University of Victoria | Graduate Studies

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

of

SAMMY WEISER-NOVAK

Division of Medical Sciences

2011 University of Guelph BSc

"Ultrastructure and Morphometric Analysis of Hippocampal Synapses in the *Fmr1-/y*mouse Model of Fragile X Syndrome**"**

Wednesday, March 25, 2015
11:30AM
Medical Sciences Building
Room 210

Supervisory Committee:
Dr. Patrick Nahirney, Division of Medical Sciences, University of Victoria (Supervisor)
Dr. Brian Christie, Division of Medical Sciences, UVic (Member)
Dr. Craig Brown, Division of Medical Sciences, UVic (Member)

External Examiner:
Dr. Paul Zehr, School of Exercise Science, Physical & Health Education, UVic

Chair of Oral Examination:
Dr. Lisa Rosenberg, Department of Chemistry, UVic

A copy of the dissertation will be available for viewing in the General Office of the Department of Political Science at least one week prior to the oral examination.

Dr. David Capson
Dean, Faculty of Graduate Studies

Abstract

Fragile X Syndrome (FXS) is a prevalent monogenic disease that presents neurological abnormalities including learning/memory deficits, autism and epilepsy. The *Fmr1* gene - transcriptionally silenced in FXS - normally encodes the Fragile X Mental Retardation Protein (FMRP), of which its function is still obscure, but has been shown to localize at dendritic spines of cortical neurons. In an attempt to understand its role, dendritic spines in the dentate gyrus (DG) and cornu ammonis 1 (CA1) hippocampal regions of 21 day *Fmr1*- mice were analyzed and compared to wildtype (WT) littermate controls using electron microscopy. Spines continuous with a parent dendrite were only included in our analyses. Morphometric studies revealed no significant differences in spine head diameters (DG: 0.529 ±0.014 vs 0.524 ±0.016; CA1: 0.515 ±0.014 vs 0.524 ±0.014 μm), total post-synaptic density length per 100 μm2 (DG: 6.180 ±0.850 vs 5.690 ±0.30; CA1: 7.55 ±0.870 vs 6.96 ±0.330μm) or spine neck lengths (DG: 0.485 ±0.019 vs 0.457 ±0.016; CA1: 0.425 ±0.017 vs 0.421 ±0.015 μm) in *Fmr1*- vs WT mice, respectively. Spine neck diameters, however, were significantly narrower in the DG of *Fmr1*- mice (*Fmr1*- 0.167 ±0.0064 vs WT 0.193 ±0.0062 μm) whereas no significant differences were observed in the CA1 (*Fmr1*- 0.161 ±0.0061 vs WT 0.162 ±0.0049 μm). Estimated resistance provided by narrower spine necks in the DG revealed a ~1.7 fold increase in the resistivity of spines. Taken together, these findings suggest that FMRP plays a role in granular cell neuron spine neck structure and may influence signal propagation in a regionally-specific manner in the hippocampus.