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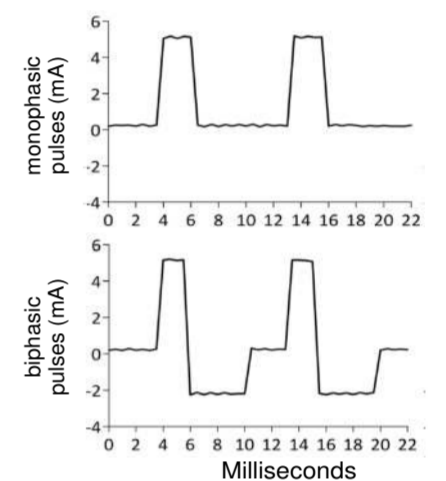
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Background and aims

Animal studies have shown that high frequency stimulation (HFS) of peripheral C-fibers induces long-term potentiation (LTP) within spinal nociceptive circuits. In humans, similar HFS applied to the skin using an electrode designed to preferentially activate nociceptive afferents induces secondary mechanical hyperalgesia, which is considered a manifestation of central sensitization. Most previous studies have delivered HFS using 100 Hz trains of square-wave pulses. Because monophasic square-wave pulses are not charge-compensated, high frequency stimulation using such pulses may induce a residual net charge which could interact with the induction of secondary hyperalgesia. Furthermore, not much is known about the after-effects of stimulation delivered using frequencies other than 100 Hz. Therefore, we conducted a first experiment comparing the secondary hyperalgesia induced by 100 Hz HFS delivered using non-charge-compensated monophasic pulses vs. charge-compensated biphasic pulses. Then, we conducted a second experiment comparing the after-effects of stimulation delivered at frequencies extending between 5 and 100 Hz.

Methods

In Experiment 1 (N=15), five 100 Hz trains of HFS lasting 1 second were delivered to the volar forearm (9s inter-train interval) using non-charge-compensated (monophasic) or charge-compensated (biphasic) pulses, in two separate sessions separated by >1 week. In Experiment 2 (N=4x15) charge-compensated 100, 42, 20 and 5 Hz trains of pulses lasting 1 s were delivered to four separate subject groups, keeping constant the total number of pulses (500) and the inter-train interval (9s). Secondary hyperalgesia was quantified as the change in intensity of perception elicited by 128 mN pinprick stimuli and the size of the area of increased pinprick sensitivity.



Results

Secondary hyperalgesia was not significantly different between 100 Hz HFS delivered using monophasic vs. biphasic pulses (Fig. 1). In contrast, secondary hyperalgesia was dependent on the frequency of the stimulation trains, and maximal at intermediate frequencies (Fig. 2; 20 and 42 Hz).

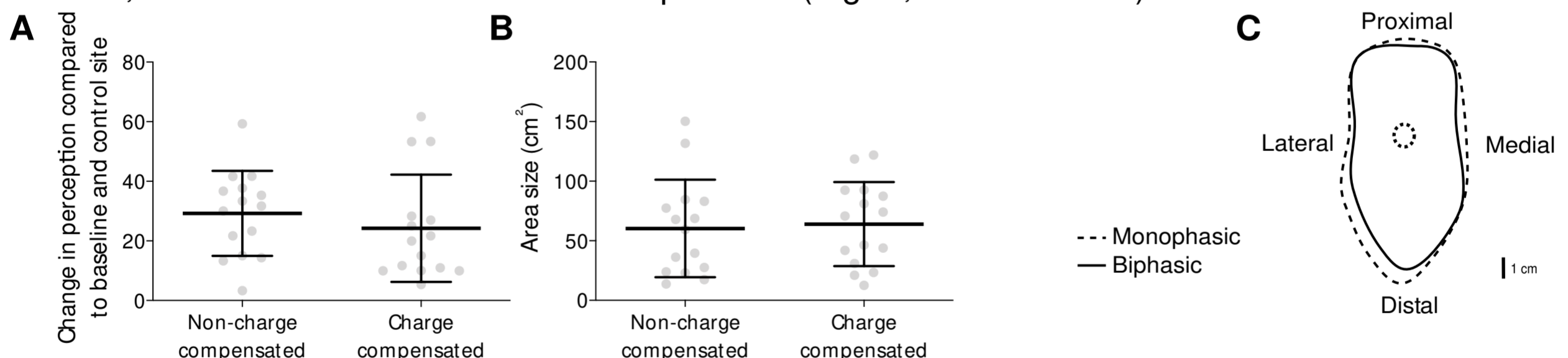


Fig 1. A. Group-level average (\pm SD) increase in numerical rating scale (NRS) compared to baseline and control site for non-charge-compensated and charge-compensated pulses. **B.** Group-level average (\pm SD) area size of the increase in pinprick sensitivity. **C.** Group-level average delineation of increased pinprick sensitivity.

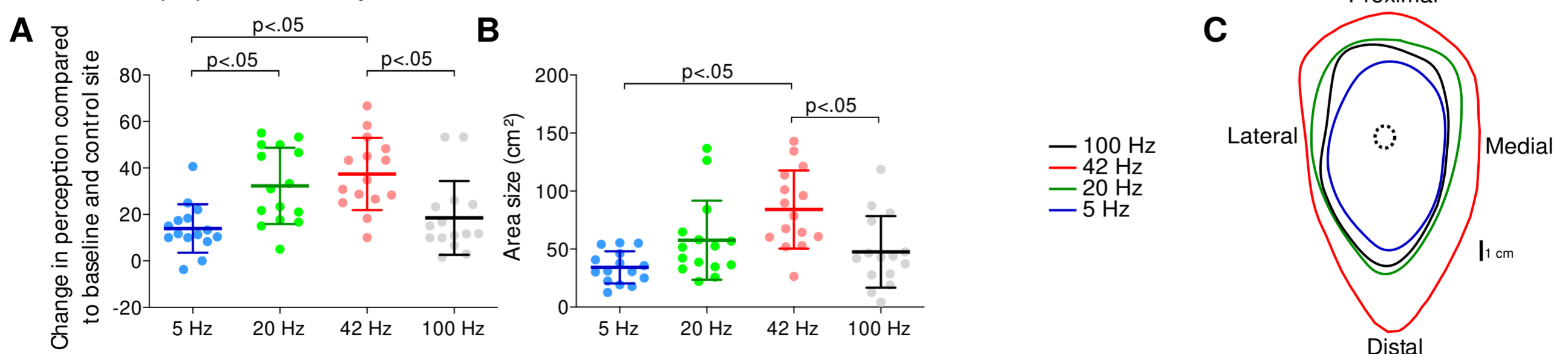


Fig 2. A. Group-level average (\pm SD) increase in NRS compared to baseline and control site after 5, 20, 42 and 100 Hz stimulation. **B.** Group-level average (\pm SD) area size of the increase in pinprick sensitivity. **C.** Group-level average delineation of increased pinprick sensitivity.

Conclusion

Possible charge accumulation induced by monophasic pulses does not significantly influence secondary hyperalgesia induced by 100 Hz HFS (Exp 1). When keeping train duration and total number of pulses constant, the secondary hyperalgesia induced by transcutaneous electrical stimulation of nociceptive afferents is maximal at intermediate frequencies of stimulation (Exp 2).