advances.sciencemag.org/cgi/content/full/5/7/eaaw1297/DC1

Supplementary Materials for

An ultrafast system for signaling mechanical pain in human skin

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Published 3 July 2019, *Sci. Adv.* **5**, eaaw1297 (2019)
DOI: 10.1126/sciadv.aaw1297

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Fig. S1. Response properties of C-HTMRs to graded mechanical stimuli.
Fig. S2. Human field afferents do not display nociceptive properties.

Supplementary Materials

Human field afferents do not have nociceptive properties

Peroneal recordings yielded 59 field afferents with the following spatial distribution: Toes 40.7%; Foot 47.4%; Ankle 8.5%; Leg 3.4% (fig. S2A). The field afferents displayed “expansive” (*16*) receptive fields that were significantly larger than those of SA1 afferents (two-tailed t-test with Welch’s correction: $P < 0.0001$). Seven field afferents were also recorded from the radial nerve (fig. S2A).

All field afferents were activated by soft brush stroking, but they were unresponsive to hair deflection and air puff. Hairs were removed by shaving from the receptive field of five field units, but this had minimal effect on their responses (example shown in fig. S2B). No particular preference for the direction of stroking was observed. The spike activity of field units increased with faster brushing, which is consistent with the known brushing profile of all A-LTMRs in human hairy skin (*8*).

The responses of field afferents plateaued as the indentation force increased (fig. S2C) with no significant differences in their responses between 20 and 3000 mN. Psychophysically, pain ratings increased with higher indentation forces, but no association was found between the peak neural response of field afferents and corresponding pain ratings. For spike numbers and mean firing, see fig. S2, D to F.

In two field units where we compared responses to sharp and blunt stimulations, no obvious differences were observed; for instance, their peak firing to a sharp 512 mN filament was 125.7 and 90.1 Hz, and to a corresponding blunt filament was 121.2 and 99.0 Hz, respectively.

Supplementary Figure 1

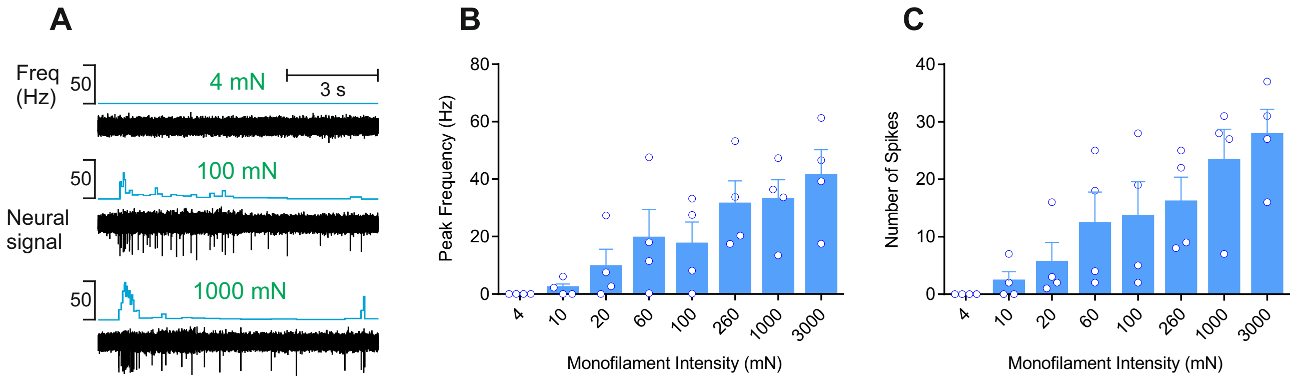

Fig. S1. Response properties of C-HTMRs to graded mechanical stimuli. (**A**) Spike activity of a C-HTMR during monofilament stimulation at three different forces. Compared to an A-HTMR (see Fig. 1F), the C-HTMR displayed a lower firing rate, and a weaker sustained response during noxious mechanical stimulation. Freq: frequency. (**B**) Peak discharge rates of C-HTMRs for monofilament stimulation. The data show individual and average (± SEM) responses of C-HTMRs to monofilament stimulation at eight different indentation forces (two units, four trial-sets). See also Fig. 2A. (**C**) Number of spikes produced by monofilament stimulation in C-HTMRs. Individual and average (± SEM) responses of C-HTMRs to monofilament stimulation at eight different indentation forces (two units, four trial-sets). See also Fig. 2D.

Supplementary Figure 2

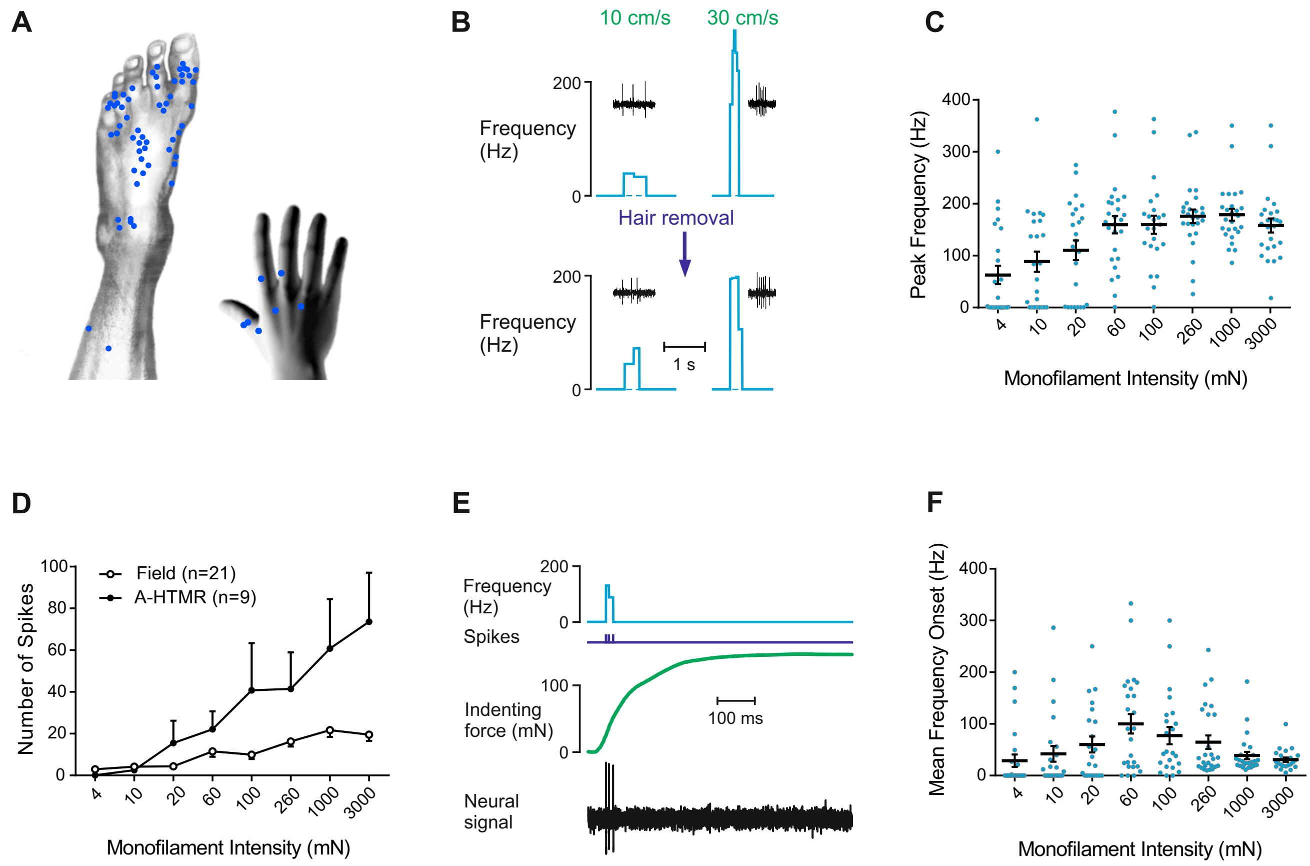

Fig. S2. Human field afferents do not display nociceptive properties. (**A**) Location of receptive fields of field afferents from recordings in the peroneal and radial nerves. Each dot represents the location of an individual field unit (n=66). (**B**) Spike activity of a field afferent to soft brush stroking before and after hair removal. Using a soft goat hair brush, a 10-cm area of skin centered on the receptive field of the recorded afferent was stroked at velocities of 10 and 30 cm/s, guided by a moving strip on a computer screen. High sensitivity to brushing was displayed by the field unit with an increase in neural discharge rate to the faster stroking velocity. The removal of hair by shaving had no effect on the responses. (**C**) Responses of field afferents plateaued during increasing indentation forces. Individual and average (± SEM) responses of 21 field units to monofilament stimulation at eight different indentation forces (26 trial-sets). No significant differences were found in the peak frequency responses between 20 and 3000 mN (Tukey's test). Further, a linear fit was not displayed between neural responses and indentation forces (R^2 = 0.1364, P = 0.3679), and no significant correlation was found with psychophysical pain ratings (*r* = 0.5608, P = 0.1482). (**D**) Different number of spikes produced by 5-s monofilament stimulation in A-HTMRs and field afferents.

Average (± SEM) response for each unit type and monofilament intensity. Both monofilament intensity (2-way ANOVA: $P < 0.0001$, $F (8, 283) = 12.52$) and unit type ($P < 0.0001$, $F (1, 283) = 31.96$) had a significant effect on spike numbers, with 1000 and 3000-mN responses of A-HTMRs significantly higher than all field responses ($P < 0.01$; Tukey's multiple comparisons test). Spike numbers for A-HTMRs were taken from Fig. 2D for comparison with field afferents. (**E**) Spike activity of a field afferent during the first 0.5 s of monofilament stimulation (with force feedback). Top panel shows neural discharge rates, middle panels show spike markers and indentation force markers, and bottom panel shows neural recording. The first 0.5 s was selected as the onset period of monofilament stimulation (total duration: 5 s). (**F**) Mean discharge rates of field afferents for monofilament onset. Individual and average (± SEM) responses of 21 field units to the onset period (0.5 s) of monofilament stimulation at eight different indentation forces (26 trial-sets).