Mapping the effects of stroke lesions on gradients of resting-state functional connectivity

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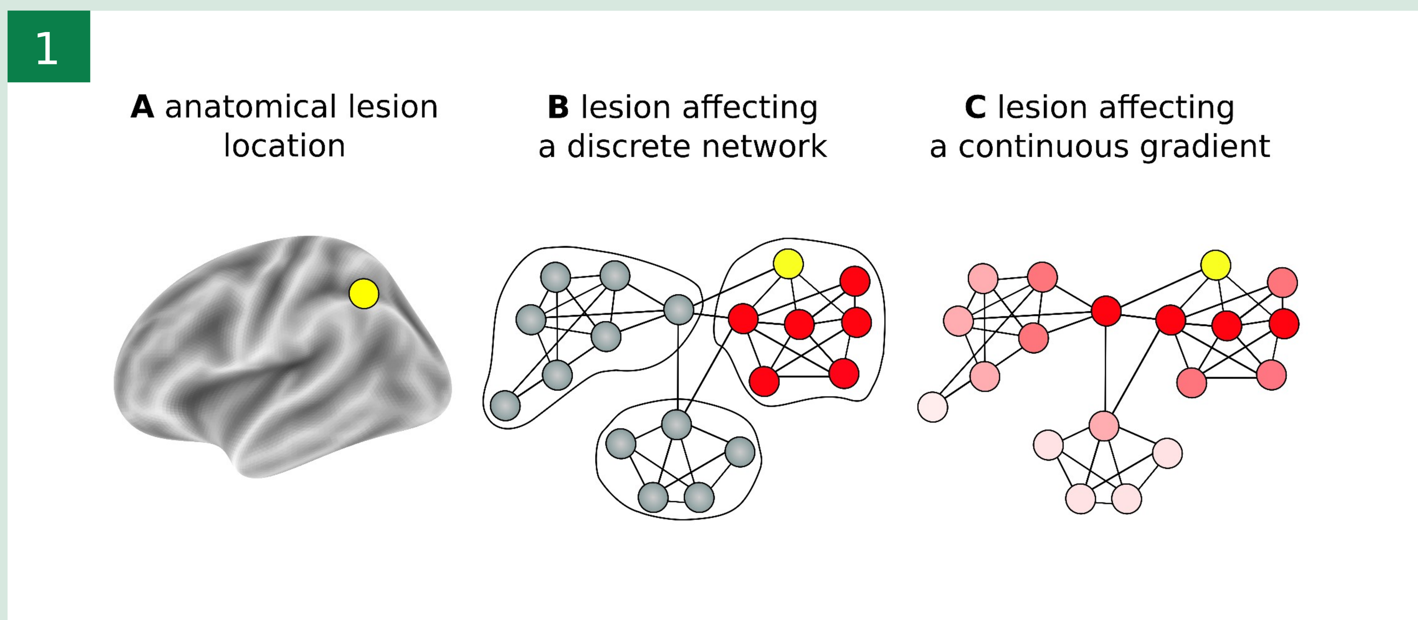
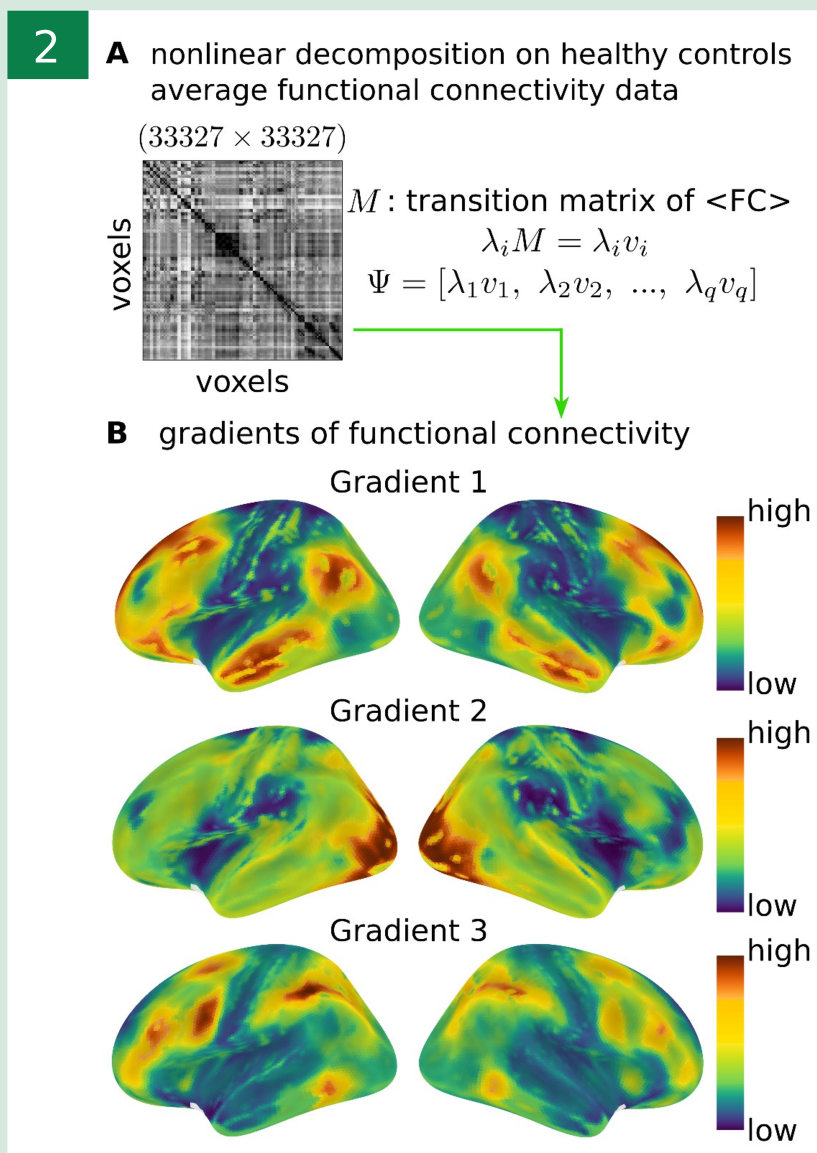
Introduction

Stroke provides a unique model to study widespread effects of a focal brain disruption. Distal effects of stroke lesions were previously studied using network parcellations [1, 2, 3]. Recently, a continuous representation of brain organization was shown by gradients of resting-state functional connectivity [4]. The advantage of gradients is that no a-priori assumption is being made concerning network boundaries, and whole-brain connectivity is represented using a low dimensional embedding.

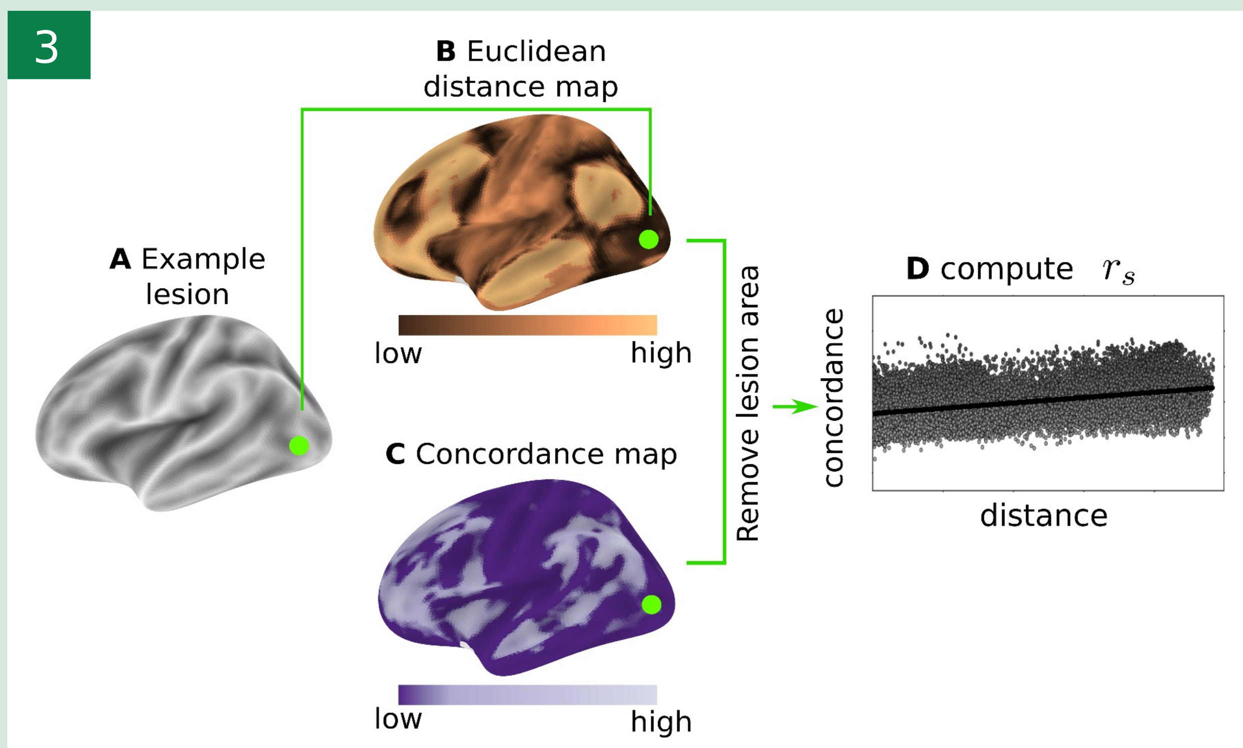


Here, we aim to study how a lesion (the acute infarct) affects connectivity changes over the course of stroke recovery, using gradients of connectivity. We hypothesized that the location of lesions along the gradients will influence the degree of changes in functional connectivity in the acute to subacute stroke phase.

Methods



Applying a nonlinear decomposition analysis to an averaged connectivity matrix based on healthy controls data revealed first three connectivity gradients.

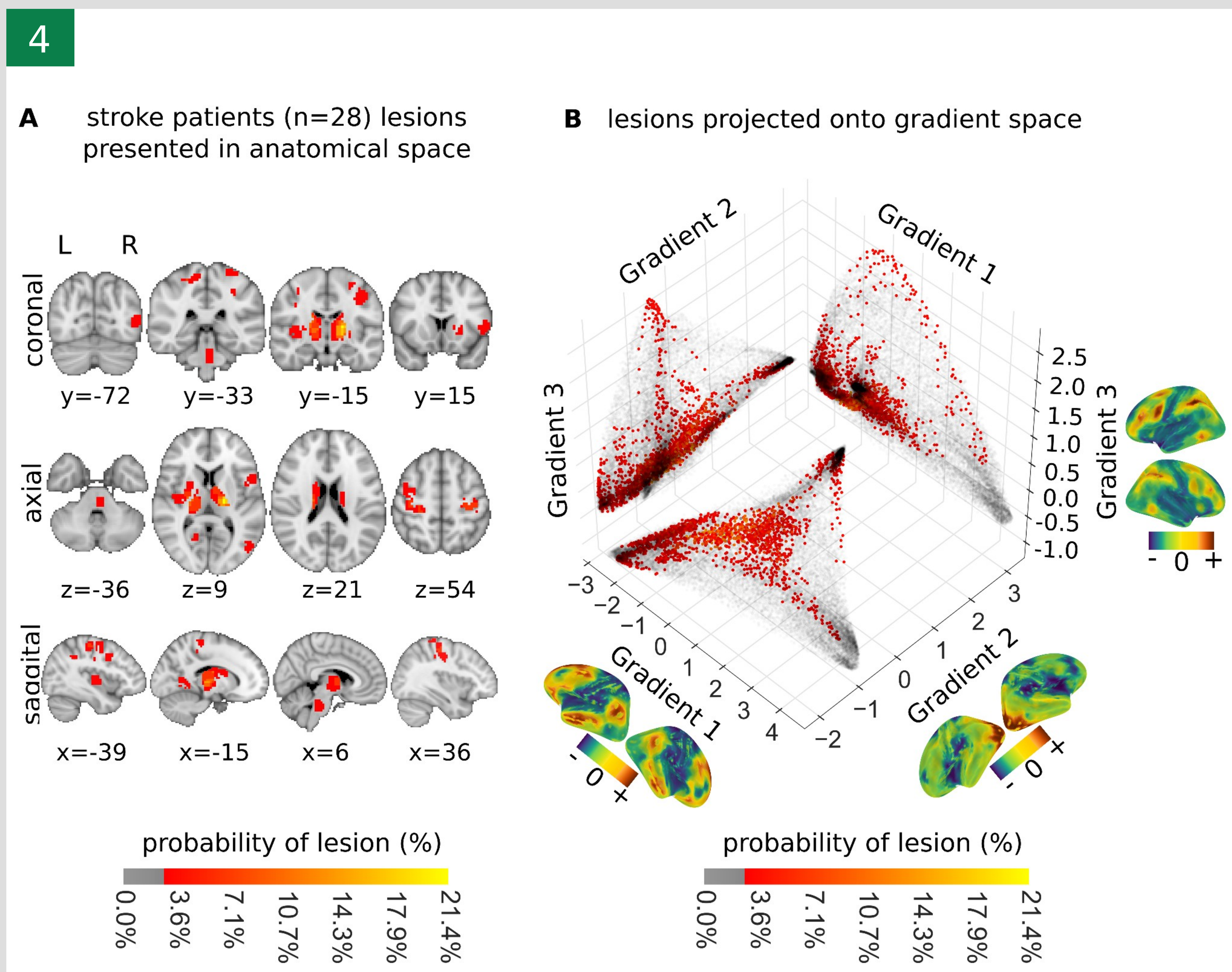


Lesion locations of stroke patients were projected onto individual gradients. For each patient, Euclidean distances from each voxel to the lesion site was computed. Functional connectivity alteration over time was quantified for each patient using voxelwise concordance correlation coefficient (CCC). A Spearman's correlation (r_s) was used to test the relationship between distances-to-lesion and concordances across voxels.

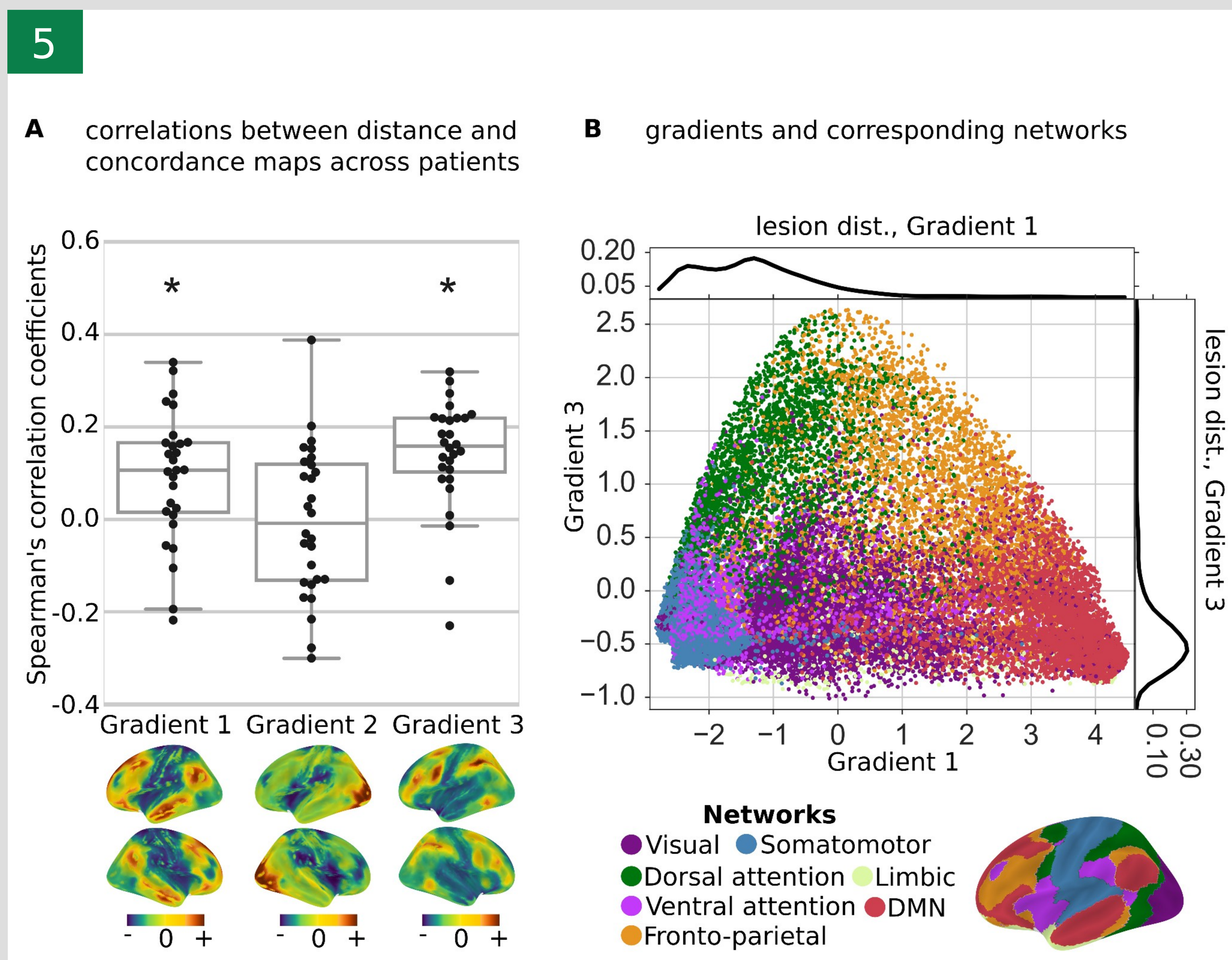
Data

Resting-state fMRI data was acquired from acute stroke patients (n=28) at three consecutive scan sessions (within 24 hours, at day 1 and day 5 following stroke symptoms onset), and from an aged-matched healthy cohort (n=28) at a single scan session.

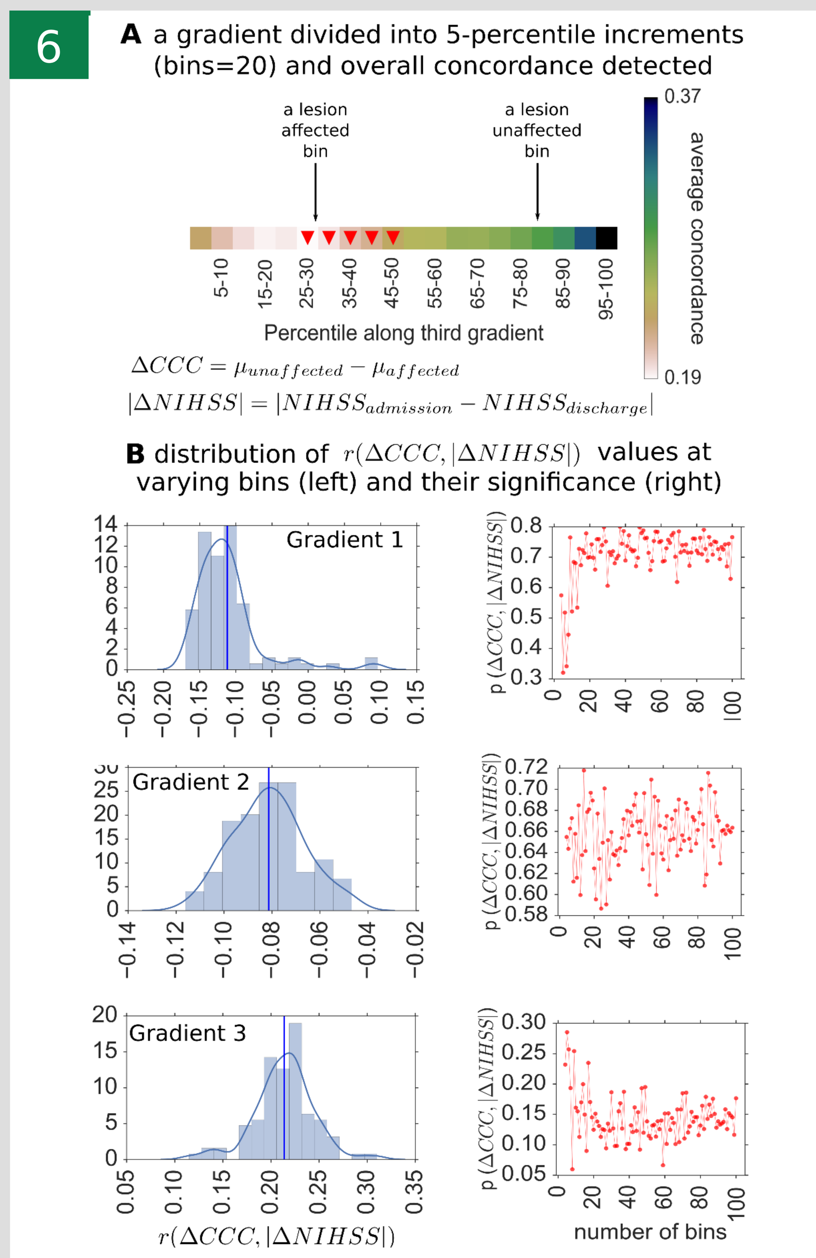
Results



As an alternative approach to traditional lesion mapping in anatomical space, we projected lesion locations onto gradients. Voxels sharing similar connectivity profiles are situated close to one another in the gradient space. Since our suggested approach was performed at individual patient level and using whole-brain functional representation, it overcomes the analytic challenge of lesion heterogeneity.



Functional connectivity in single voxels alters with respect to their distance from the lesion along Gradients 1 and 3 in connectivity space. Correlations between distance-to-lesion and concordance maps were significantly positive across patients for the first and third gradients (one-tailed Wilcoxon signed-rank test, p=0.0027 and p=0.0001, respectively), but not for the second gradient (p=0.76). Seven resting-state networks [5] are projected onto Gradients 1 and 3 to depict the functional domains associated with the space. Lesions are situated most frequently in somatomotor, visual and ventral attention network, that appear at the overlap of Gradients 1 and 3 in their lowest ends.



Correlation between the overall concordance measure (ΔCCC) and the degree of change in clinical stroke severity score (|ΔNIHSS|). The analysis was repeated for varying number of bins (4-100). Based on previous findings [2], we expected a positive relationship. No significant relationship was found. However, correlations distribution demonstrate a non-random pattern for Gradient 3 centered at r=0.21.

Discussion

- We found that stroke-induced connectivity alterations are reflected along specific gradients of a low-dimensional connectivity embedding. Brain areas close to lesion locations along Gradients 1 and 3 demonstrated a more pronounced functional connectivity alteration over time.

- Gradients 1 and 3 emphasize transmodal (DMN) and multimodal domains (attention), whereas Gradient 2 reflects a dissociation within unimodal domains (somatosensory/motor, visual) [4].

- It was previously shown that regions processing integrative functions sit central to brain's overall graph and disruptions in such associative modalities better correlated with disruptions in functional connectivity, rather than lesion anatomy [3].

- Our results extend previous findings. The extremes of Gradient 2 are dominated by short-range connections and thus were not sensitive to long-distance impact of focal lesions. Large-scale modules located at the extremes of Gradients 1 and 3 enable them to capture global and longitudinal effects of stroke lesions.

References

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