Influence of Group-Level Parcellations on Resting-state fMRI Connectome–Cognition Correlations in Brain Tumor Patients

Jian Ming Teo[1,2], Kyle R. Noll[3], Vinodh A. Kumar[4], Mu-Lan Jen[1], Sujit S. Prabhu[5], Max Wintermark[4], Ho-Ling Liu[1]

[1]Department of Imaging Physics, The University of Texas MD Anderson Cancer Center, Houston, TX,
[2]The University of Texas MD Anderson Cancer Center UTHealth Houston Graduate School of Biomedical Sciences, Houston, TX,
[3]Department of Neuro-Oncology, The University of Texas MD Anderson Cancer Center, Houston, TX, [4]Department of Neuroradiology, The University of Texas MD Anderson Cancer Center, Houston, TX,
[5]Department of Neurosurgery, The University of Texas MD Anderson Cancer Center, Houston, TX

2026 JULY 19–22 VANCOUVER, BC
JOINT AAPM | COMP MEETING

Introduction

Group-level brain parcellations provide the crucial substrate for which functional connectomics are typically calculated from. However, the specific spatial topography and labels vary across different proposed parcellations[1]. Conceivably, the choice of group-level parcellation is expected to have downstream implications on functional connectomics findings[2]. This study investigates the association between neurocognitive function (NCF) and functional connectomics derived from commonly used group-level brain parcellations on patients with brain tumors.

METHODS AND MATERIALS

Presurgical resting-state (rs) functional MRI (fMRI), T1-weighted and FLAIR MR images from a dataset of 87 patients (mean age: 50 ± 15 years; 43 Male, 44 Female) with brain tumors were analyzed. Automated Anatomical Labelling Atlas 3 (AAL3), Glasser Atlas and Schaefer 200-region atlas were registered to patient space with SPM12. For each patient and the respective atlases, Fisher's Z-transform was applied to the Pearson correlation of the average timeseries between parcels to obtain the functional connectivity matrix for calculating functional connectomics. Density thresholds of 0.1, 0.2 and 0.3 were applied to the functional connectivity matrix. Preoperative NCF measures standardized to demographically-adjusted normative data were converted to ordinal measures including normal limits and 3 levels of impairment severity for analysis. Spearman correlation was calculated between functional connectomics and NCF measures at each density threshold. NCF measures evaluated are provided in Table 1. The processing workflow and connectomic measures evaluated are provided in Figure 1

Table 1: Neurocognitive Measures Grouped by Principal Domain

Domain	Test	Abbreviation
Attention	WAIS-IV digit span	DIGITS
	WAIS-IV arithmetic	ARITHMETIC
Learning and memory	HVLT-R total recall	HVLT-R TOTAL
	HVLT-R delayed recall	HVLT-R DR
	HVLT-R delayed recognition	HVLT-R REC
Processing speed	WAIS-IV coding	CODING
	WAIS-IV symbol search	SYMBOL
	Trail making test part A	TMTA
Executive function	Trail making test part B	TMTB
	WAIS-IV similarities	SIMILARITIES
	MAE controlled oral word association	COWA
	Semantic (animal) fluency	ANIMALS
Language	Boston naming test naming	NAMING

RESULTS

For AAL3 (Figure 2), statistically significant ($p < 0.05$) correlations were found for connectomic measures and NCF measures of language, diverse executive functions, and encoding, retrieval and consolidation episode memory processes. For the Glasser atlas (Figure 3), statistically significant correlations were found for connectomic measures and NCF measures of processing speed and verbal abstract reasoning aspects of executive function. For the Schaefer atlas (Figure 4), significant correlations were found for connectomic measures and only NCF measures of processing speed.

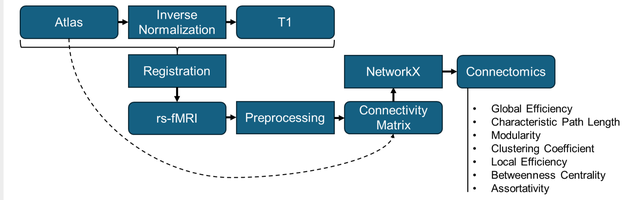


Figure 1. Processing workflow used in this study.

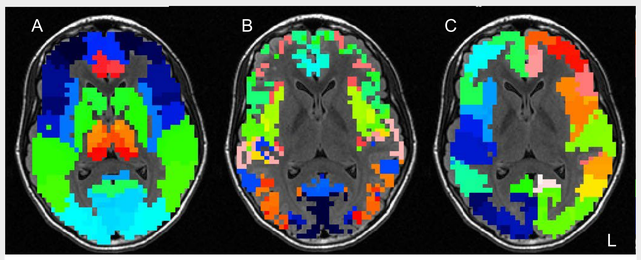


Figure 2. The three atlases used in this study overlayed on FLAIR image of a selected patient. (A) AAL3 atlas. (B) Glasser atlas (C) Schaefer 200 parcellation atlas.

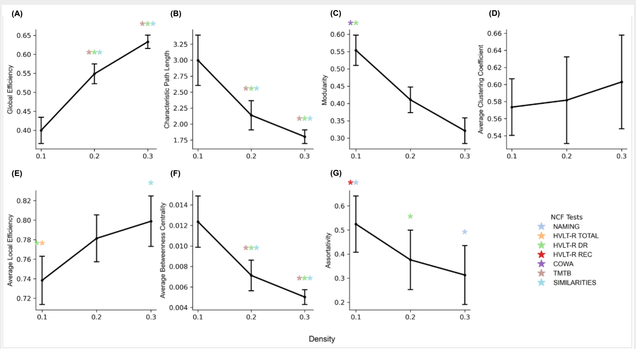


Figure 3. Values of functional connectomics measures at respective density thresholds using the Automated Anatomical Labelling 3 atlas. Colored * indicate which neurocognitive function test demonstrated significant Spearman correlation ($p < 0.05$) with respective functional connectomics measure.

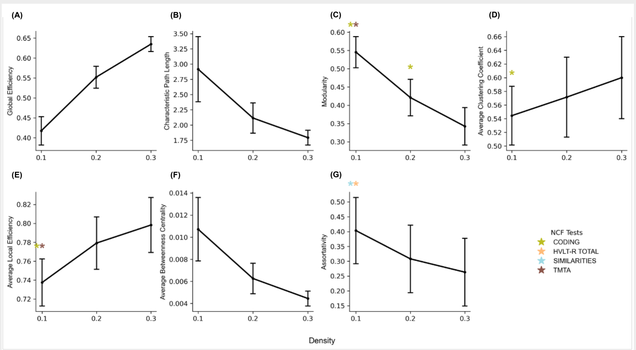


Figure 4. Values of functional connectomics measures at respective density thresholds using the Glasser atlas. Colored * indicate which neurocognitive function test demonstrated significant Spearman correlation ($p < 0.05$) with respective functional connectomics measure.

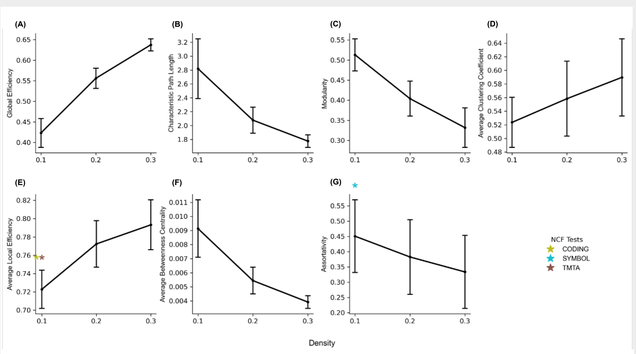


Figure 5. Values of functional connectomics measures at respective density thresholds using the Schaefer 200-region atlas. Colored * indicate which neurocognitive function test demonstrated significant Spearman correlation ($p < 0.05$) with respective functional connectomics measure.

DISCUSSION

Functional connectomics measures derived from different parcellation display similar trends with changing density thresholds. Suggesting that on the aggregate level, functional connectomics derived from different atlases describe qualitatively similar notions of the brain organization. This is unsurprising as the underlying, large-scale organization principles of the human brain (e.g. small worldness) are generally independent of parcellation methodology and parcellation resolution[3,4].

However quantitatively, the exact value of derived functional connectomics measures have changed between different parcellations. The quantitative influence on connectomic measures as been reported prior. This work contributes to growing appreciation that broader standardization of interpretating functional connectomics measures is required to facilitate comparisons between studies[1].

This work highlights how the choice of atlas can influence downstream interpretation of results. Using the AAL3 atlas, significant associations with the HVLT-R DR and HVLT-R Rec tests were found. This suggests that the AAL3 atlas is potentially better suited for studies involving learning and memory (HVLT-R) tests. However, significant associations with executive processing (CODING) tests were not found with the AAL3 atlas but found with the Glasser and Schaefer 200-region atlases. This suggests the latter two atlases are better suited for studies involving executive processing. Interpreting with only the functional connectomics results from AAL3 atlas would have resulted in the erroneous conclusion that association between connectomics and executive processing could not be found.

CONCLUSIONS

This work underscores how different group-level parcellations can influence the discovery of associations between functional connectomics and NCF measures. Despite lesion-induced anatomical distortions, group-level parcellations are commonly used in functional connectomics studies of patients with brain lesions. Knowledge pertaining to the influence of group-level parcellations on functional connectomics and their association with NCF is important to establish prediction models of NCF outcomes for the brain tumor patients.

REFERENCES

1. Kong, R. et al. A network correspondence toolbox for quantitative evaluation of novel neuroimaging results. Nat Commun (2025).
2. Furtjes, A. et al. A quantified comparison of cortical atlases on the basis of trait morphometricity. Cortex (2023).
3. Domhof, J. W. M. et al. Parcellation-induced variation of empirical and simulated brain connectomes at group and subject levels. Netw Neurosci (2021).
4. Messe, A. Parcellation influence on the connectivity-based structure-function relationship in the human brain. Hum Brain Mapp (2020).

Funding support: NIH/NCI R01 CA258788