Simultaneous Acquisition of Blood Volume, Blood Flow and Blood Oxygenation Information During Brain Activation

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Introduction

Functional MRI (fMRI) techniques based on BOLD (blood oxygenation level-dependent) and CBF (cerebral blood flow) (1,2) contrasts have been used extensively for mapping functional neuroanatomy. Recently, an fMRI technique based on cerebral blood volume (CBV) change or vascular space occupancy (VASO) contrast during brain activation was proposed (3). These MRI signals have different characteristics in terms of sensitivity and specificity in detecting brain activity. In general, BOLD imaging has higher sensitivity than ASL and CBV imaging, whereas ASL and VASO techniques provide better spatial localization by targeting signal changes more closely related to neuronal activity. Simultaneous detection of multiple fMRI signals may have a number of advantages, including efficient acquisition of multiple functional images and minimal temporal variations between the images. A combination of these complementary functional signals may offer a better understanding of the physiological and/or biophysical transduction mechanisms between neuronal activity, hemodynamics and MRI signals.

Methods

Simultaneous VASO, ASL and BOLD Acquisitions. Both VASO and ASL techniques use inversion recovery (IR) sequences. An IR sequence with multiple excitations may incorporate these two signals into a single-shot technique. For an IR sequence with two 90° excitations (Fig.1), the steady-state MR signal intensities acquired at inversion time TI_1 and TI_2 can be described as

$$S(TI_1) = M_0[1-2e^{-TI_1/T_1} + e^{-(TR+TI_1-TI_2)/T_1}]e^{-TE/T_2^*},\ S(TI_2) = M_0[1-e^{-(TI_2-TI_1)/T_1}]e^{-TE/T_2^*},$$

where M_0 is the magnetization at equilibrium, T_1 and T_2^* are the longitudinal relaxation time and effective transverse relaxation time, respectively, and TR and TE are repetition time and echo time, respectively. The blood signal nulling point is given as $TI_1(null) = T_1 \ln[2-e^{-(TR-TI_2)/T_1}]$.

Based upon the above analysis, an imaging scheme that performs concurrent acquisition of three hemodynamic images is illustrated in Fig.1. A VASO image was acquired at the blood nulling point (TI_1) for suppressing blood signal, and an ASL perfusion image was collected at a later time (TI_2) when labeled arterial spins had reached the capillary/tissue exchange sites. Two sequential gradient-echo images were acquired after the second excitation pulse, one with short TE for ASL imaging and the other with longer TE for BOLD imaging. The inversion pulse was interleaved with slab-selective or non-selective for obtaining perfusion contrast. A relatively thick slab (>100mm) is required for VASO imaging, because otherwise the inflow of non-inverted spins could confound the VASO signal. On the other hand, an extremely thick slab could reduce perfusion signal, due to reduced length of the labeled spin bolus. The slab thickness in this study was determined empirically to provide optimal quality for simultaneous VASO and ASL imaging.

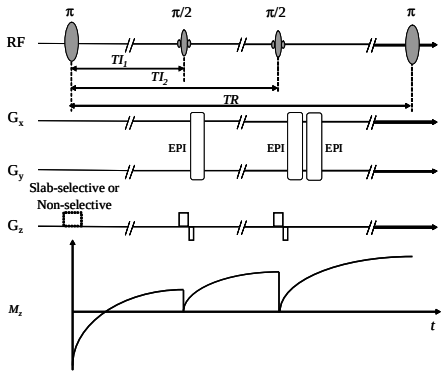

Fig.1 Schematic diagram of the pulse sequence that performs concurrent acquisition of three hemodynamic images and the corresponding longitudinal magnetization.

Functional MRI Experiments. Experiments were performed on healthy volunteers on a 3T Siemens Allegra scanner with a head volume coil. A single oblique axial slice (5mm in thickness) encompassing the primary visual cortex was chosen for functional imaging with a visual stimulation of 8-Hz black-white radial flashing checkerboard. Echo-planar imaging (EPI) was used with TE of 6.6ms for VASO image, 7.6 ms for ASL image and 27ms for BOLD image with partial (75%) k-space acquisition, and TR of 2000ms. An adiabatic inversion pulse combined with a slab selection gradient was used for alternating slab-selective and non-selective inversion. TI_1 (blood nulling point) was determined empirically by searching for minimal signal intensity of the sagittal sinus area in the inversion recovery sequence, and TI_2 was 1200 ms. During an inversion recovery cycle, three images sensitive to VASO, ASL perfusion and BOLD, respectively, were collected.

To determine the optimal inversion slab thickness, fMRI experiments with the visual stimulation were performed at different inversion thickness on 4 healthy volunteers. For each subject, 5 data sets with slab inversion thicknesses of 500, 150, 125, 100 and 50 mm, respectively, were collected. The feasibility and efficacy of the proposed sequence were evaluated by block-design fMRI experiments performed on 6 healthy volunteers. A visual stimulation paradigm that started with 24s "off" and followed by 5 cycles of 24s "on" / 24s "off" was used. Functional MRI experiment lasted 264s, during which 132 VASO, ASL perfusion and BOLD images were collected simultaneously. For comparison, individual VASO, ASL perfusion and BOLD images were acquired separately as well using conventional techniques, with the same stimulation paradigm and imaging parameters as close as possible. For perfusion quantification, apparent T_1 of the brain was measured by a set of inversion recovery experiments with TR of 10s, and inversion time of 0.03, 0.33, 0.63, 0.93, 1.23, 1.53, and 1.83s, respectively.

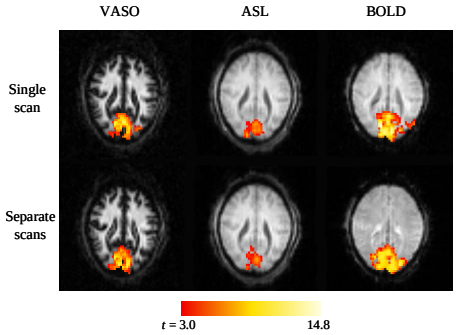

Fig.2 An example of VASO, ASL perfusion and BOLD functional maps acquired simultaneously (upper row) or separately (lower row), using a block-design visual stimulation paradigm.

Results and Discussions

The experiments to determine optimal inversion slab showed that a thickness in the range of 100-150 mm was the best for the simultaneous technique. Fig.2 illustrates simultaneously acquired (top) and sequentially acquired (bottom) VASO, ASL perfusion and BOLD activation maps with the block-design visual stimulation paradigm, from a single representative subject. As expected, while all three contrast mechanisms reflected neuronal activation within the primary visual cortex (V1), the highest contrast-to-noise ratio (CNR) was seen with BOLD, followed by VASO and then ASL. There was little qualitative difference between the combined single scan and the sequential scan acquisition methods for any of the three signals. Overall, since the proposed new technique took only 1/3 of the acquisition time but obtained similar activation maps compared to conventional techniques, a significant gain of CNR per unit time (approximately $\sqrt{3} = 1.73$) was achieved with this new technique. Perfusion maps obtained from the two techniques were also very similar. Quantitative analysis of the perfusion data showed that CBF values of gray and white matter in the brain were 66.4±8.2 and 25.2±4.3 (cc/100g/min), respectively, from data acquired simultaneously, and were 67.2±7.9 and 24.6±4.8 (cc/100g/min), respectively, from data acquired separately.

In summary, we have developed a novel imaging technique to acquire VASO, ASL and BOLD images simultaneously. Functional experiments showed that this technique can achieve significant improvement in CNR per unit time, compared to conventional techniques. With efficient measurement of three complementary functional signals associated with brain activation, this technique will provide a valuable tool to assist with data interpretation and functional transduction mechanisms.

References

[1] Ogawa et al, Magn Reson Med 1990;14:68-78. [2] Detre et al, Magn Reson Med 1992;23:37-45. [3] Lu et al, Magn Reson Med 2003;50:263-274.