The Role of Oxygen Molecule Dissolved in Rat Blood Based on BOLD MRI

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INTRODUCTION: Regarding the source of BOLD signal, it has been generally accepted that decrease in deoxyHb concentration is a main cause of increasing signal intensity (SI) during oxygen inhalation as deoxyHb is a strong endogenous T2 contrast agent. Compared with deoxyHb, the influence of oxygen on BOLD signal has took less attentions despite oxygen is also a paramagnetic material and its concentration is directly increased by oxygen inhalation [1, 2]. Therefore, to accurately interpret the meaning of BOLD signals, it is important to assess the effect of oxygen on SI changes observed during oxygen breathing. Such assessment is important particularly for explaining unusual signal intensity changes. For example, a number of regions exhibit negative conversion of SI during hyperoxic respiration, although elevated oxygen concentration usually increases SI by converting more deoxyHb to oxyHb. In these regards, (a) for analyzing the contribution of oxygen to blood SI changes, we compared T1 and T2/T2* relaxation times between normoxic and hyperoxic blood samples; and (b) for exploring the effect of tissue oxygen on BOLD signal, we compared T1 relaxation time and SI changes according to TE between normoxic and hypoxic brain tissue.

MATERIALS AND METHODS: Eight male Sprague-Dawley rats underwent inhalation of different amount of oxygen gas (20% and 100%), thereby being exposed to normoxic and hyperoxic status. In both conditions, blood gas analysis and relaxation time (T_1, T_2/T_2^*) measurement were performed. For MR images, a 4.7 T MR unit (BioSpec, Bruker) equipped with a 40 cm horizontal magnet bore was used. To measure T1 relaxation times, a RARE sequence with variable repetition times was obtained (eight TRs, 0.2 ~ 4 s; TE, 8 ms). T2 relaxation time was estimated using a multi-slice multi-spin echo sequence (TR, 4s; 30 TEs, 7.5~225ms), and T2* relaxation time using a multi-gradient echo sequence (TR, 1 s; 20 TEs, 2.5~50 ms; FA, 40°). BOLD images of rat brain were obtained by simultaneously applying gradient-echo (GRE) and spin-echo (SE) EPI sequences (TR, 3s; FOV, 3 x 3cm^2; and matrix number, 64x64) with three different TEs (15, 30, and 70 ms). SI changes from normoxic to hyperoxic respiration were calculated by applying the following equation: % change of SI = (mean $SI_{hyperoxia}$ – mean $SI_{normoxia}$) / mean $SI_{normoxia}$ x 100. Using an inversion recovery EPI sequence, T1 relaxation time of brain was compared between normoxia and hyperoxia.

RESULTS: The results of relaxation time and blood gas analysis are summarized in Table 1. In the blood examinations, increasing oxygen partial pressure from normoxia to hyperoxia led to shortening of T1 relaxation time, which was demonstrated dominantly in arterial blood. In venous blood, it was notably observed that elevated oxygen saturation by hyperoxic breathing increased T2 and T2* relaxation times. Representative BOLD signal changes with different TEs are demonstrated in Figure 1 and changes of SI are summarized in Table 2. The changes of SI in normoxia were not dependent on TEs on either GRE or SE images ($P > .05$). In hyperoxia, longer TE resulted in lower SIs on GRE images ($P < .05$) whereas SE images did not show significant changes. These results indicate that high level of tissue oxygen concentration has significant T2* effects, consequently decreasing SIs in long TEs. T1 relaxation time was decreased from normoxia (1587ms ± 28) to hyperoxia (1509ms ±45) ($P < .05$).

Table 1.

		Relaxation Times [ms]			Blood gas analysis	
		T_1	T_2	T_2^*	pO_2 [mmHg]	SaO_2 [%]
Venous blood (n=4)	Normoxia	1465±21	43.1±15.5	9.2±2.8	51	81
	Hyperoxia	1488±72	73.2±9.2	13.9±3.6	90	94
	% change	1.5	69.7	51.9	76.5	-
Arterial blood (n=3)	Normoxia	1531±27	92.7±0.9	15.6±2.7	87	96
	Hyperoxia	1379±79	94.9±2.1	16.1±2.4	586	100
	% change	-9.9	2.4	3.1	573.5	-

Table 2. The % Changes of GRE and SE BOLD Imaging.

TE[ms]	$\Delta SI_{\_GRE}$ (%)	$\Delta SI_{\_SE}$ (%)
15	-5.9	1.9
30	-23.6	3.6
70	-44.5	11.7

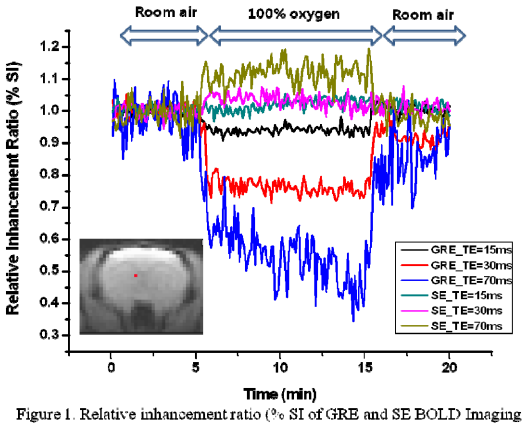

Figure 1. Relative inhancement ratio (% SI of GRE and SE BOLD Imaging

Conclusion: While high oxygen concentration increases SI by decreasing T1 and deoxyHb concentration in blood, elevated tissue oxygen concentration may decrease SI by dominantly amplifying T2* effects over T1 effect. Therefore, it is suggested that positive SI conversion on BOLD MRI is induced predominantly by oxygen effect on blood and negative conversion is related with high tissue oxygen concentration. Furthermore, the direction of BOLD signal change may be dependent on fractional blood volume and oxygen metabolism rate in tissue.

REFERENCES: [1] Yves Berthezene *et. al., AJNR* 16 2010-12 (1995), [2] Y. Ohno. *et al., European Journal of Radiology* 64 320-28 (2007)