High Frequency Oscillation analysis of CA3 interictal discharges *in vitro*, following immature Status Epilepticus

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Rational: Immature Status Epilepticus (SE) is associated with lasting neurobiological changes, some of which affect cholinergic neurotransmission. Temporal hippocampal slices display higher propensity to epileptiform-like activity compared to septal. Limbic high frequency oscillations (HFOs) are indicative of the epileptic state both *in vivo* and *in vitro*. We therefore analyzed the HFO-components of interictal-like epileptiform discharges (IEDs), recorded from adult hippocampal slices.

Methods: Temporal hippocampal-mEC slices were obtained from adult rats (>PND60), following a PND20 PTZ-induced, sustained generalized seizure (SE-slices) or their normal littermates (N-slices). Field potentials were recorded from the CA3 pyramidal layer, during 50μM 4-AP perfusion. Raw traces sampled at 25kHz, were band-pass filtered at 80-200Hz (ripple range,R) and 200-600Hz (fast ripple range,FR) and the FR:R ratio was quantified, using DFT spectra.

Results: Offline filtering uncovered HFOs in the R and FR bands in all slices. Time frequency spectral analysis, revealed that R and FR frequency volleys coincided with IEDs. CA3 FR/R ratios in SE slices (n=14) were significantly higher compared to those in N slices (n=31,$p<0.001$). CCh (25μM) decreased the FR/R ratio in SE slices but increased it in N slices (n=12SE, n=10N, $p<0.01$). The presence of mEC in the slices reduced significantly ($p<0.001$) the FR/R ratio in both groups (SE, N).

Discussion: In the *in vitro* 4-AP model, a history of immature SE is associated with enhanced FR/R ratio, which is possibly connected to increased network excitability. The CCh-induced decrease of FR/R ratio only in SE slices may reflect long-term adaptive cholinergic changes following immature SE.