PET-MRI Imaging in the Kainic Acid Model of Medial Temporal Lobe Epilepsy

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INTRODUCTION Medial temporal lobe epilepsy (MTLE) is the most common type of symptomatic epilepsy. The intrahippocampal kainic acid (KA) model is a model of MTLE in rats with a status epilepticus induced by KA injection as the precipitating insult. As functional and structural changes occur during epileptogenesis, multimodal imaging techniques such as PET-MRI can provide new insights in this process. We have investigated the metabolic and structural changes in the KA model using sequential dynamic PET and 7T MRI.

MATERIALS AND METHODS A cannula was stereotactically placed in the right intermediate hippocampus (AP=-5.6 mm, ML=+4.5 mm, DV=-5.5 mm relative to bregma) of 13 Sprague Dawley rats (male, 300g). After 1 week, PET-CT and MRI imaging was performed on a GMI Triumph II micro-PET/SPECT/CT and a Bruker Pharmascan 7T respectively. Imaging was performed on three consecutive days. On the first day a pre-injection T2-weighted (T2w) MRI was acquired. Then a CT scan was performed directly followed by a 180 min dynamic PET acquisition with continuous infusion of ^{18}F-FDG. First a 300 μCi bolus was administered followed by continuous adjustment of the infusion rate to maintain a constant radioactivity level inside the animal. After 90 min KA (n=10) or saline (n=3) was injected (0.1 μg/0.1 μl; 0.1 μl/min). Subsequently, a T2w MRI was acquired at 2h, 24h and 48h after injection. PET images were reconstructed in 10 min frames using ML-EM (50 iterations). Volumes of interest were drawn on the right and left hippocampus and the right-to-left ratio uptake ratio was calculated. The average of this ratio (= R_{avg}) within both groups was calculated in each frame. Student's t-test was used to determine significant differences ($p < 0.05$). T2w MR images were coregistered with the CT using normalized mutual information.

RESULTS Before injection, R_{avg} was between 96% and 104% in both groups. After injection R_{avg} progressively increased in the KA group (140±20 % at 75 min). In the saline group no increase was observed (104±4 % at 75 min). The difference between both groups was significant at 35 min or more after injection. On T2w MR images a small zone of oedema was visible around the injection site in the KA group 2h post-KA, which increased after 24h and 48h. In some rats oedema was also observed in the

ipsilateral and contralateral entorhinal cortex. No increased FDG uptake was seen in these regions. In the saline group no significant changes were observed on T2w MR images.

CONCLUSION We have used PET-MRI to visualize metabolic and structural changes in the acute phase of the KA model. PET imaging showed a significant increase in glucose metabolism immediately after KA injection. Structural changes were limited on T2w MR images directly after injection, but progressively increased over 48h. This may indicate that metabolic hyperactivation in the acute phase induces structural changes that occur during the post-injection period. When available, simultaneous PET-MRI could be used in this study to collect extra information during the acute phase, such as fMRI pre- and post-injection.