Correlations between BOLD and neurochemical responses measured in the human visual cortex at 7T

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Introduction. In the recent years, functional magnetic resonance spectroscopy (fMRS) has been used to investigate the brain metabolic responses to visual stimulations in the human brain. The published fMRS studies conducted at 7T [1-3] demonstrated high consistency of results and proved the ability of fMRS to measure very small changes in metabolite concentrations that indicate increased oxidative neuronal metabolism. However, to which extent the amplitude of metabolite concentration changes measured by fMRS mirror the amplitude of the blood oxygenation level dependent (BOLD) signals has not been investigated yet. The aim of the current study was to correlate the neurochemical responses measured by fMRS with the metabolic/hemodynamic responses measured by the BOLD effect.

Methods. Twelve healthy volunteers were enrolled for the fMRS/fMRI studies conducted on at 7T/90cm Agilent magnet interfaced to Siemens console. The fMRI and fMRS paradigms, along with the metabolite concentration changes were reported previously. [4] Using the same voxel utilized for the fMRS paradigm, the unsuppressed water spectra were measured per each subject during a 30s STIM - 30s REST paradigm, and the BOLD effect was derived as a line-width change of the water peak (ΔLW_{water}). Moreover, the line-width changes between STIM and REST conditions during the ~25min fMRS paradigm were evaluated per each subject using the creatine (Cr) peak at 3ppm (ΔLW_{Cr}). In order to avoid possible biases of LCModel quantification due to line-width changes,[5] metabolite concentrations were thus quantified also after line-matching the spectra acquired in STIM and REST conditions (i.e., by line-broadening the STIM spectra by ΔLW_{Cr}). Finally, a voxel mask was imported per each subject into the fMRI time-series, and the average BOLD-fMRI amplitude within the voxel was calculated using in-house written MATLAB script and SPM8 package.

Results and Discussion. The functional concentration changes in lactate (Lac), glutamate (Glu), glucose (Glc) and aspartate (Asp) observed after line-matching the STIM and REST spectra per each subject were very similar to what reported previously [4] For instance, Δ[Glu] decreased on average only by 0.06 μmol/g after line-width matching the STIM and REST spectra. The BOLD effect measured by ΔLW_{water} was strongly correlated with the BOLD effect measured by fMRI (R=0.92, p=0.0002), indicating that ΔLW_{water} during a short 60s paradigm is a good representation of the BOLD effect. On the other hand, the ΔLW_{Cr} observed during the long fMRS paradigm was less strongly correlated with BOLD-fMRI (R=0.76, p=0.0062), indicating that ΔLW_{Cr} are influenced by factors other than BOLD such as subject movement, and therefore should not be used as a reliable representation of the BOLD effect.

A strong positive correlation was observed between the amplitude of the Δ[Glu] changes and the BOLD-fMRI signals (R=0.81,p=0.0021), which remained significant also after accounting for the LW effect on LCModel quantification (R=0.67, p=0.024) (Fig 2). A trend for a correlation with BOLD-fMRI was observed for Δ[Lac] (R=0.48, p=0.13) and Δ[Glc] (R=0.64, p=0.12), but not for Δ[Asp] (R=0.29, p=0.38), likely due to less reliable quantification of such metabolites. Finally, baseline concentrations of all quantified metabolites were not correlated with the BOLD-fMRI response except for GABA for which a negative correlation with BOLD was found (R=-0.65, p=0.043) (Fig.3) in agreement with findings obtained at lower field (3T) with edited ^{1}H MRS.[6]

Conclusions: Despite the performance of LCModel is generally robust against LW changes, the subtle LW effect on LCModel quantification needs to be taken into account during fMRS experiments, especially to evaluate correlations between neurochemical changes and the BOLD effect.

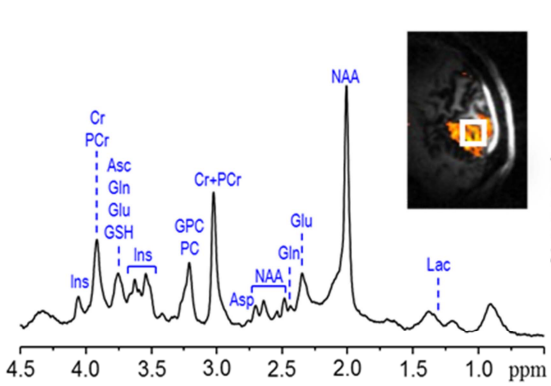

Fig.1. Metabolite spectrum from one representative subject. Semi-LASER (TR=5s,TE=26ms, NT=32, VOI=8mL).

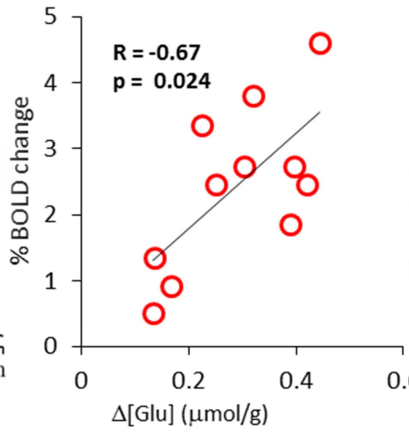

Fig.2. Correlation between the BOLD-fMRI effect and Δ[Glu] measured during visual stimulation.

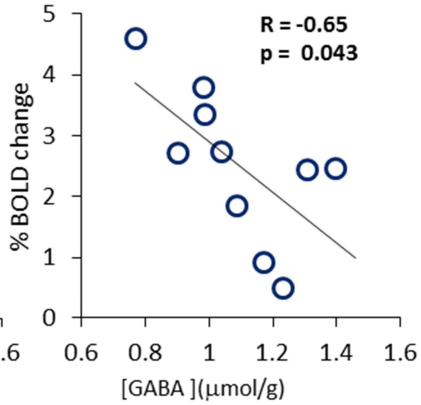

Fig.3. Correlation between the BOLD-fMRI effect and baseline GABA concentration.

References : 1. Lin et al JCBFM 2012; 32(8): 1484 **2**. Mangia et al. JCBFM 2007; 27(5): 1055 **3**. Schaller et al. Journal of Neurosc Res 2013; 91(8): 1076 **4**. Bednarik et al ISMRM 2013 **5.** Mangia et al.MRI 2006; 24(4): 343 **6**. Donahue et al. NeuroImage 2010; 53(2): 392.

Acknowledgements: CEITEC (CZ.1.05/1.1.00/02.0068) from ERDF, NIH P41 RR008079, P41 EB015894, P30 NS076408, 1UL1RR033183-01, 8UL1TR000114-02.