

Transcranial Ultrasound Improves Mood and Affects Resting State Functional Connectivity in Healthy Volunteers

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Introduction

- Transcranial ultrasound (TUS) modulates brain function [1, 2, 3] and behavior [4, 5].
- In double blind, placebo controlled trials, we showed that TUS to the right inferior frontal gyrus (rIFG) improved mood [6, 7].
- rIFG: Involved in cognitive control and emotion processing [8]; implicated among a dysfunctional network in mood disorders [9].
- Resting-state fMRI network connectivity changes were investigated here to elucidate how TUS to rIFG enhances mood.
- Prediction: TUS to the rIFG would alter connectivity in cognitive control, default mode, and affective networks.

Methods

Procedure

- Mood scales (VAMS) and resting state fMRI was recorded at baseline (N = 9).
- Focused TUS was delivered to the rIFG for 2 minutes outside the scanner; mood scales were administered.
- Mood scales and resting state fMRI was recorded again 25 minutes later
- All participants received active TUS.

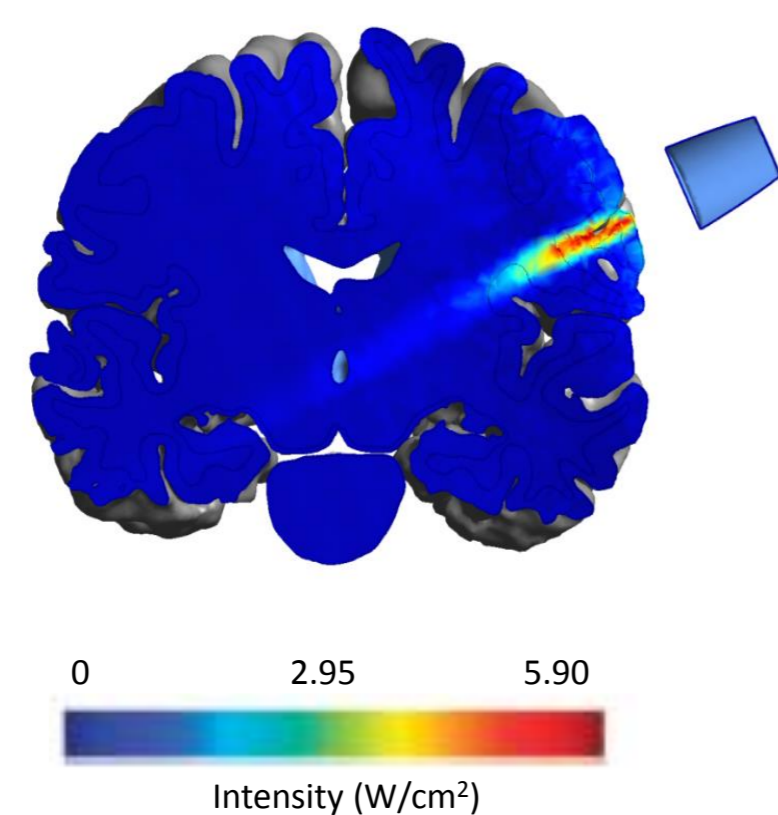
TUS Device and Waveform

- Focused ultrasound (U+, Thync, Inc.)
- 30mm focal length, 4mm focal area (FEM model, pictured right)
- 500 kHz, 40 Hz PRF, $I_{spta} = 272 \text{ mW/cm}^2$



fMRI Analysis

- Siemens SKYRA 3T MRI
- CONN Toolbox, SPM12, MATLAB
- Seed-to-voxel analysis
- Threshold: voxel-wise $p < .005$ (uncorrected), cluster-level $p < .05$ (FDR-corrected)



Seeds Regions

- Cognitive Control (IFG, DLPFC, ACC); Increased connectivity predicted (decreased in mood disorders [9])
- Default Mode (PCC, MPFC); Decreased connectivity predicted (increased in mood disorders [9])
- Affective/Reward (Subgenual, nACC, PaHC, Amygdala, Insula); decreased connectivity predicted (increased in mood disorders [9]).



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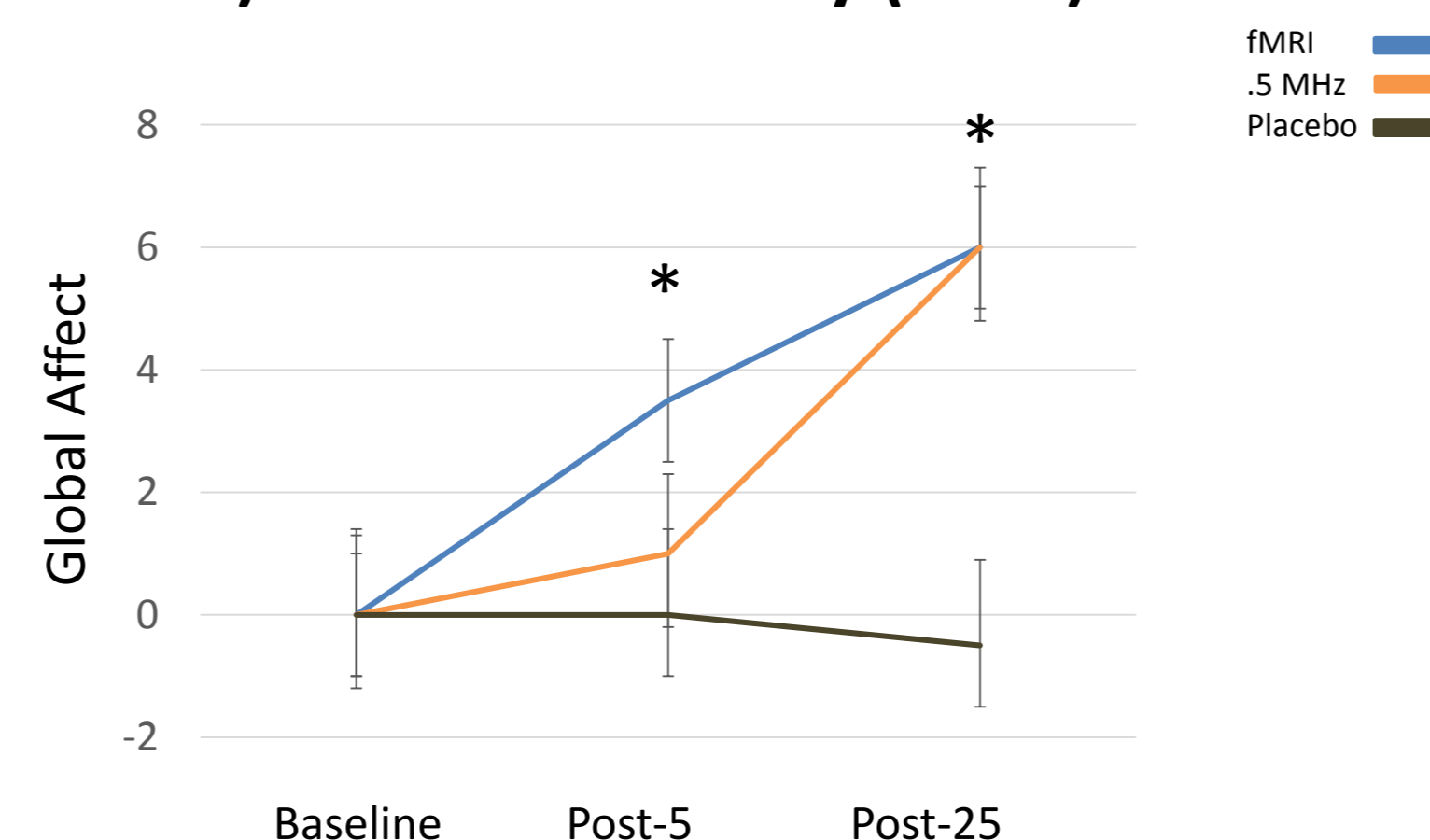
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Results Behavioral

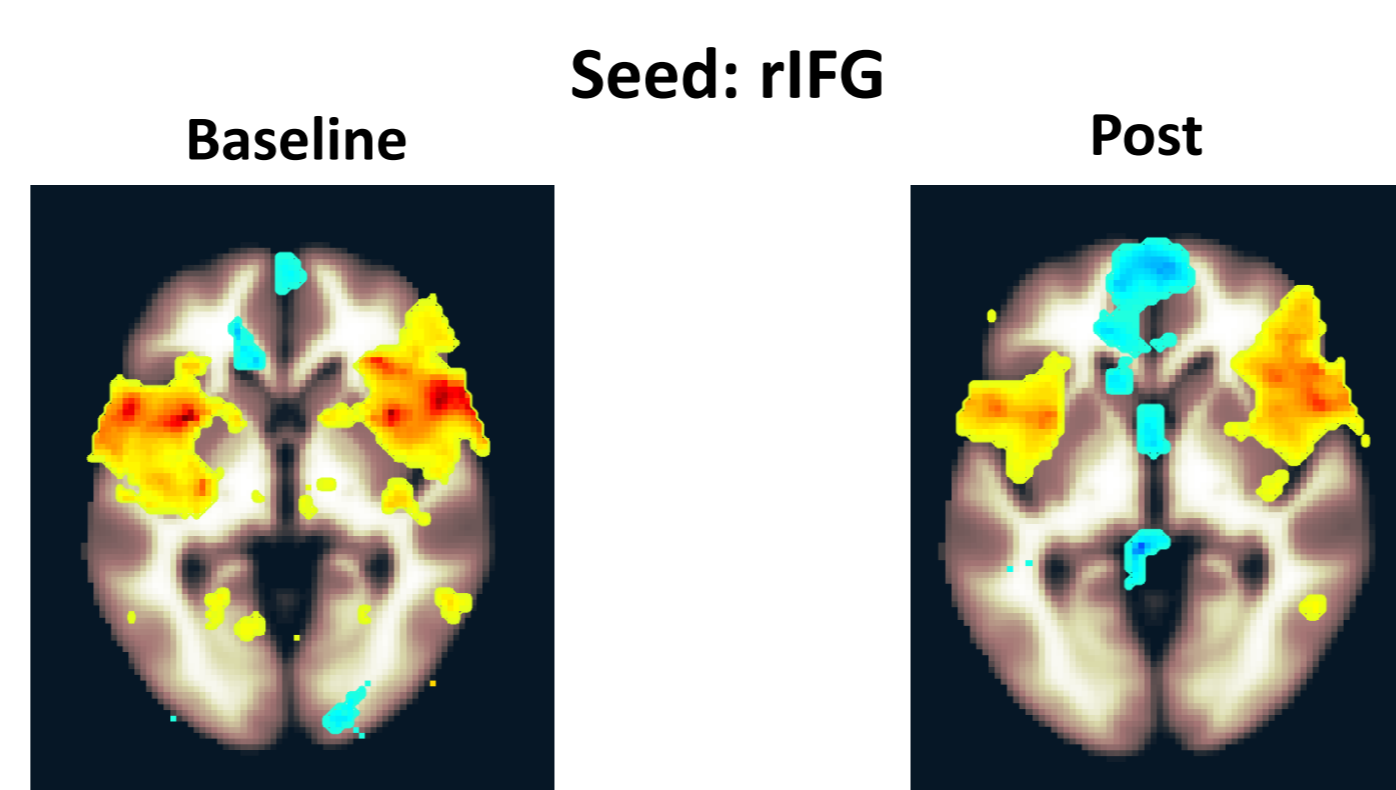
Global Affect in prior study (.5 MHz vs Placebo) and current study (fMRI)



- Behavioral replication: Participants reported enhanced affect (an increase on the scale).
- Note: There was **no** placebo control in the fMRI pilot; data for .5 KHz and Placebo are from a behavioral study and are superimposed for display purposes.

Results fMRI Connectivity

Cognitive Control Network

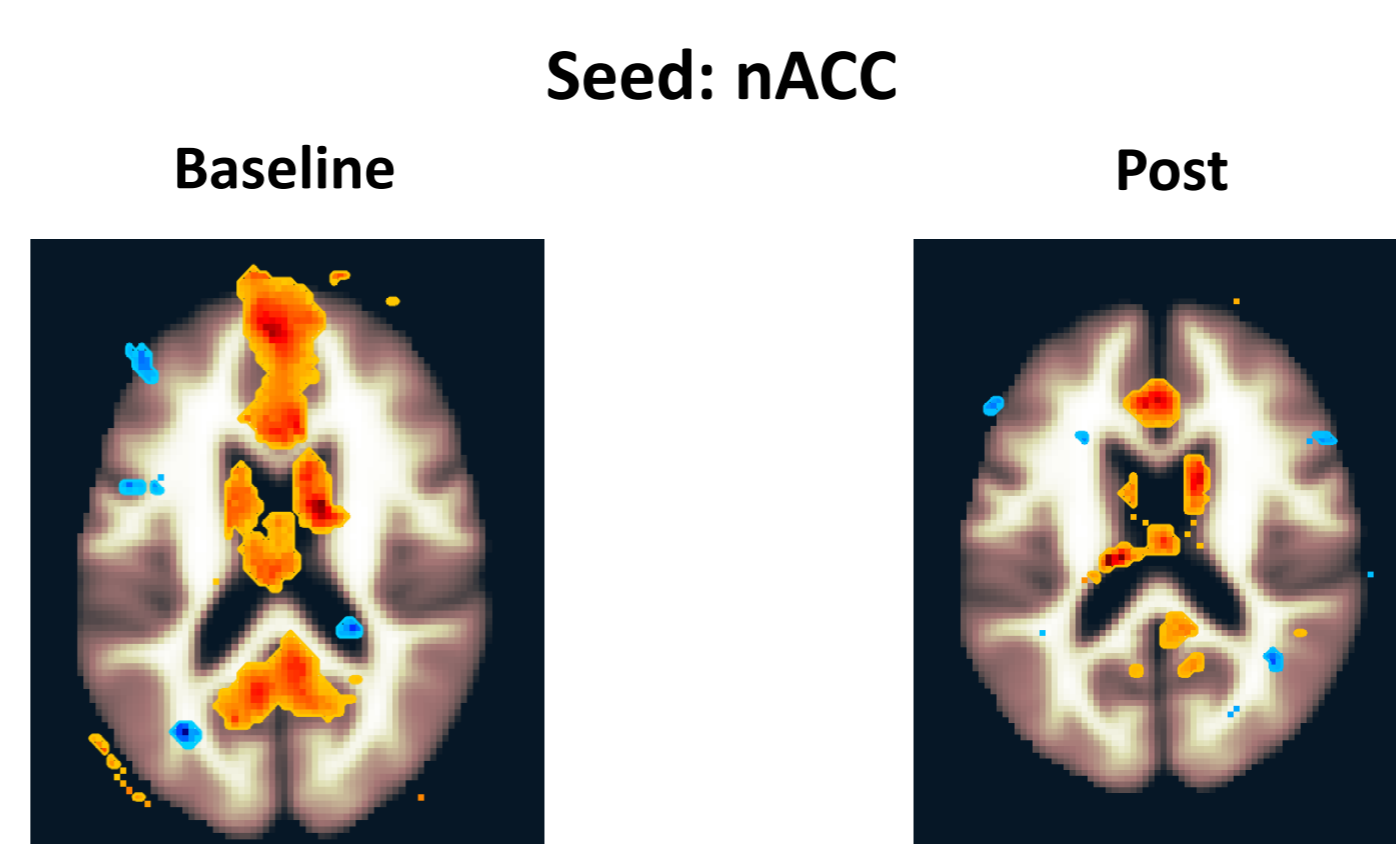


- Enhanced connectivity between cognitive control regions; decreased connectivity between frontal and affective/reward areas.

Seed	Increased Connectivity	Decreased Connectivity
R IFG (pars opercularis)	Middle & Superior FG R (0.000625)	Subcallosal, F Orbital L, nACC L, F Medial, Temp Pole L, Putamen L, Caudate L, nACC L (0.00005)
L DLPFC	Middle Frontal G R, Sup Frontal G R, Supramarginal G R, Angular Gyrus R, Parietal Lobe R (0.00046)	Intracalcarine C R, Lingual Gyrus R L, Lat Occipital, Cuneal Cortex R, Parahipp R, Temp Occipital (0.00046)
R DLPFC		Postcentral Gyrus Right (0.0036)
L ACC		Frontal Pole R, Superior FG R, Intracalcarine (0.000025)

Note: Values in parentheses reflect cluster p-val (<.05 FDR)

Affective/Reward Network



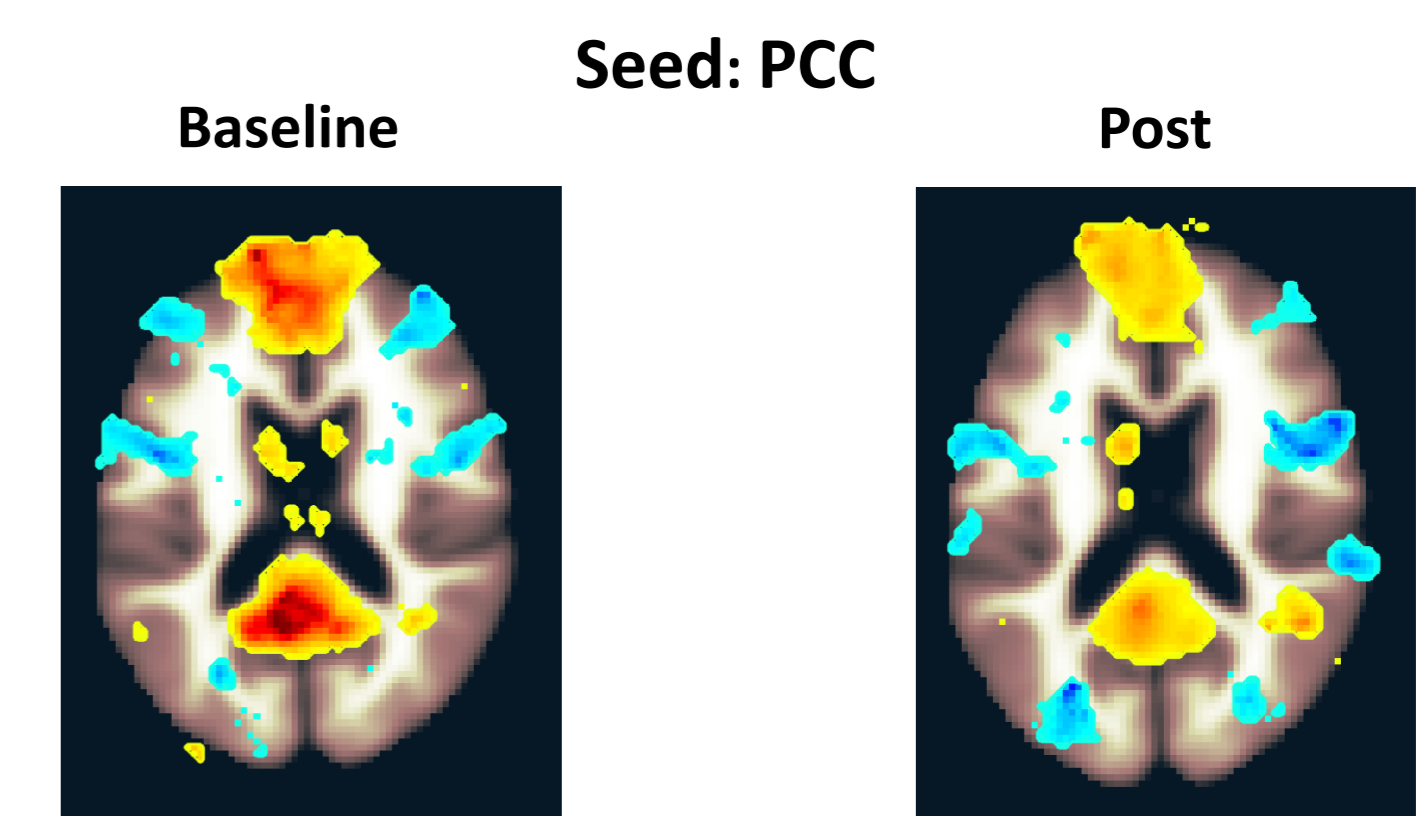
- Decreased connectivity in networks related to emotion processing, appraisal, perception, and reward.

Seed	Increased Connectivity	Decreased Connectivity
R nACC		Frontal Pole L R, S Frontal G, Paracingulate, Middle Temp G L R, Superior Temp G, Frontal Orbital, IFG R (0.000009)
Parahippocampal Gyrus Right		Caudate, Putamen, Pallidum (0.000054)
Insula		Superior Parietal R, Poscentral G R (0.015012)
L Subgenual		Supramarginal G R, Angular G R, IFG R, Frontal Operculum R (0.00068)

Note: Values in parentheses reflect cluster p-val (<.05 FDR)

Results fMRI Connectivity

Default Mode Network



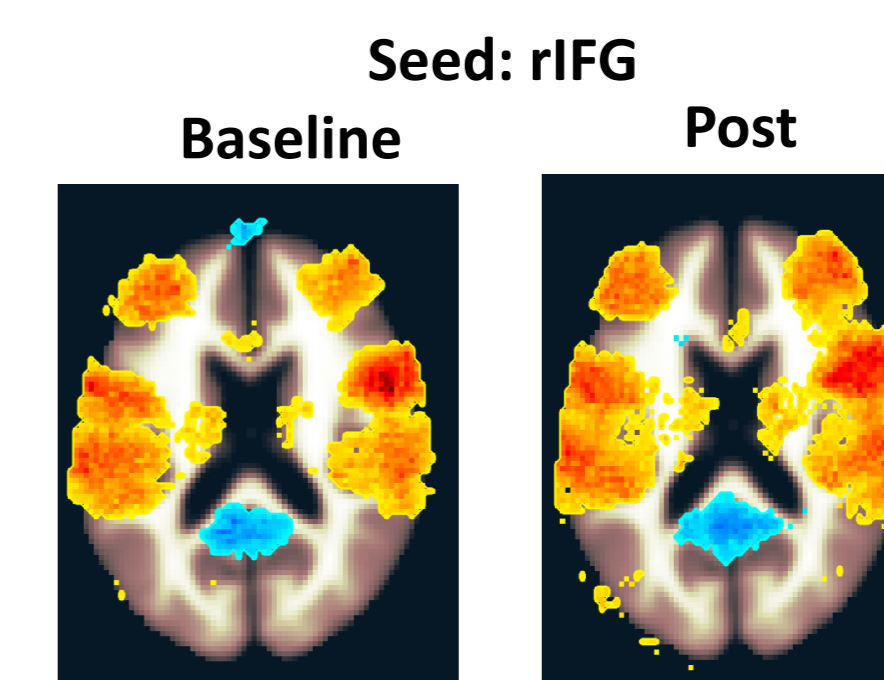
- General decreased connectivity within default mode network.

Seed	Increased Connectivity	Decreased Connectivity
PCC		Lingual Gyrus R, Fusiform R, Parahippocampal, HC R, Cer 3 R, Cer 45 R, LOC (0.001752)
MPFC	Planum Temporale R Heschl's G R, Central Opercular, Superior Temporal R (0.008094)	Juxtapositional Lobule, Superior Frontal Gyrus R L, Paracingulate Gyrus L (0.004496)

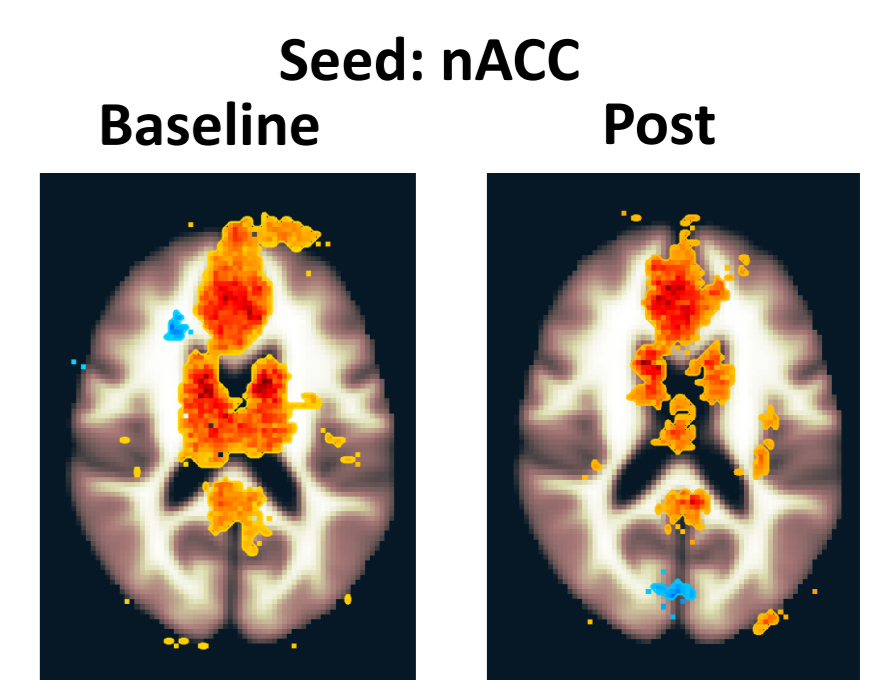
Note: Values in parentheses reflect cluster p-val (<.05 FDR)

fMRI Non-TUS Control

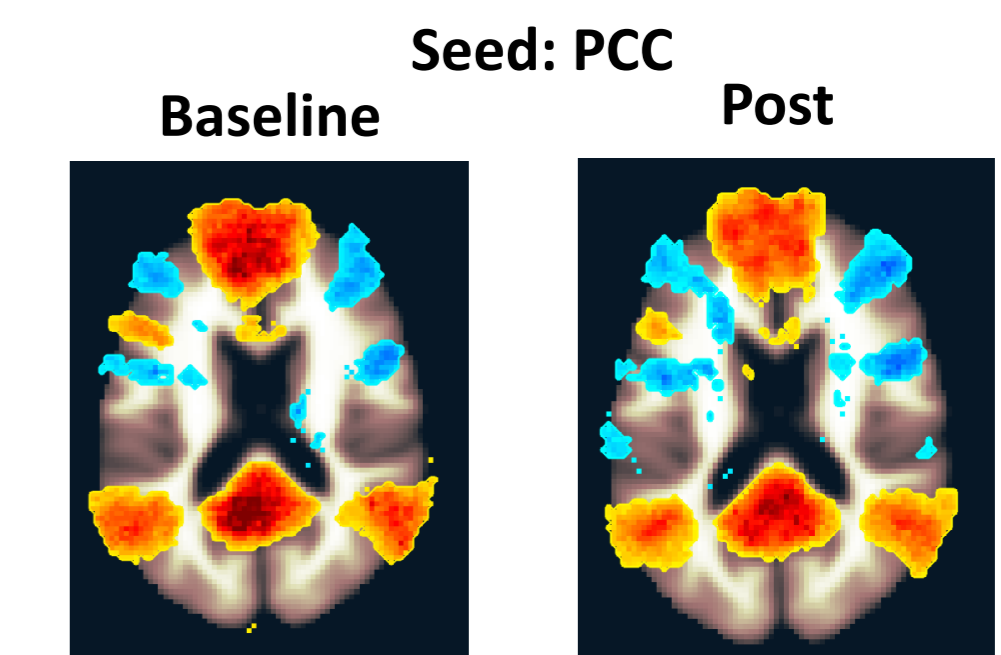
Cognitive Control



Affective/Reward



Default Mode Network



- Pre and post resting-state fMRI from a previous non-TUS experiment. "Post" = 25 minutes after baseline, following an emotion dot-probe task; participants stayed in scanner.
- Very few changes in connectivity, and the minor connectivity changes do not replicate the main experiment.

Discussion

- Altered resting state connectivity:
 - Cognitive Control Network (generally increased)
 - Affective/Reward Network (generally decreased)
 - Default Mode Network (decreased)
- TUS to rIFG may create positive mood effects by enhancing emotion regulation and decreasing perseverative thinking.
- TUS could be used to modulate mood in healthy and clinical populations (see poster: P2-162).

References

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