Reorganization of Masseter and Temporalis Muscle Single Motor Unit Activity During Experimental Masseter Muscle Pain

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Aims: To test the hypothesis that experimental noxious stimulation of the right masseter muscle results in a reorganization of motor unit activity within the right temporalis and right masseter muscles during jaw closing tasks. **Methods:** A total of 20 healthy participants received hypertonic saline (5% sodium chloride) infusion into the right masseter muscle, and pain intensity was maintained at 40–60/100 mm on a visual analog scale. Standardized isometric biting tasks were performed with an intraoral force transducer while single motor units (SMUs) were recorded from the right masseter and temporalis muscles. Tasks were repeated in four blocks: block 1 (baseline 1), block 2 (hypertonic saline [HS] infusion or isotonic saline [IS] infusion), block 3 (infusion of the other solution), and block 4 (baseline 2). The occurrences of SMUs were tabulated across blocks. Statistical significance was considered to be $P < .05$. **Results:** There were no significant effects of block on the tasks. A total of 83 SMUs were discriminated in the temporalis and 58 in the masseter. For the comparison between HS and IS across tasks, the occurrences of 74.6% to 82.8% of SMUs were unchanged (70.2% to 94.3% for masseter), while during HS, 10.3% to 17.1% of SMUs were recruited (0% to 12.8%, masseter) and 6.9% to 12.7% were de-recruited (5.7% to 17%, masseter). **Conclusion:** The present findings suggest that most biting-task–related jaw muscle SMUs remain active during experimental muscle noxious stimulation. There was some evidence in both the anterior temporalis and masseter muscles for motor unit recruitment and de-recruitment consistent with a motor unit reorganization during experimental pain. *J Oral Facial Pain Headache 2020;34:40–52. doi: 10.11607/ofph.2426*

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Temporomandibular disorders (TMD) are clinical conditions that often involve pain in the masticatory muscles, the temporomandibular joint (TMJ), and/or associated structures. Little is known of the mechanisms whereby acute TMD episodes become chronic, although clinical diagnosis and management have been influenced by earlier theories of a simple, reflex-like association between pain and muscle activity.[1–3] One of these earlier theories, the Vicious Cycle Theory (VCT), proposes a positive interrelationship between pain and muscle activity that leads to muscle hyperactivity.[1] Management strategies based on this theory attempt to break this cycle with irreversible and often invasive changes to the anatomy (eg, surgery or tooth adjustments).[4] However, in contrast to this theory's underlying assumption that painful muscles are hyperactive, many clinical and experimental studies and some comprehensive reviews in both the spinal and trigeminal systems revealed only small differences (small increases or decreases) or no change in resting electromyographic (EMG) activity between painful and nonpainful muscles.[2,4–17] The clinical significance of any of these small changes is unclear and does not appear to be supportive of a vicious cycle between pain and muscle activity.[2–4,11,17–19]

The Pain Adaptation Model (PAM)[18,20] was introduced by James Lund and colleagues to counter the VCT, and this model proposes that existing pain results in slower and smaller movements that minimize further injury and aid healing.[4,18,20] According to this model, pain results in a reflex inhibition of agonist muscle activity and a facilitation of antagonist muscle activity, which has the effect of decreasing movement velocity and amplitude during pain. Studies and reviews in both the spinal and trigeminal systems provide limited evidence, however, in support of either this model or the earlier VCT.[2–4,11,13,18,19,21–29]

Some of these earlier studies and theories are based on the underlying assumption that there are uniform increases or decreases of activity within a painful muscle. However, some of the more recent experimental muscle pain studies in limb and neck muscles[21,30,31] and in the masseter[24,25,32] have provided evidence for a reorganization of motor unit activity during noxious stimulation with changes in motor unit activity that may not be uniform across a muscle and indeed may be different between single motor units (SMUs) recorded at the same site within a muscle. For example, some of these studies have shown that these changes can manifest as a de-recruitment or silencing of one population of motor units, together with a recruitment or activation of a new population of motor units.[21,22,24,25,30,33] In the limb literature, these studies have shown that reorganization of motor unit activity can occur even in nonpainful muscles—that is, when the noxious stimulation is in another muscle or tissue.[30,33] In the jaw motor system, some surface EMG recordings have reported changes in jaw muscle activity in jaw muscles other than the one subjected to the noxious stimulation.[13,23,34,35] However, it is unclear whether the reorganization of single motor unit activity that has been described within the painful masseter muscle[24,25] is also demonstrable within other jaw muscles involved in a task that are not being subjected directly to noxious stimulation.

Whether there is a reorganization of SMU activity within jaw muscles other than the jaw muscle subjected to the noxious stimulation may have implications for understanding the progression of pain in TMD patients if some of these changes in muscle activity might predispose an individual to further pain and tenderness by involving previously nonpainful muscles. Such possible pain-related changes in motor unit activity have been proposed in the spinal motor system[36] and have also been suggested in the jaw motor system.[11] The aim of the present study was to test the hypothesis that experimental noxious stimulation of the right masseter muscle results in a reorganization of motor unit activity within the right masseter and right temporalis muscles during jaw closing tasks.

A previous paper was published with data from 18 of the participants and collected in the same experimental sessions as the present study.[37] This previous paper reported that experimental noxious stimulation of the right masseter muscle does not modify force or surface EMG activity recorded from the bilateral masseter and anterior temporalis muscles during isometric biting tasks.[37] The present paper reports SMU activity recorded from the right masseter and right anterior temporalis muscles in the same experimental sessions as the previous study.

Table 1 Overview of the Experimental Paradigm

Item	Pre	Block 1	Rest	Block 2	Rest	Block 3	Rest	Block 4
Questionnaires	×							
Tasks		×		×		×		×
Infusions				×		×		
Pain maps, VASs				×		×		
Rest			×		×		×	
MPQ					×		×	
Duration (min)		10	10	10	10	10	10	10

Block 1 = baseline 1; Block 2 = hypertonic saline infusion or isotonic saline infusion; Block 3 = infusion of the other solution; Block 4 = baseline 2; VAS = visual analog scale; MPQ = McGill Pain Questionnaire.

Materials and Methods

Twenty participants were recruited (15 women, 5 men; age range: 22 to 40 years; mean ± standard deviation [SD] age 29.5 ± 4.3 years). Participants were students of the University of Sydney and were from the general public. Exclusion criteria were neuromuscular dysfunction; systemic musculoskeletal conditions or history of chronic pain; chronic or acute pain conditions at the time of the experiment; use of medications for chronic diseases; high blood pressure; pregnancy; less than 24 teeth; an overjet or overbite that would interfere in the placement of the force transducer; dentures; or ongoing orthodontic treatment.

Participants gave written informed consent before being enrolled in the study, and the study was approved by the Human Research Ethics Committee of the University of Sydney. The study was conducted in accordance with the Declaration of Helsinki. The study was carried out over two sessions at the Jaw Function and Orofacial Pain Research Unit (Westmead Centre for Oral Health, Sydney). Many of the procedures have been previously described in detail.[13,24,25,37] The data from 18 of the 20 participants presented in this paper were collected at the same time as the data collected for a recent publication.[37]

Table 1 is an overview of the experimental paradigm. There were four blocks: block 1 (baseline 1 prior to infusion), block 2 (hypertonic saline [HS] or isotonic saline [IS] infusion), block 3 (infusion of the other

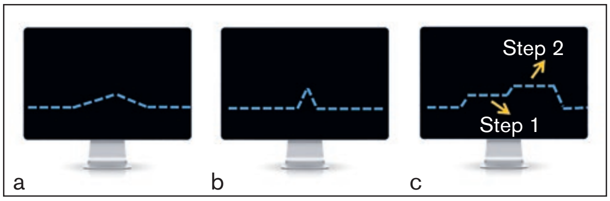

Fig 1 Schematic of the computer screen placed in front of the participant with the target force that each participant was instructed to match as closely as possible in order to achieve the same force rates and levels in every trial of a task. **(a)** Slow ramp biting task. **(b)** Fast ramp biting task. **(c)** Two-step biting task.

solution), and block 4 (baseline 2). The sequence of infusion was alternated between participants. In each of the four blocks, recordings were made of SMU activity from the masseter and temporalis muscles during task performance. The previous publication[37] reported only on the data collected in the first three blocks.

At the first session, all participants were confirmed by a single calibrated examiner to be free of TMD as defined by the Research Diagnostic Criteria for Temporomandibular Disorders (RDC/TMD).[38] The RDC/TMD was used in this study, as it is still a globally accepted standard of TMD diagnosis. Maxillary and mandibular alginate impressions were then used to construct plaster casts on which intraoral splints were fabricated for the bite force transducer (LMA-A; Kyowa Dengyo). A detailed description of the bite force device has been published.[24,25,37] In brief, custom-made polyvinal splints (Erkodent, Erkoplast-0, 1.5-mm thickness and 120-mm diameter) covered the maxillary and mandibular teeth and supported a small force transducer to measure vertical jaw closing force.

Intramuscular Electrode Placement

Bipolar Teflon-coated fine-wire electrodes (Mediwire) were placed in the approximate middle (horizontally and vertically) of the right masseter muscle. The insertion point for the temporalis intramuscular electrodes was ~1 cm posterior to the posterior border of the frontal process of the zygoma. Voluntary clenches identified the most active regions of the masseter and temporalis muscles to assist in electrode placement. Topical anesthetic was applied on the skin, and intramuscular electrode placement was made via 24- to 26-gauge needles (25 mm long) containing two fine wires that were bent back over the tip of the needle 2 to 5 mm from the ends of the wires and with 0.5 mm of exposed wire. For each electrode placement, the needle was inserted ~20 mm or until the needle contacted bone and was then withdrawn so as to leave the fine wires within the muscle. For the masseter, the needle was angled down at ~30 degrees, and for the temporalis, the needle was angled down at ~45 degrees. The electrodes were sterilized prior to placement in each muscle. EMG activity from the electrodes was confirmed by asking participants to clench. A ground electrode was attached to the left wrist.

Tasks

The participant performed three isometric jaw closing tasks (biting tasks; Fig 1) with the bite force transducer in place. Each performance of a task was termed a trial.

The slow ramp biting task involved an initial 2- to 3-second rest period, after which participants were instructed to increase jaw closing force at a low force rate (5 N/second) to a maximum force of 93 N and then to release the closing force. The task took ~40 to 45 seconds. The fast ramp biting task involved an increase in jaw closing force at a higher force rate (17 N/second) than for the slow ramp jaw closing task, up to a maximum of 119 N. This task took ~20 seconds.

In the two-step biting task, the participant increased jaw closing force to a first level (step 1), then held at that force level for 2 to 3 seconds, then increased the force to a second level (step 2) and held that force level again for another 2 to 3 seconds before relaxing. The force at each level was customized for each participant. Step 1 was determined as the force level when an experimenter noted the recruitment of at least one SMU. The step 2 force level for a participant was determined by having the participant increase closing force so that there was a clear increase in the firing rates of the existing SMU(s) and/or there was recruitment of additional SMUs. Both of the force levels were readily achievable closing forces. The step task took ~10 to 12 seconds; there was a duration of 0.5 to 1 second for the increase in force from rest to step 1, and from step 1 to step 2.

Each of the three isometric biting tasks was repeated three times. These nine trials were then repeated in each of the four blocks, which were: baseline, before any infusion (block 1); HS or IS infusion (order alternated between participants; block 2); infusion of the other solution (block 3); and baseline 2, after the two infusions were completed (block 4).

Induction and Assessment of Pain

The induction and assessment of jaw muscle pain followed the previously published protocol closely.[37,39] Briefly, a disposable 22- or 24-gauge needle–integrated IV catheter was inserted into the middle of the right masseter, and the catheter was connected to an infusion pump containing either 5% sterile saline (HS) or 0.9% sterile saline (IS). HS was infused at a rate of 4 to 6 mL/hour to achieve a moderate pain intensity of between 40 and 60 mm on a 100-mm visual analog scale (VAS) with anchors of "no pain" and "the worst pain possible." A moderate level of pain was maintained by noting the VAS score after each trial and adjusting the infusion rate as required by 1 to 4 mL/hour. IS was infused in the other block at the same rate of infusion as the HS.

Psychologic Questionnaires

To study possible associations between motor function and psychologic measures, the Depression, Anxiety and Stress Scales 21 (DASS-21)[40] and the Pain Catastrophizing Scale (PCS)[41] were completed before the experiment. The DASS-21 questionnaire is a self-report measure of depression, anxiety, and stress and consists of 21 statements scored on a 4-point scale based on how much each applied in the past week. Scores are summed to give a total for each of the depression, anxiety, and stress scales. The PCS is a questionnaire comprised of 13 statements, each rated on a 5-point scale to the degree to which the statement applies when an individual is experiencing pain. The PCS total score is the summed responses. The McGill Pain Questionnaire (MPQ)[42] is a self-report questionnaire describing the quality and intensity of a painful experience and consists of four categories of verbal pain descriptors: sensory, affective, evaluative, and miscellaneous. A pain rating index (PRI) is calculated for each category of pain descriptor from the mean of the sums of the scale values from all the words chosen in a category. The MPQ was completed after blocks 2 and 3.

Data Analyses

Across all participants, mean and SD values were calculated for each scale of the DASS-21 and subscale of the PCS (rumination, helplessness, and magnification). All data obtained during the hypertonic saline infusion or the isotonic saline infusion were grouped so as to generate the dataset for the hypertonic saline infusion block (HS block) or for the isotonic saline infusion block (IS block), respectively. For the VAS scores, there was no significant effect (repeated-measures analysis of variance [ANOVA]; $P < .05$) of repeating the trial during the HS or IS block, and mean and SD were calculated for these VAS scores. Paired *t* tests ($P < .05$) determined significant differences between the HS and IS blocks in terms of the infused volumes and the VAS scores.

Mean and SD values were calculated for each PRI for the HS block and IS block. For this analysis, the means of the summations of the scale values from the chosen words in each category of the MPQ were used. A paired *t* test compared the scores of the mean scale values between the HS and IS blocks.

The force output, recorded in volts, was converted into Newtons (N), and the maximum force achieved (amplitude) for each of the slow and fast ramp jaw closing tasks was calculated. Force rate (N/second) was calculated by dividing 40 N (for slow ramp) or 45 N (for fast ramp) by the time from force onset to these force levels. The most stable 2-second period for step 1 and step 2 in the two-step biting task was defined as the period with the lowest SD, and these force levels were recorded for each trial in each participant. A repeated-measures ANOVA was used to determine the effects of block (baseline, HS block, IS block) on the maximum force, the most stable 2-second periods, and force rates. All data analyzed with parametric statistical tests were normally distributed.

From each trial of tasks in each block, SMU activity was discriminated in the right temporalis and masseter muscles, except for the masseter in block 4, as masseter SMU analyses have already been performed in two previous recent studies.[24,25] For the slow and fast ramp biting tasks, SMUs were discriminated from the onset of an increase in force at the beginning of the task until reliable SMU discrimination was no longer possible. For each trial of the two-step biting task, the 2-second period of each step level with the lowest SD was selected for identification of SMUs. Discrimination involved the use of template-matching software (Spike2, Cambridge Electronic Design), with identified SMUs being manually confirmed that they were similar in amplitude and shape. An SMU was defined as being present during the two-step biting task if the SMU had a regular time of occurrence and fired continuously within the 2-second period for at least one step during at least two of the three repeated trials. Every SMU determined as present or not present during each jaw closing task in each block was tabulated. This allowed an assessment of whether that SMU was present in each task and block or only in some tasks or blocks.

An analysis was also done to determine whether the changes in the patterns of occurrence of SMUs in both muscles were consistent with the principles of the VCT or the PAM. For this analysis, whenever the SMU was recruited in the hypertonic saline block but was inactive (not present) in the isotonic block, the pattern of the SMU occurrence was considered consistent with the VCT, since, according to this theory, the pain would cause muscle hyperactivity and this would be associated with SMU recruitment. Contrarily, if the SMU was inactive (not present) during the hypertonic block but present in the isotonic, this pattern of occurrence was considered consistent with the PAM, since pain is related to a decrease in agonist muscle activity, and one manifestation of this would be de-recruitment of one or more SMUs.

A quantitative analysis was performed to investigate possible correlations between differences in

Table 2 Mean (Standard Deviation) Force Amplitude, Force Rates, and Step Level Amplitudes for All Participants (n = 20) During Blocks 1 to 3 for the Slow Ramp and Fast Ramp Biting Tasks and Steps 1 and 2 of the Two-Step Biting Task

	Baseline (block 1)	Hypertonic saline (block 2 or 3)	Isotonic saline (block 2 or 3)
Slow ramp amplitude, N	54.8 (12.8)	52.5 (11.2)	54.9 (10.0)
Fast ramp amplitude, N	59.7 (19.3)	62.6 (18.7)	60.9 (14.7)
Slow ramp rate, N/s	9.34 (5.4)	9.7 (5.7)	9.5 (5.1)
Fast ramp rate, N/s	20.9 (9.7)	22.6 (9.7)	21.7 (9.0)
Step 1 amplitude, N	33.3 (14.3)	32.3 (15.1)	32.1 (14.6)
Step 2 amplitude, N	66.1 (26.4)	65.6 (26.3)	65.4 (28.3)

SMU occurrences and psychologic variables. For this, PCS and DASS-21 scores of the participants in whom the occurrences of SMUs did not change during any of the infusions for the temporalis muscle were compared to the scores of those participants in whom the occurrences of SMUs did change in at least one block of infusion. The sample size was based on previous studies in both the spinal[30] and trigeminal[24] literature that have demonstrated changes in SMU recruitment patterns with comparable sample sizes of participants and numbers of SMUs that were discriminated.

Results

Psychologic Measures

For the DASS-21, the mean (SD) scores were 1.5 (1.9) for stress, 0.2 (0.7) for depression, and 0.5 (0.8) for anxiety. For the PCS scores, the mean (SD) total score was 8.3 (7.7). Rumination and helplessness had the highest group means, with 3.2 for both (SD: 3.3 and 3.2, respectively), followed by magnification, with 1.85 (1.7).

Experimental Jaw Muscle Pain

There was no significant difference ($P = .74$) between the total volume infused for hypertonic (mean 0.8 mL, SD 0.5) and isotonic (mean 0.7 mL, SD 0.4) saline solutions across the 20 participants. The VAS scores during the HS block (slow ramp biting task: mean 43 [SD 12.8], fast ramp biting task: 43.5 [10.5], two-step biting task: 47.3 [7.0]) were significantly greater ($P < .001$) than the VAS scores obtained during the IS block (slow ramp biting task: 3.9 [8.9], fast ramp biting task: 4.4 [10.3], two-step biting task: 4.0 [9.0]).

During the HS block, all 20 participants described localized pain in the area of the right masseter, and 2 participants also reported referred pain in the right anterior temporalis or around the right angle of the mandible. Participants 2, 4, 6, and 19 reported localized pain in the area of the right masseter during the IS block. The most cited words from the MPQ for the HS block were annoying (14/20), aching (13/20), pressing (12/20), and jumping (8/20); for the IS block, boring was cited by 3 people, and annoying by 2. The total PRI was 7.4 for the HS block and 2.3 for the IS block.

Force Amplitude, Rates, Levels

All participants performed all tasks under the four blocks. The force rate during the fast ramp biting task was significantly greater ($P < .005$) than for the slow ramp biting task for each of the four blocks. There were no significant effects ($P > .05$) of the repetitions on the force values for each participant during each task, and therefore mean force values were used for further analysis. The force amplitudes and rates have been documented in detail for 18 of the participants[37]; Table 2 provides a summary of mean (SD) values for force amplitude for each task, and force rates for the ramp tasks in the baseline, HS, and IS blocks. There were no significant effects ($P > .05$) of block on the force amplitudes or force rates during each task.

Occurrence of SMUs in the Right Anterior Temporalis

In total, 83 SMUs were discriminated from the temporalis muscle in 16 participants. There was a technical issue with the remaining 4 participants' recordings. Among those 83 SMUs, 75 were discriminated in at least one of the ramp biting tasks, while 62 (54 also present in at least one ramp task and 8 new SMUs) were discriminated for at least one step level (step 1 and/or step 2) of the two-step biting task.

Slow Ramp and Fast Ramp Biting Tasks. Among the 75 units present for the slow and/or fast ramp biting tasks, 35 (47%) SMUs were present in both the slow and fast ramp biting tasks for all four blocks. A total of 40 SMUs exhibited some change in the pattern of SMU occurrence between blocks. Table 3 lists the occurrences of these 40 SMUs in each block for both ramp tasks. Of these 40 SMUs, 16 (highlighted in Table 3) showed the same pattern for slow ramp and fast ramp, and 24 (nonhighlighted in Table 3) exhibited some change in the pattern of SMU occurrence between the blocks and between the slow and fast ramp biting tasks.

Two-Step Biting Task. Table 4 lists the 62 motor units present in the two-step biting tasks. Of the 62 SMUs, 8 were only present in the two-step biting task, and the remaining 54 were also present in one or more of the ramp biting tasks. From the 62 SMUs, 37 were discriminated for step 1, and 58 were discriminated for step 2; these 58 included 33 units also present for step 1, plus an additional 25 newly recruited SMUs. The greater force and higher level of EMG activity for step 2 confirmed the presence or absence of 4 SMUs (35, 45, 46, and 49) not reliable. For those cases, a question mark was used in Table 4.

For step 1 of the two-step biting task, from the 37 units discriminated, 15 (41%) were present in all four blocks, 15 were not present in some of the blocks, and it was not possible to confirm whether 7 units were present in all of the blocks because of a technical issue. For step 2 of the two-step biting task, from the 58 units discriminated, 32 (55%) were present in all four blocks, 14 were not present in some of the blocks, and it was not possible to confirm whether 12 units were present in all of the blocks because of a technical issue or due to the increased EMG activity from the greater force on level 2.

Occurrences of SMUs in the Right Masseter

A total of 58 SMUs were discriminated from the masseter muscle in 15 participants. There was a technical issue with the remaining 5 participants' recordings. From those 58 SMUs, 50 units were present in at least one of the ramp biting tasks, and 47 (39 also present in at least one ramp task plus 8 new SMUs) were present in step 1 and/or step 2 of the two-step biting task.

Table 3 Temporalis Single Motor Units (SMUs; n = 40) with Changed Patterns of Occurrence

		Slow ramp				Fast ramp			
Participant	SMU	BS1	HS	IS	BS2	BS1	HS	IS	BS2
1	**3**	−	+	+	+	−	+	+	+
	5	−	+	−	−	−	+	−	−
	6	−	+	−	−	−	+	−	−
2	8	+	+	+	+	+	−	+	+
	9	−	+	−	−	−	−	−	−
5	**18**	+	−	+	−	+	−	+	−
	20	+	+	+	+	+	−	+	−
	21	−	+	+	+	−	+	+	+
	22	−	+	+	−	−	+	+	−
6	**24**	+	−	−	−	+	−	−	−
	25	+	−	−	+	+	−	−	−
	27	+	+	+	+	+	−	+	+
	28	−	+	−	+	−	+	+	+
7	30	+	−	+	+	+	+	+	+
	31	+	−	−	−	+	−	−	−
10	**32**	+	−	+	+	+	−	+	+
	33	−	−	−	−	−	−	+	−
12	41	+	+	+	+	−	+	+	+
	43	−	+	−	−	−	+	−	−
	44	−	−	−	−	−	+	−	−
14	52	+	+	TI	TI	+	+	+	+
	53	−	+	TI	TI	+	+	+	+
	54	−	+	TI	TI	−	−	−	−
15	56	+	+	+	−	+	+	+	+
	57	+	+	+	−	+	+	+	−
	58	−	+	−	−	−	−	−	−
	59	+	+	+	−	+	+	+	−
16	61	+	+	+	+	−	+	+	−
	62	+	+	−	+	+	−	−	+
	64	−	−	+	−	+	+	+	+
17	**65**	+	−	+	−	+	−	+	−
	66	+	+	+	+	+	−	+	−
	67	−	+	+	+	+	+	−	−
	68	−	+	−	+	+	+	−	+
	70	−	+	−	−	−	−	−	−
19	79	+	+	+	−	+	−	+	−
	80	−	+	+	+	+	+	+	+
	81	−	+	−	+	−	+	−	+
	82	−	+	−	+	−	+	−	+
	83	−	+	−	+	−	+	−	+

SMUs in bold type (n = 16) indicate changed patterns of occurrence between blocks but not between slow and fast ramp tasks (n = 16). The remainig 24 SMUs indicated changed patterns of occurrence between blocks and between slow and fast ramp tasks. + = SMU present (ie, present in at least two of three trials or at least half of trials where > three trials were performed); − = not present; TI = technical issue in the recording; BS1 = baseline 1 (block 1); HS = hypertonic saline infusion block; IS = isotonic saline infusion block; BS2 = baseline 2 (block 4).

Slow Ramp and Fast Ramp Biting Tasks. From the 50 SMUs discriminated for the ramp biting tasks, 24 (48%) were present in both the fast and slow ramp tasks for all blocks. The remaining 26 exhibited some change in the pattern of SMU occurrence between the blocks (n = 10) or between the blocks and between the slow and fast ramp tasks (n = 16).

Two-Step Biting Task. From the 47 units in the two-step biting task, 29 were discriminated for step 1, and 35 were discriminated for step 2; these 35 were composed of 21 present for step 1 plus 14 newly recruited SMUs. Because of the greater force and higher level of EMG activity for step 2, 4 units were not precisely confirmed regarding their absence or presence in step 1, and 14 in step 2.

Table 4 Temporalis Single Motor Units (SMUs; n = 62) Discriminated in Two-Step Biting Task

		Step 1				Step 2			
Participant	SMU	BS1	HS	IS	BS2	BS1	HS	IS	BS2
1	1	+	+	+	+	+	+	+	+
	2	+	+	+	+	+	+	+	+
	3	+	–	+	–	+	–	+	+
	4	**–**	**–**	**–**	**–**	**+**	**–**	**+**	**–**
	5	–	+	–	–	–	+	–	+
2	7	+	+	+	TI	+	+	+	TI
	8	–	–	–	TI	+	+	+	TI
	9	+	+	+	TI	+	+	+	TI
	10	**–**	**–**	**–**	**TI**	**+**	**+**	**+**	**TI**
4	11	+	+	+	TI	+	+	+	TI
	12	+	+	+	TI	+	+	+	TI
	13	+	+	+	TI	+	+	+	TI
	15	+	+	+	TI	+	+	+	TI
5	16	+	+	+	+	+	+	+	+
	17	–	–	–	–	+	+	+	+
	19	–	–	–	–	+	+	+	+
	20	–	–	–	–	+	+	+	+
	21	–	–	–	–	+	+	+	+
6	25	–	–	–	–	+	+	+	+
	26	+	+	+	+	+	+	+	+
	27	–	–	+	+	+	+	+	+
	28	–	–	–	–	+	+	+	+
7	29	+	+	+	+	+	+	+	+
	30	+	+	+	–	+	+	+	+
	31	–	–	–	–	-	+	+	–
10	**34**	**–**	**–**	**–**	**–**	**+**	**+**	**+**	**+**
11	35	+	+	+	+	+	?	?	+
	36	+	+	+	–	+	+	+	+
	37	–	–	–	–	+	+	+	+
	38	–	–	–	–	+	+	+	–
12	40	+	+	+	+	+	+	+	+
	41	–	+	–	–	+	+	+	+
	42	+	+	+	–	+	+	+	+
	43	–	+	–	–	–	+	–	–
	44	–	+	–	–	–	+	–	–
13	45	+	+	+	+	?	?	?	?
	46	+	+	+	+	?	?	?	?
	49	**+**	**+**	**+**	**+**	**?**	**?**	**?**	**?**
	50	**–**	**–**	**–**	**–**	**+**	**–**	**–**	**–**
	51	**–**	**–**	**–**	**–**	**–**	**+**	**+**	**+**
14	52	–	–	–	–	+	+	+	+
	53	–	–	–	–	+	+	+	+
15	55	+	+	+	TI	+	+	+	TI
	56	–	–	–	TI	+	+	+	TI
	57	–	–	–	TI	+	+	+	TI
	59	–	–	–	TI	+	+	+	TI
16	60	+	+	+	+	+	+	+	+
	61	–	–	–	+	–	+	–	+
	62	+	–	–	–	+	+	+	+
	63	+	–	+	–	+	+	+	+
	64	–	–	–	–	+	–	+	+
17	67	–	–	–	–	–	+	–	–
	68	+	+	–	–	+	+	+	+
	69	**+**	**+**	**–**	**–**	**+**	**+**	**+**	**+**
	70	–	–	–	–	+	–	+	+
	71	**–**	**–**	**–**	**–**	**–**	**+**	**–**	**+**
18	72	+	+	+	+	+	+	+	+
	73	+	+	+	+	+	+	+	+
	74	+	+	+	+	+	+	+	+
	75	+	+	+	+	+	+	+	+
19	76	+	–	+	–	+	+	+	+
	77	–	–	–	–	+	+	+	+

SMUs in bold type were exclusively found in the two-step task. TI = technical issue; BS1= baseline 1 (block 1); HS = hypertonic saline infusion block; IS = isotonic saline infusion block; BS2 = baseline 2 (block 4). + = present (SMU had a regular time of occurrence and fired continuously within the 2-second period for at least one step during at least two of the three repeated trials); – = not present; ? = not possible to confirm the presence or absence of an SMU for that task.

From the 29 units discriminated in step 1 of the two-step biting task, 19 (66%) were present in the three blocks, 3 were recruited exclusively for the HS block, 2 were de-recruited only for the HS block, and the remaining 5 units were not present in some of the blocks.

For step 2 of the two-step biting task, from the 35 units discriminated, 30 were present in the three blocks, 2 were de-recruited exclusively for the HS block, 1 was recruited only for the baseline but was not present in the HS or IS blocks, and 2 units were not present in the baseline block but were present for the hypertonic and isotonic blocks.

Comparisons Between Blocks

For each of the tasks, HS was compared to block 1 (baseline 1), to the IS block for both muscles, and to block 4 (baseline 2 [BS2]) for the temporalis muscle. This comparison was done in terms of the number of units during the HS block that exhibited no change in the pattern of occurrence between the two blocks, became present in the HS block (ie, recruited), or were no longer present (ie, de-recruited) during the HS block. These analyses for the temporalis and masseter muscles are shown in Table 5 and Fig 2 (HS vs BS1), Table 6 and Fig 3 (HS vs IS), and Table 7 (HS vs BS2) for the temporalis muscle. For the HS vs IS comparison for the temporalis muscle, the occurrence of between 74.6% and 82.8% of SMUs was unchanged across the tasks; between 10.3% and 17.1% of SMUs were recruited during HS; and 6.9% to 12.7% were de-recruited during HS. For the HS vs IS

Table 5 Illustration of the Comparisons Between the Hypertonic Saline Infusion Block and Baseline 1 Block for All Tasks in the Temporalis and Masseter Muscles

	Slow ramp	Fast ramp	Step 1	Step 2
Temporalis				
No change	48/73 (65.8)	46/71 (64.8)	29/37 (78.4)	45/58 (77.6)
Recruited	18/73 (24.6)	13/71 (18.3)	4/37 (10.8)	8/58 (13.8)
De-recruited	7/73 (9.6)	12/71 (16.9)	4/37 (10.8)	5/58 (8.6)
Masseter				
No change	29/47 (61.7)	30/49 (61.2)	17/28 (60.7)	30/35 (85.7)
Recruited	9/47 (19.1)	8/49 (16.3)	4/28 (14.3)	2/35 (5.7)
De-recruited	9/47 (19.1)	11/49 (22.4)	7/28 (25)	3/35 (8.6)

Data are presented as the no. of SMUs/total no. of SMUs for that task (%). Recruited = SMU became present in the hypertonic saline block; de-recruited = SMU was not present during the hypertonic saline block but was present in baseline block.

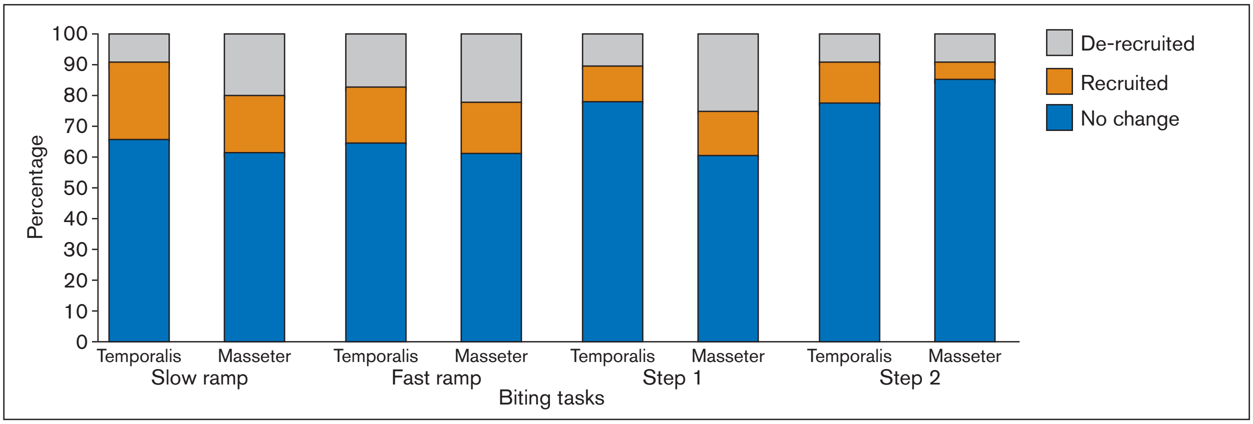

Fig 2 Comparison of single motor unit (SMU) activity between hypertonic saline (HS) and baseline 1 (BL1) blocks. Blue = percentage of SMUs that were present in both the BL1 and HS infusion blocks; orange = percentage of SMUs that were recruited (ie, became active) during HS infusion in comparison to BL1; gray = percentage of SMUs that were de-recruited (ie, became inactive) during HS infusion in comparison to BL1.

comparison for the masseter muscle, the occurrence of between 70.2% and 94.3% of SMUs were unchanged across the tasks; between 0% and 12.8% of SMUs were recruited during HS, and between 5.7% and 17% were de-recruited during HS.

From the 33 units recruited for the temporalis (when comparing the hypertonic block to the isotonic block), HS was infused as the first solution for 9 recruited units, and IS was infused as the first solution for the remaining 24. For the 15 units recruited for the masseter, 10 had HS as the first solution applied and the remaining 5 had IS applied first. From the 22 units de-recruited for the temporalis, HS was infused as the first solution for 9 de-recruited units, and IS was infused first for the remaining 13. For the 19 units de-recruited for the masseter, HS was infused first for 13 de-recruited units, and IS was infused first for the remaining 6.

For the temporalis muscle, the number of participants in which there was a de-recruitment of at least one SMU as well as a recruitment of at least one SMU at the same recording site was two for the slow ramp, two for the fast ramp, one for step 1 of the biting task, and three for step 2 of the biting task.

Changes in SMU Occurrence and Consistency with VCT and PAM

The pattern of change of SMU occurrence (ie, recruitment or de-recruitment) in each muscle for each task was assessed for consistency with the VCT or the PAM (Table 8). The pattern did not support the VCT nor the PAM for at least 70% of the SMUs.

Psychologic Variables and Associations with Occurrences of SMU Activity

Participants who exhibited no change in temporalis SMU occurrence (n = 3; participants 4, 11, and 18) were found to exhibit mostly significantly higher PCS scores for rumination, magnification, helplessness, and total PCS (respective mean [SD], *P* values: 8.3 [2.5], *P* = .003; 3.3 [1.5], *P* = .149; 7.7 [3.2], *P* = .017; 19.3 [4.7], *P* = .009) in comparison to the PCS scores (2.5 [2.5], 1.7 [1.6], 2.8 [2.6], 7.1 [6.4]) of the participants who did exhibit a change in recruitment patterns (participants 1, 2, 5, 6, 7, 10, 12, 13, 14, 15, 16, 17, 19). There were no significant associations noted for the DASS-21 scores.

Table 6 Illustration of the Comparison Between Hypertonic Saline Infusion Block and Isotonic Saline Infusion Block for All Tasks in the Temporalis and Masseter Muscles

	Slow ramp	Fast ramp	Step 1	Step 2
Temporalis				
No change	53/70 (75.7)	53/71 (74.6)	27/37 (73)	48/58 (82.8)
Recruited	12/70 (17.1)	9/71 (12.7)	6/37 (16.2)	6/58 (10.3)
De-recruited	5/70 (7.2)	9/71 (12.7)	4/37 (10.8)	4/58 (6.9)
Masseter				
No change	33/47 (70.2)	37/49 (75.6)	23/28 (82.1)	33/35 (94.3)
Recruited	6/47 (12.8)	6/49 (12.2)	2/28 (7.1)	0/35 (0)
De-recruited	8/47 (17)	6/49 (12.2)	3/28 (10.8)	2/35 (5.7)

Data are presented as the no. of SMUs/total no. of SMUs for that task (%). Recruited = SMU became present in the hypertonic saline block; de-recruited = SMU was not present during the hypertonic saline block but was present in the isotonic saline block.

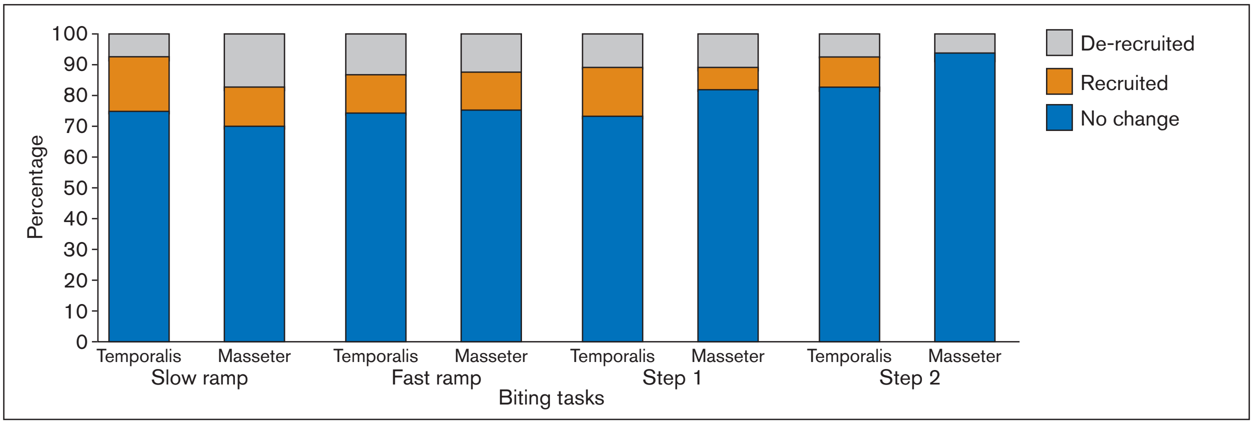

Fig 3 Comparison of single motor unit (SMU) activity between hypertonic saline (HS) and isotonic saline (IS) infusion blocks. Blue = percentage of SMUs that were present in both HS and IS infusion blocks; orange = percentage of SMUs that were recruited (ie, became active) during HS infusion in comparison to IS infusion; gray = percentage of SMUs that were de-recruited (ie, became inactive) during HS infusion in comparison to IS infusion.

Discussion

In comparison to controls, experimental masseter muscle noxious stimulation in healthy adults did not affect the performance of a set of standardized isometric biting tasks. In addition, 73% to 83% of SMUs recorded from the temporalis across the different biting tasks and 70% to 94% of SMUs recorded in the masseter were active during the HS infusion as well as during the IS infusion (control) trials. A small number of SMUs (10% to 17% in the temporalis; 0% to 13% in the masseter) were recruited (ie, became active) during the HS infusion in comparison to the IS infusion. A small number of SMUs were de-recruited (7% to 13% in the temporalis; 6% to 17% in the masseter); that is, they were active during IS infusion but not during HS infusion, irrespective of the order of infusion. The order of infusion also did not influence whether recruitment or de-recruitment occurred. Preliminary evidence was also provided that the changes in the recruitment patterns of SMU activity occurred in those individuals who had PCS scores significantly lower than those individuals who did not show any evidence of changes in recruitment patterns.

The data provide some support for the hypothesis of the study, that experimental noxious stimulation of the right masseter muscle results in a reorganization of motor unit activity within the right masseter and right temporalis muscles during jaw closing tasks. The data can therefore be cautiously considered to extend the findings of a reorganization of motor unit activity within the masseter muscle during noxious masseter muscle stimulation[24,25] to a reorganization of motor unit activity within the nonpainful anterior temporalis muscle. It is possible that reorganization of SMU activity may also be noted in other jaw muscles, and this is an avenue for further investigation. In terms of the occurrences of SMUs, there was little evidence for support of the earlier VCT (proposing generalized SMU recruitments) and PAM (proposing generalized SMU de-recruitments) (Table 8). The findings of the present study therefore point to newer models of pain-motor interaction where motor unit activity is reorganized and possibly modulated by psychologic factors as explanations for the effects of pain on motor activity.[2,11,21]

Table 7 Illustration of the Comparison Between the Hypertonic Saline Infusion Block and Baseline 2 Block for All Tasks in the Temporalis Muscle

	Slow ramp	Fast ramp	Step 1	Step 2
No change	56/70 (80)	58/71 (81.7)	19/30 (63.3)	38/46 (82.6)
Recruited	11/70 (15.7)	9/71 (12.7)	9/30 (30)	5/46 (10.8)
De-recruited	3/70 (4.3)	4/71 (5.6)	2/30 (6.7)	3/46 (6.5)

Data are presented as the no. of SMUs/total no. of SMUs for that task (%). Some units were excluded from step tasks because of technical issues. Recruited = SMU became present in the hypertonic saline block; de-recruited = SMU was not present during the hypertonic saline block but was present in the baseline 2 block.

Table 8 Summary of Single Motor Unit (SMU) Activity from the Masseter and Temporalis Muscles as a Comparison of Percentage of SMUs Supporting the Vicious Cycle Theory (VCT), Pain Adaptation Model (PAM), or Neither Theory

	Slow ramp		Fast ramp		Step 1		Step 2	
	Masseter	Temporalis	Masseter	Temporalis	Masseter	Temporalis	Masseter	Temporalis
Did not support either theory	70.2	80	75.6	74.6	82.1	73	94.3	82.8
Supported VCT	12.8	17.1	12.2	12.7	7.1	16.2	0	10.3
Supported PAM	17	7.1	12.2	12.7	10.8	10.8	5.7	6.9

If an SMU was recruited during the hypertonic saline infusion block but was inactive (ie, not present) during the isotonic saline infusion block, then that SMU was considered to be consistent with the VCT. If the SMU became inactive during the hypertonic saline infusion block in comparison to the isotonic saline infusion block, then that SMU was considered to be consistent with the PAM.

Task Performance and Neuroplasticity

Despite the moderate levels of pain, all participants generated the same force rates and amplitudes across all blocks, and this finding is in line with previous studies that have reported minimal or no effects of noxious stimulation on the kinematics or dynamics of jaw motor tasks[24,34,35,37,43–47] or on limb or trunk motor tasks.[36,48–50] Neuroplastic changes within the motor cortex may help explain how the participants were able to perform the tasks during pain. The isometric biting task in this study would most likely be driven by the primary motor cortex.[51,52] There is evidence that the face region of the primary motor cortex is inhibited by noxious stimulation,[53,54] and the site of the noxious stimulation appears to determine the region affected within the face motor cortex.[54] Localized noxious muscle stimulation may therefore result in a rapid neuroplastic reorganization of activity within the primary motor cortex to allow the task to be performed without any attenuation in force rates or force amplitudes. This neuroplastic reorganization may be manifesting as a reorganization of SMU activity within painful and nonpainful muscles that allows the task to be performed. These possible neuroplastic changes in the motor cortex may also underpin the changes in surface EMG activity that have been observed in experimental and clinical pain.[11,13,17,23,55–57]

Pain-Induced Changes in Temporalis SMU Activity

The present data demonstrate that a reorganization of SMU activity occurs not only within a painful jaw muscle, as previously demonstrated,[24,25] but also within a nonpainful jaw muscle, and this finding extends the findings from previous analogous studies in the lower limbs[30,33] to the jaw motor system.

The proportion of SMUs whose occurrences were unaffected by pain was 73% to 83% of those recorded from the temporalis and 70% to 94% of those in the masseter. These proportions are approximately comparable to the proportions of SMUs unaffected by pain in previous recordings of masseter SMUs (62% to 88% of SMUs across three tasks[24]; 58% of SMUs in one task[25]). However, the proportions are higher than in a previous limb muscle study,[30] where only 38% of quadriceps and 26% of flexor pollicis longus motor units were present during both the pain and nonpain conditions. It is not possible to draw conclusions from both sets of experiments, but future studies could consider examining whether there may be fundamental differences between the jaw motor system in comparison to the limb motor system in the effects of noxious stimulation on motor unit activity. If true, the data suggest that the jaw motor system may have less flexibility than the limb motor system in recruiting different populations of motor units as a result of a noxious stimulus. This is an avenue for further investigation.

There have been no previous studies of noxious orofacial stimulation on SMU activity in nonpainful synergistic jaw muscles. However, there have been previous reports describing noxious effects on nonpainful synergistic jaw muscle activity characterized with surface EMG electrode recordings or with multiunit intramuscular electrodes.[13,23,37,50,58–61] Some of these EMG data indicate that noxious stimulation results in EMG effects in the painful muscle, as well as in some of the nonpainful synergist muscles,[13,23,50,60,62] while other datasets show that the EMG activity of some nonpainful synergists or even the painful muscle can be unaffected.[37,59,62,63] The present findings show that about three-fourths of recorded SMUs were unaffected by noxious masseter stimulation. A comment is warranted as to how to interpret these present findings in relation to the earlier findings of an absence of, or generalized changes in, EMG activity as demonstrated by surface or intramuscular multi-unit EMG recordings.[13,23,58,62] The first point is that as both recruitments and de-recruitments of SMUs were noted at the same intramuscular electrode sites in some participants, these changes may be recorded with surface EMG electrodes as no net change in EMG activity. The second point is that some participants exhibited only recruitments in SMU activity and others exhibited only de-recruitments. Previous EMG recordings[13,23,62] have also noted that, qualitatively, individual participants could demonstrate increases in EMG activity during pain in comparison to control, while other participants could demonstrate decreases in EMG under the same conditions.

Evidence was provided for possible post-pain carryover effects on subsequent pain-free recordings. For example, SMUs 81 to 83 were present in both ramp tasks during the hypertonic saline infusion and BL2 blocks (Table 3). In this participant, the hypertonic saline infusion was done in block 3, just before the BL2 block (block 4). One interpretation of the data is that the hypertonic saline resulted in a recruitment of SMUs 81 to 83, and these SMUs remained recruited during the subsequent baseline recording. It is therefore possible that noxious jaw muscle stimulation may trigger rapid neuroplastic changes (manifesting as altered SMU recruitment patterns) that may persist after removal of the noxious stimulation (and associated pain). Although a recent jaw motor study did not provide EMG evidence of significant effects following noxious jaw muscle stimulation in comparison to control,[64] changes in muscle activity with experimental or clinical knee or low back pain have been shown to persist beyond the duration of the pain.[30,36,65–68]

Psychologic Measures

Preliminary data were provided that participants not exhibiting changes in recruitment patterns (ie, no recruitment nor de-recruitment of SMUs) during hypertonic saline infusion in comparison to isotonic saline infusion exhibited significantly higher PCS scores in comparison to participants exhibiting changes in recruitment patterns. Although the sample size is small and further data are required to confirm this observation, it is possible that individuals with higher PCS scores may exhibit a reduced ability to alter the recruitment patterns of motor units during task performance in pain. This may manifest as a loss of fine control of motor unit activity during pain in high pain-catastrophizing individuals. The individuals showing evidence of recruitments and de-recruitments of motor units during pain were those with lower pain-catastrophizing scores. These individuals may exhibit a greater ability to alter the recruitment patterns of SMUs in the presence of pain.

These preliminary data may have parallels with recent evidence showing that experimental masseter muscle pain in individuals with higher PCS scores was associated with significantly greater variability of jaw movement amplitude and velocity in repetitive open/close jaw movements in comparison to individuals with lower PCS scores.[46] The greater variability of jaw movement in the higher pain-catastrophizing individuals in pain may be a manifestation of this reduced ability to alter the recruitment patterns of motor units during task performance in pain. Previous studies have also provided evidence for associations between EMG activity and PCS scores either during or immediately after experimental pain[23,64] and add some support for the previous proposals that psychologic factors play a role in the pain-motor interaction.[2,11]

Limitations

Fatigue is a possible confounding variable to consider; however, the tasks took about 7 minutes to complete, and the alternating sequence of solutions between successive participants was a factor that mitigated against any effects of fatigue. The small sample size limits the conclusions that can be drawn, but the sample size was based on previous literature. A power calculation was not done, as the principal data analysis involved counts of occurrences of SMUs across the four blocks. All statistical tests carried out are exploratory and require further study for confirmation or refutation of the conclusions. Also, because of technical issues that arose during some recordings, it was not always possible to discriminate SMUs.

Conclusions

The present findings suggest that experimental masseter muscle noxious stimulation in healthy adults does not alter the performance of a set of standardized jaw biting tasks in comparison to control, and that most SMUs within the temporalis and masseter muscles that are recruited during control tasks were also recruited during pain. There was, however, some evidence for recruitment as well as de-recruitment of SMUs in both the painful masseter muscle and the nonpainful temporalis muscle during the biting tasks in pain in comparison to control tasks. Some preliminary evidence was provided that pain catastrophizing may influence the recruitment patterns of motor units during experimental pain, thus supporting the view that psychologic factors can influence the pain-motor interaction. The data do not support earlier theories of pain-motor interaction (VCT, PAM) that suggested uniform global changes in EMG activity throughout all muscles involved in a task, but rather point toward newer models that propose more complex effects of pain on motor activity that involve a reorganization of motor unit recruitment patterns in both painful and nonpainful muscles.[2,11,21] The reorganization appears to involve a recruitment of one population of SMUs and a de-recruitment of another population of SMUs. The present findings also provide possible insights into the spread of pain in TMD if some of these changes in muscle activity might predispose an individual to further pain and tenderness by involving nonpainful muscles. Such possible pain effects associated with changes in motor activity have been proposed in the spinal motor system[36] and have been suggested in the jaw motor system.[11]

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References

1. Travell JG, Rinzler S, Herman M. Pain and disability of the shoulder and arm: Treatment by intramuscular infiltration with procaine hydrochloride. J Am Med Assoc 1942;120:417–422.
2. Murray GM, Lavigne GJ. Orofacial pain, motor function and sleep. In: Sessle BJ (ed). Orofacial Pain: Recent Advances in Assessment, Management, and Understanding of Mechanisms. Washington, DC: IASP, 2014:75–97.
3. Svensson P, Graven-Nielsen T. Craniofacial muscle pain: Review of mechanisms and clinical manifestations. J Orofac Pain 2001; 15:117–145.
4. Stohler CS. Craniofacial pain and motor function: Pathogenesis, clinical correlates, and implications. Crit Rev Oral Biol Med 1999; 10:504–518.
5. Ahern DK, Follick MJ, Council JR, Laser-Wolston N, Litchman H. Comparison of lumbar paravertebral EMG patterns in chronic low back pain patients and non-patient controls. Pain 1988; 34:153–160.
6. Bodéré C, Téa SH, Giroux-Metges MA, Woda A. Activity of masticatory muscles in subjects with different orofacial pain conditions. Pain 2005;116:33–41.
7. Carlson CR, Okeson JP, Falace DA, Nitz AJ, Curran SL, Anderson D. Comparison of psychologic and physiologic functioning between patients with masticatory muscle pain and matched controls. J Orofac Pain 1993;7:15–22.
8. Graven-Nielsen T, Arendt-Nielsen L. Human models and clinical manifestations of musculoskeletal pain and pain-motor interactions. In: Graven-Nielsen T, Arendt-Nielsen L, Mense S (eds). Fundamentals of Musculoskeletal Pain. Seattle: IASP, 2008: 155–187.
9. 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.
10. Madeleine P, Arendt-Nielsen L. Experimental muscle pain increases mechanomyographic signal activity during sub-maximal isometric contractions. J Electromyog Kinesiol 2005;15:27–36.
11. Murray GM, Peck CC. Orofacial pain and jaw muscle activity: A new model. J Orofac Pain 2007;21:263–278.
12. Peck CC, Murray GM, Gerzina TM. How does pain affect jaw muscle activity? The Integrated Pain Adaptation Model. Aust Dent J 2008;53:201–207.
13. Sae-Lee D, Whittle T, Forte AR, et al. Effects of experimental pain on jaw muscle activity during goal-directed jaw movements in humans. Exp Brain Res 2008;189:451–462.
14. Simons DG, Mense S. Understanding and measurement of muscle tone as related to clinical muscle pain. Pain 1998;75:1–17.
15. Stohler CS, Zhang X, Lund JP. The effect of experimental jaw muscle pain on postural muscle activity. Pain 1996;66:215–221.
16. Svensson P, Graven-Nielsen T, Matre D, Arendt-Nielsen L. Experimental muscle pain does not cause long-lasting increases in resting electromyographic activity. Muscle Nerve 1998;21:1382–1389.
17. van Dieën J, Selen LPJ, Cholewicki J. Trunk muscle activation in low-back pain patients, an analysis of the literature. J Electromyogr Kinesiol 2003;13:333–351.
18. 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.
19. Murray GM, Svensson P, Arendt-Nielsen L. Musculoskeletal orofacial pain mechanisms: Insights from human experimental studies. In: Sessle BJ (ed). Orofacial Pain: Recent Advances in Assessment, Management and Understanding of Mechanisms. Washington, DC: IASP, 2014:435–454.
20. Lund JP. Persistent pain and motor dysfunction. In: Sessle BJ, Lavigne G, Lund JP, Dubner R (eds). Orofacial Pain: From Basic Science to Clinical Management. Chicago: Quintessence, 2008:117–124.
21. Hodges PW, Tucker K. Moving differently in pain: A new theory to explain the adaptation to pain. Pain 2011;152(3, suppl): S90–S98.
22. Hodges PW, Smeets RJ. Interaction between pain, movement, and physical activity. Clin J Pain 2015;31:97–107.
23. Maulina T, Amhamed M, Whittle T, Gal J, Akhter R, Murray GM. The effects of experimental temporalis muscle pain on jaw muscle electromyographic activity during jaw movements and relationships with some psychological variables. J Oral Facial Pain Headache 2018;32:29–39.
24. Malik B, Whittle T, Ogawa T, Murray GM. Reorganization of motor unit activity at different sites within the human masseter muscle during experimental pain. Eur J Oral Sci 2018;126:400–410.
25. Minami I, Akhter R, Albersen I, et al. Masseter motor unit recruitment is altered in experimental jaw muscle pain. J Dent Res 2013;92:143–148.
26. Ervilha UF, Arendt-Nielsen L, Duarte M, Graven-Nielsen T. The effect of muscle pain on elbow flexion and coactivation tasks. Exp Brain Res 2004;156:174–182.

27. 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.
28. Poortvliet PC, Tucker KJ, Hodges PW. Experimental pain has a greater effect on single motor unit discharge during force-control than position-control tasks. Clin Neurophysiol 2015; 126:1378–1386.
29. Falla D, Farina D, Dahl MK, Graven-Nielsen T. Muscle pain induces task-dependent changes in cervical agonist/antagonist activity. J Appl Physiol (1985) 2007;102:601–609.
30. Tucker K, Butler J, Graven-Nielsen T, Riek S, Hodges P. Motor unit recruitment strategies are altered during deep-tissue pain. J Neurosci 2009;29:10820–10826.
31. Falla D, Farina D, Graven-Nielsen T. Experimental muscle pain results in reorganization of coordination among trapezius subdivisions during repetitive shoulder flexion. Exp Brain Res 2007; 178:385–393.
32. Castroflorio T, Falla D, Wang K, Svensson P, Farina D. Effect of experimental jaw-muscle pain on the spatial distribution of surface EMG activity of the human masseter muscle during tooth clenching. J Oral Rehabil 2012;39:81–92.
33. Tucker KJ, Hodges PW. Motoneurone recruitment is altered with pain induced in non-muscular tissue. Pain 2009;141:151–155.
34. Kumar A, Castrillon EE, Svensson KG, Baad-Hansen L, Trulsson M, Svensson P. Effects of experimental craniofacial pain on fine jaw motor control: A placebo-controlled double-blind study. Exp Brain Res 2015;233:1745–1759.
35. 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.
36. 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.
37. Sandoval I, Moura Ferreira P, Obregon F, Whittle T, Murray GM. Experimental noxious stimulation of the right masseter muscle does not affect bilateral masseter and temporalis muscle activity and force parameters during standardised isometric biting tasks. J Oral Rehabil 2018;45:871–880.
38. Dworkin SF, LeResche L. Research Diagnostic Criteria for Temporomandibular Disorders: Review, criteria, examinations and specifications, critique. J Craniomand Disord 1992; 6:301–355.
39. 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.
40. Lovibond PF, Lovibond SH. The structure of negative emotional states: Comparison of the Depression Anxiety Stress Scales (DASS) with the Beck Depression and Anxiety Inventories. Behav Res Ther 1995;33:335–343.
41. Sullivan MJL, Bishop SR, Pivik J. The Pain Catastrophizing Scale: Development and validation. Psychol Assess 1995;7:524–532.
42. Melzack R. The McGill Pain Questionnaire: Major properties and scoring methods. Pain 1975;1:277–299.
43. Amhamed M, Whittle T, Maulina T, Gal J, Akhter R, Murray GM. Effect of experimental anterior temporalis muscle pain on jaw movements. J Oral Rehabil 2016;43:889–899.
44. Sae-Lee D, Whittle T, Peck CC, Forte AR, Klineberg IJ, Murray GM. Experimental jaw muscle pain has a differential effect on different jaw movement tasks. J Orofac Pain 2008;22:15–29.
45. Amhamed M, Whittle T, Gal JA, Murray GM. Simultaneous noxious stimulation of the anterior temporalis and masseter muscles. Part I: Effects on jaw movements. J Oral Facial Pain Headache (in press).
46. Akhter R, Benson J, Svensson P, Nicholas MK, Peck CC, Murray GM. Experimental jaw muscle pain increases pain scores and jaw movement variability in higher pain catastrophizers. J Oral Facial Pain Headache 2014;28:191–204.
47. Zhao NN, Whittle T, Murray GM, Peck CC. The effects of capsaicin-induced intraoral mucosal pain on jaw movements in humans. J Orofac Pain 2012;26:277–287.
48. Christensen SW, Hirata RP, Graven-Nielsen T. Bilateral experimental neck pain reorganize axioscapular muscle coordination and pain sensitivity. Eur J Pain 2017;21:681–691.
49. Falla D, Farina D, Kanstrup Dahl M, Graven-Nielsen T. Pain-induced changes in cervical muscle activation do not affect muscle fatigability during sustained isometric contraction. J Electromyogr Kinesiol 2008;18:938–946.
50. Gizzi L, Muceli S, Petzke F, Falla D. Experimental muscle pain impairs the synergistic modular control of neck muscles. PLoS One 2015;10:e0137844.
51. Sessle BJ. Mechanisms of oral somatosensory and motor functions and their clinical correlates. J Oral Rehabil 2006; 33:243–261.
52. Avivi-Arber L, Martin R, Lee JC, Sessle BJ. Face sensorimotor cortex and its neuroplasticity related to orofacial sensorimotor functions. Arch Oral Biol 2011;56:1440–1465.
53. Nash PG, Macefield VG, Klineberg IJ, Gustin SM, Murray GM, Henderson LA. Changes in human primary motor cortex activity during acute cutaneous and muscle orofacial pain. J Orofac Pain 2010;24:379–390.
54. Adachi K, Murray GM, Lee JC, Sessle BJ. Noxious lingual stimulation influences the excitability of the face primary motor cerebral cortex (face MI) in the rat. J Neurophysiol 2008;100:1234–1244.
55. Svensson P. Critical commentary 3: Orofacial pain and jaw muscle activity. A new model. J Orofac Pain 2007;21:284–286.
56. Mense S. Critical commentary 1: Orofacial pain and jaw muscle activity. A new model. J Orofac Pain 2007;21:279–281.
57. Lund JP, Stohler CS. Critical commentary 2: Orofacial pain and jaw muscle activity. A new model. J Orofac Pain 2007; 21:282–283.
58. Shimada A, Baad-Hansen L, Svensson P. Effect of experimental jaw muscle pain on dynamic bite force during mastication. Arch Oral Biol 2015;60:256–266.
59. Kumar A, Castrillon EE, Svensson P. Can experimentally evoked pain the jaw muscles or temporomandibular joint affect anterior bite force in humans? J Oral Facial Pain Head 2015;29:31–40.
60. Ciubotariu A, Arendt-Nielsen L, Graven-Nielsen T. The influence of muscle pain and fatigue on the activity of synergistic muscles of the leg. Eur J Appl Physiol 2004;91:604–614.
61. 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.
62. Amhamed M, Whittle T, Gal JA, Murray GM. Simultaneous noxious stimulation of the human anterior temporalis and masseter muscles. Part II: Effects on jaw muscle electromyographic activity. J Oral Facial Pain Headache (in press).
63. Hodges PW, Ervilha UF, Graven-Nielsen T. Changes in motor unit firing rate in synergist muscles cannot explain the maintenance of force during constant force painful contractions. J Pain 2008;9:1169–1174.
64. Inamoto K, Murray GM, Whittle T. Effect of a brief episode of experimental muscle pain on jaw movement and jaw-muscle activity during chewing. Eur J Oral Sci 2017;125:34–43.
65. Hides JA, Richardson CA, Jull GA. Multifidus muscle recovery is not automatic after resolution of acute, first-episode low back pain. Spine (Phila Pa 1976) 1996;21:2763–2769.
66. MacDonald D, Moseley GL, Hodges PW. Why do some patients keep hurting their back? Evidence of ongoing back muscle dysfunction during remission from recurrent back pain. Pain 2009;142:183–188.
67. Moseley GL, Hodges PW. Reduced variability of postural strategy prevents normalization of motor changes induced by back pain: A risk factor for chronic trouble? Behav Neurosci 2006; 120:474–476.
68. Tucker KJ, Larsson AK, Oknelid S, Hodges P. Similar alteration of motor unit recruitment strategies during the anticipation and experience of pain. Pain 2012;153:636–643.