Pain Modulatory Capacity in Neuropathic Pain after Spinal Cord Injury

R. Lütolf [1], I. De Schoenmacker [1], J. Rosner [1,2], L. Sirucek [3], P. Schweinhardt [3], A. Curt [1], M. Hubli [1]

[1] Spinal Cord Injury Center, Balgrist University Hospital, University of Zurich, Zurich, Switzerland
[2] Department of Neurology, Inselspital, Bern University Hospital, University of Bern, Switzerland
[3] Integrative Spinal Research, Department of Chiropractic Medicine, Balgrist University Hospital, University of Zurich, Switzerland

Contact: robin.luetolf@balgrist.ch

INTRODUCTION

Deficient endogenous pain modulation is a key feature of central sensitization and can be assessed in humans by conditioned pain modulation (CPM). In subjects with neuropathic pain after spinal cord injury (SCI-NP), previous studies have shown either deficient or intact CPM capacity.[1-4]

OBJECTIVE

- To investigate the CPM capacity above the level of lesion in SCI-NP using a sham-controlled study design
- To explore the relationship between pain modulatory capacity and NP characteristics, e.g., intensity and spatial extent

METHODS

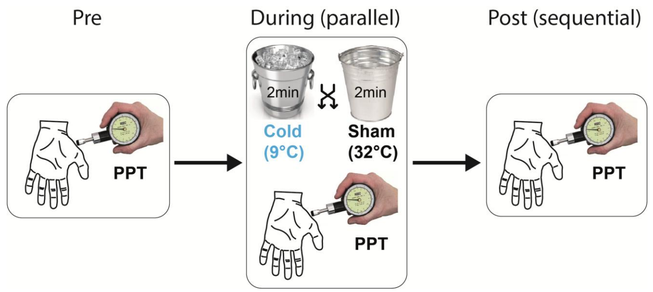

FIGURE 1: Pressure pain thresholds (PPT, test stimulus) were assessed on the thenar eminence before, during (parallel design) and after (sequential design) a 2-min immersion of the contralateral hand in a water bath (cold or sham). Subjects included SCI-NP (n=16) and HC (n=24). Readouts were normalized to the pre-assessment.

RESULTS – Conditioned Pain Modulation

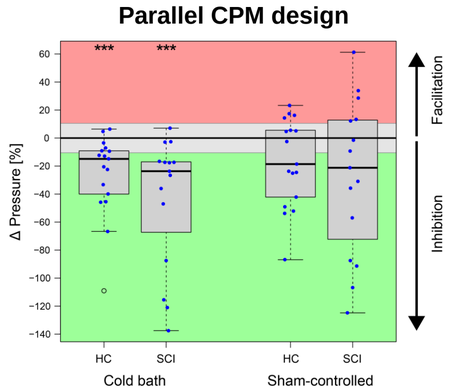

FIGURE 2: CPM effect on PPT **during** conditioning.
Clinically meaningful CPM effect beyond ±10% change (gray). Significant inhibitory effect during the cold bath for HC ($p<0.001$) and SCI-NP ($p<0.001$), but no group difference ($p=0.295$).
No significant CPM effect in the sham-controlled design for HC ($p=0.057$) and SCI-NP ($p=0.121$) and also no group difference ($p=0.655$).

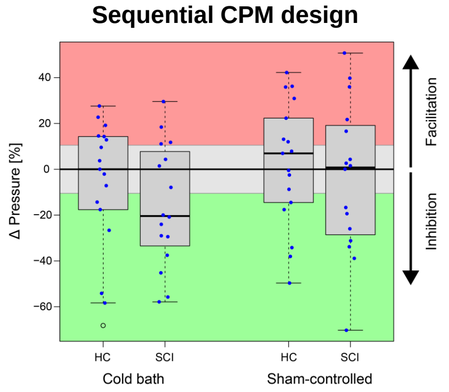

FIGURE 3: CPM effect on PPT **after** conditioning.
Clinically meaningful CPM effect beyond ±10% change (gray). The sequential CPM design resulted in no significant inhibition after the cold bath for HC ($p=0.660$) and SCI-NP ($p=0.051$).
No significant sham-controlled CPM effect in the HC ($p=0.747$) and SCI-NP ($p=0.798$). No differences between the groups ($p=0.606$).

RESULTS – Correlation with NP Characteristics

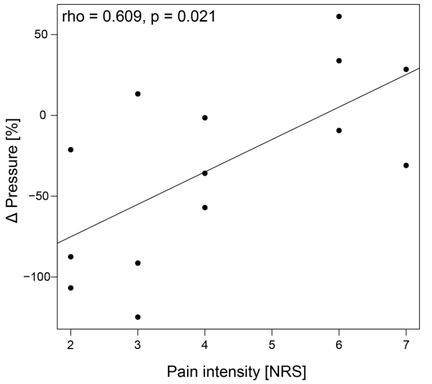

FIGURE 4: Correlation of the CPM effect with NP intensity. The sham-controlled CPM effect is presented as the change in PPT during the sequential CPM paradigm. Positive correlation of CPM magnitude with NP intensity was found. In contrast, no significant correlation of CPM magnitude with NP extent was seen (rho=-0.22, $p=0.427$).

CONCLUSIONS

- This study does not substantiate impaired descending inhibition in SCI with chronic neuropathic pain.
- However, we provided evidence that the intensity of NP matters with regard to the spectrum between pain inhibition and facilitation.
- Additionally, we highlighted the importance of a sophisticated CPM study design including a sham-controlled protocol.

OUTLOOK

Disentangling the processes of descending inhibition and neuronal hyperexcitability might improve pain modulation profiling and thereby facilitate mechanism-based treatment as well as patient stratification for clinical trials.

[1] Albu et al., 2015, Pain, Deficient conditioned pain modulation after spinal cord injury correlates with clinical spontaneous pain measures
[2] Gruener et al., 2016, Pain, Differential pain modulation properties in central neuropathic pain after spinal cord injury
[3] Gruener et al., 2020, Pain, Biomarkers for predicting central neuropathic pain occurrence and severity after spinal cord injury: results of a long-term longitudinal study
[4] Gagné et al., 2020, Neurorehabil Neural Repair, Conditioned pain modulation decreases over time in patients with neuropathic pain following a spinal cord injury

FNSNF Swiss National Science Foundation
University of Zurich[UZH]
Clinical Research Priority Program (CRPP)