Absolute CBF Quantification with PASL During Hyperoxia Corrected with the Simultaneous Measurement of the T_1 of Arterial Blood

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Introduction

A number of studies have used arterial spin labeling (ASL) approaches to investigate the regional cerebral blood flow (CBF) changes with hyperoxia (1-4). Although it is well-known that inhaled oxygen creates a significant reduction in the T_1 of arterial blood (T_{1a}) (5,6), and that T_{1a} has a substantial effect on CBF measurements using ASL (7), only a small number of these studies have incorporated T_{1a} changes in their CBF calculations (1,2). In these studies, the investigators either used the results of prior studies of T_{1a} during hyperoxia to estimate an average expected change in T_{1a} (2), or modeled the expected change in T_{1a} because the study was performed at 3T, where there is no literature data available on T_{1a} during hyperoxia (1). These approaches may be problematic for a number of reasons. First, the degree of hyperoxia may be different in a given experiment due to the gas delivery apparatus or interindividual variability in respiratory rate and other biological parameters, leading to significantly different values of T_{1a}. Second, the methods used in these particular studies (5,6) are themselves subject to a number of serious artifacts and may not be correct. Third, if different field strength is used, the longitudinal relaxivity of molecular oxygen in blood may be different. To the best of our knowledge, the in vivo measurement of T_{1a} during hyperoxia at 3T has not been reported in the literature, and no research article investigating the effect of hyperoxia on regional CBF using ASL has attempted to measure the change in T_{1a} that occurred during the experiment. In this study, our aim was to simultaneously measure CBF and T_{1a} *in vivo* during normoxia and hyperoxia. These data will allow for an accurate correction of CBF data due to reduction in T_{1a} on a per subject basis to quantify the degree to which the reduction in CBF measured with ASL is due to the reduction in T_{1a}.

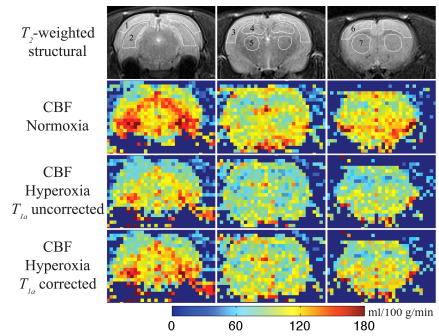

FIG.1. T_2-weighted structural images with ROIs (outlined in white) for analysis of regional CBF values (corresponding columns below), from a representative animal.

Materials and Methods

All images were collected on a whole-body clinical 3T MRI scanner (Siemens Trio; Siemens Healthcare, Erlangen, Germany) with a body coil transmitter and small (35 mm ID) receive-only surface coil passively decoupled during transmit. All data were obtained on adult male Sprague-Dawley rats (n=5; 430-470 g). Anesthesia was induced with 3% isoflurane in oxygen for approximately five minutes, and the animals were then maintained on1.5% isoflurane in 30% oxygen delivered at 1.5 L/min through a nose cone. For the hyperoxic challenge paradigm, after a five minute baseline period, gases were manually switched from 30% O2 to 100% O2 for ten minutes of hyperoxia, and then were switched back to 30% for a five minute baseline. This paradigm was repeated three times for each measurement of T_{1a} and CBF.

A pulsed ASL (PASL) approach, quantitative imaging of perfusion using a single subtraction with thin-slice TI_1 periodic saturation (Q2TIPS), based on proximal inversion with control for off-resonance (PICORE) tagging, was used in this study for regional quantification of CBF. A multi-shot fast spin echo sequence (FSE) was used for data acquisition. The imaging parameters were: TI_1 = 1200 ms, TI_{1S} = 1775 ms, TI_2 = 1800 ms, TE/TR = 6/4000 ms, slice thickness = 2 mm, slice gap = 2 mm, FOV = 40 × 40 mm, matrix size = 64 × 64. Control minus tag images were calculated according to the equation; $\mathbf{\Delta M = 2\,\alpha\,M_{0a}\,f\,TI_1\exp(-TI_2/T_{1a})}$, where α is the inversion efficiency, M_{0a} is the fully relaxed longitudinal magnetization of arterial blood, f is cerebral blood flow in ml blood/g tissue/min, and T_{1a} is the longitudinal relaxation time of arterial blood. Measurements of T_{1a} were performed using a technique employing a similar pulsed arterial spin labeling approach based on the work of Thomas, et al. (8) (pulse sequence presented in another submitted abstract).

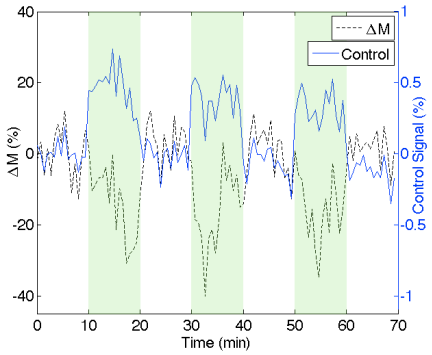

FIG. 2. Representative signal time course of ΔM (control minus tag) and control image signal intensity during normoxia (FiO2 = 0.3; white regions) and hyperoxia (FiO2 = 1.0; green regions).

Results

The measured values of T_{1a} during hyperoxia were found to decrease significantly compared to normoxia ($p < 0.01$). Mean T_{1a} decreased from 1.62 ± 0.06 s during normoxia to 1.50 ± 0.04 s during hyperoxia, which represents a decrease of 7.4%. An anatomic dataset from a representative animal is shown in Fig. 1, along with quantitative CBF maps during normoxia and hyperoxia, uncorrected and corrected for the measured change in T_{1a}. Reductions in CBF in a number of regions across the brain can be clearly visualized. Correcting for T_{1a} measured during hyperoxia reduced the degree of the differences between normoxia and hyperoxia, but reduced CBF values can still be visualized. Figure 2 demonstrates the degree of the CBF reduction during hyperoxia, and shows the time course of the average ΔM across all the ROIs during the hyperoxic challenges for a representative animal. The signal intensity of the control image was modulated by BOLD contrast. Table 1 shows that the CBF calculated in the hyperoxic condition corrected for T_{1a} exhibited a reduced, but still statistically significant change from the normoxic condition. The correction for the change in T_{1a} during hyperoxia accounted for approximately 47.5% of the overall decrease in the calculated CBF.

Table 1
Mean Calculated CBF Values from All ROIs During Normoxia (FiO_2 = 0.3) and Hyperoxia (FiO_2 = 1.0) with Correction for T_{1a} Changes

	CBF (ml/100 g/min)	% Difference
Normoxia	109.8 ± 13.4	—
Hyperoxia, uncorrected	92.0 ± 9.1**	-16.0 ± 2.6
Hyperoxia, corrected	100.4 ± 10.0*	-8.4 ± 2.9

* $P < 0.01$ from normoxia.
** $P < 0.001$ from normoxia.

Discussion

Simultaneous *in vivo* measurements of T_{1a} and CBF were performed using PASL approaches during normoxia and hyperoxia in rat brains at 3T. Baseline values of T_{1a} and CBF measured during normoxia show very close agreement with previous studies. Significant reductions in T_{1a} and CBF were measured during hyperoxia, also in agreement with previous studies. Although the effect of the correction of T_{1a} of the CBF data due to hyperoxia was substantial, it represented a smaller correction factor compared with previous studies (1,2).

References

(1) Bulte, et al. *JCBFM* (2007); (2) Zaharchuk, et al. *AJNR* (2008); (3) Sicard, et al. *JCBFM* (2003); (4) Lu, et al. *Neuroimage* (2009); (5) Tadamura, et al. *JMRI* (1997); (6) Noseworthy, et al. *JMRI* (1999); (7) Buxton, et al. *MRM* (2008); (8) Thomas, et al. *MRM* (2006)

Acknowledgements

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