Astrocyte contribution to impaired vascular-to-neuronal signaling in disease conditions

Unlike other organs, brain homeostasis requires constant cerebral blood flow (CBF). Impairments in blood flow delivery can overwhelm basic neuronal functions and accelerate neurodegenerative-related mechanisms leading to vascular cognitive impairment (VCI). Cardiovascular-related diseases are contributors to VCI. A common denominator in VCI is chronic hypoperfusion (CH) to the brain. However, the cellular mechanisms underlying progressive decline in neuronal function are complex and ill-defined. Hypoperfusion can result from conditions such as hypertension-related vascular remodeling, atherosclerosis and heart failure, to name a few. These risk factors, however, may target cells of the neurovascular unit to different degrees and/or at different time points during the disease. We previously reported that hemodynamic-related stimuli such as increases in flow and intravascular pressure increased astrocyte Ca²⁺ which in turn lowered resting pyramidal neuron firing activity, a process referred as vasculo-neuronal coupling (VNC)(2). We proposed VNC as a neuroprotective pathway that safeguards the brain from a mismatch in metabolic demand and supply (1, 2). Here, we hypothesize that vascular-related abnormalities impair flow of information at the neurovascular unit resulting in inefficient VNC. To address this hypothesis, we measured VNC using both a model of VCI and hypertension namely, bilateral common carotid artery stenosis (BCAS) and 28 day angiotensin II (Ang II) infusion in mice. I will present data on hypertension and CH-induced functional changes to the neurovascular unit. Specifically, I will address how these distinct conditions alter parenchymal arteriole vascular reactivity, astrocyte Ca²⁺ dynamics, and neuronal function.