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Enhancement of temporal resolution and BOLD sensitivity in real-time fMRI using multi-slab echo-volumar imaging

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ABSTRACT

In this study, a new approach to high-speed fMRI using multi-slab echo-volumar imaging (EVI) is developed that minimizes geometrical image distortion and spatial blurring, and enables nonaliased sampling of physiological signal fluctuation to increase BOLD sensitivity compared to conventional echo-planar imaging (EPI). Real-time fMRI using whole brain 4-slab EVI with 286 ms temporal resolution (4 mm isotropic voxel size) and partial brain 2-slab EVI with 136 ms temporal resolution ($4\times4\times6$ mm^3 voxel size) was performed on a clinical 3 Tesla MRI scanner equipped with 12-channel head coil. Four-slab EVI of visual and motor tasks significantly increased mean (visual: 96%, motor: 66%) and maximum t-score (visual: 263%, motor: 124%) and mean (visual: 59%, motor: 131%) and maximum (visual: 29%, motor: 67%) BOLD signal amplitude compared with EPI. Time domain moving average filtering (2 s width) to suppress physiological noise from cardiac and respiratory fluctuations further improved mean (visual: 196%, motor: 140%) and maximum (visual: 384%, motor: 200%) t-scores and increased extents of activation (visual: 73%, motor: 70%) compared to EPI. Similar sensitivity enhancement, which is attributed to high sampling rate at only moderately reduced temporal signal-to-noise ratio (mean: −52%) and longer sampling of the BOLD effect in the echo-time domain compared to EPI, was measured in auditory cortex. Two-slab EVI further improved temporal resolution for measuring task-related activation and enabled mapping of five major resting state networks (RSNs) in individual subjects in 5 min scans. The bilateral sensorimotor, the default mode and the occipital RSNs were detectable in time frames as short as 75 s. In conclusion, the high sampling rate of real-time multi-slab EVI significantly improves sensitivity for studying the temporal dynamics of hemodynamic responses and for characterizing functional networks at high field strength in short measurement times.

Introduction

Echo-planar imaging (EPI) using blood oxygenation level-dependent (BOLD) contrast is widely used for functional magnetic resonance imaging (fMRI) in neuroscience and clinical research applications. Although EPI is capable of sampling the time course of the hemodynamic response with a standard temporal resolution of 2–3 s for whole brain mapping and with correspondingly faster temporal resolution for partial brain coverage, there is increased interest in achieving order of magnitude faster sampling rates for whole brain mapping to resolve heartbeat-related physiological signal fluctuation to increase sensitivity in event-related fMRI, to reduce sensitivity to intra-scan head movement and to measure regional onset differences of the hemodynamic responses without resorting to jittering the task paradigm. Recent developments of high-speed fMRI include single-shot echo-volumar imaging (EVI) (Rabrait et al., 2008; van der Zwaag et al., 2006; Witzel et al., 2008), Inverse Imaging (InI) (Lin et al., 2006, 2008, 2010), highly undersampled projection imaging (PI) (Grotz et al., 2009) and more recently multiplexed EPI (Feinberg et al., 2010) and fast volumetric imaging based on single-shot 3D rosette trajectories (Zahneisen et al., 2011), all of which enable temporal resolution on the

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order of 100 ms or less. A recent study by Lin et al. using InI demonstrated considerable improvements in hemodynamic response estimation using a moving average filter to suppress physiological noise (Lin et al., 2011).

Echo-volumar imaging (EVI), one of the first 3D single-shot imaging techniques, was included in the first description of EPI and realized by Mansfield and colleagues a decade later (Mansfield and Maudsley, 1976; Mansfield et al., 1977, 1994). The method has been challenged by the inability of whole body gradient systems to encode 3D k-space sufficiently rapidly, resulting in geometrical image distortion, signal dropouts and spatially-varying blurring of the point spread function due to magnetic field inhomogeneity and transverse signal relaxation. Using the improved gradient performance afforded by a dedicated head gradient system Song et al. were able to demonstrate EVI with a $64\times32\times7$ matrix and 3.8 mm × 6.3 mm × 5 mm spatial resolution with a readout duration of 70 ms (Song et al., 1994). Using local excitation to achieve partial brain coverage Yang demonstrated a $64\times64\times10$ matrix with 3.75 mm × 5 mm × 5 mm voxel size (Yang et al., 1997). After this initial phase of feasibility studies in the 1990s using 1.5 T scanners there has been renewed interest in recent years. Van der Zwaag introduced an improved version of EVI using reduced field of view (FOV) encoding, outer volume suppression and a surface coil at 3 T (van der Zwaag et al., 2006). Integration of parallel imaging has led to considerable improvement in image quality as demonstrated in several recent studies (Rabrait et al., 2008; Witzel et al., 2008, 2011) and proof-of-concept at 7 Tesla (van der Zwaag et al., 2009). A variant of EVI using a square spiral with $14\times14\times14$ spatial matrix and 14 mm voxel dimensions enabled detection of the negative dip across the brain with 100 ms temporal resolution (Lindquist et al., 2008).

Although increasing the temporal resolution of fMRI is the principal goal, the increased efficiency (SNR per unit time) of 3D versus 2D encoding (Edelstein et al., 1986; Hu and Glover, 2007) makes EVI attractive. EVI is also considerably less sensitive to physiological noise than segmented 3D EPI methods (Poser et al., 2010), which are affected by signal fluctuations between segments that lead to ghosting and increase apparent physiological signal fluctuation. Despite the technical advances, the need for specialized hardware, persistent image quality constraints due to geometrical image distortion, blurring and signal drop outs that are exacerbated by head movement, and signal drifts due to gradient instability and steady-state effects remain considerable challenges for routine applications, in particular at high magnetic field strength. Practical applications of EVI are also hampered by time-consuming image reconstruction of large amounts of data generated by EVI, and real-time fMRI with EVI has yet to be demonstrated.

In this study we developed a new approach to whole brain EVI using multi-slab excitation and single-shot 3D encoding with GRAPPA partial parallel imaging (Griswold et al., 2002) within each slab to strongly reduce geometrical distortion and blurring while only moderately reducing temporal resolution compared to single-shot EVI. We demonstrate temporal resolution of 286 ms for whole brain acquisition (4 mm isotropic voxel size) and 136 ms for partial brain acquisition ($4\times4\times6$ mm^3 voxel size) on a conventional clinical 3 T scanner equipped with 12-channel head coil. Real-time image reconstruction was implemented using in-plane reconstruction with GRAPPA on the scanner and reconstruction in the 3rd spatial dimension on an external workstation enabling real-time fMRI analysis with time delays of less than 500 ms.

A central goal of this study was to compare BOLD sensitivity (mean and maximum percent signal change, mean and maximum t-score, extent of activation and temporal signal-to-noise ratio (tSNR)) of multi-slab EVI and conventional EPI across several tasks that engage functional brain networks in visual, auditory, motor and frontal cortex. A secondary goal was to quantify further improvement in BOLD sensitivity when applying a time domain filter that reduces physiological noise from cardiac and respiratory fluctuations (Lin et al., 2011) while maintaining an effective temporal resolution comparable to that of EPI. We also wanted to assess the feasibility of mapping major resting state networks (RSN) at 136 ms temporal resolution, as previous work has shown that the sensitivity of mapping RSNs improves with increased sampling rates compared to conventional EPI (Feinberg et al., 2010).

Materials and methods

Fifteen healthy subjects participated after giving institutionally reviewed informed consent. Data were collected on a clinical 3 T scanner, MAGNETOM Trio, A Tim System (Siemens Healthcare, Erlangen, Germany) equipped with MAGNETOM Avanto gradient system and 12-channel array receive-only head coil. Pulse and respiration waveforms were recorded with 20 ms temporal resolution. Reconstructed 2D images were exported from the scanner reconstruction computer via the scanner host computer to an external Intel Xeon E5530, 6 core, 2.4 GHz workstation for reconstruction of the 3rd spatial dimension and real-time fMRI analysis, which were integrated into the in-house developed TurboFIRE software (Posse et al., 2001).

Multi-slab EVI pulse sequence

The EVI pulse sequence, which was based on a multi-echo EPI (MEPI) sequence (Posse et al., 1999; Speck and Hennig, 1998) with flyback along the k_z-direction, is shown in Fig. 1. Multiple adjacent slabs were excited sequentially and encoded in a single TR using repeated EPI modules with interleaved phase encoding gradients. The EPI modules consisted of trapezoidal oscillating gradients (G_{RO}) along the readout direction and a series of blipped primary phase encoding gradients (G_{PE1}) that were rewound at the end of every partition. A blipped secondary phase encoding gradient (G_{PE2}) that encodes the third spatial dimension was applied after each EPI module. K_z-space was encoded symmetrically using a dephasing gradient before the first EPI module ($k_{max}/2$). The k_x–k_y space trajectories for each k_z step were traversed in the same direction using 4-fold acceleration for GRAPPA reconstruction (Griswold et al., 2002). Twenty-four GRAPPA auto-calibration signal (ACS) lines for in-plane GRAPPA reconstruction were acquired in a separate prescan using 4 interleaves.

Image distortion and BOLD contrast characteristics

Encoding of 8 slices per slab with 64×64 in-plane matrix was performed using 4-fold GRAPPA acceleration, 6/8 partial phase encoding, 2790 Hz/pixel readout bandwidth, trapezoidal readout gradients with ramp sampling and 4 mm in-plane resolution. The minimum effective TE of 28 ms for this readout corresponds to the TE routinely used with EPI sequences in our lab, which minimizes signal drop-out in the frontal lobe. The effective bandwidth per pixel in the slice direction and the in-plane phase encoding direction were 19 Hz/pixel and 149 Hz/pixel, respectively. The corresponding readout duration was 52 ms, which is approximately $1.3\times T_2^*$ in cortex and provides close to optimum BOLD sensitivity as shown in our previous studies of multi-echo EPI (Posse et al., 1999), while minimizing the degree of geometrical through-plane distortion in the frontal lobe.

Geometrical distortion was computed using Eq. (4) in (Jezzard and Balaban, 1995):

$$d_{pixel}(x,y,z) = \gamma \Delta B_0(x,y,z) T_{acq}, \quad (1)$$

where γ is the gyromagnetic ratio and T_{acq} is the sampling time. For a maximum magnetic field inhomogeneity of 0.6 ppm in the ventral prefrontal cortex, the calculated displacement was 3.9 pixels along