Functional NMR spectroscopy of the human brain at 7 T: an event-related study

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Introduction

Functional MRI techniques are generally based on local changes in cerebral blood flow, blood volume and oxygen consumption. In principle, biochemical changes related to neurotransmission could be detected by means of *in vivo* NMR spectroscopy. So far, only the time-courses of few metabolites have been reported in the literature, typically during prolonged stimulations and with low temporal resolution. Spectroscopic studies were mostly focused on lactate due to observed uncoupling between oxygen and glucose consumption during long stimuli (1) and proposed astrocyte-neuron lactate shuttle model during increased brain activity (2). Increased as well as decreased lactate levels ware reported during various functional paradigms (3-7). The aim of this study was the detection of time courses of multiple metabolites in the human brain during an event-related paradigm.

Methods

Eight healthy volunteers (19 – 26 years old) were examined on a 7 T whole-body magnet (Magnex Scientific) interfaced to Varian INOVA console. *In vivo* ^{1}H NMR spectra were acquired using an ultra-short echo-time STEAM (TE = 6 ms). The voxel selection in the visual cortex was based on fMRI maps measured in the beginning of each study. The stimulus consisted of a rotating red/black checkerboard covering all the visual field and flickering at a frequency of 8 Hz. The acquisition-stimulation paradigm involved the repetition of 64 trials composed of 5 s of visual stimulation and 22.5 s of rest condition. Data sampling was performed through an inter-leaved time-lock modality in several time points relative to the stimulus. Summing corresponding time-points resulted in 11 spectra (32 scans each) and 2.5 s temporal resolution. Concentrations of 16 brain metabolites were reliably quantified (Cramer-Rao lower bounds, CRLB < 20%) using LCModel with simulated basis set.

Results and discussion

In vivo ^{1}H NMR spectrum measured from the voxel located in the visual cortex with highest activation is shown in Fig.1. Time courses of selected metabolites that are directly linked to neurotransmission are shown in Fig. 2. Similar responses during visual paradigm were observed for all studied subjects. In spite of high precision and accuracy, CRLB(Glu) = 2%, CRLB(Gln) = 6%, CRLB(Lac) = 7%, CRLB(Cr) = 5%, CRLB(PCr) = 6%, significant changes of brain metabolites were not observed. Cramer-Rao lower bounds, i.e. estimated precision of metabolite quantification, were below 0.25 µmol/g for all sixteen quantified brain metabolites. This determined the upper limit of possible concentration changes detectable in a single subject (5 s light ON, 22.5 s light OFF). Also, no significant variations were observed for metabolites in the inter-subject analysis.

References: [1] Fox and Raichle, Science 241:462 (1988); [2] Magistretti et al. PNAS 91:10625 (1994); [3] Prichard et al. PNAS 88, 5829 (1991); [4] Sappey–Marinier et al. JCBFM 12, 584 (1992); [5] Frahm et al. MRM 35, 143 (1996); [6] Urrila et al. JCBFM 23:942 (2003); [7] Mangia et al. Neuroscience 118:7 (2003).

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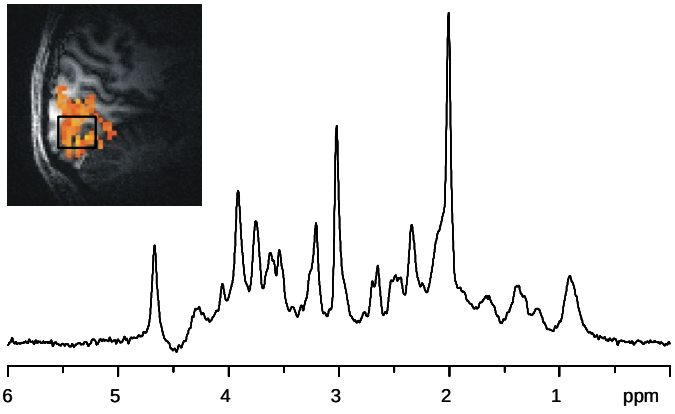

Fig. 1: *In vivo* ^{1}H NMR spectrum from the visual cortex during visual stimulation. STEAM, TE = 6 ms, TR = 5 s, NT = 32, VOI = 20 mm x 23 mm x 20 mm. Inset: sagittal image (turboflash) with superimposed fMRI data.

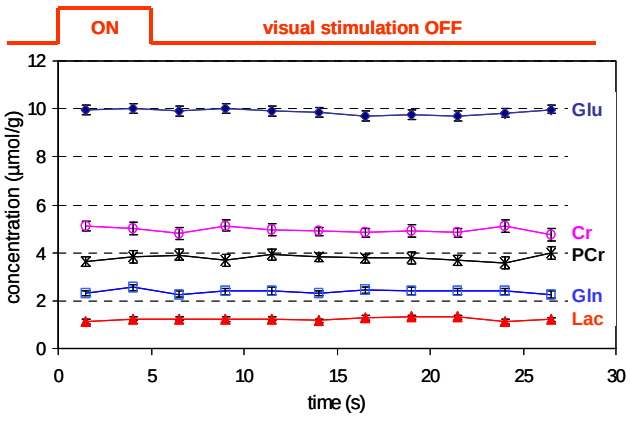

Fig. 2: Time-courses of selected metabolites during visual stimulation paradigm. Data from a single subject, each time-point corresponds to 32 averages. Error bars denote Cramer-Rao lower bounds.