

Improved DMN connectivity in patients with unilateral stenosis of internal carotid artery after carotid stent placement: A resting-state fMRI study

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Introduction

Functional connectivity (FC) within the default mode network (DMN) and its anti-correlated network (also called task-positive network, TPN) as detected by resting-state functional MRI (RS-fMRI) has generated significant interests in neuroscience and clinical studies (1). Seed-based correlation analysis (SCA) is the most common and straightforward metric to study the spontaneous neural activity with RS-fMRI (2). This study aimed to investigate the DMN FC changes in patients with unilateral stenosis of internal carotid artery (ICA) before and after carotid stent placement, with a special emphasis on the importance of seed definition. Carotid artery stenosis is highly associated with stroke and increases the risk of dementia (3). In addition, the presence of cognitive impairment and cognitive decline was observed in patients with unilateral ICA stenosis (3). Furthermore, previous studies showed that the treatment with carotid artery stenting may improve the cognitive function (4). To help understanding the mechanism of such improvement, this study assessed the effect of stenting on FC using RS-fMRI in combination with the perfusion evaluation with dynamic susceptibility contrast MRI.

Methods

Sixteen patients with unilateral ICA stenosis (Left: 10 patients, 4 females, age: 66.3±7.2y; Right: 6 patients, 2 females, age: 60.8±10.9y) were scanned twice (one week before and six months after stenting) at a 1.5T clinical MRI scanner. 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 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. 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). Data preprocessing included 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 SCA using REST (<http://resting-fmri.sourceforge.net>). Two seed regions were investigated: (1) a spherical seed ((12,-54,15); radius: 6mm) within the posterior cingulate cortex (PCC) (5) and (2) a PCC mask, obtained from ICA-based FC results of a group of normal subjects (6). The resulting correlations were transformed to approximate Gaussian distribution using Fisher's z transformation and then analyzed with one-sample t-test ($p < 0.05$, FDR corrected, cluster threshold = 10 voxels) to identify voxels showing significant correlations. In addition, the average z scores were calculated in three ROIs: medial prefrontal cortex (MPFC), left and right inferior parietal cortex (L_IPC, R_IPC). As individual level, the r-maps were thresholded with $r > 0.5$ ($p < 3.65 \times 10^{-11}$, one-sided, uncorrected). Moreover, in order to understand whether the DMN connectivity changes before and after stenting were associated with blood supply to tissues, relative cerebral blood flow (CBF) maps and the signal time courses within the bilateral IPC, obtained from DSC-MRI, were evaluated.

Results

Figure 1 shows the group results of the DMN connectivity in patients with left ICA stenosis before and after stenting. Compared to the spherical PCC seed, improved TPN connectivity was found using PCC mask. Figure 1 also illustrates improved DMN and TPN connectivity after the treatment. Average z-scores listed in the Table demonstrated increased sensitivity with the PCC mask as comparing with the seed.

Figure 2 shows the DMN connectivity maps, the relative CBF maps, and the DSC-MRI signal time courses within the bilateral IPC (red contour) from one of the patients with right ICA stenosis. For this patient, the improved FC was detected in the right IPC without apparent CBF impairments in the same region. In addition, the coincident bilateral signal time courses showed that the RS-fMRI findings in this patient were not related to potential delays of regional blood supply related to the stenosis.

Conclusion

This study found impaired FC in DMN and TPN in patients with unilateral ICA stenosis using RS-fMRI. The results were not directly related to regional perfusion deficits and thus likely linked to the neuronal origins. The impaired FC was found recovered after the carotid stenting.

References

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