Estimating the Longitudinal Decay Time of 129Xe in Rat Brain after Perturbing Cerebral Blood Flow

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Introduction

Because xenon is a lipophilic anaesthetic that demonstrates large chemical shifts in solution, it is thought that hyperpolarised ^{129}Xe may prove to be a useful MR probe of brain physiology and function. For example, several groups have measured brain perfusion using ^{129}Xe (eg. [1-2]). To make these measurements it is necessary to uncouple the MR signal decay due to perfusion from that due to intrinsic longitudinal decay. In most previous work the value of T_1 in rat brain tissue has been assumed, as estimated from simulation work [3]. The value of T_1 in rat brain has been measured in homogenates to be 18 s at 9.4 T [4]. Also, T_1 has been measured to be 3.6 s *in vivo* using a method using an intra-carotid injection of hyperpolarized xenon mixed with a lipid emulsion [5]. However, a reliable non-invasive measurement has not been published. In this work the cerebral blood flow (CBF) of rat is manipulated to estimate the longitudinal decay time of ^{129}Xe in brain tissue.

Theory

According to a simple compartment model of xenon behaviour *in vivo* [2,6], the signal from the washout of xenon can be described by $S(t) = S(0) \exp(-t/\tau)$, where τ is the washout time. In this model the washout time is related to the longitudinal decay of tissue, T_1, and cerebral blood flow, F, through $1/\tau = 1/T_1 + F/\lambda$, where λ is the brain-blood partition coefficient for xenon. Moreover, CBF can be written as $F = x\ F_0$, where x denotes the relative CBF and F_0 is the baseline global blood flow of the brain.

Methods

Two male Sprague-Dawley rats weighing around 330 g were surgically prepared under halothane anaesthesia with tail artery and vein cannulation for blood gas sampling and drug administration. An endotracheal tube (8Fr, Atom multipurpose tube) was inserted into the trachea followed by a thinner tube (PE10) coaxially inserted so that hyperpolarized gas could be almost directly inhaled into the lungs from outside the magnet. After preparation the rats were set in the magnet and the anaesthesia was maintained with α-chloralose (20-40 mg/kg/h).

Hyperpolarized ^{129}Xe gas (enriched ^{129}Xe 80% + N_2 20%) with a polarisation of around 2-6% was produced in a homemade polariser.

MR measurements were performed on a 4.7 T Varian imaging spectrometer using a custom-made 3 cm surface coil dual-tuned to the proton and xenon resonances at 200.704 MHz and 55.52 MHz, respectively. Scout images and shimming were performed at the proton resonance at the beginning of each experiment. Spectra were acquired using a single hard-pulse sequence with a bandwidth of 30 kHz and the RF pulse centred at approximately 150 ppm from the gas peak.

A strict two-pulse measurement protocol was followed. A 25cc volume of hyperpolarized gas was smoothly injected into the lungs over a period of 40 seconds. Repeated acquisition determined that the washout phase began around 3-4 seconds after the injection finished. Hence, a single spectrum was acquired 4 seconds after the injection finished followed by another acquisition at a later time Δt. This procedure was repeatedly performed for a number of different inter-pulse delays (4-16 s).

After this protocol was performed for normal CBF, the rat was injected with acetazolamide (Diamox, 20 mg/kg) via the tail vein. After the injection CBF increased by 30 ± 3% within a time-span of 10 minutes and this was maintained for approximately 30-40 minutes, during which time the acquisition protocol was repeated to obtain the xenon washout at an elevated CBF.

CBF was monitored by a laser Doppler flowmetery (LDF) (OmegaFlow FLO-C, Omega Wave) probe positioned over the thinned skull 5 mm to the left of the bregma. While the absolute value of this measurement is not indicative of the global CBF, it does give an indication of the relative increase in blood flow following the Diamox injection. For this reason all calculations were performed with respect to relative blood flow.

Results

Concurrent work has shown that the only xenon resonance in rat brain occurs at 194.5 ppm [7]. Figure 1 plots the ratio of the peak heights versus Δt for all rats on a logarithmic scale. Fitting a straight line to the logarithmic data found that the washout during normal flow was 17.4 ± 0.8 s (Fig. 1a), and that during elevated CBF was 15.1 ± 0.5 s (Fig. 1b). This clearly shows that the washout time decreased with increased flow, consistent with behaviour predicted by the simple compartment model. From the calculated washout times and the relative increase in the CBF, the T_1 of brain tissue was estimated to be 37 ± 13 s and the global blood flow was 91 ± 30 ml blood/100 g brain/min (Fig. 2).

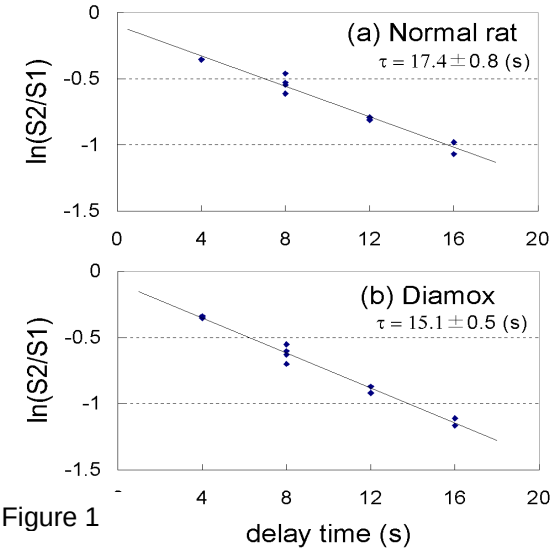

Figure 1

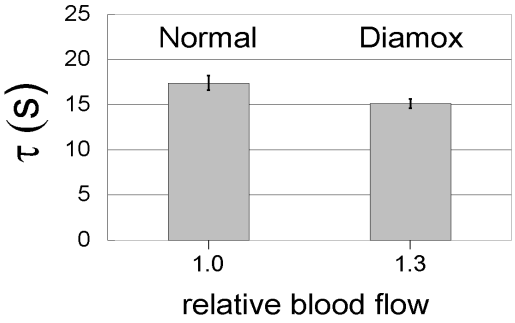

Figure 2

Discussion

The number of points with different blood flow is small and therefore the error in the T_1 estimate is relatively large. Current work is concentrating on a method to increase the number of points measured at different controlled blood flows.

References

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