

# Theta burst stimulation does not modulate functional connectivity in the primary visual cortex: A sham-controlled multi-echo fMRI study

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## BACKGROUND

□ Theta burst stimulation (TBS) is a repetitive transcranial magnetic stimulation (rTMS) protocol which has the advantage of a short delivery time over traditional rTMS<sup>1-2</sup>:

- Increases efficiency of empirical research in the lab and patient compliance in clinical settings

□ When TBS applied to motor cortex<sup>2</sup>:

- Intermittent TBS (iTBS) → Excitatory aftereffects
- Continuous TBS (cTBS) → Inhibitory aftereffects
- After a single TBS session, Aftereffects reported lasting from minutes to hours

□ However, few studies have investigated occipital TBS

□ Our lab previously examined low frequency (1 Hz) TMS to V1<sup>3</sup>:

- No immediate changes in resting state functional connectivity (FC)
- Widespread FC changes after 1 hr

## QUESTIONS

1- Does a single-session occipital TBS modulate whole brain FC measured via resting state functional magnetic resonance imaging (rs-fMRI)?

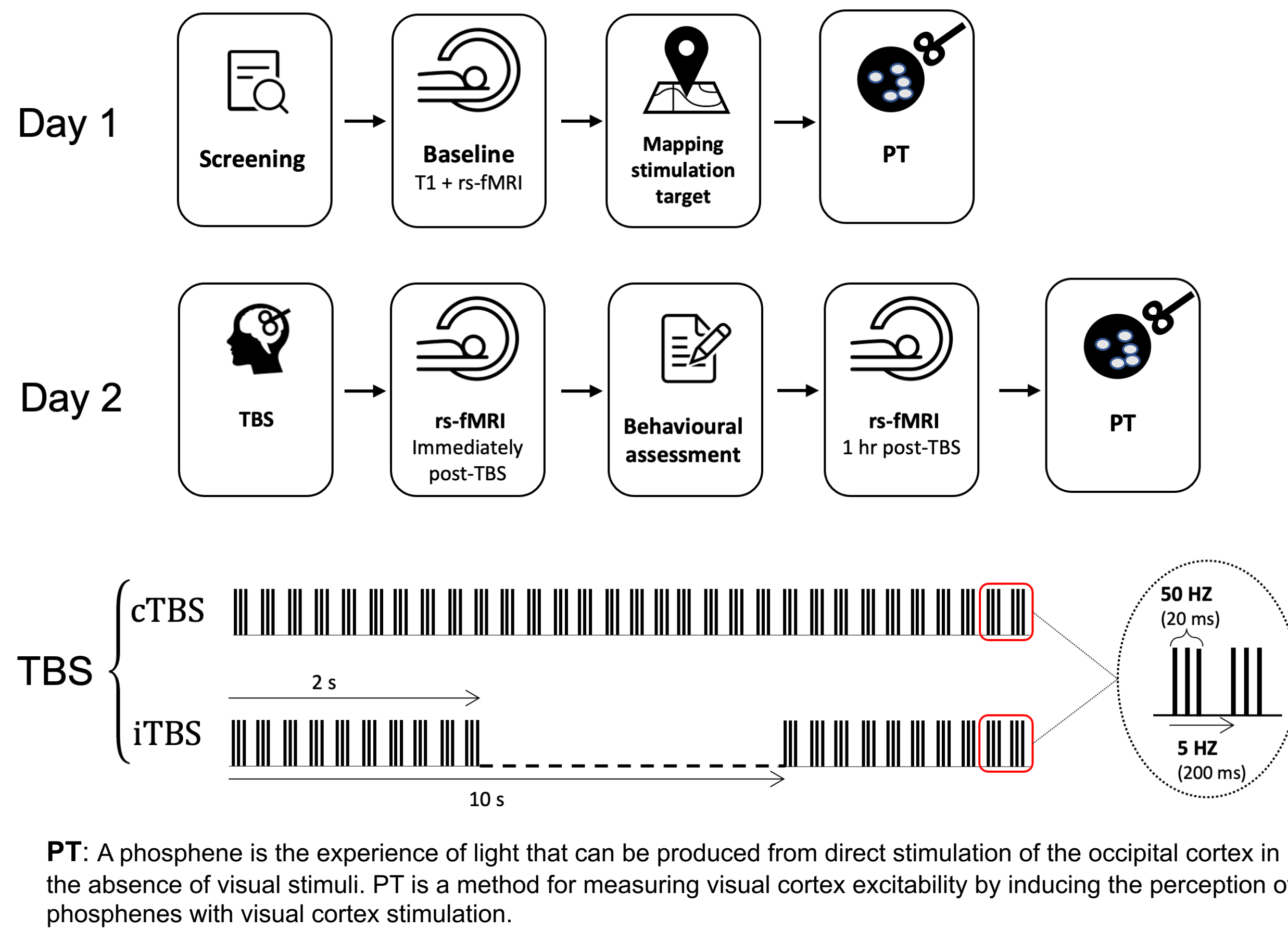
2- Do cTBS and iTBS have different effects on visual networks immediately or at 1 hr post TBS?

3- Does cTBS or iTBS to V1 affect phosphene thresholds (PTs) measured at 1 hr post-TBS?

## PARTICIPANTS

□ **N = 30**

- 17 females,  $M_{age} = 23$  years,  $SD = 4$
- Naïve to TMS, with no history of medical, neurological or psychological disorders
- No contraindications to TMS and MRI
- MoCA and vision assessment



PT: A phosphene is the experience of light that can be produced from direct stimulation of the occipital cortex in the absence of visual stimuli. PT is a method for measuring visual cortex excitability by inducing the perception of phosphenes with visual cortex stimulation.

## METHODS

**Preprocessing & Denoising:**

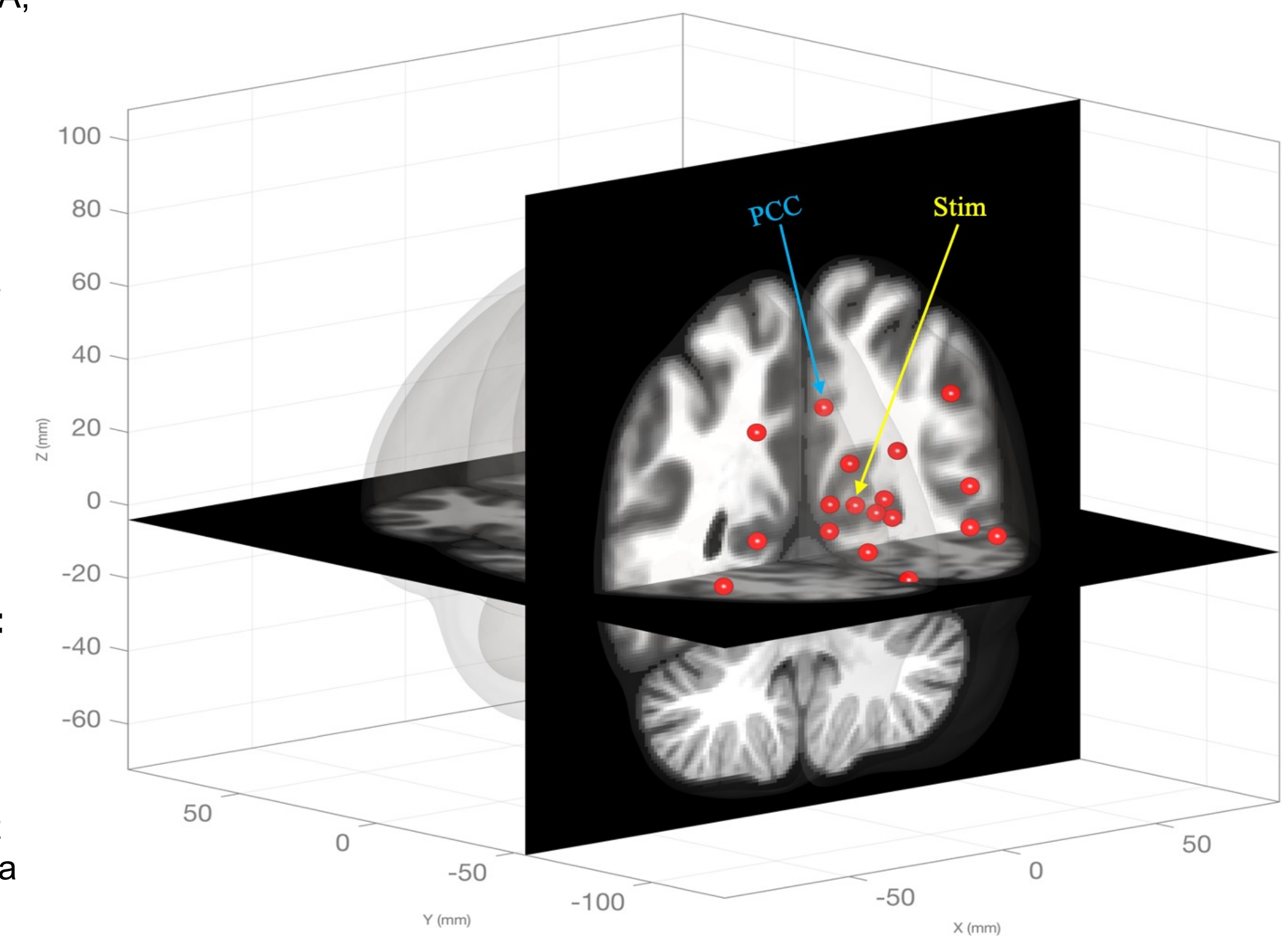
- AFNI and multi-echo independent component analysis (ME-ICA, v3.2).

**1) Volumetric seed-based FC analysis in MNI space:**

- CONN toolbox v20.b<sup>4</sup>
- 10 mm spherical ROI centred at the average stimulation site (V1) coordinates
- Whole brain seed-based FC analysis exploring stimulation site (Stim) and precuneus cortex (PCC) as seeds
- ROI-to-ROI analysis of 18 ROIs with 153 non-overlapping connections including Stim, PCC and others in occipital visual networks. (scan QR code for the list of ROIs)
- Seed-to-Target analysis between Stim and 17 other occipital targets

**2) Surface-based FC analysis with individual parcellation:**

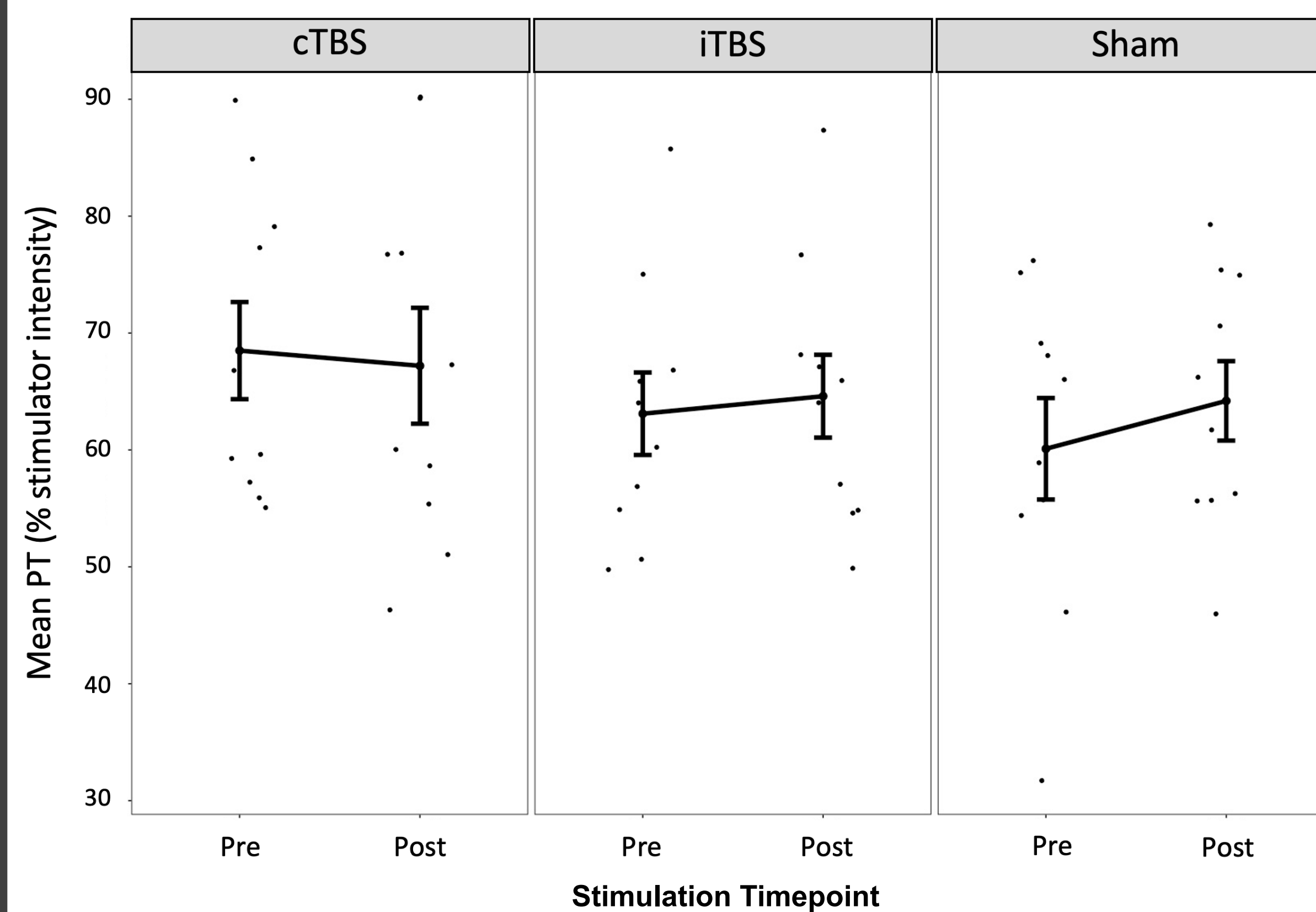
- Individual T1 images were parcellated into anatomical regions using the *recon-all* pipeline in FreeSurfer v6.0.1
- Functional data were resampled to the fsaverage5 template image
- Group Prior Individual Parcellation (GPIP)<sup>5</sup> was used to output subject-specific functional parcellations of the resting state data
- Whole brain FC analysis, ROI-to-ROI analysis and seed-to-target analysis



## RESULTS

### Phosphene Thresholds (PTs)

- No interaction between Stimulation and Time ( $F(2,27) = 2.69, p = 0.086$ )
- Main effect of Stimulation was not significant ( $F(2,27) = 0.552, p = 0.58$ )
- Main effect of Time was not significant ( $F(1,27) = 0.552, p = 0.144$ )



Note. Pre = Day 1 (baseline), Post = Day 2 (1 hr post-TBS)

### Volumetric seed-based FC analysis

**Whole brain seed-based FC (Seeds = Stim & PCC):**

- No significant within- or between-group effects

**ROI-to-ROI (18 Visual network ROIs and 153 unique connections):**

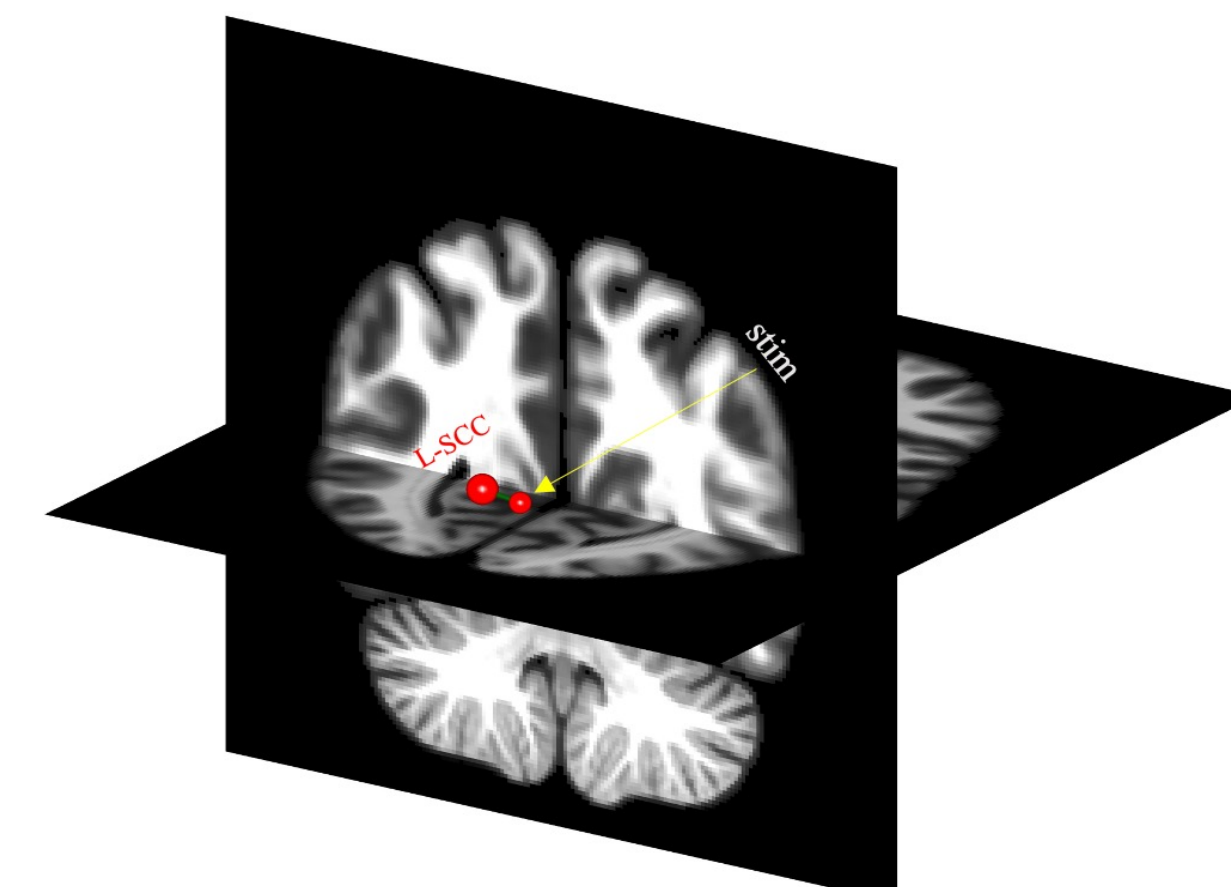
- No significant interaction, and main effects of Stimulation or Time

**Seed-to-Target (Seed = Stim, Targets = 7 visual network ROIs):**

- Between-group analysis revealed one significant connection (See table)
- **However**, within-group Stimulation main effects were not significant

Contrast	Day 2 > Day1					
	Target	Coordinates	Beta	t (18)	p-unc	p-FDR
ITBS > cTBS				N.S.		
Sham > cTBS				N.S.		
ITBS > Sham				N.S.		
	Day2-1hr-post-TBS > Day1					
	Target	Coordinates	Beta	t (18)	p-unc	p-FDR
ITBS > cTBS				N.S.		
Sham > cTBS				N.S.		
ITBS > Sham				N.S.		
	Day2-1hr-post-TBS > Day2					
	Target	Coordinates	Beta	t (18)	p-unc	p-FDR
ITBS > cTBS	L-SCC	-8, -73, 15	0.3	3.59	0.002	0.036
Sham > cTBS				N.S.		
ITBS > Sham				N.S.		

Note. Seed to target analysis results. L-SCC = Left supracalcarine cortex



### Surface-based FC analysis

**Whole brain FC analysis:**

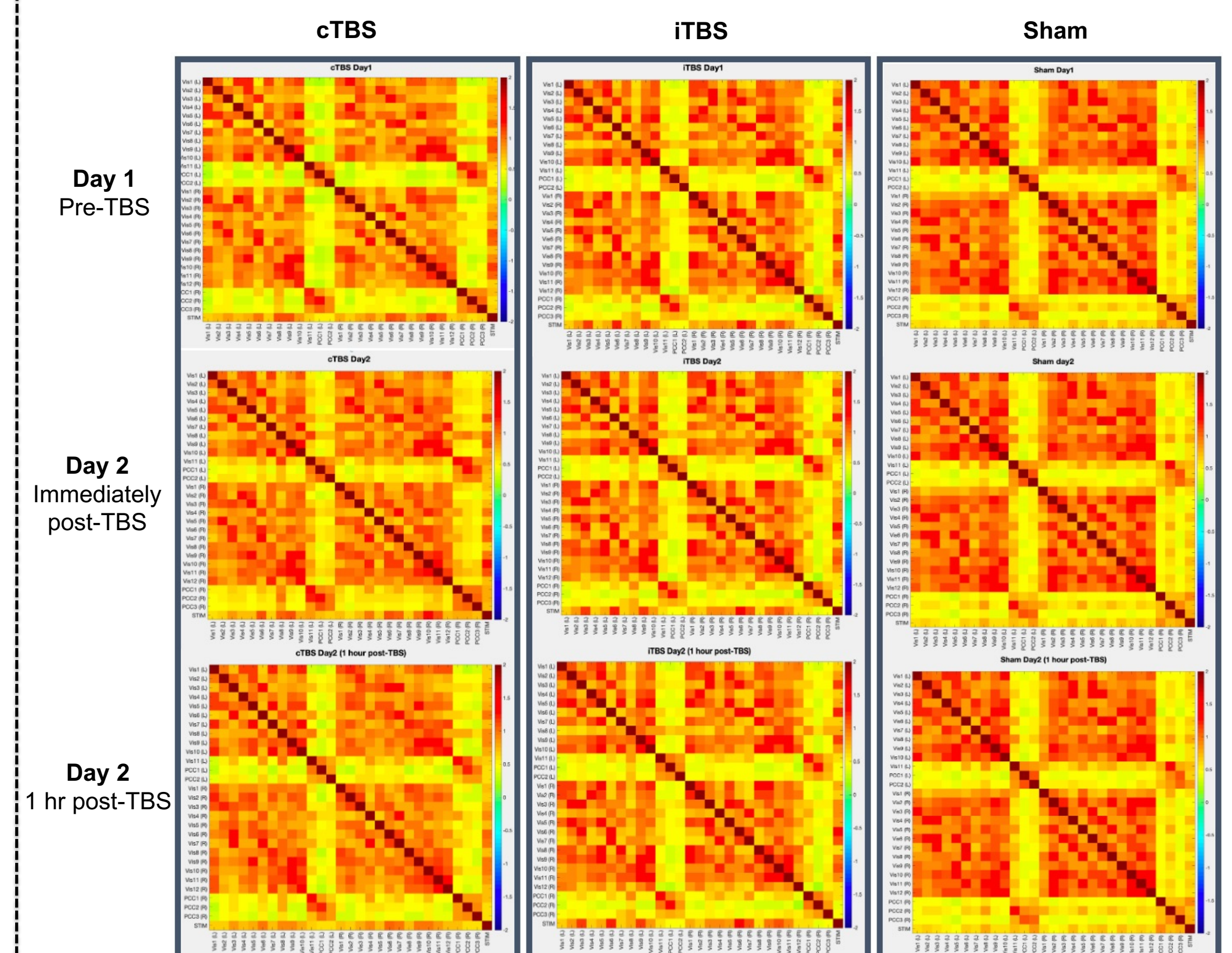
- No significant within- or between-group effects

**ROI-to-ROI:**

- No connection survived the  $p$ -FDR of  $< 0.05$

**Seed-to-Target (Seed = Stim, Targets = 7 visual network ROIs)**

- Same ROI coordinates used in volumetric analysis were converted to the homologous Schaefer atlas regions
- No connection survived the  $p$ -FDR of  $< 0.05$



Note. Uncorrected connectivity matrices using Fisher z-transformation of the Pearson correlation coefficient values for each group and timepoint. Matrices include Schaefer 200-parcel 7-network atlas left and right hemisphere visual network regions, precuneus regions, and the stimulation site.

## CONCLUSIONS

□ TBS did not modulate whole brain or focal FC:

- No significant post-TBS inhibitory or excitatory aftereffects

□ TBS did not affect PTs in any of the groups:

- No difference in PTs from pre-TBS to 1 hr post-TBS

□ These results are in contrast with our previously published low frequency (1 Hz) TMS to V1 in which we found widespread FC changes not immediately, but 1 hr post-stimulation<sup>3</sup>

□ However, these results are consistent with our previously published MRS study that showed cTBS and iTBS did not alter the concentration levels of GABA and glutamate at the stimulation site<sup>6</sup>

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