Detection of Metabolite Changes in Response to a Varying Visual Stimulation Paradigm Using Short TE $^1$H MRS at 7T


Target Audience MR spectroscopists, neuroscientists

Purpose The twofold benefit for $^1$H MR spectroscopy (MRS) at high $B_0$ fields (≥ 3T) – enhanced sensitivity and increased spectral dispersion – has previously been used to study dynamic changes of metabolite concentrations in the human brain in response to visual stimulation. In these studies, a strong visual on/off stimulus was combined with MRS data acquisition in a voxel location in the occipital cortex determined by an initial fMRI experiment. However, 1) to exclude the possibility of systemic effects (heartbeat, blood flow, etc.), which tend to be different for on/off conditions, a modified stimulation condition not affecting the target voxel needs to be employed, and 2) to assess important neurotransmitters of low concentration, in particular γ-aminobutyric acid (GABA), it might be advantageous to analyze steady-state, rather than dynamic conditions. Thus, the aim of this study was to use short TE $^1$H MRS methodology at 7T to detect differences in steady-state metabolite levels in response to a varying stimulation paradigm in the right human visual cortex.

Methods Scans were performed on a 7T whole-body system (Siemens Healthcare, Erlangen, Germany) using a custom-built shielded quadrature Tx/Rx surface RF coil. First- and second-order shims were adjusted using the spin echo full intensity acquired localized (SPECIAL) MRS technique with $\text{VOI} = 20 \times 20 \times 20 \text{ mm}^3$, TR/TE = 5000/6.0 ms, number of averages = 128, and $\gamma_{p} = 512 \text{ ms}$. Metabolite quantification was performed using LCModel. For visual stimulation, a rotating half-circle was projected onto one side of a screen (e.g. left = stimu_left), while subjects were asked to focus on a small cross in the center of the circle. The scan was subsequently repeated (same voxel) with the projection switched to the opposite side (right = stimu_right) (Fig. 1). Order of left-right projection was randomized across subjects. It was hypothesized for GABA to decrease and for glutamate (Glu) and lactate (Lac) to rise under activation. Therefore, differences in steady-state metabolite concentrations for left-right stimulation were evaluated using a one-tailed paired Student’s t-test.

Results Localized shimming resulted in water linewidths of 12.7 ± 0.8 Hz. The high spectral quality obtained (Fig. 2) enabled the quantification of 19 metabolites with Cramér-Rao lower bounds (CRLBs) < 20% including GABA, Glu, glutamine (Gln), and (Lac). Due to contra-lateral activation the selected voxel is strongly activated during stimu_left, and not or only very mildly activated during stimu_right. The average concentration of GABA was reduced by 0.06 mmol/l (9%), whereas that of Lac was increased by 0.04 mmol/l (8%) during stimu_left compared to to stimu_right (Table 1). Both changes were significant (p < 0.01). No other significant concentration changes were observed.

Discussion Using the spin echo-based SPECIAL MRS technique with short TE at 7T facilitated the detection of small differences in metabolite concentrations in the human visual cortex when comparing two different stimulation conditions. The observed reduction of the inhibitory neurotransmitter GABA can be interpreted as reduced neuronal inhibition during stimu_left, while the increase in Lac hints at an intensification of anaerobic glycolysis. The latter was also an outcome of previous studies, albeit more pronounced, while the former was not. These disparities including the absence of any changes in Glu, a precursor of GABA, but also suspected to cause Lac production, can be attributed to the different experimental and stimulus paradigm used in this study. E.g., the smaller increase in Lac can be explained by the less pronounced difference between stimu_left and stimu_right versus on and off conditions.

Conclusion Using advanced $^1$H MRS methodology at 7T it is possible to detect subtle changes in steady-state concentrations of metabolites involved in neuronal activation and inhibition including important neurotransmitters, such as GABA in a selected hemisphere.