Cerebral oxygen balance and the BOLD response

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Introduction

Several studies (1,2) have derived analytical expressions to model the BOLD response. Virtues of these models include the estimability of poorly known physiological parameters, as well as the conceptual advantage of a compact analytical form. However, the selection of parameters is often weighted by their assumed importance *a priori*. In the present study a simple but comprehensive approach is presented, in which differential equations for cerebral O_2 and hemoglobin (Hgb) transport are integrated numerically. This makes it possible to investigate the interaction of several known features of the cerebral O_2 transport, as well to test the consistency of current conceptions of BOLD responses, both when elicited by functional activation (fBOLD) and by physiological pertubation (pBOLD). Specifically the model is applied to assess the effects of arterial hematocrit, P_aCO_2 and P_aO_2.

Methods

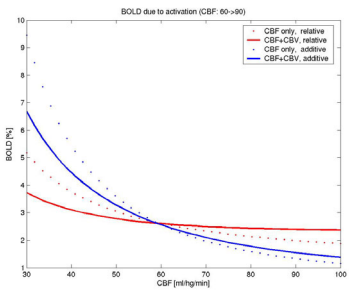
The transport of O_2 and Hgb in cerebral tissue is modelled using 4 major compartments: the arterial, capillary and venous intravascular compartments as well as an extravascular compartment. Within the intravascular compartment the distribution of O_2 between Hgb-bound and physically dissolved phases is updated for every time step, δt, as a function of local pH, PCO_2 and DPG. The transport equation between compartments takes the general form

$$\Delta C_i = \frac{\delta t}{V_i} \cdot \left(\sum_j K_{i,j} \cdot C_j - \sum_k K_{i,k} \cdot C_i \right)$$

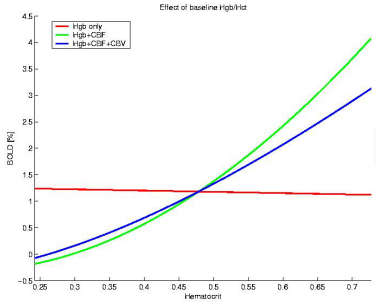
where ΔC_i is the concentration change for O_2 or Hgb in compartment i, and $K_{i,j}$ the transport constant from compartment i to j (equalling flow for intravascular and clearance for transendothelial transport), and V_i the fractional volume. In the present form diffusion of O_2 is assumed to be fast compared to other processes. The total content of deoxy-Hgb is calculated as the sum of arterial, capillary and venous concentrations weighted by their respective volume fractions. The corresponding R_2*-contribution is calculated as proposed by Ogawa et al. (3). The relationships between P_aO_2, P_aCO_2 and CBF, as well as between CBF and CBV were taken from previous empirical results (4-5)

Results

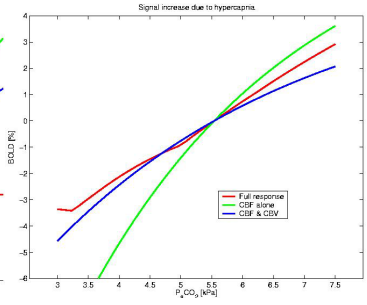
The model predicted BOLD effects of the expected magnitude (1-3% at 1.5T), and confirmed an inverse relation between baseline CBF and the oxygenation change during neural activation (left fig., seen both with additive and relative activation effect, red and blue curve). A slight decrease in BOLD response was seen with higher baseline hematocrits, but only when physiologically expected flow changes were not included (middle fig., blue vs red curve). Both of these findings are can be interpreted as effects of baseline dxHgb levels on the response magnitude (1).



fBold % vs CBF



fBold % vs Hematocrit



pBold % vs P_aCO_2

The pBOLD response elicited directly by hypercapnia was higher than explained from hemodynamic changes only (right figure, difference between red and blue curve). This was due to a significant effect of arterial hyperoxia due to increased ventilation during hypercapnia, while pH changes only had a minor influence.

Conclusion

Several physiological effects were predicted in accordance with established results. However, the model suggests that known effects of hematocrit may be due to accompanying flow changes. During hypercapnia, arterial hyperoxia is an important factor which should be taken into account when used in calibration experiments for $CMRO_2$ determination. Numerical simulation therefore seems helpful in interpreting BOLD effects caused by complex physiological responses.

References

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