T1ρ Response to the Activity-Dependent Localized Acidosis

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Introduction

Neural activity causes localized acidosis that varies in magnitude and with time. The magnitude of the pH and BOLD effects correlate closely with the stimulation intensity since greater brain activity is likely to generate a larger metabolic response and thus greater pH response [1, 2]. Recently, we found that $T_{1\rho}$ imaging can detect activity-evoked pH changes [3]. We hypothesized that $T_{1\rho}$ and pH changes depend on the degree of brain activity. To test this hypothesis, we used a visual flashing checkerboard with different temporal frequencies to alter the degree of the activation in the visual cortex. Dynamic imaging was performed using $T_{1\rho}$, BOLD, and ^{31}P spectroscopy while viewing the flashing checkerboard with different temporal frequencies.

Methods

Ten subjects (seven males and three females, 26-39 years of age) underwent BOLD, $T_{1\rho}$ study, and ^{31}P spectroscopy. A visual flashing checkerboard with different temporal frequencies of 1, 4, and 7Hz in random orders was presented for the functional and spectroscopic imaging using a block design. For BOLD and $T_{1\rho}$ dynamic imaging, 3 cycles of activation and visual fixation were presented with a 36 second block duration. These studies were repeated twice. For ^{31}P spectroscopy, the task consisted of four blocks each with 5min 18sec duration. MR images of the brain were obtained on a 3.0T Siemens Trio scanner (Siemens Medical Solutions, Erlangen Germany). Functional $T_{1\rho}$ images were collected by using an echo-planar spin-echo sequence (TR/TE=2000/12ms, FOV=220x220mm, matrix size=64x64, and slice thickness/gap=5/1mm) with two spin-lock pulses (10 and 40ms) and B1 frequency of 400Hz. BOLD imaging was performed by using a T_2^* weighted echo-planar gradient-echo sequence (TR/TE=2000/30ms, FOV=220x220mm, matrix size=64x64, and slice thickness/gap=5/1mm). The ^{31}P CSI study was collected using a free induction decay acquisition (TR/TE=4000/2.3ms, FOV=240x240mm, matrix size=8x8, thickness=30mm, average=16, vector size=1024). BOLD and $T_{1\rho}$ data were analyzed by using standard preprocessing steps including motion correction, slice timing correction, and spatial smoothing. $T_{1\rho}$ data were preprocessed by first performing motion correction followed by $T_{1\rho}$ map generation. A general linear model was used to generate individual statistical maps and calculate signal change. BOLD percent signal change and $T_{1\rho}$ time changes were mapped to MNI space where a t-test was performed across the subjects and corrected for multiple comparisons using a false discovery rate analysis. An ANOVA with the visual stimulation frequencies as a factor was performed to assess for effects in the BOLD and $T_{1\rho}$ response, which was used as a measure of brain activity. A contrast between stimulation frequencies (7Hz>1Hz+4Hz) was performed. The threshold for significance in the contrast map was set at $p < 0.05$(corrected). The ^{31}P data was analyzed by using the Siemens Syngo software to determine the chemical shift of the inorganic phosphate (Pi) and phosphocreatine (PCr) peaks in the ^{31}P spectra. The analysis included frequency filtering, frequency and phase correction, and curve fitting with prior knowledge. Brain pH was estimated by using the chemical shift between Pi and PCr in ppm. The pH estimates for the baseline and activation phases with different stimulation frequencies were compared using ANOVA.

Results

Fig 1 shows contrast maps of BOLD and $T_{1\rho}$ response between stimulus frequency of 7Hz and 1Hz+4Hz. Both BOLD and $T_{1\rho}$ responses significantly increased with the visual stimulation frequency. Furthermore, the cluster size of the activated voxels in the visual cortex increased with stimulation frequency as shown in Table 1. Fig 2 shows the BOLD and $T_{1\rho}$ percent signal change across both functional runs. It is observed that the magnitude of the $T_{1\rho}$ response depends on the temporal frequency. Fig 3 shows brain pH changes within visual cortex estimated by ^{31}P spectroscopy. During 4Hz and 7Hz visual stimulation, brain pH significantly decreased relative to the visual fixation (REST) and there was a trend relative to 1Hz visual stimulation (p=0.08). pH was slightly reduced at 1Hz relative to REST, but this was not statistically significant.

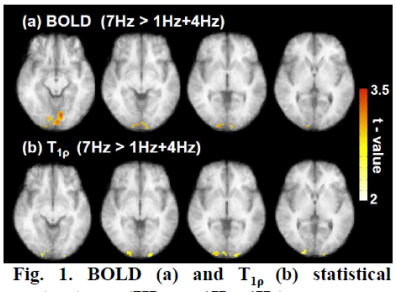

Fig. 1. BOLD (a) and $T_{1\rho}$ (b) statistical contrast map (7Hz vs. 1Hz+4Hz).

		MNI coordinates x	y	z	Cluster size	p
BOLD	1Hz	4	-90	-12	3181	<0.01
	4Hz	2	-88	-15	3257	<0.01
	7Hz	2	-88	-15	3546	<0.01
$T_{1\rho}$	1Hz	-26	-99	-8	26	<0.05
	4Hz	22 -2	-91 -101	0 3	162 35	<0.05
	7Hz	4 -18	-85 -99	-3 -10	359 128	<0.05

Table 1. MNI coordinates of the center of mass in activated cluster and cluster size.

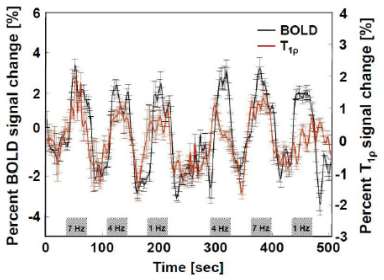

Fig. 2. Percentage changes of BOLD signal and $T_{1\rho}$ times during visual stimulation.

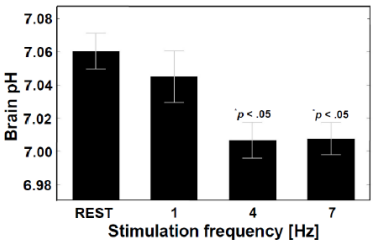

Fig. 3. Brain pH changes during different stimulus temporal frequencies.

Discussion and Conclusions

This study shows that $T_{1\rho}$ and pH changes depend on the degree of brain activity. Furthermore, this works shows a strong correlation between $T_{1\rho}$ and pH estimated by ^{31}P spectroscopy. Consequently, our findings support the hypothesis that dynamic $T_{1\rho}$ imaging is detecting activity-evoked pH changes.

References

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