Effects of Experimental Pain and Lidocaine on Mechanical Somatosensory Profile and Face Perception

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Aims: To assess the effects of experimental muscle pain and topical lidocaine applied to the skin overlying the masseter muscle on the mechanical somatosensory profile and face perception of the masseter muscle in healthy participants. **Methods:** A total of 28 healthy participants received a 45-minute application of a lidocaine or placebo patch to the skin overlying the masseter muscle followed by one injection of 0.2 mL sterile solution of monosodium glutamate. Measurements were taken four times during each session of quantitative sensory testing (QST) (T0 = baseline, T1 = 45 minutes after patch application, T2 = immediately after glutamate injection, and T3 = 25 minutes after the glutamate injection), and the following variables were measured: mechanical detection threshold (MDT), mechanical pain threshold (MPT), pressure pain threshold (PPT), pain report (pain on palpation, pain spreading on palpation, and pain intensity), pain drawing, and perceptual distortion. Multi-way within-subjects analysis of variance (ANOVA) was applied to the data. **Results:** The highest MDTs were present at T2 ($F = 49.28$, $P < .001$), the lowest PPTs were present at T2 and T3 ($F = 21.78$, $P < .001$), and the largest magnitude and area of perceptual distortion were reported at T2 ($F > 6.48$, $P < .001$). **Conclusion:** Short-lasting experimental muscle pain was capable of causing loss of tactile sensitivity as well as perceptual distortion of the face, regardless of preconditioning with a topical lidocaine patch. Short-term application of a lidocaine patch did not significantly affect the mechanical somatosensory profile. *J Oral Facial Pain Headache 2017;31:115–123. doi: 10.11607/ofph.1758*

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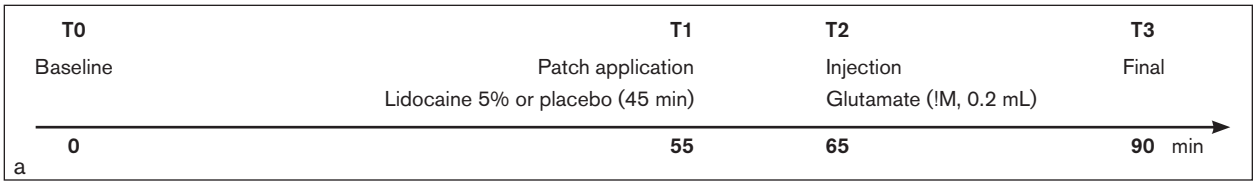
Quantitative sensory testing (QST) has been applied and recommended for somatosensory assessment in the evaluation of chronic pain conditions, including musculoskeletal pain.[1,2] In general, central sensitization processes have been considered the main factors that can explain somatosensory changes in temporomandibular disorder (TMD) patients.[3–5] However, QST assessment has limited power to localize the site or level of neuronal dysfunction along sensory pathways.[1] A recent review has endorsed the use of QST as an important additional tool for the assessment of musculoskeletal conditions, although further research is required to obtain better clarification of its assessment and methodologic aspects.[6] For instance, considering that QST provides information about pain processing in general[1] (ie, it does not clearly differentiate peripheral nociceptive function from the integrated central sensory modulation), it is important to elucidate the role of ongoing pain during the somatosensory examination. Previous neuropathic pain studies have shown that QST values can be influenced by the presence of ongoing pain[7]; however, the evidence is limited about the influence of pain on the somatosensory profile of musculoskeletal conditions, and in particular masticatory myofascial pain.

Glutamate-evoked jaw muscle pain may simulate myogenous types of TMD,[8] although it has some limitations considering the complex nature of pain and all the confounders and interrelated aspects in chronic pain patients.[9] The advantages of experimental pain models are their reproducibility, ability to control for confounders, and the possibility of



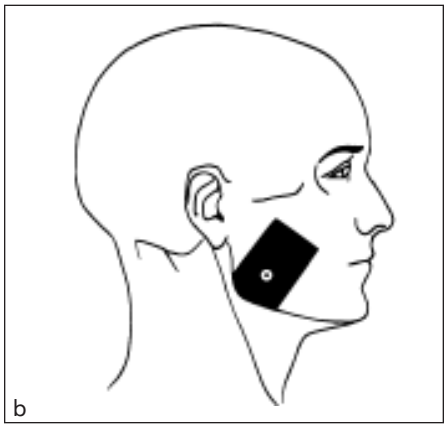


Fig 1 Flow diagram of the study procedures and the graphical representation of the patch application. **(a)** Timeline of the study phases and the outcome variables. T0 = baseline, T1 = 45 minutes after patch application, T2 = immediately after glutamate injection, and T3 = 25 minutes after the glutamate injection. Variables: Mechanical detection threshold (MDT), mechanical pain threshold (MPT), pressure pain threshold (PPT), pain intensity as measured on visual analog scale (VAS). The time points indicate the beginning of the assessments. **(b)** Patch application region *(black rectangle),* somatosensory assessment area *(white circle),* and the injection point *(black dot).* The patches covered an area of 35 cm^2 and were positioned aligned with the long axis of the masseter muscle. The injection point was the most prominent site identified during maximum tooth clenching, and a 27-gauge hypodermic needle and a disposable syringe were used. The somatosensory assessment was made within a circumference of a 0.55-cm radius around the injection point.

a clearer evaluation of the effect of peripheral pain mechanisms.[10] Accordingly, it is feasible to study the influence of deep pain on the somatosensory profile with the aid of experimental muscle pain models as a proxy of myofascial pain.

Furthermore, recent data have shown alterations in small afferent fibers of the skin in other types of chronic musculoskeletal pain; eg, fibromyalgia.[11] Although there is no evidence of cutaneous fiber damage in TMD patients, this brings attention to the need to utilize QST to test for a possible influence of cutaneous afferent inputs on the central nervous system (CNS) in order to elucidate pain mechanisms before endorsing this tool as an additional diagnostic instrument for TMD.[12] In this regard, it would be valuable to control cutaneous afferent inputs when assessing musculoskeletal pain disorders. Previous studies on masticatory muscles have reported conflicting results regarding the effect of cutaneous afferent input deprivation on sensitivity to deep painful stimuli,[13,14] but lack of a control group, clear diagnostic criteria, and a placebo effect analysis in these studies call for further systematic investigation.

In addition, a recent study has proposed the assessment of the disrupted report of one's own body image (ie, a kind of perceptual distortion of the face) in order to gain better understanding of pain mechanisms.[15] Thus, the assessment of the perceptual distortion of the face has the potential to be a novel way to evaluate persistent orofacial pain patients and obtain a better understanding of multisensory integrative mechanisms.[16] Thus, the aim of this study was to assess the effects of experimental muscle pain and topical lidocaine applied to the skin overlying the masseter muscle on the mechanical somatosensory profile and face perception of the masseter muscle in healthy participants. It was hypothesized a priori that the mechanical somatosensory profile and the face perception of the healthy participants would demonstrate changes after *(1)* the induction of experimental pain in the masseter muscle and *(2)* the application of the topical lidocaine patch.

Materials and Methods

Participants

A total of 28 healthy participants were recruited through advertisements at Aarhus University, Denmark, and through websites. The exclusion criteria were: signs and symptoms of painful TMD (TMD pain screener)[12] or other major causes of orofacial pain (eg, pulpitis, periodontal disease, or neuropathic pain); serious dental or medical illness (eg, high blood pressure or diabetes); headache complaint; psychiatric or personality disorder; regular intake of psychiatric, analgesic, or any medications that could influence a participant's response to pain; and the intake of any painkiller 24 hours prior to the procedures.

The study was conducted in accordance with the Helsinki Declaration II and had the approval from the Regional Ethics Committee as well as the Danish Data Protection Agency. All participants gave their voluntary consent after a full explanation of all procedures.

Study Design

This placebo-controlled, crossover trial was divided into two sessions separated by at least 1 week (Fig 1a). All participants received a 45-minute application of a lidocaine patch (Versatis 5%, Grünenthal GmbH) in one session and a placebo patch (self-adhesive absorbent dressing—polyurethane film, Mepore Pro, Mölnlycke Health Care) in another session. Both patches were cut to a size of 7 × 5 cm. The participants received both patches to the skin overlying either the right or left masseter. The order of patches (lidocaine or placebo) and the side of application (right or left masseter) were randomized. The injections were never applied at the same point to avoid influences of long-lasting traumatic/inflammatory changes due to needle penetration that could still be present in the second session. Furthermore, neither the examiner nor the participants were aware of the patch content (double blinded) and the examiner was not present during the patch application. The person responsible for the randomization process and patch application was not involved in the data collection or analysis.

Experimental muscle pain was induced by an injection of 0.2 mL of sterile solution of monosodium glutamate (1 mol/L; Ajinomoto Co) into the deep masseter muscle immediately after the patch application[17] with the aid of a 27-gauge hypodermic needle and a disposable syringe. The patch was completely removed prior to the injection, and the site was the most prominent point identified during maximum tooth clenching. Finally, the somatosensory assessment was made within a circumference of approximately 1 cm^2 at maximum around the injection point (Fig 1b).

Outcome Variables

Variables were assessed at four time points during each session (T0 = baseline, T1 = 45 minutes after patch application, T2 = immediately after glutamate injection, and T3 = 25 minutes after the glutamate injection), and the following variables were assessed: mechanical detection threshold (MDT), mechanical pain threshold (MPT), pressure pain threshold (PPT), pain report (pain on palpation, pain spreading on palpation, and pain intensity), pain drawing, and perceptual distortion (Fig 1a). MDT and MPT assessment sites did not coincide with the injection point. The maximum somatosensory assessment area of 1 cm^2 corresponded to the circumference of the pressure algometer probe (Fig 1b).

MDT

MDT was measured using a standardized set of von Frey filaments (OptiHair2, MARSTOCKnervtest) that applied forces between 0.25 mN and 512 mN. The area of contact between the monofilament and tissue was a rounded epoxy bead tip (diameter 0.30 to 0.45 mm) and the contact time was 1 to 2 seconds. The method of limits technique was used to determine the threshold. A series of ascending and descending stimulus intensities were applied, yielding five suprathreshold and five subthreshold reports, and the MDT was the geometric mean of these measurements.[18]

MPT

MPT was measured using a standardized set of seven custom-made weighted pinprick stimulators with fixed stimulus intensities (8, 16, 32, 64, 128, 256, and 512 mN) and a flat contact surface (diameter of 0.2 mm). Tests were made with the stimulator in a vertical and perpendicular position to the site of examination and the contact time was approximately 2 seconds. The same method of limits technique used for the MDT assessment was used to determine the MPT.[18]

PPT

PPT was measured with a digital pressure algometer (SOMEDIC Algometer, SOMEDIC Sales AB). The standard probe (flat circular tip with diameter of 11 mm) was used to apply the pressure at an application rate of close to 50 kPa/second. The participants were instructed to press a button at the first painful sensation. It was emphasized that the purpose was to measure the minimal amount of pressure at the first perception of pain, and not the pain tolerance. The PPT was determined as the arithmetic mean of three measurements.[18]

Pain Report

Pain was assessed with self-report of pain on palpation, pain spreading on palpation, and pain intensity. A mechanical device (Palpeter, SUNSTAR SUISSE SA; calibrated to deliver a pressure load of 1.0 kg) was used. Briefly, the Palpeter consists of a plastic cylindrical shell in which there is a spring composed of stainless steel with a spring constant of 0.58 N/mm. A full description can be found elsewhere.[19] The pressure was applied for 2 seconds to measure the pain on palpation (dichotomous, yes/no) and for 5 seconds to measure the pain spreading on palpation (yes/no).[12] Pain intensity was measured with the aid of a visual analog scale (VAS), which consisted of a 10-cm horizontal line with the anchor points "no pain" and "worst imaginable pain." The participants were requested to tally a vertical mark on the line at the point that best represented the pain intensity at the moment, except immediately after the glutamate injection (T2), at which point the participant was requested to mark the peak of pain intensity (recall of symptoms).

Pain Drawing

The participants were asked to use face diagrams (right and left lateral and frontal views) to draw their maximum distribution of perceived pain. The pain area was digitized (Sigma Scan Pro 4.01.003) and expressed in arbitrary units.[20]

Table 1 Somatosensory Outcomes at Each Assessment Time and Patch (Mean ± SD)

	Lidocaine Patch	Placebo Patch
T0		
MDT (mN)	0.7 ± 0.6	0.8 ± 1.0
MPT (mN)	34.2 ± 37.9	31.5 ± 32.2
PPT (kPa)	136.9 ± 31.6	130.4 ± 41.8
T1		
MDT (mN)	1.7 ± 2.6	1.6 ± 3.1
MPT (mN)	74.9 ± 103.9	39.3 ± 58.4
PPT (kPa)	136.6 ± 36.2	133.3 ± 43.8
T2		
MDT (mN)	3.8 ± 4.5	5.7 ± 8.4
MPT (mN)	49.8 ± 71.9	32.0 ± 29.8
PPT (kPa)	111.5 ± 38.0	107.5 ± 38.0
T3		
MDT (mN)	1.1 ± 1.0	1.8 ± 2.9
MPT (mN)	36.6 ± 40.4	27.4 ± 26.5
PPT (kPa)	115.8 ± 48.5	118.1 ± 47.2

T0 = baseline; T1 = 45 minutes after patch application; T2 = immediately after glutamate injection; T3 = 25 minutes after the glutamate injection; MDT = mechanical detection threshold; MPT = mechanical pain threshold; PPT = pressure pain threshold.

Perceptual Distortion

Perceptual distortions of the face, defined as changes in perceived magnitude of the concerned face areas (feelings of swelling or reduction) not related to clinical or physical signs, were measured with a numeric rating scale (NRS).[15,16] Participants were asked to give an estimate of the perceived magnitude of the face areas following the glutamate injection; ie, whether the area felt larger, smaller, or the same size as the unaffected side of the face. The contrast with the unaffected side of the face gave participants a frame of reference. The participants were asked to give an estimate of the perceived change on a scale ranging from –100% (indicating that the magnitude of the concerned face region was perceived half as large as the unaffected side of the face) through 0% (meaning that no change in magnitude of the face area was perceived) to +100% (indicating that the magnitude of the concerned face area was perceived twice as large as the unaffected side of the face).[16] The area was digitized (Sigma Scan Pro 4.01.003) and expressed in arbitrary units.[20]

Statistical Analyses

Quantitative variables (age, MDT, MPT, PPT, VAS, NRS, pain, and perceptual distortion area) were reported as mean ± SD, and the participants' sex was reported in numeric values and percentages. The quantitative variables were assessed for normal distribution by using the Kolmogorov-Smirnov test, and a $\log_{10}$ transformation was performed when the test results were significant considering an alpha level of 5% ($P < .050$). Thus, absolute values (ie, raw data) of the following variables were $\log_{10}$ transformed: MDT, MPT, PPT, VAS, NRS, pain, and perceptual distortion area.

Multi-way within-subjects analysis of variance (ANOVA) was performed as follows: the factors patch (two levels), time (four levels), and sex (two levels) were established to compare the absolute values of MDT, MPT, PPT, VAS, NRS, pain intensity, and perceptual distortion area (after $\log_{10}$ transformation), as well as the relative changes in MDT, MPT, and PPT. When appropriate, post hoc analyses were performed by using Tukey's honestly significant difference (HSD). The significance level was set at 5% ($P = .050$). In addition, Cochran Q and McNemar test were used to compare within- and between-session differences considering the pain on palpation, pain spreading on palpation, and quality of perceptual distortion. The significance level was set at 5% ($P = .05$).

For each session, the MDT, MPT, and PPT parameters were transformed into *z* values according to the following expression:

$$z \text{ score} = (\text{value single} - \text{mean group baseline}) / \text{SD group baseline}$$

A *z* score of 0 ± 1.96 represents the interval that includes 95% of the baseline data. Positive *z* scores denoted a gain of function for the tested stimulus, whereas negative *z* scores denoted a loss of function. A *z* score of 0 corresponds to the mean value of the participants at baseline.[18] A multi-way within-subjects ANOVA with the factors patch (two levels), time (four levels), and sex (two levels) were established to compare *z* scores. When appropriate, post hoc analyses were performed using Tukey's HSD. Finally, to evaluate the amount of analgesic effect, the percentage of the actual change of the thresholds from the maximum achievable threshold for the MPT was calculated to evaluate the effect of the patch application and the glutamate injection considering the following formula:

$$\%\ \text{change} = (\text{MPT T1 and T2} - \text{MPT T0}) / (724.08 - \text{MPT T0}) * 100.$$[21]

Results

Descriptive Data

A total of 28 participants (15 women, 13 men) were evaluated in two sessions in this placebo-controlled, cross-over study. The mean age ± SD of all participants was 27.3 ± 7.9 years. Of the participants, 15 (46.4%) were women with a mean age of 29.4 ± 10.5 years, and the remaining 13 (53.6%) were men with a mean age of 25.6 ± 4.6 years. The absolute baseline values for MDT, MPT, and PPT were within the normal range considering available reference data of the face.[22] Tables 1 through 3 show a complete

Table 2 Pain Outcomes at Each Assessment Time and Patch

	Lidocaine Patch	Placebo Patch
T0		
Intensity (VAS), mean ± SD	0.2 ± 0.3	0.3 ± 0.4
Area (au), mean ± SD	16.7 ± 29.6	25.8 ± 45.9
Palpation, n (%)		
Yes	16 (57.1)	19 (67.8)
No	12 (42.9)	9 (32.2)
Spreading, n (%)		
Yes	2 (7.1)	6 (21.4)
No	26 (92.9)	22 (78.6)
T1		
Intensity (VAS), mean ± SD	0.3 ± 0.4	0.3 ± 0.4
Area (au), mean ± SD	33.3 ± 45.	23.4 ± 29.1
Palpation, n (%)		
Yes	17 (60.7)	17 (60.7)
No	11 (39.3)	11 (39.3)
Spreading, n (%)		
Yes	4 (14.3)	3 (10.7)
No	24 (87.7)	25 (89.3)
T2		
Intensity (VAS), mean ± SD	5.5 ± 1.7	5.3 ± 1.8
Area (au), mean ± SD	226.1 ± 152.1	197.4 ± 151.7
Palpation, n (%)		
Yes	19 (67.9)	21 (75)
No	9 (32.1)	7 (25)
Spreading, n, (%)		
Yes	7 (25)	9 (32.1)
No	21 (75)	19 (67.9)
T3		
Intensity (VAS), mean ± SD	0.7 ± 0.7	0.6 ± 0.5
Area (au), mean ± SD	47.5 ± 61.1	43.9 ± 57.3
Palpation, n (%)		
Yes	20 (71.4)	20 (71.4)
No	8 (28.6)	8 (28.6)
Spreading, n (%)		
Yes	6 (21.4)	6 (21.4)
No	22 (78.6)	22 (78.6)

T0 = baseline; T1 = 45 minutes after patch application; T2 = immediately after glutamate injection; T3 = 25 minutes after the glutamate injection; VAS = visual analog scale; au = arbitrary units.

Table 3 Perceptual Distortion at Each Assessment Time and Patch

	Lidocaine Patch	Placebo Patch
T0		
Perceived distortion (NRS), mean ± SD	8.2 ± 10.9	5.0 ± 8.2
Area (au), mean ± SD	22.8 ± 42.2	16.3 ± 37.3
Quality, n (%)		
Enlargement	11 (39.3)	10 (35.7)
Reduction	1 (3.6)	
T1		
Perceived distortion (NRS), mean ± SD	7.1 ± 10.5	4.2 ± 8.6
Area (au), mean ± SD	32.3 ± 50.5	15.9 ± 30.4
Quality, n (%)		
Enlargement	11 (39.3)	8 (28.6)
Reduction	1 (3.6)	
T2		
Perceived distortion (NRS), mean ± SD	16.6 ± 27.9	16.4 ± 15.4
Area (au), mean ± SD	78.9 ± 107.2	88.9 ± 115.3
Quality, n (%)		
Enlargement	15 (53.6)	16 (57.1)
Reduction	2 (7.1)	
T3		
Perceived distortion (NRS), mean ± SD	9.4 ± 11.2	7.5 ± 10.7
Area (au), mean ± SD	45.9 ± 89.4)	52.5 ± 94.2
Quality, n (%)		
Enlargement	12 (42.9)	12 (42.9)
Reduction	2 (7.1)	

T0 = baseline, T1 = 45 min after patch application, T2 = immediately after glutamate injection; T3 = 25 min after the glutamate injection; NRS = numeric rating scale; au = arbitrary units.

description of the variables at each assessment time and session.

Somatosensory Outcomes

MDT absolute values showed main effects of time (ANOVA: F = 49.28, $P < .001$) and sex (ANOVA: F = 6.75, $P = .015$). The highest threshold was present at T2 (Tukey: $P < .001$), and men were less sensitive than women (Tukey: $P = .015$). MPT absolute values did not show any main effects ($P > .050$). PPT absolute values showed a main effect of time (ANOVA: F = 21.78, $P < .001$), where the lowest thresholds occurred at T2 and T3 (Tukey: $P < .001$). Finally, MDT, MPT, and PPT absolute values did not show interactions among patch, time, and sex. There was no significant effect of patch for any QST parameter ($P > .050$).

The relative changes in MDT showed a main effect of time (ANOVA: F = 4.10, $P = .008$), where higher thresholds were present at T2 (Tukey: $P = .007$) and T3 (Tukey: $P = .034$) in comparison with T0. MPT and PPT relative changes did not show any main effects or interactions ($P > .050$).

The somatosensory profiles of the participants for the MDT, MPT, and PPT throughout the time and sessions are represented in Fig 2. MDT *z* scores showed main effects of time (ANOVA: F = 49.26, $P < .001$) and sex (ANOVA: F = 6.64, $P = .015$), where the participants at T2 presented a loss of function (Tukey: $P < .001$) and men were less sensitive than women (Tukey: $P =. 016$). Again, there was no significant effect of patch ($P = .050$). MPT *z* scores did not show any main effects ($P > .050$). Finally, PPT *z* scores showed a main effect of time (ANOVA: F = 20.19, $P < .001$), where the participants at T2 and T3 presented a gain of function (Tukey: $P < .001$).

Degree of Analgesic Effect

One participant (3.6%) in the placebo session and six participants (21.4%) in the lidocaine session achieved more than 10% of the maximum achievable thresh-

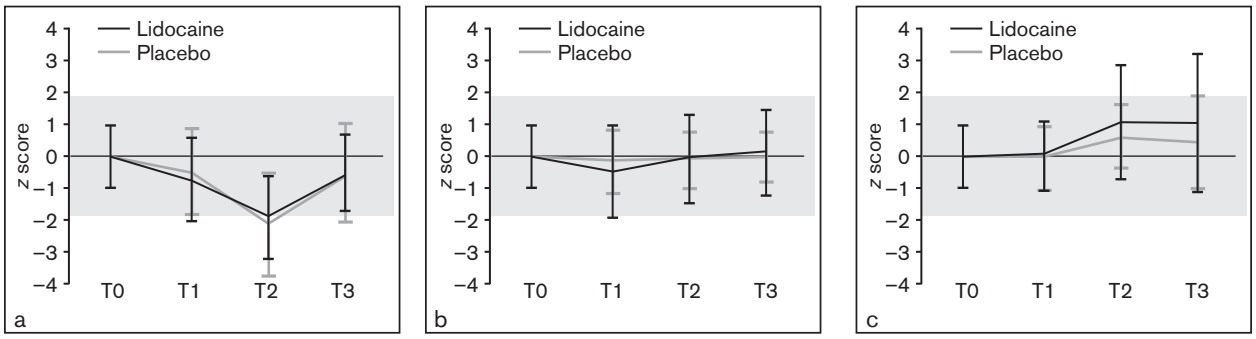


Fig 2 Mean of *z* scores of quantitative sensory testing (QST) throughout the study. T0 = baseline, T1 = 45 minutes after patch application, T2 = immediately after glutamate injection; T3 = 25 minutes after the glutamate injection. **(a)** Mechanical detection threshold (MDT). **(b)** Mechanical pain threshold (MPT). **(c)** Pressure pain threshold (PPT). Gray zone indicates a *z* score between –1.96 and 1.96, representing the normal range of baseline values. A score above 1.96 indicates a gain in somatosensory function and a score below –1.96 indicates loss of somatosensory function. Error bars indicate the standard deviation (SD) of the mean.

old for the MPT in the direction of loss of function (hypoalgesia). The percentages of actual increase of threshold were 28.9% for the single participant in the placebo session and 26.7%, 33.4%, 10.6%, 17.18%, 43.39%, and 41% for the six participants in the lidocaine session.

Pain Outcomes

Pain intensity showed a main effect of time (ANOVA: F = 186.65, $P < .001$) where the highest intensity was reported at T2 (Tukey: $P < .001$); also, there was a significant interaction between patch, time, and sex (ANOVA: F = 2.82, $P = .043$), although this was not significant considering the main comparisons (Tukey: $P > .050$). Pain area showed a main effect of time (ANOVA: F = 43.40, $P < .001$), where the largest pain area was present at T2 (Tukey: $P < .001$). In addition, there was an interaction between patch and time (ANOVA: F = 3.89, $P = .012$) where the pain area was larger at T1 (Tukey: $P = .003$), T2, and T3 (Tukey: $P < .001$) compared with T0 in the lidocaine session. Finally, pain on palpation and pain spreading on palpation did not show differences within or between sessions ($P > .050$).

Perceptual Distortion

The magnitude of perceptual distortion (NRS) showed a main effect of time (ANOVA: F = 6.48, $P < .001$), with greater values reported at T2 compared with T0 (Tukey: $P = .007$) and T1 (Tukey: $P < .001$). Similarly, the perceptual distortion area showed a main effect of time (ANOVA: F = 8.75, $P < .001$), with a larger area at T2 compared with T0 (Tukey: $P < .001$) and T1 (Tukey: $P < .001$).

Finally, the report of perceptual distortion of size magnitude showed within-session differences: T2 presented the largest percentage ($P = .018$) in the placebo session; however, there were no between-session differences ($P > .050$).

Discussion

This placebo-controlled, crossover trial tested the effects of glutamate injection and lidocaine patch application on the mechanical somatosensory profile and face perception of the masseter muscle in healthy participants. The main findings of the present study were: *(1)* a deep pain experience from the masseter muscle changed the tactile perception and generated a perceptual distortion of the face, and *(2)* a 45-minute application of a lidocaine patch seemed not to influence the mechanical somatosensory profile and the face perception.

The proxy of clinical muscle pain through injections of algesic substances is well established and has been used to help unravel deep pain mechanisms.[8,10] In the present study, it was particularly interesting to note the cutaneous mechanical hyposensitivity after the glutamate injection, regardless of the patch application. This is the first study to present results of an experimental short-lasting muscle pain model on the tactile sensitivity of the skin overlying the muscle, although impairment of touch perception as a consequence of a noxious stimulus has been reported in studies using capsaicin and tonic muscle pain models.[23,24] The putative mechanism explaining this finding is related to the suppression of low-threshold mechanoreceptive afferent inputs by the activity of nociceptive afferents in the injured muscle.[25] This mechanism is a reverse application of the well-known gate control theory,[26] which posits that touch could inhibit pain. Similar results of loss of function related to mechanoreceptive afferents associated with the presence of pain were reported in patients who underwent orthognathic surgery—only patients with ongoing pain presented cutaneous mechanical hyposensitivity in comparison to patients without pain and healthy controls.[7] Although the mechanisms underlying the sensory loss in these patients are different

from those mentioned above, it reinforces the complex interpretation of possible mechanisms underlying somatosensory profiles and the possibility that similar sensory features could be related to different mechanisms.[27] Future studies are required to explore the influence of ongoing pain on the somatosensory profile in musculoskeletal disorders.

Furthermore, since the effects did not last (ie, no significant changes 25 minutes after the glutamate injection), it could be argued that the central sensitization induced by the masseter nociceptive afferents was not primarily responsible for inhibition of touch sensation. On the other hand, when the painful stimulus is tonic (ie, 18 minutes of infusion), the effect of reduced mechanical sensitivity far outlasts the time of application,[24] which suggests that the experimental muscle pain effects are partially paradigm dependent (ie, tonic or short-lasting experimental pain).

The experimental muscle pain also affected the perception of the face independent of the patch application. The reported perceived magnitude of the distorted area was pronounced after the glutamate injection; this is in line with recent evidence that painful orofacial stimulation can cause perceptual distortions of the face in healthy subjects.[15,16] Transient cortical neuroplasticity resulting from acute pain and the correspondence of cortical and subcortical networks responsible for pain perception and body representation might account for this finding.[16,28] Finally, the lidocaine patch did not cause significant perceptual changes, which, considering that injections of anesthetics produce such disruption,[15] indicates that the route of administration and the depth of application are important to evoking perceptual distortions of the face.

The neural innervation of cutaneous and muscle structures is site specific, but a possible intercommunication occurs with the CNS.[29] Hence, a possible relationship between muscle pain and cutaneous somatosensory profiles may primarily be explained as a central effect. In fact, the somatosensory abnormalities of TMD patients (eg, cold and mechanical hyperalgesia) have been explained in terms of central sensitization processes.[4] However, recent evidence has shown alterations in the small-diameter cutaneous afferents in patients with fibromyalgia, reinforcing the discussion of the influence of peripheral factors in chronic painful disorders.[30] The present results could help in part to elucidate the contribution of such factors, considering that the study aimed to block the cutaneous afferents. Nevertheless, the main outcomes revealed no significant effects of transient deprivation of the cutaneous afferent inputs.

Even though overall significant effects of the topical lidocaine patch were not found, the present findings indicated that 21.4% of the participants achieved blockade of more than 10% of small fibers. The application time of only 45 minutes could partially explain these findings. The effects of topical lidocaine on pain relief (ie, analgesia and anesthesia) are long known as a result of a blockade of selective sodium channels in the cutaneous receptors, mainly associated with small fibers.[31] However, the magnitudes of the analgesic and anesthetic effects are different. While reported analgesia is clearly related to the application of topical anesthetics,[32] the somatosensory effects of anesthetics are inconsistent and often disappointing.[21,33] The present study found no significant difference after 45 minutes application of the topical lidocaine patch on the MPT, but such an effect has been elicited after a lengthy application period (6 hours).[21] Nonetheless, the clinical relevance seems small, considering that only a partial block of A-delta and C fibers was achieved. Most of the changes were below 10% of blockade,[21] which is in line with the present results. In addition, it could also be presumed that the degree of analgesic effects of lidocaine patches is different when considering psychophysical tests (eg, MPT) or reported pain outcomes. There is evidence that satisfactory analgesic effects require less time (around 2 hours) when lidocaine patches are used.[34] Thus, further investigations are required to determine the application time with the best cost-benefit ratio, taking into account other aspects such as drug formulation, skin characteristics, and outcome variables.

There are conflicting results about the effect of a topical lidocaine patch on large-diameter neurons (A-beta fibers) in healthy subjects.[21,35] There is some evidence of a lack of change in the tactile threshold after the application of a lidocaine patch,[21] whereas another study revealed elevation in the threshold, suggesting mild effects on tactile sensitivity.[35] Considering that A-beta fibers are not the first to be affected by lidocaine in animal experiments, probably because of the large myelinated axon diameter,[36] and even though the axon conduction velocity incompletely explains the differential sensory block with lidocaine,[37] it could be argued that the application time of 45 minutes used in the present study was also insufficient to affect these fibers. Nonetheless, this application time may only partially explain the lack of change in the tactile threshold, since no significant effects have been reported on large-diameter fibers even after 6 hours of lidocaine application.[21] The unlikely or slight skin penetration of the lidocaine through the patch formulation could better explain these findings of no effects, considering that non-nociceptive fibers are located deep in hairy skin.[38,39] Finally, there is also diverging evidence on the effect of blockade of cutaneous afferents on the PPT of masticatory muscles. One study showed that the

PPT was unaffected by iontophoretic lidocaine application[13] while another study reported intradermal lidocaine was capable of causing pressure pain hypoalgesia.[14] Since the present results also indicated no differences in PPT sensitivity after the lidocaine patch, it seems that the lidocaine effect on PPT could be depth dependent.

Finally, the present study revealed an overall sex difference in tactile sensitivity, with men presenting higher thresholds than women. Indeed, a previous study has shown that women have greater sensitivity in the face.[40] Although the present study found no interaction between sex and patch or time, there is evidence suggesting that men show greater loss of low-threshold mechanical sensitivity during tonic muscle pain, maintained for 18 minutes, than women.[24] Differences in the methods applied to determine tactile sensitivity and the experimental pain conditions may account for the conflicting findings, and further investigation is needed.

It is important to note some limitations of this study. First, the duration of application of the lidocaine patch was considered inadequate to achieve full effects in terms of somatosensory threshold changes. Even though the application period of 30 minutes was sufficient to reduce the pain intensity from lancet pricks when applying lidocaine cream[41] and considering that the analgesic effect of patch and cream formulation could be comparable,[34,42] a comprehensive evaluation of the influence of different time endpoints on the somatosensory effects of topical lidocaine is required to elucidate this matter. Second, a more comprehensive assessment of somatosensory function, including thermal sensitivity, wind-up, etc, could be warranted; however, the short-lasting effect of the glutamate injection should be taken into consideration, as it could preclude the performance of the full battery of QST, which takes approximately 30 minutes.[18] Finally, the placebo and lidocaine patches consisted of different materials, but with a similar adhesive capacity. Although it seems unlikely that this difference influenced the somatosensory profile, the possibility cannot be ignored.

Conclusions

It seems that short-lasting experimental muscle pain was capable of causing loss of tactile sensitivity as well as perceptual distortion of the face regardless of preconditioning with a topical lidocaine patch, and short-term application of a lidocaine patch did not significantly affect the mechanical somatosensory profile. These findings may have implications for a better understanding of sensory integrative mechanisms in patients with complex orofacial pain conditions.

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