

Secondary hyperalgesia is mediated by heat-insensitive A-fibre nociceptors

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Background & Aims. Secondary hyperalgesia refers to the increase in pinprick sensitivity spreading beyond the site of injury. It can be induced experimentally by transcutaneous high frequency electrical stimulation¹ (HFS). Previous studies have suggested that secondary hyperalgesia is mediated by a specific class of myelinated nociceptors: slowly adapting A-fibre mechano- and heat-sensitive (AMH) type I nociceptors. Here, we tested this hypothesis by examining whether long-lasting heat stimuli, which are known to activate AMH-type I nociceptors, elicit enhanced responses when delivered to the area of secondary hyperalgesia induced by HFS in experiment 1, and before and after an A-fiber conduction block in experiment 2.

Methods. Healthy volunteers received transient pinprick mechanical stimuli (128 mN) and suprathreshold long duration heat (30s) stimuli on both volar forearms before and 20 minutes after HFS (14 subjects, experiment 1) and before and after conduction block (4 subjects, experiment 2). Intensity of perception was recorded continuously during heat stimuli using an online visual analog scale (0-100mm). The heat rating curves obtained were analyzed with a temporal non-parametric cluster-based permutation test. Subjects rated the intensity of perception elicited by the pinprick stimulation with a numerical rating scale (NRS, 0-100). In experiment 2, long duration heat (30s) stimuli were delivered on the hand dorsum before and after a selective conduction block of myelinated fiber of the superficial branch of the radial nerve.

Results. Experiment 1, the repeated-measures ANOVA performed on the pinprick ratings confirmed a significant time $\times$ side interaction ($F(1, 13) = 38.208, p < .001$). Moreover, post-hoc tests showed a significant increase of the perceived intensity of pinprick stimuli after HFS at the treated arm (paired t-test; $t(13) = 7.177, p < .001$). For the long duration heat stimuli, the permutation test performed on the difference ratings curves (after vs. before HFS) of both arms (control vs. HFS) revealed no significant cluster. Experiment 2, descriptive analysis (4 subjects) showed that the rating response is delayed and decreased especially during the second half of the long duration stimulus.

Conclusion. While HFS induced a significant increase of the perception of mechanical stimulation, we did not observe any significant enhancement of the perception of the long duration heat stimuli. Moreover, the conduction block of myelinated fibers greatly decreased or even abolished the perception of the second half of the long duration heat stimuli. These results support the notion that AMH-type I nociceptors contribute to the perception of sustained heat, but do not mediate secondary hyperalgesia.

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¹: LaMotte et al. J Neurophysiol (1991)

²: Treede et al. J Neurophysiol (1998)