University of Victoria | Graduate Studies

Notice of the Final Oral Examination
for the Degree of Doctor of Philosophy

of

# GREOGORY PEARCEY

MSc (Memorial University of Newfoundland, 2014)
BKin (Memorial University of Newfoundland, 2012)

## "Exploiting Evolutionarily Conserved Pathways to Promote Plasticity of Human Spinal Circuits"

Division of Medical Sciences (Neuroscience)

Monday, June 10, 2019
10:00 A.M.
McKinnon Building
Room 179

Supervisory Committee:
Dr. Paul Zehr, Division of Medical Sciences, University of Victoria (Supervisor)
Dr. Craig Brown, Division of Medical Sciences, UVic (Member)
Dr. Olav Krigolson, School of Exercise, Science, Physical & Health Education, UVic (Outside Member)

External Examiner:
Dr. Jean-Sébastien Blouin, School of Kinesiology, University of British Columbia

Chair of Oral Examination:
Dr. Will Greaves, Department of Political Science, UVic

Dr. David Capson, Dean, Faculty of Graduate Studies

## Abstract

Humans evolved from species that walked on all four limbs, which means that experiments in quadrupeds can guide and support experiments in humans. This is particularly helpful for neural rehabilitation because the central nervous system is plastic in nature, meaning that activities promoting central nervous system activity can alter subsequent output properties. This is known as neuroplasticity and can be measured as changes in spinal cord excitability through reflexes as a proxy. By targeting evolutionarily conserved pathways that act on similar interneurons within the spinal cord to either increase or decrease excitability, it may be possible to preferentially modulate spinal cord excitability based on a desirable outcome. For example, rhythmic movement reduces spinal cord excitability whereas brief sensory input to cutaneous afferents increases spinal cord excitability. Alterations in spinal cord excitability have been shown to outlast the activity duration, suggesting that neuroplasticity is not transient. This evidence suggests that both rhythmic movement and sensory input can induce acute neuroplasticity of spinal cord excitability. The overall purpose of this dissertation was two-fold; 1) to provide reviews of how evolutionarily conserved pathways are studied in humans and how they contribute to human rhythmic movement, and 2) experimentally examine how these conserved pathways, which converge onto similar interneuron circuitry, can be exploited to cause bidirectional changes in spinal cord excitability. Reviews indicate that humans have retained characteristics of quadrupedal locomotion and, in particular, activity of the arms affects the excitability of the legs, and vice versa. Cutaneous input is integrated throughout the body during locomotion, such that cutaneous sensations elicit neuromechanical responses that are nerve-specific and modulated according to the phase of movement. In experiment 1, there was increased spinal cord excitability following patterned stimulation of cutaneous afferents innervating the bottom of the foot. In experiment 2, stimulation to cutaneous afferents innervating both the top and bottom of the foot amplified voluntary plantar- and dorsiflexion. In experiment 3, cervicolumbar connections were exploited to amplify plasticity in spinal cord excitability induced by rhythmic movement. Finally, in experiment 4, there were interactions of rhythmic movement and fatigue, which both reduce spinal cord excitability, with cutaneous stimulation, which increases spinal cord excitability, such that reductions in spinal cord excitability associated with fatigue were mitigated by cutaneous stimulation. Taken together, these experiments suggest that cutaneous stimulation can increase spinal cord excitability, whereas quadrupedal locomotor activity can decrease spinal cord excitability. These conserved pathways can be exploited to intentionally modify spinal cord excitability in a bidirectional fashion, which provides fruitful information for the exploration of rehabilitation and sport performance practices.