STUDY OF PILOCARPINE MODEL OF EPILEPTIC RATS AT 7 TESLA BY MAGNETIC RESONANCE SPECTROSCOPY

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INTRODUCTION

In this paper, we study the brain of the pilocarpine rat, which is a well-studied model of temporal lobe epilepsy that reproduces most of the clinical and neuropathologic features of human temporal lobe epilepsy [1]. The purpose of our study was to analyze by Magnetic Resonance Spectroscopy the hippocampus region, 24 hours after the onset of *Status Epilepticus*. Short echo-time *in vivo* signals of brains of epileptic and healthy rats were acquired at 7Tesla in the hippocampus region. Metabolites were quantitated using the method QUEST [2] combined with an *in vitro* metabolite basis set. Estimated metabolite concentrations obtained from the epileptic rats are compared with those obtained from the healthy rats.

METHODS

Eight adult male rats (Sprague-Dawley) were injected with intra-peritoneal pilocarpine (350mg/kg). Within 10-15minutes after the injection, rats developed recurrent seizures. These seizures progressed to *Status Epilepticus* at 30 minutes after the injection. The epileptic rats were examined 24 hours after the onset of *Status Epilepticus* in the hippocampus region (3.2x2x3.2 mm^3 voxel, 15 signals). For comparison, the same region of five healthy adult rats (Sprague-Dawley) was also examined (18 signals). All the experiments were performed on a 7T Biospec-BRUKER system using a bird cage coil for excitation and a receiver surface coil. A short echo-time PRESS sequence (TE=20ms, TR=5s, SW=4 kHz, 4096 data-points, 128 averages) combined with outer volume suppression was used for localization. All first- and second- order shim terms were adjusted using FASTMAP (unsuppressed water spectral linewidths of 7-11 Hz). The localization of the voxel was based on T_2-weighted RARE images (TR/TE=6500/65ms), see Figure1. The water suppressed rat brain signals were analyzed using the jMRUI software [3]. Removal of residual water components was performed in a preprocessing step using HLSVD. After the preprocessing step, quantitations were performed with QUEST combined with the 'Subtract' approach for background modeling and an *in vitro* metabolite basis set (Figure2). The reliability of the quantitation was assessed using the Cramér-Rao lower bounds. The latter were below 10% of the estimated amplitudes.

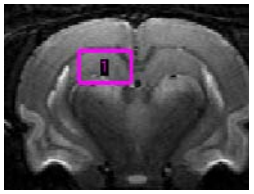

Figure1: T_2-weighted RARE image of a brain of an epileptic rat and the voxel.

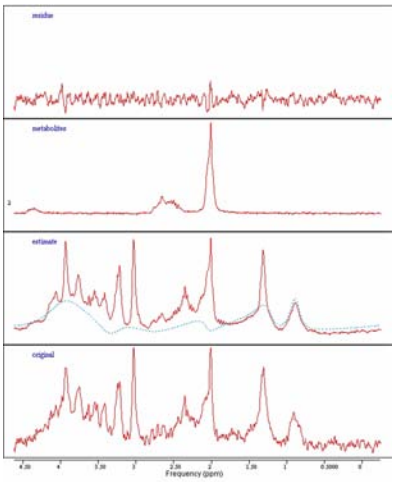

Figure2: QUEST Quantitation results. From bottom to top, original spectrum of a brain of an epileptic rat acquired *in vivo* at 7T in the hippocampus; estimated spectrum and background (dashed line); selected metabolite (NAA) spectrum; and residue.

RESULTS

All the eight rats have developed a *Status Epilepticus*. Usually, the signal intensity on the T_2 weighted images in the hippocampus area is unchanged 24 hours after the onset of *Status Epilepticus*, as confirmed in Figure1. Only a bilateral hypersignal in the piriform and enthorinal cortices and in the amygdala was observed.

Nevertheless, brain metabolism changes were detected in the hippocampus area. The mean values and the corresponding standard deviations of the estimated metabolite concentrations, obtained from the epileptic and healthy rats are shown in Figure3. Total creatine was used as internal reference and set to 7.5mmol/kg_{ww}. The most important difference between the epileptic and healthy rats observed in the hippocampus region concerns the lactate concentration, which increases in the epileptic rats. To confirm the presence of such a high concentration of lactate in the epileptic rats, acquisitions with an echo time of 136ms were also performed. This increase of lactate concentration can be explained by an anaerobic metabolism. No significant differences were observed for the other metabolites.

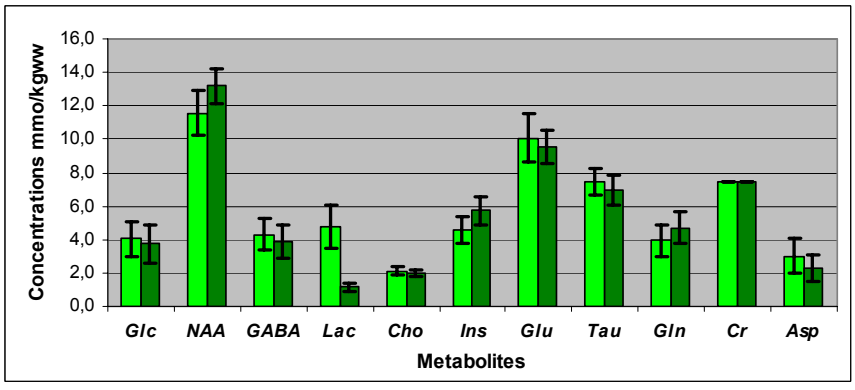

Figure3: Mean values and corresponding standard deviations of the metabolite concentration estimates obtained from 15 epileptic (light green bars) and 18 healthy (dark green bars) rat signals from the hippocampus region. Cr was used as reference and consequently has no error bars.

CONCLUSIONS

- The hippocampus region from healthy and epileptic rat brains, 24 hours after the onset of *Status Epilepticus,* was investigated at 7Tesla.
- Metabolites were well identified and successfully quantitated using QUEST and an *in vitro* metabolite basis set**.**
- We detected a significant increase of the lactate concentration in the hippocampus of epileptic rat brains. Our concentration estimates obtained from the healthy rats are in good agreement with the values from the literature [4].

REFERENCES

[1] WA Turski et al., Behav Brain Res, 9 (1983) 315. [2] H.Ratiney, et.al., NMR in Biomedicine18(2005) 1.[3] http://www.mrui.uab.es/mrui/ [4] I.Tkac,et.al., MRM50 (2003) 24.