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

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Target Audience   MR spectroscopists, neuroscientists

Purpose   The twofold benefit for ^{1}H MR spectroscopy (MRS) at high B_0 fields ($\geq 3T$) – 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[1,2]. 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-aminobutric 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.

Fig. 1. Stimulation paradigm and MRS voxel position for stimu_left (top) and stimu_right (bottom).
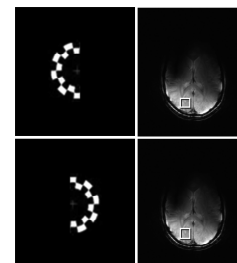
Methods   Scans were performed on a 7T whole-body system (Siemens Healthcare, Erlangen, Germany) using a custom-built shielded quadrature Tx/Rx surface RF coil. First- and second-order shims were adjusted using FAST(EST)MAP[3]. In one session, single volume data from the right visual cortex were acquired twice for N = 11 volunteers using the spin echo full intensity acquired localized (SPECIAL) MRS technique[4,5] with the following scan parameters: VOI = 20x20x20 mm^3, TR/TE = 5000/6.0 ms, number of averages = 128, and T_{acq} = 512 ms. Metabolite quantification was performed using LCModel[6]. 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.

Metabolite	stimu_left		stimu_right	
	Conc. (mmol/l)	CRLB (%)	Conc. (mmol/l)	CRLB (%)
GABA	**0.62 ± 0.16**	**8 ± 2.0**	**0.68 ± 0.17**	**7 ± 1.8**
Lac	**0.54 ± 0.06**	**6 ± 0.8**	**0.50 ± 0.08**	**7 ± 1.4**
Glu	5.60 ± 0.52	1 ± 0.5	5.63 ± 0.53	2 ± 0.5

Table 1. Quantification of selected metabolites for left-right stimulation. Absolute concentrations and Cramér-Rao lower bounds (CRLBs) are given as mean values ± standard deviations. For calculating absolute concentrations, the water signal from the VOI was used as reference. No corrections for relaxation effects or brain fractions were performed. Significant changes (p < 0.01) are in bold.

Results   Localized shimming resulted in water linewidths of 12.7 ± 0.8 Hz. The high spectra 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[1,2], 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[7] 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.

Fig. 2. [1]H spectra from the right visual cortex of a healthy volunteer acquired with the SPECIAL sequence during stimu_left condition. Data processing consisted of zero-filling up to 8-k data points, 2 Hz Gaussian weighting of the FID, Fourier transformation, and phase correction.
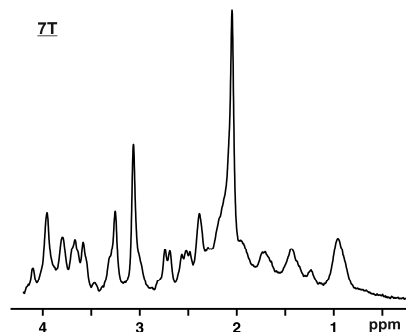
References   1. S. Mangia et al., MagnResImaging, 24(4), 343-8, 2006; 2. B. Schaller et al., J Neurosci Res, 91(8), 1076-83, 2013; 3. R. Gruetter et al., MRM, 43(2), 319-23. 2000; 4. V. Mlynarik et al., MRM, 56(5), 965-70, 2006; 5. R. Mekle et al., MRM, 61(6), 1279-85, 2009; 6. S.W. Provencher, MRM, 30(6), 672-79, 1993, 7. Mangia et al., J Cerebral Blood Flow Metab 29(3), 441-63, 2009.