From neurons to BOLD

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HIGHLIGHTS

- Blood flow and energy metabolism are driven in parallel by neuronal activity
- The "overshoot" prevents tissue oxygenation drop in between capillaries
- GABAergic neurons play a key role in neurovascular coupling
- Astrocytes may not drive CBF but contribute to BOLD by consuming O_2
- Macroscopic BOLD signal can be predicted by "bottom-up" modeling

TARGET AUDIENCE MR physicists developing models of fMRI signals and MDs/neuroscientists using fMRI as a tool.

OUTCOME/OBJECTIVES (1) Learn about recent developments in microscopic imaging that have revealed the behavior of concrete physiological parameters underlying BOLD fMRI; (2) Learn how these data can be integrated to predict macroscopic BOLD signal.

PURPOSE Understanding how neuronal activity drives changes in cerebral blood flow (CBF) and cerebral metabolic rate of O_2 ($CMRO_2$) is critical for laying a solid physiological foundation for interpreting the BOLD signal. In this talk, we will review recent data on neurovascular and neurometabolic coupling that have become available due to advances in microscopic imaging technology. Further, we will introduce a theoretical framework to bridge between micro- and macroscopic level of description and will discuss our working hypotheses on CBF regulation and neurophysiological correlates of BOLD fMRI signals.

METHODS We will review novel optical imaging methods with microscopic resolution that provide definitive and quantitative measures of concrete physiological parameters. These measures are used to predict macroscopic BOLD signal. The prediction is then tested against BOLD-fMRI data to ensure validity of the model.

RESULTS We will provide examples of (1) how in vivo microscopic imaging technology can be used to test specific hypotheses on regulation of blood flow and identify cellular players and vasoactive messengers in neurovascular and neurometabolic coupling, and (2) how these microscopic data are integrated in a mechanistic framework to predict the BOLD signal.

DISCUSSION/CONCLUSION Recent developments in optical microscopy now offer a versatile suite of tools for high-resolution, high-sensitivity measurements of vascular, metabolic, and neuronal parameters in deep tissue and local, cell-type specific manipulations of neuronal activity. These technological advances have challenged the "too hard to do" status quo for mechanistic studies *in vivo* and have defined a new standard for theoretical efforts that now can be rooted in microscopic reality of concrete physiological parameters' behavior.