T1 Effect on BOLD and CBF Functionl Magnetic Resonance Imaging of Hyperoxic Challenge in Ischemic Stroke

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INTRODUCTION Oxygen challenge (OC) has been used to test vascular function in disease conditions (1,2) and to estimate ischemic penumbra with T_2*-weighted MRI (3,4), offering an additional and unique mean to probe tissue viability. However, such T2*-weighted signal sources of OC associated with cerebral ischemia remain not well understood. OC is known to cause T1 changes which affect ASL CBF and BOLD signals if TR is insufficiently long. Ischemia also could change T1, CBF, as well the response to OC. The goal of this study was to investigate the T2*-weighted signal sources during OC by measuring T1, T2 and CBF during air and oxygen inhalation associated with ischemic brain injury.

METHODS Four male Sprague Dawley rats (250-300g) were subjected to 45-min transient MCA occlusion using intraluminal suture occlusion method (5). At 24 hour post-occlusion, animals were mechanical ventilated and maintained anesthesia with ~1.2% isoflurane in air. Body temperature, end-tidal pCO_2, PaO_2 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 T_2* weighted imaging was acquired using gradient-echo EPI with similar parameters as CBF measure except TE = 26ms, TR/FA = 1s/60° or 10s/90°. T_1 maps were acquired at baseline and under 100% O2 (steady state) using inversion-recovery gradient-echo EPI with 6 inversion times (24ms, 0.5s, 1s, 2s,4s and 8s) and TR = 12s. OC experiment paradigm was: 4 min OFF, 4 mins ON, 4 min OFF. OC response percent change maps were calculated. OC CBF time course was calculated using measured baseline T_1 map only or using T_1 map measured under 100% O_2 for OC period.

RESULTS **Figure 1** showed the ADC, CBF and T_2 maps at 24 hrs after stroke. Stroke affected the striatum and a small part of the cortex, as indicated by low ADC, hyperperfusion and high T_2. **Figure 2** showed T_1 maps at baseline, T_1 maps during O2 inhalation and the T_1 % change map. Baseline T_1 increased in the lesion area. In normal tissue, OC induced non-significant T1 change (0.4 ± 3.8%, P>0.05), while in lesion area OC induced strong T_1 reduction (-13 ± 5%, P<0.05).

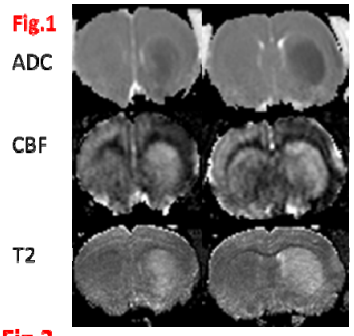
Figure 3 shows the OC-induced T2*-weighted percent change maps at 1s and 10s TR. At 1s TR, normal tissue showed increased responses as expected, whereas the lesion showed even larger response. At 10s TR, the lesion did not show the large T2*-weighted response, rather some negative responses were detected. **Figure 4** shows the OC-induced CBF changes without accounting for T1 change by OC and with accounting for T1 changes by OC. In normal tissue, OC decreased CBF slightly as expected (hyperoxia-induced vasoconstriction). In ischemic tissue, CBF changes without accounting for T1 change by OC were similar to normal tissue, whereas CBF changes accounting for T1 change by OC showed CBF increase (instead of decrease). Group-averaged T_1, BOLD and CBF percent changes for normal and lesion tissue are summarized in **Table 1**.

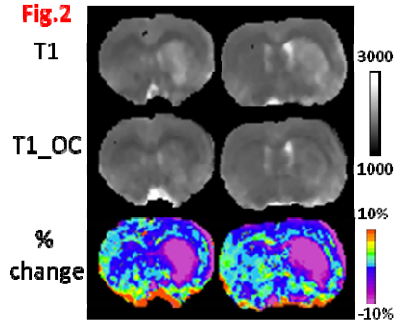
DISCUSSION & CONCLUSION The longer baseline T1 in the lesion compared to normal tissue was likely associated with edema (**Fig. 2**). OC caused little T_1 change in normal tissue, but caused strong decrease in ischemic tissue. During OC, the combination of hyperperfusion (increased O2 delivery) and dead tissue (decreased O2 metabolism) likely led to higher dissolved O_2 concentration in lesion than normal tissue, resulting in marked decrease in T1 because dissolved O2 (unbound from hemoglobin) is a paramagnetic contrast agent.

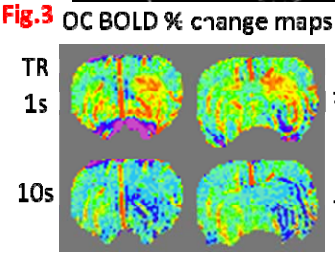
The decreased T1 in the lesion contributed to the enhanced OC T2*-weighted response at short TR due to T1 weighting. After removing T1 effect by using long TR, the strong OC T2*-weighted response disappeared (**Fig. 3**). The slight negative T2*-weighted signal response in the lesion territory was likely due to dissolved O2 because dead tissue did not metabolize O2, resulting in increased dissolved paramagnetic O2.

In the OC CBF changes, after accounting for the T_1 effect, OC increased CBF in the lesion area (**Fig. 4**), suggesting that hyperoxia-induced vasoconstriction in the lesion area had been impaired.

In conclusion, T2*-weighted MRI of OC in cerebral ischemia is complex. We concluded that it is important to take into account the T_1 and T2* effect when calculating BOLD and CBF fMRI signal changes associated with OC in ischemic brain injury. OC MRI in ischemic brain injury has the potential to offer unique information on tissue viability. Future studies will investigate OC and hypercapnic challenge MRI in acute stroke.







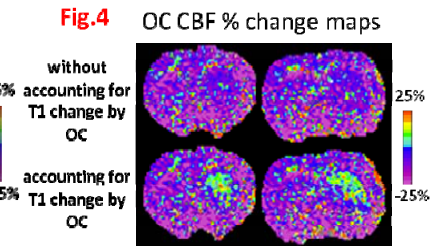


Table 1

	T1 change by OC (%)	BOLD (%)		CBF change (%)	
		TR=1s	TR=10s	w/o T1[a]	w/ T1[b]
Normal tissue	-0.9 ± 1.8	3.6 ± 2.4	3.4 ± 1.2	-9.6 ± 1.1	-8.6±2.9
Lesion tissue	-14.8 ± 2.5	**7.9 ± 2.8**	**1.3 ± 0.9**	**-8.4 ± 1.2**	**3.5±2.0**

a: without accounting for T1 change by OC. b: accounting for T1 change by OC

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