FACULTY OF MEDICINE AND HEALTH SCIENCES

Chemogenetic neuromodulation in a rat model for epilepsy

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Summary of the research

Epilepsy is a brain disorder characterized by the occurrence of recurrent spontaneous seizures. Worldwide, about 50 million people are affected by epilepsy. Unfortunately, around one third of patients does not become seizure-free, despite the availability of medication. Therefore, there is a need for novel treatments for epilepsy.

Chemogenetic neuromodulation could represent a future treatment strategy. Chemogenetics is the process by which proteins, mostly receptors, can be engineered to interact with previously unrecognized small molecules. One could make a comparison with a key that fits a lock. Chemogenetics gives the opportunity to engineer a lock that fits only the key of choice, and vice versa. By restricting the presence of the engineered receptors to a specific part of the body, e.g. a specific brain region, selective modulation of this region is possible. The region of interest is targeted through an injectable carrier containing the genetic material for the receptors, similar to what is performed in gene therapy. The receptors are inactive in the absence of the small molecule. Activation of the engineered receptors is obtained by administering the small molecule, e.g. by an injection or by ingesting a pill. In the case of epilepsy, the brain region where seizure originate from could be selectively suppressed by expressing and activating the engineered receptors in that brain region.

In this study, the **therapeutic potential** of chemogenetic neuromodulation for the treatment of temporal lobe epilepsy, a severe type of epilepsy that is often untreatable with medication, was evaluated in a **rat model**. The research demonstrated that chemogenetic neuromodulation can be used to suppress spontaneous seizures for multiple days, illustrating the promise of chemogenetics as a novel treatment for refractory epilepsy in patients. However, limitations that must be overcome before moving towards clinical translation were also uncovered. These limitations, including determination of the optimal doses of the chemogenetic receptor and the small molecule, were partly addressed in the second part of this PhD thesis.

Short Curriculum Vitae

Marie-Gabrielle Goossens (° 17th November 1993) graduated at Ghent University in 2016 as Master of Science in bioscience engineering, option cell and gene biotechnology (major biomedical biotechnology). During her higher education, Marie participated in the ERASMUS+ program and completed one semester at Aarhus Universitet in Denmark. Starting from October 2016, she worked as a PhD researcher at the faculty of medicine and health sciences at Ghent University, as part of the 4BRAIN research group. She received financial support for her research from the Flemish government through a FWO grant. During her PhD, she investigated the therapeutic potential of chemogenetic neuromodulation for the treatment of epilepsy. Her doctoral research is the result of a collaboration between the preclinical imaging core facility INFINITY and the Department of Neurology at Ghent University Hospital in the framework of a multidisciplinary research project. Marie followed multiple courses of the Doctoral Training Program of Ghent University and supervised three master thesis projects. The results of her research were presented at various national and international conferences and her name appears in 4 peer reviewed publications.

Public defense

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