

# Disruption of Small World Properties in Functional Brain Networks of Alzheimer's Disease

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**Abstract:** Alzheimer's disease (AD) is a progressive neurodegenerative disorder characterized by cognitive decline and widespread alterations in brain connectivity. In recent years, graph theory has emerged as a powerful framework for modeling functional brain networks and quantifying their topological properties. In this study we investigate disruptions in small world organizations of functional brain networks in Alzheimer's disease using graph theoretic measures. Functional connectivity networks are constructed from resting state brain regions and edges denote pairwise functional interactions. Key network metrics including clustering coefficient, characteristic path length and global efficiency are computed and compared between Alzheimer's patients and health control subjects. The results reveal a significant reduction in local clustering increased path length and decreased global efficiency in AD networks indicating impaired balance between functional segregation and integration. Furthermore, small worldness analysis demonstrates a clear breakdown of optimal network organization in Alzheimer's disease. These findings provide quantitative evidence of functional brain network disorganization in AD and highlight graph theoretic measures as potential biomarkers for neurodegenerative disorders.

**Keywords:** Alzheimer's disease, functional brain networks, graph theory, small world networks, brain connectivity, clustering coefficient, global efficiency.

## 1. Introduction

Alzheimer's disease (AD) is a progressive neurodegenerative disorder and the most common cause of dementia worldwide, characterized by a gradual decline in memory, cognition and functional abilities [1]. Despite extensive research the underlying mechanisms driving large scale brain dysfunction in Alzheimer's disease are not yet fully understood. Increasing evidence suggests that AD is not merely the result of localized brain damage but rather a consequence of disrupted interactions across distributed brain regions leading to altered functional connectivity patterns.

Functional brain networks provide a powerful framework for investigating large scale neural communication. In this context, the brain is modeled as a complex network in which nodes represent brain regions and edges represent functional interactions between them. Graph theory has emerged as an effective mathematical tool to quantify the topological organization of such networks enabling the characterization of both local and global properties of brain connectivity. Graph

theoretic approaches have been successfully applied to understand normal brain organizations as well as pathological alterations associated with neurological disorders.

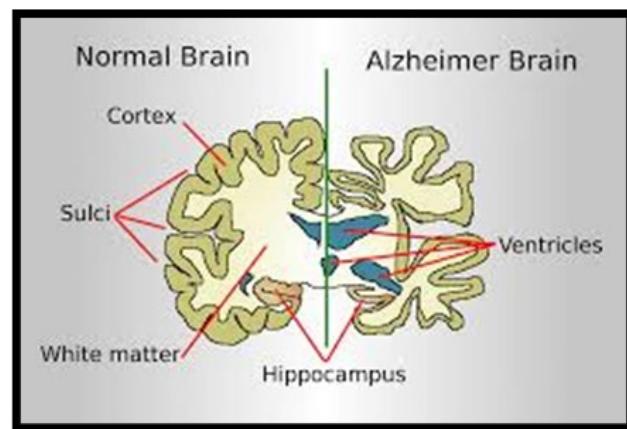


Fig. 1. Normal brain vs Alzheimer's brain

One of the most prominent features of healthy brain networks is their small world organization which reflects an optimal balance between local specialization and global integration [5,6]. Small world networks are characterized by high clustering coefficients indicating strong local connectivity and short characteristic path lengths reflecting efficient long range communication. This efficient network architecture supports rapid information transfer and robust cognitive functioning. Disruption of small world properties has been associated with impaired information processing and cognitive decline [1,2].

In Alzheimer's disease several studies have reported abnormalities in functional connectivity including reduced synchronization between brain regions and degradation of network hubs. These changes are believed to impair the brain's ability to integrate information across distributed regions contributing to the clinical symptoms observed in AD patients. However, a comprehensive understanding of how small world properties are altered in functional brain networks of Alzheimer's disease remains an active area of research particularly from a graph theoretic perspective.

Graph theoretic measures such as clustering coefficient, characteristic path length and global efficiency provide quantitative indicators of network segregation and integration.

The clustering coefficient reflects the degree of local connectivity among neighboring nodes, characteristic path length captures the efficiency of information transfer across the entire network and global efficiency offers a robust measure of overall communication efficiency. Analyzing these metrics enables systematic comparison between healthy and diseased brain networks and offers insights into the topological reorganization associated with neuro degeneration.

Motivated by these considerations this study aims to investigate the disruption of small world properties in functional brain networks of Alzheimer's disease using graph theoretic analysis. Functional connectivity networks are constructed from resting state brain signals and key network metrics are computed and compared between Alzheimer's patients and health control subjects. By quantitatively characterizing alterations in clustering, path length and global efficiency this work seeks to provide deeper insight into the network level mechanisms underlying Alzheimer's disease and to highlight graph theoretic measures as potential biomarkers for neuro degenerative disorders.

## 2. Methodology

### A. Dataset Description

Resting state brain signal data were obtained from publicly available datasets comprising subjects diagnosed with Alzheimer's disease (AD) and age matched healthy control (HC) participants. All subjects underwent standardized data acquisition protocols. The dataset was divided into two groups-

- Alzheimer's disease patients and healthy controls
- Enabling comparative network analysis.

### 1) Data Processing

To ensure signal quality and reduce noise related artifacts, standard preprocessing steps were applied.

For functional brain signals:

- Noise and artifact removal was performed.
- Signals were band pass filtered to retain physiologically relevant frequency components.
- Time series corresponding to predefined brain regions or recording channels were extracted.

Let,

$$X = \{x_1(t), x_2(t), \dots, x_N(t)\}$$

Represent the preprocessed time series from  $N$  brain regions(nodes).

### B. Functional Brain Network Construction

#### 1) Node Definition

Each node  $v_i \in V$  represents a brain region (for fMRI, defined by a brain atlas) or an EEG channel. Thus, the brain network is represented as a graph.

$$G = (V, E, W)$$

Where:

- $V$  is the set of nodes.
- $E$  is the set of edges.

- $W$  denoted the weighted adjacency matrix.
- 2) *Edge Definition and Weight Assignment*
- Functional connectivity between pairs of brain regions was quantified using Pearson's correlation coefficient [16].

For nodes  $i$  and  $j$  the edge weight is defined as:

$$w_{ij} = \frac{\text{cov}(x_i, x_j)}{\sigma_{x_i} \sigma_{x_j}}$$

Where:

- $\text{cov}(x_i, x_j)$  is the covariance between signals  $x_i$  &  $x_j$ .
- $\sigma_{x_i}$  &  $\sigma_{x_j}$  are their respective standard deviations.

This results in a weighted connectivity matrix  $W = w_{ij}$ .

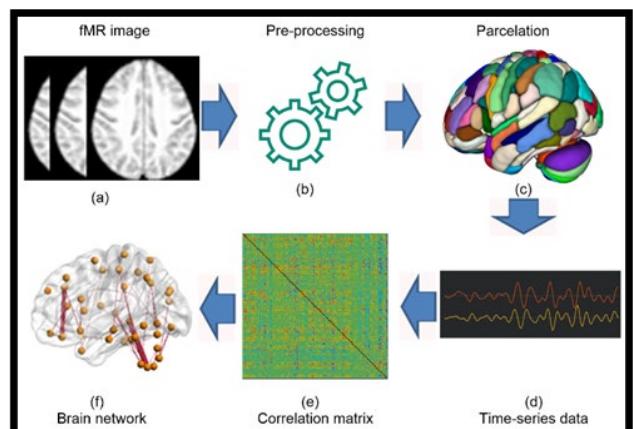


Fig. 2. Brain network

#### 3) Thresholding Strategy

To eliminate spurious connections and maintain comparable network densities across subjects a proportional thresholding approach was employed. Only the top  $p\%$  of strongest connections were retained resulting in a sparse and biologically meaningful network.

The final adjacency matrix  $A$  is defined as:

$$A_{ij} = \begin{cases} w_{ij}, & \text{if } w_{ij} \geq \tau \\ 0, & \text{otherwise} \end{cases}$$

Where  $\tau$  is the threshold value corresponding to the chosen network density.

### C. Graph Theoretic Measures

Graph theoretic metrics were computed to quantify local and global topological properties of functional brain networks.

#### 1) Clustering Coefficient

The clustering coefficient measures the degree of local interconnectedness among neighboring nodes.

For a node  $i$ , it is defined as:

$$C_i = \frac{2E_i}{k_i(k_i - 1)}$$

Where

- $E_i$  is the number of edges between the neighbors of node  $i$ .

- $k_i$  is the degree of node  $i$ .

The average clustering coefficient of the network is:

$$C = \frac{1}{N} \sum_{i=1}^N C_i$$

## 2) Characteristic Path Length

The characteristic path length quantifies the efficiency of information transfer across the network. It is defined as the average shortest path length between all pairs of nodes:

$$L = \frac{1}{N(N-1)} \sum_{i \neq j} d_{ij}$$

Where  $d_{ij}$  is the shortest path length between nodes  $i$  and  $j$ .

## 3) Global Efficiency

Global efficiency provides a robust measure of overall network integration and is defined as:

$$E_g = \frac{1}{N(N-1)} \sum_{i \neq j} \frac{1}{d_{ij}}$$

Higher global efficiency indicated more efficient information transfer across the brain network.

## D. Small World Property Analysis

To assess small world characteristics the clustering coefficient and characteristic path length of the empirical brain networks were compared with those of equivalent random networks.

The normalized measures are computed as:

$$\gamma = \frac{C}{C_{rand}}, \lambda = \frac{L}{L_{rand}}$$

Where  $C_{rand}$  and  $L_{rand}$  are the mean clustering coefficient and path length of randomly generated networks with the same number of nodes and degree distribution.

The small worldness index is then defined as:

$$\sigma = \frac{\gamma}{\lambda}$$

A network is considered to exhibit small world properties when  $\sigma > 1$ .

## E. Statistical Analysis

Graph metrics were computed for each subject independently. Group level comparisons between Alzheimer's disease and healthy control networks were performed using appropriate statistical tests. Statistical significance was assessed at a predefined significance level and results were reported as mean  $\pm$  standard deviation.

## 3. Results

### A. Functional Brain Network construction

Functional brain networks were successfully constructed for all subjects in both Alzheimer's disease (AD) and healthy control (HC) groups following preprocessing and thresholding. The resulting networks exhibited comparable densities across subjects, ensuring fair topological comparison. Visual inspection of representative networks indicated noticeable differences in connectivity patterns between the two groups with AD networks appearing sparser and less clustered than HC networks.

This figure illustrates example functional brain networks from a healthy control subject and an Alzheimer's disease subject. Nodes represent brain regions and edges denote functional connections. Compared to the healthy network the AD network shows reduced connectivity strength and fewer clustered connections.

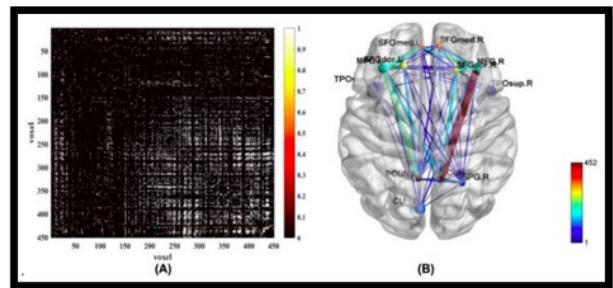


Fig. 3. Representative functional brain networks

### B. Alterations in Clustering Coefficient

The average clustering coefficient was significantly lower in the AD group compared to healthy controls. This reduction indicates diminished local connectivity and weakened functional segregation in Alzheimer's disease.

Quantitatively, healthy control networks exhibited higher clustering coefficients reflecting preserved local neighborhood organization whereas AD networks showed a marked decline in clustering.

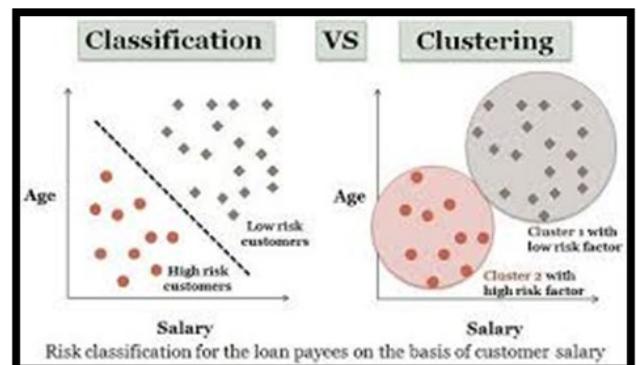


Fig. 4. Group comparison of clustering coefficient

Box plots showing the distribution of average clustering coefficient for AD and HC groups. The AD group demonstrates a significant reduction in clustering coefficient relative to healthy controls ( $p < 0.05$ ).

### C. Changes in Characteristic Path length

Characteristic path length was found to be significantly increased in Alzheimer's disease networks compared to healthy controls. This increase suggests reduced efficiency in global information transfer across the brain [11].

Healthy control networks maintained shorter path lengths indicative of efficient long range communication while AD networks exhibited longer paths between brain regions.

Bar plots representing mean characteristic path length ( $\pm$  standard deviation) for AD and HC groups. Alzheimer's disease networks show a statistically significant increase in path length ( $p < 0.05$ ).

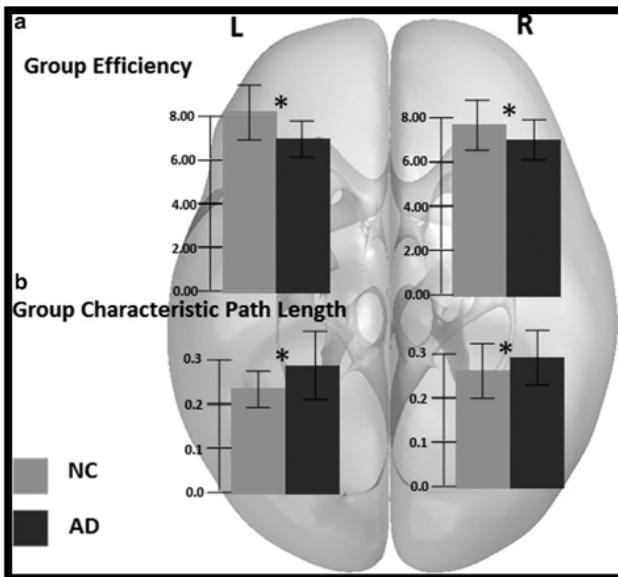


Fig. 5. Characteristic path length comparison between groups

### D. Reduction in Global Efficiency

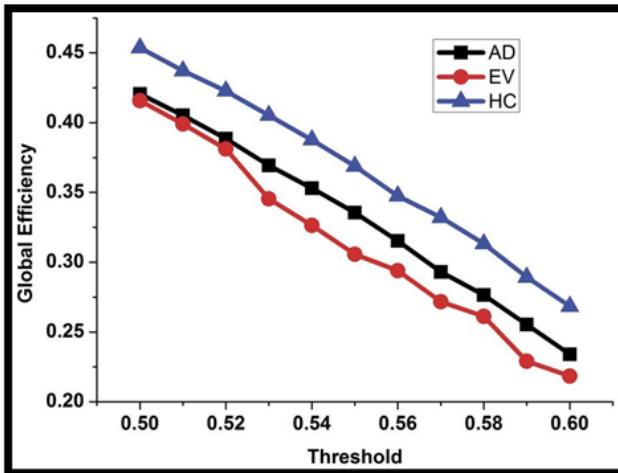


Fig. 6. Global efficiency of functional brain networks

Global efficiency was significantly lower in the AD group

relative to healthy controls. This finding further supports the presence of impaired global integration and reduced communication efficiency in Alzheimer's disease.

The reduction in global efficiency complements the observed increase in characteristic path length, confirming large – scale network dysfunction in AD.

Box plots comparing global efficiency AD and HC groups. Alzheimer's disease networks exhibit significantly lower global efficiency ( $p < 0.05$ ).

### E. Disruption of Small World Properties

To evaluate small world organization, normalized clustering coefficient and characteristic path length were compared against random networks. Healthy control networks consistently exhibited small world characteristics with small worldness index  $\sigma > 1$ . In contrast, Alzheimer's disease networks showed a pronounced reduction in small worldness with  $\sigma$  values approaching or falling below unity.

This result indicates a breakdown of the optimal balance between local specialization and global integration in AD.

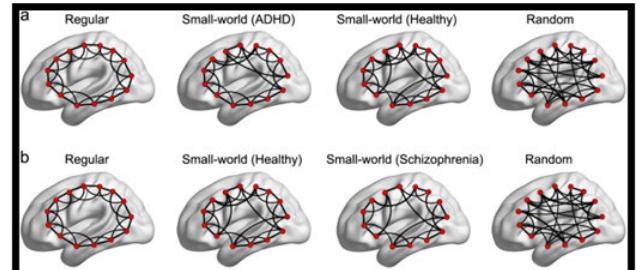


Fig. 7. Small worldness index comparison

Mean Small worldness ( $\sigma$ ) for AD and HC groups. Healthy control networks demonstrate strong small world properties whereas AD networks show significant disruption. ( $p < 0.05$ ).

### F. Network Metric Differences

A summary of group wise differences across all graph theoretic measures is provided in Table 1.

### G. Observations

- Alzheimer's disease networks exhibit reduced local clustering indicating impaired functional segregation.
- Increased characteristic path length and decreased global efficiency reflect compromised global integration.
- Small world organization is significantly disrupted in Alzheimer's disease suggesting large – scale reorganization of functional brain networks.

## 4. Discussion

The Present study investigated alterations in small world

Table 1  
Comparison of graph theoretic measures between AD and HC groups

Metric	Healthy Controls	Alzheimer's Disease	Significance
Clustering coefficient	Higher	Lower	Significant
Characteristic path length	Shorter	Longer	Significant
Global Efficiency	Higher	Lower	Significant
Small worldness index	$\sigma > 1$	Reduced	Significant

properties of functional brain networks in Alzheimer's disease using graph theoretic analysis. By comparing network metrics between Alzheimer's disease (AD) patients and healthy control (HC) subjects, observed significant disruptions in both local and global topological organization providing strong evidence of large scale functional network reorganization associated with neuro degeneration.

A key finding of this work is the significant reduction in clustering coefficient in AD networks. The clustering coefficient reflects the degree of local interconnectedness among neighboring brain regions and is commonly interpreted as a measure of functional segregation. The observed reduction indicated a weakening of localized information processing and loss of tightly coupled neural assemblies in Alzheimer's disease. This impairment in local connectivity is consistent with synaptic degeneration and neuronal loss reported in AD pathology and suggests that specialized processing within functional modules becomes progressively compromised.

In addition to local disruptions, characteristic path length was significantly increased in AD networks compared to healthy controls. Characteristic path length captures the efficiency of information transfer across the entire network. Longer path lengths indicate that information must traverse more intermediate regions to reach distant nodes, reflecting reduced global integration. This finding suggests that Alzheimer's disease impairs long range communication between distributed brain regions which may underlie deficits in memory consolidation, attention and executive functioning observed clinically in AD patients.

The reduction in global efficiency further reinforces the presence of large scale integration deficits. Global efficiency is a robust measure of network wide communication efficiency and is less sensitive to disconnected components than path length. Lower global efficiency in AD networks indicated that the brain's ability to rapidly integrate information across multiple regions is diminished. This global communication breakdown aligns with previous evidence of disrupted default mode and associative networks in Alzheimer's disease and supports the conceptualization of AD as a network disconnection syndrome rather than a purely localized disorder.

Small world analysis revealed a pronounced disruption of optimal network organization in Alzheimer's disease. Healthy control networks exhibited small world characteristics with high normalized clustering and relatively short path lengths compared to random networks reflecting an optimal balance between segregation and integration [2,3,12]. In contrast, AD networks showed a marked reduction in small worldness index ( $\sigma$ ) with values approaching or falling below unity. This loss of small world topology indicates a departure from the efficient architecture that supports normal cognitive functioning and suggests that AD leads to a suboptimal and energetically inefficient network configuration.

From a neuro biological perspective the observed breakdown of small world organization may result from progressive synaptic loss, degeneration of hub regions and disrupted functional synchronization across cortical and subcortical areas. Hub regions play a critical role in maintaining efficient

communication, their degradation can disproportionately affect global network topology, leading to widespread functional impairments. The combined reduction in clustering increased path length and decreased efficiency observed in this study collectively point toward a systematic collapse of hierarchical network organization in Alzheimer's disease.

Importantly these findings highlight the potential of graph theoretic measures as quantitative biomarkers for neuro degenerative disorders. Metrics such as clustering coefficient, characteristic path length, global efficiency and small worldness capture complementary aspects of brain network organization and may provide sensitive indicators of disease progression [12,13]. Compared to traditional region based analyses, network level measures offer a more holistic understanding of brain dysfunction and may contribute to early diagnosis and longitudinal monitoring of Alzheimer's disease.

The results of this study support the growing body of evidence that Alzheimer's disease is characterized by a disruption of both functional segregation and integration leading to a loss of optimal small world architecture [6, 9-11]. Graph theory provides a powerful and interpretable framework for characterizing these alterations and advancing our understanding of the network mechanisms underlying connectivity studies cognitive decline in Alzheimer's disease [6,10].

#### *A. Limitations and Future Directions*

Despite the promising findings of this study several limitations should be acknowledged. First functional connectivity was quantified using Pearson's correlation coefficient which captures only linear relationships between brain region time series and may not fully represent nonlinear or complex neural interactions [16]. In addition, the analysis was restricted to static functional brain networks constructed over the entire recording duration thereby overlooking the inherently dynamic nature of brain activity. Since Alzheimer's disease is known to affect temporal variability and flexibility of functional connectivity future studies may benefit from incorporating alternative connectivity measures and time resolved or dynamic network analyses [17,18]. Furthermore, the present work focused on a single neuro imaging modality, limiting the ability to integrate complementary structural and functional information. Multimodal approaches combining functional data with structural connectivity or diffusion imaging could enhance biological interpretability of network alterations [19].

Another limitation concerns methodological choices in network construction, particularly thresholding strategy and network density selection which can influence graph theoretic metrics despite the use of proportional thresholding. Future research should assess the robustness of findings across multiple thresholds or employ weighted, threshold free network analyses. Additionally, the current study emphasized global topological measures without examining regional or nodal level alterations. Investigating disrupted hubs, rich club organization and region, specific vulnerability patterns may further improve clinical relevance. Finally exploring associations between

network metrics and clinical variables such as cognitive performance, disease severity and longitudinal progression would strengthen the potential of graph theoretic measures as biomarkers for early diagnosis, disease monitoring and therapeutic evaluation in Alzheimer's disease.

## 5. Conclusion

This study employed a graph theoretic framework to investigate alterations in functional brain network organization in Alzheimer's disease with a particular focus on disruptions in small world properties. Functional connectivity networks derived from resting state brain signals revealed a significant reduction in clustering coefficient increased characteristic path length and decreased global efficiency in Alzheimer's disease patients compared to healthy controls indicating impaired local functional segregation and compromised global integration. Small worldness analysis further demonstrated a deviation from optimal network organization supporting the characterization of Alzheimer's disease as a network level disconnection disorder rather than a consequence of isolated regional damage. These findings highlight the sensitivity and interpretability of graph theoretic measures as potential biomarkers for large scale functional brain reorganization and underscore their relevance for disease characterization, monitoring and therapeutic evaluation.

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