Fast functional signal observed by diffusion-weighted fMRI

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Abstract

BOLD contrast fMRI has become the dominant method to study brain function. However, hemodynamic modulations on its signal often lead to spatial dispersions and temporal delays. It is thus of high interest to investigate alternative contrast mechanism that may offer improved spatiotemporal characteristics. We have found that by using heavy diffusion weighting to remove the vascular signal and enhance the effect of minute and incoherent spatial displacement induced by neuronal current, fast negative signal changes synchronized to the task can be detected. This finding may help take an initial step toward direct MRI detection of the neuronal activity.

Introduction

It has been routine practice for methods such as electroencephelography (EEG) or magnetoencephelography (MEG) to directly detect task-induced electrical and magnetic field changes. These methods offer high temporal resolution as the neuronal events occur, although suffer from limited ability in accurate spatial localization due to the well-known inverse problem. The possibility of using MRI to detect these effects could be the ultimate solution for achieving accurate functional localization both spatially and temporally. However, due to extremely small signal changes, the utility of MRI to directly detect these activities remains limited. Only recently have several reports demonstrated in phantoms that it is possible to directly detect minute electrical activity with MRI[1,2]. Among these methods, the Lorentz effect imaging may allow larger effects using gradient-based displacement-encoding scheme, as it could detect the destructive phase addition, and hence signal losses, caused by the electrical activity-induced incoherent displacements within a large magnetic field (due to Lorentz force). Since the incoherent phase changes ϕ can be amplified by the externally applied gradients ($\phi = \int_0^T \gamma \cdot G \cdot \Delta x \cdot dt$ where G is the amplitude of the external gradient, Δx the spatial displacement, T the duration of the gradient pulse), it is readily seen that the sensitivity of the signal detection can be high by using large G and T. Therefore, this method may be suited for directly studying minute neuronal electrical activities *in vivo* that are spatially inhomogeneous[3]. Our present study used heavy diffusion-weighted acquisition, which has a strong effect of displacement encoding and removes vascular contribution, to study functional signal changes of non-vascular origin.

Methods

Experiments using heavy diffusion weighting strategies were carried out on a GE (Milwaukee, Wisconsin) 4T whole-body MRI scanner. Normal healthy subjects were recruited under written consent approved by the Institutional Review Board of Duke University. Time-course images were collected from these subjects during visual stimulation using a flashing checkerboard stimulus. The first run was collected with a spin-echo spiral imaging sequence without diffusion weighting, thus generating the BOLD contrast. The subsequent four runs were acquired with a diffusion weighted spin-echo spiral imaging technique, with a b factor of 1980 s/mm^2 that corresponds to G = 31 mT/m and T = 50 ms for diffusion weighting gradients placed symmetrically around the 180^o refocusing pulse. These four runs were then averaged to gain statistical power. Functional volumes (containing 5 slices) were collected with a 1 s repetition time, 70 ms echo time, and a field-of-view of 24 cm with in-plane resolution of 3.75 mm^2. A total of 210 images per run were collected that consisted of seven on/off cycles, with each cycle of 30s duration. An additional set of co-planar high-resolution T1 weighted images through the visual cortex was also acquired to serve as the anatomical reference.

Results and Discussion

The diffusion weighted time-course images show prominent negative signal changes (-4.6 < z < -2.2), contrary to the conventional BOLD time-course images that are dominated by positive activations. Fig. 1(a) shows representative slice in two subjects with visual cortex activations to demonstrate such an effect. The time courses were averaged within all the respective regions of activation and are shown in Fig. 1(b). Compared with the well-studied BOLD signal changes (shown on top), the negative activation in the diffusion weighted images also showed consistent synchronization to the task. More importantly, its time course shows much faster onset (1~2s) relative to the BOLD signal (3~6 s). This rapid transition seen in the negative activation of the diffusion-weighted images could not have been caused by the vascular activity, since the hemodynamic modulation would lead to an otherwise much slower transition. Also, with the amount of diffusion weighting used in this study, there would be virtually no vascular signal present. A possible mechanism for this quick negative signal change may be related to the so-called "initial dip" observed at the onset of the stimulus, extending into the parenchyma. However, such an effect is usually transient. Being not of vascular origin, these fast and sustained negative activities provide a signal contrast that arises from an alternative mechanism of improved temporal characteristics. Although it remains difficult to determine the exact mechanism for the observed signal, its potential cause is discussed in this report.

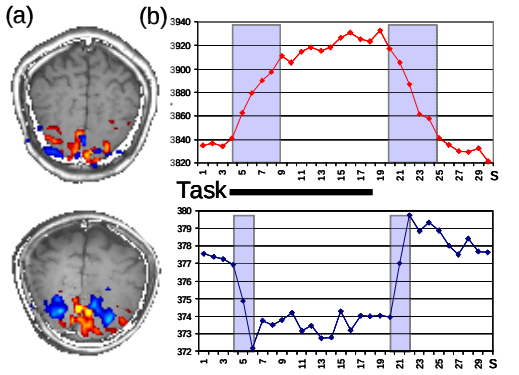

Fig. 1 (a) Representative slices from two subjects with both the positive BOLD activation and fast negative activation, (b) Averaged time course from the activated regions, respectively.

Among possible signal mechanisms for the rapid negative signal change, direct Lorentz effect due to the neuronal electrical activities remains to be a plausible contributing cause. As demonstrated in a recent phantom study, it was shown that a single conductor carrying minute electrical activity in an elastic media would induce destructive phase accumulation as a result of the intra-voxel incoherent spatial displacement within strong magnetic field used in MRI imaging. Such incoherent phase addition would be amplified by the heavy diffusion weighting gradients and, in turn, result in detectable signal attenuation rate R governed by $R = \sqrt{2(1-\cos\phi)}/\phi$. With the diffusion weighting gradients used in this experiment (31 mT/m strength and 50 ms total duration), and assuming a system detectability of 1% signal change, the experimental setting would be sensitive to a displacement of 2.5 μm. Such a signal change is on the same order as what we detected in this report (Fig. 1b) However, the neuronal electrical activities *in vivo* are more complex in that they are not currents of a single direction, but rather are spatially inhomogeneous in terms of the intensity and direction. Such activities would, however, aggravate the spatial inhomogeneity and therefore still lead to incoherent phase accumulation resulting in signal losses. Thus, this mechanism could likely be a contributing cause to the negative signal changes with the quick onset shown in Fig. 1b.

Conclusion

By using heavy diffusion weighting, fast functional signal change consequent to the task-induced brain activation was revealed. Because of its intrinsic immunity to the vascular signal, the observed signal change, primarily a synchronized, fast reduction of the MR signal, suggests an alternative origin different from the common BOLD signal sources that are closely related to the brain vasculature. Although the exact signal mechanism is still under investigation, the characteristics of the signal changes suggest that it may be more directly linked to the neuronal activity temporally and spatially. Thus, this finding may provide possibly new insight to direct MRI detection of neuronal activity and achieve more precise temporal and spatial localization for fMRI.

References

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