Connectivity network and lesion distribution in SLE

Previous work

Mapping of the hierarchical tiers (80 healthy volunteers (40 males, 40 females) aged 25–64 (median 43, IQR 17) years

Hierarchical complexity

- **Degree variance (network hubs)**
- **Assortativity (similarity of neighbouring node degrees)**
- **Clustering coefficient (tendency for nodes to cluster)**

Concepts introduced in Smith et al. 2019
From 47 patients with Systemic Lupus Erithematosus (SLE)

- **Disease activity**
  - SLEDAI
  - Ds-DNA
  - C3
  - C4

- **Accumulated damage**
  - SLICC
  - Disease duration

- **Endothelial dysfunction and inflammation**
  - Von Willebrand factor
  - Homocysteine
  - F8c
  - IL6

- **Vascular Risk Factors**
  - Hypertension (Y/N)
  - Smoking
  - Cholesterol (Total, LDL, HDL, total/HDL ratio)
  - Homocysteine
  - Acl IgG
  - Acl IgM

- **Fatigue, Depression and Anxiety**
  - FSS
  - HADS Depression Score
  - HADS Anxiety Score

- **Fibrinolysis**
  - D-dimer

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**Tractography**

**Structural MRI**
Image Processing Pipeline

Network nodes were grouped in tiers (as per Smith et al. 2019). White matter hyperintensities (WMH) and tiers were mapped in standard space for analyses.
Group comparison
(of WMH spatial distribution)

Transform continuous variables into 0/1 and/or into quartiles

Construct a 4D volume of the WMH stacking all WMH maps (in standard space)

Use functions robust4Dranksum and/or robust4Dkruskalwallis

```
[p3D,FDR3D] = robust4Dranksum(array4D,groupingvector)
[p3D,FDR3D] = robust4Dkruskalwallis(array4D,groupingvector)
```

Example: significant values (p<0.05) of the p-values map from comparing WMH from patients with high homocysteine levels vs. those with low
Regression models
(Associations between WMH and disease indicators accounting for age and biological sex)

- Import covariates and outcome variables
- Import the 4D volume of WMH containing all WMH maps (in standard space)
- Configure and use Support Vector Machine

(Sparseness, missing data, dissimilar data distributions)

Maps of voxel-based association between WMH and disease indicators or global network parameters
Voxel-based association between WMH and measures of active disease (SLEDAI + Homocysteine)

Negative association voxels: red, Positive association voxels: green
Voxel-based association between WMH and measures of anxiety and depression (HADS Anxiety + HADS Depression)

Negative association voxels: red, Positive association voxels: green
Voxel-based association between WMH and measures of clinical disease “damage” (SLICC + Lupus Duration)

Negative association voxels: red, Positive association voxels: green
Probability distribution maps of patients with Fatigue Scale Scores above the median value (upper row), below (bottom row) and an axial slice (right) showing places where there were significant differences (p<0.05)
Voxel-based association between WMH and Vascular Risk Factors (Smoker + Hypertension + Homocysteine + Total Cholesterol + anticardiolipin IgG and IgM)

Negative association voxels: red, Positive association voxels: green
Voxel-based association between WMH and D-dimer (marker of fibrinolysis)

Negative association voxels: red, Positive association voxels: green
Association with network global metrics
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