

# Human studies of functional MRS at 7T with semi-LASER

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## Introduction

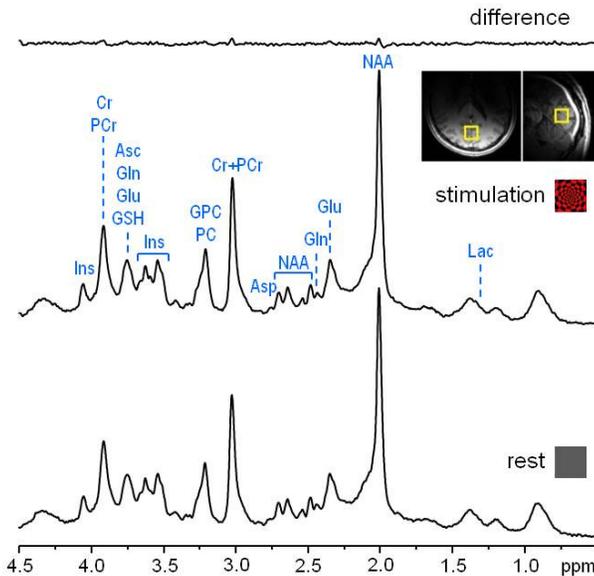
In the last years, several functional MRS (fMRS) studies from our group<sup>1</sup> and from other labs<sup>2,3</sup> have consistently demonstrated small but significant variations in concentrations of few brain metabolites in the activated human visual cortex during prolonged visual stimuli. In particular, the levels of lactate, glutamate, glucose and aspartate have been observed to change within  $\pm 0.2 \mu\text{mol/g}$  during visual stimuli<sup>1-3</sup>. Concentration changes of glutamine, glutathione, glycine and GABA have also been reported during achromatic visual stimuli (i.e., white/black checkerboard)<sup>2</sup>. Given the small concentration changes, ultra-high magnetic fields and optimized acquisition strategies are critical for conducting fMRS studies. In our previous fMRS work<sup>1</sup>, we utilized STEAM at 7 T for spectra acquisition. Most recently, spin-echo-like sequence (SPECIAL) have been used to benefit from the full-intensity MRS signal and improve sensitivity of detection in fMRS studies<sup>3</sup>. The aim of the present study was to determine whether concentration changes of glutamine, glutathione, glycine and GABA<sup>2</sup> are observed when using a full-intensity <sup>1</sup>H MRS sequence at 7 T, namely semi-LASER<sup>4</sup>, during the presentation of the same chromatic visual stimuli that we used previously (i.e., red/black checkerboard).

## Methods

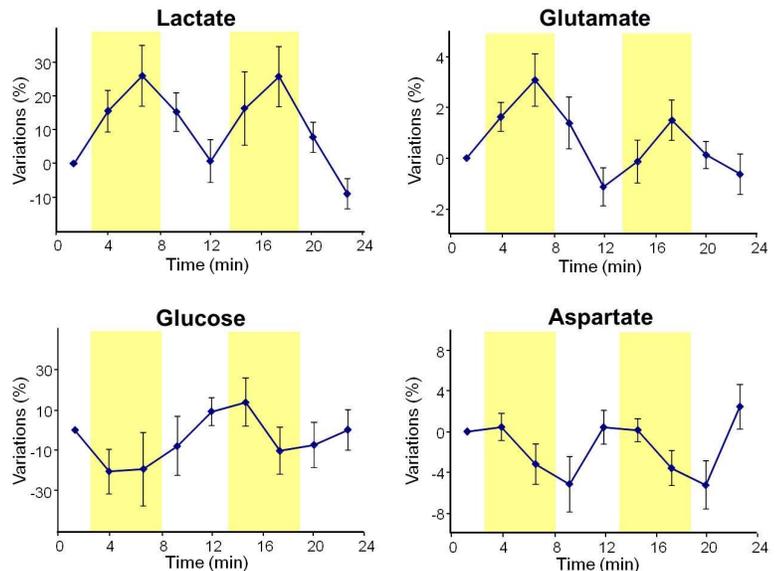
Nine healthy volunteers were examined on a 7T/90cm actively shielded Agilent magnet interfaced to Siemens console. To obtain full-intensity spectra, we utilized an optimized semi-LASER sequence<sup>4</sup>, with TE = 26 ms, TR = 5 s. Spectra were acquired with a quadrature half-volume RF coil from a 8-ml voxel localized in the primary visual cortex, during the same block-design visual stimulation paradigm as used previously<sup>1</sup>. The stimulus consisted of a rotating red/black checkerboard covering the entire visual field and flickering at a frequency of 8 Hz, while the rest condition consisted of a uniform dark background. Single scan FIDs of each subject were corrected for small frequency and phase fluctuations, summed in nine blocks of 32 scans, corrected for residual eddy currents, and finally analyzed by LCModel with simulated basis set<sup>5</sup>. Group analysis of metabolite concentrations at different time-points were performed with two-side paired t-test.

## Results and discussion

Semi-LASER spectra acquired during rest and stimulation conditions from a representative subject are shown in Fig.1. As expected, semi-LASER generally resulted in 2-fold increase of signal-to-noise (SNR) compared to STEAM. While such SNR gain could be leveraged for increased time-resolution of metabolite time-courses relative to our previous fMRS studies, we decided to use it for improving sensitivity of detection. The group analysis (Fig. 2) revealed metabolite time-courses strikingly similar to previous findings<sup>1,3</sup>. Significant concentration changes within  $\pm 0.2 \mu\text{mol/g}$  were indeed observed between stimulation periods and following rest periods ( $p < 0.05$ ) for lactate (+26%), glutamate (+3%), aspartate (-5%) and glucose (-18%). Notably, for all other 12 quantified metabolites, changes did not reach statistical significance, despite increased sensitivity. We conclude that concentration changes in glutamine, glutathione, glycine and GABA observed in other studies<sup>2</sup> are likely to be ascribed to the particular settings of the visual stimulation paradigm (e.g., chromatic vs achromatic visual stimuli).



**Fig. 1:** Semi-LASER spectra from the visual cortex during rest and stimulation. TE=26 ms, TR=5 s, NT=32, VOI=20x20x20 mm<sup>3</sup>. Inset: sagittal and transverse MP-RAGE MRI. Narrow peaks in the difference spectrum at Cr and NAA resonance frequency arise from linewidth changes due to the BOLD effect.



**Fig. 2:** Time-courses in percentage units of selected metabolites during the functional paradigm. Data are mean  $\pm$  SEM. N=9. Concentrations of the shown metabolites during stimulation periods are statistically different from the following rest periods ( $p < 0.05$ ). Shaded areas indicate stimulation periods.

**References:** [1] Mangia et al, JCBFM (2007) 27:1055. [2] Lin et al, JCBFM (2012) 32:1484. [3] Schaller et al, ISMRM (2011) Montréal, Canada. [4] Oz and Tkac, MRM (2011) 65:901. [5] Provencher, MRM (1993) 30:672. **Acknowledgments:** NIH P41RR08079 and P41EB015894, NIH P30 NS057091 and P30 NS076408, S10 RR26783, ADA 07-07-DC2, NIH KL2 RR033182, W. M. Keck Foundation and MIND Institute, CEITEC (CZ.1.05/1.1.00/02.0068) from ERDF.