Changes in T1ρ in Human Brain during Hypercapnic Challenge

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Introduction

While pH regulation is often assumed to be homeostatic, local dynamic pH fluctuations occur in the brain with neural activity and in neurological diseases. Neural activity and disease cause localized acidosis that varies in magnitude and with time. The ability to non-invasively measure brain pH dynamics holds great potential for understanding of the importance of local pH fluctuations in neurological and psychiatric disorder. This study aims to evaluate the utility of $T_{1\rho}$ MR imaging as a method to measure pH dynamics. The sensitivity of $T_{1\rho}$ to pH changes was evaluated in vivo using a CO_2 challenge to manipulate brain pH. A sheep blood phantom study was performed to determine if $T_{1\rho}$ imaging can detect pH independent of blood oxygenation signals.

Methods

MR images of the brain were obtained on a 3.0T Siemens Trio scanner (Siemens Medical Solution, Erlangen Germany) using a 12 channel head coil for RF transmission and reception. $T_{1\rho}$ weighted images were acquired using a turbo spin-echo (TSE) sequence with a spin-locking preparation pulse which created a B_1 field of 500Hz. Imaging parameters were TE=12ms, TR=2s, field of view=240x240mm, imaging matrix size=128x64, bandwidth=130Hz/pixel and slice thickness=3cm, TSL= 20, 40, 60 and 80ms. To evaluate the use of $T_{1\rho}$ to detect changes in human brain pH, $T_{1\rho}$ images were obtained from two subjects after obtaining informed consent. Imaging was performed under three conditions: 1) pre-hypercapnia (breathing room air), 2) hypercapnia (breathing 7.5% CO_2), and 3) post-hypercapnia (breathing room air). Sheep blood phantoms were prepared with fresh sheep blood. pH was adjusted with HCL and NaOH, and oxygen concentration was increased with 100% oxygen gas. pH, pCO_2 and pO_2 were measured before and after imaging with a Radiometer ABL 5 blood gas analyzer. Sheep blood phantom images were obtained on a 4.7T Varian small-bore MRI scanner (Varian, Palo Alto, CA). A single 1mm slice was acquired through the center of the phantoms. T_2^* maps were obtained using a gradient echo sequence with the following parameters: TR=2s, TE=1.7, 2, 3, 6, 9, 12, 14, 16ms. $T_{1\rho}$ maps were obtained with the same resolution with the following parameters: TE=12ms, TR=2s, TSL=10, 20, 40, 60ms, B_1=400Hz. A least squares regression analysis was used to generate T_2^* and $T_{1\rho}$ maps.

Results

Fig 1 shows the subtracted $T_{1\rho}$ maps between hypercapnia (7.5% CO_2) and pre-hypercapnia (Air^1), and between hypercapnia (7.5% CO_2) and post-hypercapnia (Air^2). The red color represents higher acidity while the blue color represents increased alkalinity. During CO_2 inhalation the widespread increases in $T_{1\rho}$ times are consistent with the expected acidosis as compared to the baseline room air condition. During post-hypercapnia $T_{1\rho}$ time returns to a level similar to the pre-hypercapnic phase as shown in Fig 2. T_2^* maps of sheep blood phantoms in control, acidified, and oxygenated conditions (Table 1) as shown in Fig. 3(a) show that BOLD is dependent of the oxygenated state of hemoglobin and independent of the pH of the blood. However, $T_{1\rho}$ increases with a decrease in blood pH and is independent of the oxygenated state of hemoglobin as shown in Fig. 3(b).

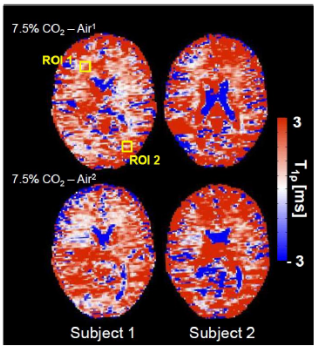

Fig. 1. Subtracted images between the $T_{1\rho}$ map with 7.5% CO2 and the $T_{1\rho}$ map with room air for two subjects.

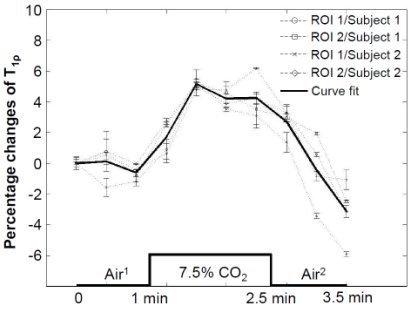

Fig. 2. Percentages of $T_{1\rho}$ times with respiratory challenges. ROIs were defined in white matter as shown in yellow color square in Fig. 1

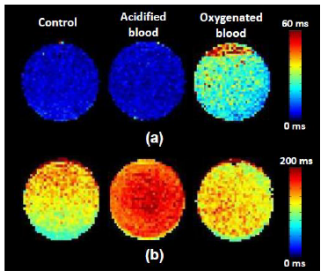

Fig. 3. T_2*(a) and $T_{1\rho}$(b) measurement of blood phantoms across a pH and oxygenated spectrums

	Control		Acidified blood		Oxygenated blood	
	Before	After 30min.	Before	After 30min.	Before	After 30min.
pH	7.12	7.10	6.49	6.49	7.18	7.17
pCO_2	71	73	187	182	52	52
pO_2	25	35	49	50	181	680
$T_{1\rho}$ [ms]	136.8 ± 4.3		173.2 ± 2.7		134.3 ± 3.2	
T_2* [ms]	5.6 ± 0.38		5.5 ± 0.4		26.2 ± 2.9	

Table 1. Blood phantoms with different pH and oxygen content

Discussion and Conclusions

This human study shows that $T_{1\rho}$ imaging is sensitive to pH changes induced by CO_2 inhalation. The respiratory acidosis by breathing 7.5% CO_2 showed increase $T_{1\rho}$ times. In addition, the sheep blood phantom data shows that there is a double dissociation between $T_{1\rho}$ and T_2^* imaging in their sensitivity to pH and blood oxygenation. In conclusion, the ability to non-invasively measure pH dynamics in vivo using $T_{1\rho}$ MRI may offer a novel, more direct approach to map brain functions as well as detect human neurological disease and assess treatment response.

This study was funded by grants from the DANA and McKnight Foundations.