T1ρ Functional Imaging Temporal Dynamics in the Human Visual Cortex

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Introduction

Brain pH has been shown to fluctuate as a result of brain activity. Many subsequent studies confirmed that local acidosis is a critical determinant of cerebrovascular tone [1, 2]. Recently, we have shown that it is possible to detect local acidosis evoked by neural activity in human brain using $T_{1\rho}$ imaging [3]. We hypothesized that pH-sensitive $T_{1\rho}$ may precede the BOLD and ASL response induced by neural activities since pH may drive the hemodynamic response. In order to investigate the temporal dynamics of $T_{1\rho}$, BOLD, and ASL, we used a phase-encoded visual stimulation, which induces traveling waves of neural activity in the visual cortex.

Methods

MR images of the brain were obtained on a 3.0T Siemens Trio scanner (Siemens Medical Solutions, Erlangen Germany). The eccentricity visual field map was simulated using expanding ring stimulation (50sec. for full expansion). BOLD imaging was performed by using a T_2^* weighted echo-planar gradient-echo sequence (TR/TE=2500/30ms, FOV=220x220mm, matrix size=64x64, 25 slices and slice thickness/gap=4/1mm). $T_{1\rho}$ images were collected by using an echo-planar spin-echo sequence (TR/TE=2500/14ms, FOV=220x220mm, matrix size=64x64, 15 slices and slice thickness/gap=4/1mm) with two spin-lock pulse (10 and 40ms) and B_1 frequency of 400Hz. Pulsed ASL (PICORE Q2T) images were collected by alternating between tag and control images (TR/TE=2500/15ms, TI1/TI2=700/1602ms, FOV=220x220mm, matrix size=64x64, 12 slices and slice thickness/gap=4/1mm). High-resolution anatomical T_1-weighted images were acquired using a 3D MP-RAGE sequence and the brain surface was reconstructed using Freesurfer. For ASL data, we calculated control-tag difference images using surround subtraction to reduce BOLD signal contamination. $T_{1\rho}$ relaxation times were calculated from the images with TSL of 10ms and 40ms, by voxel-wise fitting to mono-exponential decay. AFNI was used for pre-processing of the functional data including three dimensional motion correction, slice timing correction, and linear trend removal. In addition, time series of all functional data were high-pass filtered (cut off 0.02Hz for BOLD and $T_{1\rho}$, 0.04Hz for ASL) to remove low frequency drifts caused by subject motion and physiological noise. The phase maps were estimated taking the Fast Fourier Transform of the time series and calculating the phase at the frequency of the expanding ring. The phase data were smoothed with a Gaussian kernel of 6mm FWHM on surface. The functional images were co-registered with the anatomical T_1-weighted image and subsequently transferred onto the flattened occipital surface. To estimate the phase histogram, the $T_{1\rho}$ functional maps were thresholded to the visual cortex where a significant response ($p<0.05$, uncorrected) was found. The resulting ROI was used to mask the eccentricity map of all three functional imaging modalities: $T_{1\rho}$, ASL and BOLD.

Results

Fig 1 shows phase maps of BOLD, ASL, and $T_{1\rho}$ response to the expanding ring stimuli on the inflated (upper) and flattened (lower) cortical surface. The color scale indicates the raw phase values between 0 and 2π for eccentricity map. All eccentricity maps show a systematic increase in phase originating from the occipital pole towards more anterior regions. However, the phase lag for $T_{1\rho}$ was smaller than these for ASL and BOLD towards more anterior region, implying an earlier $T_{1\rho}$ response across the brain. The temporal dynamics presented in Fig 2 were calculated in a 2x2 pixels ROI within V1 shown in Fig 1. The same ROI region was selected for BOLD, ASL, and $T_{1\rho}$ imaging. The signal was normalized to ±1. The $T_{1\rho}$ signal (red) change appears to precede the ASL (blue) signal, followed by BOLD (black) signal. Fig 3 shows the averaged BOLD, ASL, and $T_{1\rho}$ time series for one period. Fig 4 shows histograms of the raw phase values for BOLD, ASL, and $T_{1\rho}$ eccentricity maps. The histogram indicates that $T_{1\rho}$ has relatively small phase values compared to ASL and BOLD.

Discussion and Conclusions

This study shows that $T_{1\rho}$ signal has a higher temporal resolution as compared to the hemodynamic response. This is further evidence that $T_{1\rho}$ signal is not sensitive to blood oxygenation or other blood factors. There are several potential explanations for the observed difference in phase lag. ASL signal is more closely associated with the capillary bed, but BOLD is caused by blood oxygenation and volume change in veins. This difference in the vascular sites contributing to the BOLD and ASL signal might be correlated with different hemodynamic time lag relative to each other. However, pH-sensitive $T_{1\rho}$ signal may precede the BOLD and ASL response because local acidosis evoked by the neural activity is a key factor in neurovascular coupling. Consequently, the ability to non-invasively measure pH dynamics in the human brain using $T_{1\rho}$ could provide a novel, more direct approach to map brain function.

References

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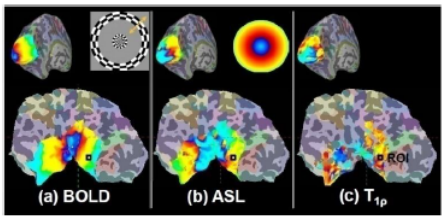

Fig. 1. Phase maps of BOLD (a), ASL (b), and $T_{1\rho}$ (c) on the inflated and flattened left hemisphere brain surface.

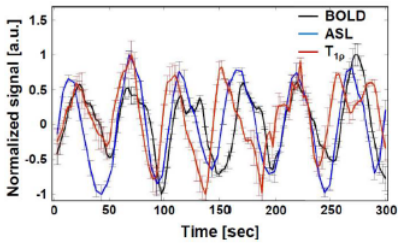

Fig. 2. BOLD, ASL, and $T_{1\rho}$ time series obtained in the ROI as shown in Fig. 1.

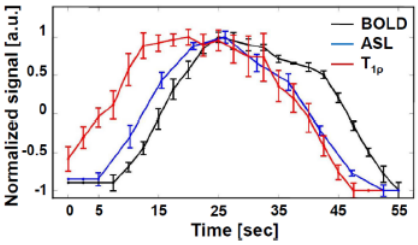

Fig. 3. Averaged BOLD, ASL, and $T_{1\rho}$ time series for one period from Fig 2.

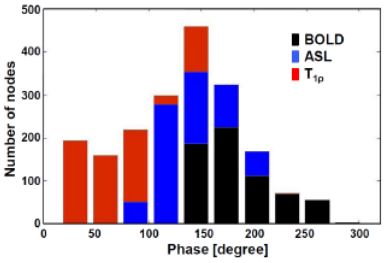

Fig. 4. Histograms of the raw phase value for BOLD, ASL, and $T_{1\rho}$ eccentricity maps.