What if rest is not best?
Considering brain state for individualized FC-based rTMS

Hallee Shearer[1], Jeffrey Eilbott[2], Fidel Vila-Rodriguez[3], Tamara Vanderwal[2,3]

[1]Northeastern University, [2]British Columbia Children's Hospital Research Institute, [3]University of British Columbia

- CONTACT -

✉ h.shearer@northeastern.edu

🦋 @HalleeShearer.bsky.social

💻 Halleeshearer.github.io

- BACKGROUND -

Individualized stimulation targets using functional connectivity (FC): an effort to optimize repetitive Transcranial Magnetic Stimulation (rTMS) for depression.

Three main stages: target definition, target localization, and treatment. All three stages usually conducted at rest.

Common individualized target: the part of the dorsolateral prefrontal cortex most anticorrelated with the subgenual cingulate cortex. Defined with resting state FC[1-2].

Three stages of individualized rTMS treatment
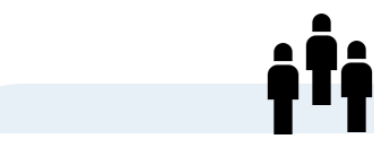
1. Target definition
Under which conditions are participants scanned to first **define** the optimal rTMS target?

2. Target localization
Under which conditions are participants scanned to **localize** their unique individualized target?

3. Treatment
Under which conditions are participants receiving their rTMS **treatments**?

Acquisition Conditions   Treatment Conditions

Figure 1. Individualized FC-based rTMS involves three stages. 1. FC signature of the optimal rTMS target is explored and defined at the group level. 2. That FC signature is localized in an individual patient. 3. rTMS treatment is administered to the patient at the previously localized target.

Effects of TMS stimulation are sensitive to the state of the brain at time of stimulation[3-5]. Brain state during first two stages has largely been overlooked

Difficult to manipulate brain state directly and precisely. Acquisition or treatment condition offers an important – and feasible – method for constraining brain state.
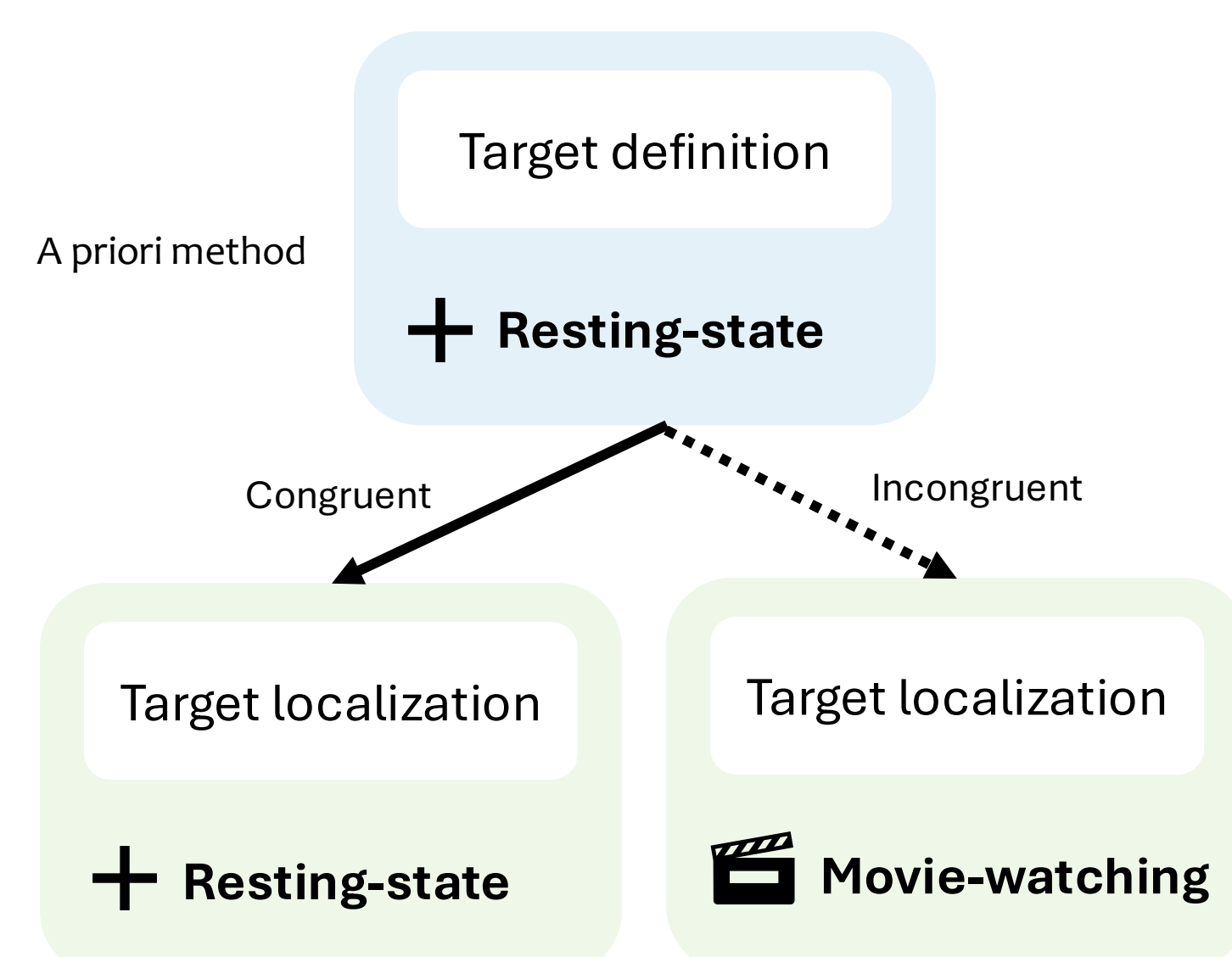
Movie-watching induces more reliable brain states across subjects and repeated scans[6]. Could be leveraged to improve consistency of brain states across stages of individualized rTMS.

- QUESTION -

Does using different scan conditions for target definition and target localization affect target location?
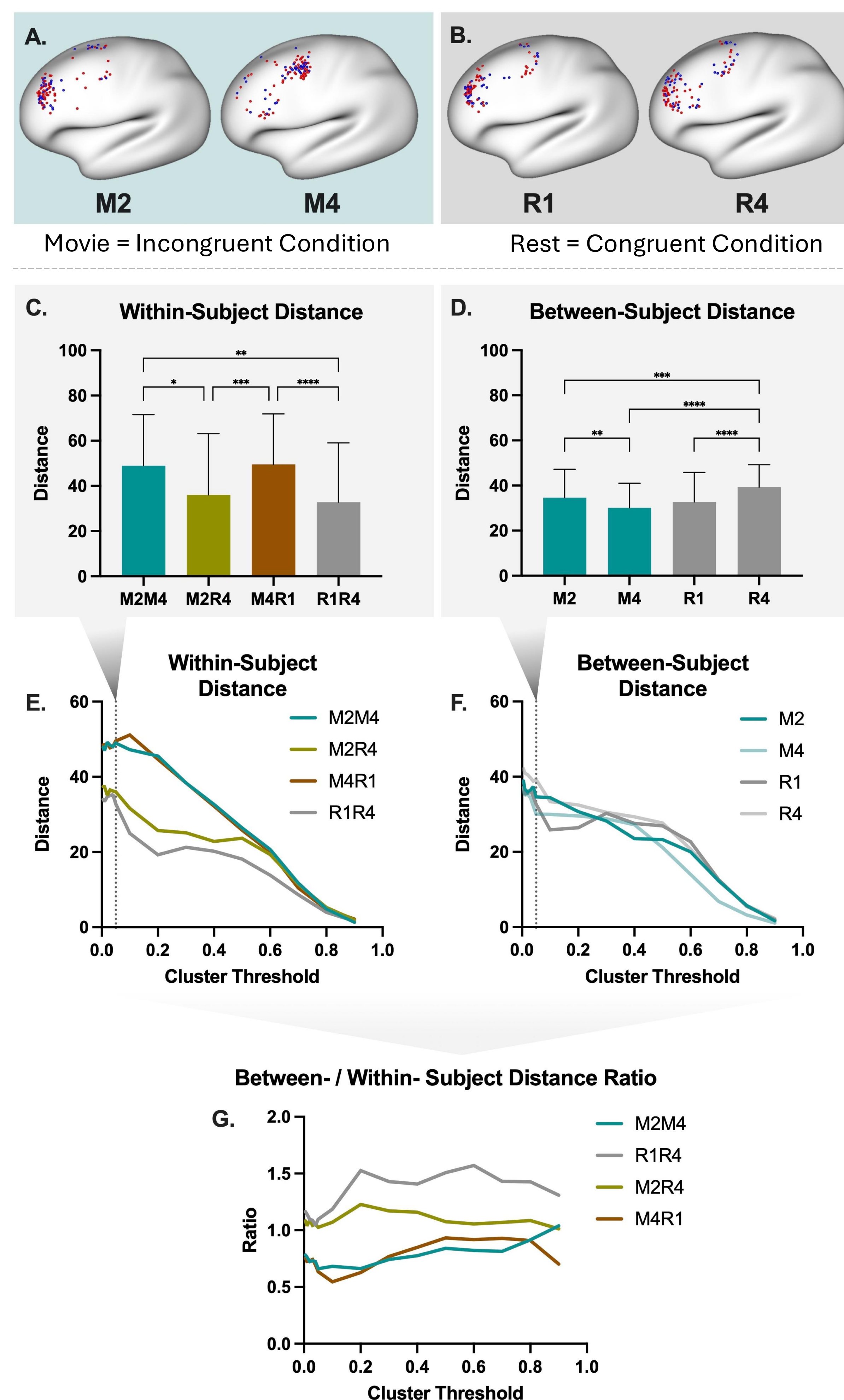
- METHODS -

- HCP 7T data[7]: two resting state scans (R1, R4) and two movie watching scans (M2, M4) were used.
- Individualized rTMS targets were localized in healthy adults (n=109) following Cash et al.[2] during movie and rest.
- Each movie run contained short clips from Hollywood movies, with different clips in each run. Both resting state runs were eyes-open. All runs were ≅ 14 min.

A priori method

Target definition
+ Resting-state

Congruent → Target localization **+ Resting-state**

Incongruent → Target localization 🎬 **Movie-watching**

HCP Data

Figure 2. The SGC-DLPFC individualized FC-based rTMS target[1-2] was defined with resting-state fMRI. We located this target with both resting-state and movie-watching FC, enabling us to assess differences in target location when either congruent or incongruent acquisition conditions were used for the target definition and localization stages.

- RESULTS -

- The locations (Figure 3A-B), reliability (Figure 3C, E), and variation between subjects (Figure 3D, F) of individualized targets varied with acquisition conditions.
- Between-/within-subject distance of targets, of which a high value is optimal, also appears dependent upon condition congruency (Figure 3G).
  - Highest for congruent resting state conditions

A. M2 M4 — Movie = Incongruent Condition
B. R1 R4 — Rest = Congruent Condition

C. Within-Subject Distance (M2M4, M2R4, M4R1, R1R4)
D. Between-Subject Distance (M2, M4, R1, R4)
E. Within-Subject Distance — M2M4, M2R4, M4R1, R1R4
F. Between-Subject Distance — M2, M4, R1, R4
G. Between- / Within- Subject Distance Ratio — M2M4, R1R4, M2R4, M4R1

Figure 3. Localization of resting-state FC defined rTMS targets with rest and movie-watching FC. M2 and M4 contain clips of different movies (not ideal test-retest conditions). M2 = Movie 2, M4 = Movie 4, R1 = Rest 1, R4 = Rest 4. Targets colored by sex in A and B (red = F, blue = M). Results in C and D are shown at a cluster threshold of 5%. Stars denote significance of p < 0.05. Distance measures are all geodesic, in mm.

- CONCLUSION -

- This exploratory initial investigation in healthy adults suggests that consistency in acquisition conditions affects the localization of individualized rTMS targets, but further investigation is required.
- The optimization of brain state for individualized rTMS could offer various advantages.
- The reproducibility of brain states during movie-watching and the goodness-of-fit between movie-fMRI and clinical populations warrant the consideration of movie-watching as an acquisition condition for the three stages of individualized rTMS.

- OPEN QUESTIONS -

- Is there an optimal brain state for rTMS target definition, localization, and treatment?
- Should rTMS treatment be administered under the same conditions as the definition and localization scans?

- ACKNOWLEDGEMENTS -

- REFERENCES -

1. Fox et al. (2013). *NeuroImage* **66**: 151-160.
2. Cash et al. (2021). *Hum. Brain Mapp.* **42**: 4155-4172.
3. Sack et al. (2023). *Biol. Psychiatry.* **95**: 536-544.
4. Silvanto et al. (2021). *Neurosci. Lett.* **742**: 1335538.
5. Fitzgerald et al. (2008). *J. Clin. Psychopharmacol.* **28**: 52.
6. Van der Meer et al. (2020). *Nat Commun.* **11**: 5004.
7. Van Essen et al. (2013). *NeuroImage.* **80**: 62-79.

CIHR IRSC — Canadian Institutes of Health Research / Instituts de recherche en santé du Canada