Compromised cerebrovascular reactivity is reversible in patients with carotid artery stenosis: A BOLD MRI study

Jian Hui-Shan[1,2], Chang Ting-Yu[1], Huang Kuo-Lun[1], Chang Yeu-Jhy[1], Chang Chien-Hung[1], Wai Yau-Yau[3], Yeh Chih-Hua[3], Lee Tsong-Hai[1], and Liu Ho-Ling[4,5]

[1]Department of Neurology and Stroke Center, Chang Gung Memorial Hospital, Taoyuan, Taiwan, [2]Departiment of Biomedical Engineering and Environmental Sciences, Tsing Hua University, Hsinchu, Taiwan, [3]Department of Medical Imaging and Intervention, Chang Gung Memorial Hospital, Taoyuan, Taiwan, [4]Department of Medical Imaging and Radiological Sciences, Chang Gung University, Taoyuan, Taiwan, [5]Department of Imaging Physics, The University of Texas M. D. Anderson Cancer Center, Houston, TX, United States

Introduction

Cerebrovascular reactivity (CVR) reflects the capacity of cerebral arteries to a dilatory stimulus and is an important mechanism to keep normal vessel blood flow.[1] CVR can be estimated by blood oxygenation level dependent functional MRI (BOLD fMRI) using hypercapnia challenges.[1] In previous studies, the impaired CVR was related to the cerebrovascular disease, e.g. unilateral stenosis of internal carotid artery (ICA).[2,3] A recent study showed great heterogeneity of CVR when comparing BOLD signal time course between ipsilateral and contralateral middle carotid artery (MCA) territories in patients with carotid stenosis before they received carotid angioplasty with stent placement (CAS).[4] However, it is unclear whether the pattern of CVR and vessel blood flow in carotid stenosis patients after received CAS would be reformed to homogeneous CVR after received CAS. In order to clarify the mechanism, this study aimed to investigate the MCA time course correlation between ipsilateral side and contralateral side in stenting subjects with unilateral ICA stenosis.

Methods

Ten patients with unilateral ICA stenosis (Left: 5 patients, Right: 5 patients, 10 males, age: 60.4±4.9y) participated in this study. The breath-holding paradigm was applied according to the previous study.[4] During the breath-holding fMRI scan, subjects were instructed to hold their breath for 15 seconds after last expiration and then to breathe naturally for the next 30 seconds. The cycle was repeated 3 times. A respiratory belt was fastened across each patient's chest to ensure that the patients followed the breathing instructions properly. The fMRI images were acquired at 3T clinical MRI scanner using a T2*-weighted single-shot gradient-echo echo-planar imaging sequence (TR/TE/FA=3000ms/30ms/90°, in-plane matrix = 64 x 64, slice thickness = 3mm). For each patient, 46 axial slices per volume and a total of 70 volumes were obtained. For the breath-holding fMRI analysis, data preprocessing included head motion correction, spatial normalization to the MNI template using SPM8 software. For each patient, voxels with significant BOLD signal changes were determined with a threshold of $p<0.05$, FWE corrected. In addition, BOLD signal time courses of the ipsilateral and the contralateral hemisphere were extracted from the MCA territory mask obtained from a previous study.[3] The Pearson correlation coefficient were calculated for the MCA time courses between the ipsilateral side and the contralateral side and then the correlation coefficient was transferred to the Z-score. Furthermore, in order to estimate the temporal variation, a convolution model was applied to fit the MCA time course.[5] Quantitative indices including full-width at half-maximum (FWHM), onset time (defined as the time to the first half-maximum) and BOLD signal change were obtained.

Results

Figure 1 shows BOLD response map before and after CAS, in one subject with left ICA stenosis ($p< .05$, FWE corrected). It can find that the BOLD responses decreased in ipsilateral side before CAS and then increased after CAS. Figure 2 shows the MCA time course of before and after CAS as averaged across all patients. For the MCA time course, the reduced BOLD signal change and obviously prolonged time curve were found in the ipsilateral side compared to the contralateral side before CAS. The quantitative indices extracted from MCA territory time courses before CAS exhibited significant differences between the ipsilateral and the contralateral sides in BOLD signal change, FWHM, onset time, (see Table). No significant difference was found after CAS. The temporal correlation (indicated by Z-score) between two hemispheres significantly improved after CAS.

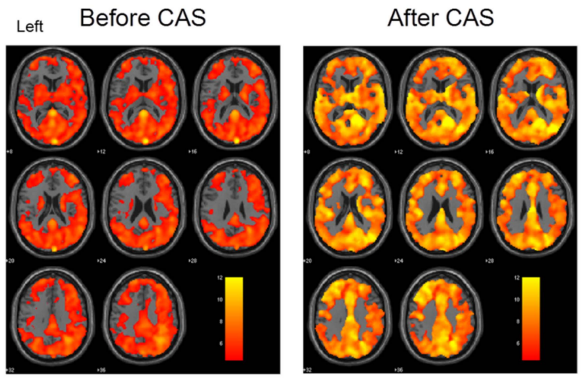

Figure 1

Conclusion

This study found a specifically temporal phenomenon of heterogeneous CVR in patients with ICA stenosis, that was the CVR of ipsilateral side appeared slower than that of contralateral side. After CAS, the heterogeneous CVR was reformed to homogeneous between the ipsilateral and contralateral sides. Whether the recovery of the slower CVR directly resulted from changes in collateral blood supply after the patients received CAS requires further investigations.

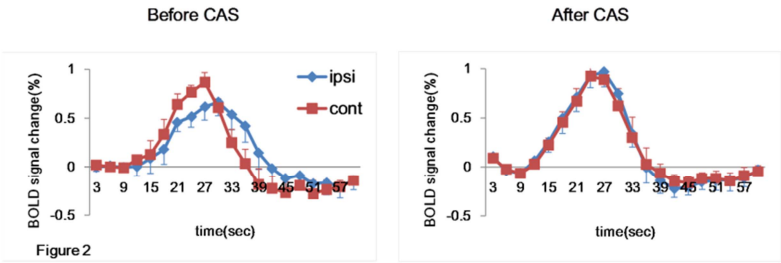

Figure 2

References

1.Kastrup A, et al., Neuroimage. 1999; 10: 675-681. 2. Kleinschmidt A, et al., Stroke. 1995; 26: 106-110. 3. Chang TY, et al., AJNR. 2009; 30: 1330-1336. 4. Chang TY, et al., PLoS ONE. 2013; 8(9): e76072. 5. Hsu YY, et al., JMRI. 2010; 31: 78-84.

	Before CAS			After CAS		
	Ipsi	Con	p-value	Ipsi	Con	p-value
BOLD signal change (%)	0.83 ± 0.24	0.95 ± 0.2	0.046	0.95 ± 0.44	0.94 ± 0.38	0.921
FWHM (s)	16.68 ± 1.13	13.59 ± 0.75	0.001	13.03 ± 0.43	13.01 ± 0.43	0.842
onset time (s)	21.24 ± 4.86	18.05 ± 2.59	0.030	19.56 ± 3.28	18.88 ± 3.19	0.071
Z-score	1.15 ± 0.48			1.88 ± 0.57		0.001