

INTRODUCTION

- Human surrogate models are commonly used to study the mechanisms associated with central sensitization in healthy volunteers, aiming to extrapolate the findings to those cases where sensitization is present as part of pathophysiological pain disorders [1].
- These models have not been extensively studied in cases when there already exists a clinical condition that affects the central nervous system, as for patients with complete spinal cord injury (SCI) [2].
- Therefore, it is crucial to determine if the protective plastic mechanisms are still functional in SCI patients, and if central sensitization models can be established in the presence of adaptive and maladaptive changes in synaptic plasticity and complete lack of descending control.

AIM

To investigate models of central sensitization in SCI patients, elicited by intramuscular injection of capsaicin, induced in the presence of altered spinal/supraspinal nociceptive processing

METHODS

- Fifteen male volunteers with complete spinal cord injury (SCI, mean age 43 years, range 27-66), classified as grade A (AIS), and fourteen non-injured volunteers (NI, 12 males and 2 females, mean age 23 years, range 19-28) participated in the experiment.
- Electrical stimulation was performed through 8 surface electrodes non-uniformly distributed on the foot sole. It consisted of a burst of 8 trains of pulses delivered at 3 Hz, in order to elicit temporal summation. Each train of pulses consisted of a–5 square-wave pulses of 1 ms width delivered at 200 Hz, generated by a computer-controlled constant-current stimulator (Fig. 1). The stimulation intensity was determined as 0.8 times the average NWR threshold over sites 2, 4 and 6.
- A solution of 10 µg of capsaicin in 0.1 ml volume was injected into the flexor digitorum brevis muscle in order to elicit central sensitization.
- RRF areas were calculated as the fraction of the sole of the foot delimited by a threshold set by the peak RMS amplitude of the NWR minus two times the standard deviation of the remaining RMS amplitudes. RRF areas were assessed before capsaicin, 1 min after capsaicin and 60 min after capsaicin.

METHODS (CONT.)

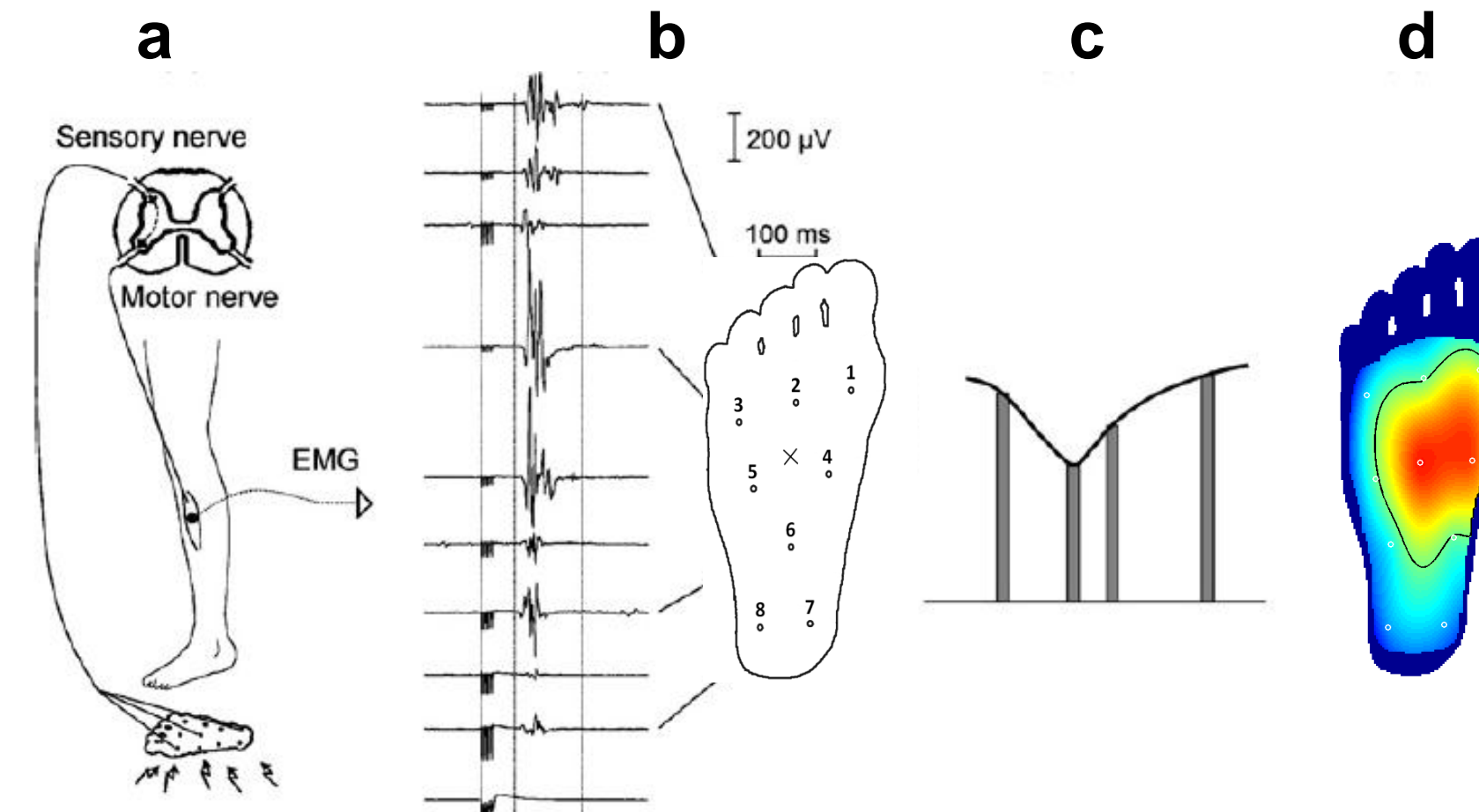


Figure 1. RRF assessment methodology. After stimulation is performed (a), the RMS amplitude of the EMG signals at each site is extracted (b), averaged across repetitions and interpolated (c) to obtain the final RRF map (d). The x marks the injection site.

RESULTS

RRF areas

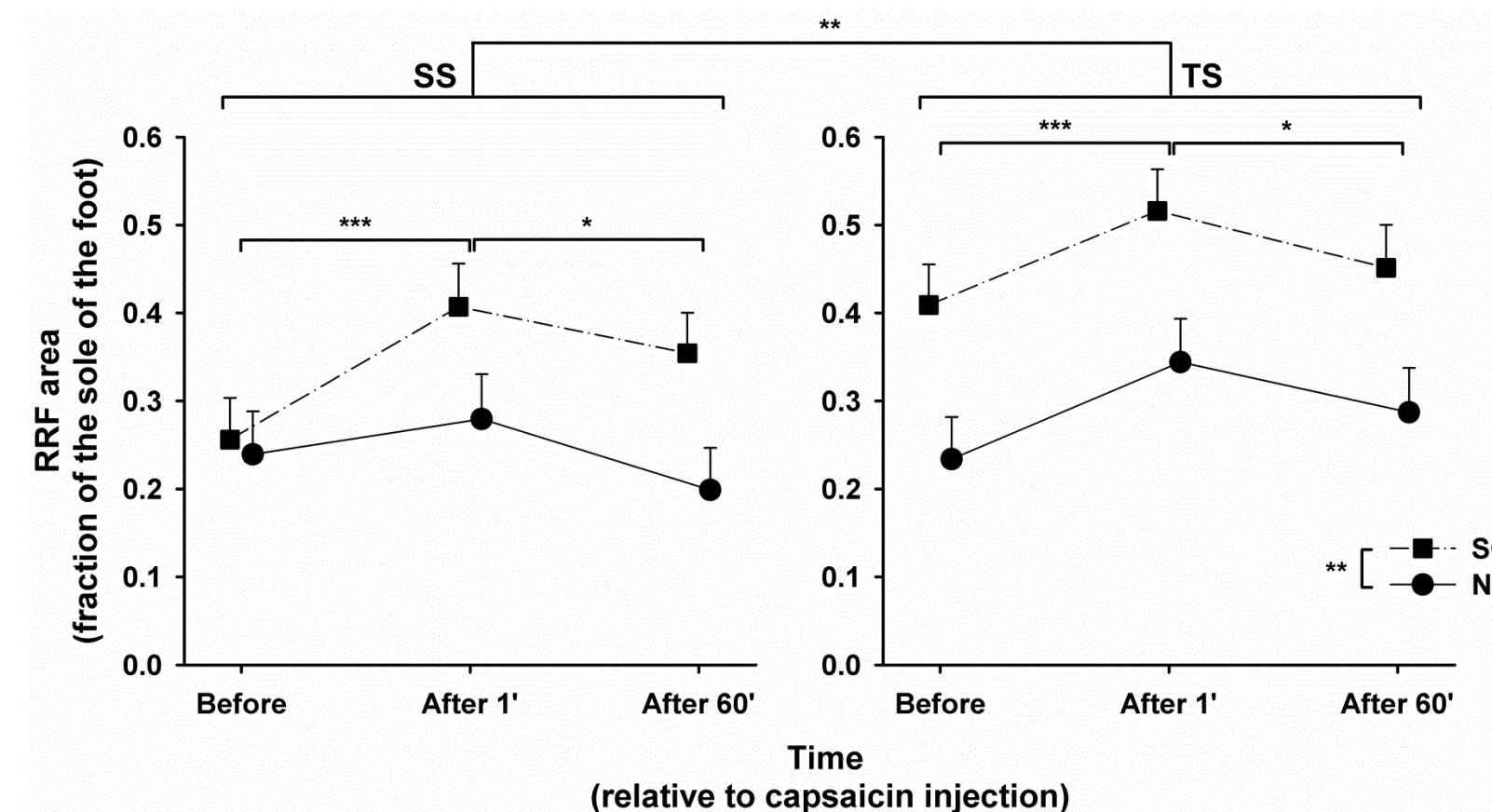


Figure 2. Reflex receptive field (RRF) areas of SCI and NI volunteers. RRF areas were larger 1 min after capsaicin than before and 60 min after capsaicin. RRF areas were also larger in SCI compared to NI volunteers. RRF areas were larger during temporal summation (TS) compared to single stimulation (SS)

RESULTS (CONT.)

RRF Maps

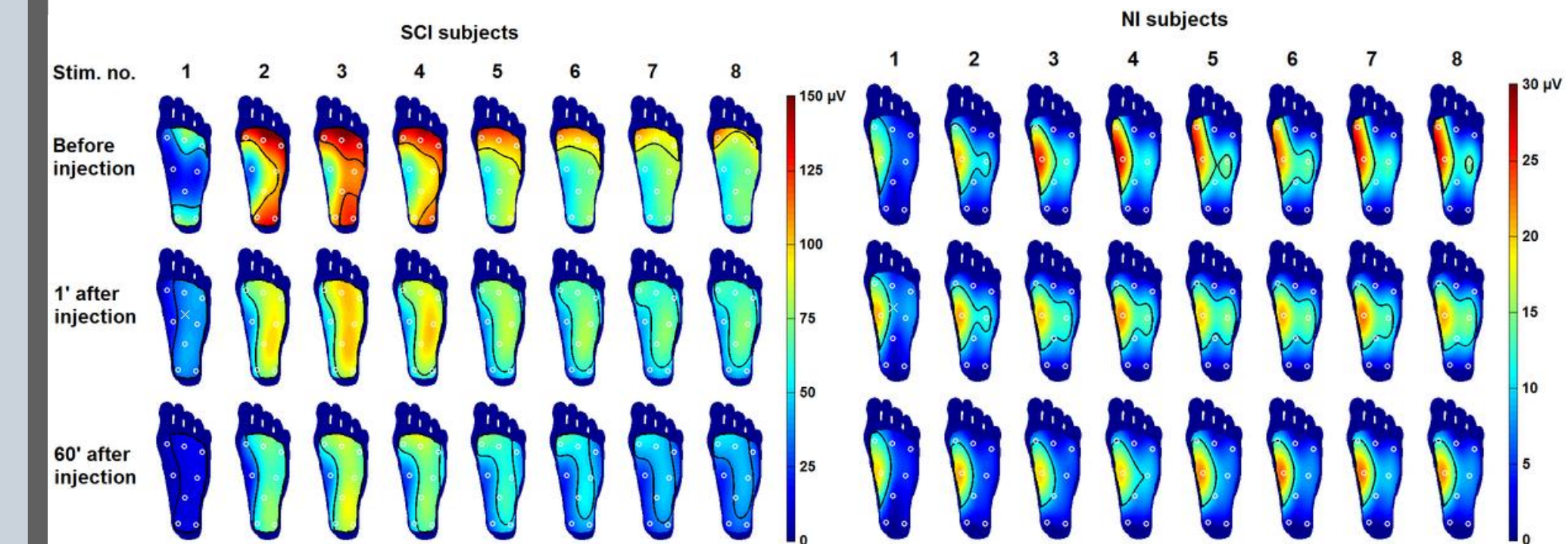


Figure 3. Grand mean RRF maps, averaged across all SCI and NI subjects. The black line delimits the RRF area.

CONCLUSIONS

- Results showed that both groups presented RRF expansion immediately after capsaicin injection (RRF areas were 28% larger in SCI volunteers and 48% larger in NI volunteers right after capsaicin injection, $p = 0.007$).
- The topography of the RRF was significantly different in SCI volunteers compared to NI volunteers in terms of size and shape (RRF areas were in average 56% larger in SCI volunteers compared to NI volunteers, $p = 0.007$). SCI volunteers not only showed larger RRF areas, but also a reversed RRF topography compared to RRF of NI volunteers (see Figure 3).
- In summary, it is possible to induce central sensitization in volunteers with complete SCI, despite adaptive changes in synaptic plasticity and lack of descending control. Moreover, central sensitization can significantly expand the RRF and this modulation is under strong influence of descending control.

REFERENCES

- Woolf CJ. Central sensitization: Implications for the diagnosis and treatment of pain. *Pain* 2011;152:S2-S15.
- Andersen OK, Finnerup NB, Spaich EG, Jensen TS, Arendt-Nielsen L. Expansion of nociceptive withdrawal reflex receptive fields in spinal cord injured humans. *Clin Neurophysiol* 2004;115:2798-2810.