

INTRODUCTION

- The 2-point discrimination threshold (2PDT) can be used to probe the sensory integration.
- Studies have shown that the 2PDT may be modulated during experimental pain sensitization in acute pain [1] and in chronic pain [2] conditions.
- Normally the 2PDT is tested using innocuous mechanical stimuli, but little is known about how the 2PDT of different intensities and modalities during pain is modulated during sensitization.
- It is likewise unknown which combinations of pain intensities and modality are more suitable to investigate change in 2PDT following e.g. sensitization.

AIM

The aim of this study was to investigate how the 2PDTs of both noxious and innocuous stimuli of mechanical and thermal stimulation modalities are modulated by hyperalgesia evoked by topical capsaicin.

METHODS

- 18 healthy subjects (6 females) participated in this study. Subjects were randomly divided into two groups. Each subject participated in two sessions, 48 hrs apart.
- During each session the 2PDT was determined in the volar forearm for four different combinations of stimulation modality and noxiousness (thermal-innocuous, thermal-noxious, mechanical-innocuous and mechanical-noxious).
- The thermal stimuli was delivered using a CO₂ laser with an advanced scanner head [3], allowing stimulation of two points simultaneously. The stimulation temperature was adjusted to reach a skin temperature of 42.1±1.6°C for the innocuous thermal stimuli and 48.7±2.0°C for the noxious thermal stimuli. Beam diameter was 5 mm.
- The mechanical stimuli were delivered using two custom-made Vernier calipers with specialized probes (Fig. 1). For innocuous stimuli the probes were blunted plastic filaments (diameter 5mm), for noxious stimuli the probes were weight-loaded (60 gr) blunted needles (diameter 200µm).
- Stimuli were delivered with point-to-point distances from 0 to 120mm, steps of 10mm. 0mm correspond to a single point. All distances were delivered twice in randomized order, 0mm was delivered four times as control.
- After each stimulus the subject had to report the perceived number of points (1 or 2), and the perceived intensity on a NRS scale anchored as 0: no perception, 3: pain threshold, 10: maximum pain.

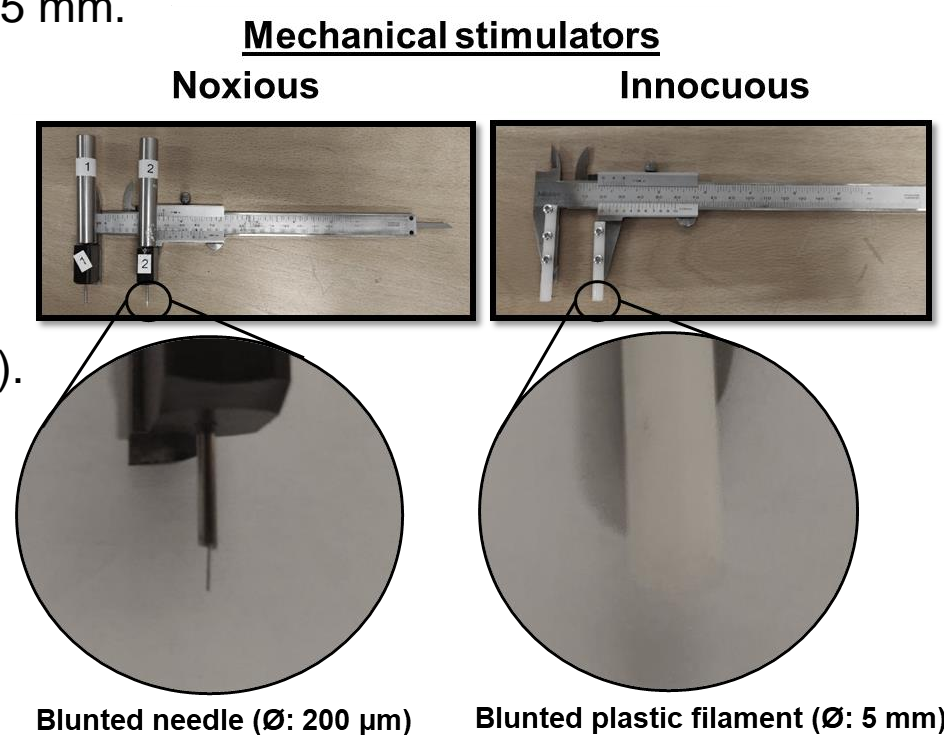


Figure 1. Mechanical stimulators. Left: noxious, right: innocuous

METHODS (CONT.)

- In session 2, one group had the skin in the stimulation area sensitized with topical capsaicin (8% Qutenza) for 30mins. The other group received placebo for 30mins. Subjects were blinded to use of either capsaicin or placebo. After capsaicin/placebo the skin was cleaned and the 2PDT was re-assessed.
- To find the 2PDT the data was fitted to a sigmoidal curve [3], for each fit the 95 % confidence interval (CI) was extracted as well.
- To analyze differences in the NRS data a 3-way ANOVA was used, with factors set as capsaicin/placebo, stimulation noxiousness and stimulation modality.
- The experiment was approved by the local ethical committee (VN-20190005). The declaration of Helsinki was respected.

RESULTS

Baseline results

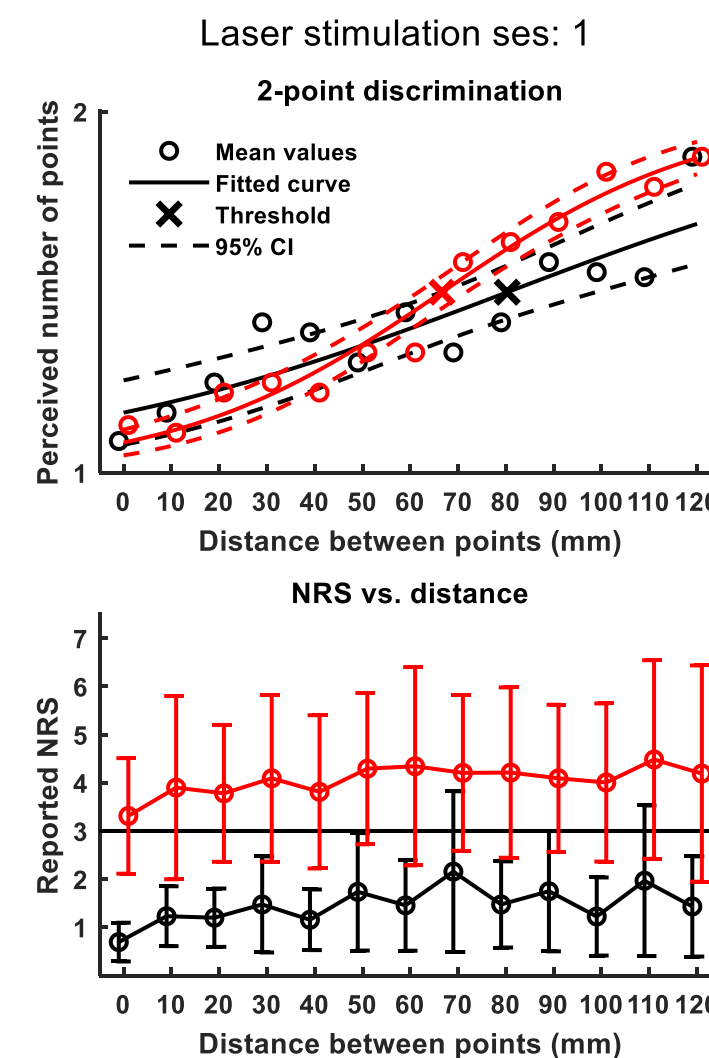


Figure 2. Thermal stimulation baseline. Top: 2PDT – bottom: NRS (mean±SD). Black: innocuous. Red: noxious.

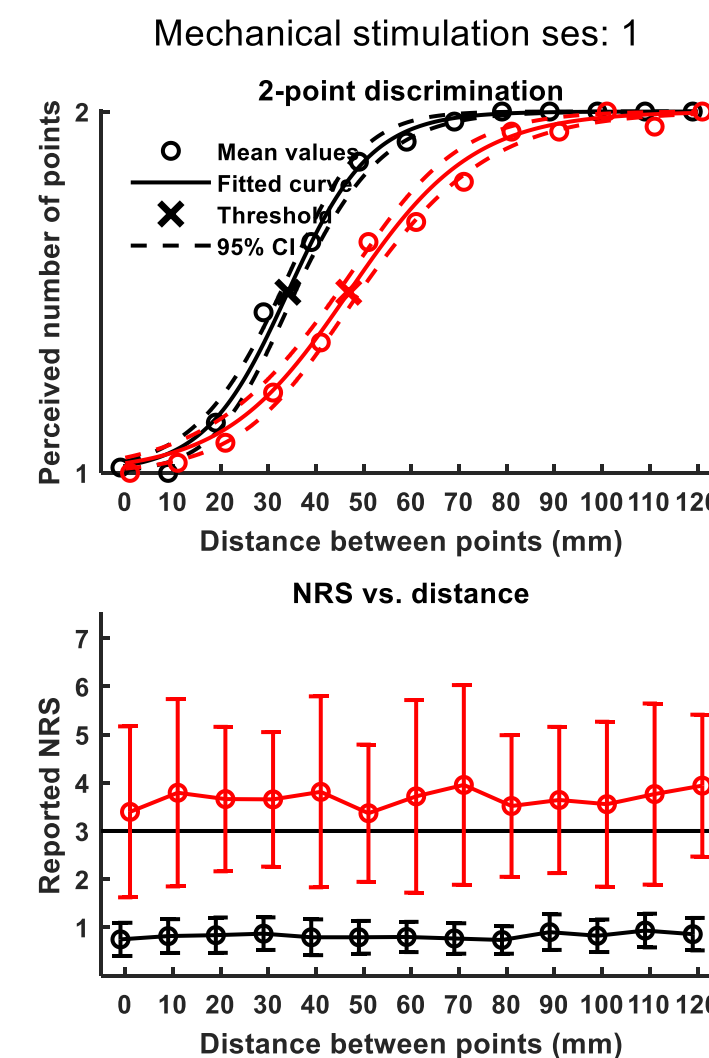


Figure 3. Mechanical stimulation baseline. Top: 2PDT – bottom: NRS (mean±SD). Black: innocuous. Red: noxious.

Table 1. Baseline 2PDT and 95 % CI for each combination of stimulation modality and noxiousness.

| | 2PDT (mm) | 95% CI (mm) |
|----------------------|-----------|-------------|
| Thermal innocuous | 80.3 | 65.5 - 95.1 |
| Thermal noxious | 66.6 | 61.7 - 71.6 |
| Mechanical innocuous | 34.1 | 32.6 - 35.6 |
| Mechanical noxious | 46.9 | 44.6 - 49.1 |

RESULTS (CONT.)

Post-capsaicin

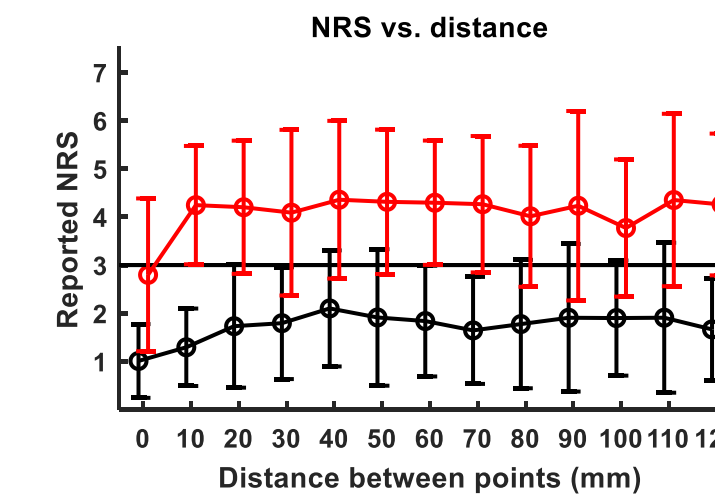
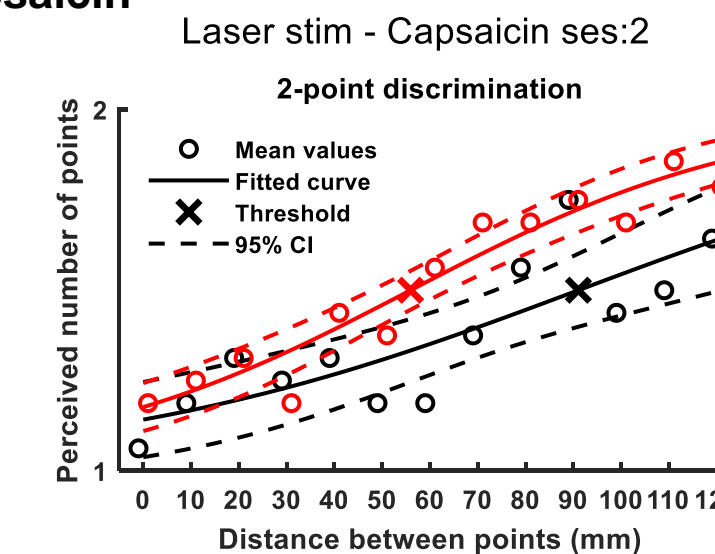


Figure 4. Thermal stimulation post-capsaicin. Top: 2PDT – bottom: NRS (mean±SD). Black: innocuous. Red: noxious.

Table 2. 2PDT and 95 % CI for each combination of stimulation modality and noxiousness following capsaicin or placebo.

| | Capsaicin | | Placebo (not depicted) | |
|----------------------|-----------|--------------|------------------------|--------------|
| | 2PDT (mm) | 95% CI (mm) | 2PDT (mm) | 95% CI (mm) |
| Thermal innocuous | 91.0 | 70.6 - 111.5 | 85.5 | 68.4 - 102.6 |
| Thermal noxious | 55.9 | 48.1 - 63.8 | 64.2 | 50.5 - 77.8 |
| Mechanical innocuous | 50.9 | 46.9 - 54.9 | 36.4 | 34.9 - 37.9 |
| Mechanical noxious | 63.0 | 56.6 - 69.5 | 48.5 | 42.2 - 54.9 |

- NRS was significantly higher after capsaicin compared to placebo (ANOVA, p<0.001). NRS was significantly higher for thermal stimuli (ANOVA, p<0.001). NRS was significantly higher for noxious stimuli (ANOVA, p<0.001).

CONCLUSIONS

- Topical capsaicin modulates the 2PDT across different stimulation modalities and noxiousness – placebo does not modulate the 2PDT.
- For innocuous and noxious mechanical stimuli capsaicin increased the 2PDT.
- For thermal stimuli the 2PDT increases slightly for innocuous stimuli, but the 2PDT decreases for noxious thermal stimuli.

REFERENCES

- [1] Kaupilla T, Mohammadian P, Nielsen J, Andersen OK, Arendt-nielsen L. Capsaicin-induced impairment of tactile spatial discrimination ability in man: indirect evidence for increased receptive fields in human nervous system. Brain Res. 1998 797:361–7.
- [2] Adamczyk WM, Luedtke K, Saulicz O, Saulicz E. Sensory dissociation in chronic low back pain: Two case reports. Physiother Theory Pract. 2018 34(8):643–51.
- [3] Frahm KS, Mørch CD, Andersen OK. Tempo-spatial discrimination is lower for noxious stimuli than for innocuous stimuli. Pain 2018. 30;159(2):393–401.