Measuring the Venous Blood Volume and Oxygenation, and Changes on Activation using CPMG EPI T_2 Measurements

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Introduction

The aim of this study is to measure cortical venous blood volume (V) and oxygenation, and changes in these parameters on neuronal activation. The method is based on measuring the change blood oxygenation on activation using the echo-time and oxygenation dependence of blood T_2. Further if a measure of total oxygenation change in a vein draining the entire active region can be found, this can be used to calculate the total excess volume of oxygenated blood arriving from the activated region in response to activation, if the blood flow in the vein is known. Ultimately this could be used to measure the mean change in oxygen extraction fraction in an activated region of interest.

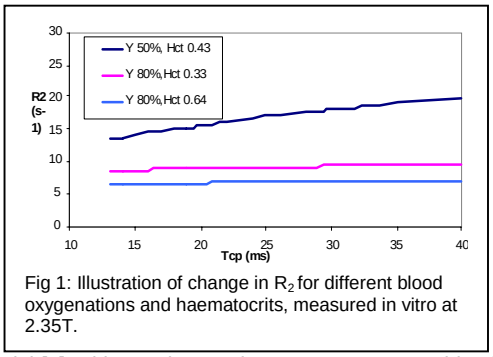

Fig 1: Illustration of change in R_2 for different blood oxygenations and haematocrits, measured in vitro at 2.35T.

Theory

In a CPMG sequence venous blood transverse relaxation rate R_2 depends on blood oxygenation level (Y), haematocrit and echo-spacing (τ_{cp}), due to exchange/diffusion between sites of different susceptibility in the erythrocytes and plasma (Fig 1). At short echo spacings the dephasing is limited and R_2 is measured close to its minimum absolute value, $R_{2,0}$. As echo spacing increases, exchange/diffusion contributions lead to an increase in apparent R_2. The Y dependence of R_2 can be described using the Luz-Meiboom exchange model [1]. This can be used to measure venous blood volume: if a voxel in the grey matter contains both venous blood and tissue (mixed tissue and arterial blood), then assuming slow exchange the measured relaxation rate is given by:

$$R_{2voxel}(\tau_{cp}) = (1-f)\, R_{2tissue} + f\, R_{2blood}(\tau_{cp})$$

where f is venous blood fraction. This also assumes that there is no significant effect of diffusion around the microvasculature, which is reasonable for the echo times used here [2]. By measuring $R_{2voxel}(\tau_{cp})$ and assuming a value of $R_{2tissue}$ equal to that of white matter which has a low blood volume (17.7 s^{-1} at 3.0 T), then this equation can be solved for f and $R_{2blood}(\tau_{cp})$ assuming the Luz Meiboom equation for R_{2blood} dependence on τ_{cp} (Fig 1), hence yielding a value of Y and f.

Furthermore, if a vein can be found that drains the entire activated region, and no other secondary activated regions, then the total excess volume of oxygenated blood arriving from the activated region in response to activation can be found. Let $\Delta Y(t)$ be the time course of change in blood oxygenation in the vein compared to baseline venous oxygenation, and v(t) be the velocity of blood flow in the vein. If A is the cross section area of the vein then $\Delta Y(t)Av(t)$, integrated over the period of the haemodynamic response gives the total change in volume of oxygenated blood from the region of interest. With measurements of perfusion in the activated region, this could be used to estimate the mean change in oxygen extraction fraction in the activated region.

Method

Three subjects were scanned according to local ethics committee procedures. An interleaved EPI, multi-echo CPMG pulse sequence, using paired hyperbolic secant 180^0 pulses for refocusing, was used to measure the τ_{cp} dependence of R_2 at 3.0 T. Interleaved EPI was used to reduce the minimum echo spacing. The repetition time was 8 s to allow complete signal recovery. R_2 values were obtained for τ_{cp} of 14, 19 and 24 ms. The paradigm consisted of 4 cycles of 80 s of visual stimulation (LED goggles flashing at 8 Hz) followed by 80 s of rest. The number of averages acquired at each τ_{cp} were optimised for signal to noise in the measurement of change in Y. This measurement time was 35 minutes. To measure the blood flow in the sagittal sinus with high temporal resolution a LLEPI-FAIR sequence [3] comprising ten 65^0 readout pulses separated by 100 ms was used. An identical visual stimulus presentation was used as for the CPMG sequence, and twenty LLEPI-FAIR sets were acquired during each rest and activation period. This measurement time was fifteen minutes.

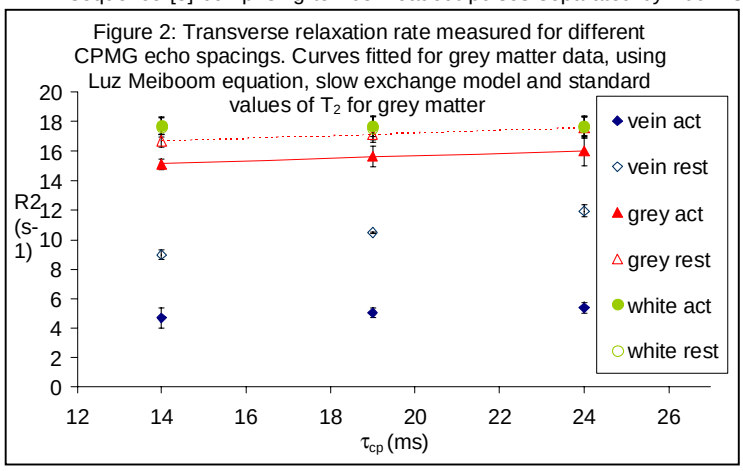

Figure 2: Transverse relaxation rate measured for different CPMG echo spacings. Curves fitted for grey matter data, using Luz Meiboom equation, slow exchange model and standard values of T_2 for grey matter

Analysis

Pixels displaying changes correlated to the stimulus paradigm were identified (p=0.001). ROIs were drawn in the sagittal sinus, activated grey matter and white matter, and R_2 values were calculated for each τ_{cp}, using a weighted linear least squares fit (Fig 2.). The grey matter data was fitted to the Luz Meiboom curves (using appropriate constants for 3T) to obtain Y and f. Flow rates were obtained from the LLEPI-FAIR data with a 2-parameter fit for flow and Mo, assuming T_{1blood} =1450ms. To calculate the total change in blood oxygenation in the activated region, the cross sectional area of the vein was estimated to be 7.8×10^{-5} m^2. Since the stimulus was 80 s long, it was assumed that the $\Delta Y(t)$ and v(t) waveforms followed a box car function for integration over stimulus duration.

Results

Fig. 2 shows the results of the CPMG study averaged over two subjects. (The third subject displayed a large degree of motion). The sagittal sinus region showed a large difference in R_2 between rest and activation and a large τ_{cp} dependency in the rest state. Conversely R_2 for white matter showed little change between rest and activation and a low dependency on τ_{cp} due to its low blood volume. Assuming $R_{2tissue} = R_{2white\_matter}$ the grey matter data was fitted for venous blood volume and blood oxygenation, and we measured Y_{act} = 0.44, V_{act} = 0.28 and Y_{rest} = 0.42, V_{rest} = 0.20. In the sagittal sinus draining the active region the mean change in Y was 0.34 and 0.38. The velocity of blood flow in the sagittal sinus averaged over 3 subjects was measured to be 8.3 +/- 0.3 cm/s with no significant change on activation. These results yield a mean total change in oxygenated blood volume of 1.8×10^{-5} litres.

Conclusions

The oxygenation change was small in the ROI, but much larger in draining vein, which is due to the fact that the vein concentrates the total change in Y across the whole region of interest. The assumption that $R_{2tissue}$ can be approximated by R_2 of white matter may underestimate the value of Y in grey matter, and overestimate the value of V, alternative methods of estimating the grey matter T_2 from multi-echo T_2 data will be investigated. The τ_{cp} dependence of R_2 for grey matter, and its dependence on rest or activation state has been demonstrated *in vivo* at 3.0 T. Using this dependency it has been possible to estimate the change in venous blood volume fraction and oxygenation in grey matter between rest and activation conditions.

References

1. Luz & Meiboom, 1963, J. Chem. Phys, 39, 366. *2. Boxerman et al, 1995, MRM, 34, 555.* *3. Francis et al,* Proc. 8th ISMRM,2000. *Funded by MRC*