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Whole-head rapid fMRI acquisition using echo-shifted magnetic resonance inverse imaging

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ABSTRACT

The acquisition time of BOLD contrast functional MRI (fMRI) data with whole-brain coverage typically requires a sampling rate of one volume in 1–3 s. Although the volumetric sampling time of a few seconds is adequate for measuring the sluggish hemodynamic response (HDR) to neuronal activation, faster sampling of fMRI might allow for monitoring of rapid physiological fluctuations and detection of subtle neuronal activation timing information embedded in BOLD signals. Previous studies utilizing a highly accelerated volumetric MR inverse imaging (InI) technique have provided a sampling rate of one volume per 100 ms with 5 mm spatial resolution. Here, we propose a novel modification of this technique, the echo-shifted InI, which allows TE to be longer than TR, to measure BOLD fMRI at an even faster sampling rate of one volume per 25 ms with whole-brain coverage. Compared with conventional EPI, echo-shifted InI provided an 80-fold speedup with similar spatial resolution and less than 2-fold temporal SNR loss. The capability of echo-shifted InI to detect HDR timing differences was tested empirically. At the group level ($n = 6$), echo-spaced InI was able to detect statistically significant HDR timing differences of as low as 50 ms in visual stimulus presentation. At the level of individual subjects, significant differences in HDR timing were detected for 400 ms stimulus-onset differences. Our results also show that the temporal resolution of 25 ms is necessary for maintaining the temporal detecting capability at this level. With the capabilities of being able to distinguish the timing differences in the millisecond scale, echo-shifted InI could be a useful fMRI tool for obtaining temporal information at a time scale closer to that of neuronal dynamics.

Introduction

Volumetric acquisitions of whole-brain functional MRI (fMRI) (Belliveau et al., 1991) using the blood-oxygen-level-dependent (BOLD) contrast (Kwong et al., 1992; Ogawa et al., 1990) typically have a sampling rate of one volume per 1–3 s with about 3-mm spatial resolution, and this is used to observe the hemodynamic response (HDR) secondary to neuronal activity (Logothetis et al., 2001). While this sampling rate has been considered sufficient for monitoring the rather sluggish HDR, higher sampling rates might help reveal underlying neuronal dynamics and their behavioral correlates (Menon et al., 1998; Ogawa et al., 2000). The high sampling rate on BOLD fMRI could also help monitor and suppress rapid physiological fluctuations in fMRI time series and accordingly to improve the detection sensitivity to brain activity (Lin et al., 2012a; Särkkä et al., 2012).

The acquisition time of traditional Fourier-encoded MRI is constrained by the *k*-space traversal time. Echo-planar imaging (EPI) (Mansfield, 1977) and spiral imaging (Blum et al., 1987) utilize high gradient slew rates and strong high strength MRI gradients to achieve fast *k*-space traversal. The sampling rate for EPI could also be moderately improved by exploiting the symmetry in the *k*-space (McGibney et al., 1993). Parallel MRI using the spatial information among different channels of a receiving coil array can also help accelerate the data acquisition, using techniques such as *k*-space SMASH (Sodickson and Manning, 1997), or GRAPPA (Griswold et al., 2002) methods, or the image domain SENSE (Pruessmann et al., 1999) method. In fMRI, parallel MRI has been successfully combined with the gradient-echo EPI accelerated acquisitions (Preibisch et al., 2003; Schmidt et al., 2005). It has also been demonstrated that incorporating a static image as prior information can further improve the sensitivity of fMRI (Lin et al., 2005).

Other multi-slice-based approaches such as echo-shifted multi-slice EPI (Gibson et al., 2006), Multiplexed-EPI (M-EPI) (Feinberg et al., 2010) and blipped-CAIPI (Setsompop et al., 2012) can acquire one brain volume in 250–400 ms. Of these techniques, echo-shifted multi-slice EPI utilizes echo shifting with a multi-slice EPI readout, while M-EPI employs spatial multiplexing and multiband RF pulses to achieve the imaging acceleration. Blipped-CAIPI, in turn, introduces an inplane image shift in the phase encoding direction between the

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simultaneously acquired slices so that they can be separated easily without the voxel tilt problem. Moreover, high-speed echo-volumar image (EVI) integrated with parallel imaging could resolve the physiological signal fluctuation to increase the sensitivity in event-related fMRI (Posse et al., 2012; Witzel et al., 2008, 2011). Taken together, these achievements have led to modest improvements on the volumetric sampling rate of fMRI.

The attainable acceleration rate of parallel MRI depends on the spatially independent information among the receiving coils. Without reaching the theoretical bounds, increasing the number of channels in a receiver coil array could improve the spatiotemporal resolution of parallel MRI by providing well-posed inverse problems (Ohliger et al., 2003; Wiesinger et al., 2004). Magnetic resonance inverse imaging (InI) is a technique that uses the spatial information among channels of a receive coil array to solve a set of ill-posed inverse problems in order to achieve highly accelerated BOLD fMRI acquisitions (Lin et al., 2006, 2012b). InI is closely related to the MR-encephalography (Hennig et al., 2007). At 3 T with a 32-channel head coil array, InI has been shown to achieve a 10 Hz sampling rate and a spatial resolution of 5 mm with the whole brain coverage (Lin et al., 2008a, 2008b, 2010; Liou et al., 2011; Tsai et al., 2012). The 10-Hz volumetric sampling rate is already a considerable improvement on the sampling rate of traditional fMRI—particularly when combined with jittered event-related stimulation paradigms. However, a further increase in sampling rate would be still desired to study a much faster event-related brain activity.

In fMRI, the 10-Hz sampling rate of InI is limited by the echo time (TE) for the optimal sensitivity to the BOLD contrast (Menon et al., 1993). Using a 2 kHz/pixel readout bandwidth, a 64×64 image matrix, and TE = 30 ms at 3 T, the repetition time (TR) cannot be shorter than 60 ms when appropriate RF excitation and magnetization spoiling are taken into consideration. This is the natural consequence of steady-state incoherent pulse sequences, which require that the TR must be longer than TE. However, echo-shifted pulse sequences (Liu et al., 1993; Moonen et al., 1992) have allowed TR < TE. It has been previously reported that the echo-shifting technique can be combined with multi-slice EPI to achieve a TR of 250 ms with the whole-head coverage (Gibson et al., 2006). Our previous work has also utilized an echo-shifting pulse sequence to achieve TR = 20 ms in single-slice 2D fMRI experiments (Lin et al., 2006). Nevertheless, using single-slice fast imaging approach was challenging because the activation sites need to be figured out *a priori*.

Here, we incorporated the echo-shifting technique with volumetric InI in order to achieve a 40 Hz sampling rate (TR = 25 ms) with the whole head-coverage and about 5 mm of spatial resolution in the cortex without shortening the TE in order to maintain high BOLD signal sensitivity in fMRI experiments. Specifically, our approach utilizes the slice selection gradient, phase encoding gradient, and frequency encoding gradient to manipulate the transverse magnetization and shift the TE by one TR to achieve TR = 25 ms and TE = 33.2 ms. We analyzed the effect of flip angle of the echo-shifted InI theoretically and empirically. In addition, we evaluated the temporal signal-to-noise ratio (tSNR) (Parrish et al., 2000) of echo-shifted InI and compared the tSNR with that of a conventional EPI acquisition.

To test the capability of echo-shifted InI on differentiating the HDR timing at tens of millisecond time scale, we applied the echo-shifted InI in a visual fMRI experiment where the onset time of the visual stimuli was shifted at 50 ms or 400 ms. Knowing that interregional vascular differences may confound BOLD timing information, our study focused on the HDR timing differences within the same region. It is also noteworthy that our ultimate goal of making the fMRI as rapid as possible may benefit certain applications beyond detecting interregional neuronal delays, such as dynamic functional connectivity analysis (Lee et al., 2012). However, this is beyond the scope of our study. The hypothesis was that if the stimulus onset latency was delayed by tens of milliseconds, the corresponding delay of a hemodynamic response could be detected using echo-shifted InI. Here, we examined this hypothesis at individual and group levels, respectively.

Theory

Pulse sequence of echo-shifted InI

Fig. 1 shows the pulse sequence diagram describing the echo-shifted InI pulse sequence to shift the TE by one TR. The gray lobes indicate the components that are used specifically to implement the echo shifting. The timing diagram is otherwise similar to a conventional single-slice 2D EPI acquisition used in applications requiring whole-brain coverage. The echo shifting gradient lobes in slice-selection, phase-encoding, and frequency-encoding directions immediately dephase the transverse magnetization so that there is no refocused magnetization in the first TR after RF excitation. After the readout, the gradient lobes with the opposite polarity—but twice the moments—dephase the transverse magnetization in the opposite direction. The echo-shifting gradient lobes in the next TR interval then refocused the transverse magnetization into a gradient echo. Taken together, the transverse magnetization excited by the RF pulse is refocused at time TR + TE after the initial excitation, which is the effective TE in echo-shifted InI.

Signal formation of echo-shifted InI

Here we derived the theoretical echo-shifted InI signal to facilitate the subsequent flip angle analysis. An echo-shifting sequence built up a coherent steady state for the transverse magnetization with the periodicity of nTR, where n denoted the number of repetitions. In our study the $n = 1$. According to previous studies (Chung and Duerk, 1999), the transverse magnetization in an echo shifting pulse sequence at time instant TE was

$$M_{xy}(TE) = \frac{M_0(1-E_1)\sin\alpha}{p} E_2(TE)\cdot\left(\frac{q}{2p}\right),$$

where

$$E_1 = E_1(t)|_{t=TR} = e^{-TR/T1}, E_2 = E_2(t)|_{t=TR} = e^{-TR/T2*}, \quad (1)$$
$$p = 1-E_1\cos\alpha-E_2^2(E_1-\cos\alpha), q = E_2(1-E_1)(1+\cos\alpha).$$

Here M_0 denotes the longitudinal magnetization in the equilibrium and α is the flip angle. Eq. (1) allowed us to check the consistency and the discrepancy between the theoretical and the measured echo-shifted InI signals at different flip angles.

Materials and methods

Participants

Eight healthy participants, with normal or corrected-to-normal vision, were recruited for this study. Two of them were excluded due to the significant head movement during experiments. Informed consent for these experiments was obtained from each participant in accordance with the experimental protocol approved by the Massachusetts General Hospital Institutional Review Board.

Task

Fig. 2 illustrates the paradigm design in the visual fMRI experiment. Subjects were instructed to maintain fixation at the center of a screen while viewing a high-contrast visual checkerboard contrast-reversing at 8 Hz. The checkerboard subtended 20° of visual angle and was