Separation of the vascular and tissue contributions to the T1rho change induced by brain activation

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Introduction

$T_{1\rho}$ is the spin-lattice relaxation time in the rotating frame during application of an on-resonance spin-locking pulse. Recently, we reported an activation induced decrease of $R_{1\rho}$ (=1/ $T_{1\rho}$) at the parenchyma of cat visual cortex [1]. It has been proposed by Hulvershorn et al. in a previous human visual stimulation study at 3 T that such functional $T_{1\rho}$ change can largely be attributed to an increase of cerebral blood volume (CBV), though other effects may also contribute [2]. Since $T_{1\rho}$ of tissue water has been found to be sensitive to many physiological parameters such as intracellular pH level [3], macromolecular composition and density, it is of particular interest to investigate whether the functional decrease of $R_{1\rho}$ at the parenchyma has a significant contribution from the extravascular tissue, which may have a different signal source from the hemodynamic response. In this work, we measured the functional response of $T_{1\rho}$ with and without the suppression of the intravascular blood signal by injecting a contrast agent.

Materials and methods

All MR experiments were carried out on a 9.4T/31-cm magnet (Magnex) interfaced to a Unity INOVA console (Varian). Four adolescent cats were anesthetized and kept under normal physiological conditions. A 1.6-cm diameter surface coil was used for high spatial resolution and high sensitivity. To achieve spin-locking (SL), the pulse sequence utilizes a non-selective adiabatic SL preparation [4], where after a 2-ms adiabatic half passage pulse the RF amplitude is decreased to the desired SL field (B_1) and then held constant for the spin-locking time (TSL). Following SL, transverse spins were imaged with double spin-echo (SE) EPI acquisition. For fMRI, a transverse slice was chosen with imaging parameters: 2×2 cm^2 FOV, 2 mm slice thickness, 64×64 matrix size, TE = 25 ms, and a repetition time (TR) of 2 s. The spin-locking frequency averaged over the gray matter of the visual cortex was $\omega_{1,SL}$ = ~500 Hz. An fMRI run of single-shot SE-EPI images with TSL of 0 or 50 ms duration was acquired sequentially, and the order of the two TSL values were reversed for different runs. The visual stimulus was a high contrast black and white square-wave drifting grating. The experiments were performed in the same session before and after an intravenous injection of ~3-5mg/kg monocrystalline iron oxide nanoparticles (MION). The block-design stimulation paradigm was 40 s control, 40 s stimulation, and 60 s control. Images were first zero-filled to 128x128, and then smoothed by a Gaussian Filter (FWHM = 3 pixels) to minimize the ringing artifacts. Functional $R_{1\rho}$ responses were calculated by pixel-wise fitting to a mono-exponential decay on TSL for each time point. The data with TSL = 0 before MION injection represents the SE-BOLD response. The percentage change maps were calculated for the SE-BOLD and the $R_{1\rho}$ responses, where activated pixels pass a Students' *t*-test threshold of $p<0.01$ and a minimal cluster size of 4 pixels. An ROI was chosen at the middle of the parenchyma based on the anatomical image (not shown), and time courses were obtained from the same ROI *regardless of* whether the pixels met the activation criteria.

Results and discussions

Functional signal increase is detected mostly within the gray matter in both SE-BOLD (Fig. 1A) and $T_{1\rho}$-weighted maps (Fig. 1B) before the MION injection, but the percentage change within the parenchyma is higher with SL preparation (more yellow pixels in Fig. 1B). The calculated relative $R_{1\rho}$ change map (Fig. 1C) shows decrease of $R_{1\rho}$ in the parenchyma but increase of $R_{1\rho}$ for some pixels at the cortical surface, similar to our previous report [1]. After the intravascular blood is suppressed by MION injection, the number of $R_{1\rho}$-decreasing pixels reduced at the parenchyma, but more $R_{1\rho}$-increasing pixels appeared at the cortical surface (Fig. 1D). Note that the data after MION were averaged two times more than those before MION, thus Fig. 1D has a higher SNR than Fig. 1C. In Fig. 1D, the $R_{1\rho}$-increasing pixels locates very well on the boundary of the gray matter and the cerebrospinal fluid (CSF), confirming the hypothesis that it is caused by an activation induced reduction in the CSF partial volume [1]. Because the $R_{1\rho}$ value of CSF (3-4 s^{-1}) is much smaller than that of tissue water (~20 s^{-1}), a small reduction in CSF volume fraction at pixels where tissue and CSF coexist would lead to an increase in $R_{1\rho}$. Such a functional change of CSF partial volume has also been observed in our recent fMRI measurements of the apparent diffusion coefficient [5]. The difference in Fig. 1C and 1D indicated that the effect of blood vessel dilation contributed to the $R_{1\rho}$ change both at the parenchyma as well as at the cortical surface.

Fig. 2 shows the time courses of the $R_{1\rho}$ responses obtained from a middle cortical ROI before and after the MION injection, where the stimulation period is indicated by the dotted gray box. The averaged relative $R_{1\rho}$ decrease at a middle cortical ROI is about -0.4% before the MION injection and is –0.25% after (n = 4). Thus, extravascular contribution accounts for about 60% of the total parenchymal $R_{1\rho}$ change in our case. Although small in magnitude, the decrease of extravascular $R_{1\rho}$ is consistently observed for all four preliminary studies. This change of $R_{1\rho}$ is not caused by the change of intravascular susceptibility effect, because compared with R_2, $R_{1\rho}$ is much less affected by the change of field inhomogeneity with our SL frequency of 500 Hz [1,2]. Moreover, with our small MION dose, for an imaging voxel at the middle of the cortex the effects of CBV and BOLD changes nearly canceled out [5], i.e., the $\Delta S/S$ or R_2 change is minimal (data not shown). Because the $R_{1\rho}$ map is calculated from two time-matched acquisitions with same parameters except two different TSL values, hemodynamic contributions such as the change of CBV and CBF are expected to be equal for the two acquisition and thus would be canceled out. Therefore, the observed extravascular $R_{1\rho}$ change may not be caused by hemodynamic effects. The exact signal source of this tissue $R_{1\rho}$ change would require further study.

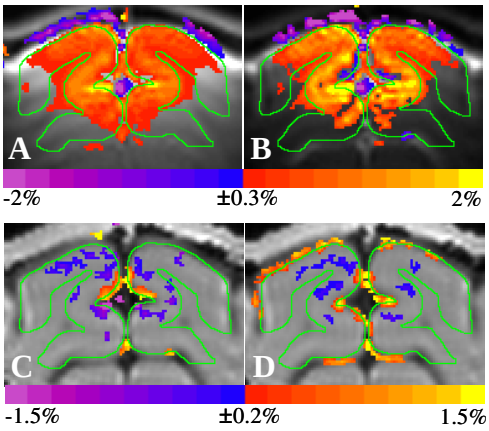

Fig. 1 Functional maps of SE-BOLD (A) and the $T_{1\rho}$ -weighted fMRI (B) without MION show signal increase at the gray matter (outlined in green). $R_{1\rho}$ decreases at the parenchyma while increases at the cortical surface for both experiments without (C) and with (D) MION.

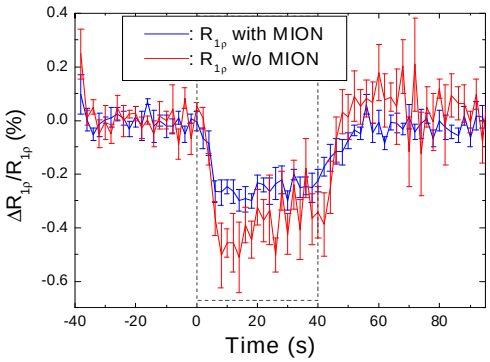

Fig. 2 The normalized time courses (n = 4) of $R_{1\rho}$ at the middle cortical ROI show small relative changes before and after MION injection.

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References: [1] Jin T and Kim S-G, *PISMRM* p2389 (2008). [2]. Hulvershorn J et al., *MRM* 54:1155-1162 (2005). [3]. Kettunen MI et al., *MRM* 48:470-477 (2002). [4] Grohn HI et al., *MRM* 51:4-8 (2004). [5] Jin T and Kim S-G, *NeuroImage*, 41:801-812 (2008).