Morphological and functional networks’ coupling by cortical lobes

Cortical thickness and functional networks modules

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1 Abstract

In this short communication I present a study on cortical thickness and functional networks’ coupling topology by cortical lobes. First, I demonstrated modular organisation of these networks by the cortical surface frontal, temporal, parietal and occipital divisions. Secondly, I mapped the coupling topology of cortical thickness and functional networks for positive and negative correlations. Finally, I showed that the coupled positive correlations map onto within-lobe cortical interactions and negative onto between-lobes interactions.

2 Introduction

Classical, localized characterization of human brain surface morphology has moved in recent years towards maps of inter-regional co-variations of cortical thickness measurements in structural magnetic resonance imaging data (sMRI) [1]. To make such cortical maps or networks (graphs) the edges (links) between pre-defined regions (nodes) are drawn based on the strength of correlation between regional thickness measurements. The anatomical substrate of variations in the thickness correlations as yet remains elusive. Recent findings suggest that strong correlations of cortical thickness are underpinned by direct axonal connections [2, 3]. However, it has been suggested that the brain functional processes can also impact cortical morphology. For example, the synchronization of neuronal activity in response to specific functional demands might induce synchronized plastic changes among related regions [4]. This may explain strong thickness correlations within the visual cortex areas [5].

The natural divisions of the cortical surface – frontal, temporal, parietal and occipital – have been defined by regional morphological characteristics, which are also known to support different functions [6, 7]. In this context, questions arise about the relationship between cortical networks of different regional measurements. To what extent regional thickness and functional correlations share similar topological organisation across cortical lobar divisions? How do networks of functional and thickness correlations map onto networks measure called modularity? If topological measures of thickness networks are functionally relevant we expect these measures may be impacted by lobar divisions of the cortical surface.
To address these questions I examined thickness and functional correlational networks based on two different neuroimaging modalities – structural and functional MRI. The networks were represented by $68 \times 68$ matrices whose individual elements map pair-wise correlations between regional Blood-Oxygen-Level-Dependent (BOLD) or thickness measurements. The main focus of the study is to illuminate intrinsic topological properties of the cortical surface frontal, temporal, parietal and occipital divisions, which may impact coupling of the structural and functional interactions across cortical lobes. To this end I studied how does modular organisation of the cortical surface divisions affect the coupling between cortical thickness and functional correlations across cortical regions.

3 Methods

3.1 Image Processing

The MRI data sets considered in this short communication are from a public database (http://fcon_1000.projects.nitrc.org/) provided by the Max Planck Institute (MPI) Leipzig. A study group included 37 (16M/21F) participants between 20 and 42 years. MRI data was acquired on 3 Tesla Magnetom Tim Trio scanner (Siemens, Erlangen, Germany) using a 32-channel head coil. T1-weighted images were acquired using a MPRAGE sequence (TR = 1.3 s; TE=3.46 ms; flip angle=10deg; FOV=256 × 240mm$^2$; 176 sagittal slices; voxel size = 1 × 1 × 1.5mm$^3$). Functional MRI/EPI data were acquired on a 3T MRI scanner (Siemens Tim Trio) using TR=2.3 sec, TE=30ms, 3 × 3 in-plane resolution, 3 mm slice thickness, 1 mm gap between slices. Each scanning session was a task-absent (“resting state”) scan lasting 7.6 minutes during which subjects were asked to fixate a fixation cross.

Processing structural MRI data was done using FreeSurfer v5.3.0 (https://surfer.nmr.mgh.harvard.edu/) pipeline according to the procedure described in more details in [5]. Cortical thickness was measured on $N = 68$ cortical surface regions segmented according to the Desikan-Kielany Atlas (DKA) [8]. FSL v5.0.11 (https://fsl.fmrib.ox.ac.uk/fsl/fslwiki/) was used to process fMRI data and extract BOLD fMRI time-series on the same 68 cortical regions of the DKA parcellations. The fMRI data processing steps were described in details in [9, 10].

3.2 Brain Graph Construction

Brain graphs considered in this study were constructed on correlations between either regional cortical thickness or BOLD activity measured by structural or functional MRI. In these correlational networks, a brain region represent network’s node and a pair-wise correlation between the regional measurements represents network’s edge/link or connection between the nodes. Fig. 1 summarizes analysis pipeline and approach.
Figure 1: Workflow diagram of the cortical networks’ construction on processed structural and functional magnetic resonance images. (Upper panel) Structural magnetic resonance images (sMRI) are processed using FreeSurfer v5.3.0 pipeline: cortical surface was reconstructed and regional cortical thickness measures were averaged over $N = 68$ structures of the Desikan-Kielan Atlas (DKA). Structural correlation network was constructed on partial correlations between regional thickness across all participants ($S = 37$) while controlling for age, sex and mean CT. (Lower panel) Functional MRI (fMRI) were parcellated and time series were averaged over the same 68 DKA regions. Individual functional correlations (FC) matrix was constructed on pair-wise correlations between the fMRI time series, Fisher z-transformed, averaged over $S$ subjects and transformed back to linear Pearson coefficient. Group-wise CT and FC matrices were reordered according to node affiliation with cortical lobes (frontal, temporal, parietal and occipital) and their coupling topology was assessed to capture positive and negative correlations maps.
3.2.1 Functional Correlations

To obtain the FC matrices, time series of the 68 DKA regions were calculated by averaging the respective BOLD signals over all regional voxels. The correlation matrices were obtained for each subject in the study. Since voxels are in MNI space and a given voxel has approximately the same anatomical position in all subjects, the individual correlation matrices can be averaged across subjects. In detail, each matrix is first Fisher z-transformed and averaged across subjects and then transformed back into correlation coefficients again as described in previous studies [9, 10]. The resulting correlation matrix $f_{ij}, (i, j = 1, N)$, was used to create a group-wise functional correlation matrix between the regions of interest. See Fig. 1 (lower panel) for analysis pipeline and approach.

3.2.2 Cortical Thickness Correlations

A group-wise structural network was constructed on inter-regional cortical thickness correlations across all study participants. The correlations were calculated between each pair of 68 regional thickness measurements while controlling for age, gender and mean CT, similarly to previously described methodology [5, 3]. See Fig. 1 (upper panel) for analysis pipeline and approach.

3.3 Brain Graph Analysis

3.4 Network Density

Network topological properties depend on the network thresholding. Threshold affects network density ($\kappa$), i.e., number of links relative to the total number of all possible links in the network [11]. A boundary for network density threshold considered here was set at the proximity of the percolation threshold. Thus, yielding to a fully connected component/network, with small-world topological organisation [9].

3.4.1 Modularity by Lobes

Each network was assessed at the scale of its lobar organisation – the frontal, temporal, parietal and occipital divisions of the cortical surface. Modularity index (Q), was calculated to determine whether cortical lobes as conventionally defined correspond to modules of the CT/FC network. This can be done by calculating the Q according to lobe (by employing vector of nodal affiliation with the particular lobe as initial community affiliation vector). The modularity index quantifies the observed fraction of within-module degree values relative to those expected if connections were randomly distributed across the network. In the context of this short communication, cortical lobes have been considered and analysed as network modules. Since the constructed CT/FC network contains both positive and negative edge strengths, I used the asymmetric
generalization of the modularity quality function introduced in Rubinov and Sporns [12]. In practice, it is accepted that a Q value above 0.3 is a good indicator of the existence of significant modules in a network [13].

4 Results

4.1 Network Density

As described in Methods, a single value for network density was obtained by considering percolation threshold for each network. This yielded network density of $\kappa = 0.16$, which includes both positive and negative edges. This choice of the threshold insures that each network has the same ($N = 362$) total number of positive and negative links.
4.2 Modularity by Lobes

Modularity index of the CT and FC networks by lobes were 0.446 and 0.442 respectively, thus indicating modular organisation of CT/FC networks by cortical lobes. To get confidence interval for network modularity distribution by lobar (frontal, temporal, parietal and occipital) divisions, 200 randomised networks have been generated on CT/FC networks (100 each), i.e., each null network model has been tested to obtain distribution of the modularity indexes (Qs) on randomly distributed correlations of the CT/FC network. Fig. 2(B) shows how the distributions of 100 Q values on random CT/FC networks differ from those calculated on real networks.

4.3 Coupling of Cortical Thickness and Functional Correlations

Coupling of thickness and functional networks was calculated by element-wise multiplication of the two matrices. Fig. 2(D) shows products of this multiplication for the coupling of positive and negative correlations/networks. The survived network edges of positive correlations map intra-lobar and inter-hemispheric homologous (off-diagonal matrix elements). In contrast, the coupled negative networks map exclusively onto inter-lobar connections. In particular, the frontal lobe regions – rostral anterior cingulate, rostral middle frontal and superior frontal – are correlated with regions of the occipital lobe. The mean distance between the coupled networks nodes ($N_{\text{agree}}$) was $(72 \pm 30)\, mm$ for positive and $(81 \pm 30)\, mm$ for negative network nodes ($p > 0.05$), Fig. 2(C).

5 Discussion

In this short communication I demonstrated coupling of the cortical thickness and functional correlations networks, with reference to modular organisation of the conventional lobar divisions. A noticeably different patterns of the coupling were observed for positive and negative correlations. In contrast to the positive networks’ coupling, which maps almost exclusively within-lobe interactions, negative networks show only between-lobes coupling.

Both cortical networks – inter-regional thickness and functional correlations – demonstrated modular organisations that mirror conventional frontal, temporal, parietal and occipital divisions of the cortical surface. Thus allowing for inferences about coupled interactions of these networks by cortical lobes. While several previous studies reported modular topology of the cortex by cortical morphological (thickness and volume) [14, 15] or functional [16] measurements, no data are available on functional modules as an instinct property of the cortical surface lobar divisions. Motivated by the lobe-specific patterns of atrophy progression in two types of dementia, we have recently reported similar findings on cortical thickness and surface area networks in healthy elderly group [5]. This short communication represent first effort to map patterns of positive and negative correlations in cortical thickness and functional networks in healthy adults.
Several interesting results observed when mapping coupling topology of the cortical thickness and functional correlations by lobar divisions need further attention. First, the approach adopted here was to compare the networks at a single value of network density. However, the obtained coupling topologies may change depending on number of correlations used for network analysis. Thus, calculation of the coupling across a range of networks densities may map all cortical interactions consistently present across different thresholds. Second, the definition of conventional lobar deviations used in this study was based on the Desikan-Kelliany cortical parcellation. Although well established, there exist alternative approaches for the cortical segmentation by using different brain templates [17]. Since adoption of different brain template may have some influences on the patterns of network correlations, further studies could validate these results using different anatomical (or functional) classifications. Finally, a study combining structural, functional and diffusion-weighted MRI data could test to what extent variations and strengths of positive and negative correlations can be inferred from underlying direct axonal links or synchronous/asynchronous functional links. These future work could also resolve issue of estimating network individually for each subject.

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