The Influence of Cutaneous Tissue Afferents on Masticatory Pain-Pressure Thresholds

Kevin I. Reid, DMD, MS
Formerly, Assistant Professor
Orofacial Pain Center
University of Kentucky
College of Dentistry
Lexington, Kentucky
Currently, Senior Associate Consultant
Department of Dental Specialties
Mayo Clinic
Rochester, Minnesota

Charles Carlson, PhD
Associate Professor
Orofacial Pain Center
University of Kentucky
College of Dentistry
Lexington, Kentucky

Mary Kay Rayens, PhD
Associate Director
Biostatistics Consulting Unit
Chandler Medical Center
Lexington, Kentucky

Richard H. Gracely, PhD
Senior Research Scientist
National Institute of Dental Research
Bethesda, Maryland

Correspondence to:
Dr Kevin I. Reid
Department of Dental Specialties
Mayo Clinic
Rochester, Minnesota 55905

Pain-pressure thresholds are routinely used in orofacial pain research to record tenderness in masticatory muscles. This method is employed to stimulate deep tissue afferents, which are thought to be at least partially responsible for pain in temporomandibular disorders. Like other psychophysical measurements, however, this technique must stimulate cutaneous tissues before stimulating deeper tissues. This study examined 39 asymptomatic volunteers to quantify the effect of cutaneous sensory afferents on pain-pressure thresholds. In a randomized, double-blind fashion, pain-pressure thresholds were recorded at four facial sites before and after subjects received intradermal local anesthetic or a dry needle stick. Pain-pressure thresholds were significantly elevated after local anesthetic (P < .0001), suggesting that cutaneous tissues contribute significantly to the pain-pressure threshold. The authors discuss potentially important roles of cutaneous tissues in the assessment of deeper tissues and offer two theories of how the skin may be an important link in the assessment of temporomandibular disorders.
J OROFACIAL PAIN 1996;10:324–329.

key words: orofacial pain, temporomandibular disorders, cutaneous, convergence

Pain-pressure thresholds (PPTs) are routinely used to evaluate the response of deep orofacial tissues to mechanical stimulation.[1,2] Studies[3,4] using either manual palpation or a variety of instruments have shown that patients with myofascial pain and fibromyalgia have lower PPTs than do pain-free control subjects. This difference is used as an indicator of deep tissue pathology. At least two studies have claimed that the technique of pressure algometry is a valid measurement of orofacial pain conditions, which, by definition, are generally considered pathologic conditions of deep tissues.[5] However, reliance on PPT as a measure of deep tissue tenderness disregards the role of cutaneous afferents. Second-order neurons in nucleus caudalis that respond to stimulation of deep tissues also receive converging input from the skin.[6] This convergence is the rule rather than the exception; it is uncommon for a second-order neuron to receive exclusive input from a deep nociceptor.[6] This neuroanatomic evidence is supported by clinical trials that have reported that a variety of electrotherapeutic and topical treatments applied to the skin routinely reduce subjective complaints of tenderness in deep tissues.[7-9] The purpose of this study was to examine the effect that anesthetization of the skin overlying the masseter and zygoma areas has on PPTs in a cohort of asymptomatic subjects. It was hypothesized that local anesthetization would result in increased PPTs as a result of convergence of cutaneous and deep nociceptors in the medullary dorsal horn.

Materials and Methods

After providing informed consent, 39 asymptomatic subjects (16 women and 23 men) with a mean age of 25 years were studied. None had temporomandibular disorders or musculoskeletal or rheumatologic diseases, and none was using regular medications other than oral contraceptives. Use of nonsteroidal anti-inflammatory, sedative-hypnotic, or opioid medications were not permitted on the day of the study.

The principle investigator recorded tactile detection thresholds at the bilateral zygomatic arches and mid masseters with von Frey filament stimulation using a modified staircase method.[10] At each trial, an ascending series of von Frey filaments was applied until a particular filament was detected. After detection, a filament of three gauges lower was administered until the filament was not detected. Subsequently, filament sizes were increased by one gauge until an affirmative response, which constituted the value for that trial. The mean of three trials determined the cutaneous detection threshold. Subjects were instructed to close their eyes during this procedure to avoid visualization of von Frey filament diameter.

Subsequently, baseline PPTs at each of the four sites were determined by the mean of three trials using the ascending method of limits with the Somedic pressure algometer (Farsa, Sweden) at a rate of 30 kPa/s. The PPTs were obtained by the

principle investigator in a balanced, sequential order. Subjects pressed a button to indicate when the pressure sensation changed to a pain sensation. The PPT was recorded by an associate investigator. Neither the subject nor the examiner could visualize the digital display of the PPT. Following baseline testing, each experimental site randomly received a double-blind intradermal injection of either 0.25 mL of 2% lidocaine hydrochloride with epinephrine 1:100,000, or an intradermal dry-needle puncture that mimicked the duration of the lidocaine injection. Injections were administered by an associate investigator. Cutaneous detection thresholds and PPTs were re-evaluated within 3 minutes of injection. Repeated measures analysis of variance (ANOVA) was used to assess the response of gender, side (right versus left), area (masseter versus zygoma), and treatment (lidocaine versus placebo). Post hoc comparisons were based on Fisher's least significant difference pairwise procedure.

Results

Compared to the placebo, injections of lidocaine with epineperine resulted in increased postinjection von Frey detection thresholds (mean increase, 3.2 g; $P < .0001$; ANOVA), confirming that anesthesia was achieved in the skin (Fig 1). Figure 2 shows that PPTs of those receiving lidocaine were significantly increased by a mean of 17 kPa compared to a *de-*
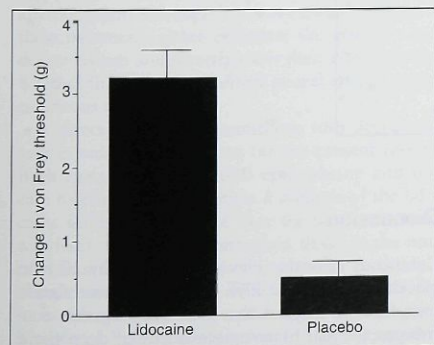

Fig 1 Change in cutaneous detection thresholds measured by von Frey filaments for subjects receiving lidocaine and placebo. The statistically significant difference ($P < .0001$) indicates that cutaneous tissue anesthesia was achieved.
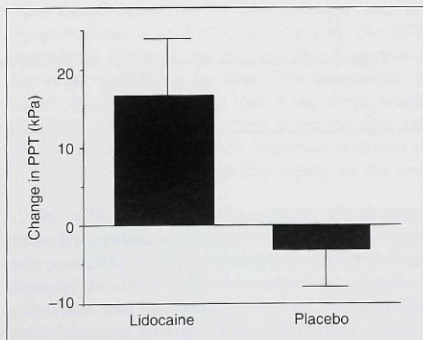

Fig 2 Change in PPTs for subjects receiving lidocaine and placebo. Pain-pressure thresholds increased 17 kPa after intradermal injection of lidocaine as compared to a decrease of 2 kPa after intradermal placebo (dry needle). The statistically significant effect ($P < .0002$) of intradermal lidocaine on PPTs suggests that cutaneous tissue contributes substantially to PPTs.
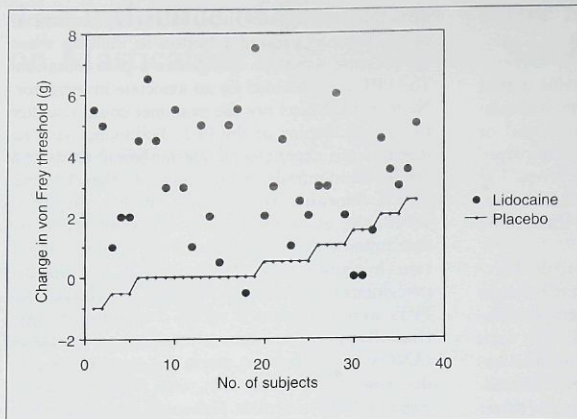
Fig 3 Change in detection thresholds to von Frey stimulation for individual subjects for both the placebo and lidocaine interventions. Subjects are ordered by effect of placebo to facilitate comparison. Thirty-three of 37 subjects showed higher thresholds in the lidocaine condition.
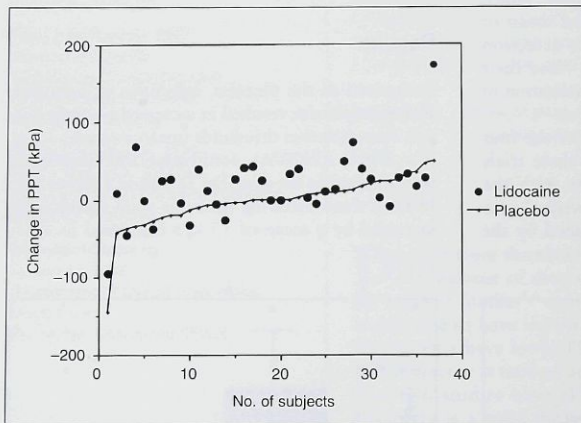

Fig 4 Pain-pressure thresholds of individual subjects for both the placebo and lidocaine interventions. Subjects are ordered by effect of placebo to facilitate comparison. Twenty-seven of 37 subjects showed higher thresholds in the lidocaine condition than in the placebo condition.

crease in the placebo group of 2 kPa ($P < .0002$; ANOVA). Site (zygoma versus masseter), side (left versus right), and gender did not influence the results. Figure 3 shows von Frey thresholds for each individual for both the placebo and lidocaine intervention. Thirty-three of 37 subjects showed higher thresholds in the lidocaine condition (binomial $P < .001$). Figure 4 shows individual PPTs for both the placebo and lidocaine interventions. Twenty-seven of 37 ($P < .02$) subjects showed higher thresholds in the lidocaine condition. Means and standard error of PPTs at the zygoma and the masseter are shown in Table 1.

Discussion

Cutaneous lidocaine elevated the PPT by 17 kPa; placebo reduced the PPT by 2 kPa. These significant findings suggest that the overlying skin contributes to quantitative assessment of deep tissue PPTs in the orofacial region in asymptomatic subjects. These results are similar to previous reports that have demonstrated that cutaneous anesthesia, achieved by local anesthetic injection[11] and anesthetic cream,[12] increases PPTs in myofascial tissues in orofacial and other regions. Together these results indicate that the evaluation of deep tissue

Table 1 Mean (and Standard Error) of PPTs (kPa)

	Men		Women	
	Before injection	After injection	Before injection	After injection
Zygomatic				
Lidocaine	264.84 (28.0)	266.00 (23.2)	198.73 (20.0)	226.31 (23.3)
Placebo	262.28 (26.0)	250.00 (19.1)	220.58 (22.0)	218.08 (22.2)
Masseter				
Lidocaine	214.22 (17.4)	227.13 (16.8)	182.38 (16.9)	194.21 (17.2)
Placebo	234.69 (26.4)	231.54 (21.4)	181.41 (16.3)	176.73 (15.1)

No statistically significant differences in PPTs of men and women were found.

pain in musculoskeletal diseases may be compromised by mechanical cutaneous sensitivity. However, it is important to recognize that the relative contributions of cutaneous and deep tissues to PPTs may be different in patients and asymptomatic subjects.

There is evidence, however, that treatments applied to the skin can result in reduction of deeper TMD-related pain. Pain-pressure thresholds in masticatory muscles were increased, ie, pain was decreased, after transient application of cold spray (Fluori-Methane, Gebauer Pharmaceuticals, Cleveland, OH) to the skin overlying masseter muscles, which were subsequently stretched.[9] Iontophoresis, the transcutaneous application of agents by electrical current, has resulted in symptom relief.[8] Common to both of these interventions is the apparent ability to alter cutaneous sensory afferent input, although it is not currently known if these treatments either penetrate the skin to reach deeper tissues and *directly* exert their effects and/or whether they exert an *indirect* neural effect on subcutaneous tissues.

A direct diffusion of anesthetic into deeper tissues is unlikely to account for the present results. Both the use of 1:100,000 epinephrine and our care to evaluate PPTs within 3 minutes of the lidocaine infiltration indicate that the local anesthetic was likely confined to cutaneous tissue at the time of evaluation.

Indirect neural effects could be either inhibitory or excitatory. According to the classic Gate Control Theory of Pain,[13] stimulation of nonnociceptive, large-diameter Aß primary afferent fibers in the skin would reduce pain sensitivity by inhibiting nociceptive transmission. Transcutaneous electrical nerve stimulation (TENS) has been shown to reduce subjective reports of myofascial pain,[14] and other forms of electrical stimulation of the skin resulted in a reduction of painful TMD-related symptoms.[7]

If pressure algometry activates cutaneous Aß afferents in sufficient numbers to evoke inhibition, we would have expected to see decreases in PPTs (increased pain) after skin anesthesia because of absence of inhibitory input from large-diameter afferents.[15] The fact that we observed marked increases instead supports an excitatory, rather than inhibitory, indirect neural effect.

An excitatory cutaneous input could contribute to the PPT in asymptomatic individuals by several mechanisms. In one mechanism, the skin and underlying tissue are innervated by separate afferent sensory channels with different nociceptive sensitivity to mechanical pressure. This mechanism could account for the present results if the cutaneous sensitivity was greater than the sensitivity of deeper tissues. Anesthetizing the skin would shift the input to the higher-threshold deeper tissue. This model suggests that anesthetizing only the deeper tissues would have no effect on the PPT, apart from changing the physical characteristics of the tissue underlying the skin. This mechanism, in which skin is the sensitive link in the chain, would function whether the afferents from the skin and deeper tissues converged on projection neurons, or provided separate independent inputs to the central nervous system.

An alternative model of excitatory input postulates convergence of cutaneous and deep tissue afferents with similar sensitivities, with PPT determined by stimulation of a sufficient number of afferents, regardless of their origin. This mechanism could account for the present results if anesthetizing the skin removed a portion of the contributing population, requiring greater stimulation to recruit the necessary threshold input from the remaining deep tissue afferents. In this model, anesthetization of only the deeper tissues also would increase the PPT because the net effect would be to remove a portion of contributing input.

This necessary-number-of-inputs model requires convergence of cutaneous and deep tissue input at some level of the afferent system.

These alternative models are of more than academic interest because they result in different interpretations of the PPT. In the sensitive link model, PPTs may reflect only cutaneous sensitivity but could indicate deep tissue sensitivity in pathologic conditions if the deep tissue sensitivity is greater than that of the skin. In the necessary-number-of-inputs model, the PPT would always indicate deep tissue sensitivity if cutaneous sensitivity remains unchanged.

In both models, changes in cutaneous sensitivity can influence the results. In the sensitive link model, an increased cutaneous sensitivity could completely mask any change in deep tissue tenderness; the PPT could remain a measure of only cutaneous sensitivity. In the necessary-number-of-inputs model, the PPT would represent a combined measure of cutaneous and deep tissue sensitivity.

To date, very little information is available regarding the influence of cutaneous tissues in what are proposed as deep tissue pain syndromes such as TMD and fibromyalgia. Reports have shown that painful syndromes attributed to musculoskeletal tissues may be related to alterations in cutaneous sensory afferents, although the mechanisms mediating these changes are not known.[16,17] For example, a recent study[18] showed that patients with fibromyalgia had significantly higher ratings of skin-fold tenderness than did control subjects, implying that pathology may involve cutaneous tissues.

Among possible explanations of these findings is that both skin *and* cutaneous tissues may be involved in the pathophysiology of musculoskeletal pain syndromes.[19] Given the absence of dermatologic pathology or cutaneous allodynia in patients with myofascial pain,[20] it seems likely that observations of alterations in cutaneous thresholds would reflect either connective tissue disorders or central nervous system changes in processing of nociceptive input.[21]

Increasing evidence from both animal and clinical studies suggests that TMD and related pain conditions may represent a central nervous system disorder.[22,23] Under these conditions, lowered cutaneous and deep tissue thresholds would be expected because nociceptors from both sources converge onto areas of the brainstem where nociceptive information is processed.[6] Current evidence, including results from the present study, suggests that future laboratory and clinical studies should evaluate the interrelationship of cutaneous and deeper tissues in patients with TMD. The poor specificity and sensitivity of current assessment methods[24] may be improved by an evaluation of cutaneous sensitivity in TMD, and the influence of this sensitivity in the measurement of deep tissue tenderness.

References

1. Jensen K. Quantification of tenderness by palpation and use of pressure algometers. In: Fricton JR, Awads E (eds). Advances in Pain Research and Therapy, vol 17. New York: Raven Press, 1990:165–181.
2. Ohrbach R, Gale EN. Pressure thresholds, clinical assessment, and differential diagnosis: Reliability and validity in patients with myogenic facial pain. Pain 1989;39:157–169.
3. Schiffman E, Fricton J, Haley D, Tylka D. A pressure algometer for myofascial pain syndrome: Reliability and validity testing. In: Dubner R, Gebhart GF, Bonds MR (eds). Proceedings of the Vth World Congress on Pain. Philadelphia: Elsevier, 1988:407–413.
4. Reid KI, Gracely RH, Dubner RA. The influence of time, facial side, and location on pain-pressure thresholds in chronic myogenous temporomandibular disorder. J Orofacial Pain 1994;8:258–265.
5. American Academy of Orofacial Pain. McNeil C (ed). Temporomandibular Disorders. Guidelines for Classification, Assessment, and Management. Chicago: Quintessence, 1993:39–60.
6. Sessle BJ, Hu JW, Amano N, Zhong G. Convergence of cutaneous, tooth pulp, visceral, neck and muscle afferents onto nociceptive and non-nociceptive neurones in trigeminal subnucleus caudalis (medullary dorsal horn) and its implications for referred pain. Pain 1986;27:219–235.
7. Taylor K, Newton R, Personius W, Bush F. Effects of interferential current stimulation for treatment of subjects with recurrent jaw pain. Phys Ther 1987;67:346–350.
8. Reid KI, Dionne RA, Sicard-Rosenbaum L, Lord D, Dubner RA. Evaluation of iontophoretically applied dexamethasone for painful pathologic temporomandibular joints. Oral Surg Oral Med Oral Pathol 1994;77:605–609.
9. Jaeger B, Reeves JL. Quantification of changes in myofascial trigger point sensitivity with pressure algometer following passive stretch. Pain 1986;27:203–210.
10. Gracely RH. Theoretical and practical issues in pain assessment in central pain syndromes. In: Casey K (ed). Pain and Central Nervous System Disease, New York: Raven Press, 1990:85–102.
11. Jensen K, Andersen H, Oleson J, Lindblom U. Pressure pain thresholds in human temporal region. Evaluation of a new pressure algometer. Pain 1986;27:203–210.
12. Kosek E, Ekholm J. Modulation of pressure pain thresholds during and following isometric contraction. Pain 1995;61:481–486.
13. Melzack R, Wall PD. The Challenge of Pain. New York: Basic Books, 1982.
14. Graff-Radford S, Reeves JL, Baker RL, Chiu D. Effects of transcutaneous electrical nerve stimulation on myofascial pain and trigger point sensitivity. Pain 1989;37:1–5.
15. Besson JM, Chaouch A. Peripheral and spinal mechanisms of nociception. Physiol Rev 1987;67:67–184.
16. Jolliffe Va, Anand P, Kidd BL. Assessment of cutaneous sensory and autonomic axon reflexes in rheumatoid arthritis. Ann Rheumatol 1995;54:251–255.

17. Granges G, Littlejohn GO. A comparative study of clinical signs in fibromyalgia/fibrositis syndrome, healthy and exercising subjects. J Rheumatol 1993;20:344–351.

18. Mikkelsson M, Latikka P, Kautiainen H, Isomeri R, Isomaki H. Muscle and bone pressure pain threshold and pain tolerance in fibromyalgia patients and controls. Arch Phys Med Rehabil 1992;73:814–818.

19. Stohler CS. Clinical perspectives in masticatory and related muscle disorders. In: Sessle BJ, Bryant PS, Dionne RA (eds). Temporomandibular Disorders and Related Pain Conditions. Progress in Pain Research and Management, vol 4. Seattle: IASP Press, 1995:3–29.

20. Fricton JR, Kroening R, Haley D, Siegert R. Myofascial pain syndrome of the head and neck: A review of clinical characteristics of 164 patients. Oral Surg Oral Med Oral Pathol 1985;60:615–623.

21. Gracely R, Lynch S, Bennet G. Painful neuropathy: Altered central processing maintained dynamically by peripheral input. Pain 1992;51:175–194.

22. Coderre TJ, Katz J, Vaccarino AL, Melzack R. Contribution of central neuroplasticity to pathological pain: Review of clinical and experimental evidence. Pain 1993; 52:259–285.

23. Maixner W, Fillingim R, Booker D, Sigurdsson A. Sensitivity of patients with painful temporomandibular disorders to experimentally evoked pain. Pain 1995;63: 341–351.

24. Dworkin SF, LeResche L, DeRouen T. Reliability of clinical measurement in temporomandibular disorders. Clin J Pain 1988;4:89–99.

Resumen

La Influencia de los Aferentes Tisulares Cutáneos sobre los Umbrales de Presión-Dolor Masticatorios

Los umbrales de presión-dolor son utilizados rutinariamente en la investigación del dolor orofacial para registrar la sensibilidad de los músculos masticatorios. Este método es empleado para estimular los aferentes tisulares profundos, los cuales se piensa que son al menos parcialmente responsables del dolor en los desórdenes temporomandibulares. Como en el caso de otras medidas psicofísicas, sin embargo, esta técnica debe estimular los tejidos cutáneos antes de estimular tejidos mas profundos. Este estudio examinó 39 voluntarios asintomáticos para cuantificar el efecto de los aferentes sensoriales cutáneos sobre los umbrales de presión-dolor. Se registraron los umbrales de presión-dolor al azar y al doble ciego, en cuatro sitios faciales antes y después de que los sujetos recibieran anestesia local intradérmica o una punción seca. Los umbrales de presión-dolor fueron elevados significativamente después del anestésico local ($P < 0,0001$), lo que indicaba que los tejidos cutáneos contribuían significativamente al umbral presión-dolor. Los autores discuten los papeles potencialmente importantes de los tejidos cutáneos en la evaluación de tejidos mas profundos y ofrecen dos teorías de como la piel puede ser un eslabón importante en la evaluación de los desórdenes temporomandibulares.

Zusammenfassung

Der Einfluß von Hautgewebeafferenzen auf die Schmerzdruckschwellen der Kaumuskulatur

Schmerzdruckschwellen werden routinemäßig bei der orofazialen Schmerzforschung benutzt um die Empfindlichkeit der Kaumuskeln zu registrieren. Diese Methode wird gebraucht, um die tiefen Gewebsafferenzen zu reizen. Man glaubt, dass die tiefen Gewebsafferenzen zumindest teilweise für die Schmerzen bei den Myoarthropathien verantwortlich sind. Bei diesem Verfahren wird aber, wie auch bei anderen psychophysischen Messungen, erst das Hautgewebe gereizt und dann die tieferen Gewebe. Diese Studie untersucht 39 asymptomatische Probanden, um den Einfluß von hautsensorischen Afferenzen auf die Schmerzdruckschwellen zu quantifizieren. In einer Doppelblindstudie wurden die Schmerzdruckschwellen an 4 verschiedenen Gesichtsstellen gemessen, vor und nach intradermaler Injektion eines Lokalanästhetikums beziehungsweise eines einfachen Nadelstiches. Die Schmerzdruckschwellen waren nach der Injektion mit Lokalanästhetikum signifikant erhöht ($P < .0001$), was nahelegt, dass das Hautgewebe signifikant die Schmerzdruckschwellen beeinflußt. Die Autoren diskutieren über die Wichtigkeit des Hautgewebes für die richtige Einschätzung von tieferem Gewebe und bieten 2 Theorien an, in welchen die Haut eine wichtige Rolle bei der Einschätzung von Myoarthropathien spielt.