

Pulse Modulation of the Occipital Nerve Using Focused High-intensity Ultrasound Improves Mechanical Thresholds in a Chronic Migraine Rat Model

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Introduction:

- Chronic migraines negatively impact the lives of 16.6% of adults
- Current treatments include steroids, occipital nerve block, radiofrequency therapy, or medical therapy
- 15% of patients remain refractory to treatment
- Therapeutic effects of high-intensity focused ultrasound (HIFU) on the occipital nerve remain unexplored

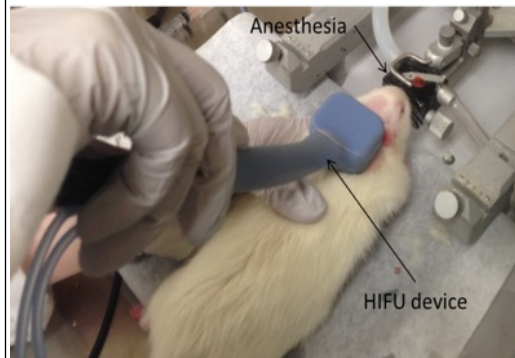
Study Objective: Explore the effects of ablative and pulsed HIFU on the occipital nerve of a rat model of mechanical allodynia secondary to chronic migraine

Learning Objectives:

1) Appreciate that mechanical thresholds are decreased by Chronic Migraine, and experience an increase following application of HIFU to the occipital nerve.

2) Discuss how both ablative and pulse modulated HIFU have resulted in increased mechanical thresholds.

HIFU application to rat occipital nerve



Methods:

Chronic Migraine (CM) model with mechanical allodynia:

- Male Sprague Dawley rats received inflammatory media via an epidural cannula over 3 weeks to induce a CM state.

HIFU application area:

- skin over occipital nerves

HIFU settings:

- pulse modulation of occipital nerve
- ablation of occipital nerve

Mechanical threshold testing:

- Mechanical thresholds assessed using vonFrey filaments
- Tests were done during peak headache, immediately after HIFU, 24h post-HIFU, and 48h post-HIFU
- Areas tested: forepaw, hind paw and peri-orbital regions.
- Mechanical thresholds obtained also compared to CM rats receiving electrical occipital nerve stimulation (ONS) (n=9) in a prior study.

External HIFU probe



Results:

- Occipital nerve ablation increased forepaw and periorbital thresholds (Figure 1)
- Pulse modulation of occipital nerve increased forepaw thresholds immediately following and 24h after HIFU treatment (Figure 2)
- Pulse modulation may produce similar results to ablative HIFU or ONS (Figure 3)

Ablative HIFU 24h after treatment

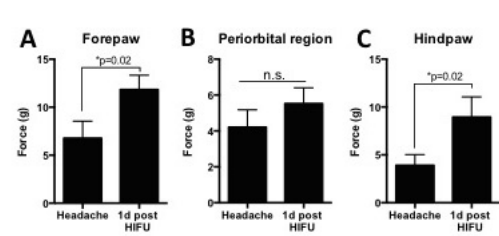


Figure 1. Ablative HIFU increases mechanical thresholds in the paws of CM rats. Significant increases in mechanical thresholds were found 24h after ablative HIFU treatment in the forepaw (p=0.02) and hindpaw (p=0.02) of CM rats (n=9). No significant changes occurred in the periorbital mechanical thresholds following this treatment. Paired t-tests, data represented as mean and SEM.

Pulsed HIFU 24h after treatment

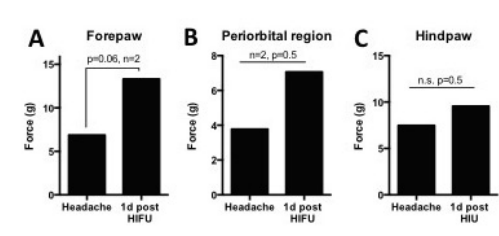


Figure 2. Pulsed HIFU treatment increases mechanical thresholds in the paws of CM rats. Paired t-tests, data represented as mean (n=2).

Occipital Nerve versus HIFU therapy

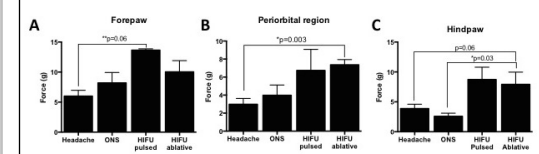


Figure 3. Mechanical threshold changes immediately following the application of ONS, pulsed HIFU or ablative HIFU. (A) Mechanical thresholds tended to increase immediately following pulsed HIFU treatment in the forepaw region (p=0.06, n=3). In the periorbital region (B), ablative HIFU treatment significantly increased mechanical thresholds (n=9, p=0.003). In the hindpaw, mechanical thresholds trended towards an increase following ablative HIFU treatment (p=0.06, n=9). Headache data includes animal data from 9 ablative, 3 pulsed and 9 ONS animals (n=21). One-way ANOVA, tukey post hoc comparison, data represented as mean and SEM.

Conclusions

Our results suggest that HIFU may be an effective noninvasive treatment for refractory CM. Furthermore, using pulse modulation instead of ablative settings, mechanical thresholds can be improved without causing damage to the occipital nerves, avoiding the aversive side effects of ablation. Future studies should address whether this noninvasive treatment is ideal and reliably effective for medically refractory CM patients.

References

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