University of Amsterdam

Technology

LIFE SCIENCES CENTER AMSTERDAM

Hippocampal EEG monitoring of effects of drugs during the development and progression of epilepsy

- **epileptogenic vs convulsive phase**
- **in-vivo 24/7 EEG recording**
- **treatment effects**
- **underlying pathological mechanisms**

Research & Enabling technologies 2011

Background

Temporal Lobe Epilepsy (TLE) is one of the most common forms of epilepsy in adult patients. Although they can be treated with anti-epileptic drugs a large percentage of TLE patients is pharmacoresistant and eventually needs to be treated surgically. Since still a lot is unknown of the mechanisms of how epilepsy develops, animal models are needed in order to develop drugs that can prevent or modify epilepsy. We use pharmacological as well as electrical stimulation models to induce status epilepticus in rat or mouse. Status epilepticus is followed by a latent period of 1 or 2 weeks after which epilepsy develops. In our epilepsy rodent models, drugs can be administered orally or via intraperitoneal injections, or via chronicallly implanted osmotic minipumps. Our focus is on anti-epileptogenic treatments but treatments in the chronic phase are also applied.

The Technology

Temporal Lobe Epilepsy (TLE) is a disorder characterized by complex partial seizures and hippocampal sclerosis. Drug discovery companies and pharmaceutical development focus on the suppression and delay of the incidence of TLE.
There is a need for established and relevant animal models to study epileptogenesis in TLE and the related evaluation of compounds in pre-clinical research.
The Neurosciences group of the Swammerdam Institute of Life Sciences can provide insight in, amongst others, the effects on the course of clinical scores and they have the ability to parallel reading of EEG patterns. Moreover they can supply information on disease and treatment effects on the underlying pathological mechanisms, including blood-brain barrier functionality and P-gp modulation.

Applications

We focus on the development and progression of epilepsy in rat and mouse models.

We are especially interested in anti-epileptogenic treatments, i.e. treatments that can delay or, in the ideal case, prevent epilepsy. Moreover we are interested in mechanisms that are related to drug resistance.

R&D Status

Rats are electrically stimulated via implanted electrodes or injected with kainate to evoke a status epilepticus. We have 16 monitoring units in which hippocampal EEG is recorded 24 hours a day 7 days a week. EEG seizures are detected using EEG software that is especially developed for epilepsy research. After EEG recording, brains are collected in order to perform histology, in vitro electrophysiology or molecular biology.

Key publications

1. Gorter JA, van Vliet EA, Aronica E, Breit T, Rauwerda H, Lopes da Silva FH, Wadman WJ (2006) Potential new antiepileptogenic targets indicated by microarray analysis in a rat model for temporal lobe epilepsy. J Neurosci 26:11083-11110.

2. Holtman L, van Vliet EA, Baas F, Aronica E, Gorter JA (2011) Complement protein 6 deficiency in PVG/c rats does not lead to neuroprotection against seizure induced cell death. Neuroscience 188:109-116.

3. van Vliet EA, da Costa Araujo S, Redeker S, van Schaik R, Aronica E, Gorter JA (2007) Blood-brain barrier leakage may lead to progression of temporal lobe epilepsy. Brain 130:521-534.

4. van Vliet EA, van Schaik R, Edelbroek PM, Redeker S, Aronica E, Wadman WJ, Marchi N, Vezzani A, Gorter JA (2006) Inhibition of the multidrug transporter P-glycoprotein improves seizure control in phenytoin-treated chronic epileptic rats. Epilepsia 47:672-680.

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