The organization of the human cerebral cortex estimated by intrinsic functional connectivity

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Contents

Introduction

- Data from 1,000 subjects were registered using surface-based alignment.
- A clustering approach was employed to identify and replicate networks of functionally coupled regions
- Within the sensory and motor cortices, functional connectivity followed topographic representations across adjacent areas.
- In association cortex, the connectivity patterns often showed abrupt transitions between network boundaries.
- Goal 1: provide reference maps that are a current best estimate of the organization of the human cerebral cortex as measured by functional connectivity.
- Goal 2: how patterns of functional connectivity might give rise to the organizational properties that underlie distributed brain systems

Organizational Properties of the Cerebral Cortex in the Nonhuman Primate

- Distributed brain systems are organized to facilitate both serial and parallel processing
- Historically, four criteria (function, cytoarchitecture, connectivity, and topography) are used to define cortical areas.
- Each distributed network consists of association areas spanning frontal, parietal, temporal, and cingulate cortices.
- Multiple distributed networks exist adjacent to each other.

Insights Into the Organization of the Cerebral Cortex Revealed Through Neuroimaging

- It is difficult to assess the organization of these distributed systems based solely on task activity because these cognitive tasks likely tap into multiple, overlapping processes

Functional Connectivity and Diffusion MRI Provide Tools to Explore Cortical Organization

- fcMRI measures intrinsic functional correlations between brain regions and is sensitive to coupling between distributed as well as adjacent brain areas.
- Limitations of fcMRI:
  - Suboptimal sensitivity to indirect anatomical connectivity and functional coupling that changes in response to recent experience and the current task being engaged.
  - Does not presently provide information about whether connections are feedforward (ascending) or feedback (descending).
- Networks identified using fcMRI have often been labeled on the basis of their relations to task-based functional networks.

Methods

- Overview
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Functional MRI Data Preprocessing

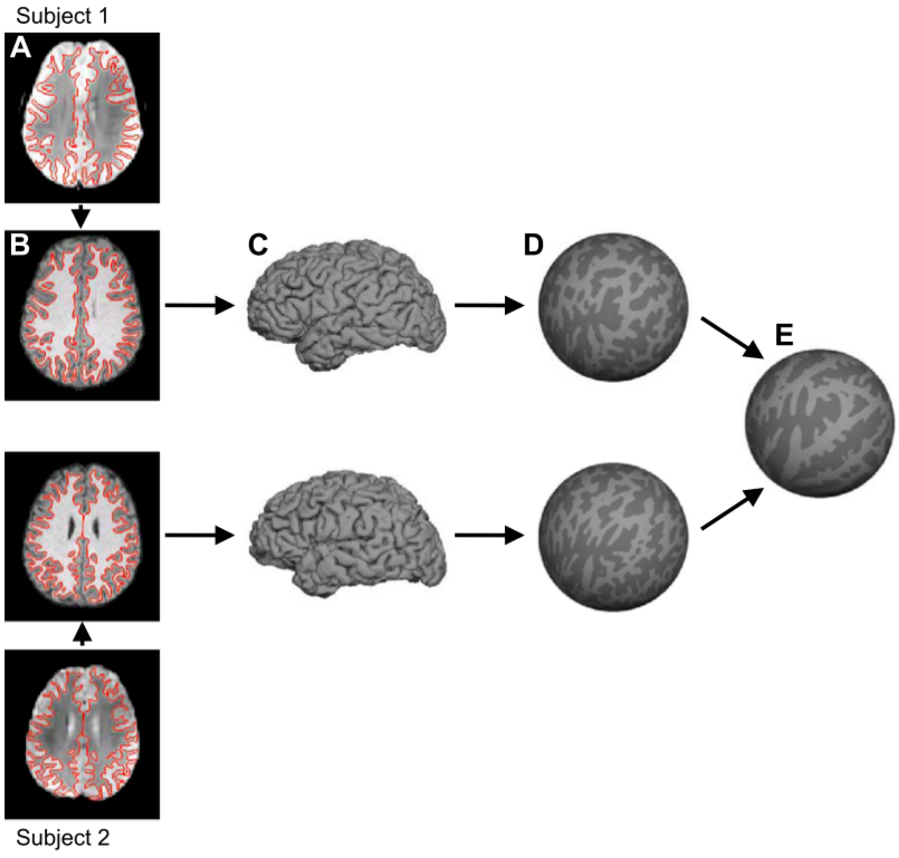
- Discarding the first four volumes of each run to allow for T1-equilibration effects.
- Compensating for slice acquisition-dependent time shifts per volume with SPM2.
- Correcting for head motion using rigid body translation and rotation with the FSL package.
- Constant offset and linear trend over each run were removed.
- A temporal filter was applied to retain frequencies below 0.08 Hz.
- Sources of spurious variance, along with their temporal derivatives, were removed through linear regression.
- No spatial smoothing of the resting-state data occurred up to this point of the preprocessing stream.

Structural MRI Data Preprocessing and Functional-Structural Data Alignment

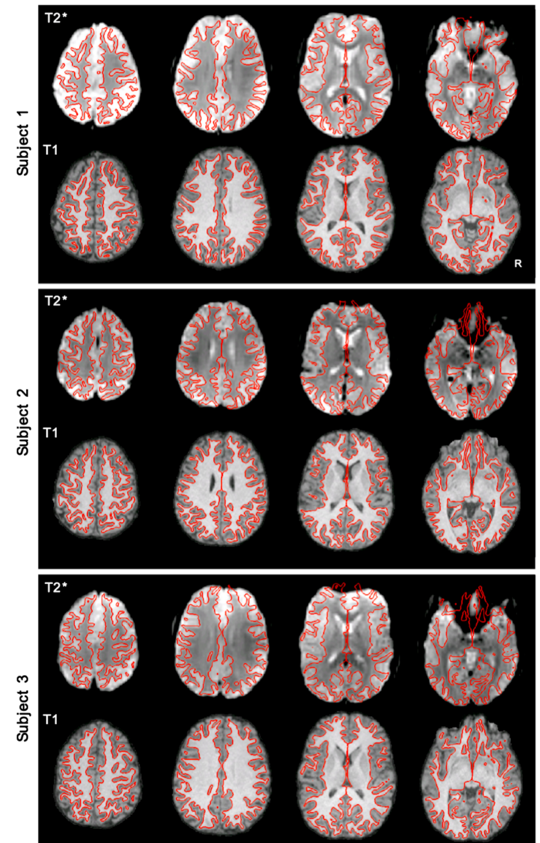
- The structural data were processed using the *FreeSurfer*.
- Correcting for intensity variations due to MR inhomogeneities.
- Removing extracerebral voxels through "skull-stripping".
- Segmenting cortical gray and white matter voxels based on the intensity difference and geometric structure of the gray-white interface.
- Computing cutting planes to disconnect the two hemispheres and subcortical structures.
- Filling the interior holes of the segmentation using a connected-component analysis.
- Tessellating a triangular mesh over the gray-white boundary of each hemispheric volume and deforming the mesh to produce a smooth representation of the gray-white interface and pial surface.
- Correcting topological defects in the surface so that the mesh achieves a spherical topology.

- Inflating each subject's surface mesh into a sphere while minimizing geometric distortion of the original cortical surface.
- Computing a smooth, invertible deformation of the resulting spherical mesh to a common spherical coordinate system.
- The structural and functional images were aligned using boundary-based registration.
- Preprocessed resting-state fMRI data were then propagated to the common spherical coordinate system via sampling from the middle of the cortical ribbon in a single interpolation step.
- 6-mm full-width half-maximum (FWHM) smoothing kernel was applied to the fMRI data in the surface space.

- Fig.1. Surface coordinate system.



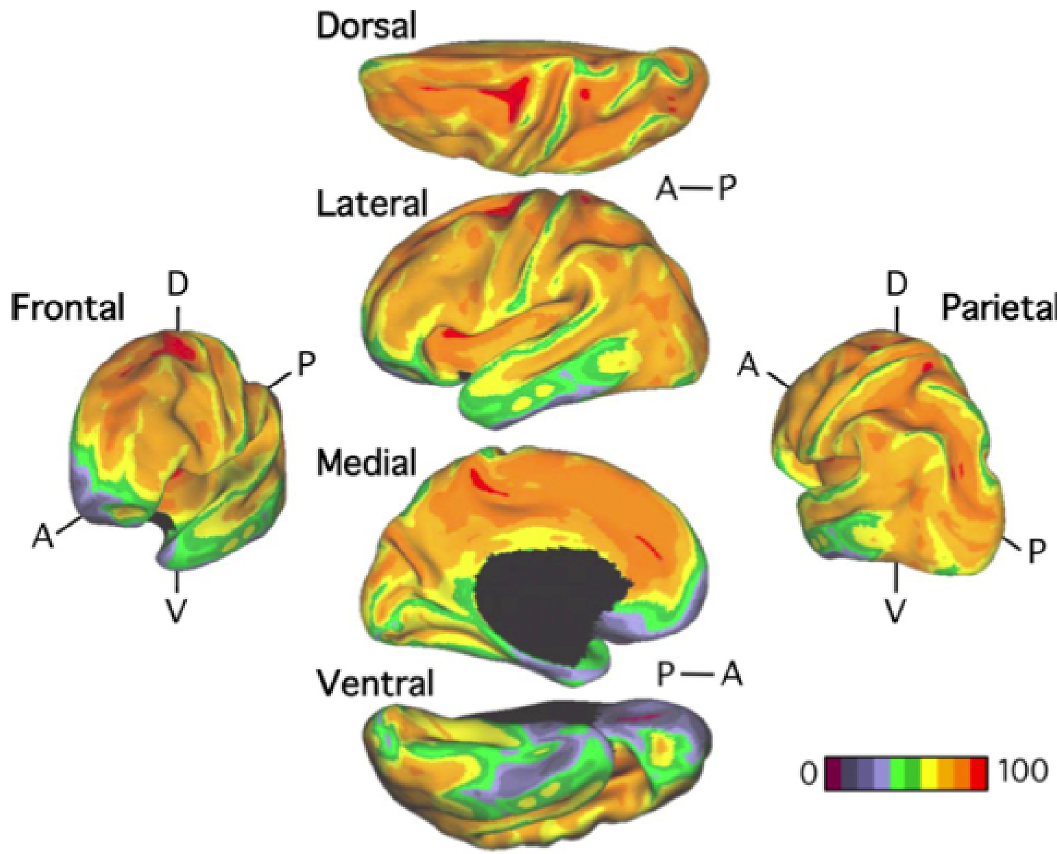
- Fig.2. Examples of intrasubject surface extraction and registration of structural-functional images.



SNR Maps

- SNR (of a voxel) equals average signal intensity across the whole run divided by the standard deviation over time.
- Help estimate the effects of susceptibility artifacts in the present data.
- If the SNR for the whole brain (mean SNR over all voxels within the brain mask) was ≤ 100 for an fMRI run, the subject was excluded.

- Fig.3. Signal-to-noise ratio (SNR) maps of the functional data from the full sample (N = 1,000).



Clustering

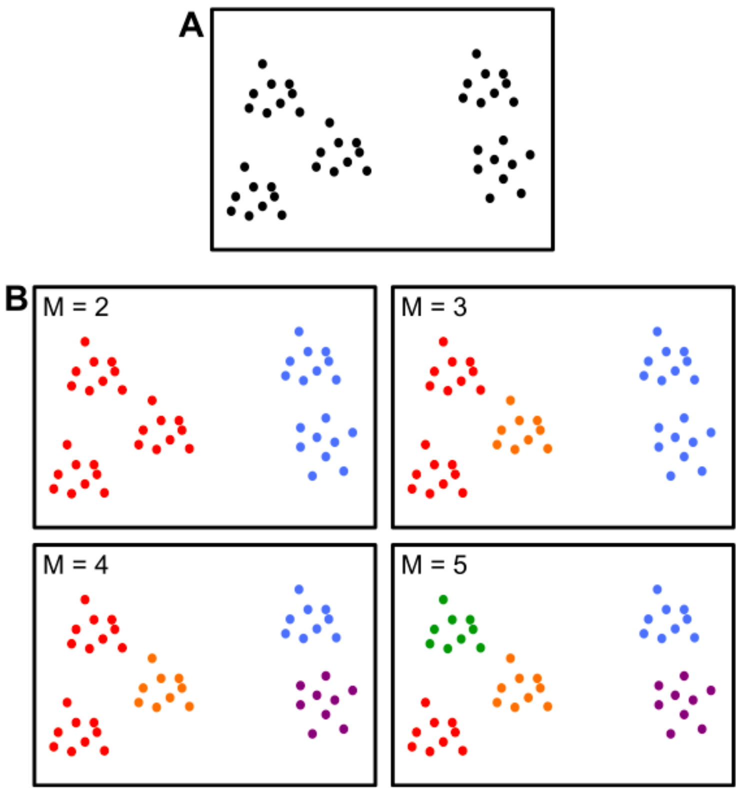
- Defined the connectivity profile of a cortical region to be its functional coupling to 1,175 region of interest (ROI) vertices
- 1,175 ROI vertices were uniformly sampled in *FreeSurfer* surface space and consisted of single vertices spaced about 16 mm apart
- Pearson's product moment correlation between the fMRI time series at each spatial location (18,715 vertices) and the 1,175 ROI vertices
- Binarized the 18,715 × 1,175 matrix of correlations for each subject by keeping the top 10% of the correlations
- Binarization of the correlation matrix leads to significantly better clustering results

- The clustering algorithm employed in this study modeled the data with a von Mises-Fisher distribution
- The data were modeled as 18,715 points on an 1,174-dimensional unit hypersphere embedded in an 1,175-dimensional Euclidean space, where distances between points were measured by their geodesic distance on the hypersphere.
- The algorithm operated by randomly assigning the 18,715 points to different groups and then iteratively reassigning the group memberships of points to maximize the agreement of connectivity profiles among points of the same group.

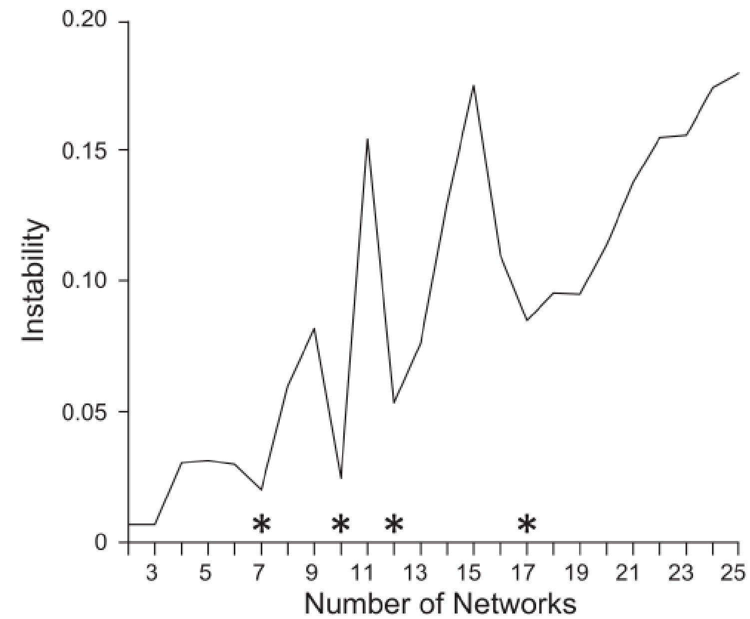
Stability Analysis

- A drawback of most clustering approaches is that one must choose the number of clusters a priori.
- One popular method for estimating the number of clusters is by analyzing the stability of the clustering algorithm.
- The stability analyses suggested 7 and 17 networks were appropriate starting points for parcellating the cortex.

- Fig.5. Toy example illustrating clustering.



- Fig.6. 7 and 17 networks can be stably estimated.



Confidence Maps

- A useful visualization of the cortical parcellation is to look at the confidence of each spatial location belonging to its assigned network.
- The **silhouette measure** (Rousseeuw 1987) from the clustering literature is used for this purpose.
- The silhouette of a data point (spatial location in our case) measures the similarity (correlation in our case) of the data point to other data points of the same cluster (network in our case) compared with data points belonging to the next closest cluster.
- A negative value indicates that the connectivity profile at the spatial location is on average closer to the next closest cluster than to its assigned cluster.

Correlation Maps and Correlations Between Regions

- Correlation maps were obtained by computing the Pearson's product moment correlation between the region's preprocessed resting fMRI time course and the time courses of all other vertices across the cortical mantle.
- The correlation map of each subject in the group was converted to individual subject z-map using Fisher's r-to-z transformation and then averaged across all subjects in the group.
- An inverse Fisher's r-to-z transformation was then applied to the group-averaged correlation z-map, yielding a group-averaged correlation map.
- Classical statistical tests, including t-tests and ANOVA, were performed on the z-transformed correlations.

Selecting Regions for Functional Connectivity Analysis

- When testing for seed-based confirmation of resolved networks, the estimated network boundaries and confidence maps of the discovery sample were used to derive regional vertices to be tested in the replication sample
- Regions were chosen for (1) maximal spatial coverage of estimated networks, (2) avoiding network boundaries, (3) their confidence in network assignments.
- For some analyses, task-based fMRI is utilized to select regions, e.g. visuotopic regions.
- Probabilistic histological maps in *FreeSurfer* surface space allowed for the selection of regions within histologically defined areas.

Distribution of Parcellations and Raw Data

- A primary result of this study is the parcellation of cortical networks and the estimation of boundaries of regions within the networks.