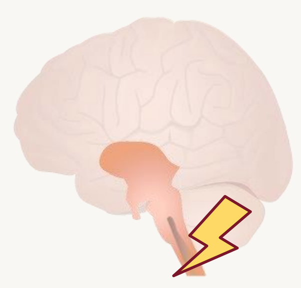
Hyperaligning brainstem connectivity during vagus nerve stimulation

Universitätsklinikum Tübingen
EBERHARD KARLS UNIVERSITÄT TÜBINGEN

Corinna Schulz[1], Anastasia Lado[1], Anne Kühnel[1,2], Vanessa Teckentrup[1,3] & Nils B. Kroemer[1]
[1] Department of Psychiatry and Psychotherapy, Center for Mental Health (TüCMH), University of Tübingen, Tübingen, Germany, [2] Department of Translational Research in Psychiatry and International Max Planck Research School for Translational Psychiatry (IMPRS-TP), Max Planck Institute of Psychiatry, Munich, Germany, [3] Trinity College Institute of Neuroscience, Trinity College Dublin, Dublin, Ireland

Introduction



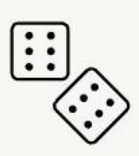
Interest: brainstem as target of large-scale modulatory input e.g., via **non-invasive vagus nerve stimulation (tVNS)** [1]

Problem: **anatomical characteristics** of small brainstem nuclei limit fMRI

Idea: applying **connectivity hyperalignment (CHA),** an **anatomy-free** alignment algorithm to capture shared information content between individuals[2,3]

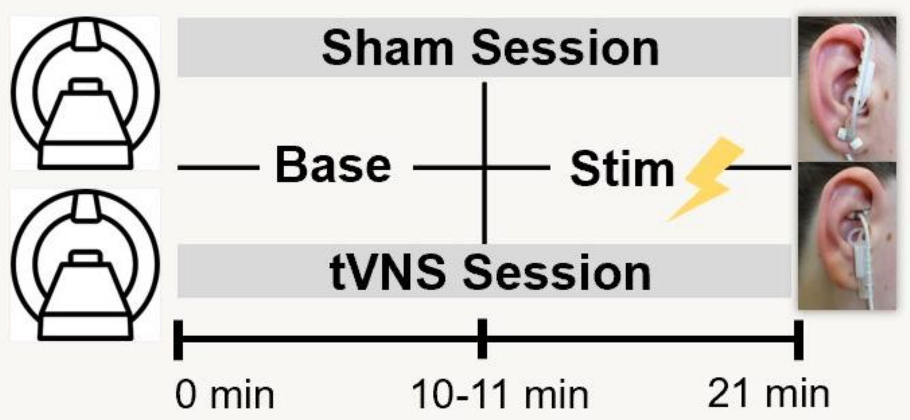
Research question:
Can connectivity hyperalignment improve robustness of brainstem fMRI, such as vagal afferent stimulation effects?

Methods

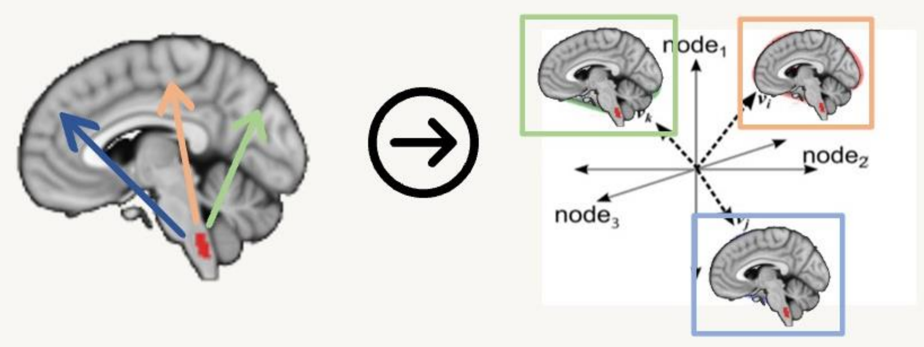


Randomized cross-over design
N = 45, N = 41 included
(22 female; M_{age} = 25.48 years)

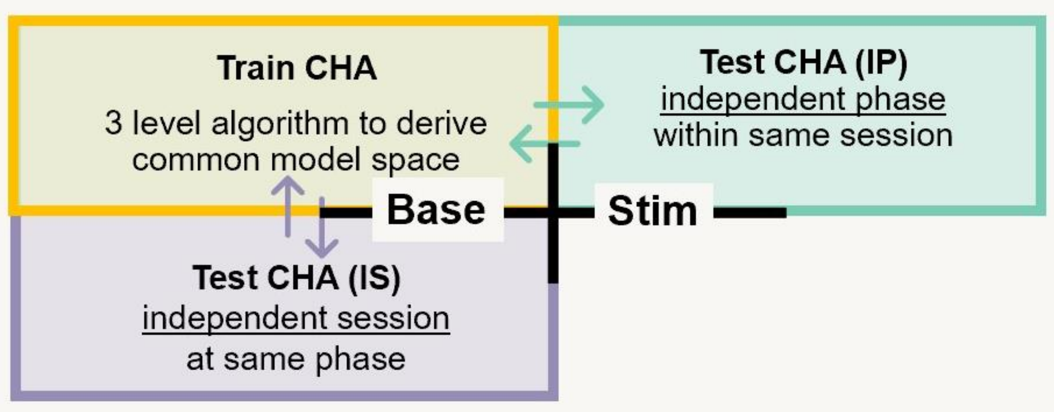
Phase: baseline vs. stimulation; **Stim**: tVNS vs. sham



Functional connectivity
Seed: **NTS** (Nucleus of the solitary tract)
ROIs: **421** cortical + subcortical



Anatomical Alignment | **Connectivity Hyperalignment**[2,3]

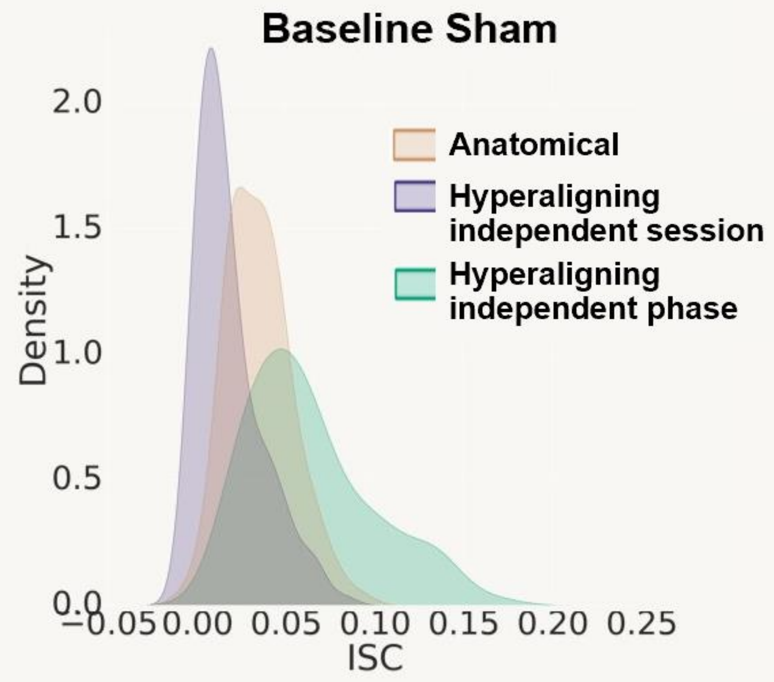


1. Validation: Inter-subject correlations (ISCs) of NTS-ROI connectivity before and after CHA.

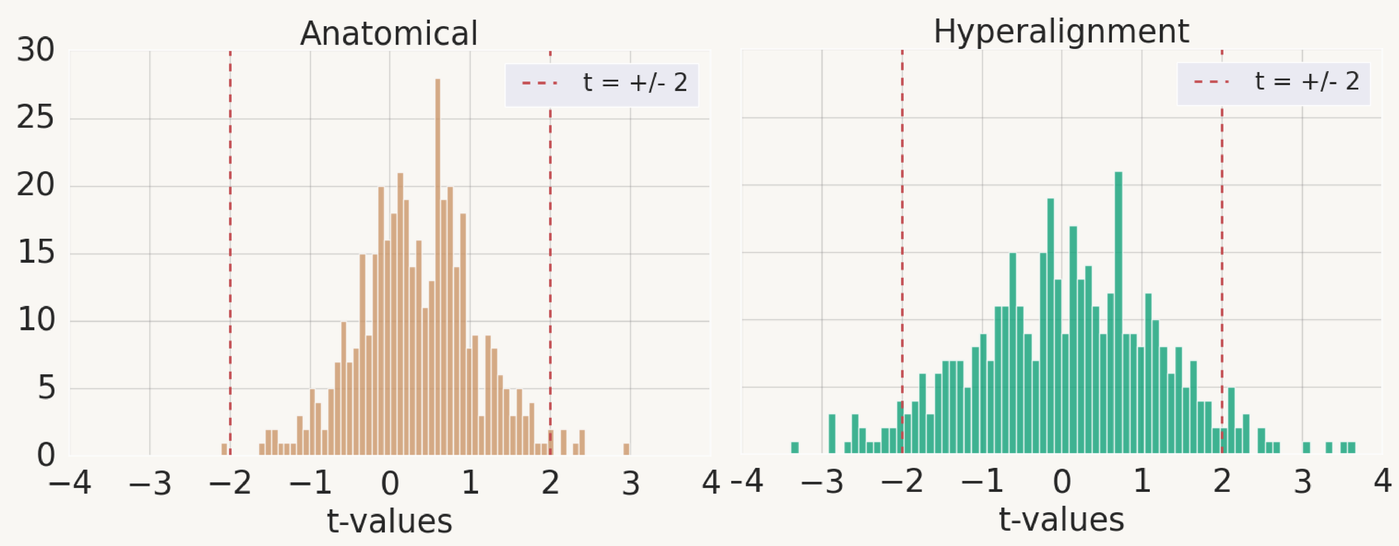
2. Stimulation Effect: Linear mixed models of NTS-ROI connectivity before and after CHA:
~ 1 + (Stim*Phase) + (1 + Stim*Phase | ID)

Results

1. Hyperaligning boosts shared information across phases, but not sessions.

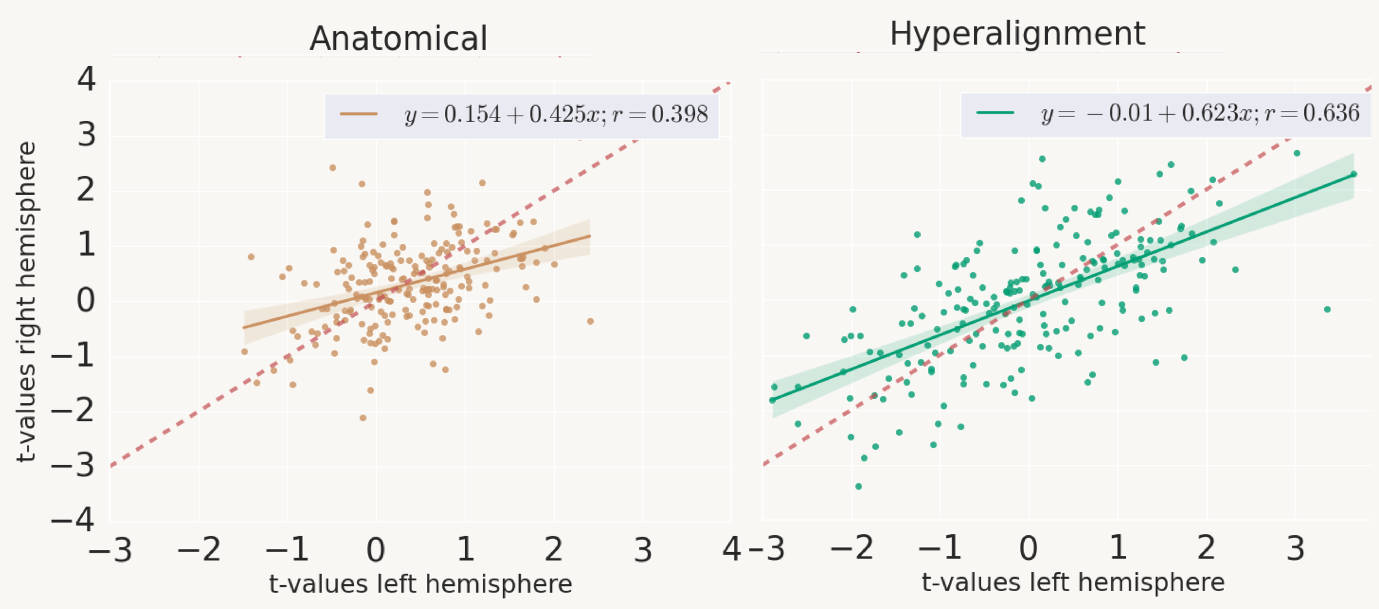


2. Hyperaligning across phases improves the ability to detect region-specific stimulation effects.



* Two Sample Kalmogorov-Smirnov Test, D(412) = 0.214, *p*-value < 0.0001

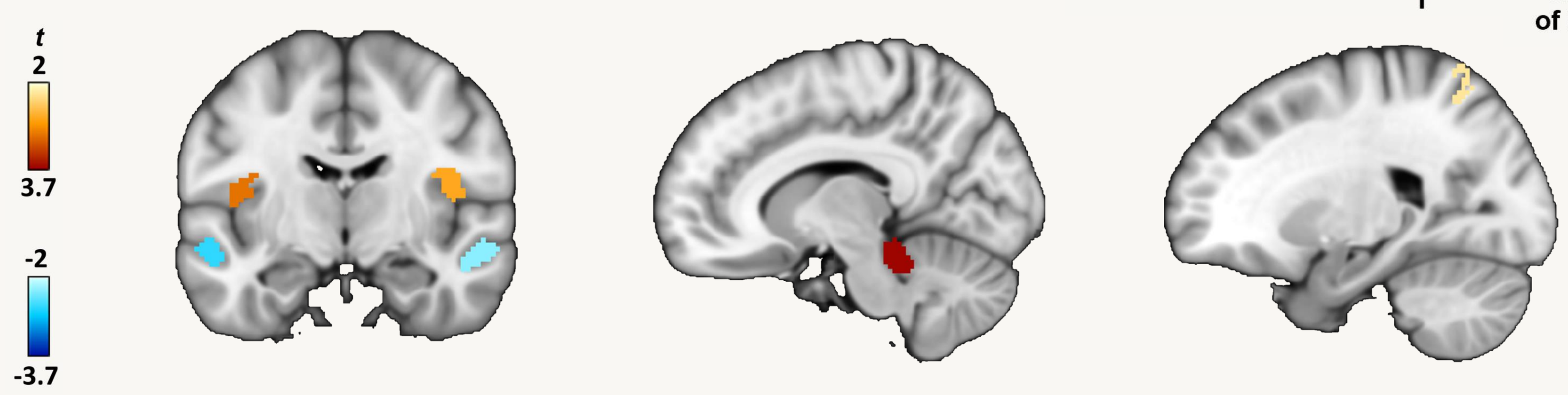
3. Improved alignment displays stronger bilaterality of region-specific stimulation effects.



4. Hyperaligning across phases shows more robust connectivity changes.

Atlas Region	*t*-value* left hemisphere	*t*-value* right hemisphere
Anatomical		
Seventh Visual Area	2.2949	2.9817
Hyperalignment		
Cerebelum 4 5	3.6609	2.2990
Area OP2-3-VS	3.0219	2.6766
Area STSd anterior	-2.6089	-2.2450
Ventral Intraparietal Complex	2.0650	2.1902

*exceeding an uncorrected p-value of 0.05 in both hemispheres



Posterior operculum Mid/Sup Temporal Lobe | **Cerebellum** | **Intraparietal Complex**

Discussion

- Potential of connectivity hyperalignment for **challenging brainstem regions** in improving alignment between participants and **more robust group level inferences** e.g., non-invasive vagus nerve stimulation effects
- **Need to improve the generalizability**: hyperaligning improved ISCs within sessions but not across; potential of hierarchical alignment that first aligns across days **within-subjects**
- **Outlook**: applying connectivity hyperalignment to task fMRI during stimulation

Hyperalignment as a promising method for anatomically challenging targets in the brain which may facilitate future clinical applications

References

[1] **Teckentrup**, V., Krylova, M., Jamalabadi, H., Neubert, S., Neuser, M. P., Hartig, R., … Kroemer, N. B. (2021). Brain signaling dynamics after vagus nerve stimulation. *BioRxiv*, 2021.06.28.450171. https://doi.org/10.1101/2021.06.28.450171

[2] **Guntupalli**, J. S., Feilong, M., & Haxby, J. V. (2018). A computational model of shared fine-scale structure in the human connectome. *PLOS Computational Biology*, *14*(4), e1006120. https://doi.org/10.1371/JOURNAL.PCBI.1006120

[3] **Haxby**, J. V., Guntupalli, J. S., Nastase, S. A., & Feilong, M. (2020). Hyperalignment: Modeling shared information encoded in idiosyncratic cortical topographies. *ELife*, *9*, 1–26. https://doi.org/10.7554/ELIFE.56601

website: neuromadlab.com
e-mail: corinna.schulz@uni-tuebingen.de
@Cor_Et_Cerebrum