

Uncovering the Latent Structure of Visuospatial Ability and Predicting Visuospatial Function

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Introduction

Visuospatial ability is the ability to perceive, understand, and utilize visual information to create a map of one's spatial environment. This higher order cognitive function can be impaired in select populations of patients with chronic (> 3 months after lesion onset) stable focal brain lesions.

- Visuospatial function is associated with the dorsal visual stream, a bilateral occipito-parietal pathway¹.
- Damage to regions outside of the dorsal visual stream can lead to visuospatial dysfunction.
- Lesion-symptom mapping, functional lesion network mapping, and white matter tractography have been used to predict deficits from lesion location²; these data can be used to improve personalized treatment recommendations and cognitive rehabilitation.

Aims

Aim 1: Identify and describe relationships between constituent processes that comprise visuospatial ability.

Aim 2: Identify neural correlates of latent variables identified in Aim 1 using multivariate lesion-symptom mapping, functional lesion network mapping, and white matter tractography.

Aim 3: Evaluate the predictive ability of factor-derived lesion-symptom maps and lesion network maps in a validation dataset.

Methods

Exploratory factor analysis was used to identify a single latent variable that best explained variance across 12 neuropsychological tests sensitive to visuospatial function (n=480). Missing data were imputed for subjects with scores for at least 8 of the 12 tests.

LESYMAP, a lesion-symptom mapping algorithm, was used to associate loci of damage with impairment in general visuospatial ability represented by a composite z-score across all 12 tests for each patient. The same behavioral data were used in functional lesion network mapping and white matter tractography analyses in FSL PALM. These approaches use resting state functional connectivity MRI and DTI datasets of healthy adults respectively to determine how whole brain networks are impacted by a lesion. Finally, we used a stepwise regression model to evaluate whether lesion-symptom mapping, functional lesion network mapping, or white matter tractography best predicts general visuospatial dysfunction in a validation dataset (n=119).

Results

Characteristic	Iowa Registry (n=480)	Iowa Clinical (n=119)
Age in years mean (sd)	52.5 (15.0)	54.8 (14.9)
Education in years mean (sd)	13.6 (2.67)	13.1 (2.45)
Gender women men	222 258	60 59
Handedness right left mixed	437 34 9	106 10 3
Race African American American Indian Caucasian Other	6 2 470 2	0 0 119 0
Ethnicity Hispanic Non-Hispanic Undeclared	2 477 1	2 117 0
Etiology ischemic stroke hemorrhage benign tumor resection focal contusion encephalitis multiple etiologies missing data	260 104 87 16 12 1 10	78 7 0 0 0 14 20

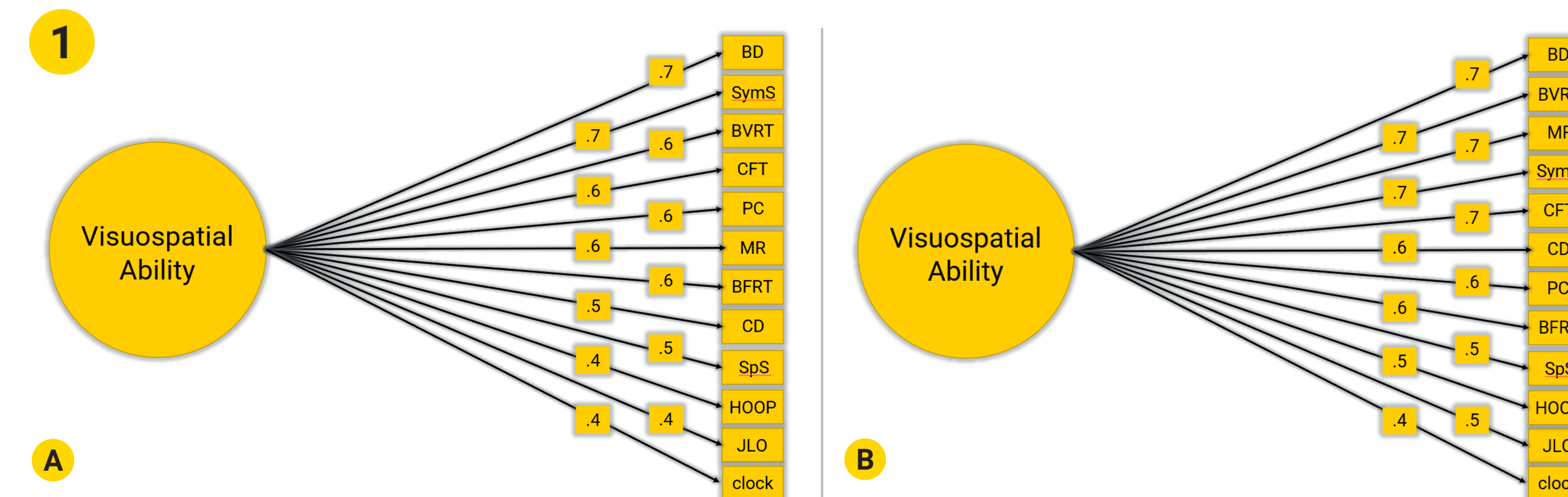


Figure 1. An exploratory factor analysis revealed a single factor best explains variance across all 12 tests. 1A shows all 480 Registry patients and uses imputed data. 1B uses data from a subset of the Registry patients who have data for all 12 tests (n=112).

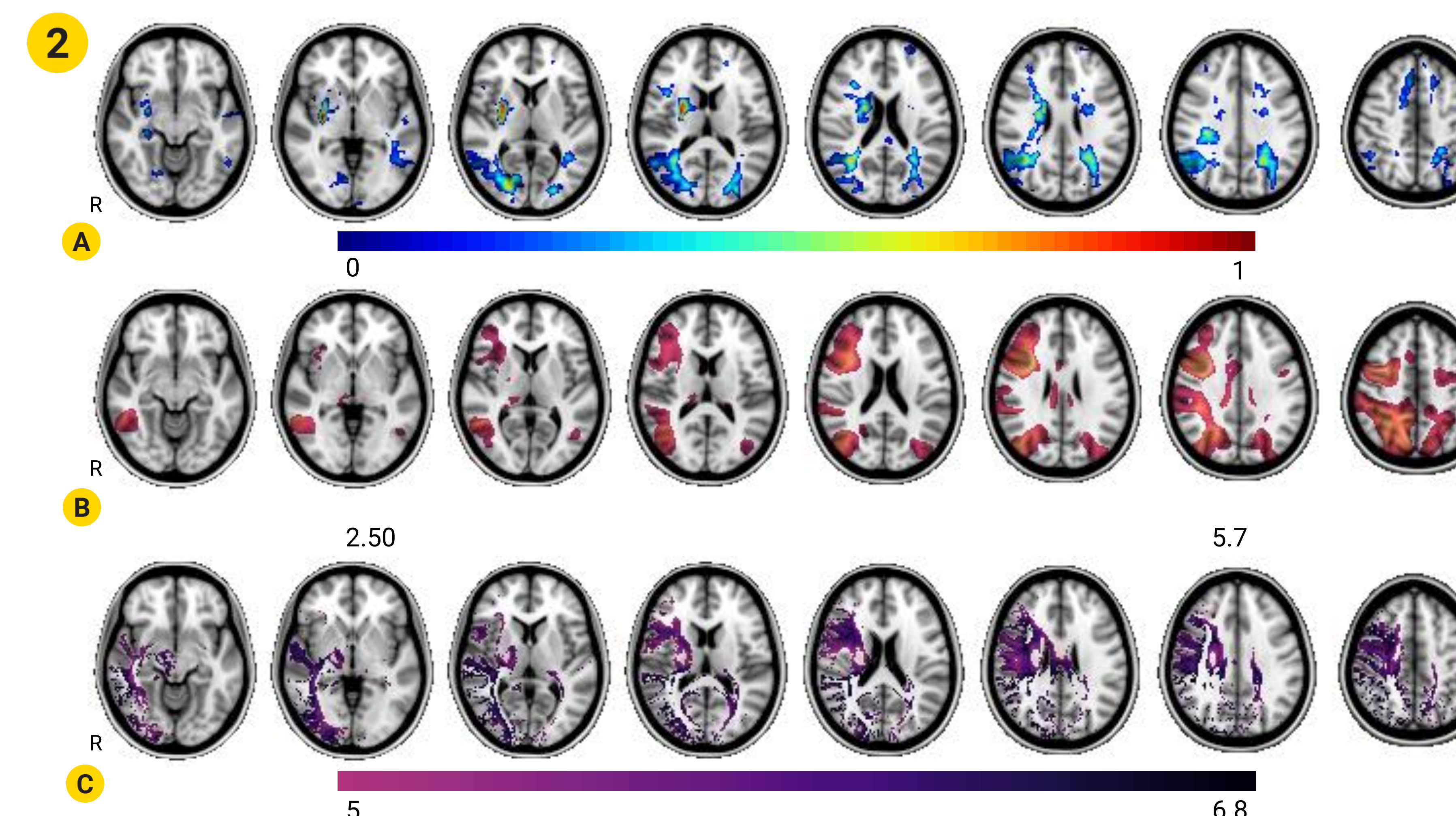


Figure 2. 2A shows lesion-symptom mapping results of the composite z-score representing general visuospatial ability in 480 Registry patients. The right putamen is most associated with visuospatial dysfunction (R= .264, p=4.56*10⁻⁹). 2B shows significant functional lesion network mapping results as t-values after FDR correction which overlaps most with the ventral attention network. 2C shows white matter tractography results as t-values after FDR correction and further thresholding to a t-value of 5 to highlight the strongest findings: long-range white matter tracts connecting the occipital, parietal, and frontal lobes.

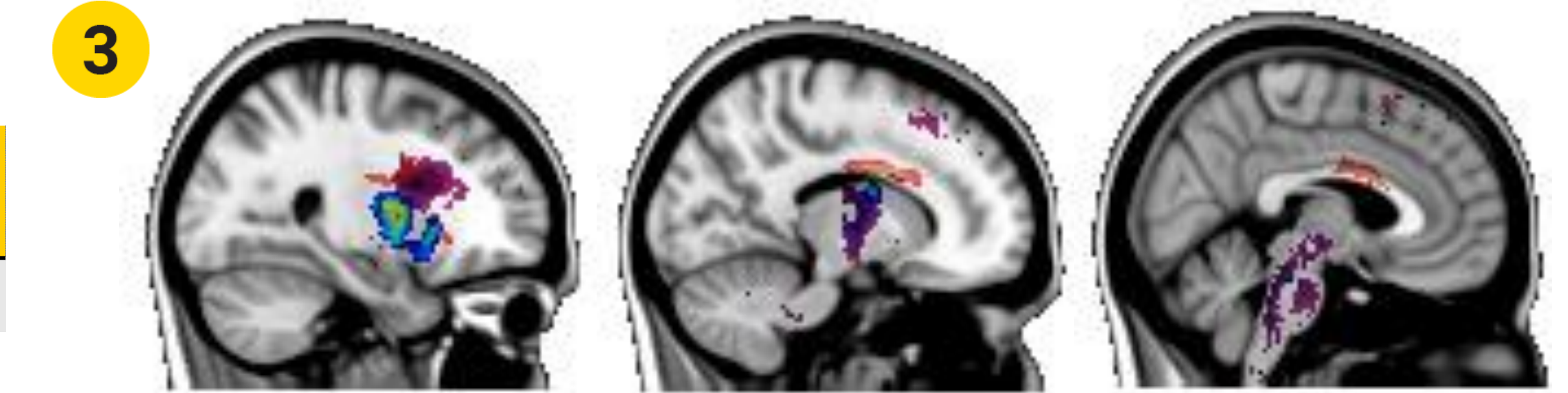


Figure 3. Lesion-symptom mapping, functional lesion network mapping, and white matter tractography results for Registry patients with scores for all 12 tests (not using imputed data, n=112) are shown in the same color scheme as Figure 2. Similar to previous results in Figure 2, these results suggest that damage to the right putamen is associated with visuospatial dysfunction and connected regions are likely also impacted.

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$$y = -7.23 \times 10^{-3} - .145_{LSM} - .206_{FLNM}$$

Figure 4. Using a stepwise regression model, we determined that lesion-symptom mapping and functional lesion network mapping but not white matter tractography predict visuospatial dysfunction in the Iowa clinical cohort.

Discussion

This study identified a single latent variable that represents visuospatial ability across 12 commonly administered neuropsychological tests sensitive to visuospatial dysfunction. White matter tracts connecting the occipital, parietal, and frontal lobes are involved in visuospatial ability, especially in the right cerebral hemisphere. Most notably, the right putamen is most associated with general visuospatial dysfunction and impaired performance on several individual tests as well. These results can be used to predict visuospatial impairment in other cohorts of neurological patients.

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References

1. Mishkin, M., Ungerleider, L. G., & Macko, K. A. (1983). Object vision and spatial vision: two cortical pathways. *Trends in neurosciences*, 6, 414-417.
2. Bowren, M., Jr, Bruss, J., Manzel, K., Edwards, D., Liu, C., Corbetta, M., Tranel, D., & Boes, A. D. (2022). Post-stroke outcomes predicted from multivariate lesion-behaviour and lesion network mapping. *Brain*. <https://doi.org/10.1093/brain/awac010>