reorganizing to drive motor unit activity to allow chewing to be performed, although at slightly lower amplitude and velocity.

In comparison with isotonic saline, during hypertonic saline, there was a decreased agonist muscle EMG slope during closing, with no significant effects on amplitude or velocity of the standardized open/close task[25]; however, there was an increased agonist muscle EMG slope during closing with significant reductions in amplitude and/or velocity of free chewing.[25] The differences in pain-related EMG and motor effects between the two tasks, under

Fig 3 The average root mean square (RMS) values of the left masseter muscle (LMAS) obtained from participants **(a)** P4, **(b)** P6, **(c)** P8, and **(d)** P14 at each 0.5-mm increment of the closing phase of the free chewing task performed under baseline and test conditions. In each participant, plots show averaged data across all cycles of the closing phases of free chewing under baseline, hypertonic saline infusion, and isotonic saline infusion conditions.

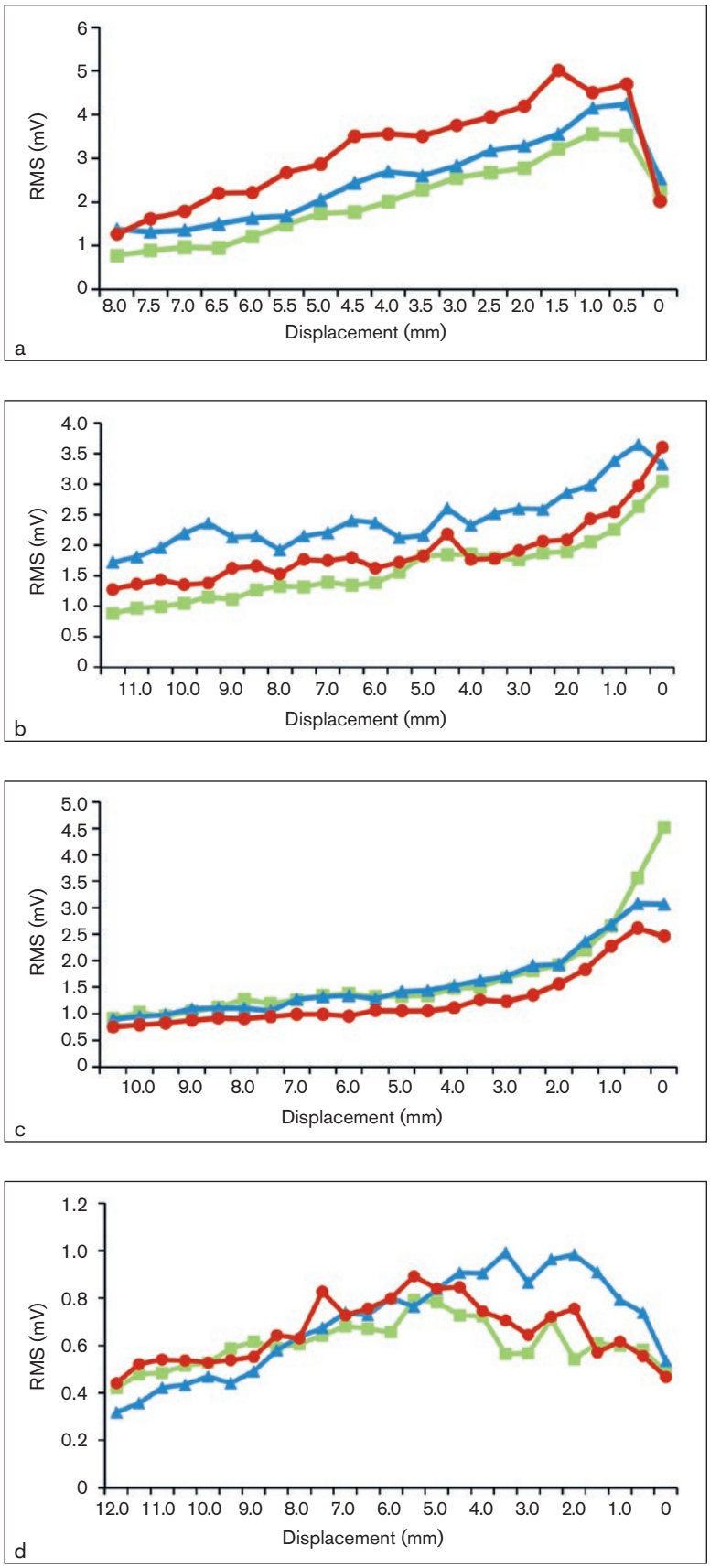

Table 4 Hypertonic Saline vs Isotonic Saline in Relation to Predictions from Vicious Cycle Theory and Pain Adaptation Model

Jaw task	Muscle	Start of movement (Table 1 data)	VCT, PAM	logRMS EMG slope (Table 2 data)	VCT, PAM
Open/close (opening)	RAT	o	X	o	X
	LAT	o	X	o	X
	RMAS	H > I	VCT	o	X
	LMAS	I > H	PAM	o	X
	RDIG	o	X	o	X
Open/close (closing)	RAT	o	X	I > H	PAM
	LAT	I > H	PAM	I > H	PAM
	RMAS	I > H	PAM	o	X
	LMAS	o	X	I > H	PAM
	RDIG	o	X	o	X
Free chewing (opening)	RAT	I > H	PAM	o	X
	LAT	o	X	o	X
	RMAS	o	X	o	X
	LMAS	o	X	o	X
	RDIG	o	X	o	X
Free chewing (closing)	RAT	o	X	H > I	VCT
	LAT	o	X	H > I	VCT
	RMAS	I > H	PAM	o	X
	LMAS	o	X	H > I	VCT
	RDIG	I > H	X	I > H	X
Standardized chewing (opening)	RAT	o	X	o	X
	LAT	o	X	o	X
	RMAS	I > H	PAM	o	X
	LMAS	o	X	o	X
	RDIG	o	X	o	X
Standardized chewing (closing)	RAT	o	X	H > I	VCT
	LAT	o	X	H > I	VCT
	RMAS	I > H	PAM	o	X
	LMAS	H > I	VCT	o	X
	RDIG	I > H	X	o	X

Direction of change in the electromyographic (EMG) activity at the start of the movement and the log-transformed root mean square (RMS) EMG slope for all tested muscles for the comparisons between hypertonic saline (HS) and isotonic saline (IS) infusions for the standardized open/close, free chewing, and standardized chewing tasks from Tables 1 and 2. The changes are also compared with the predictions of the Vicious Cycle Theory (VCT) and the Pain Adaptation Model (PAM). X = inconsistent with VCT or PAM. RAT = right anterior temporalis; LAT = left anterior temporalis; RMAS = right masseter; LMAS = left masseter; RDIG = right digastric muscle; RMS = root mean square.
Direction of effect: H > I = EMG slope during HS is greater than the EMG slope during IS infusion; I > H = EMG slope during HS is less than the EMG slope during IS infusion; o = no significant difference between HS and IS.

noxious stimulation in comparison with control, may reflect possible differences of the influence of nociceptive activity on the two motor regions driving the motoneurons in the tasks, namely the primary motor cortex for the standardized open/close task and, for free chewing, predominantly the masticatory central pattern generator, but with modulatory influences from the primary motor cortex. One possible interpretation of the data is that during light voluntary closing movements (largely driven from the face primary motor cortex, as would likely occur in the open/close task), noxious stimulation results in a decrease in the agonist EMG activity, and this may reflect the decrease in motor cortical excitability during jaw muscle noxious stimulation.[42] During gum chewing, in comparison with the open/close task, however, there are greater closing forces involved, and there is likely to be a greater influence in their generation from the masticatory central pattern generator, which appears to respond to nociceptive input by increasing the drive to agonist motoneurons. This increased agonist drive during closing, which may also involve the face motor cortex, may indeed be responsible for the small reduction in amplitude noted during free chewing during hypertonic saline infusion in comparison with isotonic saline infusion.[25]

Evidence for reorganization of motor unit activity both within muscles and between muscles has also been reported in studies of hypertonic saline–evoked masseter muscle pain,[14,15,45] hypertonic saline–evoked temporalis muscle pain,[18] and in studies of neck and limb muscle pain.[35,46–49] No significant effects were noted in any of the muscles for the analysis of EMG slope when the muscles acted as antagonists, except as noted above for a decreased RDIG activity during the closing phase of free chewing (Table 2); however, differences were noted at the start of movement (Table 1). A lack of significant effects or decreases or increases in antagonist muscle activity have been reported in other studies of experimental pain.[10,14,37,50]

Findings in Relation to the VCT and PAM

The VCT[1] and the PAM[2] have provided explanations as to how muscle activity changes during noxious stimulation. While the VCT proposes that pain results in hyperactivity—that is, increases in EMG activity—the PAM proposes decreases in activity when a muscle acts as an agonist and increases in activity when it acts as an antagonist. There are some observations in the clinical and experimental pain literature that are consistent with some of these predictions from these earlier theories,[6,51,52] but neither the theory nor the model are capable of explaining the wide range of changes in muscle activity in response to pain.[34,51,53]

Table 4 lists the changes in EMG activity at the onset of a movement (data from Table 1) and the changes

in EMG slope between hypertonic and isotonic saline infusions (data from Table 2) in relation to the predictions of the VCT and the PAM. Of the 60 comparisons in relation to these earlier theories, there were 17 changes consistent with either the VCT or the PAM, 7 consistent with the VCT and 10 consistent with the PAM. Therefore, most comparisons were not consistent with these earlier models, which suggests that they are too simplistic to explain the effects of pain on motor activity, as previously noted.[3,4,6,14,18] It may be more appropriate to consider the effects of pain on motor activity in terms of a redistribution or a reorganization of muscle activity[3,4,15,45] and as a reorganization influenced by the functional complexity of the jaw motor system and the multidimensional nature of pain.[6,14,18]

This reorganization of motor unit activity, with increases and decreases in activity occurring in the same region of the muscle, may be recorded by surface electrodes as no significant effects across blocks. Another not mutually exclusive possibility explaining the absence of changes in surface EMG activity during hypertonic saline in comparison with isotonic saline (Tables 1 and 2) could relate to the variability observed in the present study (eg, Fig 4; Table 3 in Amhamed et al[25]) between individuals in the motor response to pain. This variability has also been noted in previous studies.[3,13,14,17,18,54] The grouping of data from different individuals may result in no significant net changes in the grouped surface EMG activity between pain and no pain groups. Variability between individuals may arise because of variations in the locations of EMG electrodes and injection sites, as well as possible differences between individuals in the motor unit recruitment strategies in the presence of pain. Anatomical differences in internal muscle architecture between individuals[55] may also have an impact on how the brain motor centers alter their recruitment patterns in the presence of localized noxious stimulation within the muscle.

Despite this variability between individuals in the motor response to pain and the evidence for reorganization of motor unit activity within the jaw muscles, the hypertonic saline vs isotonic saline comparisons for some of the jaw muscles in the present study do indeed show significant EMG differences in the grouped data (Tables 1 and 2). This indicates that, while motor unit recruitments and de-recruitments might be occurring within each of the muscle regions from which surface EMG recordings are being made, for some of the muscles or regions within the muscles, the surface EMG activity appears to be predominantly increasing (or decreasing) in those regions that are being recorded by the surface electrodes. It is possible that other regions within the same muscles may show the same or different EMG effects.

Association Between Psychologic Variables and Jaw Muscle Activity During Experimental Pain

Previous studies have demonstrated associations between psychologic variables (eg, depression, anxiety, stress, pain catastrophizing, fear of movement) and pain-related changes in jaw motor activity.[10,16,18-20,23,56–58] In the present study, associations were also found between psychologic variable scores and jaw muscle activity during pain. The analyses with the psychologic variables were exploratory, with no adjustment for multiple comparisons. Nonetheless, there were 22 significant correlations between depression, anxiety, stress, and pain catastrophizing with jaw muscle EMG activity for the hypertonic saline infusion (Table 3). Of these 22 correlations, 21 were positive; that is, those individuals with higher psychologic variable scores were more likely to exhibit more EMG activity during pain in that individual during a movement. These data suggest that the degree of motor unit reorganization of motor unit activity during pain may be influenced by an individual's mood or pain-related cognition. A recent study[10] has also shown positive correlations between changes in temporalis muscle EMG activity during pain (in comparison to control) and PCS scores.

Seven of the positive correlations demonstrated were for muscles acting as agonists, and 14 were for muscles acting as antagonists. It is possible that mood or cognition may be more likely to increase antagonist EMG activity during chewing in pain. The accompanying paper[25] shows that amplitude and/or velocity were significantly smaller during hypertonic saline vs isotonic saline infusion in free chewing. These reductions may therefore be partly explained by the tendency for individuals with higher scores in mood to exhibit greater antagonist EMG activity during hypertonic saline infusion than those with lower scores, and this greater antagonist EMG activity may have contributed to the reduction in the amplitude and velocity of chewing noted in the grouped data. The absence of significant correlations between any of the psychologic scores and any of the kinematic parameters during hypertonic saline infusion (Amhamed et al[25]) despite the presence of significant EMG correlations may be reflective of the small sample size. Also, it is possible that in healthy individuals, the reorganization of muscle activity may be sufficient to allow task performance at the level occurring in the absence of pain.

Positive correlations have recently been demonstrated between PCS scores and jaw movement variability during simulated chewing, as well as brain activity within the face primary motor cortex, the trigeminal motor nucleus, and the cerebellar cortex in the presence of experimental noxious stimulation of the right masseter muscle.[16,43] These recent data

suggest that at least some of these psychologic constructs may be manifesting their effects by modifying the activity of the face M1 to provide the reorganization of motor unit activity during jaw movements that appears to be occurring in the presence of pain.

Recent comparable experiments in a different sample but involving the same tasks recorded during experimental temporalis muscle noxious stimulation did not show any significant correlations between the DASS and PCS scores and jaw muscle EMG activity.[18] The presence of many significant correlations in the present study with simultaneous masseter and temporalis muscle noxious stimulation suggest that noxious stimulation at two jaw muscle sites might allow psychologic factors to have greater effects on jaw muscle EMG activity than when only one jaw muscle site is the site of noxious stimulation. Pain location has been previously suggested as a factor that may influence the pain-motor interaction.[6]

Limitations

The small sample size derived from health professional staff and postgraduate students limits the generalizability of the findings regarding pain-motor interaction to the general population or to chronic pain patients who are likely to exhibit adaptations to pain such as pain fluctuations, long-term adaptations, functional disabilities, and psychologic distress. Another limitation is that the sample was mostly male participants, and TMD is less common in men than in women. For some analyses, no corrections were made for multiple comparisons, as this was an exploratory study and the chances of a type I error increase with the number of analyses performed. Some of the significant findings are weak, and care needs to be taken in interpreting the data. Further studies are required to confirm or not confirm the findings. Other limitations are the use of surface electrodes over only a few of the jaw muscles and quantification of the EMG signals through RMS calculations, which may not be a sensitive measure of subtle changes in the EMG activity of investigated muscles.

Conclusions

The findings from the present and the associated paper[25] show that while simultaneous experimental pain evoked from both the anterior temporalis and masseter muscles is associated with no or only mild significant changes in jaw movement, significant EMG changes were noted, and some of these EMG changes were correlated with some psychologic scores. These data add to the emerging evidence that jaw muscle activity reorganizes in the presence of pain, and the level of reorganization is modulated by psychologic measures. The findings were generally inconsistent with the earlier VCT and the PAM. The present data appear to be more consistent with a more recent theory of pain-motor interaction that implicates psychologic influences.[6] While the findings cannot be directly extrapolated to understanding how the jaw motor system adapts to pain in TMD patients, it is tempting to speculate that in most individuals, the jaw motor system can adapt to noxious stimulation through reorganization of motor unit activity with possible influence from psychologic factors. In certain individuals in whom this modulation is dependent on genetic or environmental risk factors and in whom higher psychologic distress or pain catastrophizing might be present, changes in EMG activity might occur beyond the adaptive capabilities of the muscles, which might lead to pain.

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