Correlation between hemodynamic variation and resting-state fMRI in patients with carotid artery stenosis

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Introduction

Resting-state functional MRI (RS-fMRI) has been widely applied to analyze the functional connectivity (FC) between brain regions, e.g. the default mode network (DMN) in neuroscience and clinical studies (1). The FC found from fluctuations in blood oxygenation level-dependent (BOLD) signal has been related to the spontaneous neural activity during the resting state (1,2). In patients with unilateral stenosis of internal carotid artery (ICA), a recent study showed the disrupted FC of the DMN, which correlated with cognitive impairments (3). In a previous study, the presence of cognitive impairment and cognitive decline were observed in such patient group and related to perioperative impairments in perfusion pressure or procedure-related showers of emboli released into the cerebral circulation (4). However, it is not clear whether and how the hemodynamic variations are related to the disruptions of the FC in the patients. To help understanding the mechanism, this study aimed to investigate the FC of DMM in correlation with perfusion metrics in patients with unilateral ICA stenosis.

Methods

Thirty-eight patients with unilateral ICA stenosis (Left: 21 patients, Right: 17 patients, 6 females, age: 66.1±8.3y) participated in this study. During the RS-fMRI scan, subjects were instructed to keep their eyes closed, to remain awake, to think of nothing, and to perform no specific task. RS functional images were acquired at a 1.5T clinical MRI scanner using a T2*-weighted single-shot gradient-echo echo-planar imaging (EPI) sequence (TR/TE/FA=2000ms/50ms/90°, in-plane matrix = 64 x 64, slice thickness = 5mm). For each patient, 20 axial slices per volume and a total of 150 volumes were obtained. For perfusion assessment, DSC-MRI were acquired using a T2*-weighted single-shot gradient-echo EPI sequence (TR/TE/FA=1500ms/40ms/90°, in-plane matrix = 128 x 128, slice thickness = 5mm, 20 slices, 60 dynamics). For the RS-fMRI analysis, data preprocessing included slice timing correction, head motion correction, spatial normalization to the MNI template, and spatial smoothing with a 6-mm Gaussian kernel. FC within the DMN was analyzed with seed-based analysis using REST (http://resting-fmri.sourceforge.net). The reference time course was extracted from a posterior cingulate cortex (PCC) mask obtained from a previous study (5). The resulting correlations were transformed to approximate Gaussian distribution using Fisher's z transformation. For the perfusion analysis, arterial input function was selected from six voxels around the middle cerebral artery (MCA) and then was applied to a delay-insensitive singular value decomposition method (6) to derive the relative cerebral blood flow (rCBF) map and the delay (Tmax) map. For each patient, a normalized CBF (nCBF) map was determined by the ratio of the rCBF map over the averaged rCBF value of a region-of-interest in the occipital lobule. For the DMN connectivity maps, the nCBF maps, and Tmax maps, the hemisphere ipsilateral to the ICA stenosis was defined to the left side by flipping corresponding maps from patients with right-side stenosis along the midsagittal axis. The average z scores, nCBF and Tmax values were then calculated from the DMN mask (5) in the inferior parietal cortex ipsilateral and contralateral to the carotid stenosis (IPC_sten and IPC_norm, respectivly).

Results

The IPC regions of the DMN exhibited significantly greater Tmax and smaller FC z-score in the stenotic side as comparing to the normal side (Table). No significant difference was found between the nCBF of the two sides, probably due to sufficient collateral blood supply in these patients. Figure 1 shows the rCBF map, the Tmax map, and the DMN connectivity map from one of the patients with left ICA stenosis. For this patient, the prolonged Tmax was found in the left MCA territory with normal-appearing rCBF compared to the hemisphere contralateral to the stenosis. In addition, significant DMN FC ($p<0.001$, uncorrected) was absent in the IPC_sten region. Figure 2 shows the scatter plot of the average FC z scores versus the Tmax, which demonstrated significant negative correlation in the IPC_sten region ($r=-0.27$, $p=0.048$). No significant correlation was found between the FC z-score and the nCBF in both IPC regions and between the FC z-acore and the Tmax in the IPC_norm region.

	IPC_sten	IPC_norm	P value
nCBF	1.00 ± 0.16	0.96 ± 0.19	0.07
Tmax	3.11 ± 1.99	2.36 ± 1.40	0.001
Average z scores	0.23 ± 0.22	0.29 ± 0.19	0.047

Conclusion

This study found that the prolonged blood supply to local tissues (indicated by Tmax) significantly correlated with reduced DMN connectivity in the IPC ipsilateral to the ICA stenosis, without apparent CBF deficits, in patients with unilateral ICA stenosis. Whether the delayed local blood supply directly results in disrupted FC of the brain or the BOLD signal fluctuation require further investigations.

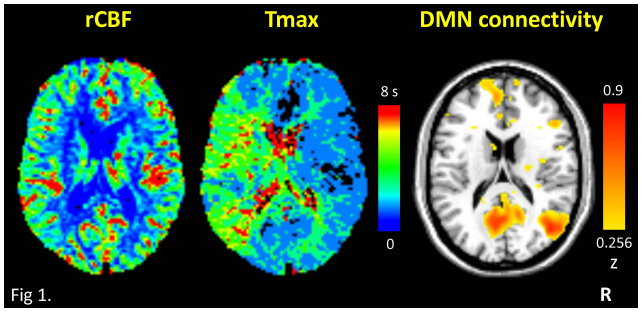

Fig 1.

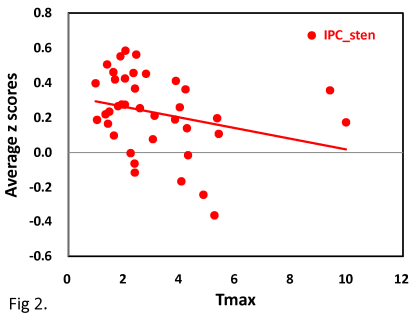

Fig 2.

References

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