Universitair Ziekenhuis Gent

UNIVERSITEIT GENT

The role of matrix metalloproteinases in excitotoxicity and neuroinflammation in temporal lobe epilepsy.

Dimitri Hemelsoet, Robrecht Raedt, Caroline Van den Broecke, Marleen Praet, Dirk Van Roost, Paul Boon

Department of Neurology/LCEN3, Ghent University Hospital, De Pintelaan 185 / 1K12A, B-9000 Ghent, Belgium. dimitri.hemelsoet@ugent.be

Research question and background

Mesial temporal lobe epilepsy (MTLE) is often caused by local brain injury that initiates a complex cascade of molecular and biochemical processes in the hippocampus, eventually leading to gliosis, neuronal reorganisation, and sprouting of axons, together called hippocampal sclerosis. These changes lead to an imbalance between excitatory and inhibitory processes, leading the development of hyperexcitable networks, and eventually epilepsy. The exact physiopathological processes underlying these processes remain unknown. Matrix metalloproteinases (MMPs) are a group of enzymes involved in the regulation of proteins and other bioactive factors in the extracellular matrix. Together with their physiological inhibitors they control cell-cell and cell-matrix interactions in physiological processes. In the central nervous system the MMP/TIMP balance has a modulating role in several physiological and pathological processes and is involved in neuro-inflammation. Recently, it was shown that MMP-9 has an important role in epileptogenesis. The role of other MMPs in epilepsy remains largely unknown. MMPs appear to be a potential therapeutic target in epilepsy.
In some inflammatory states in animals, MMP-9 forms complexes with haptoglobin. So far, a role for haptoglobin in human MTLE is unknown. The research will investigate the possible involvement of haptoglobin in human MTLE
The part of the project for which brain tissue samples are obtained form the NBB wants to investigate the expression profile of MMPs, their physiological inhibitors and related inflammatory molecules (IL-1β, TNF-α, TGF-β, haptoglobin), that are involved in mesial temporal lobe epilepsy with hippocampal sclerosis.

Methods and tissues used

MMP expression profiles will be evaluated on different levels using immunohistochemistry, zymography, immunoassay, and quantification of the transcriptional expression using quantitative real time polymerase chain reaction (qPCR). Immunohistochemical analysis of haptoglobin will also be performed. The results will be compared with those from control patients without neurological disease with hippocampal damage (6 paraffin embedded specimens and 3 cryovial specimens from the NBB will be investigated). This part of the project will add new data on the role of MMPs and related molecules in MTLE and is related to an experimental part of the research project using the kainic acid rat model for MTLE.

Results and conclusions:

Expected Q3-4 2013 & 2014