MULTIPLE FAST-ACTING SUB-PERCEPTION THRESHOLD WAVEFORMS PROVE TO PRODUCE EFFICIENT PAIN RELIEF IN AN EXPERIMENTAL ANIMAL MODEL OF CHRONIC NEUROPATHIC PAIN

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Abstract

Spinal cord stimulation (SCS) is an established treatment for chronic neuropathic pain[1]. Besides paresthesia-inducing conventional (con) SCS, paresthesia-free SCS paradigms have also been developed. They exhibit a longer analgesia wash-in, which may complicate clinical programming[2]. In contrast, Fast-Acting-Sub-Perception-Therapy SCS (FAST-SCS) is a novel sub-perception paradigm that induces a rapid onset of analgesia[3]. We assessed 4 variations of FAST-SCS in a rat model of chronic neuropathic pain to evaluate the effect of stimulation amplitude (at 40 or 60% motor threshold (MT)) and the effect of active (FAST-A-SCS) or pseudo-passive (FAST-P-SCS) charge balance.

Neuropathic pain was introduced in adult rats (n=16) using the Seltzer model[4]. Paw withdrawal threshold (PWT) was measured at baseline and Post-Seltzer to confirm pain chronification. Chronic neuropathic rats were implanted with the SCS lead (+00- cathode-anode configuration) at the L4-L6 spinal level. A con-SCS (50Hz, 200µS pulse width, 67% MT) pre-screen session was performed on SCS day one to verify lead placement. Then, five different SCS paradigms (sham, FAST-A-SCS & FAST-P-SCS at 40%, 60% MT each) were assessed on separate days for 60 minutes each

in a blinded-randomized-crossover design. PWT was measured every 15 minutes, until 30 minutes post-SCS. Statistical analysis was performed using two-way repeated-measures ANOVA with Dunnet's post-hoc test.

Within rats, all SCS paradigms except sham produced significant ($p<0.05$) increases in PWT values at various time points during stimulation compared to pre-SCS values. Between paradigms, FAST-A-SCS at 40% and 60% MT, and FAST-P-SCS at 40%MT were non-inferior to con-SCS, whereas FAST-P-SCS at 60% MT did not significantly differ from sham-SCS.

The results show that the FAST paradigms at 40% or 60% MT, except FAST-P-SCS at 60% MT, are non-inferior to con-SCS at improving mechanical hypersensitivity in an animal model of chronic neuropathic pain, suggesting effects dependent on waveform recharge type and amplitude. In addition, compared to con-SCS, FAST-SCS paradigms show a delayed therapy washout effect, that was dependent on SCS frequency (50Hz vs. 90Hz). Follow-up experiments will aim at pre-clinical testing and evaluating the behavioral effect shortly after the start of SCS as related to mechanisms of action underlying the clinically reported rapid onset of analgesia.

References

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