

INTERHEMISPHERIC STRUCTURAL AND FUNCTIONAL CONNECTIVITIES SHOW DISTINCT STRENGTHS OF ASSOCIATIONS IN HOMOTOPIC AND HETEROTOPIC CONNECTIONS

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Introduction

Functional connectivity of the brain is considered to conform to the underlying structural connectivity [1-4]. However, there exists mismatch between functional connectivity and structural connectivity partly due to limitations of current diffusion imaging approaches and analyses [5]. For instance, the reliability of the analysis is challenged when one attempts to identify intra-hemispheric cortical-cortical connections via association fibers because current tractography techniques often miss sharp turns of these fibers upon entering the cortex. To avoid this limitation, we focus on interhemispheric connection which is established mostly by a direct connection via corpus callosum, the largest white matter structure with obvious pathways. Therefore, the aim of the study is to investigate the interhemispheric structure-function relationship, specifically to characterize the features of this relationship among different lobes in the brain. We hypothesize that the structure-function relationship varies in different lobes, it is strongest in homotopic connections and the strength decreases as the degree of heterotopicity increases.

Methods

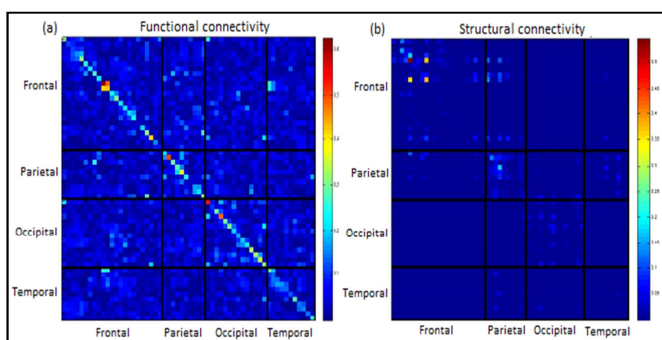
20 young healthy right-handed adults were recruited in the study (age: 19-41 yr, mean=27.7, SD=6.9; 8 males). Scanning was performed with a 32-channel head coil on a 3T MRI system. During 6-minute resting fMRI, all participants were asked to lie still with eyes closed, not to fall asleep, and think of nothing. **Image Acquisition:** The image acquisition included structure MRI, resting-state fMRI and diffusion spectrum imaging (DSI). A MPRAGE sequence was used to obtain a high-resolution T1-weighted structure image (TR/TE=2000 ms/2.98ms; voxel=1x1x1 mm³). A GRE-EPI sequence was acquired for 6 min for resting state fMRI data (TR/TE=2000 ms/24 ms, FA=90, Thickness=3 mm, FOV=256 mm²). DSI was performed using a diffusion EPI sequence (TR/TE=9600 ms/130 ms, voxel=2.5x2.5x2.5 mm³ and 102 diffusion encoding gradients with bmax = 4000 s/mm²). **Data analysis:** T1 Atlas 'aparc.a2005s.annot' was chosen from FreeSurfer (<http://surfer.nmr.mgh.harvard.edu/>), containing cortical anatomical label information of the whole brain with a total of 162 segmented regions. The fMRI images were preprocessed via SPM8: slice-timing correction, motion correction, coregistration and normalization, high-pass temporal filtering, spatial smoothing, and followed by in-house ICA-based denoising algorithm to remove artifacts. Functionally active regions were selected by the segmented cortical regions that were overlapped with the group ICA maps. These selected regions were used as cortical ROIs in the later analysis. The timecourses within the ROIs were extracted to perform partial correlation analysis to produce a functional connectivity matrix **FC**. DSI data was reconstructed via DSI Studio (<http://dsi-studio.labsolver.org/>) to perform tractography. To reconstruct the corpus callosum, we used whole brain seeding for fiber tracking and selected fibers that passed through the plane parallel to the interhemispheric fissure. The number the selected fiber tracts was set to 30,000. For each dataset, the structural connectivity matrix **SC** was quantified as the number of tracts interconnecting any pair of cortical ROIs in the contralateral hemispheres divided by the maximal connectivity in **SC**. To analyze the relationship between **SC** and **FC**, Pearson correlation analysis was employed. In addition to the analysis in a global manner, the same analysis was applied to individual lobes to explore the characteristics of the structure-functional relationship among different lobes.

Results

The **SC** and **FC** (fisher's z score) averaged across subjects were illustrated in Fig.1. In the global analysis, **SC** was correlated with **FC** (r=0.1987, p<0.001). In the lobar analysis, all lobes except temporal lobe showed significant association between **SC** and **FC** (p<0.001) with correlation coefficients being 0.3018, 0.5358, and 0.3864 in frontal, parietal, and occipital lobes, respectively [Table 1]. Particularly, parietal lobe showed the strongest structure-function relationship (r=0.5358, p<0.001). In addition, the correlation coefficients in the homotopic interhemispheric connections were stronger than the heterotopic connections in frontal, parietal and occipital lobes [Table 1].

Discussion

Consistent with a previous report [6], all lobes but temporal lobe showed significant homotopic interlobar structural and functional connectivities [Fig. 1]; little connection in temporal lobe may explain no significant correlation between **SC** and **FC** in our results. Mild structure-function correlation found in the global analysis implies a generally weak coupling between interhemispheric **FC** and **SC**. Furthermore, the lobar analysis indicated that the structure-function relation was indeed weak in the heterotopic connections which constituted the majority of the connections, but it was exceptionally strong in the homotopic connections [Table 1]. The correspondence of homotopic connections to strong structure-function relationships implies that topology may contribute to the association between structural and functional connectivities. This study also found that parietal lobe presented the strongest structure-function correlation [Table 1], consistent with a previous finding [1]. This feature is understood by the fact that parietal lobe is the hub of the brain in both structure and function. In conclusion, the interhemispheric connections are weakly coupled between structure and function in a global sense. However, when homotopicity and heterotopicity are taken into consideration, a distinct difference emerges in the strengths of associations between structural connectivity and functional connectivity.



r		Right			
		Frontal	Parietal	Occipital	Temporal
Left	Frontal	0.3018*	0.0892	-0.0264	-0.0075
	Parietal	0.0609	0.5358*	0.0553	-0.0391
	Occipital	-0.0186	0.0198	0.3864*	-0.1425
	Temporal	-0.0774	0.0487	-0.0417	0.1690

Table 1 The structure-functional correlation coefficient. (*: p<0.001)

References [1] C.J. Honey et al., Proc Natl Acad Sci U S A, vol. 106, pp. 2035-40 (2009) [2] J.M. Segall et al., Front Neuroinform, vol. 6, p. 10 (2010) [3] K. Supekar et al., Neuroimage, vol. 52, pp. 290-301 (2010) [4] M.P. van den Heuvel et al., Hum Brain Mapp, vol. 30, pp. 3127-41 (2009) [5] J.S. Damoiseaux and M. D. Greicius, Brain Struct Funct, vol. 213, pp. 525-33 (2009) [6] K. Jarbo et al., Neuroimage, vol. 59, pp. 1988-96 (2012)