Language-critical areas serve as connectors across language subnetworks

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Introduction & Approach

"Critical" brain areas are those that disrupt function during electrocortical stimulation (ECS) mapping, a standard-of-care procedure in neurosurgical procedures. ECS has a longstanding clinical history, but its underlying mechanisms remain poorly understood. This multi-center study aims to uncover the details behind ECS, for example: does ECS affect primarily local cortex? Alternately, does ECS influence remote cortical areas, and/or underlying white matter? We are currently investigating these questions in the brain's speech/language network.

Results - Static Analysis

Hsieh et al. (2024) Nat Comm 15:7897

- Critical node local connectivity (CC, LE, EC) was lower than non-critical nodes, while global connectivity (Strength) was not different
  - Language Error nodes had higher PC than others

  → Critical nodes function as connectors between regions
- Best decoding accuracy was 73% for critical nodes, 78% for language error nodes, 77% for speech arrest nodes.

Results - Dynamic Analysis

- Trial-averaged data can produce the same correlation structure as whole-record data
- Dynamic connectivity metrics--on average--follow similar patterns as static-calculated metrics, but show substantial changes during language processing.
- ΔPC alone can be used to distinguish critical from non-critical nodes
- Looking ahead: including dynamic conn. metrics as decoding features

1. METHODS

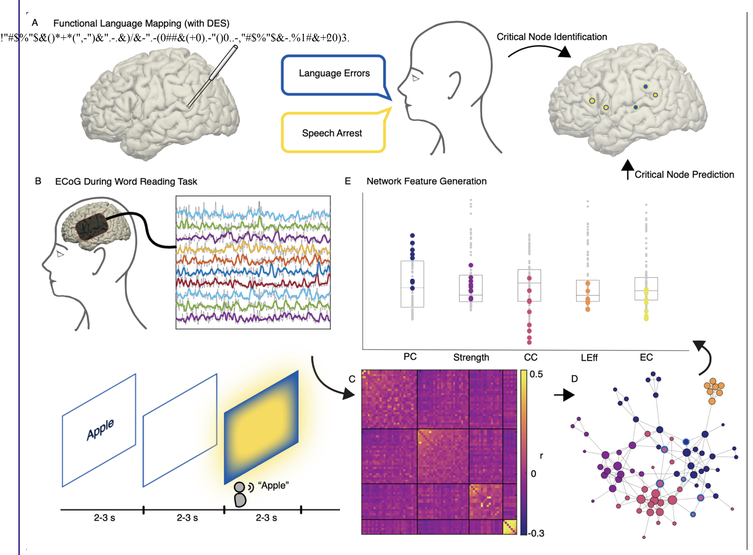


Figure 1

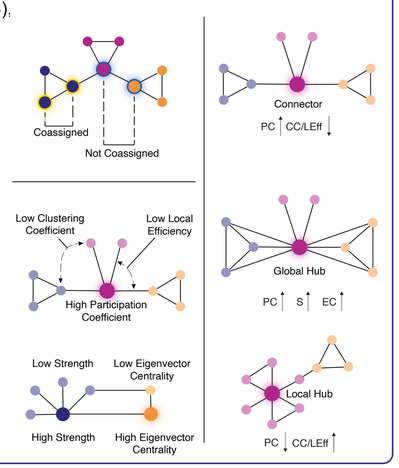
- 16 human participants underwent awake craniotomy & functional mapping (**A**) for localization of epileptogenic areas or prior to tumor resection.
- ECoG recorded (2 kHz sampling) during word-reading task (**B**).
- Static Connectivity analysis:
  - Adjacency matrix (**C**) calculated from pairwise correlations (Edges) between ECoG high-frequency power (70-300Hz), calculated at each electrode (Node).
  - Network community detection (**D**) using modularity optimization

$$Q(\gamma) = \frac{1}{2m}\sum_{ij}[a_{ij} - \gamma p_{ij}]\delta(\sigma_i, \sigma_j)$$

  then consensus community ID algorithm.
  - Calculation of 5 network metrics (**E**; see also **Figure 2**):
    - Participation coefficient (PC)
    - mean connection Strength (S), aka Degree
    - Clustering coefficient (CC)
    - Local efficiency (LE)
    - Eigenvector centrality (EC).
- Classification of critical vs non-critical nodes (top right) using metrics as input features

Figure 2

Example networks and their descriptions by the selected network connectivity metrics



2. RESULTS

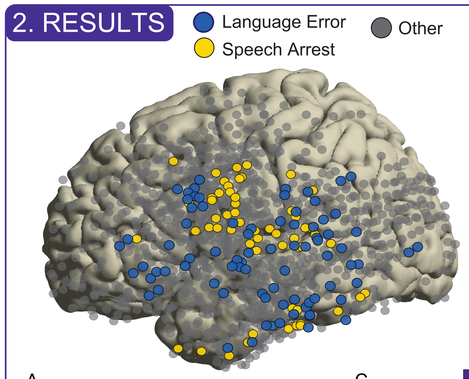


Figure 3. Composite of all electrodes (16 pts) colocalized on a template brain.

Table 1.

Mean ± S.D. number electrodes / pt (after noise channel removal)	77 ± 35
Mean ± S.D. number critical electrodes (ECS defined)	10 ± 4
Mean ± S.D. language error electrodes	6 ± 4
Mean ± S.D. speech arrest electrodes	4 ± 3

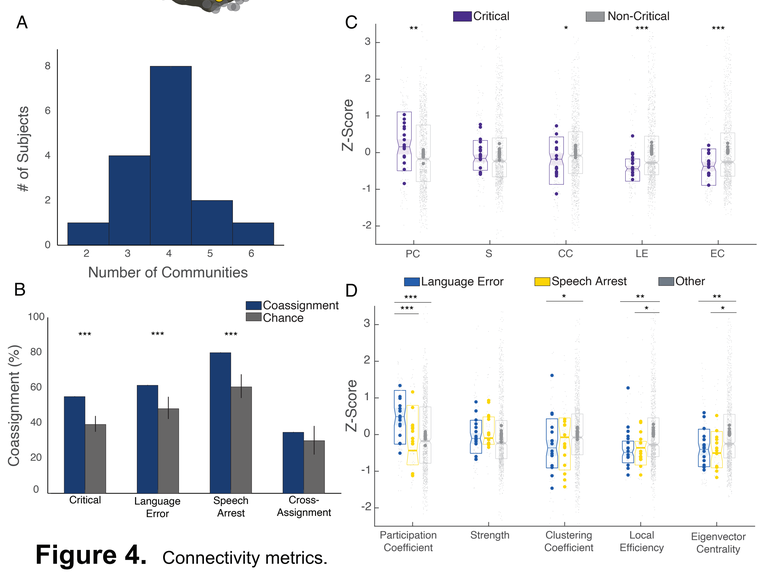


Figure 4. Connectivity metrics.

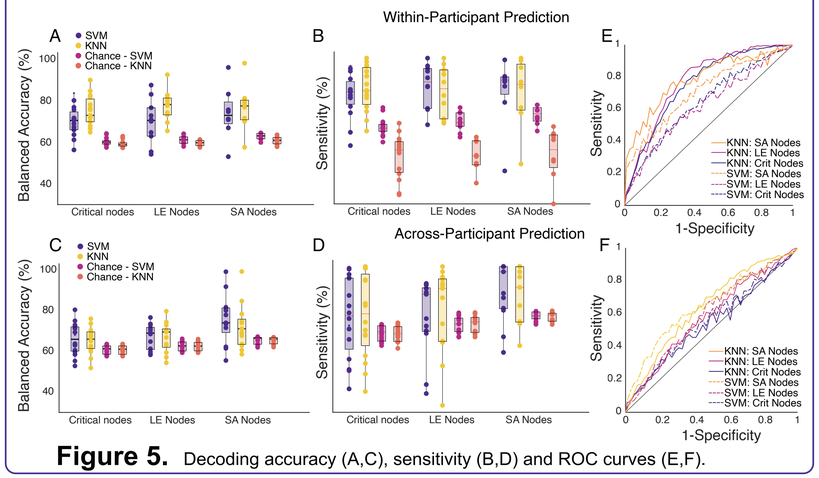


Figure 5. Decoding accuracy (A,C), sensitivity (B,D) and ROC curves (E,F).

3. RESULTS

Current → Future work

Dynamic connectivity analysis

Methods

- Data from Fig. 1-5
  - Trial-averaged around voice onset and/or stimulus presentation (~99% data length reduction)
  - Slice length 0.75s, bin at 0.075s
  - Multislice modularity[1]
  - consensus community IDs[2]
  - parameter optimization [γ,C] here, optimized based on ΔPC

$$Q_{\text{multislice}} = \frac{1}{2\mu}\sum_{ijsr}\left\{\left(A_{ijs} - \gamma_s\frac{k_{is}k_{js}}{2m_s}\right)\delta_{sr} + \delta_{ij}C_{jsr}\right\}\delta(g_{is}, g_{jr})$$

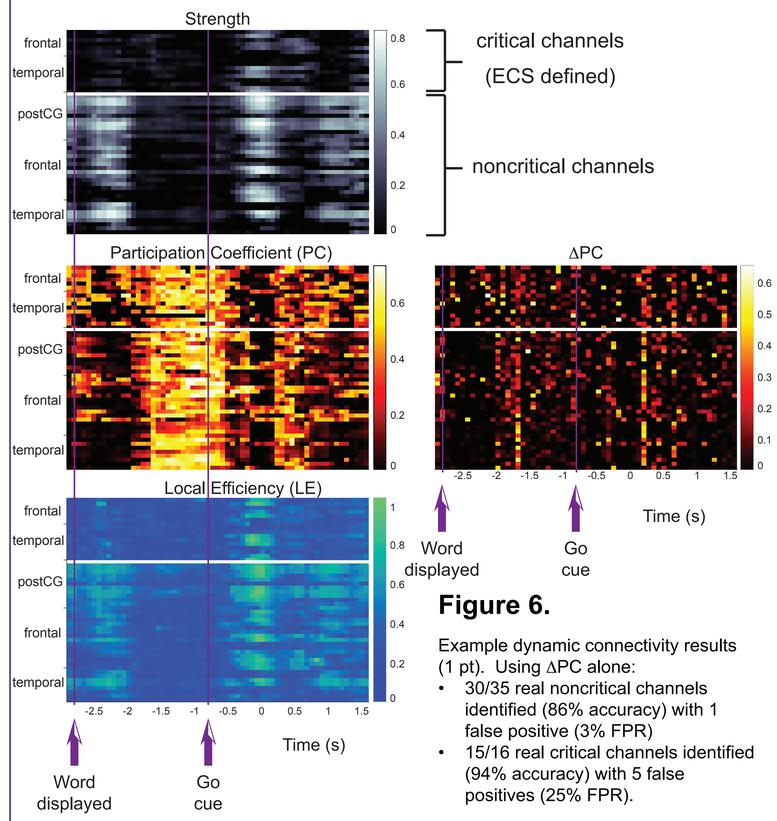


Figure 6.

Example dynamic connectivity results (1 pt). Using ΔPC alone:

- 30/35 real noncritical channels identified (86% accuracy) with 1 false positive (3% FPR)
- 15/16 real critical channels identified (94% accuracy) with 5 false positives (25% FPR).

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References

1. Mucha et al. (2010), *Science* 328:876
2. Lancichinetti and Fortunato (2012), *Sci Rep* 2:336

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