

Topographical distribution of pinprick and warmth thresholds to CO₂ laser stimulation on the human skin

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Abstract

We studied the topographical distribution of laser sensory thresholds on the human hairy skin, using a small laser beam for pinprick and a large beam for warmth sensations. The threshold for pinprick sensation correlated positively with the distance from the brain, suggesting that A δ nociceptors, the fibers which convey pinprick sensation, are more dense at proximal than at distal body sites. This finding adds information to skin biopsy studies of epidermal free nerve endings which showed a similar gradient, but could not differentiate small myelinated from unmyelinated fiber afferents. Possibly because of a diffuse low density of warmth receptors, laser warmth thresholds showed no trend. © 2000 Elsevier Science Ireland Ltd. All rights reserved.

Keywords: Laser threshold; Warm sensation; Pinprick sensation; A δ nociceptors; Warmth receptors; Free nerve endings

Skin biopsy studies have shown a higher density of epidermal free nerve endings in the neck, and back and in proximal than in distal leg sites [11,13]. Yet they could not distinguish between A δ - and C-mechanothermal nociceptors and warmth receptors.

In man, laser stimuli selectively activate epidermal free nerve endings evoking brain responses and a variety of sensations [1,3,5,14,16]. The activity arising from A δ and C afferents can be partly differentiated by studying laser perception thresholds. Pinprick sensations arise from A δ nociceptive fibers and warm or burning sensations from unmyelinated fibers [1,3–5,12,14,15].

In this study we sought information on the body distribution of free nerve endings innervated by myelinated and unmyelinated fibers by evaluating the laser thresholds of pinprick and warmth sensations at various hairy body sites.

Eight normal subjects (four men and four women, age range 22–38 years) gave their informed consent to participate in the study. The local Ethical Committee approved the experiments. From a series of laser stimuli delivered at increasing and decreasing intensities we determined perceptual thresholds [7], defined as the lowest intensity eliciting

50% of perceivable pinprick and warmth sensations. Subjects were explicitly asked to report when a pinprick or warmth sensation was first felt. Laser stimuli were randomly delivered with a 20–30 s interstimulus interval and after each pulse the beam position was changed within a target area of 3 × 2 cm². We delivered brief radiant heat pulses with a CO₂ laser stimulator (1–15 W, wavelength 10.6 μ m; Neurolas, Electronic Engineering, Florence, Italy). Laser stimuli for determining pinprick thresholds lasted 10–15 ms and had a beam diameter of 2.5 mm (irradiating an area of almost 5 mm²); those for warmth thresholds lasted 15–30 ms and had a beam diameter of 5 mm (irradiating an area of almost 20 mm²). Thresholds were measured in mmJ/mm². Pinprick and warmth sensations were determined on separate days and each session lasted about 45 min. Although the subjects were not asked to discriminate whether stimuli were painful, at the end of each session they usually reported no pain. We stimulated the skin at various body sites ranked according to their distance from the brain as assessed on a skeleton and on topometric atlases (see Fig. 1 legend). Because our laser stimuli often failed to evoke a warm sensation at the foot, for this site only the data regarding pinprick sensation were collected. Body sites were stimulated in random order.

One-way analysis of variance (ANOVA) for repeated

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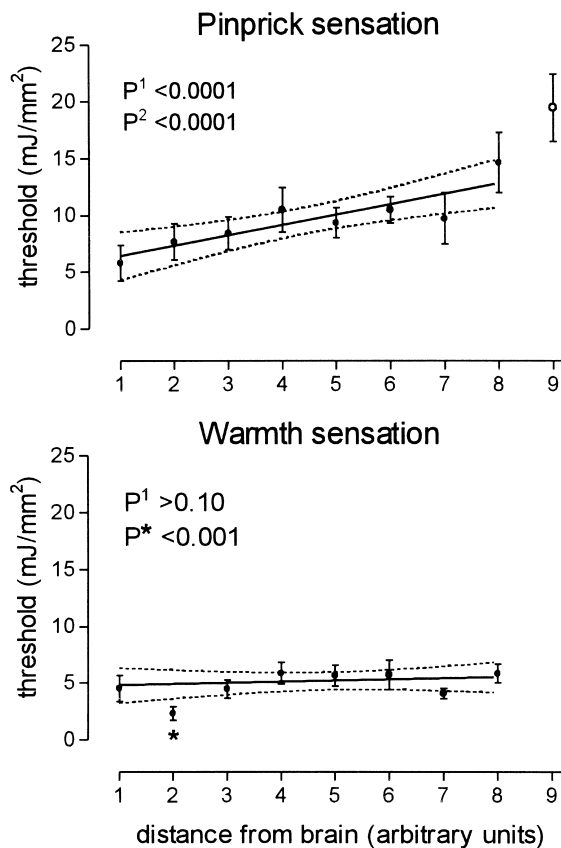


Fig. 1. Plots of the threshold values for pinprick (upper panel) and warmth (lower panel) sensations. In the X axis each stimulated body site is ranked according to its distance from the brain: (1) neck around the C5 spinal process, (2) upper lip, (3) forehead, (4) shoulder (just below the acromion), (5) dorsal trunk around the T9 spinal process, (6) T9 dermatome near the ventral midline, (7) lateral aspect of the hip, (8) hand dorsum and (9) foot dorsum. The data for the foot have been omitted from the lower panel because we failed to evoke a warmth sensation from this area. Dots are the mean \pm 1SE. The continuous lines indicate linear regression and dashed lines the 95% confidence limits. In the upper panel, P1 indicates the level of significance of the post test for linear trend when the data from the leg were included, P2 when they were excluded. The regression line in the upper panel is calculated after excluding from the analysis the data from the foot. In the lower panel P1 indicates the level of significance of the post test for linear trend. P* indicates the level of significance of the Welch's test between the data from the upper lip and those from all the other regions pooled.

measures, post test for linear trend and the post hoc Tukey's multiple comparison test were used to analyze differences in pinprick and warmth thresholds at the various body sites. The Welch's test for populations with different standard deviations was used to analyze the difference between thresholds of warm and pinprick sensations and between the warm sensation in the upper lip region and those in the remaining sites pooled.

Pinprick thresholds (Fig. 1, upper panel) were significantly higher than warmth thresholds (Fig. 1, lower panel) ($P < 0.001$; Welch's test).

The thresholds for the pinprick sensation differed at the various body sites ($P < 0.001$, ANOVA). Post hoc analysis found a significant linear trend according to distance from the brain ($P < 0.001$). Excluding foot data from the analysis left the statistical significance unchanged, indicating that thresholds values for the foot did not affect the general trend. Thresholds were higher in the foot than in any other body site ($P < 0.001$) and higher in the hand than in the neck ($P < 0.05$).

Unlike pinprick sensations, thresholds for warmth sensation showed no trend ($P > 0.10$). But post-hoc analysis showed a lower threshold in the upper lip than in the shoulder and the hand ($P < 0.05$). Upper-lip thresholds differed from those of all the other body sites pooled ($P < 0.005$; Welch's test).

In a group of healthy young subjects we consistently evoked liminal sensations of pinprick or warmth. In accordance with others, whether laser stimuli – at low stimulus intensities – evoked sensations of pinprick or warmth depended mainly on the size of the skin area stimulated [14]. Warmth receptors have a lower thermal activation threshold than A δ and C mechanothermal nociceptors [3,12,15]. But human skin contains fewer warmth fibers than A δ fibers and fewer A δ than C fibers [9,17]. Finally, A δ receptors mediating pinprick sensation reportedly have either a larger or a smaller receptive field than C nociceptors [18,19], while warmth receptors have by far the smallest receptive fields [6]. Overall these data suggest that in our subjects, CO₂ laser stimulation (at an intensity lower than the threshold for A δ nociceptors) over a large skin area recruited a sufficient number of warmth receptors. Conversely stimuli delivered to a small skin area excited too few warmth receptors. Laser pulses delivered at a slightly higher intensity also excited the A δ nociceptors mediating pinprick sensation. The activation of A δ nociceptors hindered sensations other than pinprick because the A δ fiber activity dampens the unmyelinated fiber input centrally [3,4,10].

The main finding in this study is that the pinprick threshold increased significantly as the distance from the brain lengthened, while the warmth threshold did not (Fig. 1).

The changes in pinprick threshold with the distance from the brain agree with previous data showing lower laser thresholds for pinprick sensations in the face than in the extremities [2,7]. Because spatial summation of impulses at central synapses is critical for eliciting laser perception thresholds [10,16], the proximal-distal gradient is probably a consequence of an inverse gradient in the receptor density. This conclusion concurs with biopsy findings for epidermal free nerve endings (unmyelinated and myelinated) [11,13]. Alternatively, laser thresholds may be influenced by epidermal thickness and conduction distance. The rise in temperature after short-duration laser pulses (such as those used here) reaches a lower peak and is less steep as the distance from skin surface increases [5,14]. Although epidermal thickness varies with body site, it does not follow a regular trend. Skin thickness is similar in the forehead, upper arm

and thigh, as well as cheek and trunk, and hand and ankle [20]. Furthermore skin thickness would presumably affect the thresholds of both receptor types; but warmth thresholds had no gradient. The propagation of a nervous volley certainly implies some degree of temporal dispersion, which increases with the conduction distance. Because temporal dispersion would affect sensations conveyed by unmyelinated fibers more than those conveyed by small myelinated fibers, the lack of a trend for the warmth thresholds minimizes the role of conduction distance.

The distribution of warmth thresholds differed from that of pinprick thresholds and from that of free nerve endings in biopsy studies. Warmth is mediated by thermal receptors and burning by C-fiber mechanothermal nociceptors [6]. Laser stimulation in man yields a far lower threshold for warmth sensation than for burning sensation [1,12,15]. In a recent study with feed-back control of temperature and evoked potential recordings [12], low-intensity laser stimuli (selectively activating unmyelinated fibers alone) evoked a warmth sensation in more than 50% of the trials and a burning sensation in less than 5%.

Warmth receptors are far less numerous than A- δ and C nociceptors [9,17]. The lack of a correlation between the warmth threshold and the distance of the body sites from brain probably reflects a uniform low density of warmth receptors, possibly with the exception of the perioral region (see below). The scarcity of warmth receptors has no bearing on the proximal-to-distal reduction in the density of epidermal free nerve endings found in biopsy studies [11,13]. Finally, the warmth threshold was significantly lower in the upper lip than in all the other body sites (Fig. 1, lower panel). Rabbits and cats show a clear concentration of thermal receptive fields around the nose, whisker pad and mouth [8], indicating a localized high thermal receptor density in these regions. Were this true also in man, it might explain the low value of warmth threshold we found in the upper lip.

In conclusion, the threshold for pinprick, a sensation undoubtedly related to the activation of A δ nociceptors, correlated with the distance from the brain. Concurring with data from skin biopsy studies on the distribution of free nerve endings, this finding probably reflects an inverse gradient in the density of A δ mechanothermal nociceptors. The threshold for warmth, a sensation related to the activation of unmyelinated fibers did not show the trend seen for A δ nociceptors. Assuming that under our experimental conditions the sensation of warmth mainly reflected the activation of warmth receptors rather than C nociceptors [6], the lack of correlation between warmth threshold and distance from the brain can be explained by a diffuse low density of warmth receptors.

The functional meaning of the A δ gradient is unclear. There may be no specific functional reason and the distribution of free nerve endings could simply be a phylogenetic heritage: as the process of limb development advanced, the increased skin surface led to a large increase in the number

of tactile neurons, unaccompanied by an increase in nociceptive neurons.

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