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PhD in Medical Sciences
2018-2019

INVITATION to the Public defence of

Melissa Cambron

To obtain the academic degree of '**DOCTOR IN MEDICAL SCIENCES**'

Fluoxetine in Multiple Sclerosis.

Thursday 4 April 2019

Auditorium **Vanden Driessche**, 17:00

Faculty of Medicine and Pharmacy, Laarbeeklaan 103, 1090 Brussels

How to reach the campus Jette:

<http://www.vub.ac.be/english/infoabout/campuses>

Summary of the dissertation

Multiple sclerosis is a chronic disease of the central nervous system involving two main pathophysiological processes: inflammation-mediated demyelination correlating with focal central nervous system lesions and clinical relapses, and a more diffuse mixed neurodegenerative and inflammatory process correlating with brain atrophy and slow accrual of clinical disability. Whereas multiple treatments exist for the inflammatory part of the disease, multiple sclerosis patients have been left without therapeutic options in the more neurodegenerative stages of the disease which lead to axonal degeneration. The pathophysiology of this diffuse axonal degeneration remains ill understood. One of the current hypotheses suggests that astrocyte energy failure is responsible for this axonal degeneration. Earlier data showed that reduced levels of brain creatinine kinase is responsible for a reduced astrocyte phosphocreatine metabolism in multiple sclerosis patients, generating a hypothesis that impaired energy metabolism in astrocytic end feet contacting the axonal nodes may be responsible for axonal energy failure and subsequent axonal degeneration. Fluoxetine is known to have a positive influence on the energy metabolism of astrocytes, possibly reducing the axonal degeneration in multiple sclerosis. Previous literature in other neurodegenerative diseases has also indicated a neuroprotective effect of fluoxetine. In this thesis we aim to address the questions 'Does fluoxetine influence the phosphocreatine metabolism?' and 'Does fluoxetine slow down multiple sclerosis?'

We addressed this matter in a translational way by investigating monocultures of astrocytes and *in vivo* effects using brain microdialysis in mice. Furthermore we conducted a small pilot randomized placebo-controlled trial in relapsing-remitting multiple sclerosis to investigate the metabolic repercussions of fluoxetine in the brain using magnetic resonance spectroscopy. In a second multi-center, randomized placebo-controlled trial we looked at the effect of fluoxetine in progressive multiple sclerosis and focused on the clinical effect.

Curriculum Vitae

Melissa Cambron was born on the 26th of August 1985 in Ghent, Belgium. In 2003 she started Medical School at the University of Ghent where she graduated magna cum laude. After finishing Medical school she started her residency in neurology and her PhD in 2010 at the Vrije Universiteit Brussel. She obtained a doctoral grant from the Fonds Wetenschappelijk Onderzoek and obtained grants from the Wetenschappelijk fonds MS liga and Wetenschappelijk Fonds Willy Gepts to finance her research. After four years of research and part-time residency, she focused on the treatment and diagnostics of neuroinflammatory pathologies for which she obtained a fellowship in the CHRU Lille under mentorship of Prof. Dr. Patrick Vermersch. She obtained a Horlait-Dapsens grant for this clinical training on neuroinflammation. She had the opportunity to also perform research at the CHRU Lille on JCV index evolution in Natalizumab treated multiple sclerosis patients. After her return she continued her residency in neurology part-time in the National MS Center of Melsbroek where she focused on the rehabilitation aspect of multiple sclerosis and other neurological diseases. She had the opportunity to work in the internal medicine department under supervision of Prof. Dr. Brigitte Velkeniers where she focused on infectious and autoimmune diseases. She (co)authored 25 peer-reviewed articles and she presented her work at national and international congresses.