Final Examination of

Lysanne Campeau, MD, CM, FRCSC

For the Degree of

DOCTOR OF PHILOSOPHY

COMMITTEE IN CHARGE

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Neurobiology and Anatomy

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WF Bio-Tech Place - Auditorium
June 18, 2013
9:00 a.m.
PROFESSOR(S) IN CHARGE OF RESEARCH
Karl-Erik Andersson, M.D., Ph.D.
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FIELDS OF GRADUATE STUDY
Major Subject: Physiology and Pharmacology
Regenerative Medicine and Pharmacology

SUMMARY OF DISSERTATION
CENTRAL NERVOUS SYSTEM CONTROL OF MICHTURITION IN RODENTS THROUGH NEUROPROTECTION AND ENDOCANNABINOIDS – DOPAMINERGIC AND CANNABINOID CONTRIBUTION

Micturition consists of reflexes involving the central and peripheral nervous system controlling the bladder and urethra. A better understanding of the underlying contribution of the dopaminergic and cannabinoid systems to the control of micturition could help direct therapeutic modalities for related voiding dysfunction.

Disruption of the central control of the voiding reflex, and bladder dysfunction, commonly occur with neurodegenerative disorders such as Parkinson’s disease (PD), possibly due to an imbalance in the dopaminergic system. Chronological development of bladder dysfunction has been shown after producing a unilateral lesion in the medial forebrain bundle with 6-OHDA. Rat bone marrow-derived mesenchymal stem cells (rBMSC) or cells protected by microencapsulation (ErBMSC) were transplanted into the substantia nigra pars compacta (SNpc). Urodynamic effects of the 6-OHDA lesion persisted up to 42 days after vehicle injection. Transplantation of rBMSC alone improved the urodynamic pressures at 42 days after treatment more markedly than ErBMSC. This was associated with a higher number of TH-positive neurons in the treated SNpc of rBMSC animals, suggesting that functional improvements require a juxtacrine effect.

Systemic administration of cannabinoid (CB) receptor agonists affects bladder function, but the main site of action (peripheral tissues versus central nervous system) or the contribution of individual CB receptors (type 1 [CB₁R] and type 2 [CB₂R]) to normal micturition has not been clearly defined. Central application of CB receptor agonist localized to the spinal cord with intrathecal administration was found to increase bladder capacity (BC) during conscious cystometry, possibly mediated by the activation of spinal TRPV1 channels, and likely through an afferent pathway. The overall involvement of CB₁R and CB₂R in micturition was examined individually by characterizing the in vivo and in vitro bladder function in their respective KO mouse. The absence of CB₁R was associated with a smaller BC and more spontaneous activity during cystometry and a lower response to electrical stimulation of nerves. On the other hand, lack of CB₂R was linked with lower BC and higher bladder compliance than when CB₂R is present.

In conclusion, these studies have determined that the dopaminergic and CB system play a significant role in the CNS control of micturition.
SCHOLASTIC VITAE

EDUCATION
2013 - Female Pelvic Medicine and Reconstructive Surgery ABU/ABOG Fellowship, New York University Langone Medical Center
New York, NY

2013 - PhD Candidate, Physiology and Pharmacology
Wake Forest University Health Sciences
Winston-Salem, NC

2010 - Urology Residency, FRCSC, McGill University
Montreal QC, Canada

2005 - MDCM, McGill University
Montreal QC, Canada

RESEARCH FUNDING HISTORY:
2011 Quebec Urological Association Training Scholarship
2010 American Urological Association Foundation Research Scholar Fellowship
2010 Quebec Urological Association Training Scholarship
2009 American Urological Association Foundation Research Scholar Fellowship
2009 Royal College of Physicians and Surgeons of Canada Detweiler Travelling Fellowship

RECOGNITION:
2013 Society of Urodynamics, Female Pelvic Medicine, and Urogenital Reconstruction Annual Meeting: 1st place Basic Science Presentation
2012 Wake Forest Institute for Regenerative Medicine: 2012 Retreat Poster Session: 1st Place
2009 NIDDK New Research Directions in Urinary Incontinence Symposium. Honorable Mention: Basic science research abstract
2008 Quebec Urological Association 33rd Annual Meeting: Best basic research presentation
2007 Quebec Urological Association 32nd Annual Meeting: 2nd prize Best basic science research presentation
2006 Quebec Urological Association 31st Annual Meeting: Best clinical research presentation
PUBLICATIONS
Peer-reviewed articles (selected)

Campeau L*, Füllhase C*, Sawada N, Gratzke C, Hedlund P, Howlett A, Andersson KE. Characterization of Bladder Function in a Cannabinoid Receptor Type 2 Knockout Mouse in vivo and in vitro (accepted to Neourology and Urodynamics) *both authors contributed equally to the work

Füllhase C*, Campeau L*, Sibaev A, Storr M, Hennenberg M, Gratzke C, Stief C, Hedlund P, Andersson KE. Cannabinoid receptor type 1 (CB1) is important for normal micturition – results from in vitro and in vivo bladder evaluation of a CB1 knock-out mouse model (accepted to British Journal of Urology International) *both authors contributed equally to the work

Hicks AN, Campeau L, Burmeister D, Bishop CE, Andersson KE. Lack of Nicotinamide mononucleotide adenyllyltransferase 2 (Nmat2) - consequences for mouse bladder development and function. Neourology and Urodynamics. 2013 Jan 31


