

T2*-Weighted Signal Change of Oxygen Challenge as a Potential better Penumbra Estimation—A Transient Occlusion Study

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INTRODUCTION T2*-weighted (T2*W) MRI of oxygen challenge (OC) has been used to probe tissue viability in ischemic stroke (1). We have previously shown that T2*W MRI of OC showed unique responses of at risk tissue compared to normal and ischemic core after a permanent middle cerebral artery occlusion (MCAO) in rats (2). Specifically diffusion/perfusion mismatch region showed higher than normal T2*W signal increase during OC. We hypothesized that those tissues are more amendable to treatment and T2*W MRI of OC has the potential to better approximate penumbra. To test this hypothesis, T2*W MRI associated with OC was used to study a group of transient (45-min) MCAO rats. Standard perfusion and diffusion MRI was also performed to identify perfusion-diffusion mismatch.

METHODS Four male Sprague Dawley rats (250-300g) were subjected to 45-min transient MCA occlusion using intraluminal suture occlusion method (3). Animals were mechanical ventilated and maintained anesthesia with ~1.2% isoflurane in air. Body temperature, end-tidal pCO₂, PaO₂ and heart rate were continuously monitored and maintained within normal ranges. MRI experiments were performed on a 7-T/30-cm magnet. A surface coil (2.3-cm ID) with active decoupling was used for brain imaging and a neck coil for perfusion labeling. Quantitative CBF and ADC (apparent diffusion coefficient) were measured. MRI parameters were: single shot, matrix = 96x96, FOV = 25.6mm x 25.6mm, seven 1.5mm thick slices, TR=3s, TE=10.2ms for CBF and 30ms for ADC, FA = 90°. Oxygen challenge T2* weighted imaging was acquired using gradient-echo EPI with similar parameters as CBF measure except TE = 26ms and TR=10s. OC experiment paradigm was: 4 min OFF, 4 mins ON, 4 min OFF. OC response percent change maps were calculated. CBA, ADC and OC T2*W imaging were required at before and after reperfusion. And at 24-hr post-occlusion, the animals were scanned again with the same protocol.

Three tissue types (normal, perfusion-diffusion mismatch and ischemic core) were characterized by using auto-clustering ISODATA method (4) based on 30-min ADC and CBF data. ADC, CBF and OC T2*W signal percent change of different tissue types were analyzed.

RESULTS Figure 1 showed the ADC, CBF and OC % change maps before (30-min), after reperfusion (180-min) and 24-hr post-occlusion from one animal. Figure 2 showed group averaged OC % change, ADC and CBF at three time points of three types of tissues. The inset map was the ISODATA determined normal (red), mismatch (green) and core (blue) tissues defined at 30mins after MCAO.

In perfusion/diffusion mismatch region, OC % change was significantly higher than normal before reperfusion and then changed to close to normal after reperfusion and at 24-hr post-occlusion. Slightly reduced ADC recovered after reperfusion and remained normal at 24-hr post-occlusion. Significantly reduced CBF recovered after reperfusion and show hyperperfusion at 24-hr post-occlusion in part of mismatch tissue.

In ischemic core region, negligible OC response before reperfusion changed to significantly higher than normal and then was negative or close to zero. Significantly reduced ADC transiently recovered after reperfusion and changed back to low again at 24-hr post-occlusion. Significantly reduced CBF recovered after reperfusion and show strong hyperperfusion at 24-hr post-occlusion.

DISCUSSION & CONCLUSION Before reperfusion, the mismatch region, which approximates the penumbra, was metabolically active with restricted blood flow and high oxygen extraction fraction. A higher level of deoxyhemoglobin in blood leads to a higher T2*W signal increase during OC. Normal OC response after reperfusion and at 24-hr post-occlusion indicated they were salvaged, which also indicated by normal ADC. But part of mismatch tissue showed hyperperfusion implied that they might change to lesion later.

In the ischemic core, before reperfusion, there was no blood flow and oxygen delivery during both baseline and OC, and thus baseline T2*W signal was low and there was negligible T2*W signal change during OC. After reperfusion, the OC response changed to higher than normal. We interpreted this as that the accumulated deoxyhemoglobin before reperfusion was not completely converted to oxyhemoglobin and some of the core tissue may still metabolically active, which produced more deoxyhemoglobin. Thus, the deoxyhemoglobin concentration in core region could be higher than other regions, which would lead to higher than normal OC response. The slight negative T2*W signal response at 24-hr post-occlusion in the lesion territory was likely due to dissolved O₂ because dead tissue did not metabolize O₂, resulting in increased dissolved paramagnetic O₂. Negative T2*W signal response allow us to distinguish dead tissue from normal tissue.

T2*W MRI with OC may offers a novel means to detect at-risk tissue before treatment (higher than normal OC response) and dead tissue at chronic phase (negative OC response). Further experiments will include different reperfusion time points to further explore the potential of T2*W MRI of OC. In conclusion, T2*W MRI of OC offers a novel biomarker to identify tissue salvageability that could potential complement conventional diffusion and perfusion MRI in the diagnosis and treatment of acute stroke. The higher than normal OC response after reperfusion (mostly in core region before reperfusion) may be useful for lesion prediction since ADC and CBF have changed back to normal or close to normal.

REFERENCE: 1) Sanrosh et al. JCBFM 2008; 28:1742. 3) Shen et al, ISMRM 2010; 4490. 3) Shen et al. JCBFM 2004, 24:280. 4) Shen et al, JCBFM 2004; 24:887.

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