An optimised respiratory paradigm for the Bayesian estimation of OEF by calibrated MRI

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Introduction

Estimation of the cerebral oxygen extraction fraction (OEF) using serial hypercapnic and hyperoxic stimuli has been proposed recently [1,2]. Here we expand upon this work to produce an optimised respiratory paradigm for the estimation of OEF; that is, a paradigm with the optimal number, timing and duration of hypercapnic and hyperoxic stimuli for a given acquisition time. Modelling results suggest that the proposed paradigm is able to offer a significant improvement in the accuracy of OEF estimates compared to previous experimental designs (as defined by the RMS error in simulated OEF estimates).

Methods

Pulsed ASL (QUIPSS II) datasets (each containing 1000 voxels) were simulated with echo times of 2.7 ms and 29 ms, with the acquisition scheme and echo times chosen to reflect our standard experimental protocol. ASL signal variations were calculated using the signal model described in [3]. BOLD signal variations were calculated using a multi-compartment model that accounts for contributions from one extravascular and three intravascular compartments, i.e. arterial, venous and capillary, as per [4]. Dynamic changes in signal amplitude were obtained by convolving step signal changes with a gamma-variate function. MR noise was modelled as per [5], and thus includes TE dependent and independent noise variance as well as TE dependent temporal autocorrelations. Additionally, low frequency baseline drifts were included from estimates made on dual-echo resting state data (12 subjects). The simulated MR time courses were analysed with a forward signal model, which simultaneously estimates all the model parameters from data acquired at both echo times (TE1 and TE2). The BOLD model used in the analysis is an extension of that presented in [2], with the parameter M broken down into two separate fitting parameters OEF_0 and K (where $K = A \cdot TE \cdot CBV_0$).

Data for 10,000 randomly generate respiratory paradigms were simulated and analysed, with all paradigms constrained to allow for only interleaved designs (that is periods of either elevated $PaCO_2$ or PaO_2). The optimal respiratory paradigm was identified as the design with the minimal RMS error between the estimated OEF and simulated OEF values. Using this design a further set of simulations was undertaken using a Bayesian framework to identify the hyperparameters that produced the minimum RMS error for OEF values ranging from 0.1 to 0.7.

Results

Figure 1 shows a simulated time series (TE 29 ms), produced using the optimised paradigm, overlaid with the model fit (blue). The optimised paradigm consists of 3 periods of elevated $PaCO_2$ (highlighted in red) and 2 periods of elevated PaO_2 (highlighted in green). Unlike previous designs the MR signal does not completely return to baseline between every stimulus, reducing the amount of time spent in transition and making more efficient use of the available acquisition time. Using the optimised Bayesian hyperparameters the proposed 18-minute paradigm has an RMS error (in OEF estimates) of 0.13, while simulations of previously proposed 18-minute paradigms [1,2] produce RMS errors of 0.16 and 0.17 respectively.

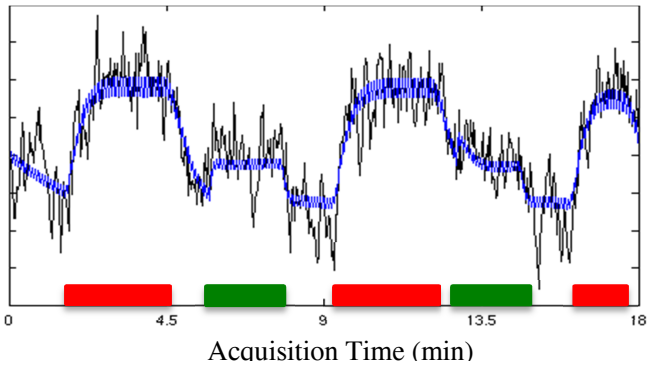

Figure 1. Simulated data (black) with model fit (blue) and gas stimulation periods (coloured blocks), CO_2 red O_2 green.

Conclusions

The respiratory paradigm presented here is tailored to produce minimal error in OEF when using an 18-minute acquisition. The new design demonstrates a significant improvement in the accuracy of OEF estimates over previous proposed designs that use the same acquisition period. Although the results still require experimental validation it is likely that the proposed experimental design will increase the accuracy and precision of in vivo quantification of OEF.

References

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