The Sound of the Future? An Introduction to Low Intensity Focused Ultrasound

Clinical Updates in Neurotherapeutics

ASCP May 2025

BROWN
Alpert Medical School

Noah S. Philip MD
Professor of Psychiatry and Human Behavior
Alpert Medical School of Brown University, Providence RI, USA

Lead, Mental Health Research
Center for Neurorestoration and Neurotechnology, VA Providence

CENTER FOR NEURORESTORATION & NEUROTECHNOLOGY

Disclosures

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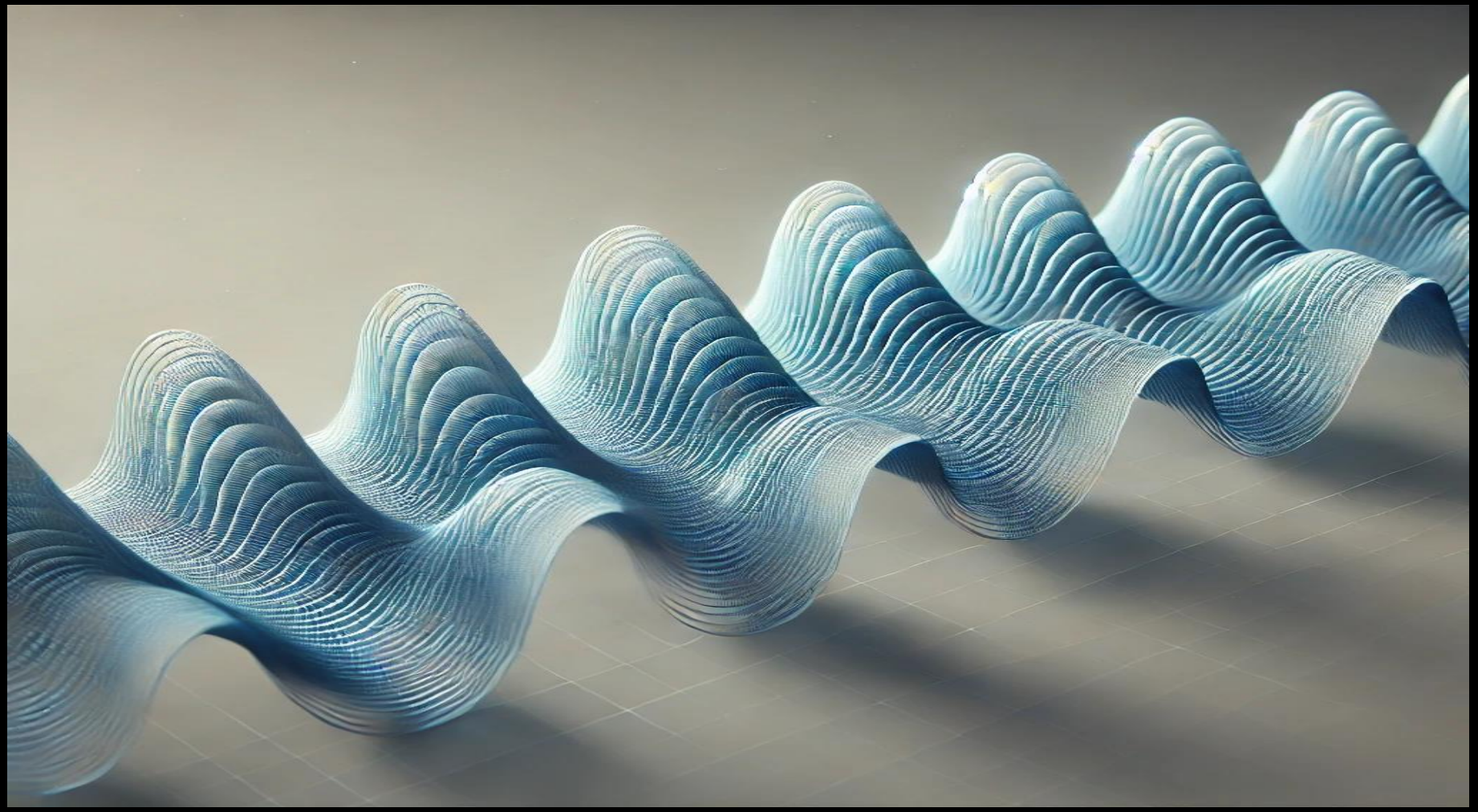
- US Dept of Veterans Affair (employment), NIMH, NIGMS, NIDA, DoD, Focused Ultrasound Foundation, BBRF/NARSAD; Scientific Advisory Board for Pulvinar, Consultant for Motif Neurotech

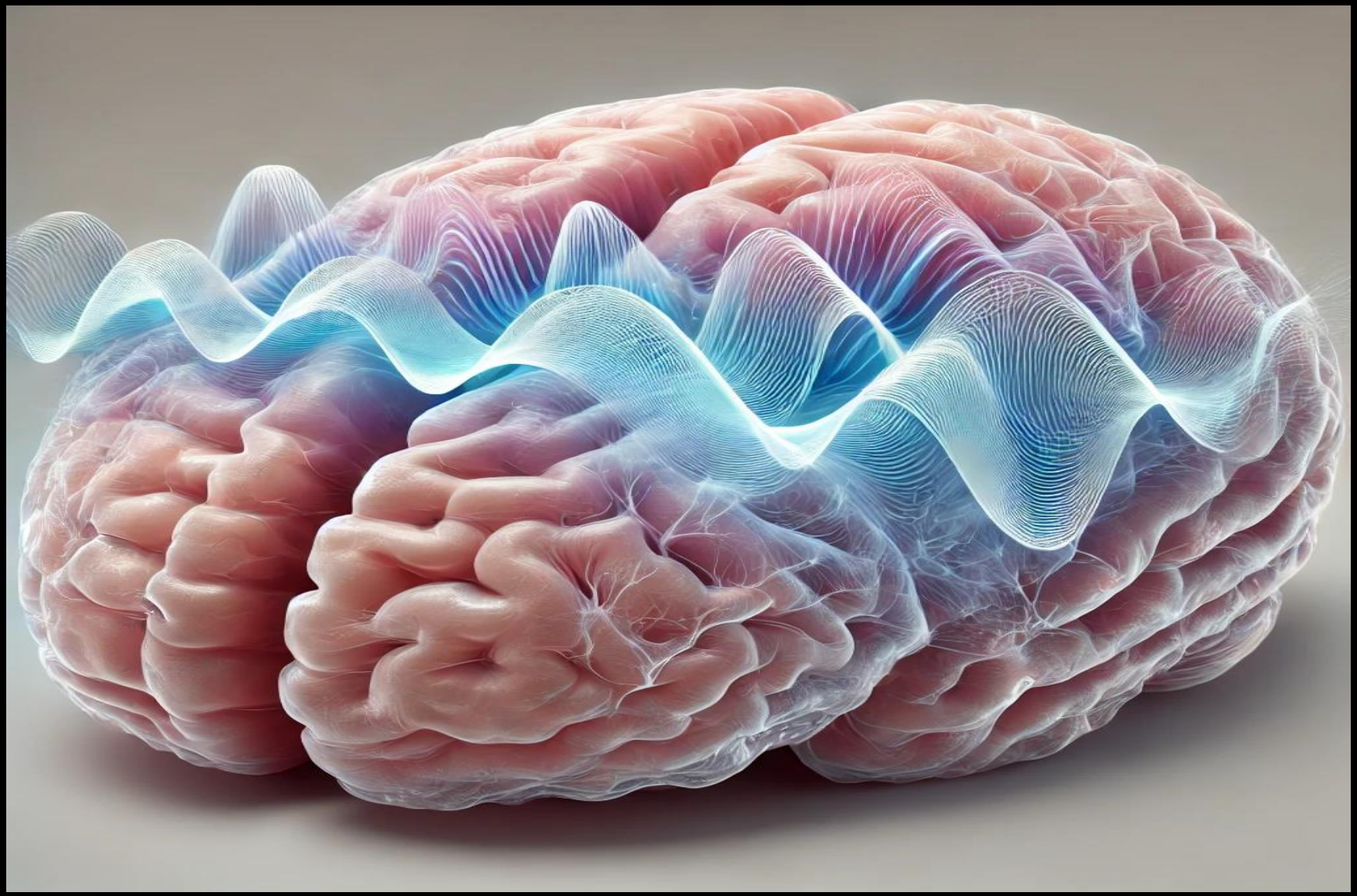
No commercial salary support, stocks, honoraria, or other material interests

Investigational use will be discussed (Ultrasound)

Opinions own & do not represent funders or employers

| Introduction to Low Intensity Focused Ultrasound |
| Recent Work – Low Intensity Focused Ultrasound in Psychiatry |
| Sneak Peak – Low Intensity Focused Ultrasound to Amygdala in Depression |
| Concluding Thoughts |





Wiliam Fry credited to ~1950, from O'Brien & Dunn; *Physics Today* 2015

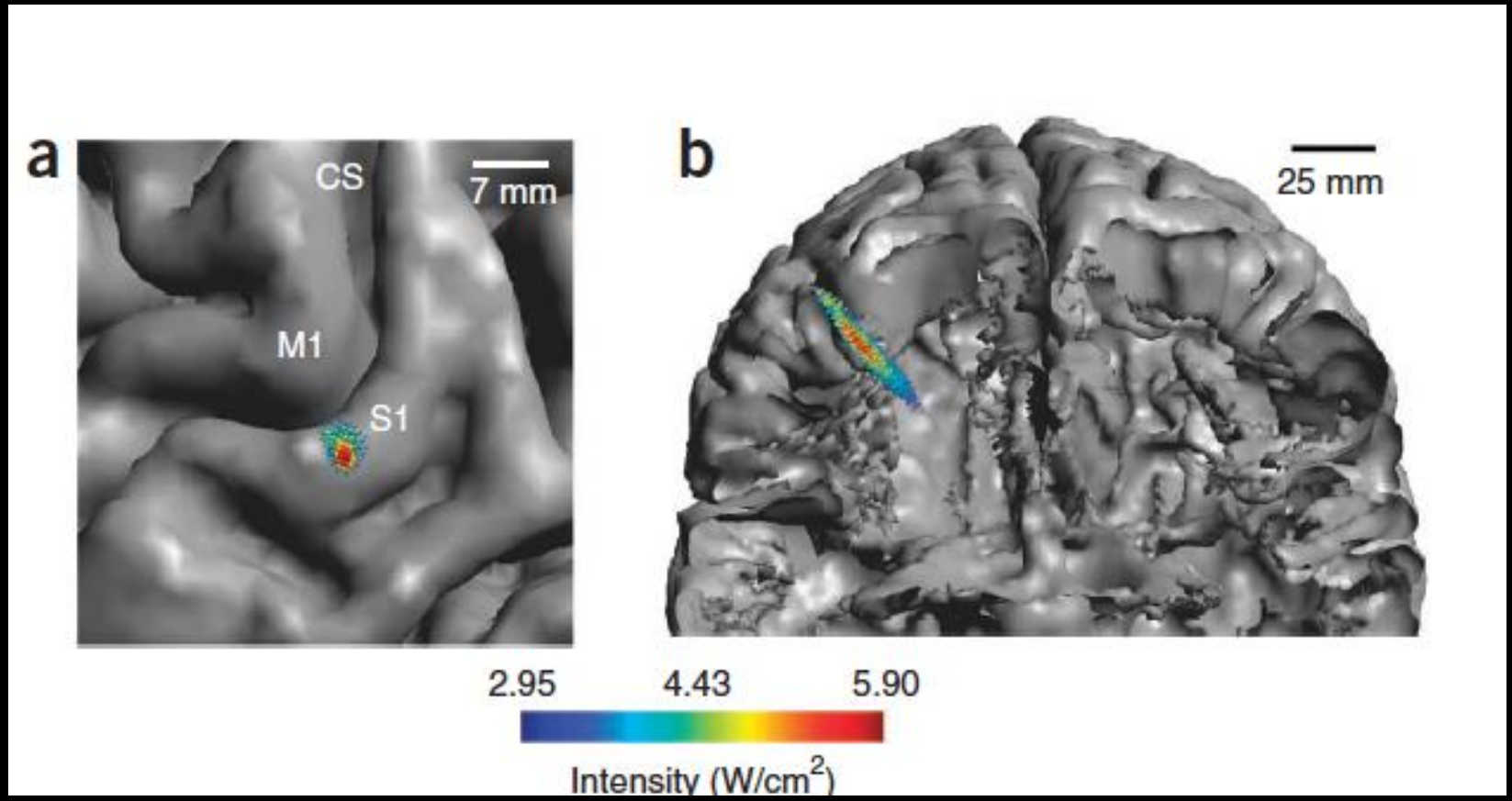
Temporal Characteristics	Spatial Characteristics

Adapted from Darmani et al., 2022

Transcranial focused ultrasound modulates the activity of primary somatosensory cortex in humans

Wynn Legon[1], Tomokazu F Sato[1], Alexander Opitz[1,2], Jerel Mueller[3], Aaron Barbour[1], Amanda Williams[1] & William J Tyler[1,3,4]

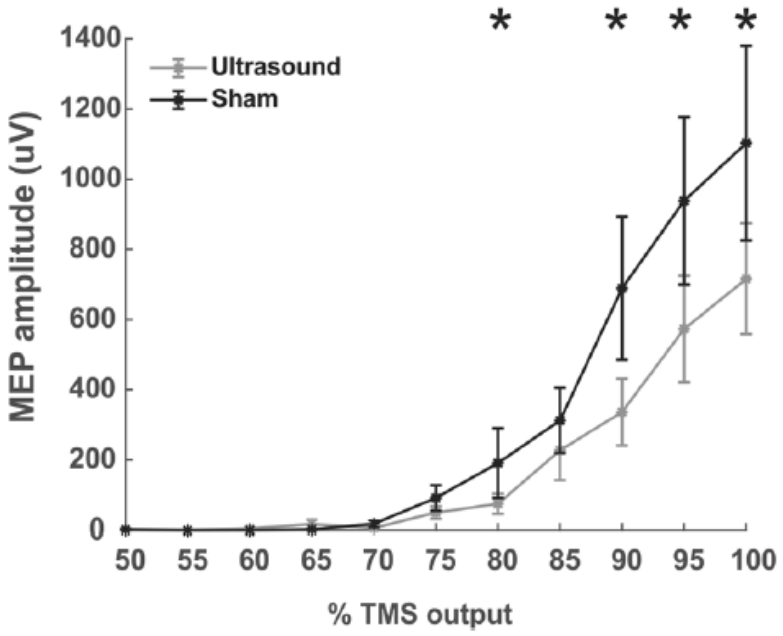
Nat Neuro 2014

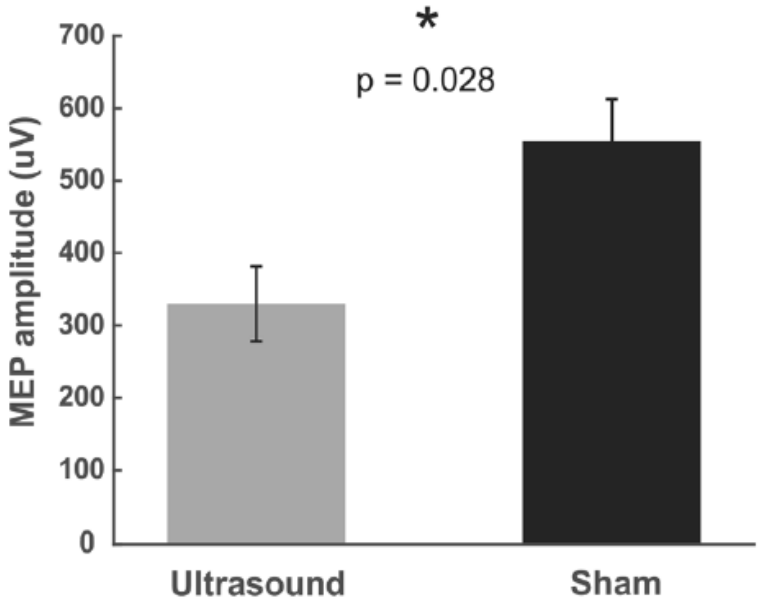


Transcranial focused ultrasound neuromodulation of the human primary motor cortex

Wynn Legon[1,3], Priya Bansal[1], Roman Tyshynsky[2], Leo Ai[1] & Jerel K. Mueller[1]

Sci Rep 2018





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Low Intensity Focused Ultrasound in Psychiatry: Neuromodulation

Low-Intensity Focused Ultrasound Targeting the Bilateral Nucleus Accumbens as a Potential Treatment for Substance Use Disorder: A First-in-Human Report

Table 1. Urine Toxicology Results: Pre-LIFU and During Post-LIFU Follow-up Evaluations

		Post-LIFU				
	Pre-LIFU	Day 1	Day 7	Day 30	Day 60	Day 90
Amphetamine	Positive	Negative	Negative	Negative	Negative	Negative
Barbiturates	Negative	Negative	Negative	Negative	Negative	Negative
Benzodiazepines	Negative	Negative	Negative	Negative	Negative	Negative
Cannabinoids	Positive	Negative	Negative	Negative	Negative	Negative
Cocaine	Negative	Negative	Negative	Negative	Negative	Negative
Ecstasy/MDMA	Negative	Negative	Negative	Negative	Negative	Negative
Fentanyl	Positive	Negative	Negative	Negative	Negative	Negative
Methadone	Negative	Negative	Negative	Negative	Negative	Negative
Opiates	Negative	Negative	Negative	Negative	Negative	Negative
Oxycodone	Negative	Negative	Negative	Negative	Negative	Negative

The participant was prescribed buprenorphine as part of comprehensive opioid addiction treatment (COAT) program. Day 0 was the day of low-intensity focused ultrasound (LIFU) sonication.

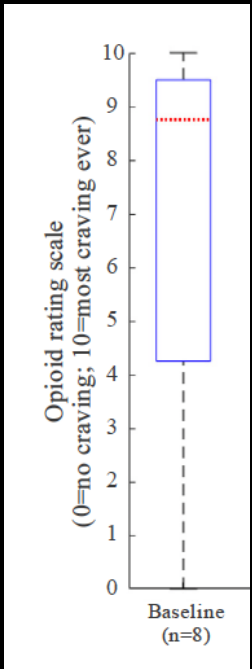
Mahoney…Rezai et al., Biological Psychiatry 2023

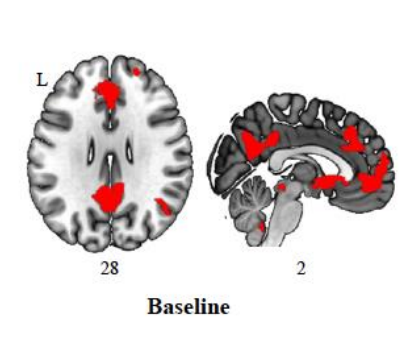
Archival Report

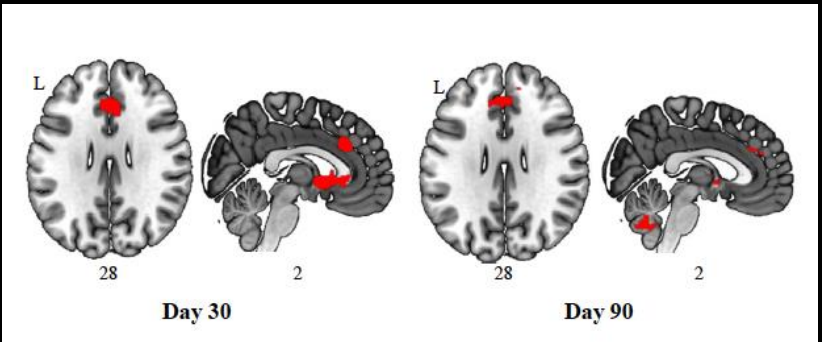
Biological Psychiatry

Focused Ultrasound Neuromodulation: Exploring a Novel Treatment for Severe Opioid Use Disorder

Ali Rezai, Daisy G.Y. Thompson-Lake, Pierre-François D'Haese, Nathalie Meyer, Manish Ranjan, Daniel Farmer, Victor Finomore, Jennifer L. Marton, Sally Hodder, Jeffrey Carpenter, Aniruddha Bhagwat, James Berry, Padma Tirumalai, Geoffrey Adams, Tasneem A. Arsiwala, Olaf Blanke, and James J. Mahoney III







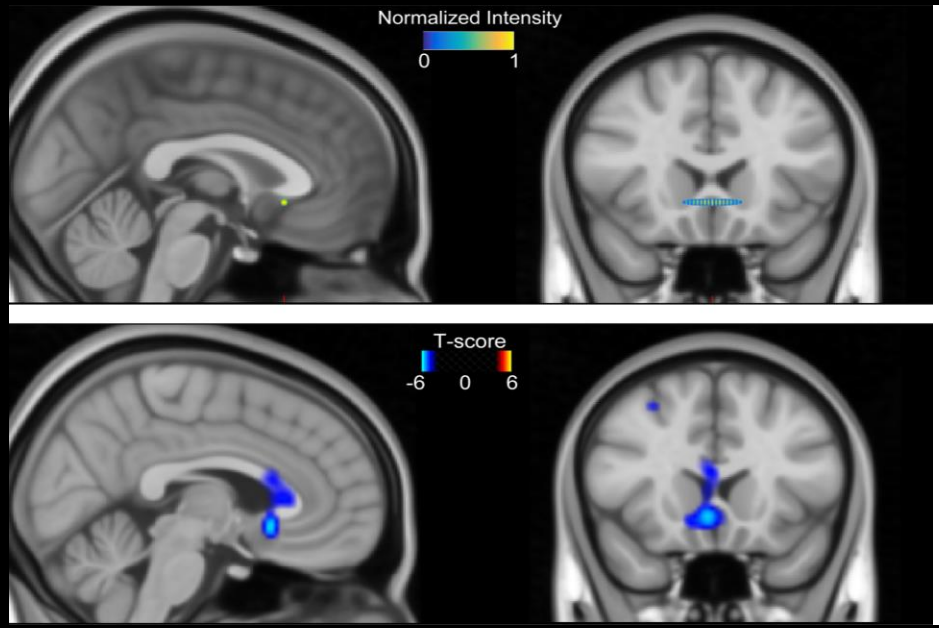
Rezai et al., Biological Psychiatry 2025

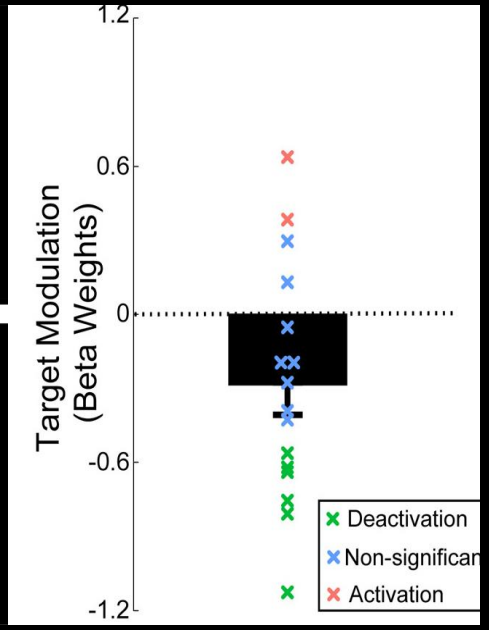
Biological Psychiatry
Available online 11 October 2024
In Press, Journal Pre-proof What's this?

Archival Report

Noninvasive modulation of subcallosal cingulate and depression with focused ultrasonic waves

Thomas S. Riis [a] *, Daniel A. Feldman [a b c] *, Sarah S. Kwon [c], Lily C. Vonesh [c], Vincent Koppelmans [c], Jefferson R. Brown [c], Daniela Solzbacher [c], Jan Kubanek [a c] *, Brian J. Mickey [a c] *





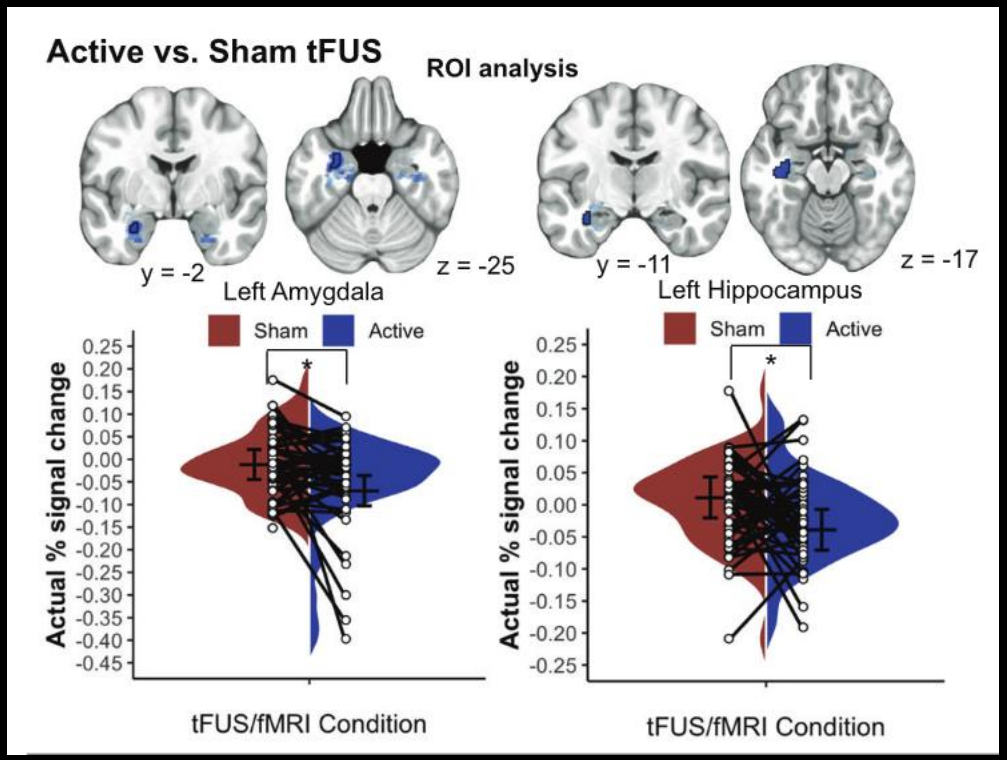
Molecular Psychiatry www.nature.com/mp

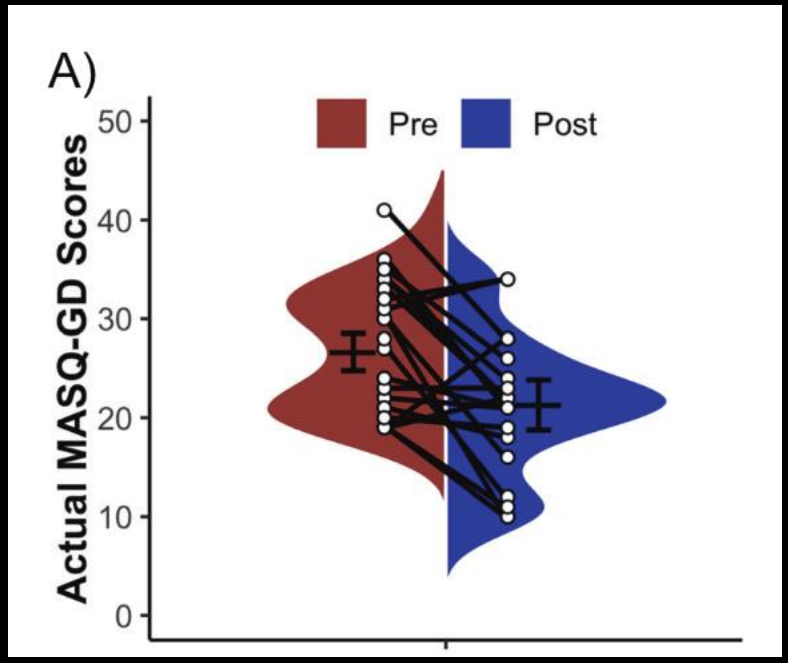
ARTICLE OPEN

Check for updates

Low-intensity transcranial focused ultrasound amygdala neuromodulation: a double-blind sham-controlled target engagement study and unblinded single-arm clinical trial

Bryan R. Barksdale[1], Lauren Enten[1], Annamarie DeMarco[1], Rachel Kline[1], Manoj K. Doss[1], Charles B. Nemeroff[1] and Gregory A. Fonzo[1]✉





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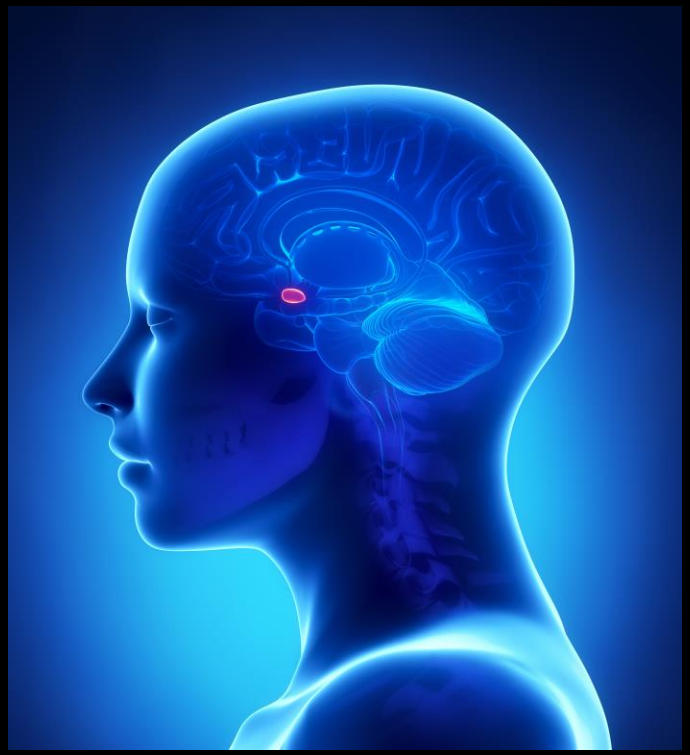
RECRUITING

ClinicalTrials.gov Identifier: NCT05147142

Low Intensity Focused Ultrasound: a New Paradigm for Depression and Anxiety (LIFU)

- Safety and tolerability
- Examine amygdala neuromodulation
- Examine simultaneous effects



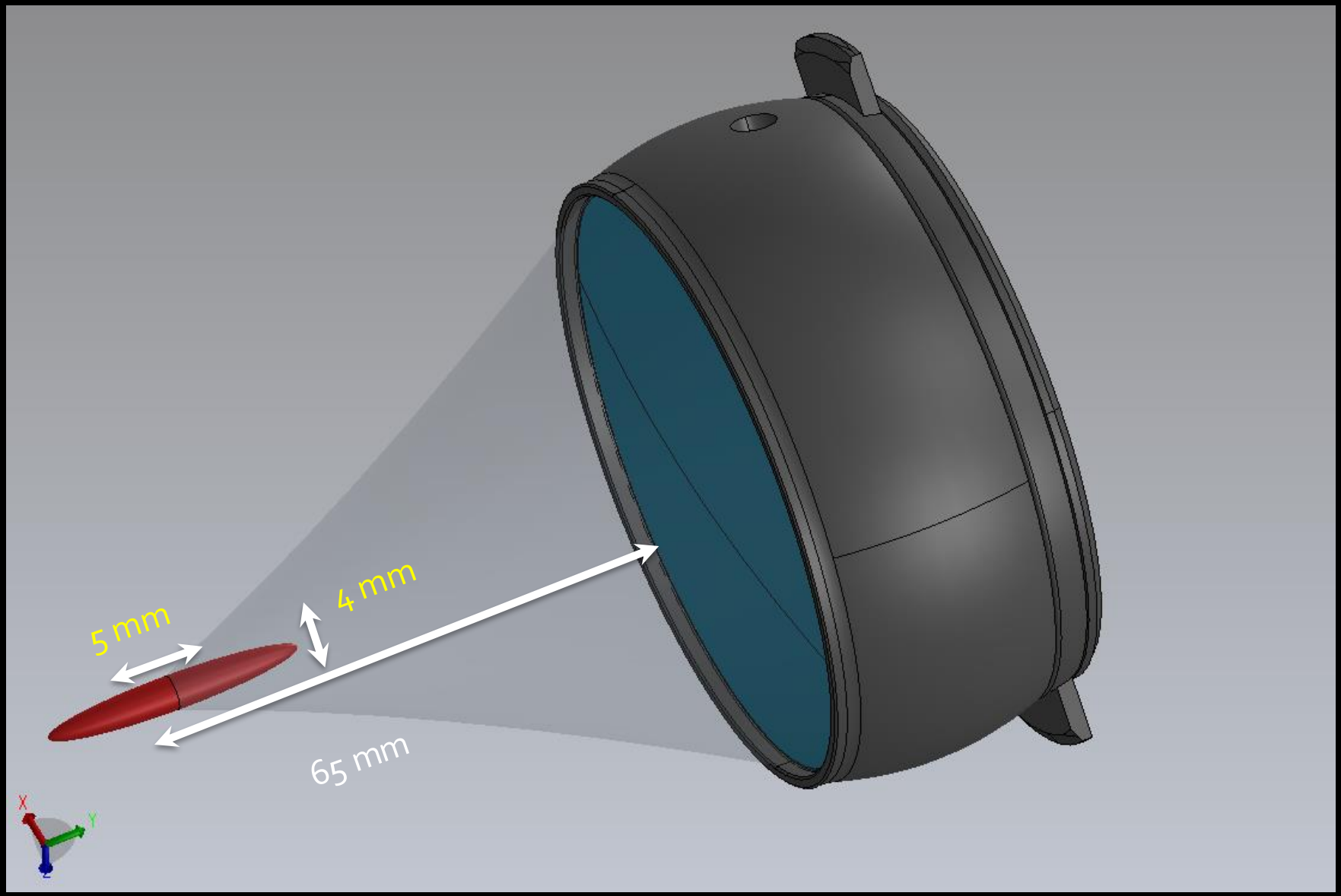
VA | U.S. Department of Veterans Affairs

FDA U.S. FOOD & DRUG ADMINISTRATION

NIH National Institute of Mental Health

VA: IS1 BX004779 (Philip PI) | FDA: IDE G200146 (Philip S/I) | NIMH: U01 MH123427 (Philip PI)


BRAINSONIX
65mm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X
Y
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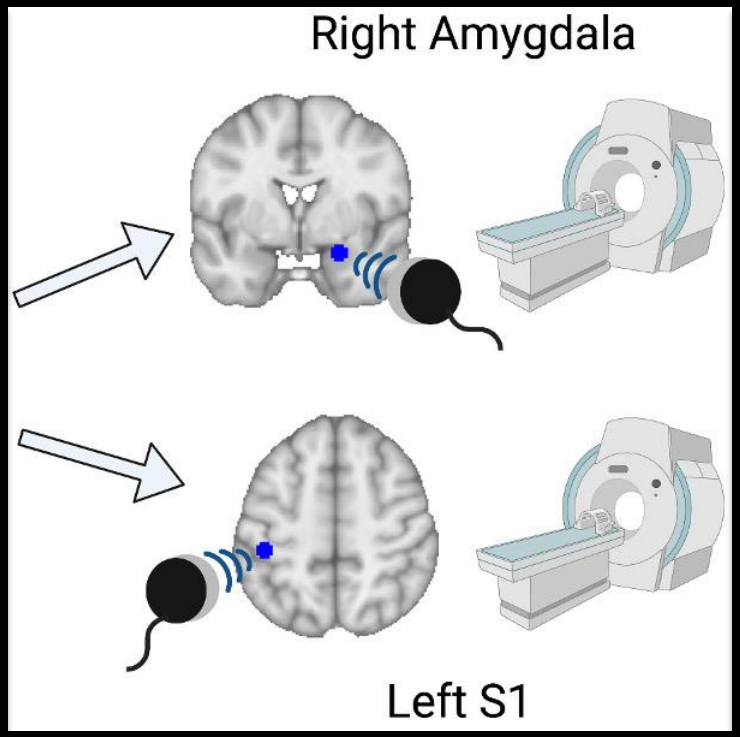
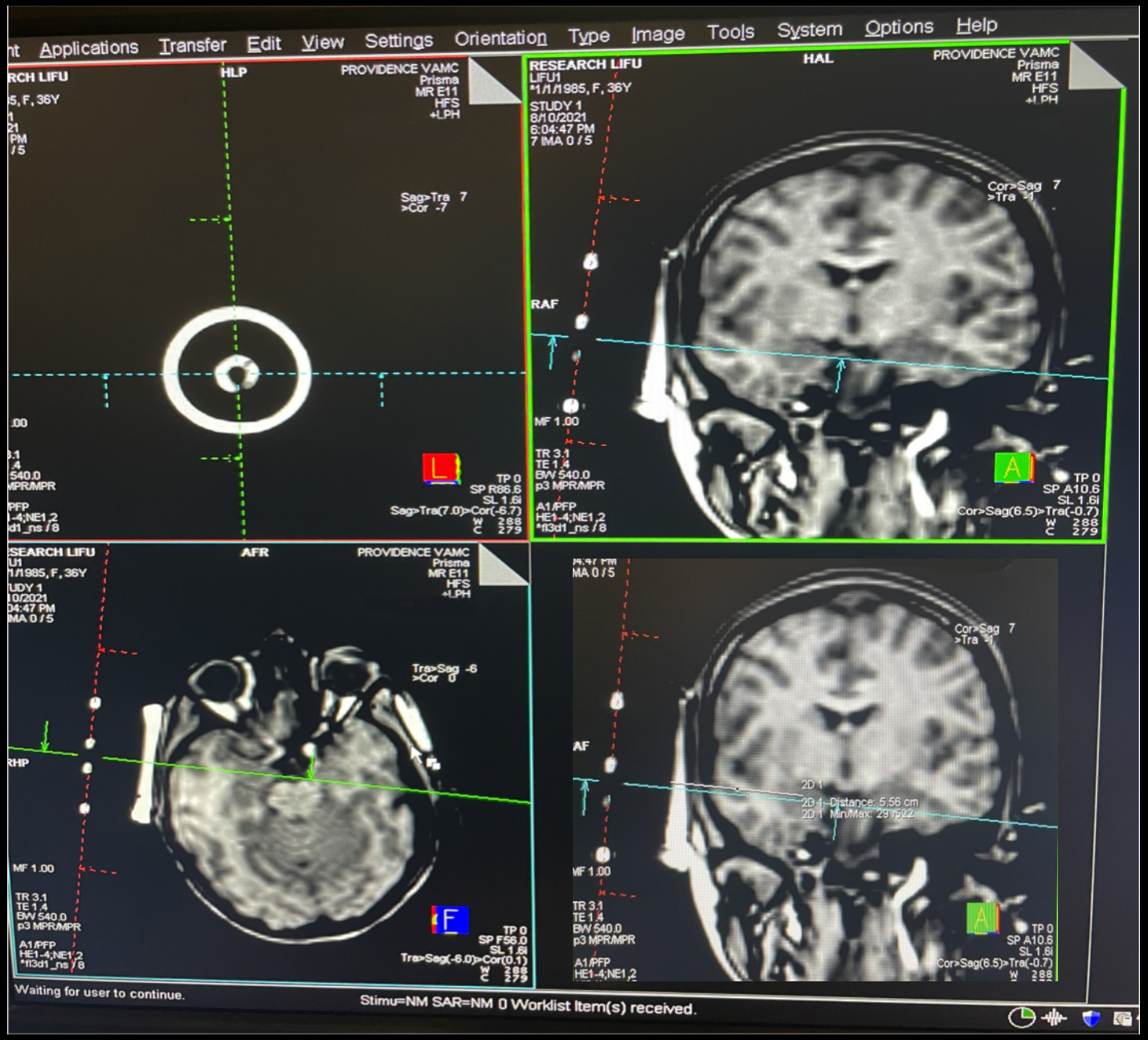

Right Amygdala
Left S1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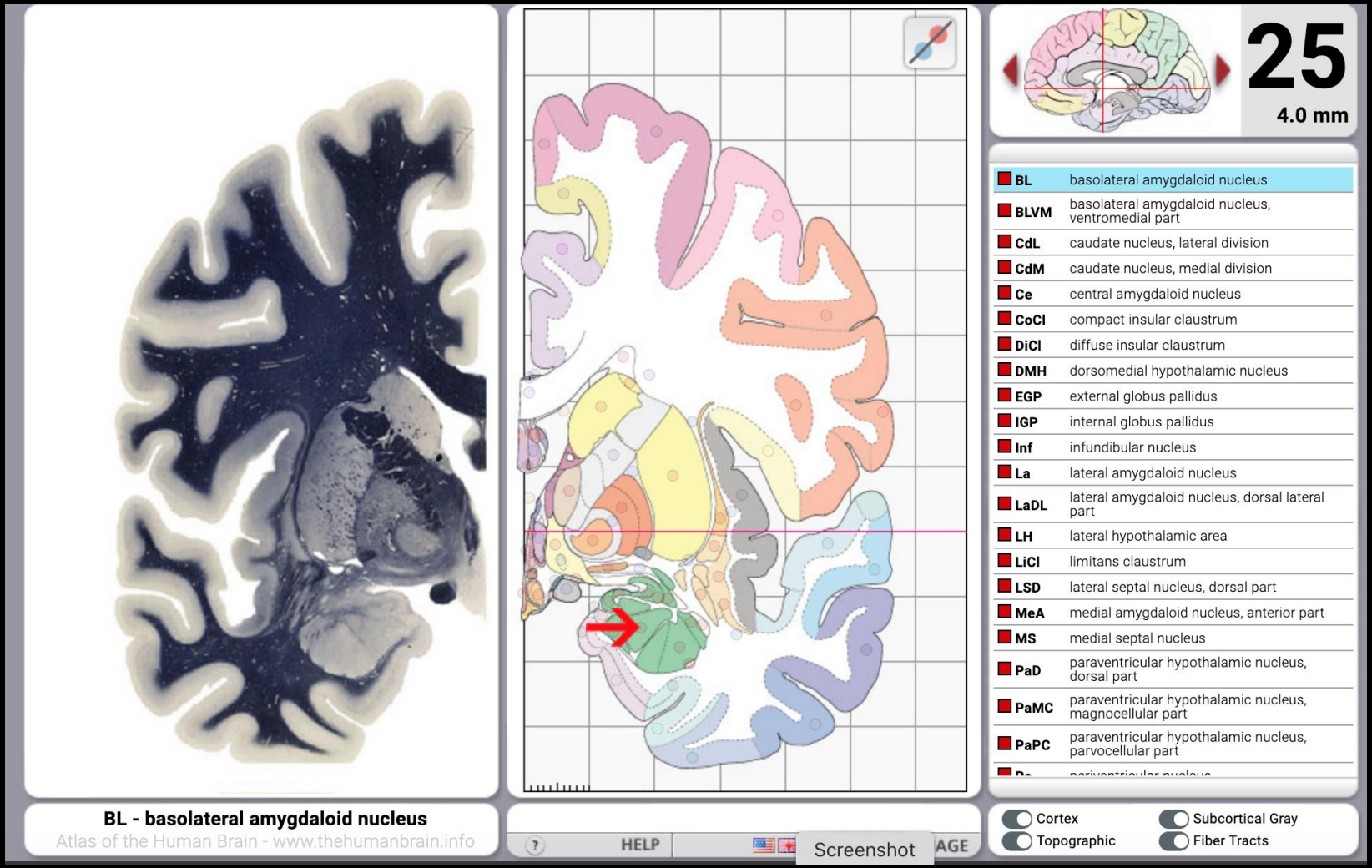
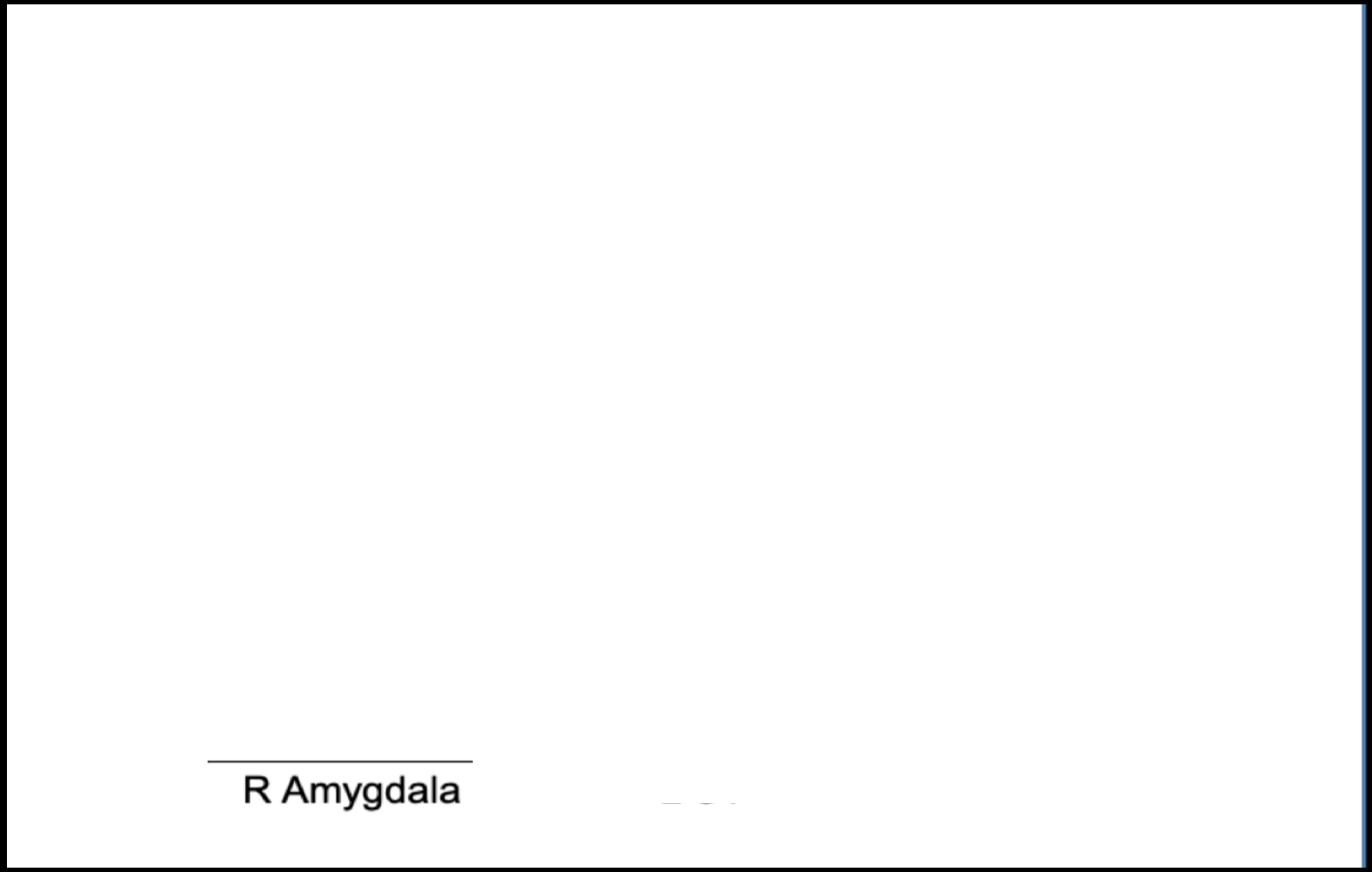

25
4.0 mm
BL basolateral amygdaloid nucleus
BLVM basolateral amygdaloid nucleus, ventromedial part
CdL caudate nucleus, lateral division
CdM caudate nucleus, medial division
Ce central amygdaloid nucleus
CoCl compact insular claustrum
DiCl diffuse insular claustrum
DMH dorsomedial hypothalamic nucleus
EGP external globus pallidus
IGP internal globus pallidus
Inf infundibular nucleus
La lateral amygdaloid nucleus
LaDL lateral amygdaloid nucleus, dorsal lateral part
LH lateral hypothalamic area
LiCl limitans claustrum
LSD lateral septal nucleus, dorsal part
MeA medial amygdaloid nucleus, anterior part
MS medial septal nucleus
PaD paraventricular hypothalamic nucleus, dorsal part
PaMC paraventricular hypothalamic nucleus, magnocellular part
PaPC paraventricular hypothalamic nucleus, parvocellular part
BL - basolateral amygdaloid nucleus
Atlas of the Human Brain - www.thehumanbrain.info
HELP
Screenshot
Cortex
Topographic
Subcortical Gray
Fiber Tracts

Mai Atlas

Target Engagement:
Change in Arterial Spin Labeling (n=10)



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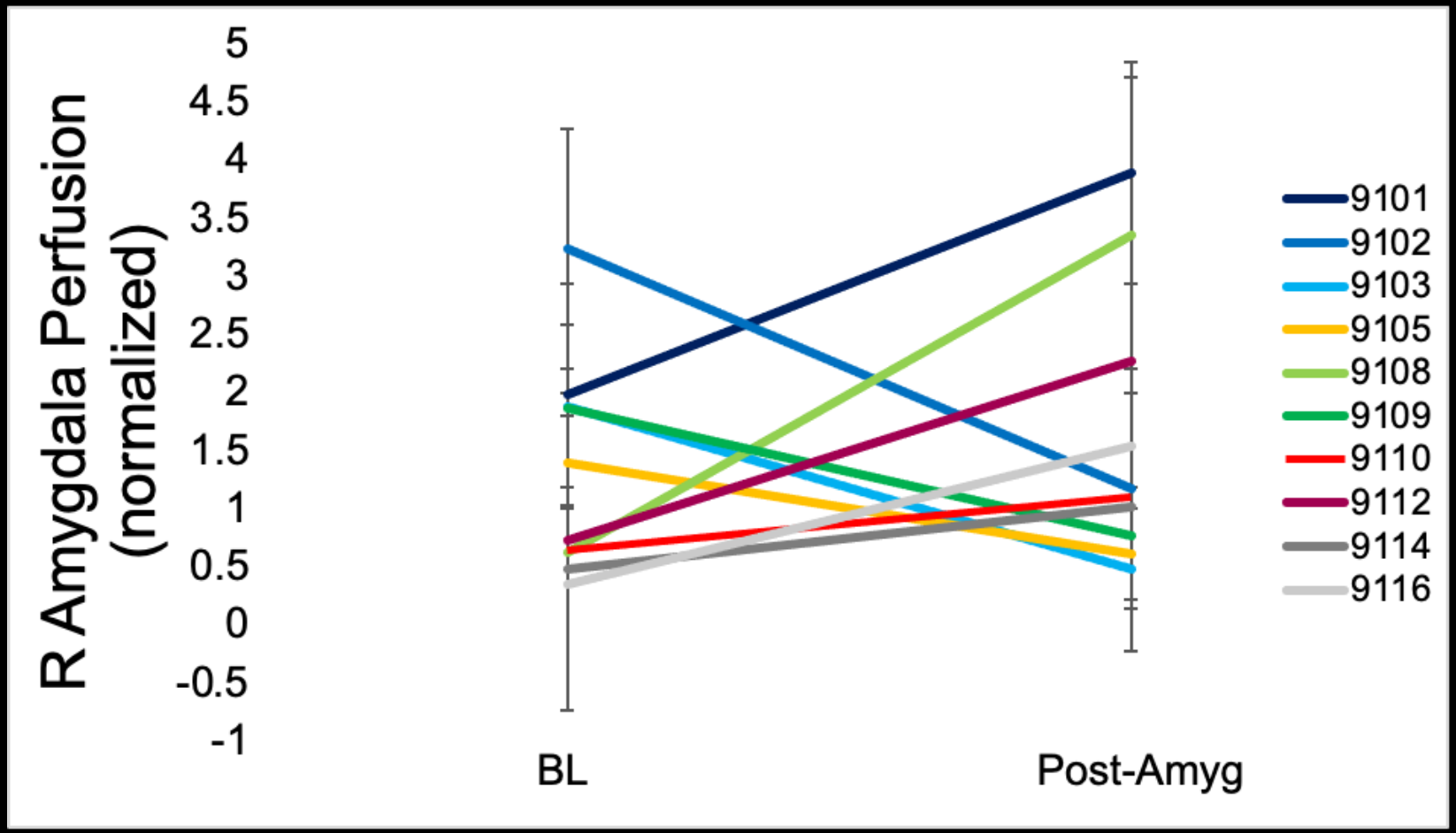

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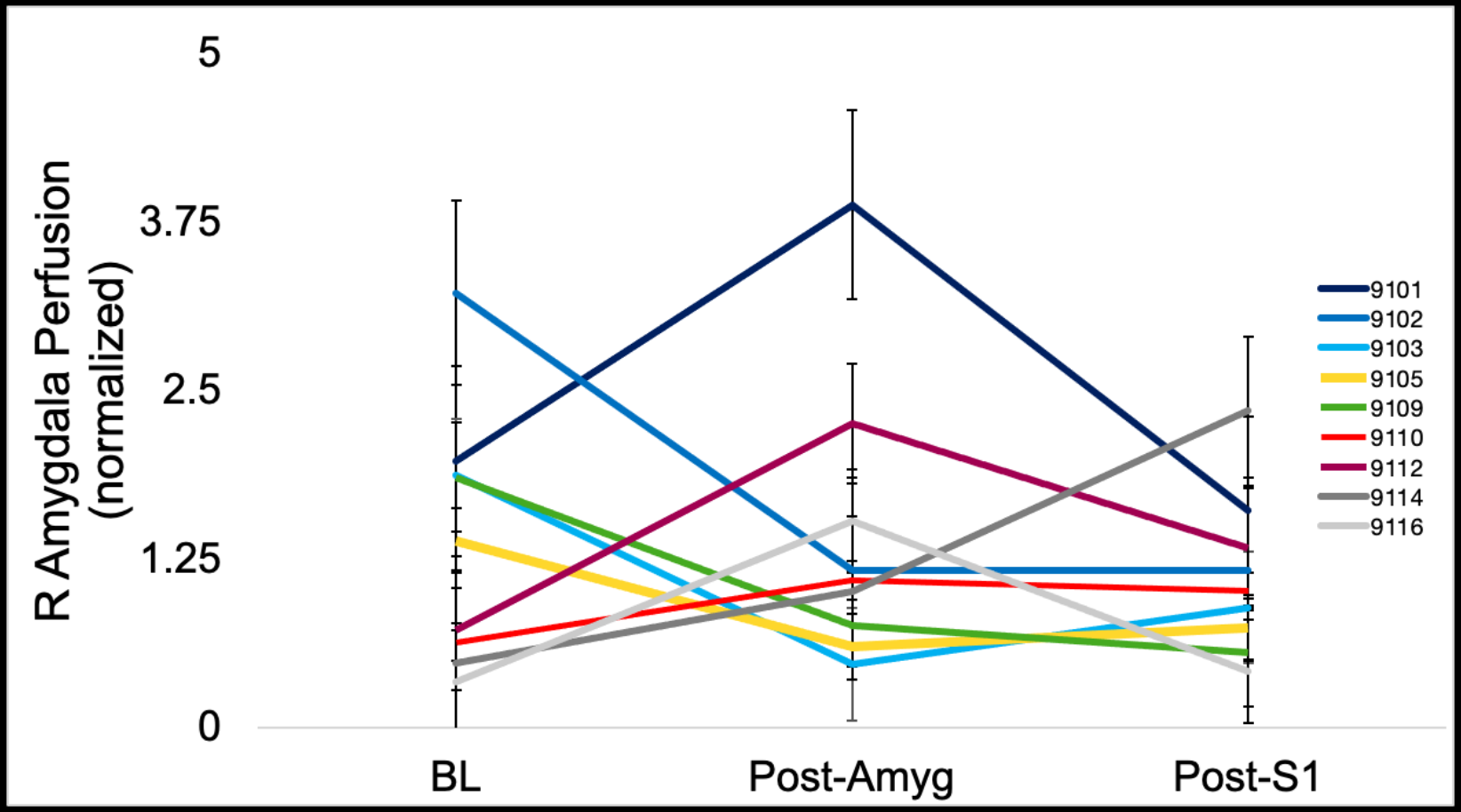

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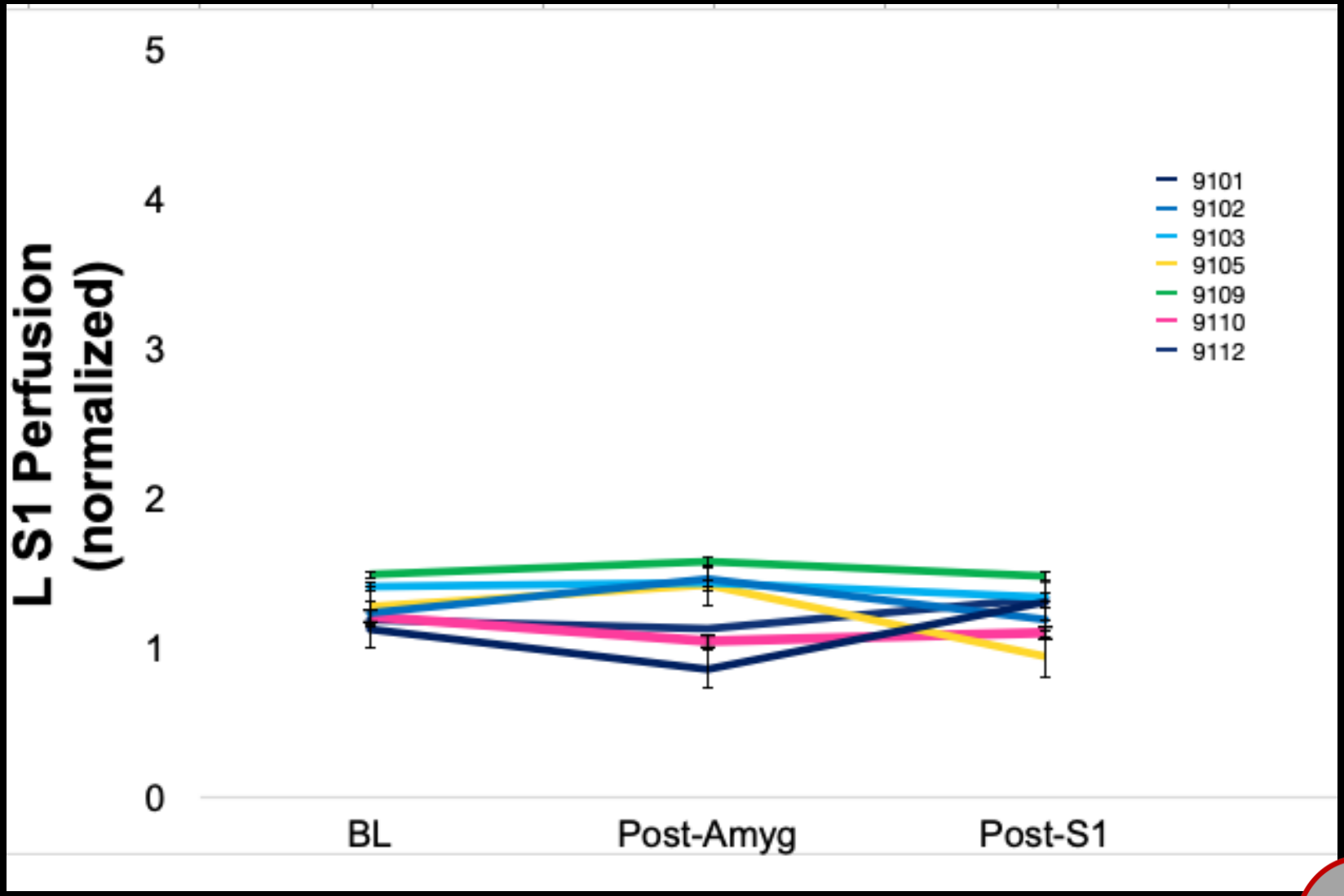
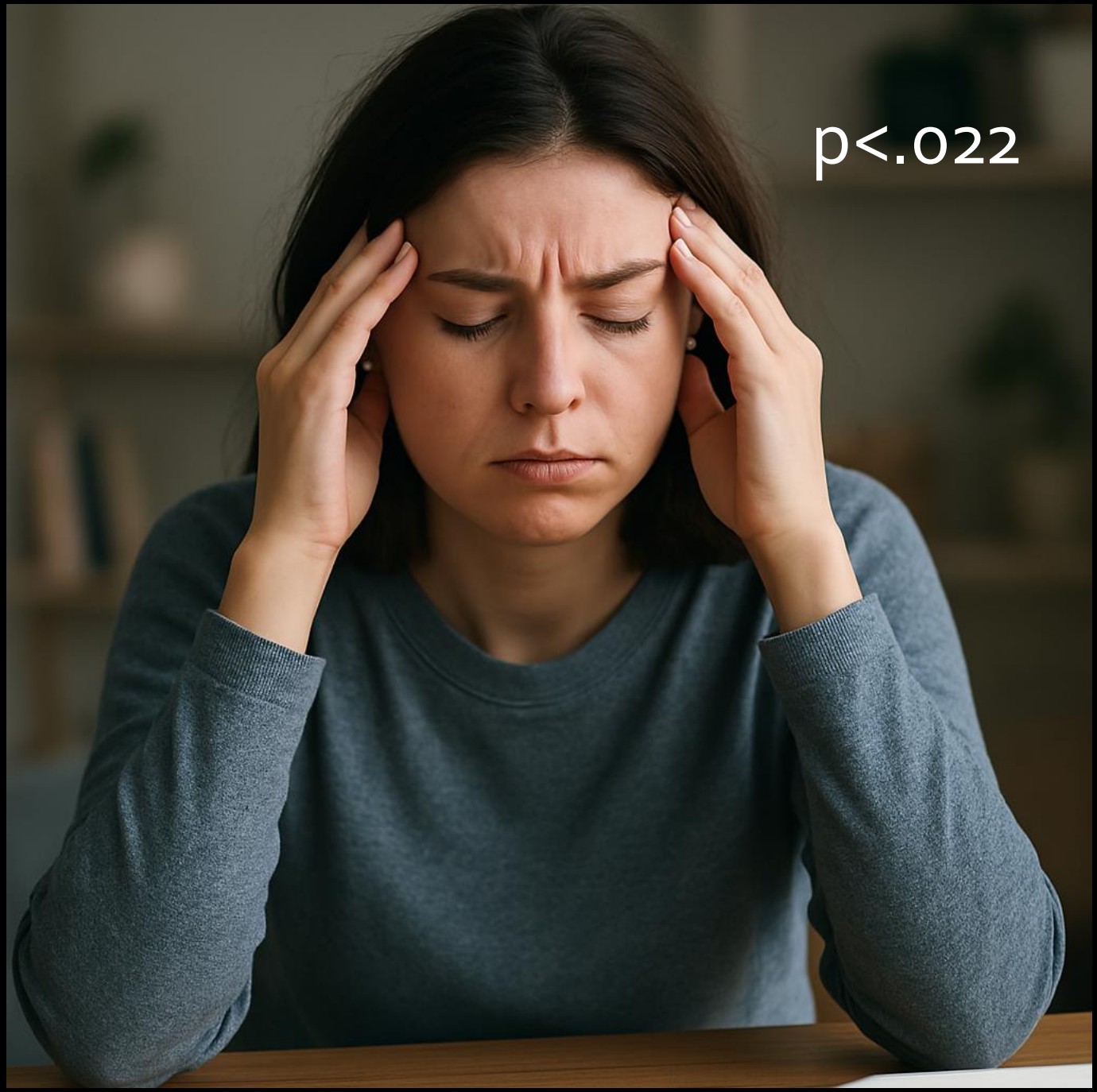


Disclaimer: Unpublished/Preliminary Data

$p < .001$

No Serious Adverse Events

YET...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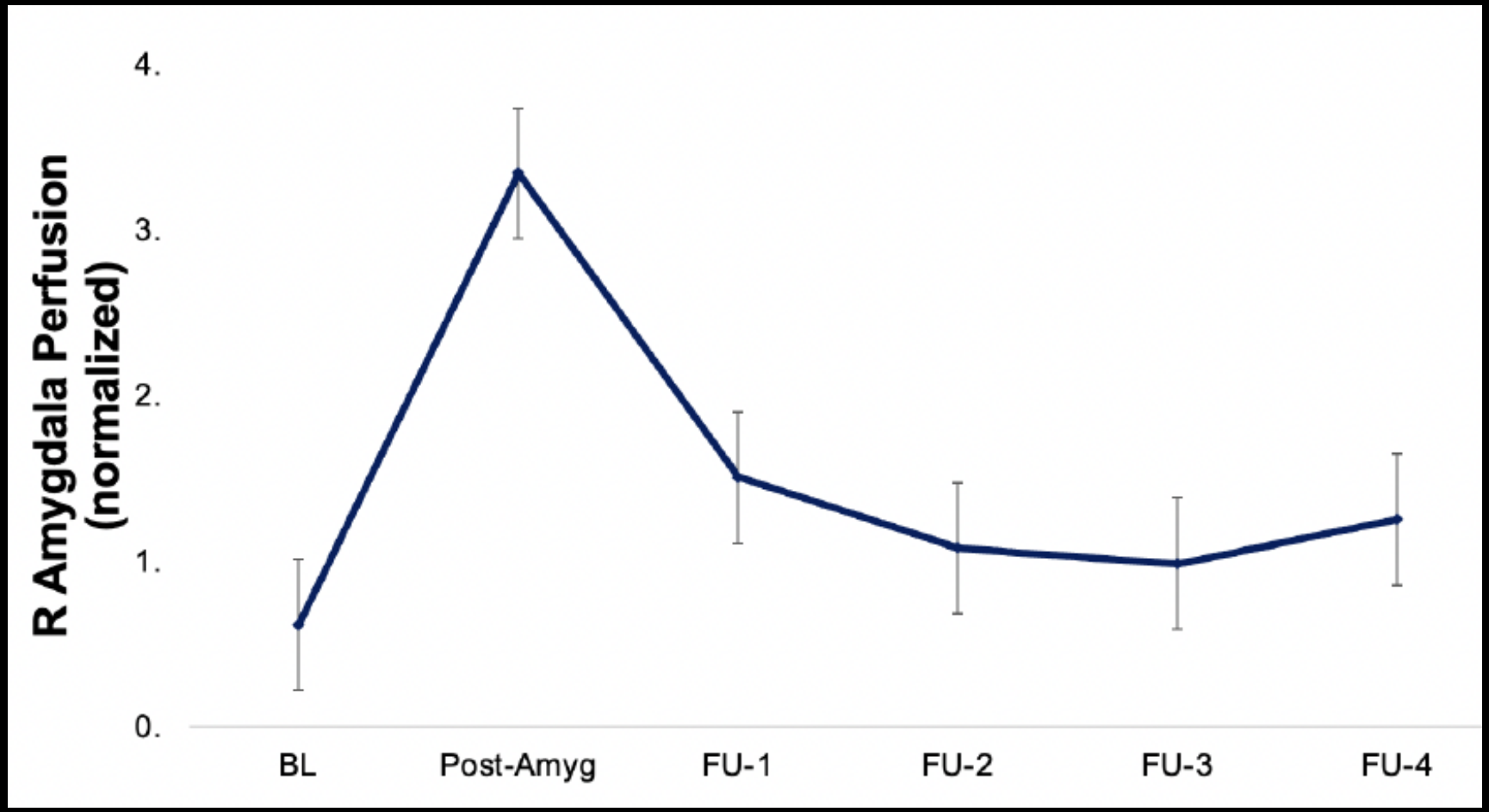

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The Team (Mental Health Research, VA Providence & Brown University)

Lead: Noah S. Philip MD

Investigators: Mascha van 't Wout-Frank PhD, Jennifer Barredo PhD, Benjamin Greenberg MD PhD, Amin Zandvakili MD PhD, Yosef Berlow MD PhD, Amanda Arulpragasam PhD, Camila Cosmo MD PhD

Affiliates: Linda Carpenter MD, Jennifer Primack PhD, Michelle Madore PhD, Leanne Williams PhD, F Andy Kozel MD, Paul Holtzheimer MD PhD, Kelvin Lim MD

Staff & Trainees: Kate Barnabe, Emily Aiken MA, Hannah Swearingen, Samantha Cilli, Noelle Marcotullio, Julia Gilotti, Alison Gorbatov JD, Miriam Goldberg MD PhD

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NIMH: R25 MH101076, R01 MH120126, U01 MH123427; NIGMS: P20 GM13045

Focused Ultrasound Foundation, NARSAD/Brain Behavior Research Foundation

Qs: Noah_Philip@Brown.edu Social: @NoahSPhilipMD & @noahsphilipmd.bsky.social