Feasibility of Localizing Epileptogenic Tissue with Naturalistic Stimulation in fMRI

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Introduction

• During engaging movie watching, fMRI reveals synchronized BOLD signals across the cortex, measurable by **inter-subject correlation (ISC)** [1].

• One in 300 people suffers from medication-resistant epilepsy, leading to significant cognitive and socio-economic impacts [2].

• Surgery, requiring accurate lesion identification, can be an effective treatment but often involves risky and expensive invasive electrode implantation.

• Could this common neural synchronization help safely and cost-effectively locate epileptogenic tissue? Do patients show asynchronous BOLD patterns compared to controls?

Methods

Dataset

• Structural and functional MRI from 47 participants (EpLink: Phase III [3]):
  19 had focal epilepsy (20-60 years)
  18 were healthy controls (19-58 years)
  3 controls and 7 patients were excluded due to hearing loss, stimulus issues or missing data

• Functional runs were acquired during an 8-minute engaging film ('Bang! You're Dead', 1961):
  384 volumes with TR=1250 ms.

Preprocessing

• Preprocessing was conducted using fMRIprep (v. 20.2.6) and FreeSurfer (v. 7.2), followed by confound removal (CSF, white matter, and motion regressors), mapping to the fsLR 32k surface [4], and parcellation utilizing the multimodal Glasser atlas [5].

Inter-subject correlation (ISC) Analysis

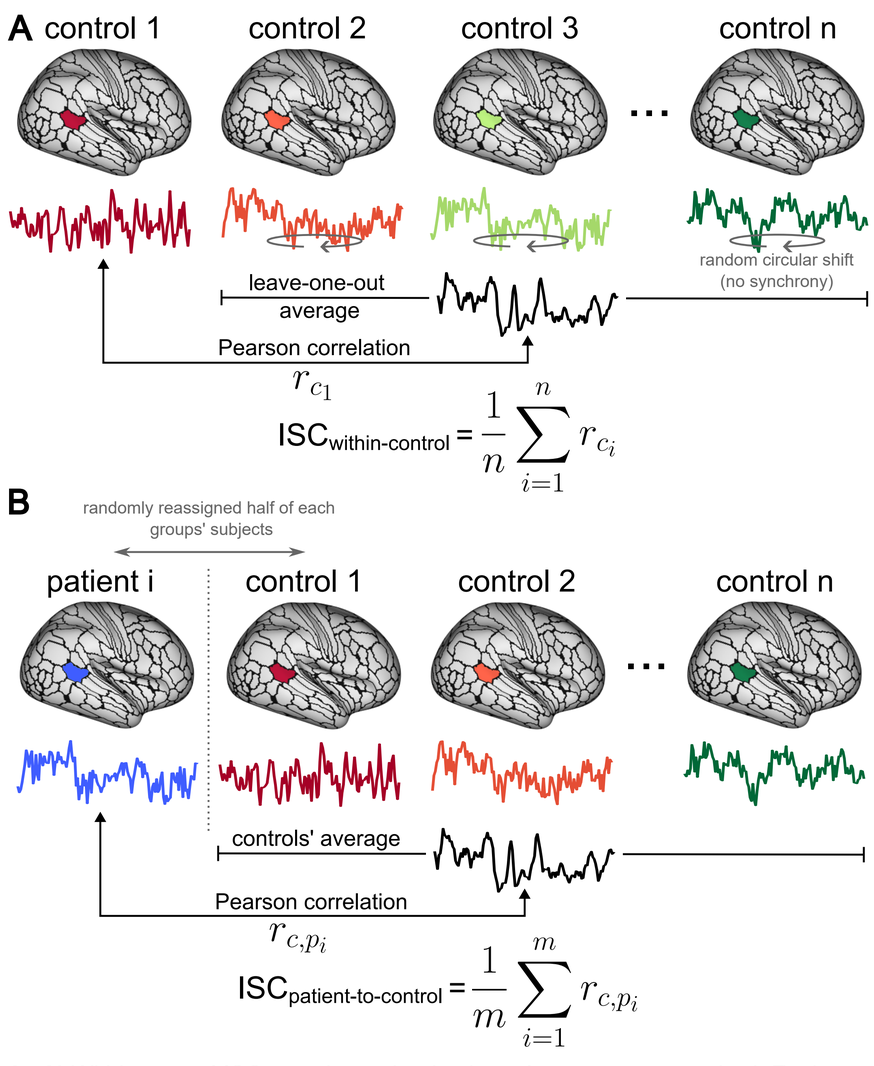
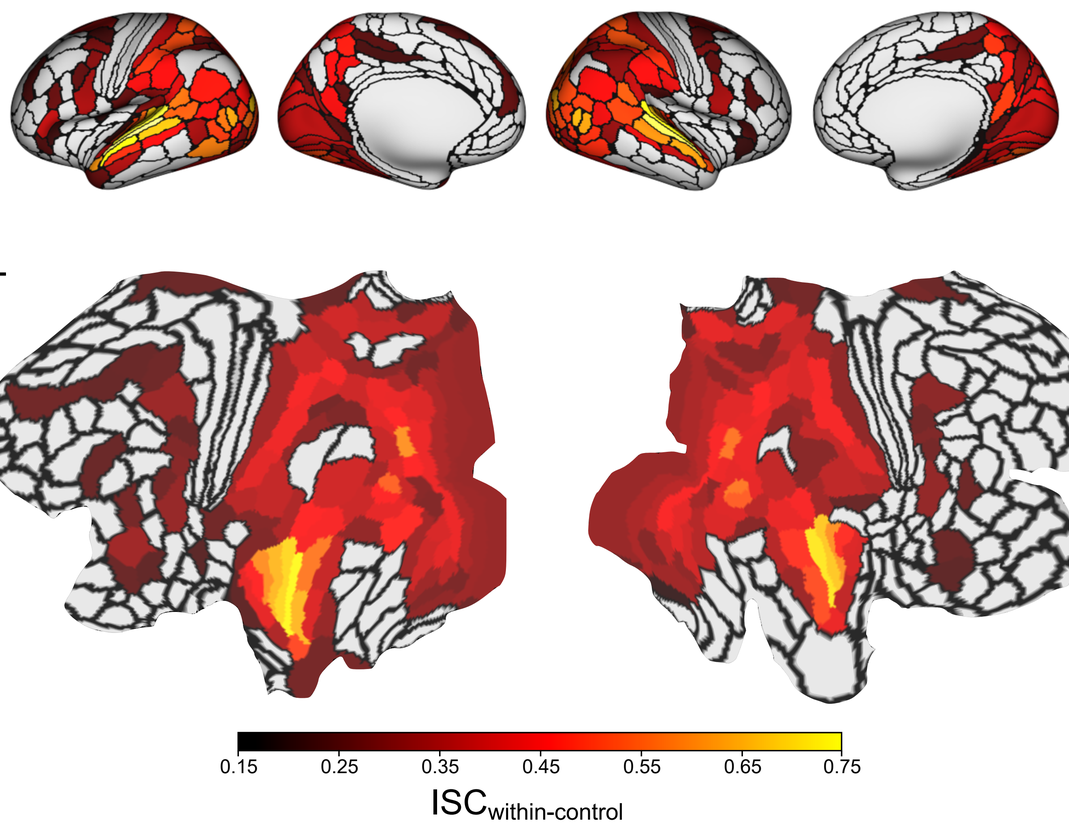


Fig. 1, Methods: A) Within-control ISC was determined using a leave-one-out method. Each control's BOLD time series was correlated (using Pearson correlation) with the average of other controls, and these correlations were then averaged across all controls. For the null distribution of non-synchrony, control time series were circularly shifted 1000 times by random values in the range (0, 384) before averaging (shown in gray)[6]. **B)** Patient-to-control ISC for each ROI involved comparing each patient's BOLD time series with the average of all controls, averaging these correlations across patients. To form the non-parametric null distribution of ISC differences (within-control vs. patient-to-control), half of each group's subjects were randomly switched 10,000 times (depicted in gray). ISCs for each random assignment were recalculated.

Results

A. Regions of interest (ROIs) that exhibit significant ISC within healthy subjects were identified using a non-parametric test



B. Among ROIs with significant ISC within the healthy group some show significantly higher ISC within healthy controls than patients-to-controls

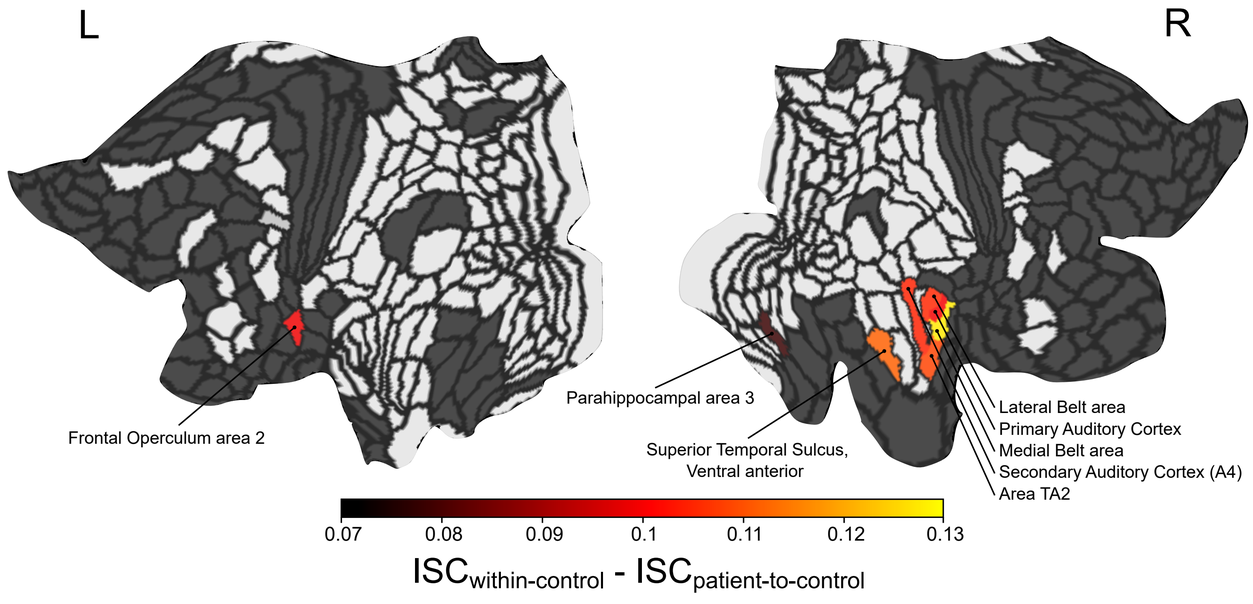


Fig. 2, Results: A) Surface flat map of within-control ISC, significant based on a non-parametric null distribution of no synchrony (N = 18, 1000 permutations, FDR q<0.01 [7]). **B)** Surface flat maps of the ISC differences between within-control (N=18) and patient-to-control (N=19). Within-control ISC was calculated using leave-one-out, and patient-to-control as the average of correlations between each patient and the control group average. Statistical inference was done by a one-tailed permutation test. Null distribution was formed by randomly switching half of each group's subjects across groups 10,000 times. P-values were derived from the proportion of null samples exceeding the original data's difference. FDR correction was applied at q<0.05 in regions from the mask in (**A**) [7]. Gray areas indicate ROIs with nonsignificant within-control ISC, considered noninformative for patient-to-control ISC divergences (inverse of mask from **A**).

Conclusions

• An 8-minute movie-watching paradigm is sufficiently brief to be incorporated into patient assessment, while eliciting robust synchrony (measured by ISC) in many brain regions. This provides wide coverage, especially in the temporal, parietal, and occipital lobes.

• ISC measurement can identify abnormal areas in our focal epileptic patient population.

• The heterogeneity within the epileptic population requires individualized patient examination. Our future research will focus on personalized assessments and evaluating if ISC can detect abnormal tissue consistent with known lesion sites from neuroimaging, surgical outcomes, or SEEG findings, especially when MRI results are negative.

References

1. Hasson, et al. 2004. “Intersubject Synchronization ofCortical Activity during Natural Vision.” Science 303.
2. Wiebe, et al. 2006. “Burden of Intractable Epilepsy.” Advances in Neurology 97.
3. The Epilepsy Research Program of the Ontario Brain Institute (EpLink), https://braininstitute.ca/eplink
4. Van Essen, et al. 2012. “Parcellations and hemispheric asymmetries of human cerebral cortex analyzed on surface-based atlases.” Cereb. Cortex 22.
5. Glasser, et al. 2016. “A Multi-Modal Parcellation of Human Cerebral Cortex.” Nature 536.
6. Tohka. 2016. “Non-Parametric Test for Inter-Subject Correlations.”https://www.nitrc.org/docman/view.php/947/2017/parametric-test-inter.pdf.
7. Benjamini and Yekutieli. 2001. “The Control of the False Discovery Rate in Multiple Testing underDependency.” Annals of Statistics 29..

CIHR IRSC Canadian Institutes of Health Research / Instituts de recherche en santé du Canada
NSERC CRSNG
CONCH Cognitive Neuroscience of Communication and Hearing

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