# Static and dynamic characteristics of resting state CBF in newborn infants

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## Introduction

Functional connectivity in the brain during the resting state has been of great interest to those who study the developmental process of the default network. Resting-state activity in infants during sleep typically has been studied using BOLD fMRI [1]. However, BOLD signals derive from the combined influences of cerebral blood flow (CBF), cerebral blood volume, and oxygen metabolism. Perfusion imaging with arterial spin labeling (ASL) is an alternative method for studying resting-state connectivity because it can directly detect changes in CBF during neuronal activation. The use of fluctuations in CBF in studies of resting-state connectivity has been limited by its low sensitivity and possible contamination from BOLD signal fluctuations. We implemented the method using high-pass filtering and demodulation [2] to reduce the potential contamination from BOLD in analyzing CBF fluctuation in newborn brains during resting state.

## Materials and Methods

The experiment was performed on a GE Signa 3T HDx system with an 8-channel head coil. A Pulsed ASL (PASL) perfusion sequence was implemented using a proximal inversion with control for off-resonance effects (PICORE) quantitative imaging of perfusion using a single subtraction (QUIPSS II) sequence [3]. A single-shot gradient-echo EPI sequence was used for image acquisition, with time to QUIPSS saturation TI1 = 500 ms and inversion time of the first slice TI2 = 1100ms. Other acquisition parameters included: FOV 19 cm, 64 x 64 matrix, TE/TR =26/2300ms, flip angle 90°, slice thickness 5 mm, inter-slice spacing 0.5 mm. Seventeen slices were acquired sequentially from inferior to superior in the brain. Each ASL scan with 151 acquisitions and 5 dummies required 5 min 59 sec. A separate M0 scan using gradient-echo EPI with TR of 15s was acquired in order to quantify CBF. The PASL data was preprocessed for head motion correction and spatial smoothing with a 6-mm Gaussian kernel. We have scanned 7 healthy newborns (aged 17±8 days). The infants were scanned during sleep without sedation. The study was approved by the local IRB, and informed content was obtained from parents of the newborns.

## Results and Discussions

An average CBF map was used to evaluate the static characteristics of CBF. The static CBF map of each infant was divided by the global mean CBF of that infant, so that the CBF map was converted to relative CBF (Figure 1). In newborns, CBF is higher near the basal ganglia, temporal lobe, and posterior cingulate cortex (PCC). The dynamic characteristics of CBF were examined by analyzing the time course of the PASL data. The simplistic way to extract the CBF and BOLD time series is to take the difference of alternate scans for the perfusion [4], and to sum alternate scans to get the BOLD. First, we applied independent component analysis (ICA) to the BOLD time series to identify resting-state components (Figure 2). We then analyzed the time courses of BOLD and CBF in the ROIs selected in the resting state components. For example, we extracted the time course of BOLD and CBF in ROIs bilaterally within the temporal lobes (Figure 3). We also used a second method to extract the CBF fluctuations from the original PASL data set, with reduced contamination from BOLD [2]. The PASL data set was first high-pass filtered with a cutoff frequency of 1/4TR. Then the filtered time course was demodulated to low frequency by multiplying $\cos(\pi n)$ (n is the scan index) (Figure 4). This approach suppressed the BOLD contamination.

As an example, we selected the ROIs defined bilaterally in temporal cortex as reference ROIs. The time course of each voxel in the brain was correlated with the average time course with the reference ROIs. The correlation coefficient map was thresholded at correlation coefficient (CC) >0.5 with a cluster size of at least 5 voxels (Figure 4). This could be an indication of resting-state connectivity that is significantly correlated with BOLD fMRI. This demonstrates that the CBF fluctuation with reduced BOLD contamination can be extracted from the PASL signals and used for detecting functional connectivity in newborns.

**References:** [1]Fransson, et al, PNAS 2007;104:15531-15536. [2]Chuang KH, et al, NeuroImage 2008;40:1595-1605. [3]Wong EC, et al, MRM 1998;39: 702-708. [4] Lu H, et al, ISMRM 2005;13:35.

**Acknowledgements:** Supported by a grant from NIDA.

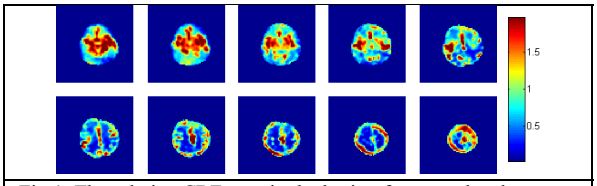


Fig 1. The relative CBF map in the brain of an unsedated, sleeping newborn infant. CBF appears highest in the basal ganglia, temporal lobe, and posterior cingulate cortex.

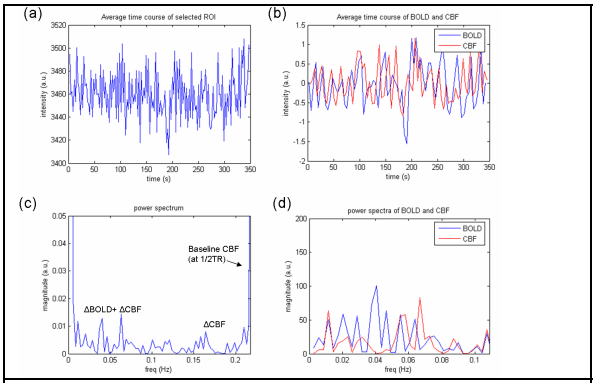


Fig 3. Time course (a) and power spectrum (b) of the PASL data of the bilateral temporal cortex ROIs. (c) The time course of BOLD is extracted from the control images; the time course of CBF is extracted from the pair-wise subtraction. A high-pass filter with a cutoff at 0.003Hz was applied to both. (d) shows the power spectra of the extracted time courses of BOLD and CBF.

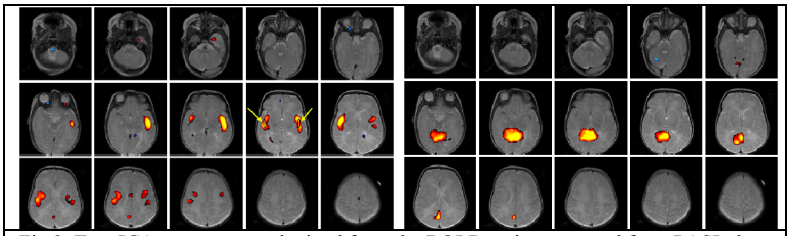

Fig 2. Two ICA components obtained from the BOLD series extracted from PASL data. (Left panel) connectivity in the temporal lobes; (right panel) connectivity in the PCC, potential physiological noise from cerebrospinal fluid. Arrows point to the reference ROIs selected in the temporal lobes.

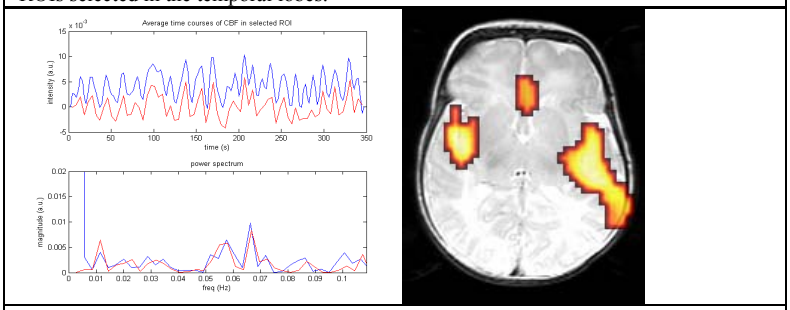


Fig 4. (Left) In the reference ROI, time course and power spectrum of CBF extracted from PASL data by using high-pass filter at cutoff frequency 1/4TR followed by de-modulation (blue line), as compared to those from CBF time series in Fig. 2 (red line). The former approach reduces the contamination from BOLD. (Right) It shows the regions in which the time course of CBF is highly correlated (CC>0.5) with that in the reference ROI.