Time resolved functional proton MR spectroscopic investigations of cortical glutamate changes during painful heat stimulation

A. Gussew[1], R. Rzanny[1], H. C. Scholle[2], W. A. Kaiser[3], and J. R. Reichenbach[1]

[1]Medical Physics Group / IDIR, Friedrich-Schiller University of Jena, Jena, Thuringia, Germany, [2]Clinic for Trauma, Hand and Reconstructive Surgery, Friedrich-Schiller-University of Jena, Jena, Thuringia, Germany, [3]IDIR, Friedrich-Schiller University of Jena, Jena, Thuringia, Germany

PURPOSE

In vivo detection of metabolic changes in the cortex may help to improve the understanding of biochemical processes involved with neuronal activity. From literature it is known that ca. 80% of brain glucose consumption is associated with glutamate metabolism in the resting state which can rise up to more than 14% during neuronal stimulation [1]. Some published *in vivo* ^{1}H-MRS studies performed during visual or painful stimulation demonstrated a correlation between subjectively perceived stimuli and detected changes of cortical glutamate (Glu) and glutamine concentrations [2, 3]. The aim of the present study was to investigate the alternation of Glu concentration in the brain with respect to different states of peripheral painful heat stimulation by using time resolved ^{1}H-MRS.

METHODS

In vivo single voxel ^{1}H-MR brain spectroscopy (PRESS, TR/TE = 5000/30 ms, V_{VOI} = 2.5 ml, manual shim, water saturation) was performed in the left anterior insular cortex (Fig.1) of three male healthy volunteers (mean age: 37±14) by using a whole body 3 T MR-scanner (Magnetom Trio TIM, Siemens Medical Solutions, Erlangen, Germany) and a 12 channel *receive only* head matrix coil in circular polarized mode. The spectroscopic measurements included the acquisition of a reference spectrum without stimulation (black arrow, NEX = 128) and two time-shifted (1 sec) series of spectra (N = 128 each) measured during short cyclic heat stimulations on the left forearm (stimulus duration: 1 sec at 48°C; rest duration: 5 sec at 32°C, see Fig.2). The heat stimulation unit (Neuro Sensory Analyzer TSA-II, Medizin-Elektronik Von Petersdorff GmbH, Munich, Germany) was triggered by the MR sequence. This synchronization allowed to separate two groups of spectra (N = 64) associated with the two different stimulation states. Finally, spectra corresponding to both stimuli time points and both resting time points were averaged. The absolute quantification of metabolic intensities was performed using the LCModel [4], including eddy current correction. Individual coil loadings were taken into account by normalizing the estimated metabolic intensities with the individually adjusted transmitter coil reference amplitudes.

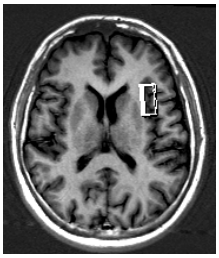

Fig.1 *Location of the 2.5 ml MRS voxel in the left insular cortex*

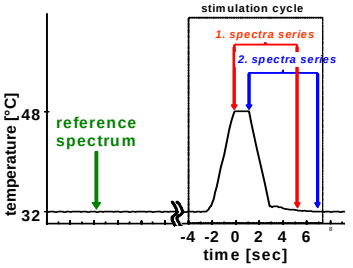

Fig.2 *Position of four discrete acquisition points (blue and red) during the time course of the heat stimulation*

RESULTS

During the stimulus state Glu intensity increased (up to 17%) in all volunteers compared to the reference condition (Figs. 3 and 4). However, observed differences of glutamate concentration during the resting period among the volunteers indicate interindividual variability. All volunteers described the perceived stimulus as painful with values between 6 and 7 on a 10-point visual analogous pain scale [5]. Cramer-Rao-Lower-Bounds below 13% for Glu and SNR_{NAA} values between 8 and 12 were obtained for all spectra.

DICUSSION AND CONCLUSIONS

The results demonstrate that changes of brain glutamate induced by painful stimuli are detectable with ^{1}H-MRS. Furthermore, synchronizing the stimulation unit and the MR-scanner allows time resolved measurements during different stimulation states. A cyclic pain stimulation technique was chosen to avoid adaptation processes Observed variations of the Glu intensity during the resting period may be caused by different adaptive individual behaviour of the volunteers. Extending the resting period between two stimuli may potentially help to avoid these variations and has to be studied in further investigations.

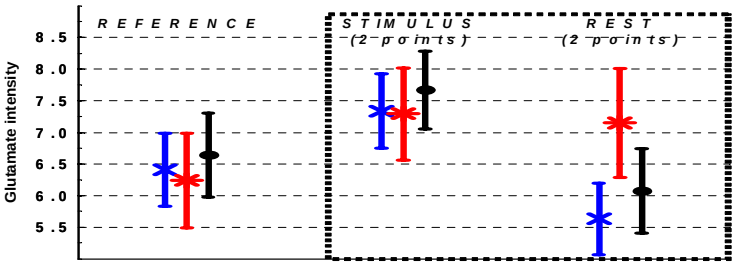

Fig.4 *The comparison of the absolute Glu intensities (arbitrary units) estimated before and during the two different stimulation states. Different colours indicate different volunteers*

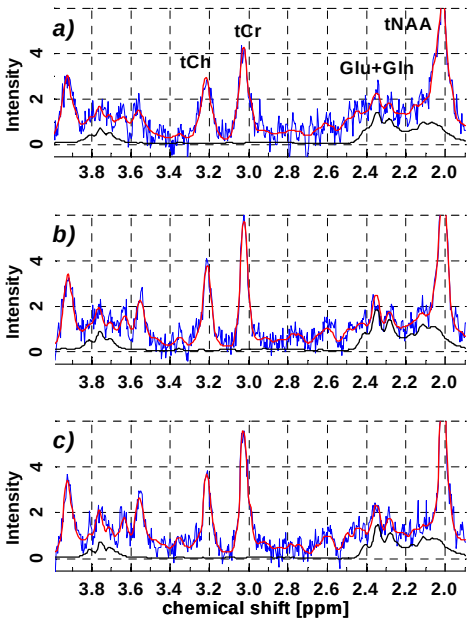

Fig.3. *Original ^{1}H-MR-spectra (blue), LCModel-fit of Glu (black) and the sum of all metabolites (red) before (a) and during the stimulation (b: averaged spectra of the two time points during stimulus state; c: averaged spectra of the two time points during rest state) for one volunteer.*

REFERENCES

[1] Danbolt NC, Progress in Neurobiology 2001; 65: 1–105; [2] Mullins PG et al., NeuroImage 26 (2005) 642– 646; [3] Peca et al., Proc. Intl. Soc. Mag. Reson. Med. 2007; 15: 767; [4] Provencher SW, Magn. Reson. Med. 1993; 30: 672-679; [5] Melzack R, Pain 1975; 1: 277-299