

INTRODUCTION

Topical application of **high-concentration capsaicin** is approved as a treatment for localized neuropathic pain. The mechanism of action is probably related to the fact that topical capsaicin activates TRPV1 afferents and that this induces a reversible intra-epidermal free nerve ending denervation resulting in reduced thermosensitivity. However the **time course** and **spatial extent** of the **denervation/reinnervation** process and the respective contribution of different **types of sensory afferents** is not well characterized. As such, we assessed the time course and spatial extent of the effects of high-concentration topical capsaicin on the **perception of noxious and innocuous heat and cold stimuli** in healthy volunteers.

METHODS

The volar forearm of **21 healthy volunteers** was treated with a single (1h) high-concentration (2% in ethanol/water) **capsaicin-patch**. Brief innocuous warm (800 ms 38°C), noxious heat (100 ms 55°C and 44°C) and innocuous cold (2000 ms 10°C) were applied within and outside the treated skin, before treatment, and **+1, +3 and +7 days** after treatment. Sensitivity based on **reaction times, intensity** and **quality ratings** was evaluated.

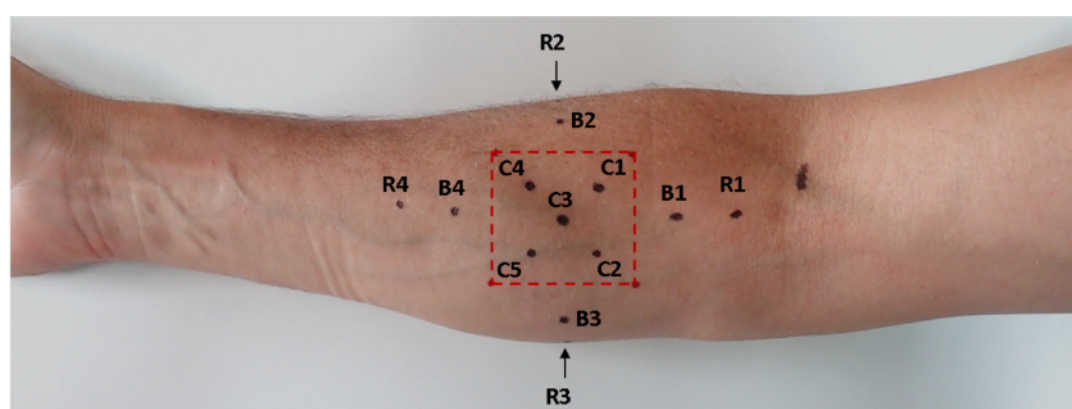


Figure 1: Placement of the testing grid on the volar forearm. Heat and cold sensitivity was tested at 13 different spots (3 measurements/spot) on the volar forearm. C1–C5 indicate the testing locations at the area of capsaicin treatment, B1–B4 the testing locations at the border of the treated skin and R1–R4 the testing area away from the borders of the treated skin. At the contralateral arm, 4 additional test locations at the area corresponding to the area of the treated skin were used as controls. Red dotted lines indicate the area of the capsaicin patch.

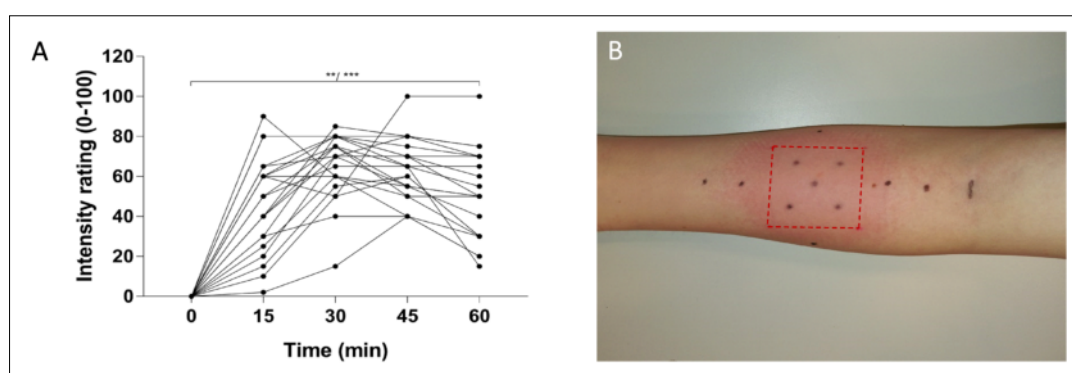


Figure 2: Intensity ratings during capsaicin treatment and flare response immediately after removal of the patch. **A)** Intensity increased after capsaicin treatment with mean scores peaking at 30–45 min after application. **B)** Flare response immediately after patch removal in one representative subject. Red dotted lines indicate the area of the patch. Generally, flare disappeared within two to three hours after patch removal.

RESULTS

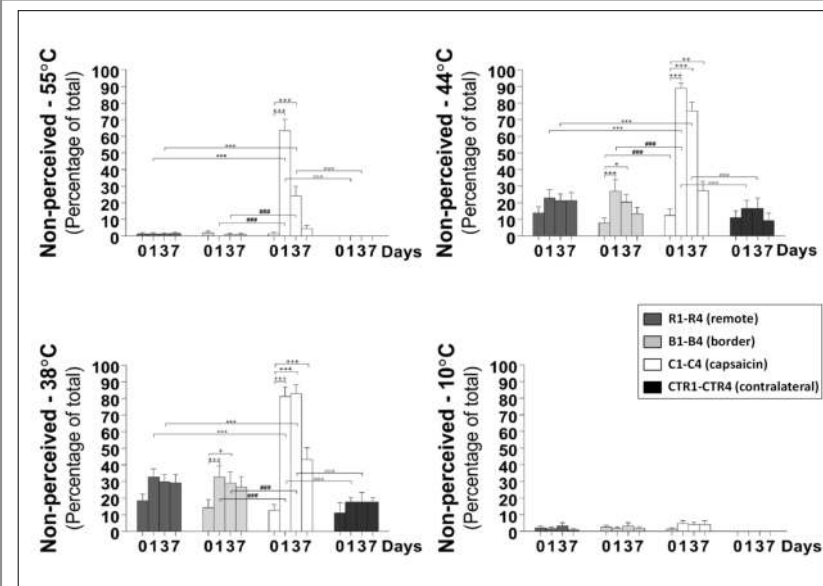


Figure 3: Percentage of non-perceived stimuli. Reduction of high-intensity heat sensitivity was restricted to the area of capsaicin treatment and returned to values before treatment, by seven days. In contrast, sensitivity to intermediate and low intensity heat stimuli was still reduced at D7 and the loss was spatially more widespread. Cool sensitivity was not affected by capsaicin.

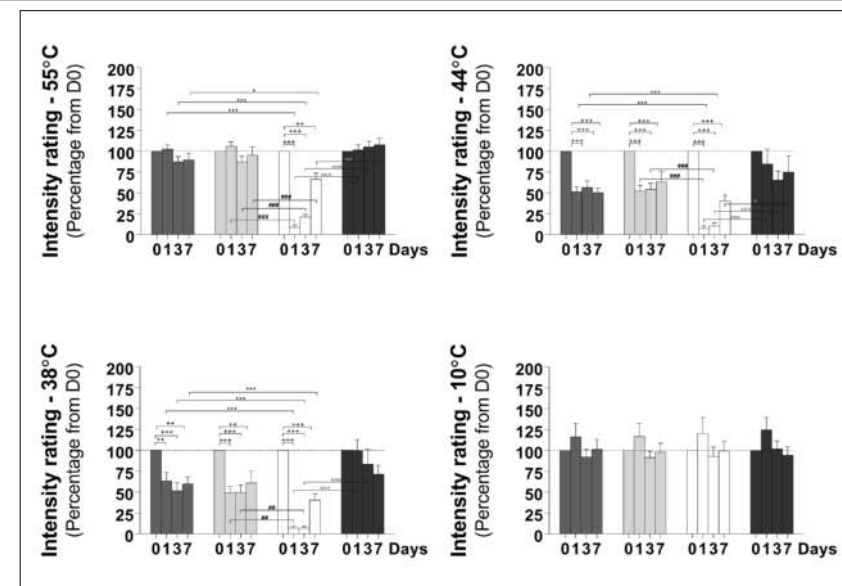


Figure 4: Intensity ratings. Intensity ratings dropped massively at the area of treatment and remained low up to seven days after capsaicin. Intensity ratings to intermediate and low intensity heat stimuli were also reduced at the border and area remote from the patch. This effect was not observed at the contralateral side. Cool sensitivity was not affected by capsaicin.

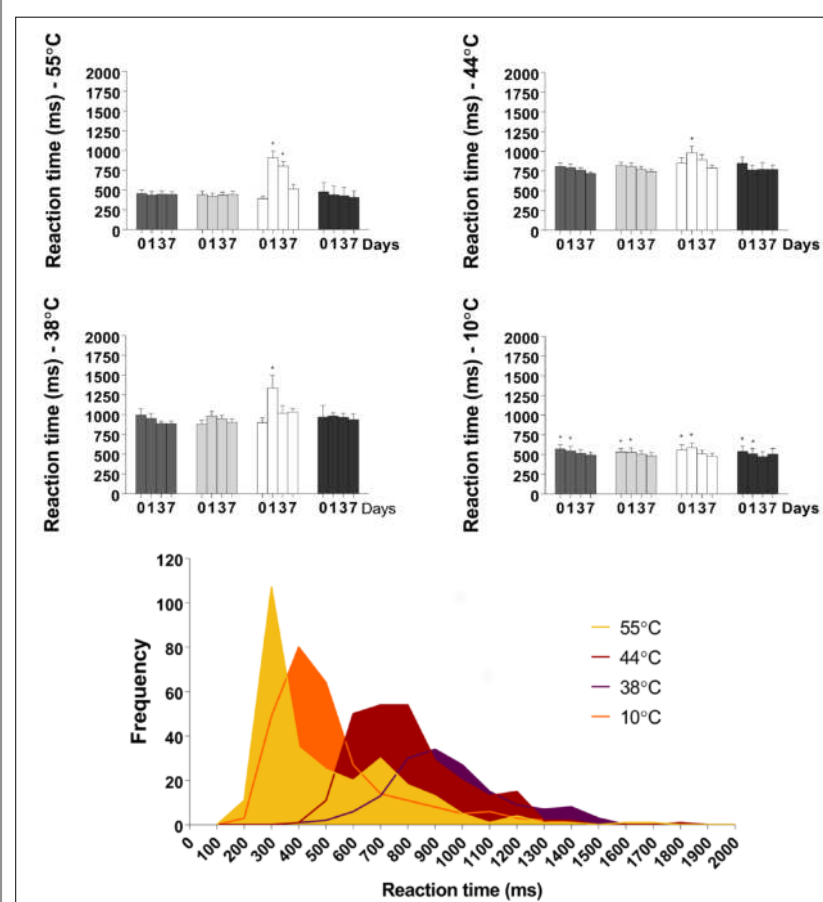


Figure 5: Reaction times. High intensity heat stimuli were detected with reaction times compatible with the conduction velocity of Ad-fibers (300 ms). Whereas intermediate and low intensity heat stimuli were detected with reaction times in C-fiber conduction range (700 ms and 900 ms).

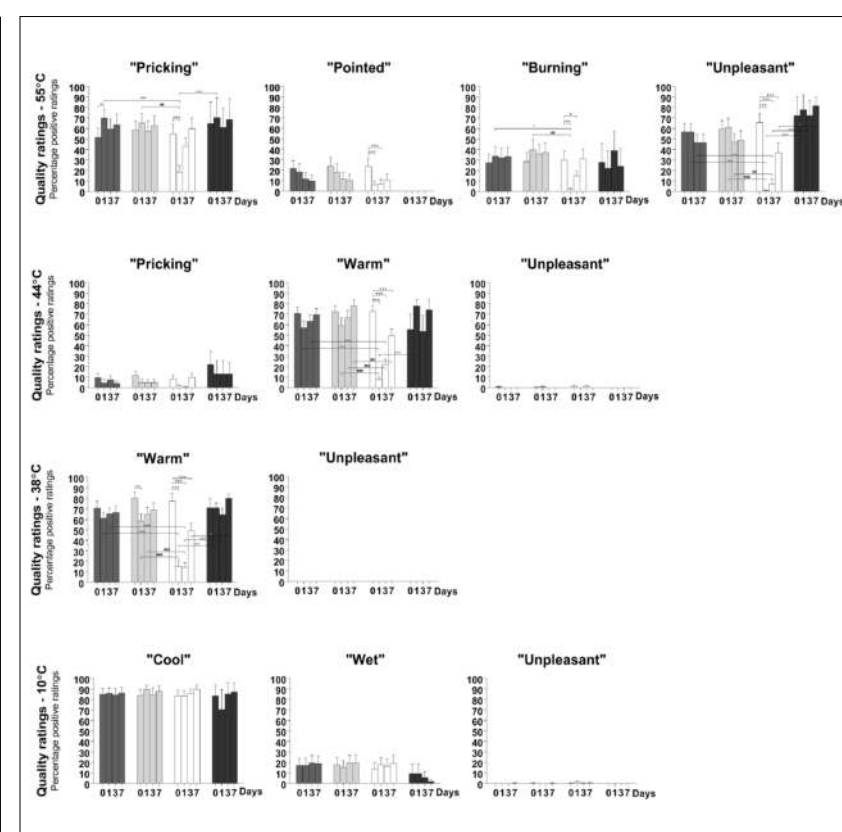


Figure 6: Quality ratings. High intensity heat stimuli elicited predominantly pricking sensations and were mostly rated as unpleasant. Intermediate intensity heat stimuli were experienced as pricking/warm. Likewise low intensity heat stimuli only elicited a (diffuse) warmth sensation and no unpleasantness. Cool stimuli were always rated as cool, sometimes as wet, and in exceptional cases as slightly unpleasant with mild burning sensations.

CONCLUSION

1) Topical capsaicin had only a temporary desensitizing effect on heating stimuli, not on the perception of cooling stimuli. **2)** The loss of sensation was not restricted to high intensity heat sensations, but it also affected innocuous warmth sensation. **3)** An additional reduction in sensitivity at area remote from the patch was observed at the treated arm. This effect was restricted to stimuli eliciting reaction times in C-fiber conduction range (38°C and 44°C), and was not observed at temperatures where reaction times suggest Ad-activation (55°C). These data support the idea that noxious and innocuous heat sensation are mediated by different afferent fibers. Moreover these observations also suggest that it is especially the C-fibers that are more affected by capsaicin, and that they may play an important role in adaptation of the sensory system to newly encountered sensory stimuli.