USING TRANSCRANIAL FOCUSED ULTRASOUND (TFUS) TO ALTER DEFAULT MODE NETWORK (DMN) FUNCTIONAL CONNECTIVITY AND SUBJECTIVE EXPERIENCE

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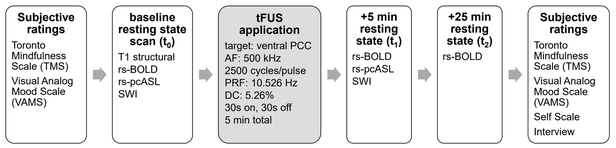
Introduction

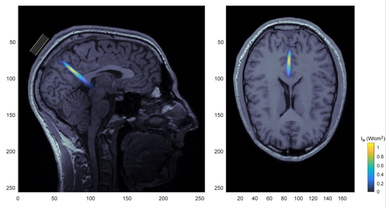
The default mode network (DMN), initially defined by Raichle and colleagues[1], comprises key midline nodes at the medial prefrontal cortex (mPFC) and the posterior cingulate cortex (PCC), along with adjacent bilateral nodes. It plays a crucial role in mind-wandering, narrative formation, and self-related processing[2]. Dysregulation of the DMN has been linked to disorders like depression, addiction, autism, ADHD, and schizophrenia, suggesting neuromodulation of it as a potential therapeutic modality. Disruption of DMN activity has been implicated as playing a central role in the effects of psychedelics[3]. Meditation can also modulate DMN activity, with PCC deactivation associated with equanimity[4]. Non-invasive brain stimulation methods that can target DMN nodes offer a way to study the causal relationship between DMN activity and internal processes. Transcranial focused ultrasound (tFUS) emerges as a promising technique due to its ability to reach subcortical brain regions with millimeter precision[5]. This study aims to use tFUS to target the PCC with a low duty cycle to inhibit DMN connectivity and explore changes in phenomenology related to mindfulness and self-related processing. This is meant as a proof-of-principle that tFUS can act as a tool for network probing and therapeutic interventions.

Methods

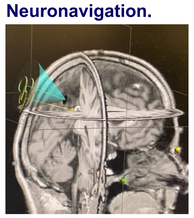
Procedure.



Acoustic Intensity Model.



Neuronavigation.



Acoustic Intensity	Free water	Skull
I_{SPPA}	5.98 W/cm^2	0.46 W/cm^2
I_{SPTA}	293.37 mW/cm^2	23.98 mW/cm2

Subjects. Thirty healthy subjects (18 female, average age 19.8 years) participated in this study.

Procedure. During MRI scans, subjects were instructed to stare at a fixation cross and allow their thoughts to flow naturally. Subjects received either active or sham tFUS to their ventral PCC in a single-blind, randomized design.

TFUS Administration. The focused ultrasound was delivered by a custom 4-channel ring transducer (Sonic Concepts, Bothell, WA, USA) with an outer diameter of 64 mm that uses a sealed membrane filled with degassed water for coupling, which is then housed inside a custom 3D-printed casing. The transducer was driven by an acoustic amplifier (TPO-203, Sonic Concepts, Bothell, WA, USA). An MRI-guided stereotactic system (Visor2, ANT Neuro, the Netherlands) was used to guide tFUS targeting to the participant's PCC.

Acoustic Intensity Measurements. Acoustic intensity was measured in a custom-built water tank using a 2.5 mm diameter needle hydrophone (HNR-0500; Onda, Sunnyvale, CA, USA) across a 12x12x68 mm scan volume. Wave output was measured in free water and through a hydrated sample of cadaver parietal bone.

Statistical Tests. Due to small sample sizes (n=15 for each condition) and skewed results in many test questions, we used non-Wilcoxon rank sum tests and linear mixed models to analyze the psychometric scales.

MRI Analysis. MRI images were preprocessed using Matlab, SPM12, and the Conn software package. A gradient-weighted Markov Random Field (gwMRF) 100-area parcellation[6] was used to predefine ROIs. A contrast that averages together both post-stimulation conditions to compare against baseline [baseline (-1) vs. t1 (1/2) vs. t2 (1/2)] was designed to fit a general model of the effects of tFUS for the active and sham group. A full ROI-to-ROI connection matrix was calculated based on spatial pairwise clustering statistics.

Results

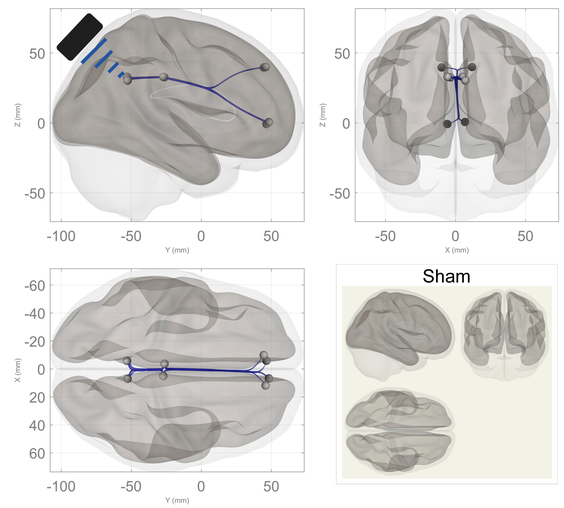
BOLD Functional Connectivity. A global ROI-to-ROI analysis showed that reductions in functional connectivity occurred in the active tFUS group across hemispheres in the cingulate cortex, and the medial and dorsolateral prefrontal cortex reduced in connectivity with the posterior cingulate. No significant effects were found in the sham group. (See figure 1 – Reductions shown in blue.)

Toronto Mindfulness Scale. Significant increases from pre to post tFUS occurred in both active and sham groups, though the effect size was much higher in the active group. (See figure 2)

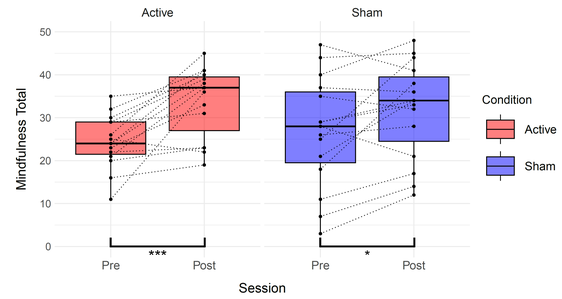
Visual Analog Mood Scale. A significant decrease in Global Vigor was detected in the active group only, with no other changes detected. (See figure 3)

Self Scale. Significant differences were detected in questions pertaining to the sense of ego, sense of time, and seeing events from the past. (See figure 4)

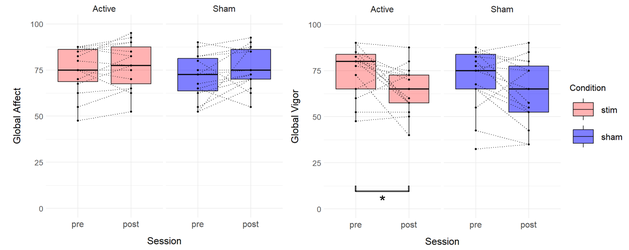
1. BOLD Functional Connectivity



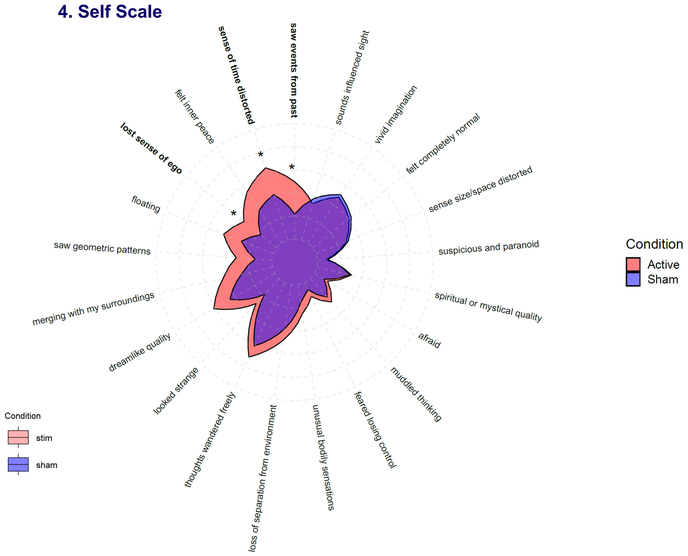
2. Toronto Mindfulness Scale



3. Visual Analog Mood Scale



4. Self Scale



Conclusions

This study shows that tFUS targeted at the PCC can disrupt DMN activity and cause mindfulness-increasing subjective effects. Given these effects, tFUS may serve as a therapeutic tool for treating network dysfunction. Future research should replicate these effects with a larger sample size, more precise targeting methods, and tFUS intensities matching previous human and animal studies. Future research may also investigate what ultrasound parameters, targeting, and modeling methods are optimal for neuromodulation.

References

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