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# Sonication of the Anterior Thalamus with MRI-Guided Low Intensity Focused Ultrasound Pulsation (LIFUP) Changes Pain Thresholds in Healthy Adults: A Double-Blind, Concurrent LIFUP/MRI Study

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## Abstract

Background: Low Intensity Focused Ultrasound Pulsation (LIFUP) is a noninvasive brain stimulation method that may modulate deep brain structures using ultrasonic waves. Presently there are limited studies in humans rigorously assessing behavioral effects following LIFUP sonication of deep brain nuclei. As an initial test, we investigated whether sonication of the anterior thalamus, a central relay structure of nociception, would modulate thermal pain thresholds in healthy individuals. Methods: We enrolled 19 healthy individuals in this three-visit, double-blind, randomized, sham-controlled, crossover trial. Participants attended a first MRI screening visit to acquire anatomical scans for LIFUP targeting. They then attended two identical experimental LIFUP/MRI visits (counterbalanced by condition) at least one-week apart. Within the MRI scanner, participants received two, 10-minute sessions of either active or sham LIFUP spread 10 minutes apart to the right anterior thalamus [Fundamental frequency:650khz,

pulse repetition frequency: 10 HZ, Pulse Width: 5ms, Duty Cycle: 5%, Sonication Duration: 30s, Inter-Sonication Interval: 30 s, Number of Sonications: 10, ISPTA.3 719 mW/cm<sup>2</sup>]. Each 10-minute session was delivered in a block design (30s ON, 30s OFF). The primary outcome measure was quantitative sensory thresholding (QST), measuring sensory, pain, and tolerance thresholds to a thermal stimulus applied to the left forearm before and after LIFUP. Thermal stimuli were also applied in the scanner during certain blocks, either alone, or during LIFUP. Results: Two 10-minute sessions of thalamic LIFUP produced a significant antinociceptive effect on pain thresholds. Temperature sensitivity increases were significantly attenuated (timeXcondition  $p=0.046$ ) after active LIFUP (0.51 degree change) relative to sham stimulation (1.08 degrees). LIFUP also changed sensory and tolerance thresholds mathematically but this was not statistically significant with this sample. LIFUP delivered concurrently with thermal pain had no immediate behavioral effect. Conclusions: Two, 10-minute sessions of anterior thalamic LIFUP has antinociceptive effects in healthy individuals. Future studies should optimize the parameter space and dose and perhaps investigate multi-session LIFUP interventions for pain disorders.

### **Competing Interest Statement**

Conflict of Interest Statement: AB is employed by BrainSonix, which manufactures the ultrasound device. He holds patents in this area. BWB owns minority stake in Bodhi NeuroTech Inc, which manufactures meditation enhancing devices and holds patents in this area. No other authors have any other conflicts.

### **Clinical Trial**

ClinicalTrials.Gov NCT# 04339972

### **Funding Statement**

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### **Author Declarations**

All relevant ethical guidelines have been followed; any necessary IRB and/or ethics committee approvals have been obtained and details of the IRB/oversight body are included in the manuscript.

Yes

All necessary patient/participant consent has been obtained and the appropriate institutional forms have been archived.

Yes

I understand that all clinical trials and any other prospective interventional studies must be registered with an ICMJE-approved registry, such as ClinicalTrials.gov. I confirm that any such study reported in the manuscript has been registered and the trial registration ID is provided (note: if posting a prospective study registered retrospectively, please provide a statement in the trial ID field explaining why the study was not registered in advance).

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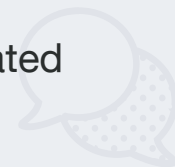
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