Investigating the Dependence of Spontaneous Fluctuations in Visual Cortex on Callosal Connectivity

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Introduction

fMRI has been widely used to investigate the spontaneous fluctuations in brain functional networks and map the functional connectivity between different cortical areas [1-3]. The underlying assumption is generally that mono-synaptic rather than multi-synaptic pathways preferentially drive these correlations. In previous work, high interhemispheric temporal correlation has been found between bilateral primary visual cortices (V1), the strength of which depended on retinotopic location [4]. Interestingly, in both humans and macaques, mono-synaptic callosal connections are virtually absent between left and right V1, apart from an area with retinotopic correspondence to the vertical meridian near the V1/V2 border [5-7]. This suggests that the strength of interhemispheric correlations may depend on the retinotopic distance from the vertical meridian. To investigate this, we functionally localized the callosal/acallosal regions in V1 and investigated their interhemispheric correlation strength during rest.

Materials and Methods

Two normal volunteers participated in the current study approved by local Institutional Review Board. All MR experiments were performed on a 7T Signa MRI system (General Electric, Milwaukee, WI, USA) equipped with a 32-channel receive-only array coil (Nova Medical, Wilmington, MA). The visual stimulus consisting of 30-degree wedge-shaped checkerboard patterns (fig. 1) was used to localize the bilateral retinotopically-organized regions in visual cortex. The checkerboard was rotated with a step interval of 4 seconds and the entire paradigm consisted of a total of 12 seven-step cycles. Functional data were acquired using a gradient-recalled echo planar imaging sequence. For retinotopic mapping, 30 axial 2 mm-thick slices with a gap of 0.2 mm covering the visual cortex were acquired and TR/TE was 2000/30 ms. The field-of-view was 260×195 mm^2 and the imaging matrix size was 128×96, using a SENSE acceleration factor of 2 [8]. For eyes-closed resting-state fMRI, 45 axial slices covering the whole brain were acquired with TR/TE of 3000/30 ms and the same voxel size as the fMRI retinotopic localizer. The numbers of scans for retinotopic mapping and resting-state fMRI were 190 and 150, respectively. The functional images were reconstructed by the use of phase-sensitive combination of individual coil data using in-house code written in IDL 8.0 (ITT Visual Information Solutions, http://www.ittvis.com).

The pre-processing of fMRI data including slice-timing correction, head-motion correction, grand mean drift scaling and co-registration between different fMRI runs was accomplished by using a combination of functions of FSL4.0 (http://www.fmrib.ox.ac.uk/fsl) and AFNI (http://afni.nimh.nih.gov/afni). Voxel time-series were normalized to their mean value. To localize the retinotopic sub-areas, the phase angles and coherence were calculated from the retinotopy fMRI data by applying the Fourier Transform method [9]. To investigate the interhemispheric correlation of resting-state fMRI data, 16 slices encompassing the visual cortex were chosen and the voxels within left and right hemispheres were separated by manually drawing the midline for each slice. To improve sensitivity, only the visual areas with coherence higher than 0.2 were considered in the subsequent analysis. The voxels within the activated visual areas were divided into 7 sub-areas corresponding to different positions of the rotating wedge. The correlation coefficients between each sub-area and all contralateral sub-areas were calculated, resulting in a 7×7 correlation matrix.

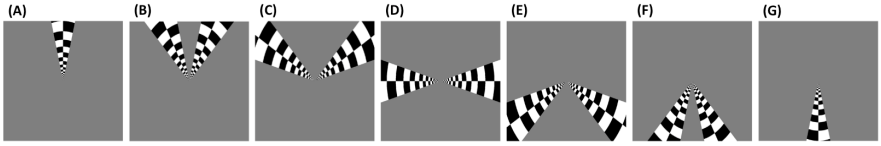

Figure 1. The visual stimuli presented in this study. The stimulus consists of a wedge-shaped checkerboard contrast flickering at 7.5 Hz. The stimulation cycle consists of a stepwise change from (A) upper vertical meridian to (G) lower vertical meridian in 7 four-second steps. The stimulus in (D) corresponds to the horizontal meridian.

Results

Sample retinotopic maps from a single subject are shown in fig. 2. The borders of different retinotopic areas are clearly visualized in the sagittal view (fig. 2A) of the mapping. Fig. 2B shows an approximately symmetric pattern of the phase angles in bilateral visual cortex, which is consistent with the expected response of the employed stimuli. The correlation matrices for both subjects are shown in fig. 3A and 3B, respectively. At first glance, both matrices show similar patterns but slightly different magnitudes of correlation coefficients. As shown in fig. 3A, significantly higher correlation coefficients ranging from 0.89 to 0.94 are found among the diagonal terms of the matrix, suggesting that interhemispheric correlations are strongest in regions with retinotopic correspondence. Relatively high correlation coefficients are also found in some of the off-diagonal terms indicated by the red rectangles, which may be due to the phase shift caused by the hemodynamic response function (HRF). Significantly lower correlation coefficients are found in the portions indicated by the white arrows, which suggests that the sub-areas related to the horizontal meridian are less correlated with the sub-areas related to the vertical meridian. Interestingly, no significant difference was found between diagional elements representing callosal and acallosal areas. Fig. 3B shows data from another subject. Although a slightly lower correlation coefficient is found in the sixth column of the diagonal terms, the overall distribution of correlation coefficients are generally similar as fig. 3A.

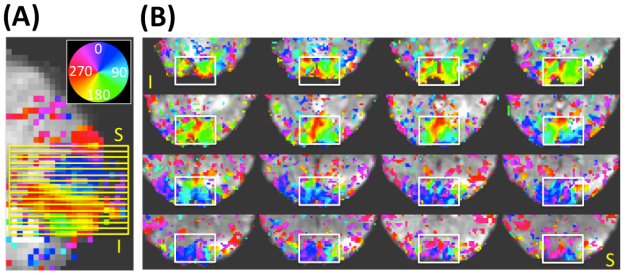

Figure 2. (A) Sagittal view of phase angle mapping. Slice positions used for further analysis are indicated by the yellow rectangles. The circular colorbar indicates the phase angles and their corresponding colors. (B) Axial slices overlayed by phase angles. The white rectangles represent the regions of interest for correlation analysis.

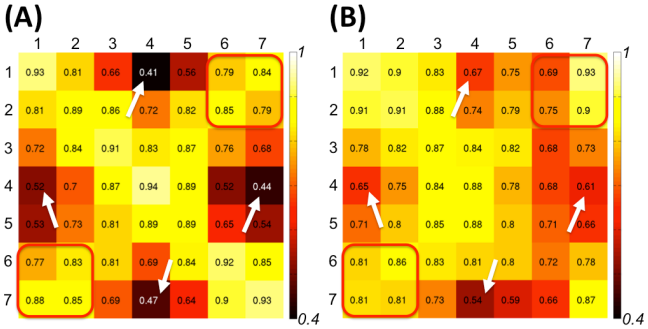

Figure 3. The correlation matrices for two subjects. The rows from top to bottom represent the sub-areas responding to the stimulus phase (as shown in fig. 2A-G) for one hemisphere. The columns from left to right are for the other hemisphere.

Discussion

In our preliminary results, relatively strong correlation coefficients were found along the diagonal terms of the correlation matrix, which shows the interhemispheric functional connectivity is organized retinotopically among these sub-areas. However, a reversed stimulus is needed to eliminate the effect of latency introduced by HRF. Moreover, there is no significant difference among the diagonal terms of the matrix, suggesting that mono-synaptic connections may not be critical for interhemispheric functional connectivity in visual cortex; rather the data suggests a dominant involvement of a mutli-synaptic pathway. Additional subjects are currently being scanned to solidify these findings.

Reference

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