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Thermode-Guided External Low Frequency Focused Ultrasound Modulation of Vincristine Induced Neuropathy

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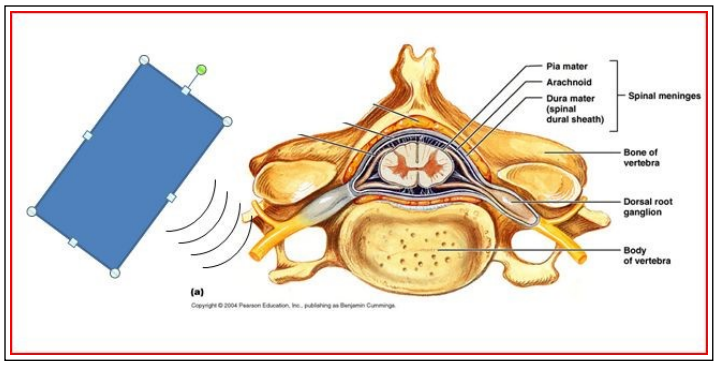
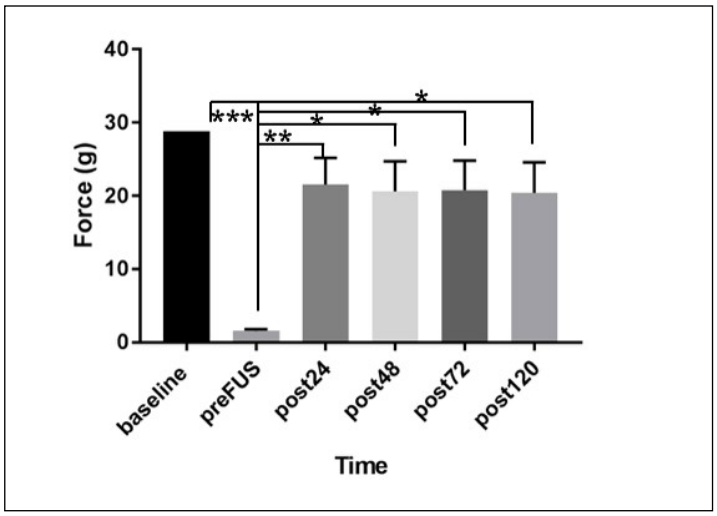


Introduction

Focused ultrasound (FUS) can modulate nervous tissue in a noninvasive format. FUS directly applied to the nerves alters mechanical thresholds in a number of rodent models of pain. Here we direct external FUS to the left L5 dorsal root ganglia using VEVO 3100 imaging guidance for targeting and using an internal thermode for therapy feedback.

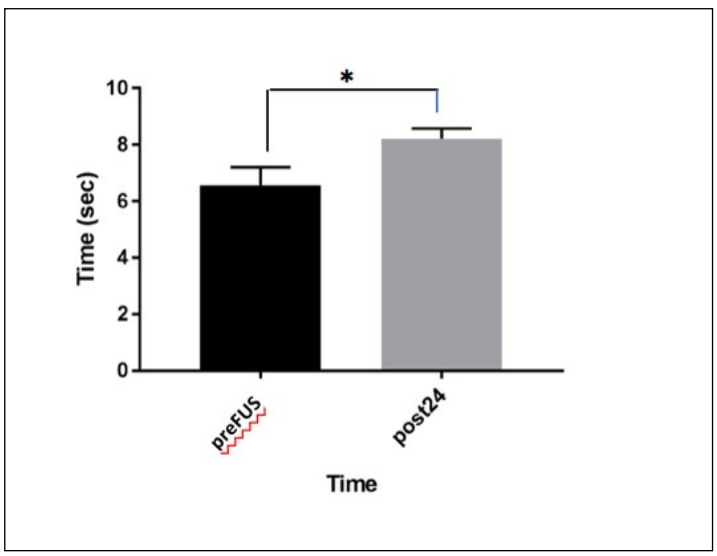
Methods

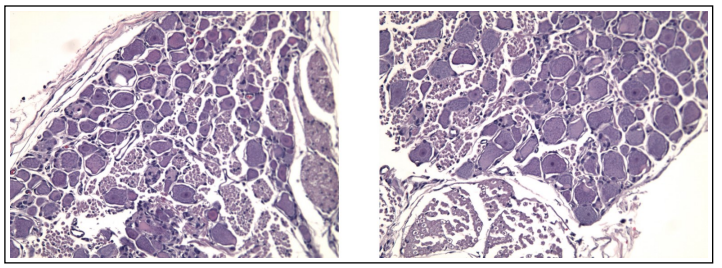
Sprague-Dawley rats were treated with intraperitoneal injections of vincristine (0.1mg/kg) to induce chemotherapy induced neuropathy. Once allodynia was induced, animals underwent general anesthesia and external FUS. The left L5 exiting nerve root (ENR) was visualized via ultrasound (VEVO 3100) and an internal thermode placed retroperitoneally to the L5 (ENR). 8W of pulsed FUS was delivered for three minutes at a frequency of 38 Hz and pulse width of 90µs. Post-procedure mechanical responses were measured using Von Frey filaments (VFF) and the Randell Selitto test (RST), and thermal thresholds via hot plate test (HPT) respectively. Open field testing (OFT) was used to ensure FUS treatment was not causing hind leg damage. Hematoxylin and eosin staining of the DRG was performed post mortem.



Results

FUS resulted in mean temperature rise of 2.73°C at the L5 DRG from a baseline of 28.5°C ± 0.68°C to 31.2°C ± 0.23°C.VFF, HPT, and RST all had significant differences 24 hours post FUS treatment (p = 0.02, p = 0.03, and p = 0.01 respectively). OFT indicated that animal movements were not hindered by FUS. There was no evident histological damage.





Conclusions

We demonstrate feasibility of delivering external FUS with direct visualization and thermal feedback. Our behavioral responses are consistent with those using internal FUS to the DRG. Future focus will be on developing external thermal monitoring to make this therapy completely non-invasive.

Learning Objectives

•To determine the thermal changes required for behavioral decreases to thermal and mechanical sensitivity

•To demonstrate feasibility of target visualization and thermal monitoring in an external model of FUS

•To create a method where the thermode can be placed internally while still performing external FUS treatment