Temporal Characteristics of the Homodynamic Response Function of Transition-band SSFP fMRI

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Introduction Steady-state free precession (SSFP) offers several unique advantages for fMRI studies. It provides improved functional contrast to noise ratio with low image distortion and signal dropout, especially in regions with large susceptibility variations (1, 2). Recently, several groups proposed improved SSFP fMRI techniques to enhance the temporal resolution, achieve whole brain coverage (3), or remove respiration artifacts (4, 5). To develop SSFP fMRI as a robust tool for a broad range of applications, several practical issues must be carefully examined. The focus of this study is to measure the hemodynamic response function (HRF) of transition-band SSFP (tb-SSFP) fMRI and describe its temporal characteristics. An accurate estimation of the HRF could increase the statistical power of fMRI analysis, especially for event-related studies.

Methods Three subjects with written informed consent participated in this study. To minimize motion artifacts, foam padding was applied between the subject's head and the RF coil and subjects were instructed to breathe evenly and avoid any voluntary motion during scans. In all fMRI experiments, an 8-Hz flickering checkerboard was used as the visual stimulus and was repeated every 30 s for 6 blocks. An additional 15 s of baseline images was acquired before the first block, for a total scan time of 195 s. Five scans were performed on each subject with stimuli duration (succeeding rest duration) of 1 s (29 s), 2 s (28 s), 4 s (26 s), 8 s (22 s), and 16 s (14 s). The whole fMRI session lasted less than 20 min.

All imaging measurements were performed on a 3T scanner (Siemens Trio TIM) using a twelve-channel product head coil. A transversal slice including the visual cortex area was selected after 3D localization. High-order shimming was targeted at the occipital lobe of the brain. For each subject, less than 15 Hz full-width at half-maximum water linewidth was achieved in the targeted volume. A 2DFT balanced-SSFP sequence was used with parameters chosen similarly to the ones used in (1): TE/TR = 3.35/6.7 ms, matrix = 128×64, flip angle = 5°, bandwidth = 205 Hz/px, 1 average. The acquisition time for each image was 0.5 s.

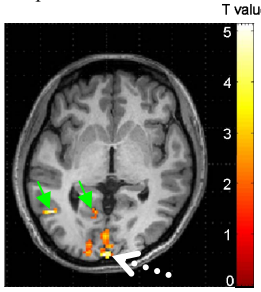

Fig.1 Transition-band SSFP fMRI activation map of 1 s visual stimulation. For HRF measurement, activated voxels outside of the shimming volume (green arrows) or in the sinus vein region (white dashed arrow) were excluded.

Data analysis and visualizations were done using Matlab 2008a. The SSFP fMRI data were analyzed using the SPM8 software package (6) without registration, smoothing, or spatial and temporal filtering. An activation map was obtained by thresholding the statistic map at P-value of 0.05. A mask was then generated based on the activation map of 1-s of stimulus, but excluding artifactual activated voxels through visual inspection, which will be explained in the Results section. The mask was applied to all five scans' original image data to extract the signal time courses. The time courses were then passed through an IIR notch filter at frequency 0.3 Hz with a Q-factor of 10. We averaged the filtered signal across all voxels for each stimulus duration to provide a measurement of the dynamic behavior.

Results Significant activation in the occipital lobe was obtained in all subjects. Fig. 1 shows a representative activation map acquired by transition-band SSFP fMRI with 1-s of checkerboard as the visual stimulus. In additional to activation area in the occipital lobe, activation responses were also observed outside the targeted shimming volume (green arrows in Fig.1) and in the sinus vein region (white dashed arrow in Fig. 1). For the purpose of measuring HRF, these regions were excluded from the region of interest (ROI). The measured dynamic responses from the remaining activation areas are displayed in Fig. 2 for stimuli with different durations. Similar to BOLD, it is apparent from these curves that amplitude of the tb-SSFP response was not linear with stimulus duration. However, there were two characteristics that differentiate tb-SSFP response from canonical BOLD response (7, 8): 1) an initial dip was clearly observed in all scans and 2) post-stimulus undershoot was unstable. As demonstrated in Fig.2, undershoot was suppressed in stimuli duration of 2 s, 4 s and 16 s.

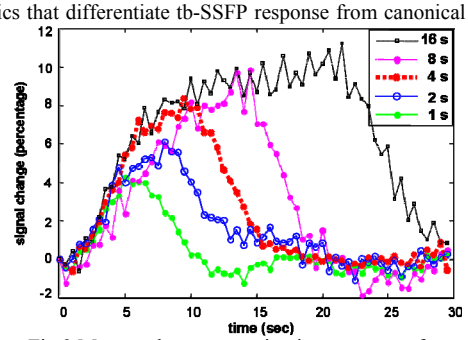

Fig.2 Measured average activation responses for stimuli of different durations in one typical subject.

The resulting response to the 1-s stimulus was taken to be an estimate of the hemodynamic response function measured by tb-SSFP fMRI. In light of the aforementioned initial dip and unstable undershoot, the measured HRF was fitted with a single gamma function, instead of the difference of two gamma functions (9). As shown in Fig. 3, the hemodynamic response was well estimated by a gamma function (R^2 = 0.89). The mean (±SD) maximum amplitude was 3.51±0.78% at time-to-peak of 5.57±0.74 s and FWHM of 4.43±0.13 s (n=3).

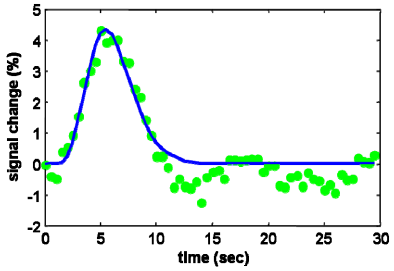

Fig.3 The measured HRF (dots) was fitted to a single gamma function (blue line), with time- to-peak of 5.43 s and FWHM of 4.56.

Conclusion and Discussion In this study, we have measured the hemodynamic response function of tb-SSFP fMRI by applying a short visual stimulus of 1 s. The measured HRF has been well characterized by a single gamma function, which models the peak. In comparison to BOLD, the signal response of tb-SSFP fMRI has exhibited a stable initial dip and an unstable post-stimulus undershoot, which cannot be modeled with a single gamma function. Moreover, similar to BOLD, the response system appears to be nonlinear since the signal change induced by a long stimulus could not be modeled by the convolution of HRF with the stimulus duration.

The result varied across subjects (n=3), especially the peak amplitude varied from 2.8% to 4.35%, while the shape and timing of response remained less variable. Although it agrees with the previous study in BOLD (10), the large amplitude variation might be due to the fact that we didn't repeat the experiment at different center frequency offsets and then combined the acquisition. However, instead of finding all activated pixels, our purpose is to measure the HRF. Therefore, this method sufficed for extracting the signal change in activated ROI, when a good high-order shimming was performed and visual inspection confirmed that the banding artifact remained stable throughout the 20-min fMRI session.

In the time course measurements, signal fluctuation caused by respiration was reduced by post processing of the raw data with a notch filter. This method worked well with our limited subject number. The respiration issue can also be compensated with real-time feedback (4, 5). These techniques can be adapted to this study to reduce temporal noise and field drift, and hence improving the accuracy of dynamic signal behavior measurements. With these improvements, our future work includes 1) a better estimation and modeling for the HRF of tb-SSFP fMRI, and 2) applying the tb-SSFP method on 7T to enhance the initial dip, using which instead of the large later positive peak might locate the oxygen extraction site, thereby improving the spatial specificity of fMRI.

References

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