Mapping resting-state functional connectivity by perfusion MRI

K-H. Chuang[1], P. van Gelderen[1], J. Bodurka[2], V. Ikonomidou[1], A. Koretsky[1], J. Duyn[1], S. Talagala[3]

[1]Laboratory of Functional and Molecular Imaging, NINDS, National Institutes of Health, Bethesda, MD, United States, [2]Functional MRI Facility, NIMH, National Institutes of Health, Bethesda, MD, United States, [3]NIH MRI Research Facility, NINDS, National Institutes of Health, Bethesda, MD, United States

Introduction

Resting-state, low frequency (< 0.08 Hz) fluctuation of BOLD signal has been shown to exhibit high correlation among functionally connected regions [1,2]. Though the underlying mechanism is unclear, observation of cerebral blood flow (CBF) fluctuations could provide further information on this phenomenon. However, until now, very few papers have reported detection of resting-state connectivity based on perfusion MRI [3,4]. The main challenges of using arterial spin labeling (ASL) perfusion MRI to detect this signal are low temporal resolution and low sensitivity and contamination of BOLD fluctuations. Use of close fitting receiver array coils can provide significant gains in ASL sensitivity [5,6]. This in turn allows increased temporal resolution via reduction of the labeling and post labeling delay times. Another issue is that, since ASL time series are modulated by perfusion as well as BOLD fluctuations, a processing strategy to isolate perfusion changes without the BOLD contribution is required [7]. In this work we demonstrate perfusion based functional connectivity using continuous ASL (CASL) with a neck labeling coil [8] and a 16 channel receiver coil array [9,10]. We also propose an analysis method to extract the CBF signal from ASL signal time-course without BOLD contamination.

Theory

The ASL signal time series with interleaved labeling RF power on/off can be formulated as

$$S(t) = M_z \cdot [1 - k \cdot F(t) \cdot \frac{1 + \cos(\pi \cdot t / TR)}{2}] \cdot e^{-[R_{20}^* + \Delta R_2^*(t)]TE},$$

where $F(t)$ is CBF; k is a function of labeling efficiency, T_1 and transit time, etc; R_{20}^* is the baseline transverse relaxation rate; and $\Delta R_2^*(t)$ is the BOLD fluctuation. Since signal changes due to CBF and BOLD fluctuations are both small and a short TE is used, the cross-term of CBF and BOLD can be neglected and this formula can be approximated as:

$$S(t) \propto 1 - \Delta R_2^*(t) \cdot TE - \frac{k}{2} \cdot F(t) - \frac{k}{2} \cdot F(t) \cdot \cos(\pi \cdot t / TR)$$

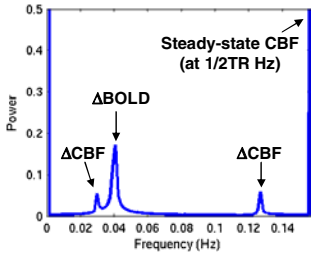

Fig 1. Spectrum of a simulated ASL signal assuming 30% ΔCBF at 0.03 Hz and 0.9% BOLD fluctuations at 0.04 Hz (TR=3.2s).

The first three terms, a mixture of BOLD and CBF, are in low frequency range, and the last term, which is steady state and fluctuating CBF modulated by the labeling on/off at 1/2TR Hz and is thus shifted to a higher frequency range. Fig 1 shows the spectrum of an ASL time-course assuming that CBF and BOLD fluctuations occur at discrete frequencies. In practice, fluctuations will occur at multiple frequencies. If TR is short enough to avoid overlapping of bandwidths of the low and high frequency components, CBF signal without BOLD contamination can be extracted from ASL signal by high-pass filtering and then restored to the proper low frequency range by demodulation.

Methods

Thirteen healthy subjects (5 males) with ages 22 to 56 years (mean = 34 years) were recruited. Informed consent was obtained from all subjects. The protocol was approved by the NINDS Institutional Review Board.

The subjects were instructed to close their eyes, lie still, and stay awake without performing any specific task. Two sets of data were acquired in two separate 10-min runs. During the first run, CASL images were acquired with interleaved control and label images. The second run was identical to the first but with no labeling RF power, and thus was sensitive to BOLD fluctuations only. Imaging was performed on a 3T General Electric Signa VH/3 MRI scanner interfaced with a custom-designed 16-channel system [9]. The neck labeling coil CASL setup [8] was used with a 16-channel receiver coil (Nova Medical Inc. Wakefield MA). The CASL and BOLD images were acquired using gradient-echo EPI with TR = 3.2 s, TE = 12.5 ms, and SENSE factor of 2. Seven axial slices with thickness of 3 mm (gap = 2 mm) covering the sensorimotor area were obtained with a 24x18-cm^2 FOV and a matrix size of 64x48. The labeling period for CASL was 2 s with a post labeling delay of 0.9 s. The respiratory and cardiac cycles were measured by a pressure belt and a pulse oximeter, respectively, and recorded by a PC.

Images were motion corrected by SPM2. CASL data were high-pass filtered (5th-order Chebyshev type I filter) at 0.08 Hz and demodulated to isolate the CBF signal. The same processing was applied to BOLD data (scan without labeling) to examine residual BOLD fluctuation in high frequency range. BOLD data were also processed with a very low cutoff (0.003Hz) high-pass filter to examine the traditional low-frequency BOLD fluctuations. Functional connectivity was detected by correlating each pixel in the filtered data with averaged time course of an ROI in the motor area.

Results

Fig 2a shows that the spectrum of the ASL data in a motor ROI contains prominent peaks at high frequency. These are attributed to CBF fluctuations modulated by labeling off/on function. No such peaks are observed at high frequency range in the BOLD data. Correlation maps of high-pass ASL data (Fig. 2b) show high correlation in the left/right sensorimotor areas across multiple slices. However, correlation is absent in the high-pass filtered BOLD data indicating that ASL connectivity maps are not contaminated by BOLD. Similar ASL connectivity maps with very good BOLD suppression were produced in 8 out of 13 subjects. ASL connectivity maps were found to be reproducible across multiple runs in the same session and corresponded well with maps produced by low-frequency BOLD fluctuations. Retrospective correction of respiration and cardiac pulsation effects did not alter the functional connectivity maps.

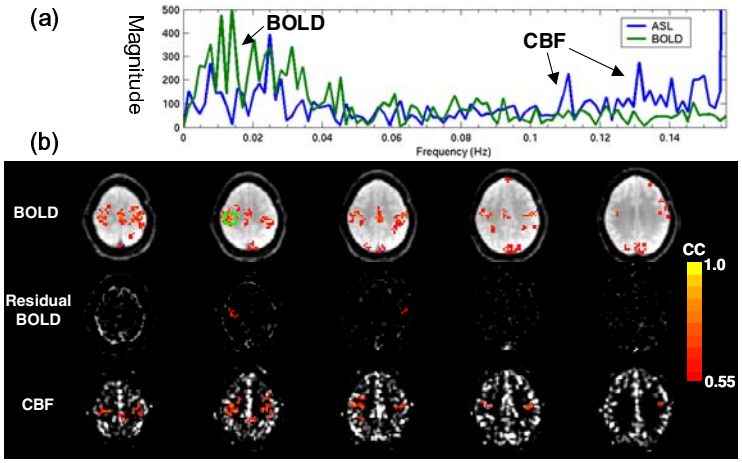

Fig 2. (a) Spectra of unfiltered BOLD and ASL signals from a motor ROI. (b) Resting state correlation maps of low-frequency BOLD (top), high-pass filtered BOLD (middle), and high-pass filtered ASL (bottom).

Conclusion

This study demonstrates that correlated CBF oscillations across different brain regions can be reliably identified at 3T by using CASL with a neck labeling coil and a 16 channel receiver coil. Though with long effective TR, physiological motions didn't affect the detection of functional connectivity. High-frequency filtering of the ASL signal allows CBF oscillations to be isolated without BOLD contamination in the majority of the subjects. This method of processing is consistent with sinc interpolation to reduce timing mismatch between control and label images [7], but has flexibility of choosing an optimal filter cutoff frequency to minimize BOLD. Combining these techniques with 3D imaging will allow CBF-based functional connectivity studies throughout the brain. This method can also be extended to higher fields.

Reference: [1] B Biswal et al, MRM 1995;34:537-41. [2] R Salvador et al, Cereb Cortex 2005;15:1332-42. [3] B Biswal et al, NMR Biomed 1997;10:165-70. [4] M Fukunaga et al, JCBFM 2005;25:S345. [5] SL Talagala et al, ISMRM 2004;12:717. [6] Z Wang et al, MRM 2005;54:732-7. [7] TT Liu et al, NeuroImage 2005;24:207-15. [8] SL Talagala et al, MRM 2004;52:131-40. [9] J Bodurka et al, MRM 2004;51:165-71. [10] JA de Zwart et al, MRM 2004;51:22-26.