Exploring the reproducibility and consistency of diffusion-weighted functional magnetic resonance imaging during visual stimulation using population-based activation map

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Introduction: BOLD contrast has been extensively used in fMRI for its relatively high sensitivity. However, the spatial specificity is compromised by the diversity of the participating vasculature [1]. Recent experiments have demonstrated that the diffusion-weighted functional magnetic resonance imaging (dFMRI) [2-11] can be used to detect brain activations, and dFMRI may provide a useful means to detect the brain activation near to the neural activation region. The spatial and temporal characteristics of the dFMRI signal changes during visual stimulation have been studied [2] [10] [11], but the influence of *b*-value on the location and spatial distribution of activation are still unknown. Here we compared the locations and distributions of dFMRI and BOLD-fMRI studies and investigated the consistency of dFMRI study using the population-based activation map.

Methods: Image Acquisition: Twelve healthy volunteers attended the present study. All subjects were scanned using a Siemens Trio 3T whole-body MR scanner. Two types of functional study, dFMRI and BOLD-fMRI, were performed, each containing 12 oblique slices centered on calcarine fissure. (*Exp-1*) dFMRI: A twice refocused spin-echo diffusion-weighted EPI sequence was applied to acquired dFMRI dataset (five *b*-values: 50, 400, 800, 1200, and 1600 s/mm^2). The sequence parameters are TR = 1500 ms, thickness = 3.3mm with 30% gap, FOV = 212mm×212mm, matrix = 64×64. (*Exp-2*) BOLD-fMRI dataset were acquired using the gradient-echo EPI sequence. The parameters are identical to those of dFMRI, but TE = 30 ms. (*Exp-3*) 3D images were obtained using T1-weighted MP-RAGE sequence. The visual stimulation paradigm comprised of a block design: the 'rest' and 'task' in 20s/20s period. The 'task' consists of a white-black-squared checkerboard pattern reversing at 8Hz, and the 'rest' was simply the fixation cross on a black screen. A total of 247 volumes functional were obtained while the subject observed the visual stimulus for functional measurement.

Data Analysis: All image analysis was carried out using FSL. For the dFMRI dataset, the brain mask was extracted from the functional dataset using BET, The effects of head motion and image distortions caused by eddy currents were corrected by selecting the first b = 0 volume as the reference volume using FLIRT. The corrected dFMRI dataset was taken as the input for the first-level statistical analysis with FEAT, including high-pass filter cut-off = 40sec to remove slow trends, spatial smoothing FWHM = 6mm, registration to structural and standard space. For the BOLD-fMRI images, the dataset were analyzed in the standard procedure using FEAT. The cluster-threshold $Z = 2.3$ and $p < 5\%$ was selected.

Activation map for group study: Two types of activation map for group study were created. One is the group statistical activation map generated from the higher-level statistical analysis using mixed-effects group analysis (FLAME1, the cluster threshold $Z = 2.3$ and $p < 5\%$). The other is the *population-based activation map*, which was created by the following two steps. *Step-1*: the activation map for each individual was calculated and transformed into MNI-152 space, then binaried. *Step-2*: all individuals' activation maps were added together in the standard space. For a given voxel in the visual cortex, thus, we can figure out the number of subjects who were detected activation under the visual stimulation.

Results: The group statistical activation maps for dFMRI and BOLD-fMRI are shown in Fig.1. Fig.2 is the population-based activation map, in which the color-coded voxels represent the number of subjects who have been detected activation. Fig.3 is the thresholded population map in which the activation region detected from more than 5 subjects is presented. The following result can be reached. The spatial location and distribution of activation maps were highly reproducible across all subjects. The consistency and spatial pattern specificity of dFMRI are significant. The activation derived from dFMRI is more localized than that from BOLD, and the extent of the activation in dFMRI study reduces with the increase of *b*-value.

Discussion: If the signal changes of dFMRI indeed originates from neuronal cells, then the most sensitive changes should occur in the middle cortical layer of the visual cortex, because layer-4 of the visual cortex [12] is known to have the highest neural activity [7, 13].

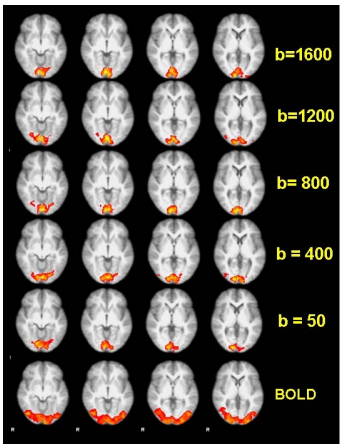

Fig.1 Comparison of group activation maps obtained from dFMRI (*b*-values = 50 / 400 /800/1200/1600 s/mm^2) and BOLD-FMRI.

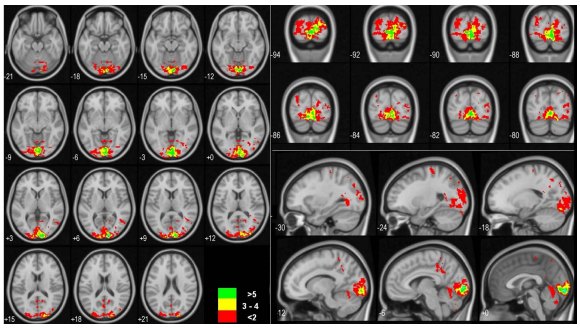

Fig.2 Illustration of the population-based activation map derived from dFMRI study. As an example, the result obtained from dFMRI with $b = 1600$ s/mm^2 is presented. The regions coded in color of red, yellow, and green indicate where the activation was detected from 1-2 subjects, 3-4 four subjects, and more than 5 subjects.

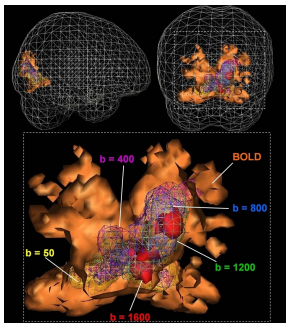

Fig.3 Rendered 3D activation map. It shows that the region has been detected activation from more than five subjects in the present study. Activation regions obtained from BOLD and dFMRI studies are coded in different colors.

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