



Schweizerische Epilepsie-Liga
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Laudation Prof. Jean-Marc Fritschy (Research Recognition Award 2016)

The Research Commission of the SLAE consisting of Dr. Günter Krämer, Dr. Klaus Meyer, Professor Christoph Michel and Dr. Markus Schmutz granted the *Research Recognition Award 2016* unanimously to

Prof. Jean-Marc Fritschy and Tilo Gschwind (University of Zürich) for their project
Using closed-loop optogenetic intervention
to investigate the mechanisms of epileptogenesis and its anti-epileptogenic effects
in a mouse model of temporal lobe epilepsy

Prof. Fritschy is one of the brightest shining stars in the field of preclinical epilepsy research in Switzerland and beyond. The project of Prof. Fritschy and his main collaborator, Tilo Gschwind, makes use of a novel technology to investigate top priorities in epilepsy research, namely mechanisms of epileptogenesis, approaches to prevent epilepsy, neuronal networks, and temporal lobe epilepsy.

Several clinical features and neuropathological changes of temporal lobe epilepsy associated with hippocampal sclerosis can be reproduced experimentally upon intrahippocampal injection of kainic acid in adult mice, the animal model used in this project. The effect of kainic acid on hippocampal activity can be divided into three phases, starting with a non-convulsive status epilepticus, followed by a latent period of about 2 weeks, and finally a persistent chronic phase of spontaneously recurring non-convulsive seizures. The latent

period is considered to represent the phase of epileptogenesis. It is characterized by the occurrence of low voltage spikes and spike-and-wave discharges. However, it has not been established so far whether such epileptiform activity is a mere manifestation of the functional alterations provoked by kainic acid or indeed the driver of epileptogenesis. The main goal of the awarded project is to investigate how epileptic discharges during the latent phase of the kainic acid model are involved in the formation of an epileptic focus.

This will be done by performing EEG recordings in kainic acid-injected mutant mice expressing light-operated channels, thus by using a novel technology: closed-loop optogenetics, an exciting field which through unprecedented specificity will allow new insights into neuronal networks. The technique applied here makes use of light sensitive proteins called opsins which are expressed in ion channels of specific neuronal populations in the hippocampus. Thus, the activity levels of such neuronal populations can be directly modulated through the delivery of light via implanted electrodes. Thereby light stimulation patterns designed to either mimick or block epileptic activity are used in an on-demand fashion, providing intervention only when needed. Hence, detected epileptic discharges can be modulated with instantaneous feedback. Towards this end Tilo Gschwind, in collaboration with the Stanford University, greatly improved the seizure detection software which now enables detection of epileptic activity within 20-40 ms and thus allows immediate closed-loop intervention upon very short epileptogenic events.

By using this technique it will now be possible to perform targeted manipulations of neuronal function on-demand during the phase of epileptogenesis in the kainic acid model, which has never been done so far. This will allow to better understand how epileptic discharges during epileptogenesis are involved in the development of spontaneously recurring seizures and the formation of epileptic foci. In addition, improving online seizure detection will contribute to advance current clinical closed-loop approaches such as interventions using deep brain stimulation.

Prof. Fritschy was born in Geneva. He completed his academic studies with the Diploma and PhD degrees at the Universities of Geneva and Lausanne, respectively. In 1996 he habilitated

at the Medical Faculty of the University of Zürich on the topic of GABAA-receptor subtypes in brain and was awarded shortly thereafter with the "Georg Friedrich Götze-Preis". Since 2004 he is Professor of Pharmacology at the Institute of Pharmacology and Toxicology of the University of Zürich and since 2010 Director of the Neuroscience Center Zürich. Since last year Prof. Fritschy is also Deputy Dean of the Faculty of Medicine of the University of Zürich. He was and still is member of many scientific societies and editorial boards and published extensively in major journals.

In the name of the Research Commission and the SLAE I cordially congratulate Prof. Fritschy and his collaborators, mainly Tilo Gschwind, on the Research Recognition Award 2016!

Markus Schmutz

- 1) Krämer G, Mühlebach C. Epilepsie. Auszeichnungen und Preise, Stipendien und Stiftungen 2012/2013. Fünfte, aktualisierte und erweiterte Auflage. Bad Honnef, Hippocampus Verlag 2012: 111–113