Institute : Institute of Zoology and Biomedical Research.

Topic: Involvement of gasotransmitter systems in the brain response to seizure activity in animal models of epilepsy.

Name of supervisor: prof. dr hab. Krzysztof Janeczko
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Background information/Information on the methods/description of work:
Temporal lobe epilepsy presents severe clinical cases of recurrent spontaneous seizures resulting in excitotoxicity, neuroinflammation, oxidative stress, and neurodegeneration and facilitating further epileptic episodes. According to classical concepts, seizure susceptibility depends on imbalances between excitatory and inhibitory neurotransmitters, mainly between glutamatergic and GABAergic systems. These concepts have been significantly modified by discoveries of cellular interactions *via* very small gaseous particles: nitric oxide, carbon monoxide and hydrogen sulfide. These molecules, called gasotransmitters, are involved in the function of several organs, including the brain and they can also affect each other functionally. However, our present knowledge about possible roles of gasotransmitters in the genesis, course and effects of epilepsy remains significantly limited. So far we know that pathological states accompanying traumatic brain injuries which are also typical of epilepsy, like neuroinflammation, oxidative stress or neurodegeneration, include gasotransmitter-involving processes. Such indirect approach to the problem does not give scientific satisfaction and is the source of inspiration for this project based on animal models.

Main research purposes and techniques to be applied:
Two well established experimental models based on pilocarpine- and electroshock-induced seizures combined with telemetric EEG recordings will be used here. Then, reactive changes in the system of gasotransmitter-producing enzymes will be characterized by:
1) changes in levels of gasotransmitters (nitric oxide, hydrogen sulfide and carbon monoxide) in the peripheral blood and brain (biochemical measurements);
2) changes in expression of enzyme proteins in the cerebral cortex, hippocampal formation and brainstem (Western blots);
3) mapping of brain areas expressing these enzyme proteins (immunohistology);
4) mapping of glial responses and the blood-brain barrier disruptions (immunohistology);
5) mapping of neurons and glial cells expressing proteins of the gasotransmitter-producing enzymes;
6) the extent of neuronal degeneration, changes in quantity and distribution.
The obtained data will be analyzed to detect possible causal relationships.

Additional information, Special requirements from the student:
The student should demonstrate:
1. knowledge of theoretical and practical research problems underlying the proposed research project;
2. certified professional abilities to perform tests on animals;
3. knowledge of appropriate research techniques;
4. abilities to teamwork confirmed by the last academic supervisor.

Place/name of potential foreign collaborator:
Professor Csaba Szabo, Faculty of Science and Medicine, University of Fribourg, Switzerland.

References:
Che X. *et al*. 2018 The Role of Gaseous Molecules in Traumatic Brain Injury: An Updated Review. Front Neurosci. 12:392. doi:10.3389/fnins.2018.00392.
Raju K. and Ischiropoulos H. 2016 Gaseous Signaling in the Central Nervous System. In: Neuroscience in the 21st Century. Springer, New York, NY. https://doi.org/10.1007/978-1-4939-3474-4_152.
Kulkarni-Chitnis M *et al*. 2019 Interaction between hydrogen sulfide, nitric oxide, and carbon monoxide pathways in the bovine isolated retina. AIMS Neuroscience, 6(3): 104-115. doi:10.3934/Neuroscience.2019.3.104.