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

of

SCOTT D. SAWCHUK

BSc Hons (University of Victoria, 2015)

“Ethanol Modulation of NMDA Receptors and NMDAR-Dependent
Long-Term Depression in the Developing Juvenile”

Division of Medical Sciences

Wednesday, April 17, 2019
11:00 A.M
Medical Services Building
Room 210

Supervisory Committee:
Dr. Brian Christie, Division of Medical Sciences, University of Victoria (Supervisor)
Dr. Pedro Grandes, Division of Medical Sciences, UVic (Member)
Dr. Raad Nashmi, Department of Biology, UVic (Outside Member)

External Examiner:
Dr. Jeremy Seamans, Centre for Brain Health, University of British Columbia

Chair of Oral Examination:
Dr. Joan Wharf-Higgins, School of Exercise, Science, Physical & Health Education, UVic

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

Long-term depression (LTD) induced by low frequency stimulation (LFS; 900x1Hz) at medial perforant path (MPP) synapses in the rat dentate gyrus (DG) has been described as both developmentally regulated and N-methyl D-aspartate receptor (NMDAr) independent, yet sufficient evidence suggest that the processes is not entirely independent of NMDAr activity. In the present study, *in vitro* DG-LTD LFS was induced in hippocampal slices prepared from rats at postnatal day (PND) 14, 21 and 28 to investigate how the sensitivity of DG-LTD LFS to the NMDAr antagonist amino-5-phosphonovaleric acid (AP5; 50µM) changes throughout the juvenile developmental period (jDP; PNDs 12-29) that occurs immediately after the period of peak neurogenesis. We further examined the acute effects of the partial NMDAr antagonist ethanol (EtOH) on DG-LTD LFS and NMDAr excitatory post synaptic currents (NMDAr-EPSCs) in dentate granule cells (DGCs) using 50 and 100mM concentrations (50mM ~0.2%BAC) of EtOH.

The magnitude of LTD induced at all three time points was not statistically different between age groups, but the probability of successfully inducing LTD did decrease with age. We found that AP5 was insufficient to inhibit DG-LTD LFS at PND14, but significantly inhibited DG-LTD LFS at PND21 and PND28. We also found that 50mM EtOH, but not 100mM EtOH, significantly attenuated the magnitude of DG-LTD LFS induced at each time point. Acute effects of 50mM EtOH had relatively little effect on NMDAr-EPSCs at PND14, and showed a slight potentiation of the response at PND21. 50mM EtOH at PND28, and 100mM EtOH at all three developmental time points showed inhibition of the NMDAr-EPSC. These findings provide insight on how developmental changes to the DG network and dentate granule cells (DGCs) influences mechanisms and processes involved in the induction and expression of synaptic plasticity in the DG.