Interaction between Magnetization Transfer (MT) and Blood-Oxygen-Level-Dependent (BOLD) Effects

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INTRODUCTION: MT effects are usually quantified using MT ratios (MTR), in which (1-MTR) is the ratio of signal intensities with and without off-resonance irradiation. It is still controversial (1-3) how MT affects signal changes during physiological alterations such as hypercapnia, hypoxia, neural activation, etc. The parenchymal BOLD effect is composed of microvascular and extravascular (tissue) contributions (4). Because MT is much larger in pure tissue than in blood ($MTR_{\text{tissue}} >> MTR_{\text{blood}}$) (5,6), the parenchymal BOLD effect will increase apparently under off-resonance irradiation. We here demonstrate these effects in the rat brain during arterial carbon dioxide tension and provide a quantitative theory capable of describing this MT-BOLD interaction.

THEORY: For parenchyma, the normalized imaging signal intensity as a function of TE is a multi-exponential decay process (4). Assuming complete relaxation ($TR >> T_1$) and negligible MT effect in the blood, which applies best when RF irradiation is far from the water resonance, the situations for an SE acquisition sequence without (unsaturated) and with (saturated) MT are, respectively:

$$S_{\text{par,unsat}} = x_{\text{tissue}}\, e^{-R_{2,\text{tissue}}TE} + \sum_{\text{i}} x_{\text{blood,i}}\, e^{-R_{2,\text{blood,i}}TE} \qquad [1]$$

$$S_{\text{par,sat}} = (1-MTR_{\text{tissue}})\left(x_{\text{tissue}}\, e^{-R_{2,\text{tissue}}TE} + \sum_{\text{i}} x_{\text{blood,i}}\, e^{-R_{2,\text{blood,i}}TE} \right) + MTR_{\text{tissue}} \sum_{\text{i}} x_{\text{blood,i}}\, e^{-R_{2,\text{blood,i}}TE} \qquad [2]$$

where x is the water fraction of a particular component (tissue, arteriole, capillary, venule) and $(1-MTR_{\text{tissue}})$ is the conventional MT signal attenuation in pure tissue. The summation for the blood compartments (i = a, c, and v) takes into account arteriolar, capillary, and venular blood, respectively. To quantify the BOLD-type effect of physiological adjustments, we define the relative signal intensity with respect to a normal physiological state. Assuming unchanged tissue MTR during blood-based physiological changes, this gives:

$$\frac{S_{\text{par,sat}}}{S^{\text{norm}}_{\text{par,sat}}} = (1-MTR_{\text{tissue}})\frac{x_{\text{tissue}}\, e^{-R_{2,\text{tissue}}TE} + \sum x_{\text{blood,i}}\, e^{-R_{2,\text{blood,i}}TE}}{x^{\text{norm}}_{\text{tissue}}\,(1-MTR_{\text{tissue}})\, e^{-R^{\text{norm}}_{2,\text{tissue}}TE} + \sum x^{\text{norm}}_{\text{blood,i}}\, e^{-R^{\text{norm}}_{2,\text{blood,i}}TE}} + MTR_{\text{tissue}}\frac{\sum x_{\text{blood,i}}\, e^{-R_{2,\text{blood,i}}TE}}{x^{\text{norm}}_{\text{tissue}}\,(1-MTR_{\text{tissue}})\, e^{-R^{\text{norm}}_{2,\text{tissue}}TE} + \sum x^{\text{norm}}_{\text{blood,i}}\, e^{-R^{\text{norm}}_{2,\text{blood,i}}TE}} \qquad [3]$$

When applied to quantify the BOLD effect, the first term in this equation is very similar (slightly smaller) to the conventional SE BOLD effects, and the second describes the BOLD enhancement due to RF saturation. In the absence of RF irradiation, MTR_{tissue} = 0, and only the first term remains.

MATERIALS AND METHODS: SD rats (300-400 g, n = 6) were anesthetized with pentobarbital (6 mg/kg/hr, i.p.). Seven successive CO_2 episodes were studied for each rat. Experiments were performed on a 4.7 T GE CSI animal imager. A train of 400 Gaussian pulses (length 6.6 ms, flip angle 180°, delay 3.4 ms, total duration 4 s, average RF power 2 μT) was used for off-resonance irradiation. Four-shot spin-echo EPI (TR 10 s, TE 50 ms) was used for data acquisition. The imaging matrix was 64×64, FOV was 40×40 mm^2, and the imaging slice thickness was 2 mm.

RESULTS AND DISCUSSION: Figure 1 shows the arterial PCO_2 dependence without (a) and with (b) RF saturation for the BOLD-type signal intensities. The solid line in (b) is the result fitted with the theory. To provide a magnitude estimation of the effects, data were also fitted linearly. The fitted slope values (Table 1) show a very similar P_aCO_2 dependence for the positive and negative offset sides. For a P_aCO_2 increase of 100 mmHg, $S_{\text{par,sat}} / S^{\text{norm}}_{\text{par,sat}}$ increases by 11-15%. These slope values for MT-modulated BOLD effect are about two times larger than those for the unsaturated signal intensities (6%), corresponding to the common SE BOLD effect. When arterial PCO_2 increases, CBV and CBF increase. When CBF increases, the tissue oxygen extraction ratio (OER) decreases, leading to decreased $R_{2,\text{blood,c}}$, $R_{2,\text{blood,v}}$, and $R_{2,\text{tissue}}$. When CBV increases, the microvascular blood fractions increase and extravascular tissue signal fractions reduce. The combined effects of these physiological changes cause the classical BOLD effect of parenchyma, giving a signal increase of approximately 6%/100 mmHg, which can be doubled by using off-resonance RF irradiation.

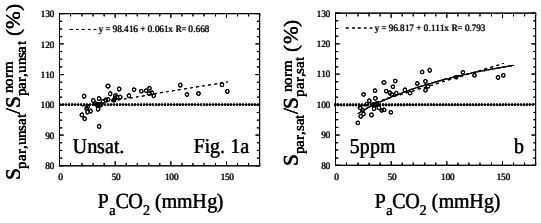

Table 1

Offset (ppm)	Slope Value (%/mmHg)
5	0.111
3.5	0.140
2	0.139
-2	0.139
-3.5	0.145
-5	0.124
Unsat.	0.061

CONCLUSIONS: The presence of weak off-resonance RF irradiation leads to an increased BOLD effect with increased arterial PCO_2 levels. These P_aCO_2 effects are attributed to the increased apparent blood fraction in the parenchyma. The findings in this paper provide a potential approach to image CBV in vivo and to manipulate the BOLD contrast in fMRI studies.

References: 1) Song et al. NMR Biomed. 1997;10:208. 2) Zhang et al. MRM 1997;38:187. 3) Stanisz et al. MRM 2002;47:472. 4) van Zijl et al. Nat. Med. 1998;4:159. 5) Balaban & Ceckler Magn. Reson. Q. 1992;2:116. 6) Pike et al. MRM 1992;25:372.