Brain inflammation and regeneration in epilepsy

Background
About 1% of the Swedish population has epilepsy. An epileptic seizure occurs when abnormal hyperactivity in the brain becomes synchronised. This results in various symptoms, such as impaired consciousness, automatisms, somatosensory or motor symptoms. Today there are few biomarkers for epilepsy and the current anti-epileptic treatment is successful in <70%. Since epileptic seizures may arise after brain diseases, there is a time window for studying potential diagnostic biomarkers during the development of epilepsy (epileptogenesis). Few of the current anti-epileptic treatments target the immune system, even though there are many studies suggesting that inflammation has a crucial role in the development of epilepsy.

Aims
1. Evaluate the immune system in the brain before and after development of epilepsy
2. Evaluate physical exercise as an immune-modulator during development of epilepsy
3. Reduce seizure-induced neurodegeneration/increase regeneration and reduce seizure frequency in epilepsy by modulating the immune system and synaptic proteins.

Materials and Methods
We have used 2 epilepsy models: electrically-induced status epilepticus (SE) in rats and synapsin 2 knockout mice. Brain and eye tissue has been evaluated with immunohistochemistry, and ELISA. Epileptiform activity with intracranial EEG. The effect of voluntary physical activity on epilepsy development was studied in the synapsin 2 KO mice. The effect of physical exercise in humans was studied in a large cohort of participants in the Swedish ski-race Vasaloppet.

Results
Epileptic rats exhibit an immune reaction in their eyes, which can be modulated by antibodies against the chemokine receptor CX3CR1. Voluntary running in synapsin 2 KO mice reduce the incidence of epileptic seizures several-folds. Preliminary data from the human study of Vasaloppet participants supports an effect on epilepsy incidence.

Conclusions
1. Epileptic seizures lead to inflammation not only inside the brain but also in the eyes of rodents. Further studies will reveal if this finding can be used as a prognostic biomarker in epilepsy.
2. Voluntary running leads to reduced seizure frequency and epilepsy development in seizure-proned mice, if initiated early during epileptogenesis. The physiology behind exercise-induced seizure reduction remains to be revealed.

Publications in PhD thesis
- Running as a modulator of the epileptogenesis in both humans and a genetic animal model of epilepsy. Matilda Ahl, Una Avdic, Stefan James, Maria Compagno Strandberg, Emelie Andersson, Ulf Hallmarker, Thomas Deireborg, Christine T Ekdahl, Manuscript

Publications not included in PhD thesis