Naturalistic Stimulation as a Localizer for Epileptogenic Zone: Insights from Homotopic Functional Connectivity

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Introduction and Background

- **Functional Connectivity (FC)** is explored as a biomarker for epilepsy as a network disorder, capturing abnormalities that structural imaging often misses.[1]
- **Resting-State (RS)** connectivity is widely used but suffers from variability: participants' sensory, perceptual, and cognitive states differ, making benchmark activity patterns hard to establish.[1,2]
- Naturalistic paradigms [e.g., **Movie-Watching (MW)**, narrative listening] present identical stimuli to all participants → align cognitive processes → synchronize neural activity.[2]
- This synchronization appears in the **Blood Oxygen-Level Dependent (BOLD)** signal across sensory regions.[2,3] (*Figure 1*)

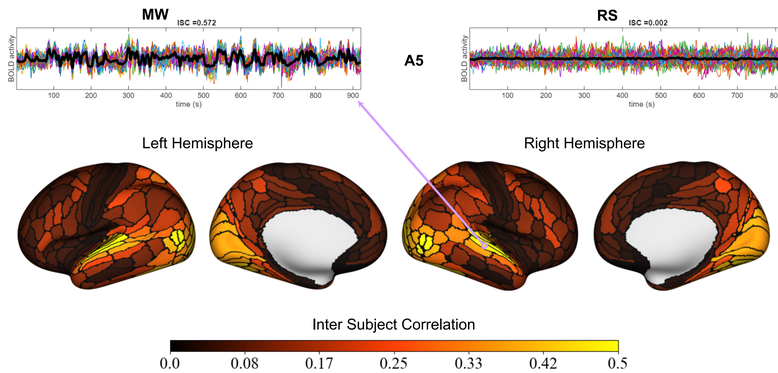


Figure 1. Inter-Subject Correlation (ISC): Average Pearson correlation of BOLD timeseries between participants within each region of interest (**ROI**) during MW. *Top*: Right A5 area BOLD time series for all participants (MW and RS). *Thick black line*: group average BOLD timeseries.

- Homotopic regions (homologous, mirror regions across the 2 hemispheres) are strongly (physically) coupled through the corpus callosum and other commissures. **Homotopic Functional Connectivity (HFC)** is normally very strong[4] and so may be sensitive to abnormal activity. (*Figure 2*)

Objective: To investigate HFC and its temporal dynamics in RS and MW, aiming to identify robust patterns (as potential biomarkers).

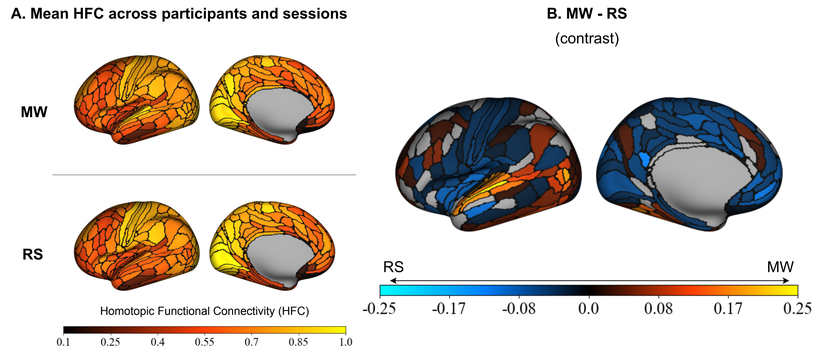
Methods and Materials

- **Participants:** 79 healthy, young, unrelated adults (41 female) from Human Connectome Project (HCP) S1200 release[5]
- **Acquisition & Preprocessing:**
  - TR = 1 s, 7T Siemens MAGNETOM scanner
  - Preprocessed with HCP pipeline, normalized to bilaterally symmetric fsLR template[6]
  - Parcellated into 7 cortical networks and 360 Regions of Interest (ROIs) based on the Glasser multimodal atlas[7]
- **Conditions:**
  - **RS:** 4 × 15 min sessions; rest in the scanner and fixation on "+"
  - **MW:** 4 × 15 min sessions; short film clips (64–259 s, mix of independent and Hollywood films)

Analysis and Results

HFC is stronger in MW than in RS in the auditory cortex

HFC Estimation: Pearson correlation between homotopic ROI time series → averaged across participants & sessions for each condition.



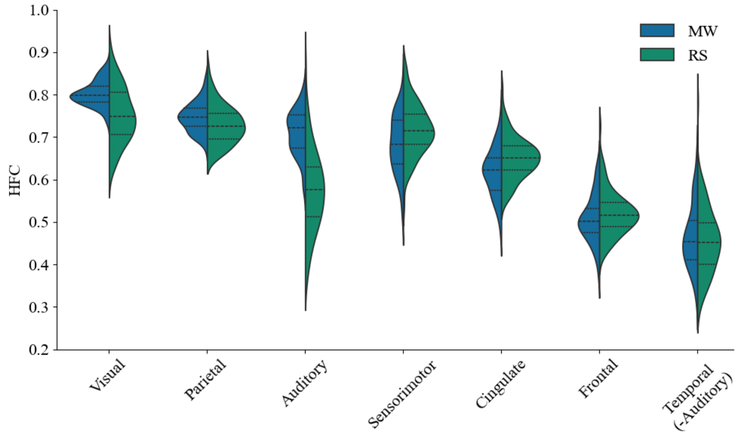


Figure 2. HFC and its distribution across the brain visualized on inflated left hemisphere templates. Black lines indicate ROI boundaries in panels A and B. In panel C, *dashed lines* represent quartiles. In panel B, contrasts are shown only for ROIs with significant differences between MW and RS *($p < 0.05$, FDR-corrected)*.

Conclusions and Discussion

- **HFC** is stronger during MW than RS, especially in the temporal lobe.
- **Dynamic HFC** synchronizes across participants during MW while there is no synchrony during RS in temporal and occipital lobes.
- **Future directions:**

1. Further investigation to clarify whether the observed synchronized connectivity is driven directly by movie stimulation or reflects a byproduct of synchronized neural activity across hemispheres.
2. Compare epilepsy patients' HFC and dynamic HFC with the healthy cohort to investigate how epileptic abnormalities appear in the comparison.

Temporal dynamics of HFC synchronize in auditory & visual cortices during MW (and not RS)

1. **Temporal profiles** for each homotopic ROI pair: Dynamic HFC estimated using non-overlapping **30-s windows** (30 TRs).
2. **Synchrony** was indexed by the average pairwise correlation of temporal profiles across participants (ISC of temporal profiles).

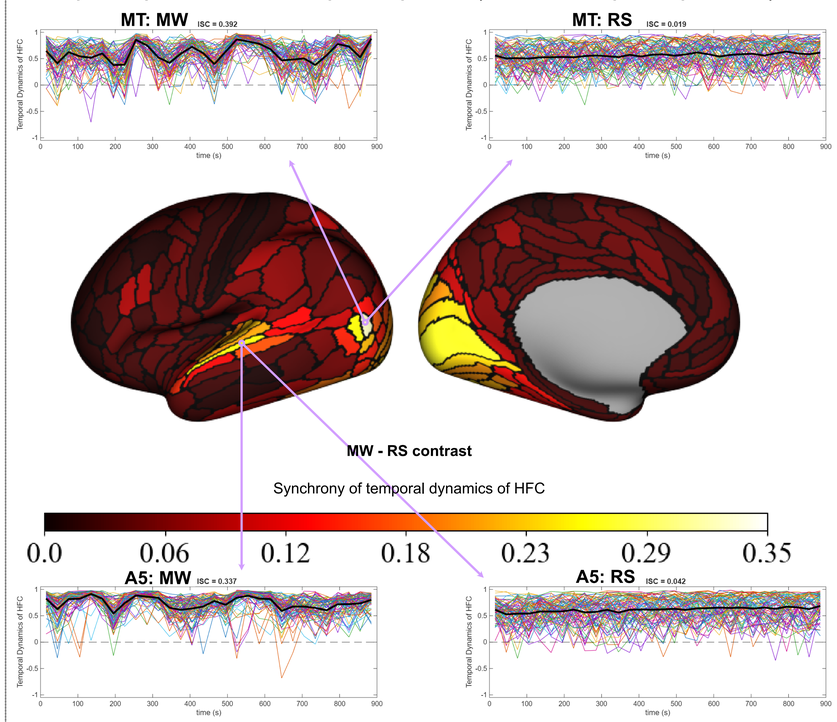


Figure 3. Synchrony of dynamic HFC across participants during MW vs. RS on inflated left-hemisphere template show strongest synchronization in **MT, V1, MST, and A5** in MW that don't exist in RS. Temporal profiles of some of these ROIs are plotted for one MW and one RS session (*thick black line*: group average).

Cortical Network	Visual Cortex	Auditory Cortex	Each of the other networks
Average synchronization change across ROIs (MW-RS)	**0.18**	**0.16**	<0.07

References

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