Impact of tube hematocrit on calibrated fMRI

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INTRODUCTION

Cerebral oxygen consumption (CMR_{O2}) – using multi-modal measurement of BOLD signal (S), blood flow (CBF), and volume (CBV) – have been thoroughly investigated and shown to be coupled to neural activity by calibrated fMRI [1], and is based on the biophysical basis of the BOLD signal, where the transverse relaxation rate term (R_2) depends on [2,3]

$$R_2 \propto (1 - Y)\ b\ \mathrm{Hct}$$

where (1 - Y) is the blood deoxygenation term, *b* is the total blood volume fraction, and Hct is the blood hematocrit. While the systemic hematocrit (discharge or macrovessel Hct) does not change during functional activity, studies have not yet assessed the impact of tissue (or microvessel) hematocrit on BOLD signal. Tube hematocrit, defined as the instantaneous volume fraction of red blood cells (RBCs) in microvessels (Hct_{micro}), depends on not only the volume ratio of RBC and plasma but also on their velocities, which may change dynamically as velocities of RBC and plasma components, especially in microvessels, are not equivalent [4]. Here we combined laser-Doppler flowmetry (LDF) and fMRI measurements of RBC (v_{rbc}) and plasma (v_{plasma}) velocities because they directly impact Hct_{micro} [4].

METHODS

We applied multi-modal measurements of BOLD, CBV, CBF with high field (11.7T) MRI and LDF techniques. We measured dynamic changes in v_{plasma} and v_{rbc} during forepaw stimulation in anesthetized rats (n=12). fMRI studies used exogenous contrast agent to measure changes in CBV_{plasma} which was then extended to v_{plasma}. The LDF provided two simultaneous measurements – the RBC flux (related to CBF) and backscattered light (related to CBV_{rbc}) – to estimate v_{rbc} from a uniform distribution of blood vessels in the layer IV of the cortex.

RESULTS

The v_{rbc} was estimated from the ratio of the LDF flux and RBC concentration, where the latter was calculated from backscattered signal. Fig. 1 shows results of our recent multi-modal studies in rats. The v_{rbc} transient arises from temporal mismatch between transients of RBC flux and concentration (Fig. 1A). The v_{plasma} was estimated from the first derivative of CBV_{plasma}. The stimulation-induced fluctuations in v_{plasma} (Fig. 1A), which arise primarily due to slow CBV_{plasma} dynamics, are significantly smaller ($p<0.001$) than changes in v_{rbc}. The dissimilar velocity patterns of RBC and plasma corresponded to Hct_{micro} decrease immediately after stimulus onset which was sustained throughout the stimulus (Fig. 1B). CMR_{O2} variations were calculated with and without the Hct_{micro} effect (Fig. 1C).

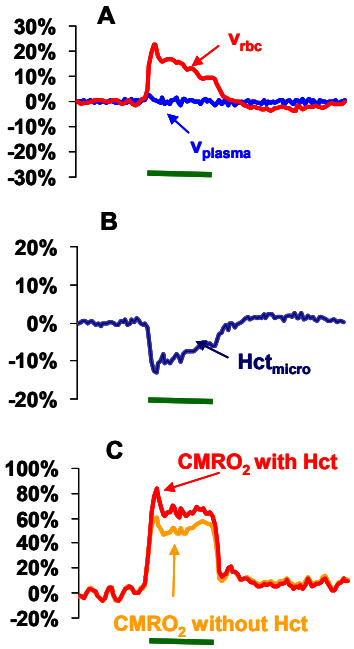

Fig 1. Hct_{micro} change during forepaw stimulation (30 s; 3 Hz; 2 mA). (**A**) Velocities of plasma and RBC (v_{plasma}, v_{rbc}) measured by fMRI and LDF. The calculated (**B**) drop in Hct_{micro} and (**C**) ΔCMR_{O2} by calibrated fMRI without and with ΔHct_{micro}.

DISCUSSION

Dynamic changes in v_{plasma} and v_{rbc} corresponded to a sustained drop in Hct_{micro}, based on the observations of Gaehtgens [4]. A key component for Hct_{micro} variation is Δv_{rbc} since Δv_{plasma} seems quite passive. In fact, even if Δv_{plasma} is allowed to vary by ±50% of Δv_{rbc}, simulations show negligible effects on ΔHct_{micro}. Recently we showed that discharge hematocrit, equivalent with volume percentage of RBCs in blood, is not appreciably affected during functional activation [5]. The hyperemia-induced decrease in Hct_{micro} is consistent with a drop in blood viscosity, which in turn would improve efficiency of RBC movement through capillaries during function. These results suggest that Hct_{micro} change need to be included in the functional hyperemic response of the BOLD signal. Given that our measured changes in Hct_{micro} are almost as large as CBV_{plasma} changes measured by fMRI, we estimate that current calibrated fMRI studies could potentially be underestimating the ΔCMR_{O2} (Fig. 1C).

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