Quantification of Load Dependent Brain Activity in Parametric N-Back Working Memory Tasks using pCASL Perfusion Imaging

Qihong Zou[1,2], Hong Gu[2], Jiongjiong Wang[3], Jia-Hong Gao[1,4], and Yihong Yang[2]

[1]*MRI Research Center and Beijing City Key Lab for Medical Physics and Engineering, Peking University, Beijing, Beijing, China, People's Republic of,* [2]*Neuroimaging Research Branch, National Institute on Drug Abuse, National Institutes of Health, Baltimore, MD, United States,* [3]*Department of Neurology, University of California Los Angeles, Los Angeles, CA, United States,* [4]*Brain Research Imaging Center, University of Chicago, Chicago, IL, United States*

Introduction

PET and BOLD fMRI studies have shown that N-back working memory tasks induce brain activation in a large-scale network including fronto-parietal cortices, thalamus, and cerebellum [1-4], as well as brain deactivation in the posterior cingulate cortex (PCC) and medial prefrontal cortex (MPFC) [5-7]. Further, load dependency of parametric N-back working memory tasks on brain activation [1, 2, 3, 7] and deactivation [3, 7] has been demonstrated. However, BOLD signal results from changes in CBF, CBV, and CMRO2 near the activated brain site [8], and its role as a surrogate of neuronal activity is still under investigation. Alternatively, ASL perfusion imaging techniques use CBF, a well understood physiological parameter closely related to cerebral metabolism, as an indicator of neuronal activity [9-10]. Compared to PET, ASL techniques provide CBF measurement without requirement of radioactive tracer injection [9-10]. However, there is no systematical investigation on the brain activation and deactivation induced by parametric N-back working memory tasks and the corresponding load effects based on quantitative CBF using ASL fMRI. Here, using a pseudo-continuous ASL (pCASL) technique [11-12], we acquired fMRI data during parametric N-back working memory tasks on a relatively large number (n=40) of subjects. Based on quantitative CBF, we investigated brain activation and deactivation, and assessed their load effects.

Methods

Experimental design: Forty healthy subjects (27.5 ± 8.2 years old, 21 females) underwent a block-design N-back verbal WM task. The task was presented as a block paradigm with four conditions: three active WM tasks [1b, 2b, 3b] and a low level vigilance task [0 back (0b)].

Data acquisition: fMRI data were acquired with a pCASL sequence on a 3T Siemens MR scanner. The parameters for pCASL sequence were as follows: TR/TE = 4000/13 ms, FA=90°, slice thickness = 5mm with 20 % gap, 20 slices, FOV = 220×220 mm^2 with in-plane resolution = 3.44×3.44 mm^2, labeling duration = 1.6 s, label offset = 80 mm, post-labeling delay = 1.2 s and bipolar gradient with b = 2 sec/mm^2.

Data analyses: All data analyses were conducted with AFNI [13] and MATLAB. Preprocessing steps for WM task data included head motion correction and spatial smoothing with a 6-mm Gaussian kernel. Label images were subtracted from control images to obtain CBF-weighted time series. Control images and CBF-weighted images were then extracted for each working memory condition based on the task design for each subject. Quantitative CBF maps for all the four working memory conditions were generated using one-compartment model [14]. Finally, the WM task CBF maps of each subject were coregistered with the corresponding anatomical maps and spatial normalized to standard Talairach and Tournoux (TT) space with a resampling resolution of 3×3×3 mm^3 to facilitate group analysis. To show the general activation and deactivation patterns of working memory tasks, paired *t*-tests were conducted between the three active working memory tasks (1b, 2b and 3b) and the baseline vigilance task (0b). Trend analyses, including linear, quadratic and cubic trends, were conducted across the four working memory conditions based on quantitative CBF. A corrected significance level of $p < 0.05$ for the resultant statistical maps was obtained by clusters with a minimum volume of 2052 mm^3 at an uncorrected individual voxel height threshold of $p < 0.01$.

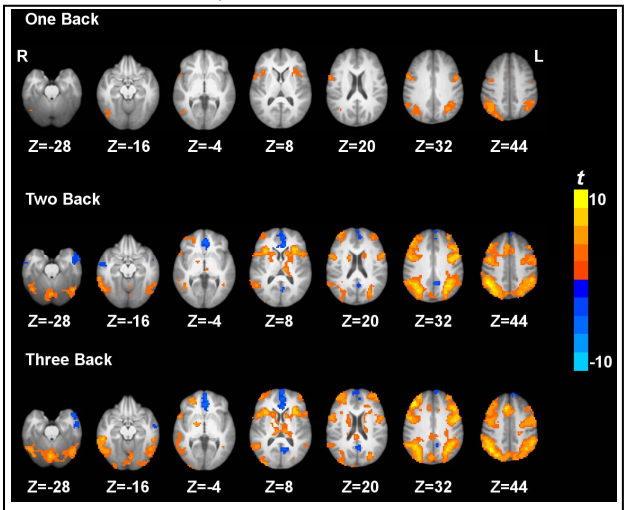

Fig. 1. *t*-maps between the three active working memory task conditions and the 0 back baseline vigilance task condition, respectively, based on quantified CBF. $p < 0.05$ corrected.

Results

Task activation and deactivation comparing the three active working memory tasks and the baseline vigilance task, respectively, are shown in Fig. 1. Task activation under 3b compared to 0b was observed in the inferior parietal lobule (IPL), middle frontal gyrus (MFG), supplementary motor area (SMA), dorsolateral prefrontal cortex (dlPFC), anterior insula (aINS), thalamus, and cerebellum. On the other hand, task deactivation under 3b compared to 0b was observed in the PCC, MPFC and anterior temporal gyrus (Fig. 1). Similar patterns of activation and deactivation were observed when comparing 2b to 0b. Brain activation was detected in the similar regions, although with less intensity and extent, when comparing 1b to 0b. These results are generally in agreement with previous working memory data [3, 4, 7]. Fig. 2 shows the brain regions exhibiting the linear, quadratic and cubic trend contrasts. The regions that showed a linear increase of CBF with task loads were located at cortical regions including IPL, MFG, SMA, dlPFC, aINS, thalamus, and cerebellum. The only regions that showed a linear decrease of CBF with task loads were only located at cortical regions including PCC, MPFC and anterior temporal gyrus. The regions that showed a quadratic trend of CBF were located at bilateral IPL. Right IPL activation also showed a cubic trend. No brain regions showed a significant quadratic or cubic trend of CBF in the task deactivated brain regions.

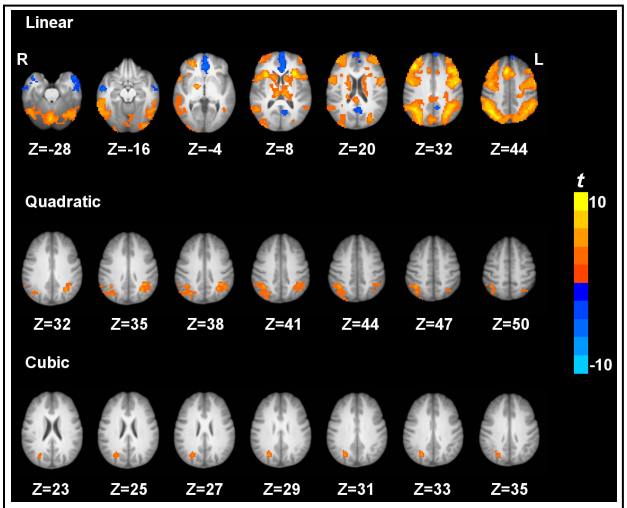

Fig. 2. Trend t-maps across the four working memory conditions based on quantified CBF. $p < 0.05$ corrected.

Summary and Discussion

The current study systematically investigated the patterns of brain activation and deactivation induced by parametric N-back working memory tasks based on quantitative CBF. Further, we investigated the load effects of N-back working memory tasks on brain activity. To the best of our knowledge, this is the first study to investigate the load effects of parametric N-back working memory tasks on brain activity based on quantitative CBF using pCASL. Our findings are in agreement with those measured by PET [3] and BOLD fMRI [1, 2, 4-7], which are mainly located at the fronto-parietal cortices, thalamus, caudate, cerebellum, PCC and MPFC. Our findings suggest potential applications of ASL fMRI techniques, with advantages of quantitative measurements at both baseline and activated states, to the assessment of neuropsychiatric and neurological populations with cognitive deficits.

References

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