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Shedding light on the brain: multimodal imaging from two-photon microscopy to fMRI-BOLD

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Blood Oxygen Level Dependent functional Magnetic Resonance Imaging (BOLD-fMRI) is a powerful tool to measure brain activity non-invasively. Over the past 25 years, it has become widely used in neuroscience research. However, BOLD does not measure neurons directly, but instead results from a complex interplay of vascular and metabolic processes, termed the 'hemodynamic response'. Therefore, BOLD is influenced by various cell types as well as individual physiology and must be interpreted with caution. In particular, the use of BOLD to compare brain activity between groups with known physiological systematic differences, such as sex or age groups, is subject to bias.

My work makes use of a combination of imaging techniques (multimodal imaging), animal models, and biophysical modeling to measure and compute a maximum of physiological parameters influencing BOLD. The goal is to improve interpretation of past and future neuroscience studies based on BOLD and to improve its applications in atypical populations (e.g. persons with diseases that affect brain blood flow).

In this talk, I will present different brain imaging techniques and briefly discuss their biophysical basis. I will discuss our results from a study on the effects of aging on vascular physiology and how it affects the BOLD. This two-part study was conducted both in humans using non-invasive imaging and in a rat model of aging using microscopy.

Understanding the relation of BOLD to neural activity requires elucidating the mechanisms of what we call 'neuro-vascular coupling', i.e. the relation between neural activity and changes in local cerebral blood flow. One of the most exciting recent tools available to study this in animal models is the use of optogenetics, which allows control of specific cell types by means of laser illumination. I will illustrate how, combined with two-photon imaging of blood vessels, optogenetics allowed us to measure the contribution of specific neuronal types (e.g. excitatory vs inhibitory neurons) to the BOLD signal.

I will finally present my most recent work from imaging in awake, normally behaving mice, to elucidate the origins of the BOLD signal. I will discuss potential applications of these techniques in models of disease affecting blood flow and oxygenation, such as tumors.

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