Balanced Steady State Free Precession fMRI Using Intravascular Susceptibility Contrast Agent

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INTRODUCTION

The major challenges in EPI-fMRI are the image distortions and constraint in spatial resolution, thus limiting accurate and high-resolution mapping of brain functions, especially in small animals at high fields. Balanced steady-state free precession (bSSFP) imaging has been proposed as a promising alternative to EPI for fMRI [1]. The short repetition time (TR) and high signal efficiency of bSSFP allow high-resolution, high-speed imaging and distortion-free acquisition [2]. Recently, it has been demonstrated that the functional contrast can be achieved by utilizing the relatively large flat portion of the bSSFP off-resonance profile rather than the steep magnitude/phase transitions [3]. The contrast mechanism of the so-called "pass-band bSSFP" is similar to conventional BOLD and less sensitive to motion and physiological noise [4]. CNR and detection sensitivity are also the key factors in fMRI. Using intravascular susceptibility contrast agent, CBV-weighted fMRI provides larger CNR and robust signal changes with less contamination from large vessels compared to BOLD fMRI [5]. However, the contrast agent induced susceptibility also causes severe signal dropouts and image distortions at high fields in EPI. Balanced SSFP fMRI can potentially be used to mitigate these limitations. In this study, we proposed and examined a new fMRI approach that was based on the bSSFP fMRI in combination with intravascular susceptibility contrast agent MION. Visual stimulation of rodent brains was examined and results were compared with conventional SE-EPI and GE-EPI fMRI.

MATERIALS AND METHODS

Animal Preparation: Adult Sprague-Dawley rats (220~250g, 3 months, N=8) were anaesthetized with isoflurane (3% induction, 1.5% for surgery, and 1% maintenance) and the left femoral vein was cannulated for injecting 15 mg Fe/kg of monocrystalline iron oxide nanocolloid (MION). In Group 1 (N=5), an optical fiber connected to a LED was placed at 5 mm in front of the left eye and the LED was flashed at 1 Hz with a duty cycle of 0.05. Stimuli were synchronized with the scanner using LabVIEW. A standard block-design paradigm of 40s of rest followed by stimulation for 20s repeated for 4 blocks was employed. Animals from Group 2 (N=3) were subjected to 5% CO_2 hypercapnia challenge with 2-min baseline followed by 4-min gas condition and 4-min recovery. All animals were allowed to rest for ~10 minutes between stimulation sets, and 2~4 sets of data were recorded from each rat. ***MRI Protocols:*** All MRI experiments were conducted using a 7 T Bruker scanner with a surface coil. Prior to fMRI scans, FieldMap was employed to perform localized shimming. The bSSFP images were acquired with TR/TE=3.8/1.9 ms, 1 coronal slice with FOV=3.2x3.2cm^2, matrix=64x64, averaging = 4 (temporal resolution=1s).The flip angle was set to create a maximally flat pass-band region in the bSSFP profile (α=18^o). For comparison, post-MION single-shot SE-EPI fMRI with TR/TE=1000/21ms and GE-EPI fMRI with TR/TE=1000/18ms, flip angle=30^o were also performed in one rat in Group 1 with the same slice orientation and stimulation paradigm as the bSSFP fMRI. ***Data Analysis:*** The first 5 images of bSSFP and EPI images were discarded to eliminate non-equilibrium effects. All fMRI data was co-registered, detrended and temporally filtered. Cross-correlation analysis was performed using the STIMULATE software with a correlation threshold of 0.35 and a cluster of 2 pixels.

RESULTS AND DISCUSSION

As shown in Fig.1 left column, the strong distortions seen in EPI images were absent in bSSFP images, which exhibited better conformity to the anatomical T2W image. At 15 mg/kg of MION, the signal in blood vessels was dramatically reduced due to MION T2-shortening effect [6], but the surrounding tissue was not as strongly affected and heavily distorted in bSSFP data as in EPI images. During unilateral flashing stimulation, activations in contralateral superior colliculus (SC) and bilateral visual cortices were observed by all three techniques. However, activation patterns in EPI results were displaced to varying extents due to the image distortion, which could affect the fMRI interpretation and was difficult to correct by most co-registration techniques. Single-voxel time profiles indicated that bSSFP also had robust CBV-weighted signal changes whose percentage amplitude changes were larger than SE-EPI and smaller than GE-EPI (Fig.1, right column). Fig.2 (left) showed that distortion-free bSSFP result yielded better agreement between the activation patterns and known brain structures. For example, the cortical activation in binocular area (V1B) was more lateral than in monocular area (V1M), which was consistent with the atlas but not observed in GE- or SE-EPI, especially for the ipsilateral V1B (more medial in EPI images, Fig.1 left). Average time series from both the single voxel and activated regions showed robust activations in all Group 1 animals with small SDs (Fig.2, middle & right). Although both tissue T1 & T2 were shortened after MION injection, T2 changes were found to dominate the bSSFP signal changes (data not shown). Thus the post-MION regional bSSFP changes upon stimulation were mainly sensitized to the functional CBV changes. The strong negative signal changes from cortical and subcortical regions observed in Group 2 hypercapnia experiments (Fig.3) further confirmed the CBV-weighted functional contrast in post-MION bSSFP fMRI [7]. In conclusion, bSSFP fMRI with intravascular susceptibility contrast agent produces distortion-free data with robust CBV-weighted functional signal changes. This approach can be readily adopted for 3D fMRI by using 3D bSSFP [8] and is particularly suited for high-resolution high-fidelity fMRI study of animal models at high fields.

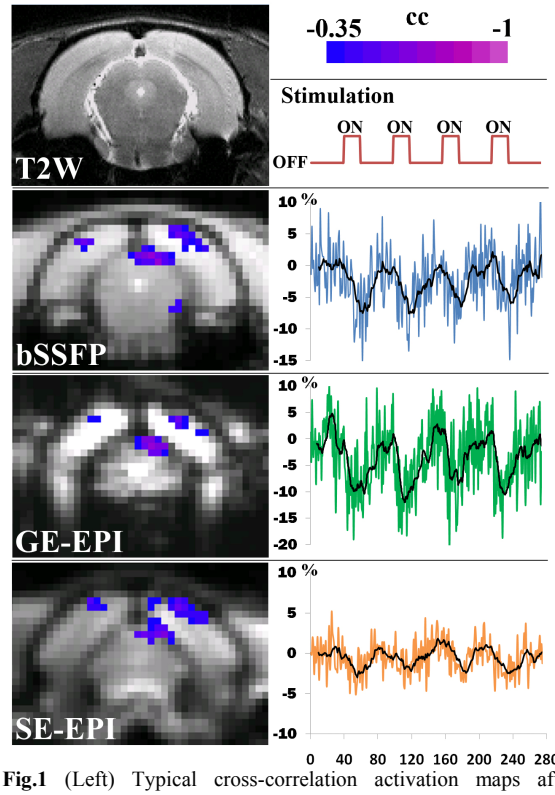

Fig.1 (Left) Typical cross-correlation activation maps after unilateral visual stimulation overlaid on post-MION bSSFP, GE-EPI and SE-EPI images at Bregma -7.2mm. (Right) Raw (colored) and low-pass filtered (black) time profiles collected from the most activated pixels (highest cc value) in superior colliculus.

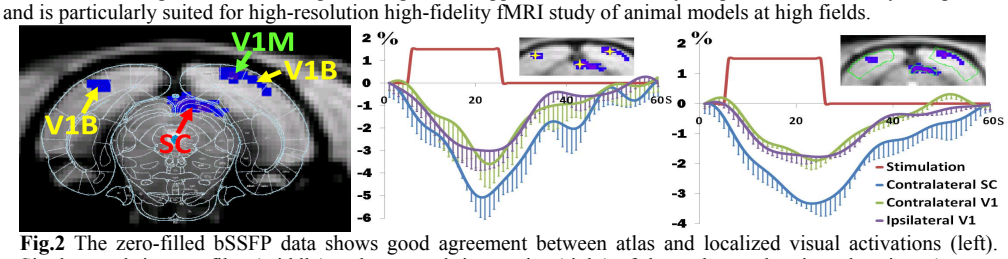

Fig.2 The zero-filled bSSFP data shows good agreement between atlas and localized visual activations (left). Single voxel time profiles (middle) and averaged time series (right) of three clustered activated regions (contra-SC, contra-V1 and ipsi-V1 shown in small inserts) are plotted by averaging all Group 1 animal datasets.

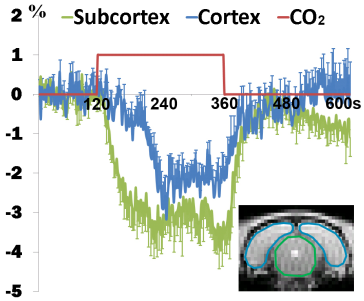

Fig.3 Average bSSFP time series from cortical and subcortical regions during hypercapnia in Group 2.

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