The resting-state topological organization damage of language-related brain regions in post-stroke cognitive impairment

Sirui Wang1 · Bo Rao2 · Guofu Miao1 · Xin Zhang1 · Jun Zheng1 · Junbin Lin1 · Minhua Yu2 · Xiaoli Zhou2 · Haibo Xu2 · Weijing Liao1

Accepted: 14 August 2022 / Published online: 22 September 2022
© The Author(s), under exclusive licence to Springer Science+Business Media, LLC, part of Springer Nature 2022

Abstract
The topology of brain networks is the foundation of cognition. We hypothesized that stroke damaged topological organization resulting in cognitive impairment. The aim was to explore the damage pattern of the resting-state topology in post-stroke cognitive impairment (PSCI) patients. Thirty-seven patients with PSCI and thirty-seven gender- and age-matched healthy controls (HC) were recruited. The structural and functional data were collected from all subjects. The degree centrality (DC), betweenness centrality (BC), and global properties of brain networks were analyzed between groups. Spearman correlation analysis was performed between topological properties that changed significantly and clinical cognitive function scale scores. Compared with HC, the PSCI patients had significantly reduced DC in language-related brain regions and significantly higher DC in the right frontal lobe, hippocampus, and paracentral lobule. The decreased BC was located in the left caudate, thalamus, temporal, and frontal lobes. The increased BC was detected in the left cuneus and right precuneus. In addition, PSCI exhibited increased characteristic path length and decreased small-worldness. PSCI patients had impaired functional topology of the language-related brain regions, mainly in the left hemisphere. The enhanced processing and relaying information of some right high-order cognitive brain regions may be a compensatory mechanism. However, the whole brain's function integration was reduced, and there was an imbalance between efficiency and consumption.

Keywords Post-stroke cognitive impairment · Resting-state functional magnetic resonance imaging · Degree centrality · Betweenness centrality · Small-worldness

Introduction
Post-stroke cognitive impairment (PSCI) is a clinical syndrome of cognitive impairment that occurs after a stroke, affecting approximately one-third of stroke survivors (Iadecola et al., 2019; Sun et al., 2014). They manifest as impairments in various cognitive domains (e.g., attention, memory, executive function, language, and visual space) (Mijajlovic et al., 2017). Several studies have confirmed that abnormal functional connectivity may be related to PSCI pathophysiological mechanisms, notable alterations in the default mode network (DMN), and language-related network (Ding et al., 2014; Hartwigsen & Saur, 2019; Thiel & Zum-bansen, 2016; Tuladhar et al., 2013). In addition, studies have shown changes in the topological organization of brain networks in cognitive impairment patients (Dai & He, 2014; Xiang et al., 2013).

The human brain is a complex network that achieves an optimal balance of efficiency and cost. Graph theory is a powerful mathematical method that quantifies network representations' topology to understand better complex systems (Bullmore & Sporns, 2009). Accumulating evidence has indicated that it was feasible to explore brain network organization using a complex network theory based on graph theory, and network topology is the base of cognition (Bullmore & Sporns, 2009, 2012; Sporns, 2018). Studies have demonstrated that the human brain's complex network features, such as small-world properties and highly connected hubs, reflect the optimal balance of efficiency and cost.
(Farahani et al., 2019). However, pathological injury may affect network organizations differently, resulting in cognitive impairment (delEtoile & Adeli, 2017; Wright et al., 2021). Some studies have used graph-theoretic analysis to characterize the topological changes of neural networks in cognitive impairment patients. Xiang et al. demonstrated changes in nodal properties of brain regions presented in Alzheimer’s disease (AD) patients using graph-theoretic analysis (Xiang et al., 2013). Network function in various brain regions progressively deteriorates, increasing with cognitive impairment. The topological organization of the large-scale brain network was disrupted in mild cognitive impairment patients, significantly associated with a decline in cognitive function (Dai & He, 2014).

Furthermore, recent research has revealed that the topology of the brain network changes in stroke patients (de Pasquale et al., 2021; Miao et al., 2021; Shi et al., 2021). Blaschke et al. found similar changes in small-worldness and characteristic path length in stroke mice and stroke patients in the first few days after stroke (Blaschke et al., 2021). Shi et al. found that the topological properties of the functional brain network were disrupted in patients with acute brainstem ischemic stroke (Shi et al., 2021). The relationship between changes in topological properties and cognitive function in patients with post-stroke cognitive impairment is unclear. Our previous study found that PSCI patients showed disrupted low-degree rich club organizations (Miao et al., 2021). However, the topological properties of PSCI patients have not been sufficiently studied.

Based on the prior study, we hypothesized that impairment in the topological properties of cognitively relevant nodes existed in the PSCI, which could be caused by a stroke. We validated the impairment pattern of cognitive-related nodes in the topological organization of PSCI patients. We also explored the potential relationship between topological properties that changed significantly and clinical symptoms.

Materials and methods

Participants

This study included 37 PSCI patients and 37 demographically matched healthy controls (HC). We used G*power 3.1 to calculate the sample of our study with two-sample t-tests (effect size = 0.8, α = 0.05, power = 0.90, two tails) (Dai & He, 2014; Faul et al., 2007). We recruited the PSCI patients from the Department of Neurological Rehabilitation in Zhongnan Hospital of Wuhan University and recruited the HCs by advertisement. We have admitted these participants from November 2019 to December 2020. Fulfillment of the following inclusion criteria was confirmed for all stroke subjects: 1) met the cerebral apoplexy diagnostic criteria and were confirmed by CT or MRI; 2) first-ever stroke with an early phase (Bernhardt et al., 2017); 2) 40 to 80 years old; 3) cognitive impairment as assessed by the cognitive screening, Montreal Cognitive Assessment (MoCA) < 26 (Yin et al., 2020); 4) right-handed; and 5) participate voluntarily and sign an informed consent form. The exclusion criteria were as follows: 1) unstable vital signs; 2) other brain diseases such as intracranial inflammation, Parkinson’s disease, intracranial space-occupying lesions; 3) a history of pre-stroke cognitive impairment such as Alzheimer’s disease, dementia, and mild cognitive impairment; 4) severe aphasia or any mental illness that could not complete the cognitive test; and 5) MRI contraindications.

The Medical Research Ethics Committee and Zhongnan Hospital’s Institutional Review Board approved this study (2,019,012). All individual participants signed informed consent.

Behavioral assessment

Professional therapists carried out neuropsychological exams. The Mini-Mental State Examination (MMSE) and the Montreal Cognitive Assessment (MoCA) were selected to evaluate the neurocognitive state of all participants.

Data acquisition

A MAGNETOM Trio 3.0 Tesla MR scanner obtained all resting-state fMRI and T1-weighted images (Siemens, Germany). Resting-state data were acquired using a gradient-echo planar imaging (EPI) sequence for this analysis. The scanning parameters were as follows: TR/TE = 2000 / 30 ms, FOV = 240 mm × 240 mm, flip angle (FA) = 78°, matrix = 64 × 64, thickness = 4.0 mm, number of slices = 35, and voxel size = 3.75 × 3.75 × 4 mm³. High-resolution sagittal T1-weighted images were collected using a three-dimensional magnetization-prepared rapid gradient echo (3D-MPRAGE) sequence, and the scanning parameters were as follows: TR/TE = 2000 / 2.3 ms, thickness = 1.0 mm, FA = 8°, FOV = 225 mm × 240 mm and voxel size = 1 × 1 × 1 mm³. Participants were told to lie down in a comfortable position, close their eyes, stay awake, and avoid thinking about anything during functional MRI scanning. To ensure the MRI scan’s smooth progress and the image’s quality, use two foam pads to fix the patient’s head and use rubber earplugs to reduce the noise generated during the MRI scan.

Data preprocessing

Data preprocessing was performed in the MATLAB environment (Mathworks, Natick, MA, USA) using the SPM 12 (http://www.fil.ion.ucl.ac.uk/spm) based DPABI software.
v6.0 (http://rfmri.org/DPABI). First, we conversed the Neuroimaging Technology Initiative (NIFTI) format from the raw DICOM images and removed the first 10 volumes. The remaining images were then slice timing and realignment corrected for head motion. Participant data demonstrating head movement > 2.0 mm translation or > 2.0° rotation were excluded from the analysis. Then, the structural and functional images were coregistered and spatially normalized to the standard Montreal Neurological Institute (MNI) space with 3 × 3 × 3 mm³ resample, followed by the smoothing with a 4 × 4 × 4 mm³ full-width-half-maximum (FWHM) Gaussian kernel. In addition, linear regression excluded many sources of spurious variances, including the Friston 24 motion parameters and the white matter and cerebrospinal fluid signals (Friston et al., 1996). Finally, 0.01–0.08 low-frequency filter was done (Biswal et al., 1995).

Network construction

The functional brain network was constructed by a graph theoretical network analysis toolbox named GRETNA (Wang et al., 2015). The cortical surface was segmented into 90 regions (45 regions in each hemisphere) as network nodes using the Automated Anatomical Labeling (AAL) 90 template (Tzourio-Mazoyer et al., 2002). The edges were formed by Pearson’s correlation coefficients between a node and the remaining nodes of the averaged time series of the BOLD signal. The 90 × 90 functional connectivity matrices were successfully created for all participants.

Functional brain network analysis

The sparsity threshold was set in the range of 0.05 to 0.50, and the step size was set to 0.01 for node and global topological property analysis (Achard & Bullmore, 2007). The node topology properties included degree centrality (DC) and betweenness centrality (BC). DC is calculated by counting the number of direct connections from one node to all others. Given an entire network, DC can indicate communicating ability of the information flow between other nodes (Fagerholm et al., 1995). DC is calculated by counting the number of direct connections from one node to all others. Given an entire network, DC can indicate communicating ability of the information flow between other nodes (Fagerholm et al., 1995). The cortical surface was segmented into 90 regions (45 regions in each hemisphere) as network nodes using the Automated Anatomical Labeling (AAL) 90 template (Tzourio-Mazoyer et al., 2002). The edges were formed by Pearson’s correlation coefficients between a node and the remaining nodes of the averaged time series of the BOLD signal. The 90 × 90 functional connectivity matrices were successfully created for all participants.

SPSS 23.0 software was used for data analysis, and numerical variables were expressed as mean ± standard deviation. We used the Shapiro–Wilk (S-W) test to analyze the normal distribution. A chi-square test for gender was performed. Two independent samples t-test was used to test the difference in age, years of education, duration of disease, MMSE score, MoCA score, and AUC for each nodal and global attribute index. The between-group differences in DC and BC were assessed using permutation tests (5000 times, P < 0.05) (Winkler et al., 2016). Spearman correlation analysis was performed between topological properties that changed significantly and clinical parameters. P < 0.05 indicates a statistically significant difference.

Results

Demographic and clinical results

Thirty-seven patients with PSCI and thirty-seven HCs were included in this study. The baseline information of the study subjects was shown in Table 1. After statistical analysis, the differences in gender, age, and years of education between the two groups were not statistically significant (P > 0.05). The MoCA and MMSE scores were significantly lower in the PSCI group than in the HC group (P < 0.001). The

| Table 1 Demographic and clinical data in PSCI group and healthy control group (HC) |
|---------------------------------|-----------------|----------------|
| Variables                      | PSCI(n = 37)    | HC(n = 37)     | p value |
| Age (years)                    | 57.78 ± 10.38   | 57.97 ± 10.43  | 0.94    |
| Sex(male/female)               | 30/7            | 30/7           | 1       |
| Education(years)               | 11.92 ± 3.07    | 11.81 ± 2.61   | 0.87    |
| Disease duration (days)        | 44.43 ± 23.89   | -              | -       |
| Site of lesion (cortical/sub-cortical) | 18/19          |                |         |
| MMSE                           | 19.49 ± 5.24    | 28.84 ± 0.76   | <0.000  |
| MoCA                           | 15.97 ± 4.92    | 28.30 ± 1.22   | <0.000  |

A chi-square test for gender was performed. Two independent samples t-test was used to test the difference in age, years of education, MMSE and MoCA scores. MMSE: Mini-Mental State Examination; MoCA: Montreal Cognitive Assessment.
lesions in 19 patients with PSCI were located in the thalamus and basal ganglia, while those in 18 patients with PSCI were mainly cortical damage (see Table S1).

**Between-group differences in DC**

Compared with HC, the PSCI patients showed reduced DC in the bilateral caudate, left angular, and left temporal pole compared with the HC group. In contrast, increased DC in the right middle frontal gyrus (orbital part), hippocampus, and paracentral lobule was observed in the PSCI group (Fig. 1 and Table S2).

**Between-group differences in BC**

The results showed that the differences in BC between the PSCI and HC groups were statistically significant in some brain regions. The brain regions with decreased BC in the PSCI group were: the left precentral gyrus, middle frontal gyrus, inferior frontal gyrus (orbital part), caudate, thalamus, temporal pole, and inferior temporal gyrus. The brain regions with increased BC in the PSCI group were: the left rolandic operculum, left cuneus, right precuneus, and right paracentral lobule (Fig. 2 and Table S3).

**Between-group differences in global topological properties**

A comparison of global topological properties showed that the small-worldness was more significant than 1 in the threshold range in both groups (Fig. 3). Compared with the HC group, the AUC of $L_p$ and $\lambda$ increased, and the AUC of $\gamma$ and $\sigma$ decreased in the PSCI group, and the differences were all statistically significant ($P < 0.05$). There were no differences for the AUC of $C_p$ (Fig. 4 and Table S4).

**Correlation analysis**

No areas were correlated with MoCA and MMSE scores.

**Discussion**

This study investigated the resting-state topological properties in PSCI patients. The results supported our hypothesis that related cognitive nodes have abnormal topological properties in PSCI patients.

![Fig. 1 The nodes with differential DC in the PSCI group compared to the HC group. Red color represents nodes with increased DC, and blue color represents nodes with decreased DC. DC: degree centrality; PSCI: post-stroke cognitive impairment; HC: healthy control; ANGL: left angular gyrus; CAUL: left caudate nucleus; CAUR: right caudate nucleus; TPOsupL: left temporal pole: superior temporal gyrus; ORBmidR: right middle frontal gyrus, orbital part; HIPR: right hippocampus; PCLR: right paracentral lobule](image)
Between-group differences in DC

Our study found that the DC of the left angular gyrus and left temporal pole was significantly reduced in the PSCI group compared with the HC group. The angular gyrus belongs to Wernicke's area, a sensory-linguistic center involved in language-related cognitive studies, such as phonological, semantic, episodic, and speech comprehension (Fujii et al., 2016; Humphreys et al., 2021; Leff et al., 2009; Seghier, 2013). The decreased DC observed in the angular gyrus was consistent with previous findings in stroke with basal ganglia and cognitive impairment patients (Yao et al., 2020). Zhao
et al. found that the reduced DC of the left anterior temporal lobe and the bilateral anterior cingulate cortex correlated significantly with the severity of semantic performance deficits, consistent with our study (Zhao et al., 2017). We found significantly lower DC in the bilateral caudate in PSCI patients. The caudate nucleus is the most significant input nucleus to the basal ganglia and is involved in cognitive processes and sensory processing, reward processing, learning, and memory (Grahn et al., 2008; Haber, 2016). The caudate nucleus is a crucial node of the frontal-subcortical circuit.

Guo et al. found that post-stroke aphasia patients presented abnormalities in the integration capacity of the caudate and thalamus (Guo et al., 2019). These results may suggest that PSCI patients had impaired function of the language-related brain regions, resulting in patients with language-related cognitive deficits in multiple aspects of phonological and semantics.

Our study found increased DC in the right middle frontal gyrus (orbital part) and hippocampus for PSCI patients. The left orbital of the middle frontal gyrus is related to emotional regulation (Hiser & Koenigs, 2018). The brain would undergo self-repair and reconstruction after injury (Szelenberger et al., 2020). Enhanced DC in the right middle frontal gyrus may reflect compensatory mechanisms. The hippocampus plays a critical role in memory function and stores and retrieves situational memories (Lisman et al., 2017). Xi et al. found that the amplitude of low-frequency fluctuations values in the right hippocampus was positively correlated with MMSE scores (Xi et al., 2012). These studies supported our results to some extent, emphasizing that enhanced processing information of some nodes of the right hemisphere act as a compensatory mechanism.

**Between-group differences in BC**

The BC of the left caudate, the left inferior frontal gyrus (orbital part), the left temporal pole, and the left inferior temporal gyrus was reduced, indicating the relay function impairment for communication between nodes. Yao et al. found that patients with mild cognitive impairment and AD showed reduced BC in the medial temporal gyrus, generally consistent with previous results (Yao et al., 2010). The damage to these brain regions led to language function disorder. Also, we found that the left middle frontal gyrus and left thalamus of PSCI patients had significantly reduced BC. The middle frontal gyrus is associated with cognitive control processes and language switching (Sierpowska et al., 2018). Decreased BC in the middle frontal gyrus suggested partial damage to the connection between the nodes with the middle frontal gyrus as a relay. The thalamus is the relay station of the higher cortical-thalamocortical classical circuit (Wolff & Vann, 2019). Stebbins et al. suggested a central role for the thalamus volume in the developing cognitive impairment after ischemic stroke (Stebbins et al., 2008). As a result, the

Fig. 4 The global properties between PSCI and HC groups. PSCI: post-stroke cognitive impairment; HC: healthy control; Cp: clustering coefficient; Lp: characteristic path length; γ: normalized clustering coefficient; λ: normalized characteristic path length; σ: small-world-ness; AUC: area under the curve
damage to the cortical-thalamocortical circuit may result in cognitive impairment.

In addition, BC was significantly increased in the left cuneus and right precuneus, which belong to the DMN (Raichle, 2015). Chen et al. found significantly enhanced DMN node properties in subjective cognitive decline patients compared to healthy people (Chen et al., 2020). Similar to DC, strengthened BC in the left cuneus and right precuneus may represent compensatory mechanisms.

**Between-group differences in global topological properties**

Functional segregation and integration are the fundamental organizing principles of brain networks (Wang et al., 2021). The network topology of PSCI exhibited roughly similar Cp, but increased Lp compared with HC. The Cp assesses the nodes’ interconnectivity neighboring the node of interest and reflects network segregation (Bullmore & Sporns, 2009). On the other hand, the Lp quantifies the mean distance between a node and other nodes, reflecting network integration. Kabbara et al. found that AD networks are characterized by reduced integration and increased segregation (Kabbara et al., 2018). Our results found that the difference in Cp between PSCI patients and HC was not statistically significant, indicating no difference in segregation ability. Compared with the HC group, the Lp was significantly higher in the PSCI patients, indicating that the network information transfer decreased and more resources were consumed. Our result was inconsistent with previous studies, probably because the affected nodes were distinct due to different pathological mechanisms.

Our study showed that both groups had small-world characteristics, but PSCI patients had lower small-worldness than HC. Our results were consistent with Shi et al.’s study, which indicated that both unilateral acute brainstem stroke patients and HCs exhibited small-world characteristics (Shi et al., 2021). The small-worldness is characterized by the balance between efficiency and cost, which is key to functional cognitive networks (Humphries & Gurney, 2008). Siegel et al. revealed that the small-worldness significantly reduced in patients with acute stroke and partially recovered by three months (Siegel et al., 2018). Vecchio et al. found similar results and concluded that small-worldness played a vital role in the recovery prediction (Vecchio et al., 2019). Our study showed that PSCI patients had lower small-worldness than HC, indicating an imbalance in efficiency and cost, representing a low-inefficient and high-cost state.

**Correlation analysis**

We found that no areas were correlated with MoCA and MMSE language items. We have done the supplementary analysis based on MMSE and MoCA language items. No areas were correlated with MoCA and MMSE language items. This may be related to the heterogeneity of the patient, such as the type and location of the stroke. It may also be associated with the small sample size.

**Limitations**

This study had several limitations. Firstly, this study had a small sample size. Thus, future studies should be performed on PSCI patients with larger sample sizes. Secondly, the location of the lesion in stroke patients may be crucial information for differences between groups. We should study further by group according to their stroke type and lesion in the future. Thirdly, stroke patients with non-cognitive impairment should also be set as a control group to explore the effect of stroke on graph theory properties. Finally, we should divide patients into different groups to investigate whether topological properties progressively deteriorate with the progression of cognitive impairment.

This study could be replicated in the future by grouping according to stroke type and location of stroke lesions with larger sample sizes. We should also use language-specific behavioral evaluations, such as the Boston naming and word fluency tests.

**Conclusions**

The language-related brain regions (angular gyrus, temporal pole, inferior temporal gyrus, and caudate), mainly in the left hemisphere, were functionally impaired in patients with PSCI. The enhanced processing and relaying information of some right high-order cognitive brain regions (middle frontal gyrus, hippocampus, cuneus, and precuneus) may compensate for the left-side damage. However, the whole brain’s function integration was reduced, and there was an imbalance between efficiency and depletion. Our findings may provide a neuroimaging pathology mechanism and new insights for PSCI patients.

**Supplementary Information** The online version contains supplementary material available at https://doi.org/10.1007/s11682-022-00716-8.

**Acknowledgements** Thanks to all those who helped our department in this study and to all those who participated.

**Author contributions** Author contributions included conception and study design (Sirui Wang, Bo Rao, Haibo Xu and Weijing Liao), data collection or acquisition (Guofu Miao, Xin Zhang, Jun Zheng, Junbin Lin, Minhua Yu and Xiaoli Zhou), statistical analysis (Sirui Wang, Bo Rao and Guofu Miao), interpretation of results (Sirui Wang and Bo Rao), drafting the manuscript work or revising it critically for important intellectual content (Sirui Wang, Bo Rao, Haibo Xu and Weijing Liao) and approval of final version to be published and agreement to
be accountable for the integrity and accuracy of all aspects of the work (All authors).

**Funding** This study was supported by the National Key Technology Research and Development Program of China (2018YFC2002300), and the research fund from medical Sci-Tech innovation platform of Zhongnan Hospital, Wuhan University National (PTXM20222020).

**Data availability** All data generated or analyzed during this study are included in this article and its supplementary information files.

**Declarations**

**Ethical approval** The Medical Research Ethics Committee and Zhongnan Hospital’s Institutional Review Board approved this study (2,019,012).

**Consent to participate** Informed consent was obtained from all individual participants included in this study.

**Consent to publication** Not applicable.

**Conflict of interest** None of the authors have a conflict of interest to declare.

**References**

Achard, S., & Bullmore, E. (2007). Efficiency and cost of economical brain functional networks. PLoS Computational Biology, 3(2), e17. https://doi.org/10.1371/journal.pcbi.0030017

Bernhardt, J., Hayward, K. S., Kwakkel, G., Ward, N. S., Wolf, S. L., Borschmann, K., ..., Cramer, S. C. (2017). Agreed definitions and a shared vision for new standards in stroke recovery research: The Stroke Recovery and Rehabilitation Roundtable taskforce. International Journal of Stroke, 12(5), 444–450. https://doi.org/10.1177/1747493017711816

Biswal, B., Yetkin, F. Z., Haughton, V. M., & Hyde, J. S. (1995). Functional connectivity in the motor cortex of resting human brain using echo-planar MRI. Magnetic Resonance in Medicine, 34(4), 537–541. https://doi.org/10.1002/mrm.1910340409

Blaschke, S. J., Hensel, L., Minassian, A., Vlachakis, S., Tscherpel, C., Vay, S. U., ..., Rueger, M. A. (2021). Translating Functional Connectivity After Stroke: Functional Magnetic Resonance Imaging Detects Comparable Network Changes in Mice and Humans. Stroke, 52(9), 2948–2960. https://doi.org/10.1161/STROKEAHA.120.032511

Bullmore, E., & Sporns, O. (2009). Complex brain networks: Graph theoretical analysis of structural and functional systems. Nature Reviews Neuroscience, 10(3), 186–198. https://doi.org/10.1038/nrn2575

Bullmore, E., & Sporns, O. (2012). The economy of brain network organization. Nature Reviews Neuroscience, 13(5), 336–349. https://doi.org/10.1038/nrn3214

Chen, H., Sheng, X., Luo, C., Qin, R., Ye, Q., Zhao, H., ..., Bai, F. (2020). The compensatory phenomenon of the functional connectome related to pathological biomarkers in individuals with subjective cognitive decline. Transl Neurodegener, 9(1), 21. https://doi.org/10.1186/s40035-020-00201-6

Dai, Z., & He, Y. (2014). Disrupted structural and functional brain connectomes in mild cognitive impairment and Alzheimer’s disease. Neuroscience Bulletin, 30(2), 217–232. https://doi.org/10.1007/s12264-013-1421-0

de Pasquale, F., Chiacchiaretta, P., Pavone, L., Sparano, A., Capotosto, P., Grillea, G., ..., Baldassarre, A. (2021). Brain Topological Reorganization Associated with Visual Neglect After Stroke. Brain Connect. https://doi.org/10.1089/brain.2020.0969

delEtoile, J., & Adeli, H. (2017). Graph theory and brain connectivity in Alzheimer’s disease. The Neuroscientist, 23(6), 616–626. https://doi.org/10.1177/1073858417702621

Ding, X., Li, C. Y., Wang, Q. S., Du, F. Z., Ke, Z. W., Peng, F., ..., Chen, L. (2014). Patterns in default-mode network connectivity for determining outcomes in cognitive function in acute stroke patients. Neuroscience, 277, 637–646. https://doi.org/10.1016/j.neuroscience.2014.07.060

Fagerholm, E. D., Hellyer, P. J., Scott, G., Lecch, R., & Sharp, D. J. (2015). Disconnection of network hubs and cognitive impairment after traumatic brain injury. Brain, 138(Pt 6), 1696–1709. https://doi.org/10.1093/brain/awv075

Farahani, F. V., Karwowski, W., & Lighthall, N. R. (2019). Application of graph theory for identifying connectivity patterns in human brain networks: A systematic review. Frontiers in Neuroscience, 13, 585. https://doi.org/10.3389/fnins.2019.00585

Faul, F., Erdfelder, E., Lang, A. G., & Buchner, A. (2007). G*Power 3: A flexible statistical power analysis program for the social, behavioral, and biomedical sciences. Behavior Research Methods, 39(2), 175–191. http://doi.org/10.3758/bf03193146

Friston, K. J., Williams, S., Howard, R., Frackowiak, R. S., & Turner, R. (1996). Movement-related effects in fMRI time-series. Magnetic Resonance in Medicine, 35(3), 346–355. https://doi.org/10.1002/mrm.1910350312

Fuji, M., Maesawa, S., Ishiai, S., Iwami, K., Futamura, M., & Saito, K. (2016). Neural basis of language: An overview of an evolving model. Neurologia Medico-Chirurgica (Tokyo), 56(7), 379–386. https://doi.org/10.2176/nmca.2016-0014

Grahn, J. A., Parkinson, J. A., & Owen, A. M. (2008). The cognitive functions of the caudate nucleus. Progress in Neurobiology, 86(3), 141–155. https://doi.org/10.1016/j.pneurobio.2008.09.004

Guo, J., Yang, M., Biswal, B. B., Yang, P., Liao, W., & Chen, H. (2019). Abnormal functional connectivity density in post-stroke aphasia. Brain Topography, 32(2), 271–282. https://doi.org/10.1007/s10548-018-0681-4

Haber, S. N. (2016). Corticostriatal circuitry. Dialogues Clin Neurosci, 18(1), 7–21. https://doi.org/10.31887/DCNS.2016.18.1/shaber

Hartwigsen, G., & Saur, D. (2019). Neuroimaging of stroke recovery from aphasia - Insights into plasticity of the human language network. Neurolmage, 190, 14–31. https://doi.org/10.1016/j.neuroimage.2017.11.056

Hiser, J., & Koensigs, M. (2018). The multifaceted role of the ventromedial prefrontal cortex in emotion, decision making, social cognition, and psychopathology. Biological Psychiatry, 83(8), 638–647. https://doi.org/10.1016/j.biopsych.2017.10.030

Humphreys, G. F., Lambon Ralph, M. A., & Simons, J. S. (2021). A unifying account of angular gyrus contributions to episodic and semantic cognition. Trends in Neurosciences, 44(6), 452–463. https://doi.org/10.1016/j.tins.2021.01.006

Humphries, M. D., & Gurney, K. (2008). Network ‘small-world-ness’: A quantitative method for determining canonical network equivalence. PLoS One, 3(4), e0002051. https://doi.org/10.1371/journal.pone.0002051

Iadecola, C., Duering, M., Hachinski, V., Joutel, A., Pendlebury, S. T., Schneider, J. A., & Dichgans, M. (2019). Vascular cognitive impairment and dementia: JACC scientific expert panel. Journal of the American College of Cardiology, 73(25), 3326–3344. https://doi.org/10.1016/j.jacc.2019.04.034

Kabbara, A., Eid, H., El Falou, W., Khalil, M., Wendling, F., & Has san, M. (2018). Reduced integration and improved segregation of functional brain networks in Alzheimer’s disease. Journal of...
Neural Engineering, 15(2), 026023. https://doi.org/10.1088/1741-2552/aaa776
Leff, A. P., Schofield, T. M., Crinion, J. T., Seghier, M. L., Grogan, A., Green, D. W., & Price, C. J. (2009). The left superior temporal gyrus is a shared substrate for auditory short-term memory and speech comprehension: Evidence from 210 patients with stroke. Brain, 132(Pt 12), 3401–3410. https://doi.org/10.1093/brain/awp273
Lisman, J., Buzsaki, G., Eichenbaum, H., Nadel, L., Ranganath, C., & Redish, A. D. (2017). Viewpoints: How the hippocampus contributes to memory, navigation and cognition. Nature Neuroscience, 20(11), 1434–1447. https://doi.org/10.1038/nn.4661
Miao, G., Yao, B., Wang, S., Fang, P., Chen, Z., Chen, L., …, Liao, W. (2021). Decreased functional connectivity of low-degree level rich club organization and caudate in post-stroke cognitive impairment based on resting-state fMRI and radiomics features. Frontiers in Neuroscience, 15, 796530. https://doi.org/10.3389/fnins.2021.796530
Mijailovic, M. D., Pavlovic, A., Brainin, M., Heiss, W. D., Quinn, T. J., Ihle-Hansen, H. B., …, Bornstein, N. M. (2017). Post-stroke dementia - a comprehensive review. BMC Medicine, 15(1), 11. https://doi.org/10.1186/s12916-017-0779-7
Raichle, M. E. (2015). The brain’s default mode network. Annual Review of Neuroscience, 38, 433–447. https://doi.org/10.1146/annurev-neuro-071013-040300
Seghier, M. L. (2013). The angular gyrus: Multiple functions and multiple subdivisions. The Neuroscientist, 19(1), 43–61. https://doi.org/10.1177/1073858412459606
Shi, M., Liu, S., Chen, H., Geng, W., Yin, X., Chen, Y. C., & Wang, L. (2021). Disrupted brain functional network topology in unilateral acute brainstem ischemic stroke. Brain Imaging and Behavior, 15(1), 444–452. https://doi.org/10.1186/s11682-020-00353-z
Siegel, J. S., Seitzman, B. A., Ramsey, L. E., Ortega, M., Gordon, E. M., Dosenbach, N. U. F., …, Corbetta, M. (2018). Re-emergence of modular brain networks in stroke recovery. Cortex, 101, 44–59. https://doi.org/10.1016/j.cortex.2017.12.019
Sierpowska, J., Fernandez-Coello, A., Gomez-Andres, A., Camins, A., Castaner, S., Juncadella, M., …, Rodriguez-Fornells, A. (2018). Involvement of the middle frontal gyrus in language switching as revealed by electrical stimulation mapping and functional magnetic resonance imaging in bilingual brain tumor patients. Cortex, 99, 78–92. https://doi.org/10.1016/j.cortex.2017.10.017
Sporns, O. (2018). Graph theory methods: applications in brain networks. Dialogues Clin Neurosci, 20(2), 111–121. https://doi.org/10.31887/DCNS.2018.20.20sporns
Stebbins, G. T., Nyenhuis, D. L., Wang, C., Cox, J. L., Freels, S., Bangen, K., …, Gorelick, R. B. (2015). Gray matter atrophy in patients with Parkinson disease: Epidemiology, mechanisms and management. Ann Transl Med, 3(8), 80. https://doi.org/10.3978/j.issn.2305-5839.2014.08.05
Szelenberger, R., Kostka, J., Saluk-Bijak, J., & Miller, E. (2020). Pharmacological interventions and rehabilitation approach for enhancing brain self-repair and stroke recovery. Current Neuropathol, 18(1), 51–64. https://doi.org/10.2174/1570159X17666190726104139
Thiel, A., & Zumbansen, A. (2016). The pathophysiology of post-stroke aphasia: A network approach. Restorative Neurology and Neuroscience, 34(4), 507–518. https://doi.org/10.3233/RNN-150632
Tuladhar, A. M., Snapthaan, L., Shumskaya, E., Rijkema, M., Fernandez, G., Norris, D. G., & de Leeuw, F. E. (2013). Default Mode Network Connectivity in Stroke Patients. PLoS One, 8(6), e66556. https://doi.org/10.1371/journal.pone.0066556
Tzourio-Mazoyer, N., Landeau, B., Papathanassiou, D., Crivello, F., Etard, O., Delcroix, N., …, Joliot, M. (2002). Automated anatomical labeling of activations in SPM using a macroscopic anatomical parcellation of the MNI MRI single-subject brain. NeuroImage, 15(1), 273–289. https://doi.org/10.1006/nim.2001.0978
Vecchio, F., Tomino, C., Miraglia, F., Iodice, F., Erra, C., Di Iorio, R., …, Rossini, P. M. (2019). Cortical connectivity from EEG data in acute stroke: A study via graph theory as a potential biomarker for functional recovery. International Journal of Psychophysiology, 146, 133–138. https://doi.org/10.1016/j.ijpsycho.2019.09.012
Wang, J., Wang, X., Xia, M., Liao, X., Evans, A., & He, Y. (2015). Corrigendum: GREtNA: A graph theoretical network analysis toolbox for imaging connectomics. Frontiers in Human Neuroscience, 9, 458. https://doi.org/10.3389/fnhum.2015.00458
Wang, R., Liu, M., Cheng, X., Wu, Y., Hildebrandt, A., & Zhou, C. (2021). Segregation, integration, and balance of large-scale resting brain networks configure different cognitive abilities. Proceedings of the National Academy of Sciences of the United States of America, 118(23). https://doi.org/10.1073/pnas.2022288118
Watts, D. J., & Strogatz, S. H. (1998). Collective dynamics of ‘small-world’ networks. Nature, 393(6684), 440–442. https://doi.org/10.1038/30918
Wilk, M., & Vann, S. D. (2019). The cognitive thalamus as a gateway to mental representations. Journal of Neuroscience, 39(1), 3–14. https://doi.org/10.1523/JNEUROSCI.0479-18.2018
Wright, L. M., De Marco, M., & Venneri, A. (2021). A graph theory approach to clarifying aging and disease related changes in cognitive networks. Frontiers in Aging Neuroscience, 13, 676618. https://doi.org/10.3389/fnagi.2021.676618
Xi, Q., Zhao, X., Wang, P., Guo, Q., Jiang, H., Cao, X., …, Yan, C. (2012). Spontaneous brain activity in mild cognitive impairment revealed by amplitude of low-frequency fluctuation analysis: A resting-state fMRI study. La Radiologia Medica, 117(5), 865–871. https://doi.org/10.1007/s11547-011-0780-8
Xiang, J., Guo, H., Cao, R., Liang, H., & Chen, J. (2013). An abnormal resting-state functional brain network indicates progression towards Alzheimer’s disease. Neuro Regeneration Research, 8(30), 2789–2799. https://doi.org/10.3969/j.issn.1673-5374.2013.30.001
Yao, G., Ji, L., Liu, S., Wang, J., Cao, X., Li, X., …, Xu, Y. (2020). Alterations of functional connectivity in stroke patients with basal ganglia damage and cognitive impairment. Frontiers in Neurology, 11, 980. https://doi.org/10.3389/fneur.2020.00980
Yao, Z., Zhang, Y., Lin, L., Zhou, Y., Xu, C., Jiang, T., Neuroimagining, A. D., & I. (2010). Abnormal cortical networks in mild cognitive impairment and Alzheimer’s disease. PLoS Computational Biology, 6(11), e1001006. https://doi.org/10.1371/journal.pcbi.1001006
Yin, M., Liu, Y., Zhang, L., Zheng, H., Peng, L., Ai, Y., …, Hu, X. (2020). Effects of rTMS treatment on cognitive impairment and resting-state brain activity in stroke patients: A randomized clinical trial. Frontiers in Neural Circuits, 14, 563777. https://doi.org/10.3389/fncir.2020.563777
Zhao, Y., Song, L., Ding, J., Lin, N., Wang, Q., Du, X., …, Han, Z. (2017). Left anterior temporal lobe and bilateral anterior cingulate cortex are semantic hub regions: Evidence from behavior-nodal degree mapping in brain-damaged patients. Journal of Neuroscience, 37(1), 141–151. https://doi.org/10.1523/JNEUROSCI.1946-16.2016
Zuo, X. N., & Xing, X. X. (2014). Test-retest reliabilities of resting-state fMRI measurements in human brain functional connectomics: A systems neuroscience perspective. Neuroscience and
Publisher's Note Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.