The vascular steal phenomenon is an incomplete contributor to negative cerebrovascular reactivity in patients with symptomatic intracranial stenosis

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Target Audience: Researchers interested in the physiological mechanisms of fMRI signal origins in healthy and ischemic cerebrovascular disease.

Purpose: The overall goal of this work is to apply simultaneous hypercarbia-induced measurements of cerebral blood flow (CBF) and blood oxygenation level-dependent (BOLD) cerebrovascular reactivity (CVR) in patients with symptomatic intracranial stenosis to better understand the physiological origins of negative BOLD CVR. Magnetic resonance imaging (MRI) protocols that exploit the BOLD contrast are capable of measuring CVR in response to a global vasodilatory hypercarbic gas stimulus (4,5), and these approaches are now being used with increased frequency in cerebrovascular disease, dementia, and tumor applications. However, fundamental gaps remain in our knowledge regarding the physiological underpinnings of the BOLD contrast mechanism, and importantly how the BOLD contrast in patients with intracranial vessel disease correlates with prognosis. As such, changes in regional cerebral perfusion (rCBF) in patients with intracranial vessel disease have been demonstrated with hypercarbia (3), and these approaches are now being used with increased frequency in cerebrovascular disease, dementia, and tumor applications. However, fundamental gaps remain in our knowledge regarding the physiological underpinnings of the BOLD contrast mechanism, and importantly how the BOLD contrast in patients with intracranial vessel disease correlates with prognosis.

Methods: Symptomatic intracranial stenosis participants (n=40) and healthy control volunteers (n=8) provided informed, written consent in accordance with local IRB and HIPAA guidelines and underwent a multimodal 3.0T MRI protocol including structural (T1-weighted and T2-weighted fluid attenuated inversion recovery, FLAIR) and hemodynamic (BOLD; TR=35 ms, in-plane spatial resolution=3x3 mm) and CBF-weighted (pCASL; TR/TE=4000/17 ms, in-plane spatial resolution=3x3 mm) functional MRI during resting state, hypercarbic hyperoxia (carbogen; 5% CO2/95% O2) gas administration (3 min x 2). Carbogen was used as many patients were in the subacute phases of stroke, and it was not appropriate to reduce FIO2 through hypercarbic or hypoxic gas stimuli. Ramifications of carbogen administration are discussed below. CBF was quantified, upon administration of the flow-modified Bloch equation (including a 200 ms reduction in blood water T1 upon carbogen administration), as well as symmetric hemispheres by infant and lateralizing clinical symptoms were also recorded.

Results: Fifteen of 40 participants exhibited negative BOLD reactivity. Of these, three participants exhibited significant (P<0.01) reductions in CBF with hypercarbia consistent with vascular steal phenomena; six participants exhibited increases (P<0.01) in CBF and the remaining participants exhibited no statistical change in CBF.

Conclusion: The primary finding of this study is that in patients with symptomatic intracranial steno-occlusive disease, regions of hypercarbia-induced negative BOLD reactivity cannot be exclusively explained by “vascular steal” phenomena. Rather, while a subgroup of such cases does appear to suggest steal phenomena, the majority of participants exhibited no or increased CBF response in such regions. Secondaries findings are that negative BOLD reactivity correlated with symptomatic hemisphere by lateralizing clinical symptoms and prior infarcts(s), that a strong inverse correlation (P=0.048) exists between the volume of the negative BOLD region and the magnitude of the negative response.

Discussion: The origin of negative BOLD responses in stroke patients is heterogenous, likely containing differential contributions from vascular steal, autoregulation and/or metabolic upregulation.

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