Supplementary Material 8

Global Network Metrics

Methods

Assortativity

Assortativity (R) quantifies the tendency of a network's nodes to connect to other nodes that are similar in some specified attribute, such as degree, which in this context refers to the number of connections a node has. High assortativity indicates that nodes tend to link to others with a similar degree, while low assortativity (or disassortativity) suggests the opposite. The formula for calculating assortativity, focusing on degree assortativity, is:

$$R = \frac{\sum_{ij} jk(e_{jk} - q_j q_k)}{\sigma_q^2}$$

Here, e_{jk} is the proportion of edges that connect nodes of degrees j and k, q_j and q_k are the expected proportions of these degrees under randomness, and σ_q^2 is the variance of the degree distribution.

Hierarchy

The hierarchy coefficient is used to identify the presence of a hierarchical organization in a network that measures the extent to which a network is organized in a hierarchical manner, with some nodes acting as hubs that are more central than others. This can be quantified by examining the distribution of paths or the levels of organization within the network, where a high level of hierarchy implies a structured tier of node interactions.

$$\text{bzscore} = \frac{\text{b} - \text{mean (brand)}}{\text{std (brand)}}$$

Where b is hierarchy of network, $1 \times N$ array, N is the number of threshold sequences; bzscore is the z-score of hierarchy of network, $1 \times N$ array, N is the number of threshold sequences. brand is a $R \times 1$ array, R is the number of randomized network. It is the hierarchy of randomized network.

Synchronization

Synchronization refers to the extent to which the activity of different nodes (or regions in the context of brain networks) in a network becomes synchronized, indicating coordinated activity. In brain networks analyzed through fMRI, synchronization often involves measuring the statistical correlation or coherence of the BOLD signal between regions over time. While synchronization itself is a property observed through these correlations, rather than being calculated through a simple mathematical formula, it can be quantified using measures such as phase locking value (PLV) or Pearson correlation coefficients between pairs of nodes:

$$\text{Syncrhonization between nodes i and j} = \text{Correlation}\ (\text{BOLD}_i, \text{BOLD}_j)$$

Clustering coefficient (C_p)

The clustering coefficient (Cp) indicates the likelihood that the neighbors of a given node i in a network are also neighbors with each other. The network's overall clustering coefficient is the average of the clustering coefficients for all nodes within the network. This metric is used to measure the degree of cliquishness or local groupings within the network. The formula for calculating the clustering coefficient is as follows:

$$C_p(G) = \frac{1}{N}\sum_{i=1}^{N}\frac{2a_i}{k_i(k_i - 1)}$$

Here, k_i is the degree of node i, a_i is the actual number of edges between the neighbors of node i, and N is the total number of nodes in the network.

Shortest Path Length (L_p)

The shortest path length (Lp) represents the optimal path for information to travel from one node to another within a network. The network's shortest path length (Lp) is the average value of the shortest paths between all pairs of nodes in the network. This metric is used to measure the efficiency of global path connectivity for information transmission across the network. The formula to calculate the shortest path length is:

$$Lp(G) = \frac{1}{N(N-1)}\sum_{i \neq j \in N} L_{ij}$$

where L_{ij} is the length of the shortest path between nodes i and j in the network G, and N is the total number of nodes in the network.

Small-worldness (Sigma)

Regular networks are characterized by high clustering coefficients and longer shortest path lengths, in contrast to random networks, which have lower clustering coefficients and shorter shortest path lengths. Small-world networks possess the high clustering coefficients of regular networks as well as the short shortest path lengths of random networks. The small-world property index (Sigma) represents the ratio of the normalized clustering coefficient (Cp) to the normalized shortest path length (Lp). The formula for calculating Sigma is:

$$\mathrm{Sigma} = \frac{\mathrm{Cp}/\mathrm{Cp_{rand}}}{\mathrm{Lp}/\mathrm{Lp_{rand}}}$$

where $\mathrm{Cp_{rand}}$ and $\mathrm{Lp_{rand}}$ are the average clustering coefficient and average shortest path length for 5000 random networks, respectively. When the ratio exceeds 1, the network is considered to have small-world properties.

Global Efficiency (E_{global})

Global efficiency (E_{global}) reflects the overall capacity of a network for transmitting information. The higher the global efficiency of a network, the faster the rate at which information can be exchanged between nodes. The formula for calculating global efficiency is:

$$E_{global}(G) = \frac{1}{N(N-1)} \sum_{i \neq j \in G} \frac{1}{L_{ij}}$$

Here, L_{ij} is the length of the shortest path between nodes i and j in the network G, and N is the total number of nodes in the network.

Local Efficiency (E_{local})

Local efficiency (E_{local}) reflects the capacity of a network for local information transmission, and, in a sense, represents the network's resilience to random attacks. The formula for calculating local efficiency is:

$$E_{local}(i) = \frac{1}{N-1}\sum_{i \neq j \in G}\frac{1}{L_{ij}}$$

Here, L_{ij} is the shortest path length between nodes i and j within the subnetwork G formed by the neighbors of node i, and N is the total number of nodes in the network.

Results

No significant variations were detected in global network metrics under sparsities ranging from 0.14 to 0.5, when comparing the effects of circuits-based PAS and sham interventions in aMCI patients. Analysis covered various graph theory metrics, including assortativity, hierarchy, synchronization, clustering coefficient (C_p), shortest path length (L_p), small-world index (Sigma), global efficiency (E_{global}), and local efficiency (E_{local}) (all $p > 0.05$) (Figure S8-1).

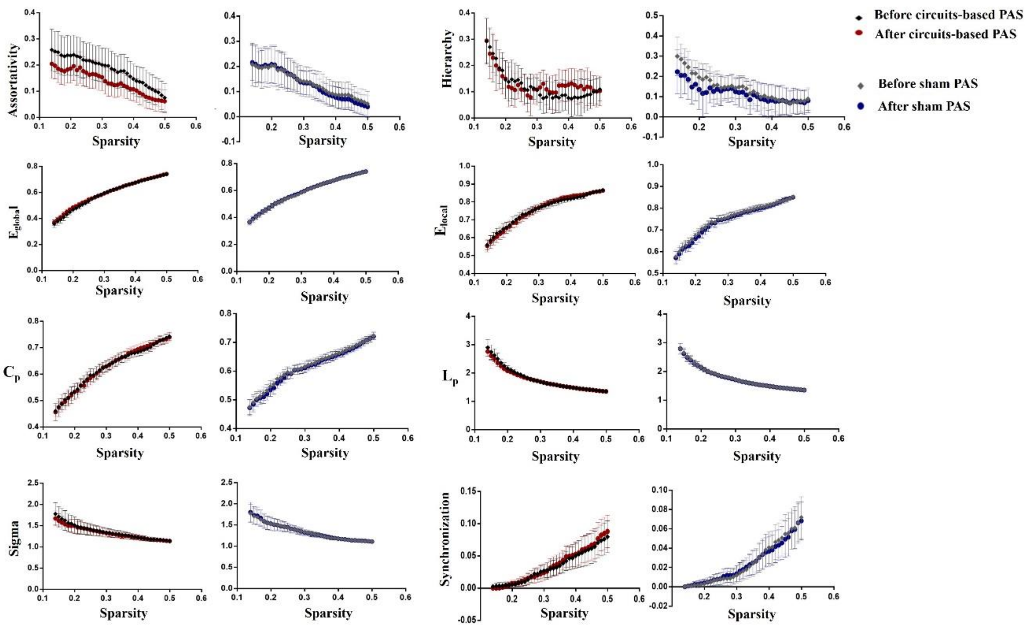

Figure S8-1. Graphical representation of brain network attributes before and after circuits-based PAS and sham intervention in aMCI patients. Global graph theory metrics, including assortativity, hierarchy, synchronization, clustering coefficient (C_p), shortest path length (L_p), small-worldness (Sigma), global and local efficiency (E_{global}, E_{local}), were assessed at varying sparsity thresholds from 0.14 to 0.5. Data points show no significant difference between pre- and post-intervention states for both treatments (all $p > 0.05$). PAS: paired associative stimulation; aMCI: amnestic mild cognitive impairment.