Effect of short-term synaptic plasticity on the relationship between neuronal activity, BOLD, CMRO2 and CMRGlc studied by metabolic modeling of neuron-glia interaction

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INTRODUCTION AND PURPOSE

The pivotal work by Logothetis and colleagues on the relation between brain electrophysiology and BOLD signal demonstrated that the latter is better correlated to the local convergent synaptic processing rather than divergent spiking activity [1]. However, how this finding can be rationalized in terms of neurometabolic coupling is not yet fully understood. In this study, we sought to examine in detail the coupling between neuronal activity, BOLD, and cerebral metabolic rates of oxygen ($CMRO_2$) and glucose (CMRGlc). To this end, we developed a kinetic model of rat brain metabolism including electrophysiological information related to short-term synaptic plasticity (STP). In particular, the inclusion of a form of neuronal habituation such as STP implies that energy consumption of APs and EPSPs scale differently with mean neuronal firing rate.

METHODS

The present metabolic model is largely based on previously published theoretical accounts [2]. We made the following major additions/changes: (i) pre- and post-synaptic neuronal compartments separated, (ii) action potentials (APs) and excitatory post-synaptic potentials (EPSPs) determined with a phenomenological model of STP [3]; (iii) Na^+ and K^+ ion fluxes explicitly accounted for with a detailed kinetics of neuronal and astrocytic Na^+/K^+-ATPase isoforms.

RESULTS AND DISCUSSION

Figure 1 shows that when mean neuronal firing rate increases from 2 Hz to 9 Hz both the BOLD signal and the $CMRO_2$ reaches a plateau, whereas the CMRGlc increases almost linearly. The different changes in $CMRO_2$ and CMRGlc result in the well-known decrease of the oxygen-carbohydrate index, which departs towards lower values as the neuronal activity increases.

Dendritic activity (i.e., EPSPs) drives the oxygen consumption in the transition from suppressed to basal activity, then oxidative capacity saturates (Figure 2A). On the other hand, axonal APs (i.e. spiking activity) are found to be the primary determinants for the up-regulation of glucose metabolism out of proportion compared with oxygen (Figure 2B). Astrocytes also contribute to the "anaerobic" shift when mean neuronal firing rate increases above 2 Hz. However, at firing rates above 5-6 Hz the axonal energy demand is the only increasing factor and this increase is met almost exclusively via non-oxidative glucose metabolism.

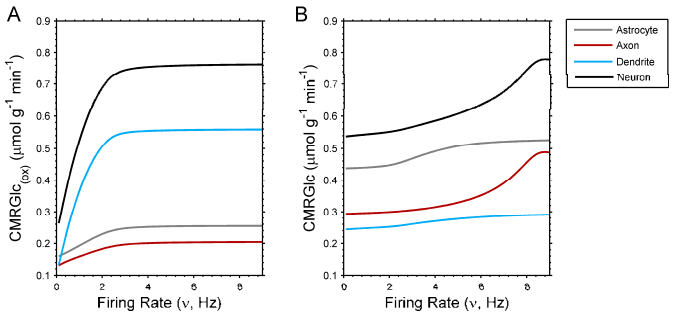

Figure 2. Oxidative (A) and non-oxidative (B) energy consumption by individual cellular compartments as a function of mean neuronal firing rate varies in the interval 0-9 Hz. Data points are determined as the value reached by the relevant variable at the end of a 60 secs activation (i.e., departure of mean neuronal firing rate from the basal value of 2 Hz).

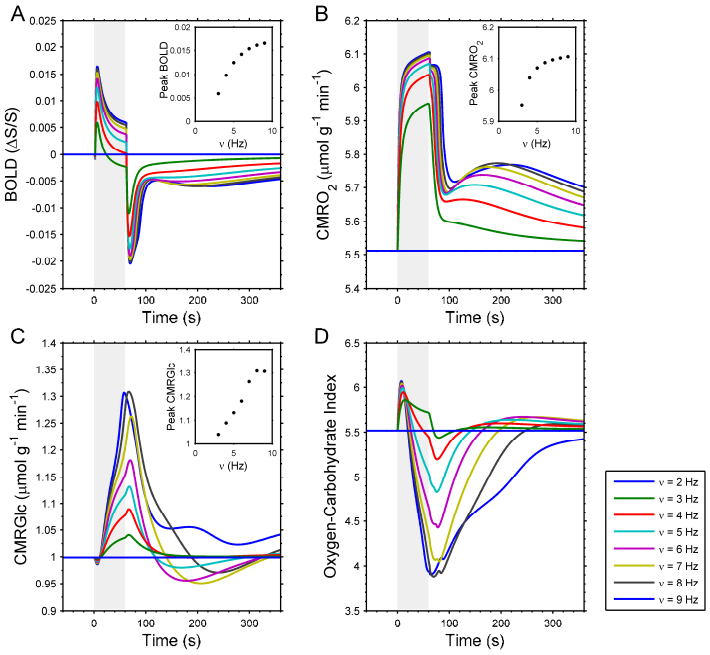

Figure 1. Main outcomes of the model as a function of mean neuronal firing rate during a 60 secs activation. Mean neuronal firing rate increases in the interval 2-9 Hz. (A) BOLD signal. (B) $CMRO_2$. (C) CMRGlc. (D) Oxygen-Carbohydrate Index. The insets in each plot shows the peak amplitude of the relevant variable. The ratio between CMRGlc and either BOLD or $CMRO_2$ increases as mean neuronal firing rate increases.

CONCLUSION

Our modeling outcomes suggest that post-synaptic activity correlates with $CMRO_2$ and BOLD, while pre-synaptic spiking activity correlates with CMRGlc. These results are relevant for further understanding the coupling between neuronal activity, vascular response and oxidative/non-oxidative metabolism.

REFERENCES

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Acknowledgments: NIH KL2 RR033182