Negative BOLD signal response to inhaled carbon dioxide correlates with decreased cerebral blood flow on arterial spin labeling

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Introduction:

Exhaustion of cerebrovascular autoregulation can occur in patients with carotid artery stenosis or occlusion. One can assess cerebrovascular autoregulation by measuring the change in cerebral blood flow induced by an exogenous vasodilatory stimulus such as inhaled carbon dioxide. This response is called cerebrovascular reactivity. A relatively new approach to imaging cerebrovascular reactivity is the use of BOLD (blood oxygen level-dependent) MRI. In cases with severe impairment of blood flow, BOLD MRI signal can actually decrease in response to a vasodilatory stimulus – a paradoxical response. We hypothesize that this paradoxical response represents vascular steal.

Methods:

Cerebrovascular reactivity was mapped using both a BOLD MRI pulse sequence and a FAIR (flow-sensitive alternating inversion recovery) arterial spin labeling sequence. The BOLD sequence was a gradient echo EPI acquisition with the parameters: TR 2000 ms, TE 30 ms, FOV 23.6 x 23.6 cm, matrix 64 x 64, 30 slices, slice thickness 4.4 mm, scan duration 6 minutes. The FAIR sequence was a spin echo EPI acquisition with the parameters: TR 2000 ms, TE 22.2 ms, TI 1000 ms, FOV 23.6 x 23.6 cm, matrix 64 x 64, 4 slices, slice thickness 5 mm, scan duration 6 minutes. A unique gas sequencer and rebreathing mask was used, enabling near square wave changes in end tidal CO2 between 40 and 50 mm Hg. Quantitative maps of cerebrovascular reactivity were obtained by using r value correlations of the end-tidal CO2 waveform with the MRI signal for each of the pulse sequences. We identified 4 patients with a region of negative response on BOLD MRI, and then quantified cerebrovascular reactivity on the FAIR map in this region of interest. The underlying diseases were carotid artery stenosis (2), Moya Moya disease (1), and cocaine-induced vasculitis (1). Parenchymal changes in the regions of interest were infarct, severe microangiopathic change, normal, and infarct, respectively.

Results:

In all cases, the negative response on BOLD MRI correlated with reduced cerebral blood flow on arterial spin labeling MRI. Mean percentage signal change per mm pCO2 change for the regions of interest on the FAIR maps were -0.92 ($\sigma = 0.37$), -0.11 ($\sigma = 0.18$), -2.75 ($\sigma = 2.54$), and -0.63 ($\sigma = 0.25$) for the four patients, respectively.

Discussion and Conclusion:

Inhaled carbon dioxide normally dilates the cerebral vasculature, decreasing vascular resistance, and increasing cerebral blood flow. Carotid artery stenosis or occlusion can result in autoregulatory maximal vasodilatation of a downstream brain territory, leaving no capacity for further dilatation in response to inhaled carbon dioxide. In such cases, there can be shunting of blood from the abnormal region of brain where carbon dioxide does not reduce vascular resistance, to a normal region of brain where resistance decreases in response to carbon dioxide. This decrease in blood flow in the abnormal region would result in decreased signal on BOLD MRI. Unfortunately, a decrease in cerebral blood flow is not the only factor that can cause decreased signal on BOLD MRI. In particular, we were concerned that the observed negative response on BOLD MRI might be due to increased cerebral blood volume with little change in cerebral blood flow. Compared with BOLD MRI, the FAIR sequence is specific to measurement of changes in cerebral blood flow. Our combination of findings on BOLD and FAIR show that a negative BOLD signal response to inhaled carbon dioxide does actually represent a decrease in cerebral blood flow, that is, vascular steal.