

Assessment of Regional Rates of Change in CBF in Response to Changes in PaCO₂: A Combined ASL and Phase Contrast Study

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Introduction

Arterial blood flow to the brain is strongly modulated by arterial partial CO₂ pressure (PaCO₂) level. Therefore respiratory manipulation of PaCO₂ is an effective means for manipulation of CBF for clinical and for investigational purposes. Limited information, however, is available regarding how different regions in the brain response to global change in arterial blood flow. Invasive studies in adult patients during Sevoflurane anesthesia utilizing transcranial Doppler provide evidence for possible differences in the degree of auto regulation between the anterior and posterior circulation [1]. Development of a practical noninvasive protocol for assessment of regional cerebral blood flow response to global change in PaCO₂ may provide a quantitative and more direct means for assessing regional blood flow autoregulation and regional cerebral vulnerability. The proposed protocol utilizes whole brain Pulsed Arterial Spin Labeling (PASL) and phase contrast scans and is thus noninvasive. ASL is utilized in conjunction with 3D-T1W scan to assess mean CBF in selected anatomical regions, and phase contrast MRI (PCMR) measurements of total arterial inflow of tCBF are used to quantify the subject's response to change in PaCO₂. Therefore, this approach eliminates the need to directly measure PaCO₂, which requires blood test. Manipulation of the tCBF over a wide range is obtained by manipulating the end tidal pCO₂ level with the application of continuous positive airways pressure (CPAP).

Methods

Five healthy subjects (2M:3F, ages 24 to 39 years) underwent MRI scans using 3T (Verio, Siemens Healthcare), which included whole brain ASL and cine phase contrast repeated at 3 physiological states: rest, moderate (up to 6mmHg) and high (12 mmHg) continuous positive airway pressure. End tidal pCO₂ level ranged from 45 to 20 mmHg. CBF in a normal subject is reduced by approximately 3% per mmHg. Total cerebral blood flow (tCBF) from PCMR was obtained by summation of the arterial inflow through the two internal carotids and vertebral arteries [2]. The PCMRI imaging parameters were FOV of 14x14 cm, slice thickness of 6 mm, matrix of 256x192, flip angle of 20 degrees, minimum TR/TE of 10/4ms, and VENC of 70 cm/sec. Total cerebral blood flow from PASL was obtained by summation of the relative CBF values over the entire brain volume. A brain volume mask was obtained using the high resolution 3D T1-weighted MPRAGE data set which was then registered with the ASL volume. The masking of the non brain regions was obtained using the FSL-BET (Brain Extraction Tool) [3]. Registration of the HR T1W and ASL volumes was obtained through a rigid body transformation using FSL-FLIRT [4]. The PASL imaging parameters were FOV of 22x22 cm, slice thickness of 3 mm, acquisition matrix of 80x80, flip angle of 90 degrees, TR/TE 2500/11ms, T1/TI2 1500/600 ms, and 105 measurements resulting in total scan time of 5min. In addition to whole brain ASL derived total CBF, regional mean CBF (perfusion values in mL/min/100gm) were calculated separately for the following regions: cerebral GM and WM, thalamus, Palladium, hippocampus, putamen and the amygdala. The brain masks for the selected brain regions was obtained using the subcortical segmentation routine in FreeSurfer [5].

Results

Fig. 1 demonstrates the relationship between ASL-derived whole brain CBF and the PC and the value for the 3 states of CO₂ levels from all 5 subjects (each subject is shown in different colors). A strong linear correlation with R value of 0.94 demonstrates the reliability of PCMR based tCBF measurement as a surrogate measure for the change in PaCO₂. Regional CBF regulation is estimated by the slope of the mean regional ASL derived CBF vs. the global blood flow, i.e., tCBF. The steeper the slope the less is the degree of flow regulation. The mean slope for each of the brain regions are summarized in Table 1, and plots of rate of change of CBF as a function of global blood flow from 4 different brain regions are shown in Figure 2.

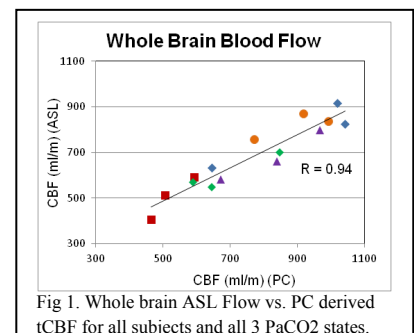


Fig 1. Whole brain ASL Flow vs. PC derived tCBF for all subjects and all 3 PaCO₂ states.

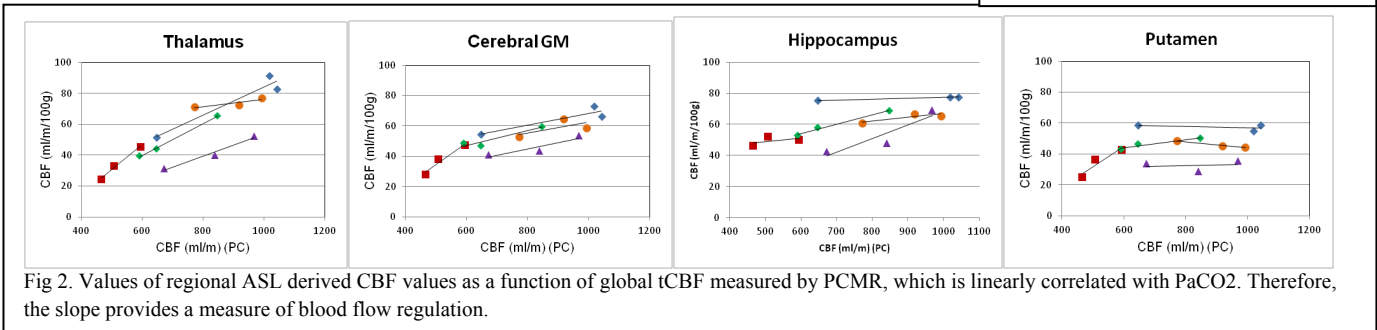


Fig 2. Values of regional ASL derived CBF values as a function of global tCBF measured by PCMR, which is linearly correlated with PaCO₂. Therefore, the slope provides a measure of blood flow regulation.

Conclusions

Large differences in CBF response to changes in PaCO₂ were found across different brain regions. For example, a significantly larger mean slope (0.075) was found for the thalamus compared with the putamen (0.023). This difference can be attributed to the fact that the thalamus is supplied by the vertebrobasilar arterial system which is part of posterior circulation, which has less sympathetic innervations compared with the anterior circulation. The putamen is supplied by branches of the middle cerebral arteries, which is part of the anterior blood supplies. The slopes in 4 of the 5 individuals demonstrate consistency within each brain region, while the fifth subject (red markers) has relatively larger slopes compared with the other subjects. The lesser blood flow regulation in this subject may be explained by the overall much lower tCBF values compared to the other subjects. These preliminary promising results warranted further validation in larger number of healthy subjects as well as in patients.

References

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Table 1. Mean regional CBF slope

Region	Mean Slope
Thalamus	0.075
Cerebral GM	0.051
Cerebral WM	0.034
Hippocampus	0.033
Putamen	0.023
Pallidum	0.008