Estimating dynamic CMRO2 from dynamic CBF and BOLD fMRI measurements

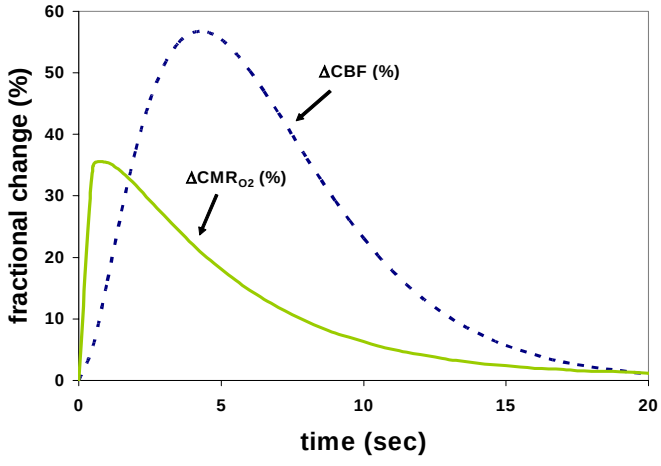
P. K. Maciejewski[1], I. Kida[2], F. Hyder[2]

[1]Psychiatry, Yale University, New Haven, CT, United States, [2]Diagnostic Radiology, Yale University, New Haven, CT, United States

Introduction: Currently there are no direct MR methods for measuring CMR_{O2} as a function of time during transient brain activation. However, parameters that are closely related to changes in CMR_{O2} evoked during functional activation, e.g., CBF and parameters associated with BOLD signal, can be measured dynamically with MRI techniques. Proposed methods for estimating changes in CMR_{O2} during transient brain activation using these types of MRI measurements have appeared only recently [1-3], and reflect the early development of this new class of MR-based measurement techniques. Each of these recent studies has assumed that CMR_{O2} is proportional to CBF and the arteriovenous oxygen difference. Although this assumption is valid at steady state, it is not valid during transient changes in blood and tissue oxygen concentration. Here we adopt an alternative view. Because both changes in CBF (ΔCBF) and BOLD signal (ΔS) are linked to alterations in CMR_{O2} (ΔCMR_{O2}) through processes of O_2 transport from blood to tissue [4], we propose that ΔCMR_{O2} transients may be obtained from modelling O_2 in blood ($[O_2]_b$) and tissue ($[O_2]_t$) compartments within a microvascular unit. Accordingly, we use a non steady-state O_2 transport model to estimate changes in $[O_2]_b$, $[O_2]_t$, and CMR_{O2} as functions of time based on measured time courses of ΔCBF and ΔS during brief sensory stimulation in a rat model [5].

Methods: Since details of animal preparation and sensory stimulation in the rat model have been previously described for quantitative fMRI experiments at 7T [4, 5], here we describe the modelling of the measured ΔCBF and ΔS time courses for an 8s long stimulation period to determine the dynamics of $[O_2]_b$, $[O_2]_t$, and CMR_{O2}. The rate of O_2 transport was modelled in two domains sharing a common boundary: the first domain representing brain tissue and the second domain representing a capillary that supplies O_2 to the brain tissue. A simple cylindrical geometry was considered, in which blood flow through a tube of circular cross section supplies O_2 to a concentric cylindrical tissue volume. Within the tissue domain, the rate of O_2 transport as a function of time was modelled as a diffusion process in both axial and radial directions. CMR_{O2} was modelled to be uniform in tissue space but allowed to vary in time. Within the capillary domain, the rate of O_2 transport was modelled as a process of convection. CBF was assumed to be uniform in space but allowed to vary in time. Blood O_2 concentration was considered to be a function of axial distance along the length of the capillary domain and of time. Numerical solutions for the problems specified within each domain were constrained to ensure continuity of the rate of O_2 transport in space and time between the two domains across their common boundary. Predicted values of the BOLD signal were inferred from calculated values for deoxyhemoglobin concentration derived from blood O_2 concentration and Hill's equation for a hemoglobin saturation. Using this O_2 transport model, ΔCMR_{O2} (t), $\Delta[O_2]_b$ (t), and $\Delta[O_2]_t$ (t) were estimated for specified ΔCBF(t) and ΔS(t).

Results: The figure below displays results for $\Delta CMR_{O2}(t)$, estimated on the basis of measured values of ΔCBF(t) and ΔS(t). CMR_{O2} reaches its peak value approximately one second after the onset of sensory stimulation, prior to the time at which CBF reaches its peak value at approximately 4.5 seconds after the onset of sensory stimulation. This suggests that increases in tissue demand for O_2 precede increases in blood flow supply of O_2**.**



Conclusion: A model for non steady-state O_2 transport from blood to tissue can be used to estimate CMR_{O2} as well as O_2 concentration in blood and tissue during transient functional activation using time courses of ΔCBF and ΔS measured using fMRI techniques.

References:

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