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

of

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BSc (McGill University, 2018)

“The Impact of Congenital Long QT Syndrome on First Nations Children and Youth in Northern British Columbia”

Interdisciplinary Studies

Monday, August 17th 2020
4:15pm
Remote Defence

Supervisory Committee:
Dr. Laura Arbour, Division of Medical Sciences, University of Victoria (Co-Supervisor)
Dr. Carmen Rodriguez de France, Department of Indigenous Education, UVic (Co-Supervisor)
Dr. Rod McCormick, Faculty of Education and Social Work, Thompson Rivers University
(Outside Member)
Dr. Shubhayan Sanatani, Department of Pediatrics, University of British Columbia
(Additional Member)

External Examiner:
Dr. Francis Choy, Department of Biology, UVic

Chair of Oral Examination:
Dr. Christopher Darimont, Department of Geography, UVic

Dr. Stephen V. Evans, Acting Dean, Faculty of Graduate Studies
Abstract

Background: Long QT syndrome (LQTS) is a cardiac condition which predisposes individuals to syncope, seizures, and sudden cardiac death. There is a high prevalence of congenital LQTS in a First Nations community in Northern British Columbia due to the founder variant p.V205M in the KCNQ1 gene. Additionally, two other variants of interest are present in this population: the KCNQ1 p.L353L variant, previously noted to modify the phenotype of LQTS in adults, and the CPT1A p.P479L variant, a metabolic variant common in Northern Indigenous populations associated with hypoglycemia and sudden unexpected infant death.

Methods: We performed a mixed methods study to better understand the impact of LQTS in children and youth in this First Nations community. To learn about the clinical impact of LQTS, and better understand the effects of the KCNQ1 and CPT1A variants in children, we used statistical analysis to compare the cardiac phenotypes of 211 First Nations children with and without the p.V205M, p.L353L and p.P479L variants, alone and in combination. Ordinary Least Squares linear regression was used to compare the highest peak corrected QT interval (QTc). The peak QTc is an electrocardiogram measurement used in risk stratification of LQTS patients. Logistic regression was used to compare the rates of syncope and seizures experienced in childhood. Additionally, to learn about the lived-experience of LQTS, we interviewed one young First Nations adult about her experiences growing up with LQTS as a teenager. From this interview, we conducted a qualitative case study analysis using Interpretative Phenomenological Analysis. All research was done in partnership with the First Nations community using community-based participatory methods.

Results: We found that the p.V205M variant conferred a 22.4ms increase in peak QTc (p<0.001). No other variants or variant interaction effects were observed to have a significant impact on peak QTc. No association between the p.V205M variant and loss of consciousness (LOC) events (syncope and seizures) was observed (OR(95%CI)=1.3(0.6-2.8); p=0.519). However, children homozygous for p.P479L were found to experience 3.3 times more LOC events compared to non-carriers (OR=3.3(1.3-8.3); p=0.011). With regard to the qualitative portion of the thesis, four superordinate (main) themes emerged from the case study: Daily life with Long QT Syndrome, Interactions with Medical Professionals, Finding Reassurance, and The In-Between Age. We found that even though our participant was asymptomatic and felt that she was not impacted by LQTS in her daily life, she considered certain elements of the condition to be stressful, such as taking a daily beta-blocker.

Conclusion: These results suggest that while the KCNQ1 p.V205M variant is observed to significantly prolong the peak QTc, the CPT1A p.P479L variant is more strongly associated with LOC events in children from this community. More research is needed to further determine the effect of these variants; however, our preliminary findings suggest management strategies, such as whether beta-blockers are indicated for p.V205M carriers, may need to be reassessed. The importance of developing a holistic, well-balanced approach to medical care, taking into consideration the personal perspectives and unique medical circumstances of each child is exemplified in this study.