Notice of the Final Oral Examination
for the Degree of Master of Science

of

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“Sex Differences in Hippocampal Cell Proliferation and Inflammation Following Repeated Mild Traumatic Brain Injury in Adolescent Rats”

Division of Medical Sciences (Neuroscience)

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Remote Defence

Supervisory Committee:
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Dr. Patrick Nahirney, Division of Medical Sciences, UVic (Member)
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Dr. Michael Masson, Department of Psychology, UVic

Dr. David Capson, Dean, Faculty of Graduate Studies
Abstract

Traumatic brain injury (TBI) is becoming increasingly recognized as a global health issue. Each year over 160,000 Canadians experience some form of TBI, which can be caused by sportrelated injuries, motor vehicle accidents, or assault. Adolescents are especially susceptible to repeat head injury and represent an at-risk population for sustaining sports-related concussions. The hippocampus, known for its role in learning and memory, is vulnerable to this injury. Although most TBI studies exclude females, there are important sex differences in outcomes and recovery following brain injury. A greater understanding of how sex differences contribute to the heterogeneity of this disease is critical for clinical care and potential treatments. Currently, few preclinical studies have assessed sex differences in adolescents following repeated mild traumatic brain injury (rmTBI). This study uses an awake closed head injury (ACHI) paradigm in male and female adolescent rats to investigate acute injury-induced changes to the hippocampus after rmTBI. A neurological assessment protocol (NAP) administered immediately after each impact showed that the ACHI acutely alters state of consciousness, and results in deficits after each impact. Following 8 ACHIs spaced 2 hours apart, adolescent rats were injected with the thymidine analogue BrdU and perfused 2 hours later on either post injury day (PID) 1 or 3. BrdU was used to identify cells undergoing DNA synthesis, and Ki-67 – expressed during all active phases of the cell cycle – was used as an endogenous marker for proliferation. Results indicate a robust and diffuse increase in cellular proliferation in male rmTBI animals that was not present to the same extent in female rmTBI animals. Triple labeling experiments revealed a higher proportion of microglia/macrophages in the subgranular zone of rmTBI animals, indicating an immediate inflammatory response in both sexes. This study shows sex differences in the pathophysiology of rmTBI in adolescent rats. Further investigation will reveal the detrimental versus neuroprotective contributions of this effect on learning and memory.