**Network analysis of anatomical brain regions' synchronization and competition**

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**Abstract**

**Objective**: This project aims to investigate the network characteristics of brain functional connectivity during the resting state, and focuses on comparing pre-task and post-task networks and exploring inter-individual differences.

**Methods**: We preprocess the original fmri scan data at first. Then we compute the functional connectivity matrices for each participant by correlating time series extracted from predefined regions of interest (ROIs) using the Automated Anatomical Labeling (AAL) atlas and additional atlases for comparison. We set up the network according to the matrices and apply network metrics such as degree distribution, clustering coefficient, and small-world properties to characterize the network organization. We evaluate the consistency of network metrics both across the 33 participants and between pre- and post-task resting states.

**Results**: Key findings reveal decreased synchronization and clustering coefficients post-task, increased modularity indicating greater network segregation, and higher variance in synchronization during sleep. Temporal brain regions consistently emerged as central nodes, reflecting their critical role in brain dynamics. These results provide new insights into the interplay between local specialization and global integration in brain networks under varying conditions.

**Discussion**: The study faces challenges with neuroimaging data complexity, method selection, and parameter optimization for network construction. Integrating EEG data offers potential insights but increases processing demands. The small dataset size limits generalizability, and preprocessing is still ongoing. Future efforts will focus on refining methods, completing analysis, integrating multimodal data, and validating findings with larger datasets.

**Conclusion**: Our findings highlight how task-related activities and sleep states influence brain connectivity, suggesting that modularity and centrality measures can reveal key aspects of neural adaptability. Further exploration of multi-modal neuroimaging data could enhance our understanding of these dynamic processes.

**Introduction**

Resting-state functional MRI (R-fMRI) has become a critical method for understanding the brain's intrinsic activity. By capturing spontaneous fluctuations in the blood oxygen level-dependent (BOLD) signal, R-fMRI provides unique insights into the brain's baseline functional organization, offering a different perspective from traditional task-based neuroimaging approaches (Wang et al., 2010).

Graph theory has emerged as a powerful analytical framework for characterizing functional brain networks. By representing the brain as a network of interconnected regions, researchers can quantify critical network properties like small-worldness, modularity, and hub structures. These metrics reveal how brain networks balance local specialization with global integration.

This study utilizes a multimodal neuroimaging dataset from Pennsylvania State University, which includes simultaneous EEG and fMRI recordings during resting and sleep states (Gu et al., 2023). We conducted a graph-based analysis of functional connectivity in 33 healthy participants, focusing on network characteristics across pre-task and post-task resting states. Our research aims to explore how task engagement influences intrinsic brain connectivity and examine the methodological implications of using different brain atlases in functional connectivity research.

**Materials and Methods**

The dataset used in this study consists of resting-state fMRI data from 33 healthy participants, collected at Pennsylvania State University with informed consent. Resting-state data were acquired using a Siemens 3T Prisma scanner with a 20-channel receive-array coil. Each participant underwent a 10-minute pre-task resting-state scan, during which they were instructed to remain still with their eyes closed.

Functional imaging data were acquired using an echo-planar imaging (EPI) sequence with the following parameters: repetition time (TR) = 2100 ms, echo time (TE) = 25 ms, slice thickness = 4 mm, field of view (FOV) = 240 mm, in-plane resolution = 3 mm × 3 mm, and 35 axial slices. Anatomical images were also acquired using a T1-weighted MPRAGE sequence for spatial normalization and ROI definition.

Regions of interest (ROIs) were defined using the Automated Anatomical Labeling (AAL) atlas, and additional analyses were conducted using alternative atlases for comparative purposes. Time series data were extracted from each ROI for subsequent functional connectivity analysis.  
  
**Methods**

**Workflow Overview**

Our analysis involves the construction and investigation of functional brain connectivity networks derived from resting-state functional MRI (fMRI) data. The workflow encompasses data preprocessing, region-of-interest (ROI) definition, time series extraction, functional connectivity computation, and network analysis. Below, each step is described in detail.

**Tools**

We use various tools to support different aspects of data handling, analysis, and visualization. Numpy and Pandas , as well as matplotlib subprocesses are used for basic operations and debugging. Nibabel was employed for loading and saving MRI data, enabling smooth access to both anatomical and functional scans. nipype for interface to various neuroimaging tools and software, especially FSL in our project, and managing preprocessing workflow. Docker ensured a reproducible and isolated environment for preprocessing pipelines and enhanced the consistency of our workflow. NetworkX facilitated the construction and analysis of connectivity networks. Additionally, Gephi is used for visualizing and exploring network structures.

**Data Preprocessing**

We do the data preprocessing to clean, normalize, and transform data for ensuring quality and reliability. Here are key preprocessing steps we do:

* Skull-stripping: Removing non-brain tissues such as the skull, eyes, and face from anatomical MRI scans.
* Affine Registration: Aligning brain scans to the MNI 152 template to achieve consistent spatial orientation using transformation matrices.
* Nonlinear Registration: Refining alignment through complex transformations to match the field of view, resolution, and anatomical position to the template.
* Motion Correction: Adjusting fMRI images to account for head movements and ensure accurate analysis.
* Spatial Smoothing: Reducing noise by averaging voxel intensities using a Gaussian kernel.
* Warping: Mapping functional data into standard MNI space for cross-subject analysis using computed transformations.
* Nuisance Regression: Removing physiological noise (e.g., heart rate, respiration) and motion artifacts via linear regression.
* Temporal Smoothing: Enhancing neural signal detection by filtering high and low-frequency noise.
* Defining Regions of Interest (ROIs) & Extracting Time Series

After that, brain atlases were utilized to segment the brain into predefined anatomical regions. The mean signal for each region was calculated to enable correlation analysis.

**Functional Connectivity Matrix**

Correlation coefficients between time series of each pair of ROIs were computed to construct connectivity matrices. Both positive and negative correlations were considered, with absolute values used as edge weights for network construction.

**Challenges in Preprocessing**

* Misalignments in Real-World Coordinates:Affine registration failures led to faulty mapping matrices with unusually large translation components, requiring numerous adjustments and retries.
* The final workaround involved nonlinear registration without initialization, though suboptimal, it yielded acceptable results.
* Misalignments impacted grey/white matter and cerebrospinal fluid segmentation, introducing noise. Despite this, noise effects on temporal correlations were minimal due to graph construction on temporal relationships within the same brain regions.

**Network Construction**

Network construction in this study involved creating graphs that represent functional connectivity patterns in the brain based on resting-state fMRI data. The process is detailed as follows:

#### 1. Define Nodes: Regions of Interest (ROIs)

* **Selection of Brain Atlas:** The Automated Anatomical Labeling (AAL) atlas was used to segment the brain into approximately 90 predefined regions, each serving as a node in the network. These regions represent specific anatomical or functional brain areas.
* **Time Series Extraction:** For each ROI, the mean Blood Oxygenation Level-Dependent (BOLD) signal was calculated across all time points. This time series captures the average activity level within each region over time.

#### 2. Define Edges: Functional Connectivity

* **Correlation Computation:** Pairwise Pearson correlation coefficients were computed between the time series of all ROI pairs. This correlation quantifies the linear relationship between activity in different brain regions.
  + **Positive Graphs:** Retain connections with positive correlations.
  + **Negative Graphs:** Retain connections with negative correlations.
  + **Edge Weights:** The absolute value of the correlation coefficients was used as edge weights to represent the strength of connectivity.

#### 3. Graph Construction

* Using the processed connectivity matrix:
  + **Nodes:** Represent ROIs.
  + **Edges:** Represent significant connections (either weighted or binary).
  + Graphs were constructed as **undirected** and **one-mode**, meaning that connections are symmetrical and only between ROIs.

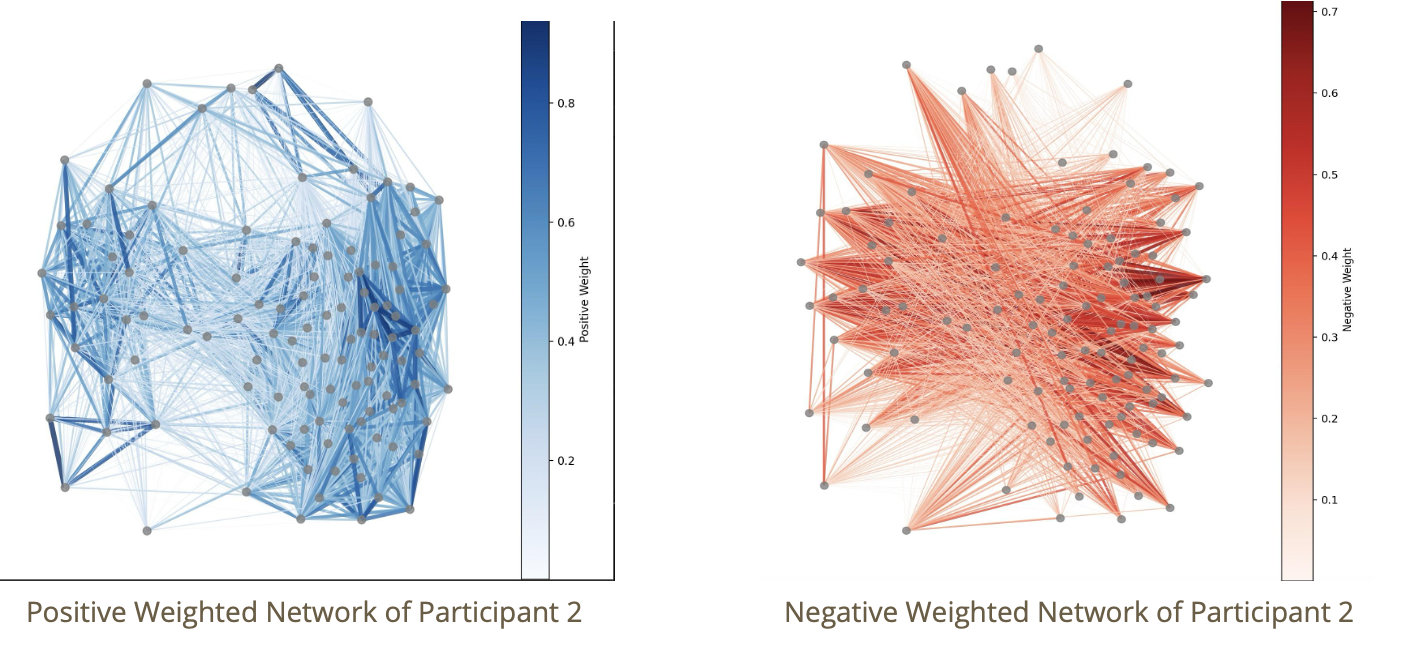
#### 4. Individual Networks

* Separate graphs were constructed for each participant and for each state:
  + **Pre-task:** Represents baseline functional connectivity.
  + **Post-task:** Captures changes in connectivity after task performance.
  + **Sleep:** Represents functional connectivity during sleep.

#### 5. Visualization

* The constructed graphs were visualized to provide insights into the network structure:
  + Dense regions in the graphs indicate areas of high connectivity.
  + Sparse regions highlight areas with limited interactions.

The visualization of our network is shown at **Figure1**.



**Figure 1.** Visualization of Network

**Metrics**

We computed several key metrics to analyze the dynamic changes in brain connectivity across different states (pre-task, post-task, and sleep):

#### 1. Clustering Coefficient

* The clustering coefficient measures the tendency of a node’s neighbors to form tightly-knit groups. It provides insight into local connectivity and integration within the network.
* Relevance to Brain Networks:
  + A high clustering coefficient suggests specialized processing within localized clusters of brain regions.
  + Lower clustering coefficients post-task indicate a shift from localized integration toward global network integration, which may facilitate broader information flow across the brain.

#### 2. Degree Centrality

* Definition: Degree centrality represents the number of direct connections (or edges) a node has within the network. For weighted graphs, it considers the sum of connection strengths (edge weights) instead of binary counts.
* Relevance to Brain Networks:
  + High degree centrality nodes are considered hubs, playing a critical role in boosting activity across the network.
  + In positive graphs, higher degree centrality reflects greater synchronization across regions, whereas lower centrality indicates reduced synchronization post-task.
  + In negative graphs, increased degree centrality post-task suggests energy reallocation and reduced regional synchronization.

#### 3. Modularity

* Modularity quantifies the degree to which a network can be divided into distinct modules or communities. Modules are groups of nodes that are densely connected internally but sparsely connected to other groups.
* Relevance to Brain Networks:
  + An increase in modularity post-task suggests the brain’s reorganization into more segregated functional modules, potentially improving task efficiency and adaptability.
  + Modular structures reflect the brain’s ability to compartmentalize functions and maintain efficient processing despite changing demands.

#### 4. Node-Specific Metrics

* Key Nodes Identified:
  + Temporal regions, including Temporal\_Mid\_L (Node 84), Temporal\_Sup\_L (Node 80), and Temporal\_Inf\_L (Node 88), consistently appeared as top-ranked nodes for clustering coefficient and degree centrality.
  + These regions are critical for integrating sensory information and mediating neural processes during both resting and task states.
* State-Specific Observations:
  + During sleep, temporal regions exhibited higher variance, reflecting more dynamic and diverse connectivity patterns.
  + Post-task states showed the emergence of new central nodes, indicating task-induced shifts in network synchronization.

#### 5. Comparison Across States

* Pre-Task vs. Post-Task:
  + Lower clustering coefficients and increased modularity post-task suggest a functional reorganization of the brain to facilitate global integration.
  + The emergence of new high-degree nodes highlights adaptive changes in neural synchronization dynamics.
* Post-Task vs. Sleep:
  + Sleep networks showed greater variance in metrics like degree centrality and clustering coefficients, indicating a more diverse and less stable synchronization state.
  + Negative graphs during sleep exhibited even greater diversity in top central nodes, suggesting unique neural resource allocation during sleep.

**Table 1.** Common notation used in this study with their corresponding definitions.

| **Notation** | **Description** |
| --- | --- |
|  | A set of events |
|  | A set of sequences |
|  | A sequence, which consists of a series of events in order. |
|  | A set of blocks |
|  | A block, which is a series of events in order. |
|  | A revised sequence, which consists of blocks. |
|  | A set of revised sequences |
|  | A set of topics |
|  | An asymmetric matrix representing the relations between events |
|  | A symmetric matrix representing the relations between blocks |
|  | A matrix representing the relation between sequences in and blocks in |

***Topic-level Workflows***

**Results**

The results of the study reveal distinct differences in brain network characteristics across resting, post-task, and sleep states, as highlighted below:

* Degree Centrality
  + For Positive Graphs:
    - Post-task, a decrease in the ability of brain regions to provoke synchronization was observed, indicated by lower mean degree centrality.
    - Sleep state exhibited higher variance in degree centrality, reflecting greater instability in brain synchronization dynamics.
  + For Positive Graphs:
    - Degree centrality increased post-task, signifying a decrease in overall synchronization and aligning with results from the positive graphs.The sleep state showed even higher variance, suggesting heightened diversity in brain dynamics during this state.
* Clustering Coefficient
  + A general decrease in clustering coefficients post-task indicates reduced local clustering of brain activity, potentially reflecting an increase in global integration of neural signals.
* Modularity
  + Modularity increased for most subjects post-task, suggesting that brain networks became more compartmentalized. This highlights a shift towards specialized neural processing following task engagement.
* Node-Specific Observations
  + For Positive Graphs:
    - Top nodes pre- and post-task displayed some overlap, but new prominent nodes emerged post-task, signifying a shift in synchronization dynamics.
    - In the sleep state, node 84 (Temporal\_mid\_L) emerged as a consistently dominant node across subjects.
  + For Negative Graphs:
    - Greater diversity was observed in top nodes compared to positive graphs, with even more pronounced variability during sleep states. This suggests different mechanisms underlying synchronization and resource allocation.
* Clustering Coefficient Nodes:
  + Similarities were found across subjects but less so across states. Key nodes included 80 (Temporal\_Sup\_L), 84 (Temporal\_Mid\_L), and 88 (Temporal\_Inf\_L).

**List of Abbreviations Used in this Paper:** fMRI: Functional Magnetic Resonance Imaging, BOLD: Blood Oxygenation Level Dependent (signal), ROI: Region of Interest, AAL: Automated Anatomical Labeling (Atlas), MNI: Montreal Neurological Institute (Template Space), CSF: Cerebrospinal Fluid, FSL: FMRIB Software Library, NiPype: Neuroimaging in Python (workflow management tool), Nilearn: Statistical learning and visualization for neuroimaging data.

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