

## Graph Network Analysis for Predicting Cognitive and Survival Outcomes in Glioma Patients

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### Abstract

Graph theory provides a framework for analyzing brain networks. This review explores the role of graph network analysis in predicting cognitive function and overall survival (OS) in glioma patients, focussing on studies that applied graph theory metrics to evaluate cognitive and survival outcomes in glioma patients.

Various studies showed that graph network alterations in glioma patients were associated with cognitive decline and worse OS. Small-world network properties were disrupted, with reductions in global efficiency and clustering coefficients correlating with neurocognitive deficits. Network hubs, which are critical for brain integration, were significantly affected, further contributing to functional impairments. These findings have implications for personalized neurosurgical planning and patient prognosis.

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### Introduction

Graph theory, in neuroscience, analyzes the brain as a complex network of regions and the structural and functional connections between them. Structural networks are derived from diffusion tensor imaging (DTI) while functional networks may be assessed by imaging (functional MRI (fMRI)) or electrophysiological measures such as Magnetoencephalography (MEG). The "graphs" are composed of nodes (specific brain regions) and edges (connections between them).<sup>1</sup>

There are various network measures/properties or 'graph metrics', such as centrality (how important a node or brain region is within the network), clustering coefficient (reflects local efficiency), and network efficiency (how effectively information is transferred across the network).<sup>2</sup> Healthy brains exhibit small-world networks that show high clustering (efficient local processing) and short path lengths (rapid communication between distant brain

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regions). This organization supports optimal cognitive function, however, tumour-induced network disruptions may alter this balance.<sup>2</sup> Another key concept in graph theory is network hubs, which are highly connected brain regions important in the communication and integration of information. Damage to these hubs can lead to widespread network dysfunction, contributing to cognitive impairment and poorer clinical outcomes.<sup>2</sup>

As graph theory is being widely utilized in neuroscience, several studies have assessed its neurosurgical applications. This article reviews the studies that used graph measures to predict outcomes in glioma patients, including cognitive status and overall survival.

### Literature Review

Graph network analysis of brain tumour patients has been used to predict cognitive outcomes<sup>3-7</sup> and overall survival<sup>8,9</sup> in glioma patients.

Friedrich et al. utilized graph metrics to identify critical cortical nodes from DTI and predicted the cognitive test scores of high-grade glioma (HGG) patients following their treatment. Overall the cognitive scores of HGG patients were lower than healthy controls and were strongly related to structural connectivity between multiple brain networks depending on the integrity of known network hubs.<sup>3</sup>

De Roeck et al. also studied the structural network metrics and their association with cognitive functioning in 50 glioma patients (WHO grade 2-3). They reported that the network of glioma patients was less integrated and exhibited higher segregation. This was associated with intelligence. They also showed that the assortative of hubs is vital in predicting cognitive outcomes of glioma survivors.<sup>4</sup>

Huang et al. assessed graph metrics via fMRI of 12 frontal lobe low-grade glioma (LGG) patients, and reported that clustering coefficient and local efficiency were lower in both LGG groups as compared to healthy controls, and the cognitive scores positively correlated with global efficiency. Furthermore, the small-worldness was disrupted and the authors proposed that this may be responsible for cognitive decline in these patients.<sup>5</sup>

Noll et al. assessed functional network properties of left perisylvian glioma patients and also reported that most exhibited cognitive decline in verbal memory, processing speed, executive functioning, receptive language, and a composite index shortly after the resection, along with a decrease in metrics of betweenness centrality and assortativity. They further reported that reductions in these measures were associated with better cognitive outcomes, implying that patients with the least postoperative decrease in network properties, mainly hubness and segregation, tend to exhibit poorer cognitive outcomes.<sup>6</sup>

Bosma et al. used MEG scans to study the network properties and cognitive outcomes of 17 LGG patients and reported a decline in psychomotor functioning, attention, information processing, and working memory compared to healthy controls. They also reported that disrupted graph networks were correlated with cognitive performance.<sup>7</sup>

Liu L et al. conducted a graph-theoretic analysis of functional networks and developed machine-learning-based individualized overall survival (OS) prediction. Their model achieved a high accuracy (86.8%) on segregating the individuals with bad OS from those with good OS based on network features, however, the accuracy was lower (63.2%) if only conventional features such as age and tumour characteristics were used.<sup>8</sup>

Wei et al. also predicted the OS of Glioblastoma (GBM) patients, however, their study was based on structural network disruptions. They reported that GBM disrupts the structural network beyond the site of the lesion and may alter the complete network topology, which is associated with worse cognition and survival.<sup>9</sup>

## Conclusion

Graph theory measures improve our understanding of how gliomas disrupt the overall brain connectivity and influence patient outcomes. The given studies demonstrate that gliomas alter both structural and

functional networks, leading to cognitive decline and impacting overall survival. Graph metrics, such as clustering coefficient, global efficiency, centrality, and network hubs, provide insights into these disruptions. Furthermore, the small-world network alterations and hub dysfunction may serve as biomarkers for predicting neurocognitive. Machine-learning models integrating graph metrics have shown superior predictive accuracy compared to conventional clinical features alone. Therefore, graph network analysis may enhance personalized neurosurgical planning to minimize cognitive deficits and maximize treatment efficacy.

## References

1. Sporns O. *Networks of the brain*. Cambridge, Massachusetts London, England: The MIT Press; 2011. 412 p.
2. Mithani K, Suresh H, Ibrahim GM. Graph Theory and Modeling of Network Topology in Clinical Neurosurgery. In: Di Ieva A, Suero Molina E, Liu S, Russo C, editors. *Computational Neurosurgery [Internet]*. Cham: Springer Nature Switzerland; 2024 [cited 2025 Jan 15]. p. 107–22. Available from: [https://doi.org/10.1007/978-3-031-64892-2\\_7](https://doi.org/10.1007/978-3-031-64892-2_7)
3. Friedrich M, Filss CP, Lohmann P, Mottaghy FM, Stoffels G, Weiss Lucas C, et al. Structural connectome-based predictive modeling of cognitive deficits in treated glioma patients. *Neuro-Oncol Adv*. 2024;6:vdad151.
4. De Roeck L, Blommaert J, Dupont P, Sunaert S, Sleurs C, Lambrecht M. Brain network topology and its cognitive impact in adult glioma survivors. *Sci Rep*. 2024;14:12782.
5. Huang Q, Zhang R, Hu X, Ding S, Qian J, Lei T, et al. Disturbed Small-World Networks and Neurocognitive Function in Frontal Lobe Low-Grade Glioma Patients. *PLOS ONE*. 2014 ;9:e94095.
6. Noll KR, Chen HS, Wefel JS, Kumar VA, Hou P, Ferguson SD, et al. Alterations in Functional Connectomics Associated With Neurocognitive Changes Following Glioma Resection. *Neurosurg*. 2021;88:544–51.
7. Bosma I, Reijneveld JC, Klein M, Douw L, van Dijk BW, Heimans JJ, et al. Disturbed functional brain networks and neurocognitive function in low-grade glioma patients: a graph theoretical analysis of resting-state MEG. *Nonlinear Biomed Phys*. 2009;3:9.
8. Liu L, Zhang H, Wu J, Yu Z, Chen X, Reikik I, et al. Overall survival time prediction for high-grade glioma patients based on large-scale brain functional networks. *Brain Imaging Behav*. 2019;13:1333–51.
9. Wei Y, Li C, Cui Z, Mayrand RC, Zou J, Wong ALKC, et al. Structural connectome quantifies tumour invasion and predicts survival in glioblastoma patients. *Brain*. 2023;146:1714–27.