LONG TERM OBSERVATIONS ON STATUS-EPILEPTICUS INDUCED NEURODEGENERATION: A 7TESLA MR STUDY IN A RAT MODEL

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Introduction: Temporal lobe epilepsy is a common cause of complex partial seizures that most often originate in mesiotemporal structures. Although this epilepsy is frequently characterized by hippocampal sclerosis, lesions are found in other brain areas such as the amygdala, the thalamus, and the parahippocampal region. The present study aims to identify critical structures during epileptogenesis in an animal model by using a long term (until 8 months) MR imaging follow up. We used a well-established pilocarpine model[1] that reproduces most clinical and neuropathological features of temporal lobe epilepsy (TLE). In the following we report first results on our pilot study.

Materials and methods: The study was approved by the local Animal Welfare Committee. Three naive female Sprague Dawley rats were chosen for the pilot study to evaluate the methods. Status epilepticus (SE) of the rats was induced by administering pilocarpine. MR scans were performed at timepoints -1h, 1h, 48h, 1week, 1months, 3months, 6months and 8months after SE onset, to include the acute, latent and chronic phases of epileptogenesis. All MR examinations were carried out on a 7 Tesla animal scanner (Pharmascan 70/16, Bruker BioSpin MRI Ettlingen) with identical scan protocols. In addition to a T1-MDEFT sequence for imaging anatomic structures the protocol included two MSME-T2-Map sequences containing different echoes with the aim to find out the effect of echo numbers on T2 determination. T2 maps were obtained on a voxel-by-voxel basis using a nonlinear least-square fit from either 3 echo images or 16 echo images. In both cases the quantitative T2 values of the gray and white matter were measured in exemplary regions of interest identified on basis of a rat brain atlas [2]. The time dependent structural changes were analyzed qualitatively (morphological scoring) and quantitatively (T2 relaxation time measurements).

Results: Both morphological and quantitative analyses showed that increasing cellular edema occurred immediately after SE with a maximum at 48 h post SE. Subsequently a continued degeneration of the tissue becomes obvious with loss of volume. Different brain structures were involved: Thalamus, AL Cortices, entorhinal cortices, parahippocampal region, hippocampus, mesencephalon. Especially the neurodegenerative changes are continuously going on until the end of the measurement period, i.e. until 8 months after SE. This is most prominent at the hippocampus with a volume loss of more than 50%.

Conclusions: This pilot study showed that status-induced neurodegenerative change is a very long lasting process. Even after 3 months changes could be detected. This should be taken into consideration by making neuroprotective treatment in clinical applications.

Fig.1 T2 relaxation time [ms] in exemplary regions (WM=white matter) at dedicated timepoints.
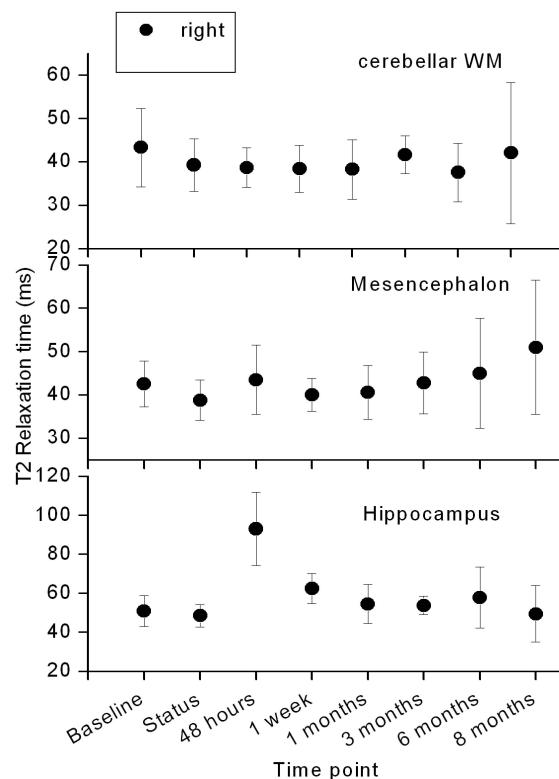
(1)Glien et al., Repeated low-dose treatment of rats with pilocarpine: low mortality but high proportion of rats developing epilepsy, Epilepsy Res. 46 (2001), pp. 111–119

(2)Paxinos, G., and Watson, C. The Rat Brain in Stereotaxic Coordinates, Elsevier/Academic Press, New York, 2007