Epilepsy is a group of neurological disorders characterized by recurrent epileptic seizures caused by abnormal electrical activity of the brain. It is estimated that approximately 65 million of people suffer from epilepsy. The etiology of epilepsy is complex and includes structural and metabolic abnormalities, genetic factors, and unknown causes. Despite many advances in biomedical science, treatment of epilepsy continues to be a challenge as pharmacotherapy is often unsatisfactory and associated with numerous adverse effects. In only 60–70% of epileptic patients seizures can be controlled with a single antiseizure drug. Many patients fail to become seizure free with adequate trials of two antiseizure medications (whether as monotherapies or in combination), which is defined as drug-resistant epilepsy. Thus, there is still a need to develop novel therapeutic strategies for epilepsy management.

The microbiota-gut-brain axis is a complex system in which the gut microbes communicates with the brain *via* neuroanatomical, neuroimmune, neuroendocrine, and metabolic pathways. Emerging evidence indicate that the gut microbiota may be also involved in the pathogenesis of seizures and epilepsy. Several studies demonstrated the differences in the gut microbiota composition between patients suffering from epilepsy and healthy subjects as well as between drug-resistant and drug-sensitive epileptic patients, which suggests that epilepsy may be associated with gut microbiota dysbiosis. Accordingly, the gut-microbiota orientated treatments (e.g. probiotics) may open up new avenues for the management of epilepsy. The concomitant usage of probiotics and antiseizure drugs may however alter the pharmacokinetic and pharmacodynamic profile of the drugs. Probiotics may influence metabolism and absorption of the drugs as well as affect drug's pharmacokinetics by modulating the composition or metabolic activity of the gut microbiota. Unfortunately, studies exploring the influence of gut microbiota and its manipulation by probiotics on the therapeutic efficacy and/or pharmacokinetics of antiseizure drugs are scarce.

In the view of the above, the aim of our study is to provide more insight into the role of the gut microbiota in the treatment of epilepsy by:

(1) Investigation of the influence of a probiotic supplementation on seizure activity as well as therapeutic efficacy and pharmacokinetic profile of selected antiseizure drugs.
(2) Investigation of the influence of gut microbiota (by using antibiotic-induced microbiota depletion model) on seizure susceptibility as well as therapeutic efficacy and pharmacokinetics of antiseizure drugs; and *vice versa*, evaluation of the influence of prolonged treatment with antiseizure drugs on the gut microbiota.
(3) Evaluation of possible mechanisms underlying the observed effects by broad examinations of the host-gut microbiota interactions including analysis of the gut microbiota composition and fecal metabolome, neurochemical changes in the brain, inflammatory and gut permeability markers, ribosomal sensing system and stress response in the liver, expression of selected drug transporters and drug-metabolizing enzymes in the intestine.

The results of our study will allow for a better understanding of the role of the gut microbiota in the treatment of epilepsy. We will evaluate possible interactions between three antiseizure drugs and the gut microbiota. The potential benefits of a new probiotic in reducing seizures alone or as add-on therapy to conventional antiseizure medicines will be also recognized. In the further perspective, the results of our studies may contribute to the development of novel gut microbiota-orientated treatment strategies for epilepsy.