Dynamics of human brain metabolites during prolonged visual stimulation as revealed by 1H-MRS at 7 T

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Introduction

Localized ^{1}H-MRS has been used to identify in humans variations of metabolite concentrations, primarily lactate, using a variety of stimuli [1-5]. The results have been contradictory even for very similar paradigms; for example, long photic stimuli were reported to cause either 50–60% [1,3] or 150% [2] transient increases in lactate concentration. In addition, lactate is a low concentration metabolite (about 1 µmol/g) and therefore its reliable detection even in basal condition was not always possible. In this context, the increased sensitivity afforded at ultra-high magnetic field (7 T) can provide more reliable and accurate time-courses of metabolites, with a detection threshold that has been shown to be equal to 0.2 µmol/g [6]. The aim of the present study was to determine the time-course of lactate and other metabolites during prolonged visual stimulation at 7 T.

Methods

Twelve healthy volunteers were examined on a 7T/90 cm magnet (Magnex Scientific, UK), interfaced to Varian INOVA console. Ultra-short echo-time STEAM (TE = 6 ms, TR = 5 s) [7] was used to acquire spectra from a voxel localized in the primary visual cortex, during the following paradigm of visual stimulation: 32 scans OFF – 64 scans ON – 64 scans - 64 scans ON – 64 scans OFF, similar to [3]. The stimulus consisted of a rotating red/black checkerboard covering the entire visual field and flickering at a frequency of 8 Hz. After having applied frequency and phase corrections on single scans, 9 spectra (32 scans each) were obtained, then corrected for residual eddy currents, and finally analyzed by LCModel with simulated basis set [8]. Metabolites quantified with Cramer Rao Lower Bounds (CRLB) < 30% were included in the analysis.

Results and discussion

Spectra obtained during rest and stimulation conditions from a single subject are shown in Fig.1. Sixteen brain metabolites were quantified by LCModel with CRLB < 30%. The group analysis (Fig. 2) revealed significant concentration changes between stimulation periods and following rest periods ($p<0.05$) for lactate (+20%), glutamate (+2%), aspartate (-20%) and glucose (-15%). In general, changes in metabolite concentrations were within ±0.2 µmol/g, whereas, for all other metabolites, changes did not reach statistical significance. The increase in lactate and the decrease in glucose reported in the present study qualitatively agreed with previous findings [3], but we observed a persistent increase in lactate within 1-2 min of 0.2 µmol/g, that was restored to baseline after the stimulus ended. Furthermore, we reported significant changes of opposite sign in aspartate and glutamate, implicating that amino-acid homeostasis is affected by physiological stimulations.

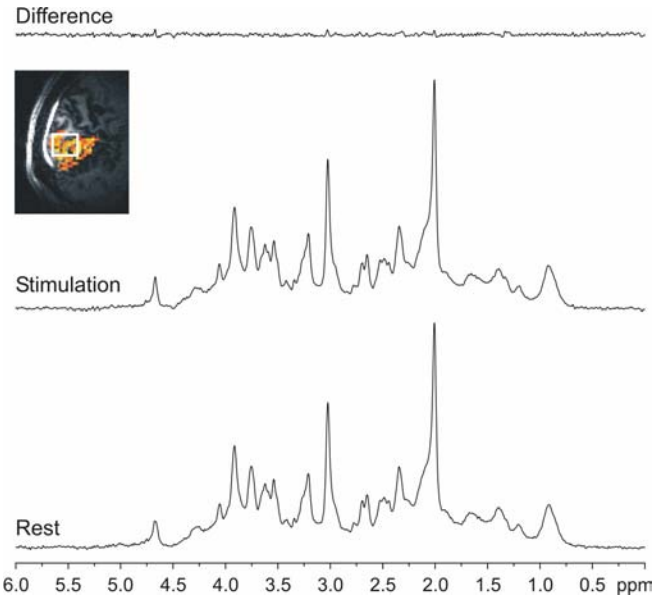

Fig. 1: *In vivo* ^{1}H-NMR spectra from the visual cortex during rest and prolonged visual stimulation. STEAM, TE = 6 ms, TR = 5 s, NT = 32, VOI = 20 x 22 x 20 mm^3. Inset: sagittal image (turboflash) with superimposed fMRI data. Small narrow peaks in the difference spectrum on singlets of Cr and NAA arise from linewidth changes due to the BOLD effect.

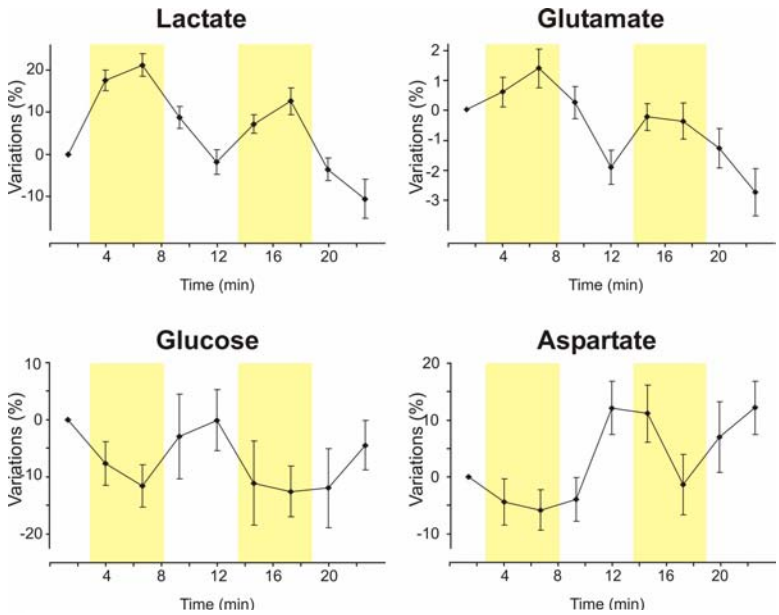

Fig. 2: Time-courses in percentage units of selected metabolites during the functional paradigm. Data are AVG ± SEM. N=12. Concentrations of the shown metabolites during stimulation periods are statistically different from the following rest periods ($p< 0.05$). Shaded areas indicate stimulation periods.

References: [1] Prichard et al. PNAS 88:5829 (1991); [2] Sappey–Marinier et al. JCBFM 12:584 (1992); [3] Frahm et al. MRM 35:143 (1996); [4] Urrila et al. JCBFM 23:942 (2003); [5] Mangia et al. Neuroscience 118:7 (2003); [6] Mangia et al. MRI (in press) ; [7] Tkac et al. App Magn Reson 29:139 (2005); [8] Provencher MRM 90:672 (1993).

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