Simultaneous SE-BOLD and T2* Measurement by Functional MRS of Water Signal

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INTRODUCTION: Blood-oxygen-level-dependent (BOLD) contrast is known to be modulated by vascular origins such as intravascular, extravascular, venular and capillary. The relative contributions of these factors to BOLD signal is dependent of magnetic field strength and whether spin echo (SE) or gradient echo (GE) detection is used [1, 2]. Characterization of SE and GE BOLD may provide new perspectives to our understanding of BOLD mechanism. However, here is a lack of methods to simultaneously measure SE-BOLD and GE-BOLD, the precise comparison of SE and GE BOLD signals can be compromised due to scan to scan variations. By using MRS voxel selective excitation method (e.g. PRESS) instead of the conventional imaging method (e.g. EPI), the acquired SE-FID contains both SE-BOLD (i.e., amplitude of SE) and the T2* (i.e., the FID decay rate) information. Taking advantage of predominantly extravascular signal at 7T and the complete absence of static dephasing effects due to the pure SE measurement, the direct comparison between simultaneously acquired SE-BOLD and T2* information may provide insights into the BOLD mechanism. In this study, we investigated the auditory activation characteristics in inferior colliculus (IC) using dynamic single voxel MRS.

MATERIALS AND METHODS: Animals: Male Sprague-Dawley rats (N = 4) were employed. Animals were anesthetized with 1% isoflurane and mechanically ventilated. A receive-only quadrature surface coil was placed over the dorsal surface of rat head. The sound transmission tube was inserted into the right ear. Animal rectal temperature, respiration rate, heart rate, and oxygen saturation were monitored (SA Instruments). **Acoustic stimulation**: Stimulation during fMRI was transmitted from a high frequency speaker (MF1, TDT) to the animal's right ear. The stimulus was a bandlimited noise burst pulsed at 10Hz and 85dB SPL. The stimulus was set such that most of IC regions could be stimulated. The stimulus was presented in a block design paradigm with 40s stimulus off followed by four repetitions of 20s stimulus off and 40s stimulus on [3]. **MR experiments**: fMRS experiments were performed on a 7T MRI Bruker scanner. One standard GE-EPI fMRI (with TE/TR=20/1000ms) was first acquired with block design stimulation paradigm [3]. Period cross correlation was applied to identify the IC regions activated by the acoustic stimuli (cc>0.2, cluster>3). Then PRESS region of interest (ROI) with a fixed size of $2.24\times3\times2.3mm^3$ was placed on the active region of left IC based on the cc map (obtained by GE-EPI fMRI) and high resolution T2WI. This ensured the ROI spanned the same brain region in different animals. One fMRS acquisition, consisting of dynamic PRESS acquisition and block design paradigm, lasted for 280s. PRESS sequence used TE/TR = 40/1000ms, 280 repetitions, triggered by ventilator and no water suppression. Another PRESS acquisition with diffusion weighting was performed with δ/Δ =5/15ms and b=600s/mm^2. All scans were repeated six times per animal. In total, 48 PRESS datasets were acquired. 5 datasets that showed apparent baseline distortion were excluded before the data analysis. **Data Analysis**: Analysis of PRESS dataset was performed using JMRUI software. Amplitude of SE and T2* were quantified by fitting the FID signal to a Lorentzian line shape using AMARES algorithm. Detrending for removing baseline drifting (only removed linear trend) was applied to each hemodynamic response before the summation and further analysis.

RESULTS AND DISCUSSIONS: Fig.1a shows the PRESS ROI that covered the active regain of left IC. Fig. 1b illustrates the SE-BOLD and T2* can be calculated as the amplitude and the decay rate of FID. Fig. 2 shows the stack view of a set of SE-FIDs acquired during stimulation, computed SE-BOLD and T2* time courses from one representative animal. Four essential elements (i.e., PRESS sequence, mechanical ventilation and synchronization with MR acquisition and baseline detrending) together provided robust measurement of BOLD SE and T2* time courses (Fig. 2b). As seen in Figs. 3a and 3c, the BOLD signal changes with and without diffusion weighting were similar, suggesting that the predominantly extravascular signal was measured because of the intravascular signal suppression by diffusion weighting, the high field strength (i.e., 7T) and relatively long TE (40ms). In Figs. 3b and 3d, SE-BOLD and T2* hemodynamic responses were closely correlated largely in a linear manner (Fig. 3b). They were also largely overlapped during the post-stimulation undershoot after scaling (Fig.3b). This observation was in line with a previous study that demonstrated no difference in temporal response in terms of positive/negative ratio between SE and GE at 3T [4]. The authors argued that that if the undershoot in GE was solely caused by CBV effects, post-stimulation undershoot should have been absent in the pure SE data [4]. An recent review commented on this argument that it holds true for extravascular signal, but a delayed recovery of CBV in venules or capillaries could in principle cause a undershoot for both SE and GE data due to the short vessel water T2 [1]. In present study, the temporal characteristics (including post-stimulation undershoot) of SE-BOLD and T2* were similar and were mainly from exptravascular signal when large b value was used. Therefore, the present finding could serve as evidence for that post-stimulus undershoot is caused by elevated post-stimulus deoxyhemoglobin concentration in the small vessels. As shown by Figs.3b and 3d, the T2*/SE-BOLD ratio increased from 2.3 to 2.7 after applying diffusion gradient. This might be caused by the diffusion suppression of arterial signal that has relatively long T2.

CONCLUSION: Our experiment demonstrated that fMRS could measure the SE-BOLD and T2* changes simultaneously. For the first time, the SE-BOLD and T2* from the same fMRS scan were directly compared. The results revealed the similarity between these two independent BOLD contrasts. Regarding post-stimulation undershoot, our result supported that post-stimulation undershoot is mainly caused by elevated post-stimulus deoxyhemoglobin concentration in the small vessels.

REFERENCES: 1. van Zijl P. C., Neuroimage 2012;62:1092-102; **2.** van Zijl P. C., Neuroimage 2012;62:1092-102; **3.** Norris D. G. Neuroimage 2012;62:1109-15; **4.** Norris D. G. Neuroimage 2012;62:1109-15.

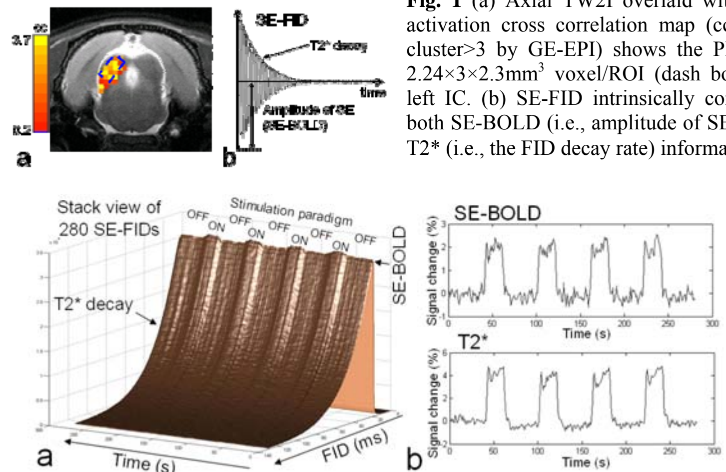

Fig. 1 (a) Axial TW2I overlaid with the activation cross correlation map (cc>0.2, cluster>3 by GE-EPI) shows the PRESS $2.24\times3\times2.3mm^3$ voxel/ROI (dash box) in left IC. (b) SE-FID intrinsically contains both SE-BOLD (i.e., amplitude of SE) and T2* (i.e., the FID decay rate) information.

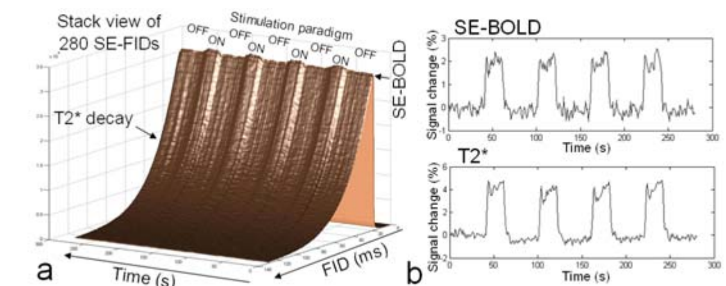

Fig. 2 SE-FIDs, SE-BOLD, and T2* acquired from one representative animal. (a) Stack view of 280 SE-FIDs that were averaged across six scans. (b) SE-BOLD and T2* time profiles derived from the same SE-FID dataset.

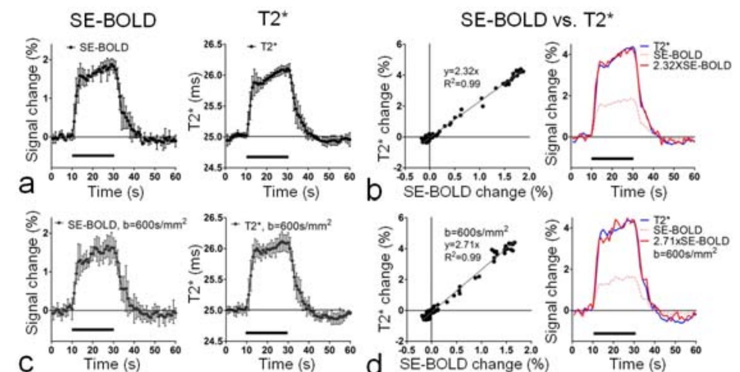

Fig. 3 (a) Time courses of SE-BOLD and T2* averaged across four blocks and four animals (mean±standard deviation). (b) Scatter plots of SE-BOLD and T2*, and their overlaid view, including magnified SE-BOLD. (c-d) Same measurements but with diffusion weighting (b=600s/mm^2) to eliminate the intravascular signal.