Exp Brain Res (1997) 114:390–392

RESEARCH NOTE

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Human intramuscular and cutaneous pain: psychophysical comparisons

Received: 30 July 1996 / Accepted: 28 November 1996

Abstract We used psychophysical methods to compare the central processing of nociceptive inputs from skin and muscle in ten normal humans. Both intramuscular electrical and infrared CO_2 laser cutaneous stimulation showed increasing but decelerating (downward concave) stimulus-response curves and similar temporal summation characteristics. Intramuscular stimulation was rated significantly more unpleasant than cutaneous stimulation. The results are consistent with a common mode of central nociceptive processing for skin and muscle pain intensity but suggest a relatively larger activation of affective mechanisms by muscle afferents.

Key words Pain assessment · Muscle pain · Cutaneous pain · Central neural summation

Introduction

Activation of deep nociceptive afferents can be accomplished by electrical stimulation using intramuscular electrodes (Duranti et al. 1983; Giamberardino et al. 1988; Simone et al. 1994). The evoked perception is described as a cramp-like pain unrelated to the simultaneous muscle twitch. At low stimulus intensities large-diameter myelinated mechanoreceptive fibers are activated, but at higher stimulus intensities small-diameter nociceptive fibers must be recruited to evoke pain (Simone et al. 1994). The relative advantages and disadvantages of electrical stimulation in pschophysical studies of pain have been reviewed recently (Handwerker and Kobal 1993). Activation of cutaneous nociceptive afferents by high-energy lasers has previously been described in detail (Bromm et al. 1984; Treede et al. 1995). If the central processing of nociceptive input from muscles and skin is similar, one would expect similarities in psychophysical stimulus-response (S-R) curves and temporal summation characteristics.

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Materials and methods

Ten subjects (2 women and 8 men; mean age±SE, 24.9±2.3 years) participated in the study. Written informed consent was obtained from each subject before inclusion in the study, in accord with the Helsinki-II declaration. All subjects were healthy with no neurological, psychiatric or physical disabilities, and were not taking any medication.

An infrared CO_2 surgical laser (wavelength 10.6 μm, Model 20, Directed Energy Inc., USA) was used for radiant heat stimulation of the skin (Pertovaara et al. 1988). The pulse duration was 60 ms with a beam diameter adjusted to 10 mm (79 mm^2). The laser beam was focused on the hairy skin overlying the left brachioradialis muscle 5 cm below the elbow (C7 dermatome). To avoid sensitization or habituation the beam location was moved for each stimulus.

An electrical constant current stimulator (Spectrum 32, Cadwell Laboratories, USA) generated 250-μs square-wave pulses which were applied to the left brachioradialis muscle of the forearm. Two disposable 20 mm long sensory needle electrodes (13R27, 28G, Dantec, Denmark), uninsulated for 3 mm at the tip, were inserted 10 mm apart along the muscle fiber direction (Giamberardino et al. 1988). The electrical stimuli generated small muscle twitches which the subjects were told to neglect and to focus on the sensation generated by the stimulus. The readings of the stimulus intensity were made in integers of milliamps.

Pain thresholds (PTs), summation PTs, and S-R curves for each subject were determined. The PT was defined as the lowest stimulus intensity required for the subject to report a "just barely painful" sensation. The summation PT to repeated stimuli was determined using single pulses repeated five times at a frequency of 1 Hz. The summation PT was defined as the stimulus intensity required for the subject to report an increasing perceived intensity in

the course of the successive stimuli and to rate the fifth stimulus as "just barely painful" (Arendt-Nielsen et al. 1994). The PTs and summation PTs were determined as the mean of three ascending and three descending series of stimuli using the methods of limits. Approximately 30 s elapsed between successive series of stimuli.

For the S-R curves, the stimuli were rated on a scale of 0–100 where 0 denoted "no sensation" and 100 denoted "nearly intolerable pain" and 70 was "just barely painful" (Casey et al. 1993, 1994). This intensity scale allowed ratings of both nonpainful and painful stimulus intensities. The unpleasantness was rated from 0, denoting "not unpleasant at all," to 100, denoting "extremely unpleasant." The difference between pain intensity and unpleasantness was explained to the subjects by reading a narrative description similar to Price et al. (1983). S-R curves were constructed by presentation of five different stimulus intensities each repeated five times in random order. The stimulus intensity was kept as individual percentages of the PT with two intensities within the nonpainful range, one intensity just at PT, and two intensities above PT. About 30 s elapsed between successive stimuli.

Analyses of variance (ANOVA) with repeated measures were used for statistical analysis of the data. Paired *t*-tests were used when appropriate. The null hypothesis was rejected if $P<0.05$.

Results

At painful levels (PT=11.6±3.4 W), the CO_2 laser stimulus was described as a distinct and localized pin-prick sensation followed by a burning after-sensation. The intramuscular stimulation (PT=29.6±10.2 mA) was consistently described as a brief but deep painful cramping, stinging sensation which was fairly well localized around the stimulating electrodes, although four subjects reported a deep sensation radiating towards the wrist. The summation PTs for cutaneous infrared laser stimulation (7.8±1.9 W) and for intramuscular electrical stimulation (20.1±8.3 mA) were significantly lower than PTs to single stimuli (–31.5±8.9%, $P<0.001$; –33.2±17.2%, $P<0.001$). There was no significant difference between these decreases ($t_9=0.102$, $P=0.921$).

The S-R curves for the perceived intensity of intramuscular and cutaneous stimulation were both downward concave (Fig. 1). A log-log plot yielded different power exponents for intramuscular stimulation (0.58±0.08) than for cutaneous stimulation (1.17±0.15, $t_9=4.348$, $P<0.002$). To compare directly the responses for intramuscular and cutaneous stimulation, the relative unpleasantness, defined as the ratio between perceived unpleasantness and intensity (U/I ratio), was calculated (Rainville et al. 1992). This analysis showed that the U/I ratio increased significantly with increasing stimulus intensity [$F(4,9)=12.38$, $P<0.001$] and that U/I ratios for intramuscular stimulation were greater than for cutaneous stimulation [$F(1,9)=6.21$, $P=0.034$] (Fig. 1).

The increasing ratings of perceived intensity and unpleasantness appeared to be parallel for intramuscular stimulation, but to diverge in the case of cutaneous infrared laser stimulation. We compared the ratings of perceived unpleasantness and intensity at each stimulus intensity for both electrical intramuscular and cutaneous infrared laser stimulation. Two-way ANOVAs showed a significant interaction between the ratings of unpleasantness and intensity at the five applied intensities of cutaneous infrared laser stimulation [$F(1,4)=11.0$, $P<0.0001$], but a similar interaction was not shown for intramuscular electrical stimulation [$F(1,4)=1.41$, $P=0.250$].

Discussion

The intramuscular and cutaneous S-R curves were similar in form. One factor that may contribute to this similarity is the pattern of recruitment of afferent fibers as the intensity of the single pulse increases. For both forms of stimulation, the rate of afferent fiber recruitment may be highest within the low-intensity range and decrease at higher stimulus intensities. However, the S-R curve for cutaneous stimulation was steeper than that for intramuscular stimulation, suggesting that cutaneous heat stimulation provides better intensity discrimination than intramuscular electrical stimulation.

An especially salient observation was that relative intensity and unpleasantness were rated differently for cutaneous and intramuscular stimulation. Thus, relative unpleasantness (U/I ratio) was larger for intramuscular stimulation than for cutaneous stimulation. This is in ac-

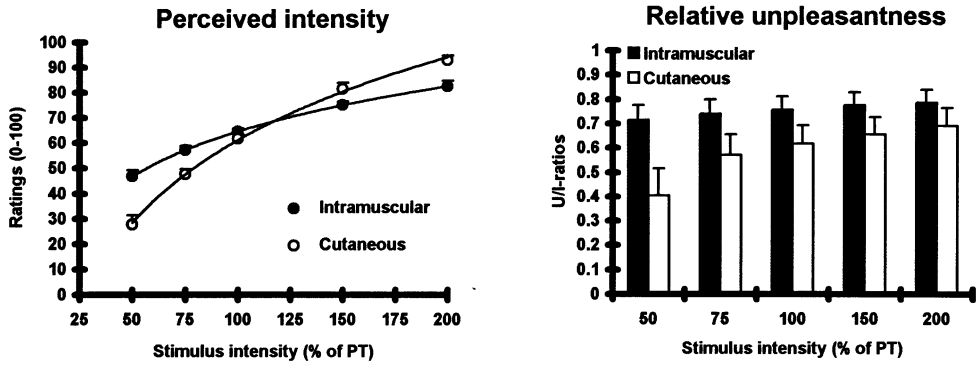

Fig. 1 Perceived intensity and relative unpleasantness of intramuscular electrical and cutaneous infrared laser stimulation. Stimulus intensity on the abscissa is expressed in percentages of pain threshold (*PT*) intensity. The slope of the cutaneous stimulus-response (S-R) curve was significantly steeper than that of the intramuscular S-R curve ($P<0.002$) and intramuscular unpleasantness/intensity (U/I) ratios were significantly greater than cutaneous ratios [$F(1,9)=6.21$, $P<0.034$]. Values are the mean and SE ($n=10$)

cord with the findings of Rainville et al. (1992) who showed that the U/I ratio for deep cold stimulation was significantly higher than for contact heat stimulation. It is likely that the unpleasantness of the intramuscular pain is due, in part, to the types of afferent fibers stimulated and not simply to the electrical mode of stimulation. Unlike the results obtained with cutaneous electrical (Rainville et al. 1992) stimulation, we found no evidence that unpleasantness and intensity ratings diverged as intramuscular electrical stimulus intensity increased. Indeed, in contrast with the ratings of cutaneous laser stimulation, these ratings showed a slight, but statistically insignificant, tendency to converge at the higher stimulus intensities.

The observation that summation PTs to repeated cutaneous infrared laser or intramuscular electrical stimuli were significantly lower than PTs to single stimuli demonstrates the existence of temporal summation mechanisms for both skin and muscle pain. It is unlikely that the accumulation of heat produced by repeated infrared laser stimuli could account for the decrease in laser threshold, because after 1 s the temperature at the surface of the skin is within 2°C of the baseline temperatures (Haimi-Cohen et al. 1983). Temporal summation has previously been demonstrated for cutaneous C-fiber mediated pain sensations when the stimulus frequency is higher than 1/3 Hz (Price et al. 1977). Furthermore, Pertovaara et al. (1988) found evidence of temporal summation with cutaneous CO_2 laser stimulation. Recently, Arendt-Nielsen and collaborators have shown that temporal summation mechanisms may be activated with electrocutaneous stimulation and that these mechanisms could be related to central hyperexcitability and hyperalgesia (Andersen et al. 1994; Arendt-Nielsen et al. 1994, 1995; see also Price et al. 1994). Duranti et al. (1983) presented evidence for a temporal summation mechanism in muscles but did not attempt to quantify the phenomenon. Recently, Graven-Nielsen et al. (1996) have shown temporal summation for muscle pain produced by repeated injections of hypertonic saline. Together, these results suggest that intramuscular, like cutaneous nociceptive information, may summate in central neurons.

The present results are consistent with a common mode of central processing for skin and muscle pain intensity. Convergence of nociceptive afferents from skin and muscle onto wide dynamic range neurons in the spinal cord could be an underlying mechanism (Foreman et al. 1977; Mense 1993). However, the data also suggest a relatively larger activation of affective mechanisms by muscle afferents than by cutaneous afferents.

Acknowledgements This work was supported by the US Department of Veterans Affairs Merit Review Program and by grants from the Danish Medical Research Council, the Danish Dental Association's FUT and Calcin Foundations and Foght's fund to P.S.

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