Decreased Baseline Microvascular Volume in Acute Ischemia Induces Hemispherically Deficient Cerebrovascular Response to Hypercapnia: MRI Study using Permanent MCAO rat model

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INTRODUCTION: Systemic hypercapnia, often induced by inhaling excessive CO₂, is known to evoke significant cerebral vasodilation and to dramatically elevate the overall cerebral blood volume (CBV) and blood flow (CBF) under the normal healthy conditions. Previously, in order to characterize the altered vascular function, vasoreactivity to a hypercapnic stimulation was often used for the investigation of CBF affected by the ischemic stroke. However, the relationships between the hypercapnia-induced vascular responses and the baseline vascular states have not been investigated under the acute ischemic stroke. In this study, using an alternating gradient and spin echo (GE/SE) EPI and superparamagnetic intravascular contrast agent (SPION) in rats with permanent occlusion of middle cerebral artery (MCAO), we monitored multiple hemodynamic parameters in response to systemic hypercapnia. Our results demonstrated alterations of the cerebral vasoreactivity in relation to MRI-derived baseline tissue/vascular parameters during acute cerebral ischemia.

MATERIALS & METHODS: In vivo MRI experiments were performed using a 9.4T magnet immediately following the suture occlusion of the MCA of Wistar rats (n=13). For the real time monitoring of cerebrovascular parameters during hypercapnia (inhaling of 5% CO₂), T2- and T2*-weighted images were acquired alternatively using GESE EPI sequence with TR/TE = 4000/15.16 ms for GE and 4000/27.73 ms for SE before and after administering SPION. Dynamic changes of the CBV (ΔR2*), microvascular volume (MVV, = ΔR2), and vascular size index (VSI, = CBV/MVV) were quantified from four ROIs defined by the percent decrease of apparent diffusion coefficient (ADC) as compare to the contrallesional cortex area. (1) core: area with more than 75% decreased in ADC, (2) peri: area with ADC decrease between 25% and 75%, (3) sub-normal: subcortex area with normal ADC (4) cortex-normal: cortex area with normal ADC. ROIs in contrallesional hemisphere were placed in the homologous regions of the ipsilesional hemisphere.

RESULTS & DISCUSSION: Previously, we demonstrated the significant increase of cerebrovascular responses to systemic hypercapnia in normal rat brains [1]. In the current study using permanent MCAO models, we observed no baseline CBV decrease in the ipsilesional hemisphere, but the reduction of baseline MVV in the ipsilesional hemisphere was conspicuous (Fig.1). During exposure to 5% CO₂, the percent responses of both CBV and MVV from the baseline were not dependent on the ADC-defined stroke severity and hemispherically deficient in all areas including the normal ADC regions (Fig. 2). Interestingly, unlike previous results from the normal rat brains, the percent response in MVV surpassed that in CBV in both hemispheres, resulting in decreases of VSI (Fig. 2). This finding suggests the globally altered cerebral hemodynamic properties. In this work, we observed changes in the baseline MVV, rather than the baseline CBV, has decisive effects on the decreased vasoreactivity upon CO₂ stimulation. Secondly, the magnitudes of the percent response both CBV and MVV is not dependent on the local severity of stroke defined by ADC. Thirdly, the baseline MVV is particularly vulnerable to the ischemic damage, implying an impaired microvascular environment, possibly even in the contrallesional hemisphere. Such drastic changes in MVV may influence the overall cerebrovascular activity, hence, suppressing the CO₂ reactivity in the entire ipsilesional hemisphere. Our results provide an important basis for understanding the impaired cerebrovascular reactivity due to occlusion of major cerebral arteries.


Fig. 1. Normalized baseline CBV, MVV and VSI in ADC derived ROIs

Fig. 2. Comparison of percent responses in CBV, MVV and VSI during hypercapnia stimulation (left) and an example of activation maps (right).