FMRI and Carotid Artery Intima-Media Thickness in Patients with Cardiovascular Disease

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Introduction

Patients with cardiovascular disease often exhibit cognitive deficits even when they do not meet clinical criteria for dementia.[1] Such impairment may be mediated through abnormalities in cerebral blood flow and oxygenation due to poor cardiac function or through compromises in the structural integrity of blood vessels supplying blood to the brain. Because many cardiovascular risk factors are treatable, it is important to elucidate the relationships between cardiovascular health and brain function. The purpose of this study was to examine the association between a non-invasive marker of arterial health, common carotid artery intima-media thickness (CCA IMT), and fMRI activation during a verbal working memory task (VWM) in stable outpatients with cardiovascular disease.

Method

Eight cognitively intact (Mean Mini Mental Status Exam Score = 29.25 ± 1.04) patients diagnosed with cardiovascular disease, mean age 68 ± 8.5 years, underwent fMRI during a 2-Back VWM task[2] and B-mode ultrasound of the far wall of the left CCA, approximately 1 cm proximal to the carotid bulb. All participants performed above 70% accuracy on the 2-Back task. CCA IMT was defined as the distance between the luminal-endothelial interface and the junction between the media and the adventitia, and calculated with an automated algorithm based on a validated edge-detection technique.[3] Whole brain echo-planar fMRI was performed on a 1.5T Siemens Symphony scanner with TR/TE = 3860/38 ms, 90 flip angle, 3 mm thick slices, FOV = 192cm^2, matrix size of 64x64. AFNI[4] was used for image processing including motion correction, temporal smoothing, spatial filtering, linear detrending, and transformation to standard stereotaxic space.[5] An empirically defined group mask was created by averaging the results of individual multiple regression analyses, which were transformed to z-scores, corrected for multiple comparisons, filtered with a 5 mm Gaussian kernel, and thresholded at z = 1 and a 400 μL volume. Eight regions of interest (ROIs) resulted (Fig. 1). This empirically defined mask was applied to individual data to determine mean task-related effect (intensity) and number of significantly active voxels (volume) within the ROIs (FDR-corrected p<0.05). Mean signal intensity and volume were correlated with CCA IMT controlling for the effect of age.

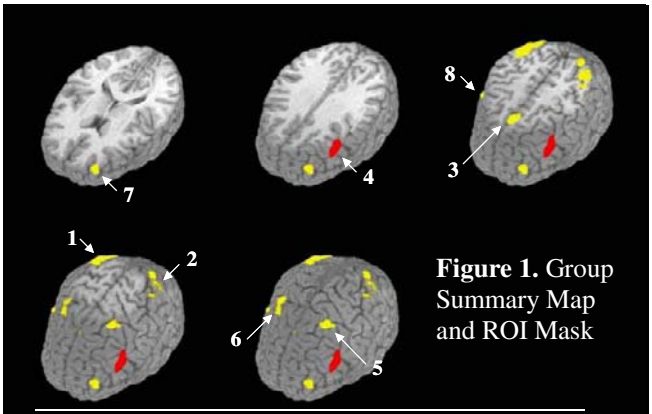

Figure 1. Group Summary Map and ROI Mask

ROI	x	y	z	Region
1	38	-59	47	Right Posterior Parietal Cortex
2	-38	-63	45	Left Posterior Parietal Cortex
3	-4	19	44	Left Premotor Cortex
4	-51	23	26	Left Dorsolateral Prefrontal Cortex
5	-32	2	58	Left Premotor Cortex
6	30	3	61	Right Premotor Cortex
7	-34	52	12	Left Prefrontal Cortex
8	47	7	35	Right Premotor Cortex

Results and Discussion

Consistent with previous studies of VWM, we found that the 2-Back task was associated with activation in dorsolateral prefrontal cortex (DLPFC), posterior parietal cortex (PPC), and supplementary motor areas (SMA).[2,6] Independent of age, increased CCA IMT was associated with significant decreases in both mean signal intensity ($r = -0.80$, $p < 0.05$) and number of active voxels ($r = -0.82$, $p < 0.05$) in the left DLPFC of patients with cardiovascular disease (coded in red on Fig. 1). Decreases in mean signal intensity and number of recruited voxels within the DLPFC ROI were also correlated with poorer performance on a similar VWM task, digit span backwards ($r = 0.85$, $p < 0.05$). As DLPFC is implicated in attention/executive components of VWM[2], these results fit well with our previous imaging and neuropsychological studies documenting that attention-executive-psychomotor networks are particularly vulnerable to subcortical ischemic vascular disease.[7] They also support the idea of a continuum of vascular-related cognitive impairment where subtle decline in attention/executive functions is evident even in the absence of dementia. The demonstrated relationship between fMRI activation and CCA IMT also reaffirms the need for studies aimed at elucidating the complex relationships between vascular health, cerebral perfusion, and brain function.

References: **(1)** Paul, R. et al. Cardiovasc Dis 2005; 20(2):129-133; **(2)** Smith, E.E. & Jonides, J. Cog Psychol 1997;33:5-42; **(3)** Stadler, R.W. et al. Ultrasound Med Biol 1996;22:25-34; **(4)** Cox, RW Comput Biomed Res 1996;29:129-173; **(5)** Talairach, J. & Tournoux, P. Thieme Medical Publishers, New York, NY, 1988; **(6)** Sweet, L.H. et al. J Neuroimaging 2004;14:150-7; **(7)** Cohen, R.A. et al. JINS 2002:8:743-752.