Comparisons of Neuronal Activations from BOLD and ASL fMRI during an associative working memory task in patients with cognitive normal, mild cognitive impairment, and Alzheimer's Disease

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Target Audience: Clinicians and physicists who work for a neurodegenerative diseases.

Background: The blood oxygen level-dependent (BOLD) fMRI technique is the most popular functional MRI (fMRI) method to observe the changes in the metabolic activity [1]. BOLD signals depended on several physiological parameters, including oxygen consumption, blood volume, and blood flow. Cerebral blood flow (CBF) is a well-established correlate of brain function and therefore is an essential parameter for studying the brain at both normal and diseased states. Arterial spin labeling (ASL) can be used to fMRI studies based on alternations of CBF between different conditions [2]. CBF values measured by an ASL technique were able to measure perfusion changes in dementia [3].

Purpose: The objective of this study, therefore, was to estimate the neuronal activations during an associative working memory task in patients with cognitive normal (CN), mild cognitive impairment (MCI) and Alzheimer's diseases (AD) with two different fMRI methods, BOLD and ASL.

Materials and Methods: BOLD and ASL fMRI data were obtained from 25 CN (mean age = 64.28, 19 females and 6 males), 19 MCI (mean age = 67.95, 14 females and 5 males), and 23 AD subjects (mean age = 75.69, 18 females and 5 males) after informed consent during a face–name association encoding task. Figure 1 shows that the fMRI paradigm was used a block design with three conditions: novel (face–name pairs), un-novel (repeated face–name pairs), and fixation (baseline). The MR imaging was performed on 3T MR system (Achieva, Philips Medical system) with an 8 channel phase-array SENSE coil. BOLD and ASL fMRI paradigm were performed that each novel pair was presented once for 4 sec, un-novel pair was for 3.5 sec and fixation pair was for 0.5 sec. BOLD fMRI data were acquired using a two-dimensional gradient-echo (FFE) EPI sequence and the ASL fMRI data were acquired using PULSAR sequence [4]. Other acquisition imaging parameters for two sequences were: TR = 3 sec, the number of dynamics = 96, and total scan time = 4 min 48 sec. Furthermore, sagittal structural three-dimensional T1-weighted (3DT1W) images were acquired with the MPRAGE sequence for image registration. The ASL data processing was performed to estimate CBF using an SPM based an ASL data processing toolbox (ASLtbx) [5]. CBF values were corrected ($CBF_{correct}$) to minimize partial volume effect and increase the statistical power using a formula: $CBF_{correct} = CBF_{uncorrect}/(GM+0.4*WM)$ [3]. SPM8 program was used to pre-processing and a voxel-based statistical analysis. The differences of BOLD and ASL fMRI among the three groups were investigated by using a one-way analysis of variance (ANOVA) test. The gender and age information were included as covariates.

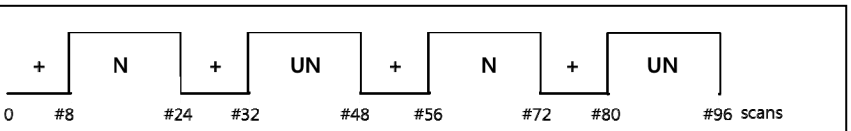

FIG.1. Task design for the fMRI experiment. The block design paradigm with three conditions. (**N**=novel, face-name; **UN**=un-novel, face-name; **+**=fixation, baseline)

Results: Figure 2 demonstrates the differences between the novel and the fixation contrast among the three different groups for BOLD (upper) and ASL (low) fMRI data. For BOLD (A, B, and C), CN subjects between the novel and the fixation contrast showed greater activations than AD subjects in the left cingulate gyrus and anterior cingulate regions, but AD subjects had no greater activation region than CN subjects. MCI subjects showed greater activations than AD subjects in the left cingulate gyrus regions, but AD subjects had no greater activation region than MCI subjects. The activation regions between un-novel and the fixation contrast were similar to those of the novel and fixation contrast. For the un-novel and the novel contrast, the activation regions were similar to other contrasts, but there were no significant differences between MCI subjects and CN subjects for the un-novel and the fixation contrast in BOLD fMRI data.

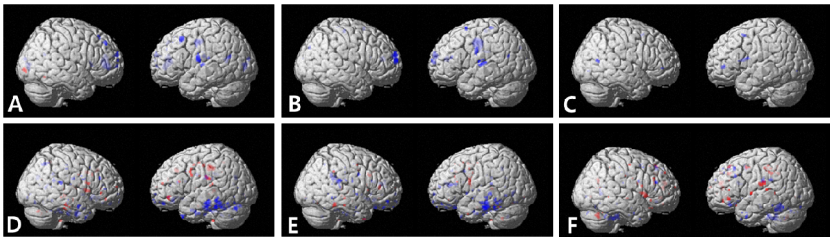

FIG. 2. The results of difference of BOLD (A, B, and C) and ASL (D, E, and F) fMRI data for the novel verse fixation contrast among three subjects. A and D: AD>CN (Red), AD<CN (Blue), B and E: AD>MCI (Red), AD<MCI (Blue), and C and F: MCI>CN (Red), MCI<CN (Blue).

For ASL (D, E, and F), CN subjects between the novel and fixation contrast showed greater activations than AD subjects in the right uncus region, but lower activations in the left sub-gyral and precentral gyrus regions. MCI subjects showed greater activations than AD subjects in the left cingulate gyrus and the right sub-gyral regions, but lower in the right inferior temporal gyrus region. MCI subjects showed greater activations than CN subjects in the left sub-gyral region, but lower in the right insula and the left postcentral gyrus region. The activation regions between un-novel and the fixation contrast were similar to those of the novel and fixation contrast. For the un-novel and the novel contrast, the activation regions were similar to those of other contrasts.

Discussions: In the study, we have investigated the fMRI contrast using BOLD and ASL fMRI sequences during the face-name association encoding task. We found that more differences between AD and MCI groups and between MCI and CN groups were found in ASL fMRI data compared to BOLD fMRI data. CBF values of ASL fMRI data decreased from CN to MCI and to AD for all contrasts.

Conclusion: The ASL fMRI technique offered more efficiency information for the neuronal activity effects than the BOLD fMRI technique and was useful to investigate functional changes for early diagnosis for AD.

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