Temporal variations of the hemodynamic response onset estimated by perfusion-based event-related fMRI

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Synopsis

This study aims to conduct perfusion-based ER-fMRI technique to assess the temporal resolution of ER-fMRI at different levels of contrast-to-noise ratio (CNR) and further to compare with BOLD-based ER-fMRI technique. Brief visual stimulation experiments were applied both on BOLD and perfusion experiments. Based on the application of the repeated-single-trial averaging technique, remarkably smaller variability (standard deviation) of the onset times was observed on the perfusion data than the BOLD data at equal CNR level. From the results, we suggest that perfusion-based techniques may lead to higher temporal resolution of fMRI.

Introduction

Since 1997, Kim et al has demonstrated two major effects on the temporal limitation of blood oxygenation level dependent (BOLD) fMRI responses: the intrinsic blurred BOLD hemodynamic response (HDR) and the low CNR (1). Previous investigators have demonstrated that by using a deconvolution method on the basis of the linear model can differentiate successfully the superimposed components of the blurred BOLD HDR (2). However, when comparing the temporal responses between spatially distinct brain regions, the temporal resolution was no longer defined by the linear model but affected by a finite CNR. Thereafter, the event-related (ER) fMRI with single-trial averaging was suggested to improve the CNR of the ER-fMRI signals (3). By using the averaging technique, we have proposed a relationship between the CNR and the temporal resolution by the computer simulation (4). However, when verifying with the empirical BOLD fMRI data, we have observed a remarkable offset when estimating the minimal resolvable temporal onset delays between voxel-wise signals within brain regions, as well as notable variability between subjects (5). This was suggested due to contamination by more signals originated from the large veins and different anatomical structure distribution of the large veins between subjects (3, 6). Therefore, in this study, we will propose a non-typical BOLD imaging technique, perfusion-based ER-fMRI technique, to demonstrate that perfusion imaging may lead to more stable evaluation of the onset times of the HDRs between and/or within brain regions (7) due to its good property of the detection of the smaller vessels, and further we will compare the results between perfusion-based and BOLD-based data.

Methods

Four healthy subjects were studied with both BOLD and perfusion ER-fMRI experiments. All the experiments were performed on a 1.5-T Magnetom Vision MRI Scanner. The paradigmatic design for the BOLD experiment was consisted of 50 repeated trials, with each trial consisting of 1-sec brief visual stimulation state and 13-sec resting state. 8-Hz-flashing annular checkerboards with a crosshair in the center were displayed as the visual stimuli. The BOLD images were acquired by using a single-shot T2*W GRE-EPI sequence, with the acquisition parameters: TR/TE/FA = 1000ms/60ms/90^0, NEX = 710 and in-plain resolution = 3.3 x 3.3mm^2. Single slice with slice thickness 8-mm was imaged along the calcarine fissure to cover the visual cortices. For the perfusion studies, an inversion recovery pulse slice selective (IR-SS) sequence and an inter-trial interleaf method were applied to obtain high sampling rate perfusion images. Six separate runs were designed to include three non-time-shift repeated runs and three 1-sec-time-shift repeated runs, with each run consisting of 17 repeated trials. The imaging parameters were as the following: TI/TR/TE/FA = 1200ms/2000ms/9.3ms/90^0, NEX = 124, and in-plain resolution = 2.0 x 2.0mm^2. The imaging position as well as slice thickness were the same as the BOLD study, and so as the materials of the visual stimuli. Prior to all the runs, there were 10-sec dummy scans for the imaging system reaching the steady state, and throughout all the entire runs, the subject was instructed to exactly gaze on the fixation crosshair in the center. For image data processing, voxels with statistically significant activation ($p<0.01$) were detected by correlating with a gamma reference function (8):

$$h(t) = c1 * (t - c2)^{c3} \exp(-t / c4)$$

where c1, c2, c3 and c4 were constants. After manually selecting the regions-of-interest (ROIs) within the visual cortices, the BOLD and IR-SS time series were extracted pixel by pixel and averaged randomly across 50, 40, 30, 20, 10 and 1 repeated single trials, respectively. By employing curve fitting method using a gamma variate function, the onset times were thus determined at the time to half maximum of the fitted curves and the CNRs were determined as the contrast of the fitted curves divided by the noise, measured as the standard deviation of the differences between the fitted curves and the raw time series (4, 5).

Results

Fig. 1 demonstrated the relationship between CNR and standard deviation (SD) of the onset times measured from averages across four subjects for IR-SS and BOLD data. From left to right, the six points for both IR-SS and BOLD data were represented 1, 10, 20, 30, 40 and 50 trials, respectively, for averaging. For IR-SS, the CNR measured by averaging across 50 trials was comparable with that for BOLD when averaging across 20 trials. While increasing numbers of trials, the measured CNR for IR-SS and BOLD both increased. As the CNR increased, SD of the onset times significantly decreased. When comparing at equal CNR level, we observed remarkably smaller SD of the onset times for IR-SS than BOLD. Fig. 2 showed IR-SS and BOLD fitted curves of the averaged time series from left (pink) and right (blue) visual cortices, respectively, from one of the four subjects. It revealed that a notably smaller offset of the onset times between the two visual cortices could be observed for IR-SS than that for BOLD.

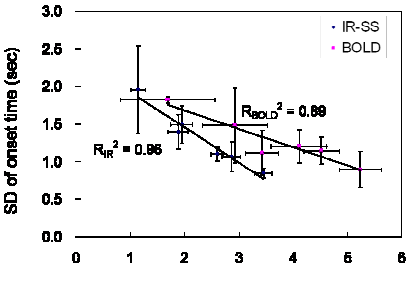

Fig. 1

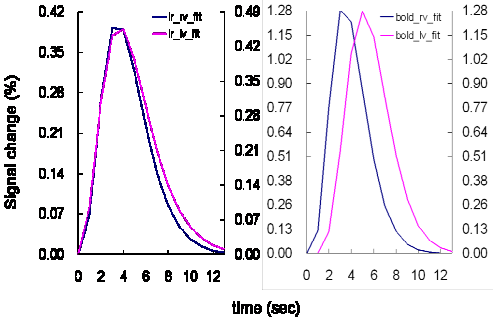

Fig. 2

Discussion

From fig. 1 and 2, we observed that the onset time distribution of the perfusion-based HDR showed a much smaller variance in onset time than that of the BOLD-based HDR. Since perfusion imaging technique is more sensitive to the smaller vessels, thus we can use it to detect more accurate onset latencies within single brain region and/or onset time delays between spatially distinct brain areas. Smaller onset variation is expected when CNR is further increased for the perfusion-based measurements. In addition, the interaction between the onset variation of voxel-based signals within a brain region and that of the mean signals between regions requires further investigations.

References

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