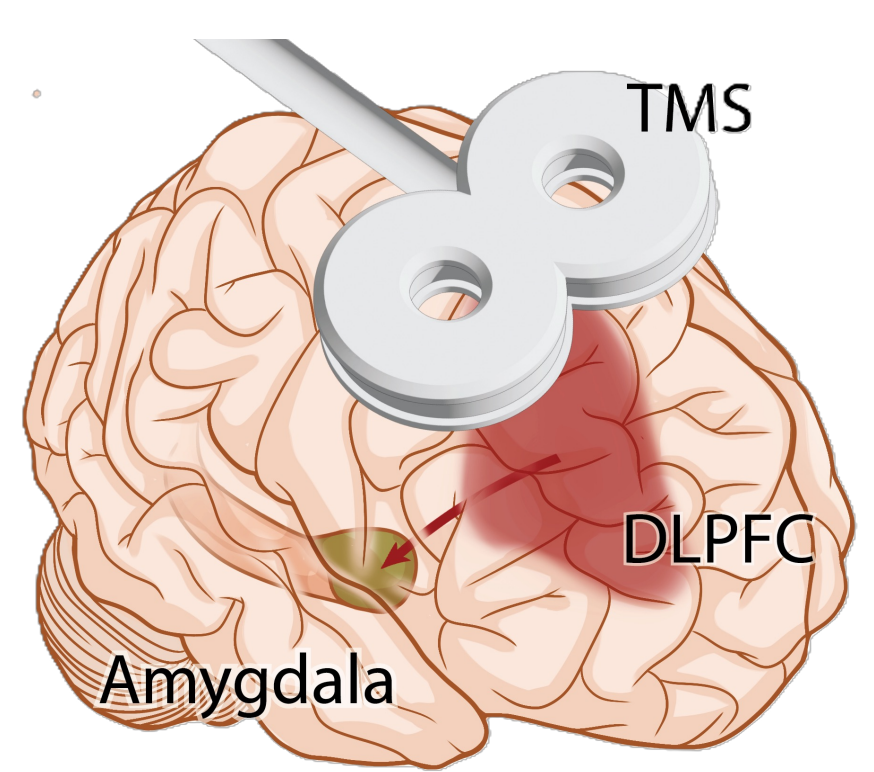


**Patlapa Sompolpong**<sup>1</sup>, Sean Minton<sup>2</sup>, Cecilia Hinojosa<sup>2,3</sup>, Joshua Lukemire<sup>4</sup>, Rebecca Hinrichs<sup>2</sup>, Natalie Merrill<sup>2</sup>, Timothy Ely<sup>2</sup>, Kristina Dahlgren<sup>2</sup>, Patricio Riva Posse<sup>2</sup>, Paul Holtzheimer<sup>5, 6</sup>, Vince Calhoun<sup>2,7</sup>, Joan Camprodon<sup>8,9</sup>, Sheila Rauch<sup>2</sup>, Nadine Kaslow<sup>2</sup>, Kerry Ressler<sup>2,8,10</sup>, Tanja Jovanovic<sup>11</sup>, William McDonald<sup>2</sup>, Sanne van Rooij<sup>2</sup>

<sup>1</sup>Emory University, Graduate Division of Biological and Biomedical Sciences, <sup>2</sup>Emory School of Medicine, Department of Psychiatry and Behavioral Sciences, <sup>3</sup>University of New Mexico, Department of Psychology, <sup>4</sup>Emory University Rollins School of Public Health, Department Biostatistics and Bioinformatics, <sup>5</sup>National Center for PTSD, <sup>6</sup>Dartmouth Geisel School of Medicine, Departments of Psychiatry and Surgery, <sup>7</sup>Tri-institutional Center for Translational Research in Neuroimaging and Data Science, Georgia State, Georgia Tech, <sup>8</sup>Harvard Medical School, Department of Psychiatry, <sup>9</sup>Mass General Brigham, Division of Neuropsychiatry and Interventional Psychiatry, <sup>10</sup>McLean Hospital, Division of Depression and Anxiety Disorders, <sup>11</sup>Wayne State University, Dept. of Psychiatry and Behavioral Neuroscience

## Background

- Up to 50% of patients with posttraumatic stress disorder (PTSD) do not respond to first line treatment<sup>1</sup>.
- Amygdala hyperreactivity is a main driver of PTSD symptoms and treatment non-response<sup>2</sup>.
- Modulating the threat circuitry via transcranial magnetic stimulation (TMS) is promising as an alternative PTSD intervention<sup>3</sup>.
- TMS to right dorsolateral prefrontal cortex (DLPFC) attenuates PTSD<sup>4</sup> and results in downstream modulation<sup>5</sup> and inhibition<sup>6</sup> of amygdala activity.



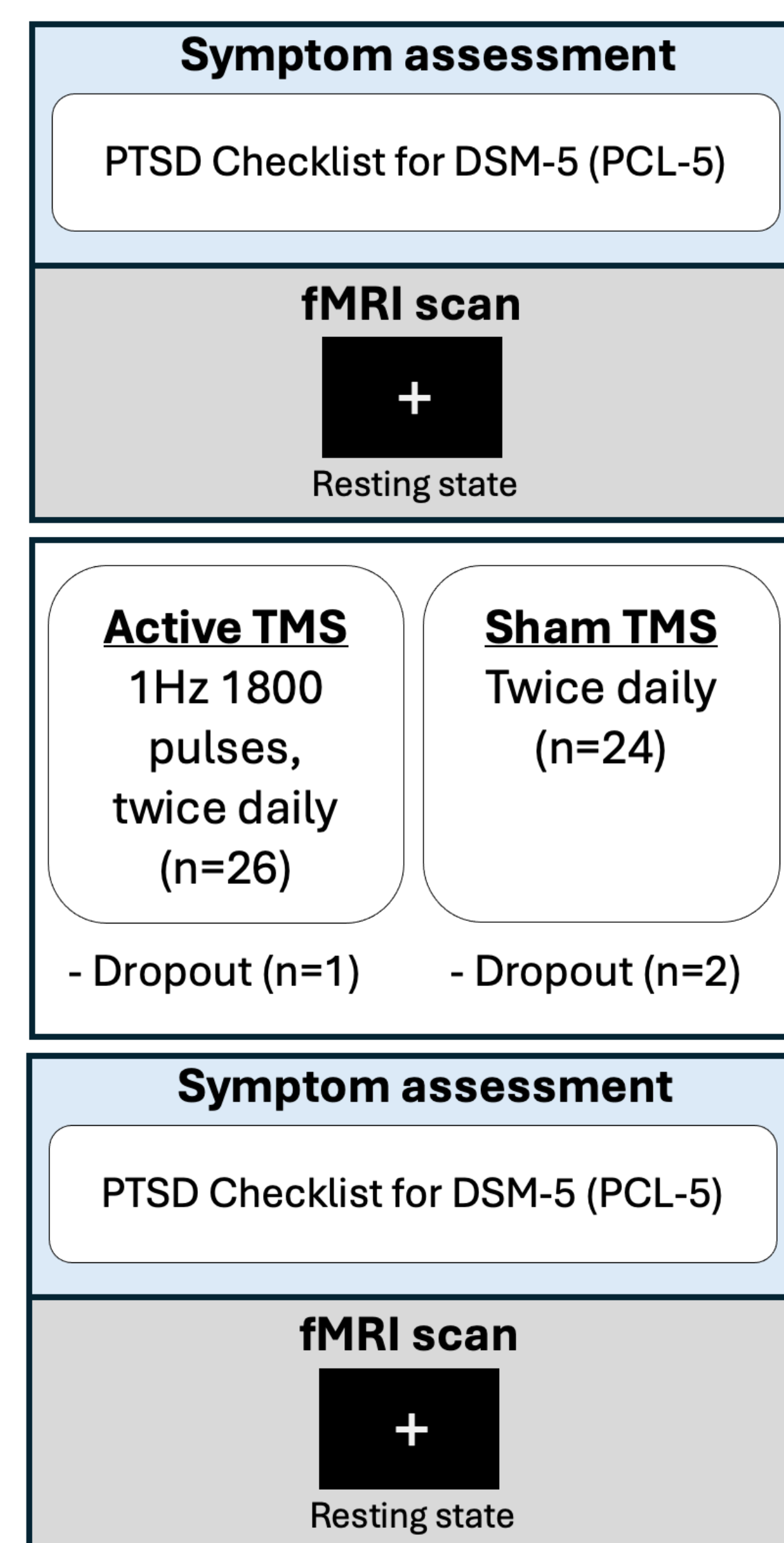
We developed a **functional connectivity (FC)-guided approach to indirectly target the right amygdala through functional connections with rDLPFC**.

This is the first clinical trial to show that personalized neuroimaging-guided TMS targeting the threat circuitry dampens amygdala hyperreactivity and leads to long-term improvements in PTSD<sup>7</sup>.

## Objectives

- Determine topographic variability of personalized targets
- Determine effect of active versus sham TMS on target topography

## Methods



Pre-TMS visit  
+ 2-3 days  
TMS treatment (10 days)  
+ 4 days  
Post-TMS visit

	Sham (n=24)	Active (n=26)	Overall (n=50)
	Mean (SD)		
Age	45.3 (10.1)	38.3 (11.7)	41.7 (11.4)
Pre-TMS PCL-5 total	35.4 (12.3)	39.9 (12.4)	37.7 (12.4)
Post-TMS PCL-5 total	25.9 (16.3)	25.9 (13.2)	25.9 (14.5)
	N (%)		
<b>Sex</b>			
Male	3 (12.5)	4 (15.4)	7 (14.0)
Female	21 (87.5)	22 (84.6)	43 (86.0)
<b>Gender</b>			
Man	2 (8.3)	4 (15.4)	6 (12.0)
Woman	20 (83.3)	21 (80.8)	41 (82.0)
Nonbinary	2 (8.3)	1 (3.8)	3 (6.0)
<b>Race</b>			
White	15 (62.5)	15 (57.7)	30 (60.0)
Black	6 (25.0)	9 (34.6)	15 (30.0)
Asian	1 (4.2)	10 (3.8)	2 (4.0)
Other/Mixed	2 (8.3)	0 (0.0)	2 (4.0)
Missing	0 (0.0)	1 (3.8)	1 (2.0)

Table 1. Participant demographics

Figure 1. Study design

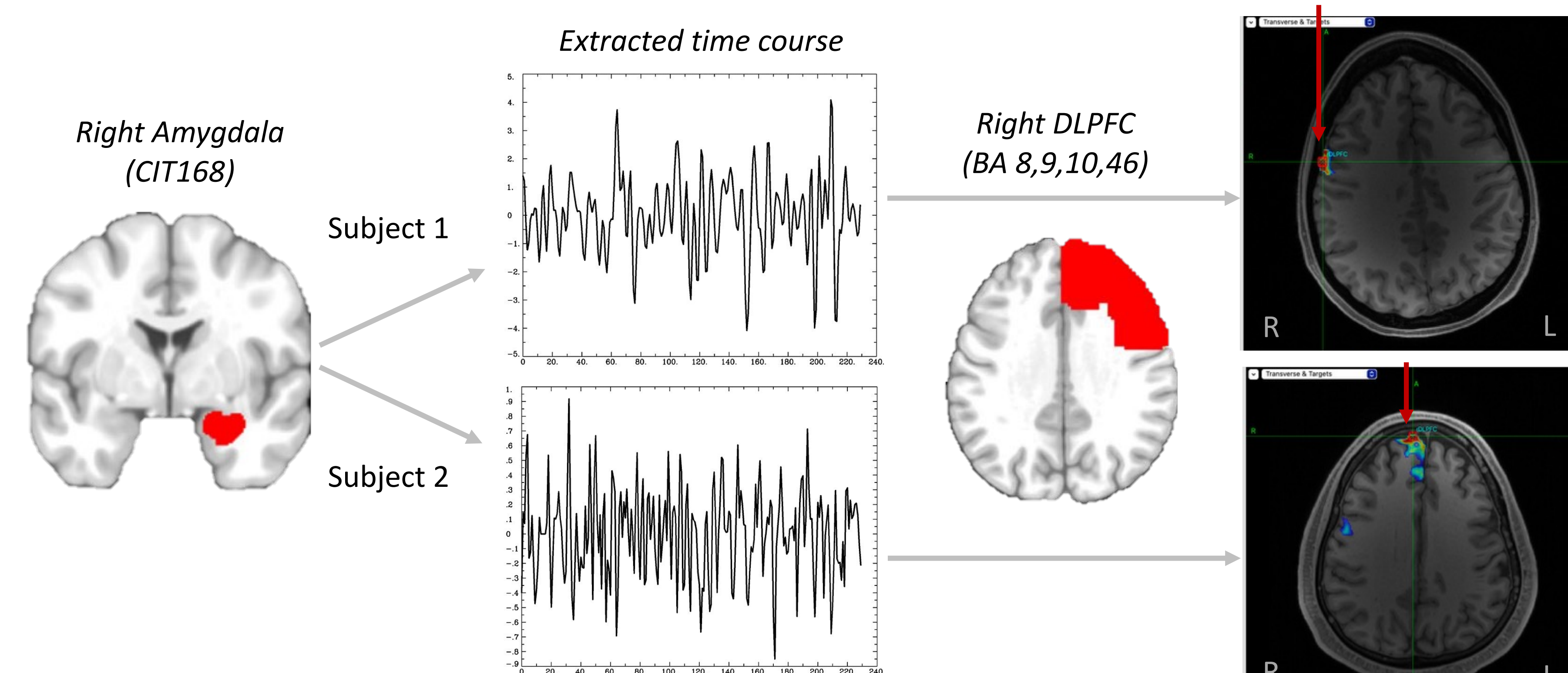
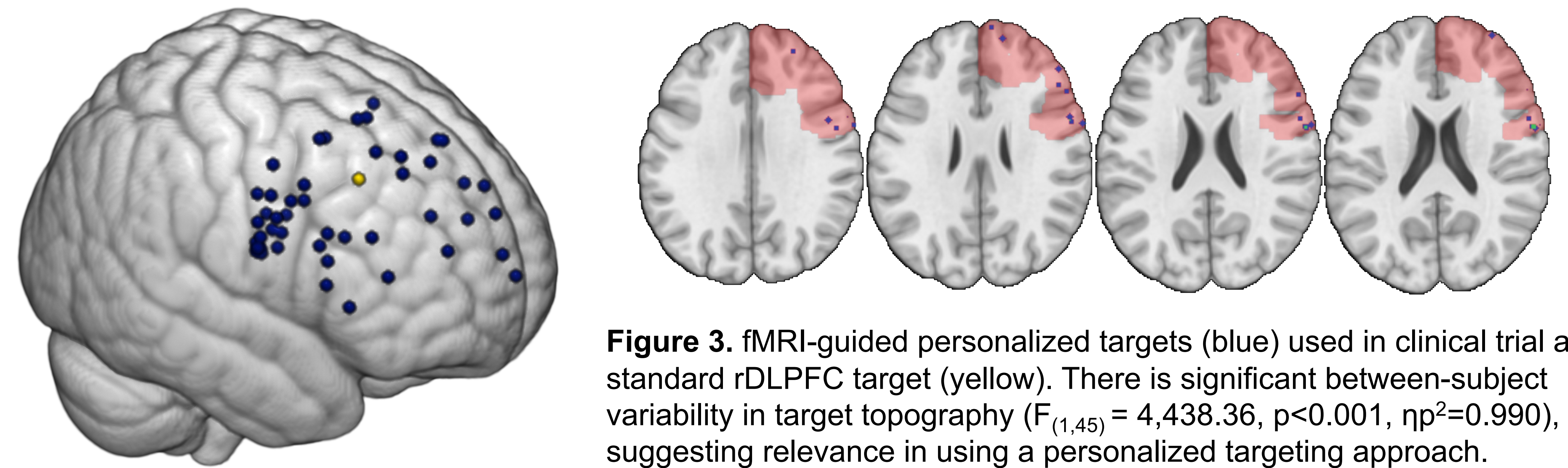


Figure 2. Personalized targeting pipeline. Targets in rDLPFC were defined using positive FC to right amygdala and according to three criteria: 1. Largest FC peak cluster, 2. Within 1.0 cm of the cortex, 3. Location tolerable for 3600 1Hz TMS pulses per day.

## Results: Between-subject target variability



## Results: Effect of active versus sham TMS on target topography

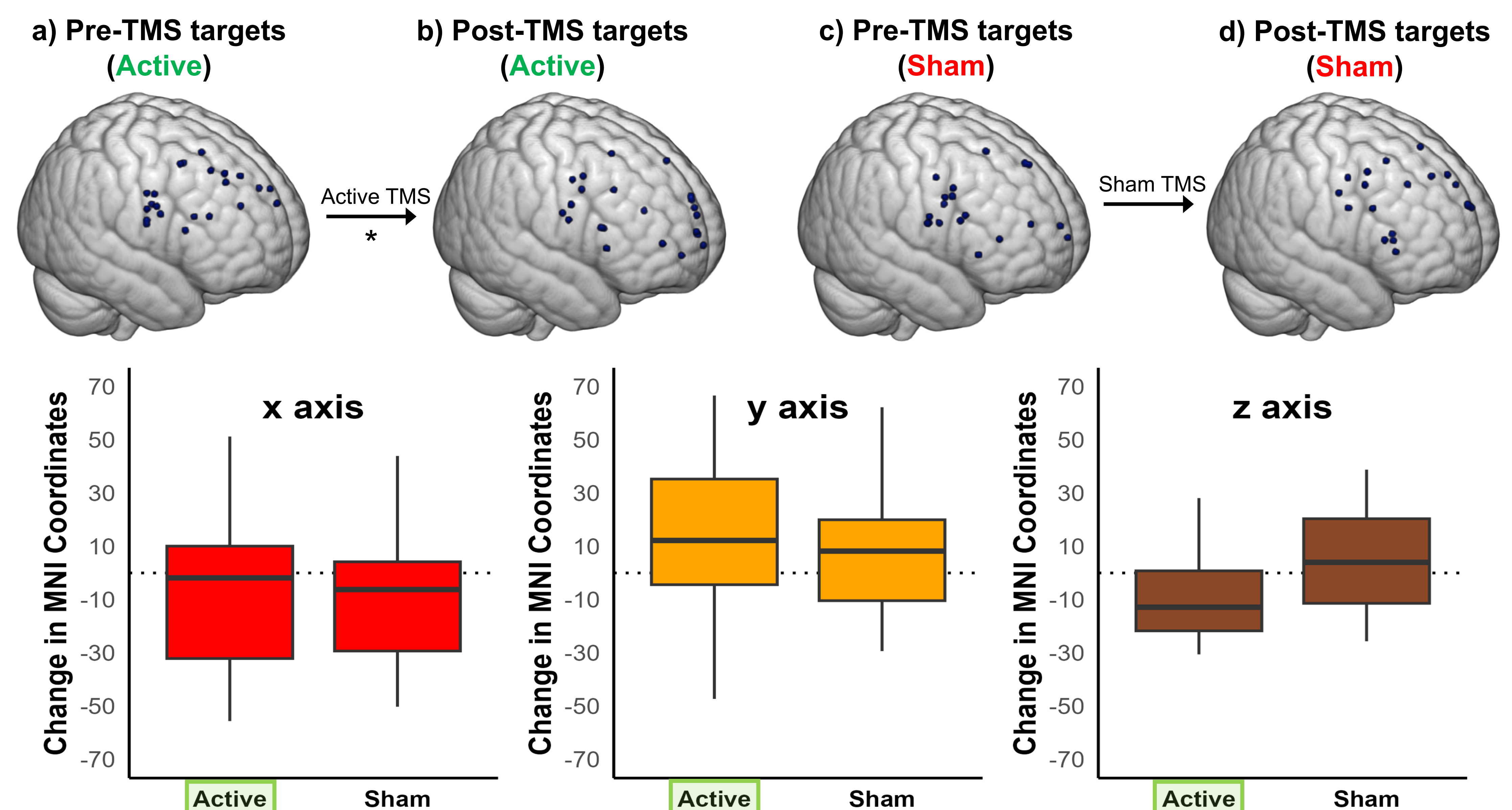


Figure 4. (Top) Pre- and post-TMS targets for active (n=22) and sham (n=19). (Bottom) Box plots showing pre- to post-TMS vector change for x, y, and z direction. There was a significantly different effect of active versus sham TMS on change in topographic location over time (interaction,  $F_{(1,39)} = 4.49$ ,  $p = 0.040$ ,  $\eta^2 = 0.103$ ). Active TMS, but not sham, significantly changed target location  $F_{(1,21)} = 5.65$ ,  $p = 0.027$ ,  $\eta^2 = 0.212$ ). Exploratory correlation analyses in the active group found greater PTSD improvement to be associated with greater change in the x (more medial;  $r = 0.45$ ,  $p = 0.034$ ) and y direction (more anterior;  $r = -0.44$ ,  $p = 0.043$ ).

## Conclusion

- Variability in target location indicate topographic heterogeneity of the threat circuitry across individuals and supports the use of personalized TMS targeting approaches.
- A clinical course of TMS changes target location, suggesting that amygdala-guided TMS alters FC within the threat circuitry.

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Contact: Patlapa Sompolpong ([patlapa.sompolpong@emory.edu](mailto:patlapa.sompolpong@emory.edu))  
Sanne J.H. van Rooij, PhD ([sanne.van.rooij@emory.edu](mailto:sanne.van.rooij@emory.edu))