Neuromodulation of pain by small fibre matrix stimulation in a human surrogate model using capsaicin

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BACKGROUND

Pain can be distressing, and its pharmacological management may be insufficient. Further strategies such as non-invasive neuromodulation using small fibre matrix stimulation seem promising in palliative care patients. However, mechanisms of action for this type of electrical stimulation and involved spinal cord projection pathways are unclear.

AIM

We used a human surrogate model for neuropathic pain known to induce central sensitization of dorsal horn nociceptive neurons (wide-dynamic-range neurons, WDR). We aimed to (1) show involvement of WDR neurons by reducing capsaicin-induced hyperalgesia after 4 Hz matrix stimulation, and (2) to determine a sham frequency to be used in future trials.

METHODS

We examined N=16 healthy human subjects after conditioning by intracutaneous injection of 50 µg capsaicin into the volar forearm, each at 4 Hz (test stimulus) and 40 Hz (control condition) matrix stimulation versus no stimulation using a single-blinded, balanced crossover design. Sensitivity to pin prick and light touch to the skin was tested by using quantitative sensory testing (QST) at different time points (10-180 minutes) to characterize mechanical hyperalgesia and allodynia. Statistical testing was done using ANOVA.

Forearm with matrix-electrode

Quantitative Sensory Testing Set for testing
(A) light touch and (B) pin prick

Reference: Mücke M, Cuhls H, Radbruch L, Weigl T, Rolke R. Evidence of Heterosynaptic LTD in the Human Nociceptive System: Superficial Skin Neuromodulation Using a Matrix Electrode Reduces Deep Pain Sensitivity. PLoS One 2014

RESULTS

Both 4 and 40 Hz matrix stimulation resulted in significant reduction of mechanical pain sensitivity (MPS) ($p < 0.001$) but not dynamic mechanical allodynia (DMA) compared to 'no stimulation'. Four Hz stimulation reduced mechanical pain sensitivity more than 40 Hz.

CONCLUSIONS

- (1) 4 Hz matrix stimulation was effective in reducing capsaicin-induced mechanical hyperalgesia. This finding is consistent with the concept of matrix neuromodulation turning down hyperexcitability of spinal cord WDR neurons. It may be used by palliative care patients in addition to standard analgesic regimens.
- (2) 40 Hz did not serve as an ideal sham stimulation. We suggest to use slightly higher frequencies when performing future RCTs.

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