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High-Efficiency Graph Measures for Discriminating Schizophrenia Patients from Healthy Controls Using Structural and Functional Connectivity

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Abstract

Purpose: Schizophrenia (SZ), which affects 0.45% of adults worldwide, is a complex mental illness with unknown causes and mechanisms. Neuroimaging techniques have been used to study changes in the brain of patients with SZ. In this study, we aim to construct brain subnetworks, analyze the association of structure with function, and investigate them with graph measures. We hope to identify important subnetworks and graph measures for SZ diagnosis.

Materials and Methods: This study investigates the structural and functional brain connectivity of 27 Healthy Controls (HC) and 27 patients with SZ. Independent Component Analysis (ICA) and joint ICA (jICA) are used to construct subnetworks based on functional and structural connectivity. An association between structural and functional connectivity is examined. Joint functional and structural subnetworks are also examined and compared with independent analysis of functional and structural subnetworks. Several graph measures are used in the whole brain and its subnetworks.

Results: In this study, we investigated brain connectivity in HC and SZ patients using graph measures. The study analyzed both the whole brain and brain subnetworks to better understand the importance of partitioning the brain into subregions. Our results suggest that analyzing the whole brain may not be the most effective method for studying the brain peculiarities of SZ patients. In addition, multimodal brain analysis has proven to be effective in understanding SZ. There is no one-to-one relationship between structural and functional connectivity in the brain. Certain measures such as maximum modularity, clustering coefficient, network strength, global efficiency, and path length were important in distinguishing patients with SZ from HCs in specific subnetworks. This study recommends further investigation of specific subnetworks that overlap with default mode, visual, and somatomotor resting state networks.

Conclusion: This study emphasizes the importance of subnetwork and multimodal analysis for understanding SZ disease.

Keywords: Schizophrenia; Independent Component Analysis; Subnetworks; Functional Connectivity; Structural Connectivity; Graph Theory.

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1. Introduction

Schizophrenia (SZ) is a debilitating, complex, and serious mental illness [1]. This psychiatric disorder is rooted in genetic and environmental factors [2]. This chronic mental disease affects approximately 0.45% of the adult population worldwide [3]. However, the causes and pathophysiological mechanisms of this complex mental disorder remain largely unknown [4]. Researchers have attempted to investigate pervasive changes, especially abnormal interactions, in the brains of patients with SZ. Some neuroimaging techniques, such as resting-state functional Magnetic Resonance Imaging (fMRI) and Diffusion Tensor Imaging (DTI), have been used to elucidate the neurobiological basis of schizophrenia [1]. fMRI examination shows blood oxygen level-dependent signals between different Regions Of Interest (ROI). This technique drives Functional Connectivity (FC) [4]. DTI is a diffusion-weighted MRI method that evaluates accurate fiber structural information. DTI technique drives Structural Connectivity (SC) [1]. SZ disrupts functional and structural patterns of the brain [5]. Most SZ studies with neuroimaging methods used functional and structural networks separately to investigate changes in the whole brain network. However, some studies have used more modalities in the whole brain and subnetworks. Contradictory and unclear results have been reported by these studies [6-8].

In brain networks, there are variations of algorithms such as blind Independent Component Analysis (ICA) for subnetwork creation. To quantitatively analyze the brain, graph theory has predominantly been used to investigate functional and structural topologies. However, most previous studies have used few graph measures and have reported unclear results [6, 9].

In this paper, we aim to construct brain subnetworks with both single modality and multimodality to elucidate the association between structural and functional brain subnetworks. In addition, we analyze 11 graph measures in brain subnetworks (betweenness, clustering coefficient, characteristics path length, radius, diameter, eccentricity, optimum and max modularity, local and global efficiency, and strength). Furthermore, we want to find important subnetworks and graph measures in SZ diagnosis. We expect our approaches to lead to improvements in the diagnosis of SZ using subnetworks.

2. Materials and Methods

Methods and materials of our cohort study are presented in this section

2.1. Data and Preprocessing

This study consists of a total of 27 healthy controls (HC) and 27 SZ patients with structural and functional MRI data. The mean age of SZ subjects was 41.9±9.6 years and 35±6.8 years, respectively. It is a public dataset in the Zenodo platform https://doi.org/10.5281/zenodo.3758534). More details about this data such as data acquisition, data preprocessing, SC, FC, inclusion and exclusion criteria, and ethics statement, are described in detail elsewhere [10].

2.2. Network Reconstruction

In our study, we used the Desikan– Killiany atlas along with considering parcellation in the Cammoun study. The brain was divided into 129 ROIs [11, 12]. For partitioning the brain, several algorithms, such as Principal Component Analysis (PCA) were used to reduce the dimensionality of data, and independent component analysis (ICA) was then applied to identify subnetworks based on Functional Connectivity (FC) and SC, separately. jICA was further used to identify subnetworks using both SC and FC. In addition, a modified version of ranking and averaging ICA by reproducibility algorithm (RAICAR) was used to identify reproducible components across multiple runs of ICA, ensuring consistency in component ordering. More details about our methods are provided in [13].

2.3. Subnetworks Relationship

In our study, we found an association between SC and FC by investigating common edges in the connectivity matrix when using the ICA algorithm and independent functional and structural subnetworks and when using the jICA algorithm and joint subnetworks. To calculate association, we converted FC and SC subnetworks into binary. With this technique, we have only edge connectivity between nodes in subnetworks without values. Using (Equation 1), we calculated the percentage of common edges in each subnetwork:

$$\frac{edges\ connectivity\ of\ FC \cap edges\ connectivity\ of\ SC}{edge\ connectivity\ FC \cup edge\ connectivity\ SC} \times 100 \qquad (1)$$

According to changes that structural information creates in functional subnetworks in joint mode, and vice versa, we examined joint functional and structural subnetworks to investigate how they differ from functional and structural independent subnetworks.

2.4. Network Examination

We used a network-based approach to investigate specific neural signatures of schizophrenia brain connectivity. Altered brain networks and connectivity describe the neurobiological underpinnings of schizophrenia. Graph theory characterizes the organization of brain networks. We used the following graph measures from our undirected, weighted matrices: betweenness, clustering coefficient, characteristic path length, radius, diameter, eccentricity, optimal and maximum modularity, local and global efficiency, and network strength. In this study, we computed graph measures using the Brain Connectivity Toolbox implemented in MATLAB version 2021b [14].

2.5. Statistical Analysis

We performed statistical analysis of network properties using Python version 3.10. To compare graph measures in subnetworks, we employed the t-test or Mann–Whitney U test, as appropriate. A significance threshold of 0.05 was used in this study.

3. Results

Structural and functional connectivity assess in vivo deviation of water molecules along white matter fiber structure and pairwise correlations of brain activity time series during brain rest, respectively [7]. Next, we will review the investigation of connections results.

3.1. Subnetworks Relationship

In this study, we investigated the correlation between SC and FC. We calculated common edges in the same subnetworks and common nodes using (Equation 1).

3.1.1. ICA FC and SC Subnetworks

Table 1 shows the percentage of common edges in the same FC and SC ICA subnetworks and nodes. For example, ICA subnetwork #1 SC and FC have 14.1705% common edge connectivity. For visualization of subnetworks in the study, the nodal strength of each region to map subnetworks was used. Figure 1 shows ten ICA brain subnetworks.

Table 1. The percentage of common edge connectivity between FC and SC in the ICA subnetworks according to Equation 1

ICA subnetworks	percentage %
#1	14.1705
#2	13.0416
#3	13.5109
#4	15.7167
#5	12.6606
#6	9.9096
#7	14.5541
#8	13.8249
#9	9.1605
#10	12.7259

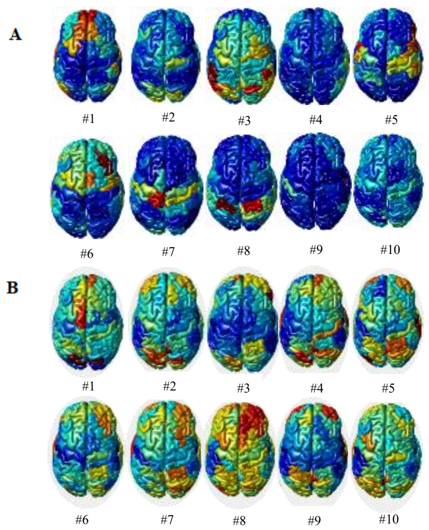

Figure 1. ICA brain subnetworks A) FC and B) SC

3.1.2. JICA FC and SC Subnetworks

Table 2 shows the percentage of common edges in jICA FC and SC subnetworks. Figure 2 shows ten jICA brain subnetworks.

Table 2. The percentage of common edges connectivity between FC and SC in jICA subnetworks

jICA subnetworks	percentage %
#1	13.0434
#2	13.2347
#3	13.7822
#4	14.8742
#5	15.0613
#6	11.4071
#7	16.2841
#8	10.6024
#9	11.1609
#10	14.2513

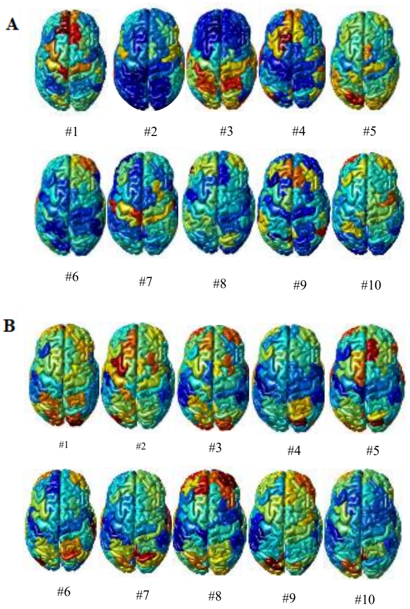

Figure 2. JICA brain subnetworks A) FC and B) SC

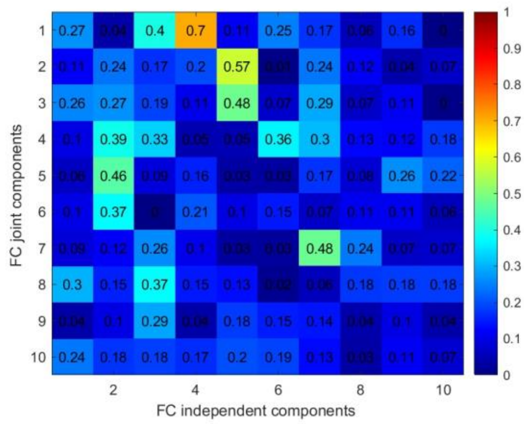

Figure 3. Percentage of similarity (correlation coefficient) of ICA FC and the FC joint of components separately. Please zoom in

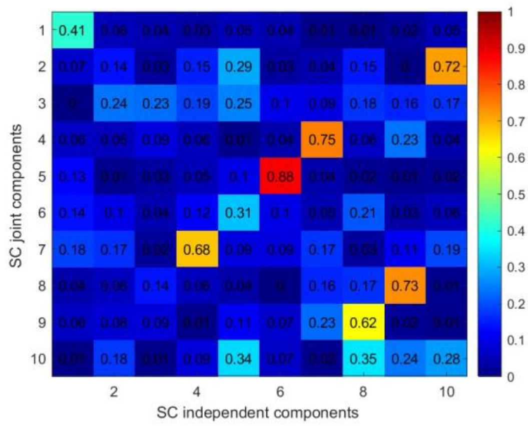

Figure 4. Percentage of similarity (correlation coefficient) of the SC independently and the SC joint of components separately. Please zoom in

3.1.3. ICA and JICA FC Subnetworks

Figure 3 shows the percentage of similarity (correlation coefficient) of SC independent and SC joint of components separately. In Figure 3, changes in functional subnetworks due to the addition of structural information can be seen.

3.1.4. ICA and JICA SC Subnetworks

Figure 4 shows the percentage of similarity (correlation coefficient) of the SC independent and the SC joint components separately. In Figure 4, changes in structural subnetworks due to the addition of functional information can be seen.

3.2. Whole Brain Statistical Analysis

Whole brain Functional Connectivity (FC) and Structural Connectivity (SC) were analyzed using various graph measures. The clustering coefficient was significantly different between SZ and HC for both FC (0.1845±0.0333 vs. 0.0642±0.0102, $P < 0.0001$) and SC (0.0009±0.0001 vs. 0.0004±6.1491×10-5, $P < 0.0001$). Max modularity (0.5011±0.0165 vs. 0.4861±0.0189, $P = 0.0097$) and network strength (0.1138±0.0086 vs. 0.1085± 0.0072, $P = 0.0215$) were also significantly different between SZ and HC for whole brain SC. More details on the results of the statistical graph measure analysis for FC and SC are shown in Tables 3 and 4, respectively.

Table 3. Statistical investigation 11 graph measures FC in the whole brain analysis

Graph measures	Mean HC	SD HC	Mean SZ	SD SZ	P-value
Clustering coefficient	0.1845	0.0102	0.0642	0.0333	<0.0001
Radius	4. 9197	0.4166	5. 1027	0.3644	0.0589
Local efficiency	0.2031	0.0364	0.1888	0.0328	0.0746
Network Strength	30.9940	4. 6837	29.0485	4. 1793	0.0805
Global efficiency	0.3083	0.0300	0.2957	0.0263	0.0901
Eccentricity	5. 9203	0.4483	6. 0857	0.3965	0.0973
Characteristic path	3.6803	0.3382	3. 8069	0.3022	0.1424
Betweenness	80.7883	9. 6914	83.4990	8. 7069	0.2069
Diameter	7. 1388	0.6441	7. 3581	0.6087	0.2279
Max modularity	0.1341	0.0196	0.1306	0.0184	0.2939
Optimum modularity	2. 0847	0.4565	2. 0896	0.3104	0.8671

Table 4. Statistical investigation 11 graph measures SC in whole brain analysis

Graph measures	Mean HC	SD controls	Mean SZ	SD SZ	P-value
Clustering coefficient	0.0004	0.00006	0.0009	0.0001	<0.0001
Max modularity	0.4861	0.0189	0.5011	0.0165	0.0097
Network Strength	0.1085	0.0072	0.1138	0.0086	0.0215
Global efficiency	0.0052	0.0003	0.0054	0.0004	0.3355
Betweenness	450.31	25.866	454.1	21.86	0.4601
Local efficiency	0.0014	0.0001	0.0014	0.0002	0.4706
Characteristic path	259.05	20.145	254.9	21.345	0.6554
Radius	480.9	107.8	490.7	121.5	0.8369
Optimum modularity	38.702	0.7763	39.144	0.7657	0.8469
Eccentricity	640.58	135.54	651.16	151.69	0.8503
Diameter	925.82	203.59	921.32	194.56	0.959

3.3. ICA FC Subnetworks Statistical Analysis

This study used an Independent Component Analysis (ICA) algorithm to divide the whole brain into subnetworks. Each subnetwork was analyzed using graph analysis techniques, focusing on brain functional information. The results revealed several significant differences between individuals with SZ and HC. In subnetwork #5, the characteristic path length was longer for SZ than HC. This difference was also observed in subnetworks #7 and #9. The clustering coefficient was lower in SZ for subnetworks #5, #7, and #9. Furthermore, SZ exhibited a larger diameter in subnetwork #1, and eccentricity was higher for SZ in subnetworks #1 and #7. The radius was also significantly different in subnetworks #1, #7, #8, and #10. Regarding network strength, SZ showed lower values in subnetworks #5, #7, and #9. The global efficiency was lower in SZ for subnetworks #7, #9, and #10. The local efficiency was lower in SZ for subnetworks #5, #7, and #9. Finally, maximum modularity was significantly different between SZ and HC. More details are shown in Table 5. SD is the standard deviation in Tables.

3.4. ICA SC Subnetworks Statistical Analysis

In individuals with SZ and HC structural networks, the clustering coefficient was significantly lower in SZ than in HC in three subnetworks #1, #2, and #10. The network strength was significantly lower in SZ than in HC in subnetworks #1, #2, #4, #5, #6, #7, and #10. The betweenness was significantly lower in SZ than in HC in two subnetworks #1 and #8. The local efficiency was significantly lower in SZ than in HC in two subnetworks #1 and #10. The maximum modularity was significantly lower in SZ than in HC in three subnetworks #1, #6, and #7. The optimum modularity was significantly lower in SZ than in HC in four subnetworks #1, #2, #6, and #9. More details are shown in Table 6.

Table 5. Statistical graph measures ICA FC subnetworks analysis

ICA subnetwork	Significant graph measure	Mean and SD HC	Mean and SD SZ	P-value
#1	Max modularity	0.2236±0.0159	0.2109±0.0153	0.0074
	Eccentricity	7.5383±0.6867	8.0193±0.7077	0.0153
	Diameter	9.5028±1.0687	10.190±1.1309	0.0196
	Radius	6.0951±0.5390	6.4006±0.5429	0.0441
#5	Clustering coefficient	0.0929±0.0172	0.0806±0.0178	0.0082
	Local efficiency	0.1640±0.0276	0.1457±0.0283	0.0139
	Network strength	9.3982±1.3596	8.4650±1.4123	0.0146
	Characteristic path length	5.0278±0.5156	5.3170±0.5082	0.0372
#7	Clustering coefficient	0.0807± 0.0169	0.0686±0.0132	0.0008
	Network strength	9.9264±1.6259	8.8630±1.3269	0.0026
	Local efficiency	0.1485±0.0275	0.1310±0.0231	0.0028
	Radius	6.5527±0.5724	6.9812±0.5899	0.0045
	Global efficiency	0.2278±0.0249	0.2132±0.0210	0.0102
	Eccentricity	8.1626±0.78529	8.5957±0.7353	0.0298
	Characteristic path length	4.9885±0.5166	5.2596±0.4703	0.0388
#8	Radius	6.0142±0.6194	6.3854±0.4672	0.0139
#9	Network strength	6.2364±1.0911	5.6457±0.8649	0.0237
	Global efficiency	0.1965±0.0246	0.1824±0.0201	0.0272
	Characteristic path length	5.8382±0.6970	6.2393±0.6449	0.0298
	Local efficiency	0.1241± 0.0266	0.1106±0.0200	0.0340
	Clustering coefficient	0.0586± 0.0139	0.0515± 0.0097	0.0423
#10	Radius	7.3427±0.8911	7.7424±0.6326	0.0237
	Global efficiency	0.2013±0.0225	0.1912±0.0193	0.0460

Table 6. Statistical graph measures ICA SC subnetworks analysis

ICA subnetwork	Significant graph measure	Mean and SD HC	Mean and SD SZ	P-value
#1	Max modularity	0.5863±0.0205	0.5702±0.0209	0.0037
	Betweenness	522.50±22.802	542.26±29.584	0.0139
	Optimum modularity	5.5584±1.1535	4.8326±0.9988	0.0189
	Network strength	0.0776±0.0065	0.0735±0.0053	0.0169
	Local efficiency	0.0034±0.0003	0.0032±0.0002	0.0311
	Clustering coefficient	0.0022±0.00022	0.0021±0.0001	0.0356
#2	Optimum modularity	7.5363±2.1985	5.9239±1.7111	0.0075
	Clustering coefficient	$0.0004\pm7.1401\times10^{-5}$	$0.0003\pm6.4026\times10^{-5}$	0.0423
	Network strength	0.0460±0.0037	0.0441±0.0036	0.0480
#4	Network strength	0.0427±0.0044	0.0396±0.0040	0.0260
#5	Network strength	0.0320± 0.0031	0.0293± 0.0028	0.0010
#6	Max modularity	0.6138±0.0158	0.5949±0.0239	0.0013
	Network strength	0.0431±0.0038	0.0398±0.0035	0.0026
	Optimum modularity	6.7244±1.5115	5.8145±1.7840	0.0218
#7	Network strength	0.0288±0.0030	0.0271±0.0021	0.0125
	Max modularity	0.6213± 0.0263	0.6084±0.0189	0.0372
#8	Betweenness	550.43±29.411	573.78±43.805	0.0226
#9	Optimum modularity	8.6655±2.2835	7.3853±1.7369	0.0418
#10	Network strength	0.0367±0.0039	0.0339±0.0029	0.0113
	Local efficiency	$0.0004\pm 9.3316\times10^{-5}$	$0.0004\pm6.064\times10^{-5}$	0.0311
	Clustering coefficient	$0.0003\pm7.1815\times10^{-5}$	$0.0002\pm4.8002\times10^{-5}$	0.0311

3.5. JICA FC Statistical Analysis

FC joint subnetworks in patients with SZ were compared to HC in terms of several metrics.

A metric that showed significant differences was the clustering coefficient. Subnetworks #3 and #7 showed lower clustering coefficients in SZ patients than in HC. This suggests that these subnetworks are less interconnected in patients with SZ. Another metric that showed significant differences was network strength. Subnetwork #3 showed lower network strength in SZ patients compared to HC. This suggests that this subnetwork is less active in SZ patients. Eccentricity showed in Subnetworks #2, #10, and #1 were higher in SZ patients than HC. This suggests that these subnetworks are more disrupted in patients with SZ.

Local efficiency showed significant differences in subnetworks #3, #7, and #1, with lower values observed in SZ patients.

Global efficiency showed lower values in subnetwork #1 in SZ than in HC. This suggests that information transfer is less efficient across the whole brain network in SZ patients.

Characteristic path length showed higher values in subnetwork #2 in patients with SZ than HC. This suggests that the average distance between pairs of nodes is greater in this subnetwork in patients with SZ.

Maximum modularity showed significant differences in subnetworks #4 and #9, with lower values observed in SZ patients. This suggests that these subnetworks are less modular in patients with SZ.

The diameter and radius showed significant differences in multiple subnetworks. This suggests that the overall structure of these subnetworks is disrupted in patients with SZ. For a more detailed analysis of graph measure values and their changes in each jICA FC subnetwork, readers refer to Table 7.

3.6. JICA SC Statistical Analysis

Statistical analysis of the SC joint network reveals, significant differences between SZ and HC.

Subnetworks #1, #3, #5, #6, and #9, there had lower network strengths in SZ than HC. Additionally, maximum modularity was significantly lower in subnetworks #1, #4, and #6 in SZ than in HC. These findings suggest that there are disruptions in the SC joint network in individuals with SZ.

Other graph measures that showed significant differences between SZ and HC included local efficiency, clustering coefficient, betweenness, and global efficiency. These measures were significantly lower in subnetwork #3 in SZ than in HC. For a more detailed analysis of graph measure values and their changes in each jICA SC subnetwork, readers refer to Table 8.

Table 7. Statistical graph measures jICA FC subnetworks analysis

jICA subnetwork	Significant graph measure	Mean and SD HC	Mean and SD SZ	P-value
#1	Global efficiency	0.2099±0.0112	0.2042±0.0132	<0.0001
	Local efficiency	0.1648±0.0120	0.1587±0.0154	0.0200
	Eccentricity	9.5580±0.6444	9.9980±1.0318	0.0385
#2	Radius	5.7011±0.6478	6.1749±0.6096	0.0040
	Eccentricity	7.072±0.6884	7.603±0.7694	0.0089
	Diameter	8.8182±0.9284	9.5426±1.3534	0.0140
	Characteristic path length	4.3129± 0.4279	4.5421±0.4584	0.0466
#3	Radius	5.6983±0.5456	6.1127±0.5228	0.0092
	Network strength	17.2231±3.5778	15.529±2.3429	0.0441
	Local efficiency	0.1794±0.0426	0.1601±0.0281	0.0480
	Clustering coefficient	0.1330±0.0357	0.1164±0.0220	0.0480
#4	Max modularity	0.2196±0.0162	0.2075±0.0137	0.0053
#7	Radius	5.9906±0.58855	6.3525±0.4977	0.0234
	Clustering coefficient	0.0851±0.0145	0.0784±0.0136	0.041
	Local efficiency	0.1580±0.0255	0.1470±0.0235	0.0460
#9	Max modularity	0.2029±0.0122	0.1944± 0.0134	0.0224
#10	Eccentricity	8.0484±0.7478	8.5843±0.7648	0.0107
	Diameter	9.9852±1.0309	10.858±1.2485	0.0204

Table 8. Statistical graph measures jICA SC subnetworks analysis

jICA Subnetwork	Significant graph measure	Mean & SD HC	Mean & SD SZ	P-value
#1	Max modularity	0.5250±0.0208	0.5057±0.0208	0.0015
	Network strength	0.1302±0.1571	0.1038±0.0077	0.0429
#3	Network strength	0.0323±0.0033	0.0275±0.0041	<0.0001
	Local efficiency	$0.0004 \pm 9.92\times10^{-5}$	0.0003±0.0001	0.0003
	Clustering coefficient	$0.0004 \pm 8.26\times10^{-5}$	0.0003±0.0001	0.0006
	Global efficiency	00016± 0.0001	0.0014±0.0002	0.0009
	Betweenness	627.44±36.55	661.60±48.583	0.0077
#4	Max modularity	0.6454±0.0201	0.6393±0.0195	0.0292
#5	Network strength	0.0392±0.0046	0.0356±0.0028	0.0013
#6	Network strength	0.0233±0.0027	0.0214±0.0021	0.0077
	Max modularity	0.6989±0.0318	0.6793±0.0309	0.0333
#9	Network strength	0.0374±0.0041	0.0346±0.0034	0.0062

4. Discussion

In this study, we investigated brain connectivity in HC and SZ patients using graph measures in 2 states: first, whole brain, and second, brain subnetworks. These investigations were aimed at finding the importance of brain partitioning into subregions, finding important regions and graph measures in SZ diagnosis, and investigating the association between FC and SC in SZ.

In the whole brain analysis according to Tables 3 and 4, few measures can distinguish SZ patients from HC. Structural connection differs in clustering coefficients, max modularity, and network strength. Functional connection differs only in clustering coefficients.

So, our results showed that analyzing the whole brain may not be the most effective method for studying the brain peculiarities of SZ patients in our data.

Using jICA and ICA, we can partition the brain into 10 subnetworks. A similar study has shown that subnetworks analysis is an effective approach to understanding SZ disease. This study showed that functional and structural brain changes are observed in some brain regions, but many regions only change in FC or SC connectivity [15].

This suggests that there is no simple one-to-one relationship between these two types of connectivity in the brain.

In addition, overlap values between structural and functional connectivity in Tables 1 and 2 confirm the relation between brain structure and function, a finding that is consistent with recent studies [16].

Also, according to Figures 3 and 4, we can infer that adding structural information to functional subnetworks, and vice versa, can cause extensive changes in subnetworks.

According to topological changes in subnetworks, when using the jICA algorithm, we recommend investigating subnetwork #3 in both SC and FC. When using the ICA algorithm, we recommend subnetworks #7 and #5 in FC and subnetwork #1 in SC. The abovementioned subnetworks overlap the most with Default Motor (DMN), visual, and Somatomotor (SM) Resting State Networks (RSNs). Our results show the jICA functional and structural subnetwork #3 is important in SZ and extensive changes in these regions have been reported in various studies. Therefore, by utilizing the jICA algorithm, we can elicit more structural and functional information that relates to SZ because both of them were involved in the construction of subnetworks. This is not possible with the ICA algorithm. A similar study showed that multimodal ICA fusion models are effective for SZ diagnosis. Also, some studies have assessed the correlation between structural and functional connectivity as multimodality. They used ICA to identify associations. Consistent with our findings, they proved the good potential of the brain networks method for investigating individuals with mental disease [17, 18].

Additionally, examining graph measures in each subnetwork reveals extensive changes that these parameters undergo, which is not possible when examining the whole brain. According to Tables 5, 6, 7, and 8, our findings in topology changes are supported by several studies. The results indicate that network strength, global efficiency, maximum modularity, clustering coefficient, and path length are important measures in examining topology changes in patients with SZ [19-24].

Global efficiency is an important measure that helps us understand network topology and the efficiency of parallel information transmission. Furthermore, path length relates to a complex disorder that affects cognition, emotion, and behavior, and is characterized by a reduced ability to process and integrate information across different brain regions. Additionally, clustering coefficients measure the interconnectedness of nodes in a network. Recent research suggests that individuals with SZ have less efficient brain networks than HC, which may contribute to cognitive and social deficits associated with the disorder. Furthermore, modularity is a network topology measure that quantifies the degree to which a network can be subdivided into densely interconnected modules. Also, mean network strength relates to disruption in information integration. that reduced brain [22-24].

5. Conclusion

This study aimed to investigate brain connectivity in HC and SZ patients using graph measures in two states: whole brain and brain subnetworks. Results showed that just a few measures can distinguish SZ patients from HC in whole-brain analysis, suggesting that whole-brain analysis might not be the optimal method for brain analysis. This study also found that multimodal brain analysis in understanding SZ disease is an effective approach. Examining graph measures in each subnetwork revealed extensive changes that these measures undergo, which is not possible when examining the whole brain. The most important differentiators between HC and SZ were in maximum modularity, network strength, global efficiency, and clustering coefficient in various subnetworks. This study's authors recommend investigating SC and FC of SZ patients in specific subnetworks that overlap with DMN, visual, and SM RSNs. Overall, this study highlights the importance of investigating brain connectivity using a multimodal approach and analyzing subnetworks for a more detailed understanding of SZ disease.

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