Measuring Regional Blood Flow in the Rat Brain using Indirect ^{17}O Magnetic Resonance Imaging

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Introduction

Cerebral blood flow (CBF) has been estimated in the rat [1] and in the cat [2] using direct ^{17}O nuclear magnetic resonance spectroscopy. Here we demonstrate the feasibility of measuring regional blood flow in the rat brain using proton $T_{1\rho}$-dispersion magnetic resonance imaging [3] and the Kety-Schmidt approach [4]. We also quantify the in vivo sensitivity of our technique for proton detection of ^{17}O.

Methods and Materials

Animal Preparation

Two Female Sprague-Dawley rats (~150 g each) were anesthetized with Nembutol® (50 mg/kg) via IP injection. A catheter was inserted into the right external carotid artery towards the common carotid bifurcation so that a bolus could be delivered entirely into the blood stream going from the common carotid to the internal carotid artery. The animals were wrapped with an insulating pad to help maintain body temperature.

Imaging

The animals were placed in a specially designed head coil optimized for proton $T_{1\rho}$-dispersion imaging on a 4T GE-Signa Scanner. The coil was mounted on a motion-resistant platform and equipped with a head restraint system to minimize cardiac and respiratory pulsation artifacts. A spin-locking length (TSL) of 120 ms and high and low spin-locking frequencies of 1500 (ω_h) and 125 Hz (ω_l), respectively, were determined to be optimal (maximum $H_2{}^{17}O$ sensitivity and SNR=50) and used as sequence parameters. Five images were collected at 1500 Hz immediately before and after a series of images collected at 125 Hz. The total scan time was 10 s, and there was a 3 s delay between scans. The total volume of the catheter, fitting, and tubing (which extended to the outside of the magnet bore) was 0.2 ml. During the low frequency imaging series, 0.2 ml $H_2{}^{17}O$ (29 a%) was injected via the catheter over a period of 30 s. This was immediately followed by 0.5 ml of Heparinized (15 units/ml) saline injected over a period of 1 min. For control, 0.7 ml of Heparinized saline was injected at a similar rate.

Data Analysis

Mean pixel intensities (S) were determined for various ROIs in the images. The concentration of $H_2{}^{17}O$ (f) was computed based on the following equation derived in [3]:

$$f = \frac{\ln\left[S(\omega_h)/S(\omega_l)\right]}{TSL\left[R_{1\rho}(\omega_l) - R_{1\rho}(\omega_h)\right]}$$

The difference of the relaxivities (R) was estimated based on the natural abundance of ^{17}O (~14 mM in brain tissue). Blood flow was computed based on the following equation derived in [2]:

$$C_b(t) = C_b(0)e^{-\frac{Qt}{\lambda}}$$

where $C_b(t)$is the concentration of $H_2{}^{17}O$ in excess of natural abundance in brain tissue as a function of time, $C_b(0)$ is the peak concentration after bolus injection, λ is the brain/blood partition coefficient (0.90 ml/g [5]), and Q is blood flow.

Results and Discussion

The figure provides time courses for the $H_2{}^{17}O$ concentration for three ROIs (as shown) and for the control. Data from only one animal is shown. The control time course is independent of the ROI and is steady at 14 ±0.5 mM. The top panel of the figure provides images corresponding to the labeled time points on the graph.

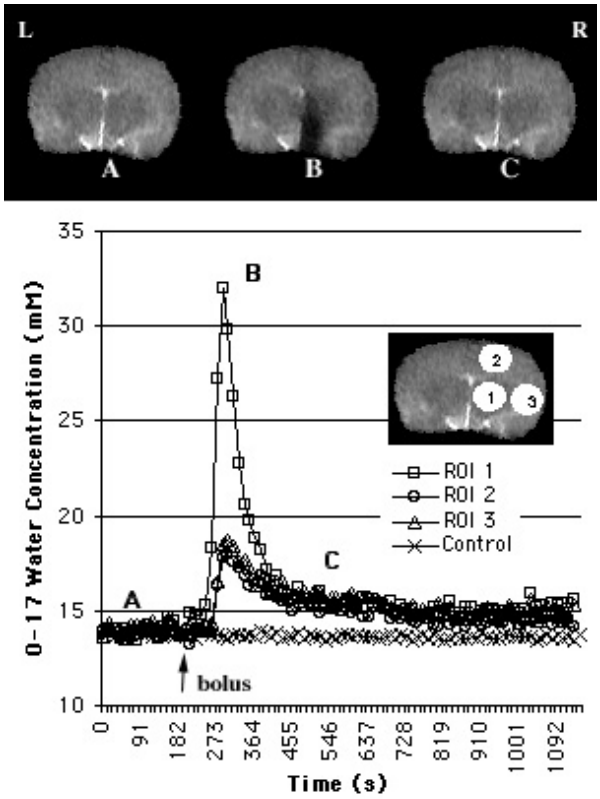

Figure 1

As predicted physiologically, the "wash-out" curves (i.e. the decay of $[H_2{}^{17}O]$ from the peak to equilibrium) fit well to an exponential: the correlation coefficients are 0.99, 0.91, and 0.89 for ROI 1, ROI 2, and ROI 3, respectively. The cerebral blood flow (CBF) in ROI 2 and ROI 3 is 0.37 and 0.36 ml/g/min, respectively. The blood flow in ROI 1 is 1.09 ml/g/min. The difference between natural abundance and the plateau after wash-out is a discernable 1-2 mM. Hence, 1-2 mM is the resolution of our indirect imaging technique for detecting ^{17}O in the rat brain.

In summary, we have demonstrated the utility of our technique for measuring regional blood flow and for monitoring small $[H_2{}^{17}O]$ changes in the rat brain. The former is a step closer towards high-resolution mapping of CBF and the latter may prove sufficient for detecting minute amounts of $H_2{}^{17}O$ generated metabolically from inhaled $^{17}O_2$ gas. Both are necessary for mapping cerebral metabolic rate of oxygen, which is critical for several important applications.

References

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