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 damage/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 i.e. the immune system, even though there are many studies suggesting that inflammation has a crucial role in the development of epilepsy. Therefore, we need to know more about how the pro/anti–inflammatory systems interact with neuronal function in the brain, where inflammation is located and may be propagate in epilepsy during epileptogenesis.

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

Materials and Methods
Both an electrically induced status epilepticus (SE) model in rat, and a genetic mouse model of epilepsy have been used. With immunohistochemistry, and Elisa an evaluation of inflammation in both the brain and the eyes have been performed. In our genetic mouse model we have also evaluated if running could affect the seizure onset and seizure frequency. In addition, we have also investigated in a large cohort study, the effect of exercise in humans with participants from Vasaloppet.

Preliminary results
There is an increased inflammation in the eyes of epileptic rats, the origin of this inflammation however, we currently do not know. Furthermore, running had strong inhibitory effect in the genetic mouse model of epilepsy, with delayed or complete inhibition of seizure onset. Levels of inflammation was not different between running and non-running animals hence the mechanism behind this phenomenon is not elucidated. Lastly, the human data from Vasaloppet participant further confirmed that exercise seems to have an inhibitory effect on epilepsy, since skiers had a significantly lower incidence of epilepsy compared to non-skiers.

Conclusion
In epilepsy, it is not only the brain that that shows signs of inflammation, but also the eyes seems to be involved. We hope that further studies will reveal if the eyes could be used as clinical tool to be used as a prognostic biomarker in epilepsy. Furthermore, exercise seem to have a beneficial inhibitory impact on epilepsy development, in both animals and humans. If the same mechanism can be targeted in treatments to interfere with early epileptogenesis, we hope to reveal in the future.

Publications
- **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 Hallmark, Thomas Deireborg, Christine T Ekdahl, *Manuscript*