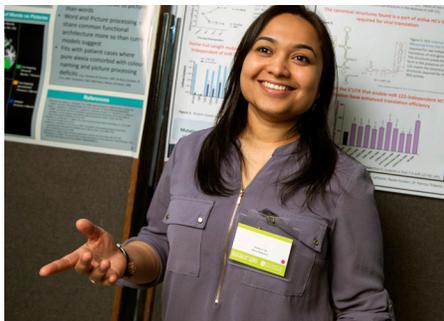




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Health Sciences
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2021 LIFE AND HEALTH SCIENCES RESEARCH EXPO



ACKNOWLEDGING EXEMPLARY RESEARCH AND LEARNING
AT THE UNIVERSITY OF SASKATCHEWAN

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Agenda and livestream links*

9 – 10:30 a.m.

CONCURRENT PRESENTATIONS IN THE STUDENT RESEARCH COMPETITION

Undergraduate Research 1

- Live feed: <https://youtu.be/X46etYMxENU>

Basic Science 1

- Live feed: <https://youtu.be/ro7bqxYfrNE>

Basic Science 2

- Live feed: <https://youtu.be/rJx3V2Hxlx4>

Clinical Science 1

- Live feed: <https://youtu.be/jel8n4lzqvA>

Social & Population Health 2

- Live feed: <https://youtu.be/YEJwUsDwS-w>
-

10:30 a.m.

Adjudicator deliberations (private)

11:30 a.m. – 1 p.m.

CONCURRENT PRESENTATIONS IN THE STUDENT RESEARCH COMPETITION

Undergraduate Research 2

- Live feed: <https://youtu.be/1t8RvnYGNJM>

Basic Science 3

- Live feed: https://youtu.be/HMeltYw_ZNw

Basic Science 4

- Live feed: <https://youtu.be/a3fIBPhMa0o>

Clinical Science 2

- Live feed: <https://youtu.be/AU0HVkmowtw>

Social & Population Health 1

- Live feed: <https://youtu.be/mZAResib93Q>
-

1 p.m.

Adjudicator deliberations (private)

2:30 p.m.

Awards ceremony and special presentations

- Live feed: <https://youtu.be/MXqyYomfRIk>

**Links will only be available during the time noted. Presentations will not be recorded.*

2021 Best Supervisor Award

**Congratulations to the winner of the
2021 Life and Health Sciences Research Expo
Best Supervisor Award**



Dr. Anne Leis, PhD

Professor and Department Head
Community Health & Epidemiology
University of Saskatchewan College of Medicine

Nominated by Kavitha Ramachandran

2021 Best Paper Awards

BEST PAPER – BASIC SCIENCE

Daniel Udenze

School of Public Health

The African strain of Zika virus causes more severe in utero infection than Asian strain in a porcine fetal transmission model

Daniel Udenze, Ivan Trus, Nathalie Berube, Volker Gerdtts & Uladzimir Karniychuk (2019) The African strain of Zika virus causes more severe in utero infection than Asian strain in a porcine fetal transmission model, *Emerging Microbes & Infections*, 8:1, 1098-1107, DOI: 10.1080/22221751.2019.1644967

BEST PAPER – CLINICAL SCIENCE

Heloisa Westphalen

College of Engineering

Assessment of hemodialysis clinical practices using polyaryl ether sulfone-polyvinylpyrrolidone (PAES: PVP) clinical membrane: Modeling of in vitro fibrinogen adsorption, in situ synchrotron-based imaging, and clinical inflammatory biomarkers investigations

Westphalen H, Abdelrasoul A, Shoker A, Zhu N. Assessment of hemodialysis clinical practices using polyaryl ether sulfone-polyvinylpyrrolidone (PAES: PVP) clinical membrane: Modeling of in vitro fibrinogen adsorption, in situ synchrotron-based imaging, and clinical inflammatory biomarkers investigations. *Sep Purif Technol* 2021;259:118136. <https://doi.org/10.1016/j.seppur.2020.118136>.

BEST PAPER – SOCIAL POPULATION HEALTH

Stephanie Ortynsky

Johnson Shoyama School of Public Policy

Budget practices in Canada's K-12 education sector: Incremental, performance, or productivity budgeting?

Ortynsky S, Marshall J & Mou, H (2021). Budget practices in Canada's K-12 education sector: incremental, performance, or productivity budgeting? *Canadian Public Administration/Administration Publique du Canada*, Mar.

Undergraduate Research 1

1. A SOCIAL MEDIA CAMPAIGN IN SASKATCHEWAN TO ENHANCE FOOD SECURITY DURING THE COVID-19 PANDEMIC

Presenter: Jordyn Grantham
Collaborators: Carrie Verishagen
College: Pharmacy and Nutrition
Supervisor: Jessica Lieffers

Background:

Social media use amongst health professionals has increased in recent years, because it can be a cost effective way to share evidence based health information to large audiences. Eat Well Saskatchewan (EWS), a dietitian contact service that provides nutrition advice to Saskatchewan residents for free, implemented a social media campaign, #eatwellcovid19, from May 2020 to August 2020. #eatwellcovid19 utilized a storytelling approach to encourage Saskatchewan residents to tell their story and share their experiences and coping strategies during COVID-19. Additionally, EWS shared credible and evidence based nutrition information to counteract readily available misinformation regarding nutrition and COVID-19 on social media.

Methods:

EWS collected stories from Saskatchewan residents and featured 1-3 stories per week that detailed unique and practical coping strategies for the various food security and nutrition challenges during COVID-19 on EWS social media platforms (Facebook, Twitter, Instagram). Evidence-based information that supplemented featured stories and general nutrition information was also shared. Residents were incentivized to submit their stories with weekly draws for \$100 grocery gift cards. We used the social media insights provided by the respective social media platforms and semi-structured qualitative interviews to evaluate #eatwellcovid19.

Results:

EWS featured 42 of the 75 stories submitted by Saskatchewan residents. The stories fell into numerous categories, including, traditional skills and foraging, changes to grocery shopping habits, gardening, and cooking. The campaign reached 100,571 people on Facebook, left 128,818 impressions and 9,575 engaged with posts. On Instagram the campaign reached 11,310 people, made 14,145 impressions, and received 823 likes. On Twitter the campaign made 15,199 impressions and received 424 engagements. EWS experienced an increase in following on all platforms, with the EWS Instagram experiencing the largest increase with a 30% growth in following. Analysis of qualitative interviews demonstrated followers appreciated the positive tone and storytelling approach of the campaign, they felt it connected them to their community while social distancing and restrictions were in place. Interview participants also appreciated the reliable, attainable, and evidence based nutrition information shared by EWS.

Conclusion:

Social media can be a useful tool for health promotion campaigns, especially when social distancing measures are in place. EWS followers appreciated the storytelling component of the #eatwellcovid19 social media campaign and EWS experienced an increase in reach, engagement, and followers while utilizing this approach. Health professionals may considering utilizing a storytelling approach in future social media health promotion campaigns.

Keywords:

COVID-19; food security; health promotion; social media; dietitian; Saskatchewan; storytelling

2. MODELLING THE EFFECTS OF DYNAMIC PHYSICAL DISTANCING MEASURES IN THE COVID-19 PANDEMIC: APPLICATION TO SASKATCHEWAN, CANADA

Presenter: Robert D. E. Henderson
Collaborators: Carolyn Augusta, Rob Deardon, Graham Taylor
College: Medicine
Supervisor: Carolyn Augusta

Background:

The COVID-19 pandemic has resulted in widespread changes to daily life, and the impact on Canadian public health outcomes of gradually re-opening several economies is expected to be dramatic. We explore the effects of reopening the Saskatchewan economy at various time points, and examine the potential outcomes on ICU and acute care case load.

Methods:

We propose a compartmental infectious disease model with application to the province of Saskatchewan. The model is fit to publicly available case data. We estimate effects of physical distancing and suggest approaches to minimise future outbreaks, using cumulative hospital and ICU admission counts per day to aid in fitting. This approach is helpful in cases of rare event data and serves as an example approach which could be adapted to other jurisdictions.

Results:

Our base model predicts a total caseload of just over 1,000 individuals, approximately 68% of whom are detected. We find that relaxing physical distancing restrictions one month in results in a high number of deaths and hospitalizations. Returning to an interaction level of 25% of normal before 3 months results in a severe spike in cases (>10,000).

Conclusion:

Long-term population-level health outcomes from a pandemic disease process are exquisitely sensitive to physical distancing practices. Strain on hospital capacity can be avoided by aggressive physical distancing over a sustained period. In our model for Saskatchewan, Canada, a reduction of physical interaction to below 20% of normal is required over a period of at least 6 months to significantly reduce disease spread.

Keywords:

COVID-19, Infectious Disease Modelling, Epidemiology, Saskatchewan

3. NORDIC WALKING INTERVENTION FOR RESIDENTS IN LONG TERM CARE: IDENTIFYING CARE-LEADERS' INTERESTS AND PREFERENCES

Presenter: Aafia Maqsood
College: Kinesiology
Supervisor: Dr. Saija Kontulainen

Background:

Residents in long term care homes are at increased risk of fracture. Risk factors for fracture include impaired balance, mobility, and posture. Nordic walking in community dwelling older adults has shown to be safe as well as decrease these risk factors. However, there is no evidence if residents of long-term care would benefit from Nordic walking. The objective of my honours thesis was to contact care-leaders of the long-term care homes in Saskatoon and inquire their interest to co-design a Nordic walking intervention, and availability of related personnel and infrastructure at their facility.

Methods:

This cross-sectional study involved emailing a 7-question survey to 30 care-leaders of long-term care homes in Saskatoon. I used descriptive statistics to characterize interest among responders, available personnel and infrastructure.

Results:

The response rate was 37% and out of the 11 facilities that responded to the survey, 9 showed an interest in co-designing the intervention (82%). One facility had a day program (13%), 1 had trained personnel (13%), 1 had poles available (13%), and 7 had an indoor and/or outdoor walking space available (88%).

Conclusion:

Majority of responders were interested in co-designing a Nordic walking intervention in summer 2022. The next step will be to contact these facilities and work alongside residents, care-leaders, and residents' families to create a patient-oriented approach to a Nordic walking intervention for residents to see if they will receive benefit from this.

Keywords:

Nordic walking, long term care, survey, patient-oriented, residents

4. AN ENVIRONMENTAL SCAN OF INTERVENTIONS TO SUPPORT WOMEN WITH METHAMPHETAMINE USE IN PREGNANCY AND THEIR CHILDREN: A DEVELOPMENTAL ORIGIN OF HEALTH AND DISEASE LENS

Presenter: Melissa Ackerman
Collaborators: Claudia Madampage, Lynette Epp
College: Medicine
Supervisor: Alexandra King
Co-supervisor(s): Kali Gartner

Background:

Developmental origins of health and disease (DOHaD) is a multidisciplinary field which studies the delicate interaction between the environment, genetics, and one's susceptibility to disease. It emphasizes the significance of the first 1000 days of life starting at conception, considering how one's health may be influenced and potentially predicted from exposures during this time. During fetal growth, tissue development occurs in stepwise manner, dependant on gestational timing. However, due to an intricate relationship between the environment and one's genes, this development may be significantly influenced by factors such as substances, poor nutrition, prenatal stress and environmental pollutants. DoHAD suggests that such insults may induce adaptive processes in the fetus and may inflict permanent changes in health throughout their lifetime. Methamphetamine (MA), or "meth," is a central nervous system stimulant which has seen an extensive upsurge in its number of users in the last few decades. Alongside increased prevalence, there is rising concern for its use among women of childbearing years due to the limited evidence of its effects when used in pregnancy. However, it is suspected such that effects of MA may manifest in a delayed presentation. Additionally, a DOHaD lens emphasizes effects of environmental stressors such as prenatal methamphetamine exposure (PME) that may transmit across several generations. Our objectives were (1) to identify the effects of MA use in pregnancy, specifically among pregnant women who are living with or at risk of becoming HIV positive; and (2) to identify interventions that might be useful to minimize or mitigate these effects. This work was done in association with Sanctum 1.5, a prenatal/postnatal wrap around care home located in Saskatoon SK, whose objective is to provide prenatal and postnatal support to women who are HIV positive, or at risk of becoming positive, and/or using substances during pregnancy. We anticipate that our findings will inform practices at Sanctum 1.5, and provide evidence for decision-makers and health care providers managing PME in both acute and non-acute care settings in future.

Methods:

The search protocol included a total of five databases, Ovid Medline, Embase, CINAHL, ProQuest-Public health, and Google (which provided the majority of grey literature). Academic search results were exported into Zotero (open access reference management tool). Duplicates across the databases were then manually merged into one citation within Zotero. The remaining citations were exported into Rayyan (a free web tool to assist screening/selection of articles). Articles were excluded based on initial review of their title, abstract, and contextual use of keywords. A PRISMA (preferred reporting items for systematic reviews and meta-analysis) chart was created to depict the search protocol. The

final selected literature for analysis were annotated and outcomes were extracted to include similar outcomes of interest.

Results:

Data extracted from 80 articles identified 481 outcomes and six programs. The results were presented as changes pertaining to one/or more of the following seven categories: maternal, neonatal/infant, cognitive, behavioural, visual, and neurological, and interventions. Mothers had an increased risk for a spectrum of diagnoses from hypertensive diseases, which were most prevalent, to psychiatric disorders. The most prevalent outcomes in children with PME pertained to the category of neonatal/infant outcomes. One study reported nation-dependent changes in anthropometric measures which they attributed stemmed from differences in government policies and support.

Conclusion:

The research articulates recommendations for acceptance of MA use disorder as a disease that requires multidisciplinary interventions. Interventions that embody this theory have the potential to minimize the effects of MA use in pregnancy in mother and baby, as well as subsequent generations.

Keywords:

Fetus, pregnancy, women, maternal exposure, prenatal exposure, methamphetamine, crystal meth.

5. INVESTIGATING THE CLEARANCE OF AN ANTIPSYCHOTIC MIXTURE FROM ISOLATED PERFUSED LIVERS OF RAINBOW TROUT

Presenter: Zoey Bourgeois
Collaborators: Jonathan Challis, Matthew Schultz, Jenna Cantin
College: Arts and Science
Supervisor: Markus Brinkmann

Background:

Environmental risk assessment of chemicals relies, among other endpoints, on estimations of their bioaccumulation potential, such as the bioconcentration factor (BCF). BCF is considered the gold standard metric for gauging this criterion, though scientists and regulators have been looking for alternatives due to the high cost and animal use. One such alternative might be recently developed in vitro biotransformation assays in combination with in vitro-in vivo extrapolation (IVIVE) models. However, IVIVE of in vitro clearance rates to BCF has been complicated due to various factors, including the potential for extrahepatic biotransformation. Previous research has indicated that by isolating the liver as the main detoxification organ, a more reliable in vivo measure of xenobiotic biotransformation can be obtained. The purpose of this study was to obtain hepatic clearance rates of a pharmaceutical mixture in isolated perfused fish livers, to generate urgently needed data to validate IVIVE models.

Methods:

Livers of juvenile rainbow trout were cannulated through the hepatic portal vein and perfused with a physiological buffer that was spiked with a mixture of 9 anti-psychotic, anti-depressant, and anti-convulsant drugs at a nominal concentration of 5 µg/L. Afferent and efferent samples were taken in 15-minute intervals for 5 hours. The samples were analyzed using liquid chromatography-mass spectrometry (LC-MS) to determine the hepatic clearance of the individual compounds over time.

Results:

The results show, for the first time, that this experimental model can be used to test mixtures of chemicals for the measurement of the hepatic clearance of individual chemicals in fish.

Conclusion:

Ultimately, this approach will allow for reduced animal use while at the same time improving the confidence in IVIVE for chemical risk assessment.

Keywords:

Biotransformation, bioconcentration, effluent, hepatic, mode ling, in vivo, in vitro

6. MENSTRUAL FUNCTION AND DYSFUNCTION RATES AND EXPERIENCES IN FEMALE ATHLETES

Presenter: Alexandra Bristow
College: Kinesiology
Supervisor: Marta Erlandson
Co-supervisor(s): Margo Adam

Background:

Menstrual dysfunction is not an uncommon phenomenon in female athletes, with the majority of them reporting dysfunction in their menstrual cycle. Many female athletes also perceive their menstrual cycle as negatively affecting their performance, possibly creating an overall negative experience in the sport. Currently, our understanding of the menstrual cycle and its impact on sport remains physiological, with little knowledge of female athletes' in-depth lived experiences. Additionally, it has been found that menstrual dysfunction rates differ between leanness and non-leanness sports; however, it is unknown if there is variation within sports based on competition level. Therefore, the purpose of this study is to explore if menstrual function/dysfunction rates and experiences differ between levels of competition within female athletes.

Methods:

An online embedded mixed-methods study was conducted, which integrated qualitative and quantitative data to represent all aspects of the study. Participants (n=63) aged 14 to 39 were gathered using snowball sampling. Data was collected using an online conversation-style survey that was designed to imitate a one-on-one interview. During this process, information on menstrual and sport history was obtained, with a detailed perception of athlete's experiences of menstruation within a sports context. Data analysis for this project was an iterative process but was generally analyzed in two phases. Data was first analyzed using various quantitative measures, such as descriptive statistics and independent t-tests. Subsequently, data was coded by hand and analyzed for themes. Integrating the quantitative and qualitative data to represent all aspects of the study is essential to this study as it allowed us to explore both the rates of menstrual dysfunction and the experience female athletes had with their menstrual cycle within a sport context.

Results:

After completing the data analysis, no significant differences were observed from the variables between competition levels within both the qualitative and quantitative data. Qualitative data analysis resulted in three generated themes. The first theme, attitude, describes the participant's feelings and thoughts about menstruation. Within the data, the normalization of dysfunction is very common among female athletes, as only 27% reported menstrual irregularities; however, 50% of our sample disclosed an absence of 3-months or longer where they did not experience a menstrual cycle (secondary amenorrhea). The second theme, symptoms, deals with the females' expressed symptoms due to their menstrual cycle. Our data revealed a high number of female athlete's experience dysmenorrhea, painful menstrual cycles, with painful abdominal cramps being cited eighty-five times within the data to describe menstrual periods. The third theme, impact, describes how the menstrual cycle impacts participant's daily lives, ultimately influencing their participation in sport. Within our sample, 20% of athletes refrained from participating due to symptoms of their menstrual cycle, which is considerably higher than stated in previous literature.

Conclusion:

In contrast to previous research, no differences were found among competition levels for both menstrual dysfunction rates and experiences within female athletes. However, generally female athletes perceived their menstrual function as having a negative impact on their sport experience. Highlighting that dysfunction rates and experiences are common among female athletes.

Keywords:

Female athlete, mixed methods, women's health

Undergraduate Research 2

7. EXAMINING VENTRAL SHARED STREAM ADVANTAGES: SEMANTIC PRIMING OF LEXICAL DECISION WITH OBJECT PICTURE AND ACTION VIDEO STIMULI

Presenter: Chantal Chabot
College: Arts and Science
Supervisor: Ron Borowsky

Background:

Lexical and visual semantic processing of objects are associated with ventral brain regions, whereas sublexical processing and visual semantic processing of object interaction are associated with dorsal regions. We hypothesized better performance would occur in the object condition than the action condition, along with better performance in related conditions than unrelated conditions, and that greater priming would be observed with object primes than action primes.

Methods:

In a lexical decision task, prime-target relatedness was manipulated while participants viewed picture object primes and video action primes prior to target word presentation.

Results:

Reaction times showed the object condition was significantly faster than the action condition, and error rates showed that the priming effect was greater for object than action primes.

Conclusion:

These results extend previous research by indicating ventral shared stream advantages for object and lexical processing. Our research may have clinical applications for patients with acquired impairments to lexical reading or object identification.

Keywords:

Lexical decision, visual semantic processing

8. EVALUATION OF A NEW HARM REDUCTION COMMUNITY BASED MODEL OF MANAGING MOTHER-NEWBORN DYAD'S WITH NEONATAL OPIOID WITHDRAWAL SYNDROME/OPIOID EXPOSURE

Presenter: Ishita Patel
Collaborators: Emma Maelde
College: Arts and Science/College of Medicine
Supervisor: Dr. Mahli Brindamour
Co-supervisor(s): Dr. Kali Gartner

Background:

Rise in the rates of opioid usage during pregnancy results in more infants being diagnosed with Neonatal Opioid Withdrawal Syndrome (NOWS). A majority of health care institutions in Canada use the Finnegan Scale to diagnose and manage NOWS. The Finnegan Scale tends to recommend the use of pharmacotherapy, requiring the infant to be admitted to the NICU for treatment, which often leads to separation of the infant from its mother. Sanctum 1.5 is a Saskatoon community residence that provides prenatal and postpartum care for women and children with or at high risk of HIV. Sanctum 1.5 uses the Eat, Sleep, and Console Scale to manage and diagnose NOWS, as it promotes the use of nonpharmacological interventions that emphasize mother-infant bonding.

Methods:

This study has received Operational Research Approval from the Biomedical Research Ethics Board at the University of Saskatchewan. As a retrospective chart review study pre-recorded patient-centric data from January 2017 to January 2020 at the Royal University Hospital, Jim Pattison Children Hospital, and Sanctum 1.5 in Saskatoon, Saskatchewan was retrieved. Two separate lists of patients were compiled through the NICU and Pharmacy databases at the hospital. The first list of patients consisted of women who received medically-assisted methadone treatment prenatally on the labor and delivery ward during the time period. The second list consisted of any neonates admitted to the NICU with a diagnosis of NOW. Data will be collected from charts at the Royal University Hospital Health Records Office, Westside Clinic, and Sanctum 1.5 for mother-infant dyads who fit the inclusion and exclusion criteria.

Results:

After evaluating the inclusion and exclusion criteria the data from 126 mother-infant dyad pairs was analyzed; 110 from RUH and 16 from Sanctum. Prenatally, 61% of moms reported smoking and 56% reported drug usage during pregnancy. The 3 most common prenatal complications included 1) Hep C (60.6%), 2) Mental Health (31%), and 3) HIV (22.9%). 93% of women used Methadone as their Maternal Opioid, and 7% used Suboxone. Out of 126 babies, 67 developed NOWS which makes up 53% of the total sample. Although the age at which morphine medication started was similar across both groups, Sanctum weaned neonates off medication earlier at 9.4 days compared to 12 days at RUH. A similar pattern was noted for Clonidine, in which Sanctum weaned neonates at 14 days compared to 25 days at RUH. 90% of infants were discharged with outpatient medication, which is medication administered in the community, increasing the total dosage and length of pharmacotherapy which was noted as something of concern. The results show a much greater

reduction in dosage of medication that is administered at Sanctum, compared to RUH/JPCH, due to its alternative non-pharmacotherapy interventions. In terms of total medication received by infants with NOWS, the total cumulative dose of morphine at RUH 54.3 ug and at Sanctum 21.1 ug. The total cumulative days at RUH was 46.3 days, and at Sanctum 21.8 days, empirical showing a drastic reduction. The average length of hospital days was 12 days. . At RUH, 54% returned home to immediate family, 15% to extended family, and 31% when into foster care.

Conclusion:

Results showed that community-based models, such as Sanctum 1.5, improved health outcomes for infants diagnosed with NOWS compared to the standard care currently offered in our province and elsewhere in Canada. Furthermore, monitoring prenatal conditions is critical in order to improve neonatal care overall, as adverse health conditions increase the risk of infants being diagnosed with NOWS. More so, as a large portion (31%) of infants went into foster care, it is important to include the caregiver during treatment, as short-term and long-term health outcomes can be improved for infants with NOWS, which is greatly emphasized at family-centric care such as Sanctum 1.5. Evaluation of how NOWS is managed at both institutions, allowed for critical appraisal of current protocol for the treatment of NOWS in Saskatoon and will allow for potential implementation of the best practice for neonatal care across the province.

Keywords:

Keywords: Neonatal Opioid Withdrawal Syndrome, Community Based Model, Pharmacological and Nonpharmacological Interventions, Retrospective Chart Review and Neonatal Care

9. SASKATCHEWAN DANCE TEACHER DEMOGRAPHICS AND PRACTICE

Presenter: Madison Rajchyba
Collaborators: Muhammad Siddiqui
College: Medicine
Supervisor: Dr. Amanda Kleisinger

Background:

The main purpose of this study was to explore the profile of dance teachers and their demographics such as age, sex, location, dance and teacher training and experience, teaching volume, work or education outside of dance, style of dance, number of studios, and recommendations to their students for accessing the health care system.

Methods:

This is a cross-sectional exploratory survey. Data was gathered utilizing an electronic questionnaire distributed via email and social media available from January 1-February 24, 2021. 87 dance teachers from any genre completed the study questionnaire with a mean age of 33.11 ± 10.8 (range 18 -73) years.

Results:

82.8% respondents have obtained a qualification or certificate to teach, therefore, 17.2% teach dance without certification. ($p < 0.001$) Royal Academy of Dance (RAD) was the most common technique taught without obtaining qualification at 13.8%, and Canadian Dance Teachers Association (CDTA) 10.3%. Note, 43.7% do not teach without first obtaining a formal certification, which means 56.6% teach dance technique without certification. ($p = 0.51$). Of all respondents, only 36.4% have more than 1 year of professional dance experience, therefore, 63.6% have less than or equal to 1-year experience as a professional dancer. ($p < 0.001$) 68.9% of dance students are less than 18 years old. ($p < 0.001$) 50% of teachers do not have a process for reporting injuries, 46.7% do not have a protocol for injury recovery, and 20% do not modify classes for that injured dancer.

Conclusion:

There is a large variety of dance genres being taught in this province. A significant number of teachers do not obtain teaching certifications and a large majority do not have professional dance experience. Most dancers are under the age of 18 years old. Half of the respondents do not have a reporting process or protocol for injured dancers. Further research with a larger sample size and a multicentre setting is warranted to explore dance teaching practices and injury prevention protocols to learn how to keep dancers safe.

Keywords:

Dance, teachers, student, injury, prevention, studios, certification.

10. SELF-PERCEIVED RISK OF HEART DISEASE IN CANADIAN SOUTH ASIANS

Presenter: Saiyuga Suthaakarann
Collaborators: Dr. Kathryn King-Shier, PhD
College: Kinesiology
Supervisor: Dr. Corey R Tomczak, Associate Professor
Co-supervisor(s): Natasha G Boyes, PhD Candidate

Background:

South Asians are the fastest-growing minority population in Canada. They have a higher prevalence of heart disease compared to other ethnic groups. A language barrier is a key factor driving lack of knowledge and misconceptions in modifiable cardiovascular risk factors. Language barrier may be different between those South Asians born in Canada (i.e. second-generation) compared to those who immigrated to Canada (i.e. first-generation). As such, the perception of heart disease risk may be different between first- and second generations of South Asians in Canada. The purpose of this study is to investigate the difference in perception of heart disease risk between Tamil Sri Lankan first generation immigrants and second-generation Tamil Canadian-born Sri Lankans. We hypothesized that the second generation would have a higher perception of getting heart disease compared to the first generation of Tamil Sri Lankans in Canada.

Methods:

We had 151 Tamil Sri Lankans in Canada complete an online Perceived Risk of Heart Disease Scale questionnaire to assess their perception of risk of getting heart disease. Participants were split into second generation (n=90; 22.9±3.4 years) and first generation (n=61; 56.5±7.1 years) groups. Each item on the 20-item questionnaire is scored on a continuum of higher perception to lower perception. The risk perception scores are then split into three categories: dread risk (7 questions), risk (6 questions), and unknown risk (6 questions). Dread risk is perceived as lack of control of getting heart disease; risk is perceived as having moderate awareness of getting heart disease; and unknown risk is perceived as being unaware or perceiving the risk of getting heart disease to be delayed.

Results:

Total PRHDS scores were not significantly different between first generation (47.4±14.9) and second generation (50.9.5±6.7; p=0.089) groups. Dread risk was not significantly different between first generation (14.5±6.4) and second generation (13.3±4.0; p=0.192) groups. Second generation scored significantly higher in risk (16.8±2.8) and unknown risk (17.9±2.4) perception scores compared to the first generation (15.3±5.1, p=0.025; 14.9±4.8, p<0.001, respectively).

Conclusion:

First generation Sri Lankans in Canada had a significantly lower perception of heart disease risk compared to their second-generation counterparts. Low perception of risk is associated with lower knowledge of cardiovascular risk factors. More education programs about raising awareness risk factors targeted towards older adults should be in place.

Keywords:

Cardiovascular Disease, Sri Lankan, Tamil, Perceived Risk of Heart Disease Scale Questionnaire

11. IMPLEMENTATION OF A CLOZAPINE CLINICAL TOOLKIT AT THE DUBÉ CENTRE FOR MENTAL HEALTH: AN ASSESSMENT OF NURSING CONFIDENCE AND KNOWLEDGE

Presenter: Brooke Gessner
College: Pharmacy and Nutrition
Supervisor: Katelyn Halpape
Co-supervisor(s): Rohit Lodhi

Background:

Clozapine is the most efficacious antipsychotic and it is the only approved pharmacotherapy for treatment-resistant schizophrenia. Despite this, it is grossly underutilized as there are many barriers to its use. One barrier is health professional confidence and knowledge related to clozapine. A standardized, evidence-based protocol to care for patients on clozapine may increase appropriate use of this medication. A clozapine Clinical Toolkit (CTK) was developed and implemented in Vancouver, British Columbia, and, with permission, was adapted to the Dubé Centre for Mental Health (DCMH). Small group education sessions on the CTK were provided to the DCMH nursing staff. The objective of this study was to determine the impact of the education sessions on nurses' confidence and knowledge related to clozapine.

Methods:

Groups of one to five nurses at the DCMH were provided mixed-media education sessions on the clozapine CTK. Sessions were led by one or two researchers and ranged between 15 to 20 minutes in duration. Pre- and post-education questionnaires were administered to assess nurses' knowledge and confidence related to clozapine. Questionnaire completion was voluntary and anonymous. The results were analyzed using simple summary statistics.

Results:

The pre-education questionnaire was completed by 81 nurses and 80 nurses completed the post-education questionnaire. The small group, mixed-media education sessions, improved nursing knowledge on three out of five clozapine knowledge-based questions and overall enhanced nurses' confidence related to clozapine. These results provide an understanding of nurses' knowledge and confidence related to clozapine and inform future nursing education strategies at the DCMH.

Conclusion:

Keywords:

Psychiatry, clozapine, nursing

12. BUILDING VALIDITY EVIDENCE FOR THE QUAL (QUALITY OF ASSESSMENT FOR LEARNING) SCORE AS A MEASURE OF THE QUALITY OF NARRATIVE COMMENTS IN COMPETENCY BASED MEDICAL EDUCATION

Presenter: Sim Singh
Collaborators: Rob Woods, Brent Thoma, Teresa Chan
College: Medicine
Supervisor: Rob Woods

Background:

Competency based medical education (CBME) relies heavily on narrative comments from entrustable professional activities (EPA) for programmatic assessment, but the quality of these comments are usually left unassessed. There is validity evidence supporting the QuAL (Quality of Assessment for Learning) score for rating narrative comments within workplace-based assessments, but its utility for rating EPAs has not been evaluated. We sought to establish validity evidence for the QuAL score in the context of EPAs by investigating the perspectives of residents, academic advisors, and competence committee members.

Methods:

The authors randomly selected 52 de-identified narrative comments from two emergency medicine EPA databases using purposeful sampling. Six collaborators (two residents, two academic advisors, and two competence committee members) were recruited from each of four EM Residency Programs (Saskatchewan, McMaster, Ottawa, and Calgary) to rate these comments with a utility score and the QuAL score. Correlation between utility and QuAL score was calculated using Pearson's correlation coefficient. Sources of variance and reliability were calculated using a generalizability study.

Results:

All collaborators (n=24) completed the full study. The QuAL score had a high positive correlation with the utility score amongst the residents ($r=0.80$) and academic advisors ($r=0.75$) and a moderately high correlation amongst competence committee members ($r=0.68$). The generalizability study revealed the major source of variance was the narrative comment. The QuAL score inter-rater reliability ranged from 0.72-0.94 among the cohorts of raters.

Conclusion:

The QuAL score is a simple tool that demonstrates acceptable reliability and correlates well with utility for narrative comments in EPA assessments for residents, academic advisors, and competence committee members. The QuAL score may serve as an outcome measure for program evaluation and as a resource for faculty development.

Keywords:

Faculty Development, narrative Comments, feedback, CBME

Basic Science 1

13. CALORIE RESTRICTION MIMETICS EFFECTS ON CELLULAR PHENOTYPES ASSOCIATED WITH THE EXPRESSION OF AN ALZHEIMER DISEASE-RELATED PRESENILIN-1 PROTEIN SPLICE VARIANT IN CAENORHABDITIS ELEGANS

Presenter: Carla Almendáriz-Palacios
Collaborators: Cheng-Wei Wu, Brandon M. Waddell, Carlos E. De Carvalho, Christopher H. Eskiw, Darrell D. Mousseau
College: Agriculture and Bioresources
Supervisor: Christopher H. Eskiw
Co-supervisor(s): Darrell D. Mousseau

Background:

As we age, our brain undergoes a number of changes at the cellular and molecular levels. These changes, such as those associated with protein removal through autophagy, lead to the aggregation of misfolded proteins and eventually to the disruption of the nuclear membrane. Age-related disruption of these cellular events is strongly associated with diseases, such as Alzheimer's disease (AD), the most common form of dementia. Much of the brain malfunction during AD is related with the beta-amyloid peptide that is generated because of incorrect cleavage of the amyloid precursor protein (APP). This incorrect cleavage of APP has been associated with dysfunction of the presenilin-1 (PS-1) protein. Alterations in the PS-1 gene have been associated with nuclear membrane disruption and autophagy impairment. A screen of mRNA transcripts in our laboratory identified a splicing variant of PS-1 (PS-1 (SV)) that is highly expressed in AD brain samples. The role of PS-1(SV) during AD and aging is unknown. Since current AD pharmacological therapies are not effective, there is critical need to find treatment strategies. One promising alternative is caloric restriction (CR), the reduction in dietary caloric intake without inducing malnutrition, which has been shown to increase autophagy, reduce risk of AD and extend lifespan in various species. A new class of compounds called CR mimetics (CRms), which mimic the effects of CR without the need for dietary intervention, have been identified. The *C. elegans* model is widely used to study aging and neurodegeneration. The sel-12(or131) strain, which carries a loss-of-function sel-12, the worm homologue of PS-1, exhibits an egg-laying defect (which is often associated with aging), a reduction in lifespan and a loss of nuclear membrane integrity.

Methods:

- Generation of stable *C. elegans* lines expressing PS-1(WT) and PS-1 (SV). - Egg-laying and lifespan *C. elegans* assays. - qPCR and Western Blots against autophagy and nuclear membrane integrity markers. - Treatment of PS-1 (WT) and PS-1 (SV) *C. elegans* lines with caloric restriction mimetics: metformin, resveratrol and everolimus.

Results:

Our preliminary results, based on transient expression of PS-1 in the sel-12(or131) background, confirms that PS-1(WT) can rescue the egg-laying defect, but that PS-1(SV) cannot. Once we have generated the stable expressing PS-1 (WT) and PS-1 (SV) C. elegans lines we can be able to perform the following experiments.

Conclusion:

According to the egg-laying preliminary results PS-1(SV) is non-functional, which might underlie its influence on age-related phenotypes.

Keywords:

Aging, Presenilin-1, calorie restriction mimetics, autophagy, nuclear membrane

14. TARGETING PD-1 WITH RADIOIMMUNOTHERAPY AS A THERAPEUTIC STRATEGY FOR MULTIPLE SCLEROSIS

Presenter: Connor Frank
Collaborators: Dr. Ravendra Garg, Dr. Kevin Allen, Dr. Hannah Salapa
College: Pharmacy and Nutrition
Supervisor: Dr. Ekaterina Dadachova
Co-supervisor(s): Dr. Wojciech Dawicki, Dr. Michael C. Levin

Background:

Multiple sclerosis (MS) is a chronic inflammatory, demyelinating and neurodegenerative disease of the central nervous system (CNS). The cause of this demyelination seen in MS can be attributed to inappropriate stimulation of myelin specific CD4+ T cells responding to antigen present cells (APC) presenting major histocompatibility 2 complexes (MHC 2) bearing myelin peptides. Subsequent immune invasion coordinated by myelin specific CD4+ T cells leads to a degeneration of the myelin sheath and loss of electrical conduction in the nervous tissue in patients.

Methods:

This project will entail using PD-1 specific monoclonal antibodies (mAbs) radiolabeled with ²²⁵Ac and ¹⁷⁷Lu to specifically target and eliminate PD-1+ CD4+ T cells with cytotoxic doses of radiation. Anti-PD-1 mAbs conjugated to tetraxetan (DOTA) will enable the addition of radioactive metals that can deliver toxic radiation to PD-1+ cells.

Results:

Conjugated of anti-PD-1 mAbs to DOTA chelating agent show minimal disruption of immunoreactivity towards PD-1 protein in vitro. Stability and radiolabeling efficiency with ²²⁵Ac labeled anti-PD-1 mAbs demonstrated remarkable stability of radiolabeled construct up to 7 days in human serum.

Conclusion:

We hypothesize that a reduction in myelin specific CD4+ T cells will lead to a reduction in symptoms in MS patients.

Keywords:

Multiple sclerosis, radioimmunotherapy, PD-1 targeting, anti-PD-1 therapy

15. IDENTIFICATION OF AMINO ACID DIFFERENCES IN THE SEQUENCE OF SYSTEMIC- AND JOINT-SPECIFIC SERUM AMYLOID A ISOFORMS

Presenter: Roman Koziy
Collaborators: J.L. Bracamonte, S. Yoshimura, P. Chumala
College: Veterinary Medicine
Supervisor: Elemir Simko
Co-supervisor(s): George Katselis

Background:

Serum amyloid A (SAA) is an important acute phase protein in horses. It is mainly produced in liver (systemic), but several tissue-specific isoforms have been identified in humans and animals. In horses, joint-specific isoforms are found in inflamed joints; however, their amino acid sequence is not known. Identification of joint-specific SAA isoforms can be useful in diagnosing inflammatory joint diseases in horses. The objective of this study is to identify amino acid differences in the sequence of systemic- and joint-specific SAA isoforms.

Methods:

We performed liquid chromatography-tandem mass spectrometry on equine synovial fluid and blood, and matched the results to SAA sequence entries from all animal species available in UniProt and NCBI protein databases.

Results:

We analyzed data obtained from 2 experiments. In experiment-A, we compared SAA sequences from SF and blood of horses with either septic arthritis or aseptic synovitis. One peptide sequence (FGDSGHGAADSR) was unique to synovial fluid in both septic and aseptic samples. This peptide differed in one amino acid location from a peptide identified in both synovial fluid and blood (FGDSGHGAEDSR). In experiment-B we compared SAA sequences from SF of horses with septic arthritis, aseptic synovitis, and systemic inflammation. Peptide FGDSGHGAADSR, which we identified previously only in synovial fluid, was also found in synovial fluid of horses with septic arthritis and systemic inflammation. However, we did not find this peptide in SF samples from aseptic synovitis cases in this experiment.

Conclusion:

Our results suggest that there are potential differences in the amino acid sequence of the liver-produced systemic and local joint-specific SAA isoforms in horses. However, the results of the second experiment indicate that the presence of SAA isoforms in different conditions must be investigated further. The horse species is not well annotated and SAA database entries are limited, therefore SAA isoform isolation and de-novo amino acid sequencing may be necessary to identify further differences.

Keywords:

Serum amyloid A, isoform, proteomics, liquid chromatography-tandem mass spectrometry

16. INVESTIGATING THE ROLE OF THE ANAPHASE PROMOTING COMPLEX IN BREAST CANCER PROGRESSION

Presenter: Gabrielle Mercier
College: Medicine
Supervisor: Dr. Troy Harkness

Background:

High mortality rates in triple negative breast cancer (TNBC) are attributed to multiple drug resistance (MDR) causing innate aggressiveness compared to estrogen receptor positive cancers. The aggressive nature of TNBC relies on its hormonal independence making routine hormone therapy ineffective, causing a reliance on limited toxic chemotherapy. However, there are mechanisms in place, such as those provided by the Anaphase Promoting Complex (APC), that activate stress response pathways that facilitate apoptosis in TNBC cells. The APC is an E3 ubiquitin ligase that targets many substrates for proteasomal degradation through polyubiquitination during the M and G1 phases of the cell cycle. Studies in yeast have provided evidence that APC activation interacts with various stress response pathways, antagonizing genomic instability, potentially leading to anticancer effects. Activating the APC may push malignant cells through premature mitosis while harboring high levels of chromosome instability, resulting in mitotic catastrophe and death of MDR cells. When combined with DNA damaging chemotherapy, premature progression of these cells through mitosis could be even more debilitating. Therefore, we hypothesize that increasing the activity of the APC through novel binding and activating peptides will slow cancer cell migration, tumor growth and will behave synergistically with chemotherapy agents. This project will extend the current knowledge base of the APC and its relation to TNBC while attempting to counter MDR and create a less toxic more effective form of treatment to improve patient outcomes.

Methods:

To test these hypotheses, the MDA MB 231 TNBC cell line was transfected with peptide expression plasmids that were shown to bind and activate the APC: peptides termed C43.4 and C13.3 expressed from a pcDNA3.1 plasmid. These modified cells were used for cell derived xenotransplantation (n=12/group), immunofluorescence, cell viability assays (MTT & Trypan Blue), wound healing assays to assess levels of cell migration and western analyses of downstream APC targets as well as apoptotic, mitotic and DNA damage markers. Tumors were grown in female NSG mice who were treated with doses of doxorubicin, Mad2- inhibitor (M2i-1) and APC inhibitor (APCIN). Behavioral analysis was conducted on these mice throughout the experimental period, and upon completion, tumor fragments were excised and used for western analyses and RNA sequencing.

Results:

In vivo, tumors were grown with modified TNBC cells, C13.3, C43.4 and the pcDNA empty vector control and treated with doxorubicin, M2i-1 and/or APCIN. C43-4 significantly slowed tumor growth and synergized with doxorubicin, while C13-3 did not. Consistent with this, we observed an M2i-1 dose dependent reduction in pcDNA and C43.4 tumor growth in mice. Finally, as predicted, inhibition of the APC using APCIN in an early pilot study increased tumor growth in mice. Western analyses indicated that C43.4 and C13.3 were degrading more APC substrates showing a more active complex. There were also increased expression of apoptotic and DNA damage markers compared to the pcDNA control. Furthermore, cell migration in the C43.4 cell line was slower than the C13.3 and the pcDNA.

These results were consistent with the cell viability assays showing that C43.4 had fewer viable cells, followed by C13.3.

Conclusion:

Increased APC activity reverses the MDR nature of TNBC cells as supported by our results of slowed cell migration, decreased cell viability, and stalled tumor growth.

Keywords:

APC, TNBC, MDR, apoptosis, genomic instability, mitotic progression.

17. ENHANCED DIFFERENTIATION OF DENTAL EPITHELIAL STEM CELLS FOR IN VITRO DENTAL ENAMEL PRODUCTION

Presenter: Fatemeh Mohabatpour
Collaborators: Ildiko Badea, Mays Al-Dulaymi
College: Engineering
Supervisor: Petros Papagerakis, Xiobgbiao Chen, Silvana Papagerakis

Background:

Mature dental enamel, unlike other mineralized tissues in the body, lacks the ability to repair and regenerate. Enamel-making cells, ameloblasts, die after completion of the tooth eruption early in life. One of the promising approaches to regenerate dental enamel after apoptosis of ameloblasts is stem cell-based strategies. However, the development of an efficient method to induce ameloblast differentiation of dental epithelial stem cells into regenerated enamel tissue that mimics natural enamel development remains a challenge

Methods:

Herein, using an optimized gemini surfactant-based delivery system, we delivered Tbx1 encoding gene, a key ameloblast differentiation inducing factor, into the rat dental epithelial stem cells (HAT-7). HAT-7 cells are cultured in two- and three-dimensional cell culture systems, after being transfected with Tbx1, and then long term ameloblast differentiation and enamel formation are evaluated.

Results:

Immunocytochemistry and quantitative polymerase real time chain reaction (qRT-PCR) show high levels of expression for ameloblast markers, both in enamel secretory and maturation stages, in Tbx-1 transfected cells. Alizarin red S and von Kossa staining revealed that transfection of HAT-7 cells with Tbx1 could increase the deposition of calcium and calcium phosphate minerals, respectively. More intense staining of alkaline phosphatase (ALP) was detected in Tbx1-transfected cells compared to control, suggesting enhanced mineralization potential. Scanning electron microscopy (SEM) indicated that Tbx1-transfected cells are able to produce more extensive mineralized nodules and enhanced the elongation of crystals.

Conclusion:

Therefore, our study suggests that inducing initial epithelial stem cell differentiation by Tbx1 gene delivery could be used to enhance ameloblast differentiation and enamel mineralization in in vitro. Our study provides foundation for engineering approaches to repair defective enamel.

Keywords:

Tooth regeneration, gene delivery, Tbx1, dental stem cells, ameloblast differentiation

18. BIOMECHANICS OF OLDER MEN AND WOMEN DURING CONTROLLED FORWARD DESCENTS IN RESPONSE TO FALL ARREST STRATEGY TRAINING (FAST)

Presenter: Justin Pifko
Collaborators: Catherine Arnold, Jonathan P. Farthing, Joel Lanovaz
College: Kinesiology
Supervisor: Joel Lanovaz

Background:

Reaching hands forward to protect the body from injury is a common reaction during forward falls. Improving upper body capacity to effectively land and descend may help to mitigate forward fall-related injuries in older adults. The purpose of this study was to determine sex-related biomechanical changes and quantify fall arrest capacity in older adults in response to a unique intervention program, Fall Arrest Strategy Training (FAST).

Methods:

FAST was led by two physical therapists for 45 minutes twice per week for 12 weeks to improve upper extremity (UE) strength, reaction, and movement time along with fall prevention goals. Participants completed lab-based testing at Baseline, Pre (after a 12-week control), and Post (after FAST). Testing consisted of three push-up-like descents at 60° from horizontal starting with 90° shoulder flexion, elbows extended, and hands shoulder-width apart with an end target of 90° elbow flexion in 1.5s. Bilateral force platforms (OR6-7, AMTI, fs=2000Hz) collected reaction forces while a motion capture system (VICON, fs=200Hz) recorded bilateral 3D UE kinematics. Outcome variables included elbow range of motion (eROM), maximum ground reaction forces (mxGRF), and overall energy absorption (OE). Independent t-tests compared sex demographics and 3 x 2 (time x sex) mixed-design ANOVAs examined outcome variables.

Results:

Fifty-five participants (29 women) completed all testing sessions. Age (\bar{x} Men=73.5±8.2years, \bar{x} Women=69.7±6.9years, range=60-93years, $p=0.062$), body mass index (M:28.7±3.6kg/m², W:27.8±5.5kg/m², $p=0.447$), and FAST attendance (M:82.5±13.6%, W:81.2±14.4%, $p=0.722$) were similar by sex. eROM had no sex or time effects. mxGRF showed a main effect of time ($p<0.001$, Base-Post, Pre-Post) and sex (M>W, $p=0.007$). OE had a time main effect ($p=0.018$, Pre-Post).

Conclusion:

After FAST, participants shifted loading away from their upper extremity while descending, reducing upper extremity overall energy demands. While older men applied higher forces than older women, FAST had similar effects on controlled forward descent biomechanics.

Keywords:

Fall risk, intervention, older adults

19. DROSOPHILA AS A MODEL TO CHARACTERIZE THE HUMAN HOMOLOG OF THE ANTI-HUNGER PROTEIN NUCB1

Presenter: Narsimha Pujari
Collaborators: Shreyas Jois V., Adelaine K.W. Leung,
College: Veterinary Medicine
Supervisor: Dr. Adelaine K.W. Leung

Background:

Metabolic regulation is a complex process with a multitude of regulators. The multifunctional protein Nucleobindin-1 (NUCB1) was discovered to have anti-hunger function in several animal models. Our lab would like to utilize the fruit fly model and our expertise in structural biology to unravel how different structural domains present in the NUCB1 protein coordinate energy metabolism in the whole animal. In silico analysis shows the presence of NUCB1 in the fly genome. However, nothing has been published on its function in metabolic regulation. We hypothesize that, like its mammalian homologue, dNUCB1 also plays a role in regulating energy metabolism in flies.

Methods:

We utilized immunochemistry approach to characterize tissue expression of dNUCB1 and RT-PCR of fly tissues to investigate the influence of diet on the expression level of dNUCB1 mRNA.

Results:

We discovered that dNUCB1 is expressed in neurons that are known to secrete insulin-like peptides and cells in the gut that may have a high population of intestinal stem cells. We observed that dNUCB1 mRNA level is increased in flies fed with high carbohydrate diets. In contrast, dNUCB1 mRNA level is decreased in the body tissue of flies fed with high protein and high fat diets. Starvation on the other hand increases the expression level of dNUCB1 mRNA.

Conclusion:

Our current results support our hypothesis that dNUCB1 plays a role in regulating energy metabolism in flies. The observation that dNUCB1 expression is increased upon starvation needs further investigation. It could be related to its function in endoplasmic reticulum stress management as identified in mammalian cell lines (Tsukumo et al, 2007). The presented data opens up several angles for further investigation. We will use genetic tools to confirm the identity of the cells that express dNUCB1 and to manipulate dNUCB1 expression followed by physiological and behavioural analyses.

Keywords:

Energy metabolism, Drosophila, Neuroscience, Diet studies, Obesity

20. DEVELOPMENT OF APTAMER-BASED ENZYME-LINKED IMMUNOASSAY FOR DETECTING SALIVARY BIOMARKERS LINKED TO CIRCADIAN RHYTHM SLEEP DISORDERS

Presenter: Meenakshi Pundir
Collaborators: L. Lobanova
College: Engineering
Supervisor: Petros Papagerakis, Daniel Chen, Silvana Papagerakis

Background:

Circadian rhythms sleep disorders (CRSDs) are linked to the levels of circulating melatonin and its main precursor, L-tryptophan. Current CRSDs diagnostic approaches are typically based on questionnaires (which lack objectivity), and/or on dim light melatonin onset tests (which are costly, cumbersome, and lack sensitivity), thereby leaving a lot to be desired. In the present study, we aim to develop an aptamer-based enzyme-linked immunoassay for detecting melatonin and L-tryptophan in saliva. We hypothesize that the developed immunoassay can provide high sensitivity and specificity to detect both melatonin and L-tryptophan for CRSDs diagnosis.

Methods:

Competitive aptamer-based immunoassay assay was developed based on the standard protocols, where the levels of melatonin and L-tryptophan are detected through colorimetric characterization. The performance of varying DNA aptamers is evaluated in terms of the melatonin and tryptophan detection levels and the influence of assay conditions. The assay for detecting melatonin and L-tryptophan is performed in phosphate buffer solutions and artificial saliva.

Results:

Our results illustrate that the melatonin and L-tryptophan in phosphate buffer solutions can be detected with a sensitivity of 0.0346 fg/mL to detect melatonin in a range from 0.199 mg/mL to 0.0346 fg/mL, and a sensitivity of 4.0846 ng/mL to detect L-tryptophan in a range from 2.28 mg/mL to 4.0846 ng/mL.

Conclusion:

Our data demonstrates the effectiveness of aptamer-based assays for detecting both melatonin and L-tryptophan, which are biomarkers linked to the CRSDs. The aptamer-based assay, as a proof-of-concept, provides a foundation for accomplishing our long-term aim, i.e., developing an aptamer-based point-of-care detection device for the CRSD diagnosis. Our approaches also provide foundation for optimal saliva diagnosis of circadian clock disruption linked to systemic and oral diseases beyond sleep disorders.

Keywords:

Circadian rhythm sleep disruption, Aptamers, Melatonin, L-tryptophan, Enzyme-linked aptamer-based immunoassay

21. EXPRESSION OF MUTANT HETEROGENEOUS NUCLEAR RIBONUCLEOPROTEIN A1 IN PRIMARY NEURONS TO MODEL NEURODEGENERATION IN MULTIPLE SCLEROSIS

Presenter: Hashim M. Abidullah
Collaborators: Dr. Patricia Thibault, Dr. Hannah Salapa, Cole Libner
College: Medicine
Supervisor: Dr. Michael Levin

Background:

Neurodegeneration (NDG), or neuronal cell death, is a hallmark of progressive Multiple Sclerosis (MS). NDG is thought to lead to permanent disability in persons living with MS; however, no currently available disease modifying therapies target NDG, as the mechanisms driving it are poorly understood. Therefore, it is important to study pathways of NDG in order to help mitigate MS disease progression. Our lab has identified a number of connections between NDG and the RNA binding protein heterogeneous nuclear ribonucleoprotein A1 (A1). A1 is mislocalized to the cytoplasm in the neurons of brains of MS patients, and its mislocalization is temporally and anatomically associated with NDG markers and disease severity in an animal model of the disease. Both somatic mutations in A1 and auto-antibodies to A1 have been identified in patients with progressive MS, and exacerbate A1 mislocalization and NDG markers in cell lines and animal models. Thus, we hypothesize that A1 mislocalization results in NDG. To study the causal link between A1 mislocalization and NDG, we utilized Adeno-associated virus (AAV) vectors to deliver wild-type A1 (A1[WT]) or mutant A1 (A1[mut]) (previously identified in MS patients) to primary embryonic neurons, and quantify downstream markers of NDG.

Methods:

We created mCherry-tagged A1 constructs in an AAV9-encapsidated expression vector to ensure neurotropism. We will use these to assess the cytoplasmic mislocalization of A1[WT] and five mutants derived from progressive MS patients: F263S, F273L, P275S, M276L, and F281L. Mouse primary embryonic neurons will be transduced with A1[WT] or A1[mut], then assessed at various timepoints for A1 mislocalization markers of NDG. We will assess neurite number and length, stain for stress granule markers like G3BP, and programmed cell death markers such as pMLKL (necroptosis), and monitor cell viability via LDH assay.

Results:

Currently, we have generated AAV backbones of A1[WT] and all five of the A1[mut] of interest, and have produced stocks of A1[WT] and A1[mut]-containing viruses. We have successfully transduced primary neurons with mCherry-tagged A1[WT], and next will test our newly-generated A1[mut] constructs. We anticipate that neurons transduced with A1[mut] will demonstrate increased A1 accumulation in the cytoplasm, leading to exacerbated NDG as compared to A1[WT].

Conclusion:

Keywords: Circadian rhythm sleep disruption, Aptamers, Melatonin, L-tryptophan, Enzyme-linked aptamer-based immunoassay

Keywords:

hnRNPA1, RNA binding protein, neurodegeneration, Multiple Sclerosis

Basic Science 2

22. ALTERED EXPRESSION OF THE RNA BINDING PROTEIN HETEROGENOUS NUCLEAR RIBONUCLEOPROTEIN A1 (A1) CONTRIBUTES TO THE PATHOGENESIS OF NEURODEGENERATION IN MULTIPLE SCLEROSIS

Presenter: Amber Anees
Collaborators: Dr. Hannah Salapa
College: Medicine
Supervisor: Dr. Michael Levin

Background:

Multiple Sclerosis (MS) is a disease of the central nervous system characterized by autoimmune mediated destruction of myelin and a significant neuronal/axonal degenerative component, known as neurodegeneration (NDG). NDG is known to underlie permanent disability in MS but the etiology of NDG in MS is incompletely understood. Dysfunctional RNA binding proteins (RBPs) have been established as a hallmark feature in many other neurological diseases, including MS, and are thought to underlie NDG. Dysfunctional RBP features include mislocalization of A1 from its homeostatic nuclear location to the cytoplasm and reduced nuclear expression. Our lab was the first to show pathogenic features of a dysfunctional RBP known as heterogeneous nuclear ribonucleoprotein A1 (A1) in neurons from the brains of MS patients and other relevant MS models. These studies suggest that dysfunctional A1 contributes to the pathogenesis of NDG in MS similar to other neurologic diseases. However, the exact mechanism of how A1 dysfunction affects neuronal health is not yet known. Therefore, we hypothesize that decreased nuclear expression of A1, a characteristic of A1 dysfunction, will negatively impact neuronal health and viability.

Methods:

First, we established an in vitro model of decreased nuclear expression of A1 using differentiated Neuro-2a cells (N2a; a neuronal cell line) and siRNA to A1 (siA1). Molecular consequences of decreased nuclear A1 expression were analyzed using immunostaining and western blotting for the cell death markers, active caspase-3 (apoptosis) and phospho-mixed lineage kinase domain-like protein (P-MLKL; necroptosis), as well as effects on neurite outgrowth. Cytotoxicity assays were performed to assess the effect of decreased A1 nuclear expression on cell viability and cytotoxicity.

Results:

We successfully established a differentiated N2a model in which fluorescently tagged siRNA entered neurons and significantly reduced A1 protein expression as compared to control ($p=0.0003$; $p<0.0001$). SiA1 treated neurons showed a significant reduction in neurite branching and neurite length as compared to control ($p<0.0001$), as well as increased levels of P-MLKL (necroptosis; $p=0.02$), but no change in active caspase-3 (apoptosis). Assessment of cellular cytotoxicity revealed that

decreased A1 nuclear expression resulted in increased cellular cytotoxicity as compared to control ($p=0.04$).

Conclusion:

These findings suggest that there is a mechanistic link between reduced A1 nuclear expression and decreased neuronal health and viability. This model mimics the decreased nuclear expression observed in MS brains and relevant animal models and provides a relevant system to assess the consequence of A1 dysfunction on neuronal health and viability. By determining functional and molecular consequences of decreased A1 nuclear expression in neurons, we can fill a major gap in our understanding of NDG in MS, which could ultimately aid in the development of novel therapies that target A1 dysfunction.

Keywords:

Multiple Sclerosis, Neurodegeneration, RNA binding proteins, Heterogeneous nuclear ribonucleoprotein A1

23. IDENTIFICATION AND CHARACTERIZATION OF THE ACTIVITIES OF GLYCOGEN DEGRADING ENZYMES OF GARDNERELLA SPP.

Presenter: Pashupati Bhandari
Collaborators: Jeffrey P. Tingley, D. Wade Abbott
College: Veterinary Medicine
Supervisor: Professor Janet Hill

Background:

Glycogen is a major nutrient source available to the vaginal microbiota. This complex polysaccharide consists of linear chains of glucose molecules covalently linked with α -1, 4 glycosidic linkages, with branches attached through α -1, 6 glycosidic bonds. Digestion of glycogen into products that can be taken up by bacteria requires the combined activities of several enzymes collectively known as “amylases”. Our current objective is to identify and characterize the activities of extracellular amylases, belonging to the glycosyl hydrolase family 13 (GH13), of Gardnerella spp. that are associated with vaginal dysbiosis.

Methods:

dbCAN webserver was used for the automated annotation of carbohydrate active enzymes belonging to glycosyl hydrolase family 13 (GH13) in the predicted proteomes of 37 Gardnerella isolates and the results were filtered to search for the signal peptide-containing sequences. To verify the sequence-based functional predictions, genes encoding these enzymes are being cloned and expressed for activity studies. The amylase and pullulanase domains of the amylopullulanase enzyme, identified through dbCAN annotation, were expressed and purified separately to characterize the activity.

Results:

Identified proteins included a single domain α -amylase (found in 32/37 isolates) and a multidomain amylopullulanase (25/37 isolates) containing both α -amylase and pullulanase domains. The amylase domain was able to release maltose, maltotriose and maltotetraose from glycogen and the pullulanase domain released was active against its predicted substrate.

Conclusion:

These results suggest that Gardnerella amylopullulanase is capable of digesting glycogen to oligosaccharides by breaking α -1,4 and α -1,6 glycosidic bonds. These breakdown products can be transported inside the cell for use in the metabolism. Combining knowledge of the activities of these enzymes and their distributions among Gardnerella spp. will contribute to our understanding of the contributions of these bacteria to the nutrient pool in the vaginal microbiome, and how glycogen utilization may affect the composition of the vaginal microbiota.

Keywords:

Gardnerella, glycogen, glycosyl hydrolases, amylopullulanase

24. MUSCLE METABOREFLEX SLOWS POST-EXERCISE HEART RATE KINETICS: A MULTI-MODEL PILOT STUDY

Presenter: Natasha G Boyes
Collaborators: Nicole Rapin, Joseph Mannozi, Dana S. Lahti
College: Kinesiology
Supervisor: Dr. Corey R. Tomczak
Co-supervisor(s): Dr. Donal O'Leary

Background:

A delay in the post-exercise recovery heart rate is a strong predictor of mortality that may be mediated by autonomic nervous system dysfunction (e.g., impaired parasympathetic reactivation and/or augmented sympathetic nerve activity, SNA). Muscle metaboreflex activation (MMA) increases SNA to the heart, potentially slowing post-exercise heart rate recovery. Phenylephrine is known to activate the arterial baroreceptors, subsequently inhibiting SNA to the heart. In phase 1, we tested the hypothesis that augmented SNA via MMA during exercise recovery would delay the rate of post-exercise heart rate decay (i.e., slow post-exercise heart rate kinetics) compared to a control condition (CTL). In phase 2, we hypothesized that phenylephrine administration (PE) would reverse the delay in post-exercise heart rate decay, thereby confirming that elevated SNA during post-exercise recovery is the culprit for slowed heart rate recovery observed during MMA.

Methods:

In phase 1, twenty-two healthy adults (13 f; 22 ± 2 yrs; peak $\text{VO}_2 = 47 \pm 7.4$ mL/kg/min; BMI = 23.4 kg/m²) performed heavy-intensity exercise above the ventilatory threshold at $90 \pm 6\%$ peak heart rate for 5 min during CTL (no SNA augmentation) and during an experimental (EXP) condition. The EXP condition entailed SNA augmentation via the muscle metaboreflex following 2 min of bilateral isometric handgrip exercise at 30-40% maximal voluntary contraction. Bilateral circulatory occlusion was performed during the last 1 min of exercise and continued during 5 min of recovery. In phase 2, two healthy Mongrel canines (2 f; 1 ± 1 years; 20-25 kg) completed the above mentioned heavy-intensity exercise and post-exercise recovery protocols during CTL (treadmill running at 6.4 km/h) and MMA (hind-leg 50% circulatory occlusion during 6.4 km/h treadmill running), as well as a MMA+PE condition (10μ PE/kg body weight administered intravenously) in one canine so far. Phase 2 canine data collection is ongoing and aims to reach a sample size of 6 canines. Human post-exercise heart rate kinetics were analyzed using paired t-tests; canine post-exercise heart rate kinetics will be analyzed using repeated measures ANOVA when sample size allows. Significance was accepted at $P < 0.05$.

Results:

In phase 1, there was a significant difference in heart rate kinetics between CTL (57 ± 3 beats/min) and EXP (69 ± 5 beats/min, $P = 0.009$). There was no difference in end-exercise heart rate (last 1 min) between CTL (159 ± 3 beats/min) and EXP (158 ± 3 beats/min, $P = 0.592$), amplitude of heart rate recovery between CTL (-61 ± 2 beats/min) and EXP (-64 ± 2 beats/min, $P = 0.178$), or end recovery heart rate between CTL (98 ± 3 beats/min) and EXP (94 ± 3 beats/min, $P = 0.068$). In phase 2, both canines showed rapid CTL post-exercise heart rate kinetics (9 ± 3 beats/min) compared to MMA (26 ± 1 ; no P-value). Further, PE administration appears to attenuate the MMA-induced delay in heart rate kinetics in one canine (CTL 12 beats/min vs. MMA 25 beats/min vs. MMA+PE 13 beats/min).

Conclusion:

MMA significantly slowed post-exercise heart rate recovery in healthy humans. The slowed tau was not attributed to change in pre-recovery heart rate or heart rate recovery amplitude; therefore, the slowed tau is likely attributed to increased SNA activity alone. These findings suggest that augmented SNA may modulate a delay in the recovery time for heart rate following heavy intensity exercise. Phase 2 canine data collection is ongoing and will provide mechanistic insight into MMA regulation of post-exercise heart rate kinetics.

Keywords:

Canine, sympathetic nerve activity, autonomic nervous system, phenylephrine, cardiovascular physiology

25. THE INFLUENCE OF NUTRIENT- AND STRESS-RELATED SIGNALLING ON ANAPHASE PROMOTING COMPLEX-DEPENDENT LONGEVITY

Presenter: Jordan Brakstad
College: Medicine
Supervisor: Dr. Terra Arnason

Background:

The Anaphase Promoting Complex (APC) has been identified as a protein complex that aids in genomic stability and cell-cycle progression. It has been well demonstrated in yeast, *S. cerevisiae*, that when the APC is dysfunctional, cellular longevity is shortened and cells age at a greater rate. Specifically, the nutrient- (Sch9/Tor1) and stress-(Snf1) sensing upstream kinase pathways influence the APC through the evolutionarily conserved Forkhead Proteins. Fkh1 and Fkh2 are transcription factors that independently play roles in stress response and cellular longevity. Fkh1 and Fkh2 play a crucial role in mitotic progression by stimulating the expression of multiple APC target genes. The yeast Fkh1 is predicted to be phosphorylated at multiple serines and threonines, although not yet defined. We propose that Fkh1 stability is dependent on its phosphorylation, and that the status of phosphorylation is due to the competing upstream kinase signaling pathways responding to nutrient abundance. The signalling pathway of abundance (feasting) is Sch9/Tor1. The signaling pathways of energy limitation (fasting) is SNF1 kinase. We hypothesize that Fkh1 is differentially phosphorylated by Sch9/Tor1 and Snf1 at discrete sites to influence the APC-dependent ubiquitination and degradation of Fkh1.

Methods:

Each of these yeast strains express a genomic version of FKH1 that carries an in-frame C-terminal TAP tag to allow quantifiable detection reflecting Fkh1 protein abundance through Western blot analysis. Secondly, in WT cells, Fkh1 abundance is maximal at mitosis, so we will arrest cells at mitosis with the spindle-poison, nocodazole, and follow Fkh1 stability from this point forward when the upstream SNF1 kinase and Sch9/Tor signalling pathways are disrupted. The addition of cycloheximide to cells arrested at mitosis prevents further protein translation as we sample Fkh1-TAP abundance for 2 hours. Our strains include an isogenic wild types strain with all signalling pathways intact for comparison. Western blot probing for TAP is performed to quantify Fkh1-TAP abundance using the VersaDoc molecular imager and Quantity One software (Bio-Rad) following synchronization and arrest.

Results:

We predicted that Fkh1 protein stability would be affected by the nutritional and energy growth environment of the cells, under the distinct and specific influences of phosphorylation by the anabolic signalling pathways of nutrient abundance (Sch9/Tor1) versus that of the catabolic signalling pathways of nutrient and energy limitations (SNF1 kinase).

Fkh1 normally accumulates in mitosis. Comparing the Fkh1 protein abundance of asynchronous logarithmically dividing yeast cells and that of mitotically arrest cells, we noted a marked decrease in Fkh1-TAP protein abundance specifically within the snf1 Δ -Fkh1-TAP strain, suggesting that protein

degradation was enhanced by its absence. The WT strain, and that deleted for sch9 or tor1 showed various degrees of Fkh1 accumulation most notable in WT and tor1 Δ , as was previously known. We next assessed the protein stability of Fkh1-TAP over a 2-hour period following mitotic arrest. Because the liquid cultures were grown in the presence of cycloheximide, which prevents protein translation from mRNA, no further protein accumulation is possible over the experimental timeline. The abundance of Fkh1-TAP is maximal at mitotic arrest (time 0) and steadily decreases over 2 hours in WT cells. This was similar to that observed in the tor1 Δ strain. It was revealed that there was a distinct stabilization of Fkh1-TAP in the sch9 Δ strain, and a marked and rapid destabilization of Fkh1-TAP in the snf1 Δ strain. These results suggest that normal function of SNF1 kinase is to stabilize Fkh1, and that of Sch9 to destabilize it. Tor1 does not appear to influence Fkh1 abundance.

Conclusion:

These results support our hypothesis that under conditions of nutrient limitation and energy stress (when lifespan is extended, and stress pathways are activated), that SNF1 kinase signalling promotes Fkh1 activity through its stabilization, presumably through a stabilizing phosphorylation event(s). Furthermore, these results also support our hypothesis that under conditions of nutrient abundance (when lifespan is shortened, and stress pathways are quiescent), that Sch9 signalling results in decreased Fkh1 activity through degradation, presumably through a distinct destabilizing phosphorylation event(s). The phosphorylation sites on Fkh1 are not reported in the literature, nor it is known if they are single, multiple or mutually exclusive between SNF1 kinase and Sch9.

Keywords:

Anaphase Promoting Complex, DNA Damage, Longevity

26. UTILIZING COMPARATIVE ONCOLOGY APPROACH FOR THE DEVELOPMENT OF RADIOIMMUNOTHERAPY FOR OSTEOSARCOMA

Presenter: Jaline Broqueza
Collaborators: Dr. Ryan Dickinson, Dr. Valerie MacDonald-Dickinson
College: Pharmacy and Nutrition
Supervisor: Dr. Ekaterina Dadachova
Co-supervisor(s): Dr. Maruti Uppalapati

Background:

Osteosarcoma (OS) is a type of bone cancer and is the most common primary malignant bone cancer in children wherein the overall 5-year survival rate is approximately 70%. In addition, OS is one of the most widespread cancers in companion dogs, particularly larger breeds, and closely resembles human OS. Unfortunately, in over 30 years, there has been no significant advancement in treatment options in humans; and canine treatment options are also limited. A protein receptor called cation independent mannose-6-phosphate/insulin-like growth factor-2 receptor (IGF2R) was found to be overexpressed on multiple standard OS cell lines and on patient-derived xenografts, as well as on tumors from dogs with OS, making it a promising therapeutic target for radioimmunotherapy (RIT). RIT involves the use of an antibody labeled with an alpha- or beta- emitting radioisotope which delivers cytotoxic radiation to targeted cells. Our objective is to develop a novel, effective and safe treatment for OS using radioimmunotherapy (RIT) and have a comparative oncology approach.

Methods:

Antibodies against IGF2R were developed using phage-display, a combinatorial protein engineering technique wherein bacteriophages are used to select for high affinity reagents. The IGF2R-specific antibodies were tested in vivo using SCID mice by performing microSPECT/CT imaging to confirm that the antibodies bound to the OS tumors in mice.

Results:

Antibodies that were cross-reactive with IGF2R human, canine and murine were generated. Best-binding antibodies were radiolabeled with the isotope Indium-111 and have been confirmed by microSPECT/CT that the radiolabeled antibody bound to human and canine OS tumors in SCID mice.

Conclusion:

Future studies will include therapy studies which will involve the testing of the best binding IGF2R-specific antibodies radiolabeled with Lutetium-177, a β -emitting theranostic radioisotope, for therapeutic efficacy studies in mouse models of human and canine OS. Afterwards, research will move forward with canine OS patients. The development of IGF2R-specific RIT will lead to a better therapeutic strategy for not only human OS but also for canine and will pave way to increase survival for both.

Keywords:

Osteosarcoma Radioimmunotherapy IGF2R Phage-display

27. OPTOGENETICS DEFINES RNA BINDING PROTEIN DYSFUNCTION IN A MODEL OF NEURODEGENERATION IN MULTIPLE SCLEROSIS.

Presenter: Joseph-Patrick Clarke
College: Medicine
Supervisor: Dr. Michael C. Levin

Background:

Canada has one of the highest rates of Multiple Sclerosis (MS) in the world, with Saskatchewan being the highest in Canada. Current evidence indicates that neurodegeneration (NDG) is a prominent feature of the pathogenesis of MS and the primary cause of disability in MS patients. Yet, knowledge of the molecular mechanisms of NDG in MS, as well as treatment options to that reverse NDG are lacking. Previous data from our lab indicates that dysfunction of the RNA binding protein (RBP) heterogeneous ribonucleoprotein A1 (A1) may contribute to MS pathogenesis. To examine A1 dysfunction, we utilized a cutting-edge optogenetic technology, and examined how somatic (acquired) MS-associated genetic mutations in A1 cause its molecular dysregulation in the pathogenesis of NDG in a cellular model of MS.

Methods:

Reversible, blue light (BL) stimulated, optogenetic A1 protein expression plasmids, containing wild-type (WT) and mutant A1 (p.P275S and p.F281L), tagged with both the optogene Cryptochrome 2 (Cry2) and mCherry, were used to examine the effects of mutations on protein dynamics and associated downstream cellular pathways in real-time. We established an in vitro optogenetic paradigm of A1 dysfunction in HEK293T cells and analyzed how mutations affect A1 cellular localization, cluster kinetics and stress granule (SG) formation – a marker of NDG.

Results:

Using an acute BL stimulus followed by a steady period of recovery (imitating an acute environmental cell stress), revealed that MS-associated A1 mutations p.P275S and p.F281L caused significant A1 cytoplasmic mislocalization compared to WT (cytoplasmic/nuclear localization ratio: p.P275S=1.14; p.F281L=0.85; WT=0.59). The kinetics of cytoplasmic cluster formation [half-maximal formation time (minutes): p.P275S=40; p.F281L=42; WT=55] and dissociation of A1 [half-maximal dissociation time (minutes): p.P275S=11; p.F281L=21; WT=18] were significantly altered with A1 mutations. Additionally, percent dissociation efficiency was significantly altered with A1 mutations (p.P275S=69±8%; p.F281L=49±9%; WT=67±8%). Further, A1 mutations altered the quantity (clusters/cell: p.P275S=3.2; p.F281L=2.1; WT=3.4) and size [average cluster size (µm²): p.P275S=0.49; p.F281L=0.37; WT=0.24] of A1 clusters. A1 mutations also caused SG formation to occur more quickly [half-maximal formation time (minutes): p.P275S=55; p.F281L=51; WT=73] and frequently (fold change of cells with SG: p.P275S=1.6; p.F281L=2.3; WT=1.1) in response to their cluster formation by BL stimulation.

Conclusion:

Using an in vitro optogenetic approach, this study presents evidence that mutations in A1 promote A1 mislocalization, self-association clustering, altered RBP function, and cell stress leading to SG

formation. These results indicate a potential link between A1 protein dysfunction and NDG in MS pathogenesis and may allow us to develop therapies that attenuate NDG, and inhibit disability and improve the quality of life of persons living with MS.

Keywords:

hnRNPA1; mutations; optogenetics; stress granules; multiple sclerosis

28. A CLINICAL EXERCISE TRAINING PROGRAM IMPROVED CEREBROVASCULAR INSULIN SIGNALING AND OXIDATIVE STRESS REGULATION IN A PORCINE MODEL OF AGING

Presenter: Zeyad El Karsh
Collaborators: Rory A. Marshall, Cameron J. Morse, Yehia El Karsh
College: Veterinary Medicine
Supervisor: Dr. T. Dylan Olver

Background:

Selective insulin resistance in the cerebrovasculature is characterized by augmented vasoconstriction and attenuated vasodilation in response to insulin. The manifestation of selective insulin resistance is associated with a poor diet, ageing and physical inactivity, all of which promote an increase in oxidative stress. Regular exercise has been shown to normalize vascular responses to insulin, but the mechanisms responsible remain unknown. This study tested the hypothesis that exercise training ameliorates cerebrovascular selective insulin resistance in juvenile and mature pigs by improving the regulation of oxidative stress.

Methods:

Twenty juvenile (n=10F/10M; 3±1 months; mass=11±3kg) and seventeen mature (n=9F/7M; 14±1 months; mass=83±9 kg) Ossabaw miniature swine were divided into sedentary or exercise training groups (matched for age, sex and body mass). Pigs in the exercise training groups completed high intensity interval training three times per week for eight weeks. All animals were group housed with access to Western diet feed (1 kg per pig per day) as well as sugar water (10% solution; provided ad libitum). At euthanasia, their brains were harvested and cerebral arteries were dissected for pressure myography experiments. Vascular diameter was tracked continuously and vasomotor responses to insulin (1e-9-1e-6 M) were studied under two conditions: 1) untreated (vehicle); and 2) NADPH Oxidase inhibition (Apocynin; 1e-4 M). Physiologic maximum and cumulative change in diameter (area under the curve; AUC) for all groups were compared using a two-way ANOVA.

Results:

Indices of insulin-induced vasodilation were significantly higher in exercise-trained vs. age-matched sedentary controls (p<0.001). Pre-treatment with NADPH oxidase inhibitor normalized differences between groups (p≥0.85).

Conclusion:

Our results indicate that exercise training can augment insulin-induced cerebral vasodilation. Further, improvements in selective insulin resistance were coupled with attenuated insulin-stimulated production of reactive oxygen species. By improving the regulation of oxidative stress mechanisms, high intensity interval exercise training may prevent or reverse selective insulin resistance associated with a poor diet, aging and physical inactivity.

Keywords:

Aging, inactivity, exercise, cerebrovascular disease, insulin resistance, oxidative stress

29. EFFECT OF THE MUSCLE METABOREFLEX ON HEART RATE KINETICS DURING LOW-MODERATE EXERCISE IN YOUNG HEALTHY ADULTS

Presenter: Cole Elaschuk
Collaborators: Natasha G Boyes, Dana S Lahti, Ramlah Iqbal
College: Kinesiology
Supervisor: Dr. Corey Tomczak

Background:

The muscle metaboreflex increases sympathetic nerve activity (SNA) to the heart which may speed heart rate kinetics.

Methods:

We studied the effects of the muscle metaboreflex activation (MMA) on heart rate (HR) kinetics during a square-wave exercise transition, on a cycle ergometer in the low-moderate exercise intensity domain. MMA was elicited using isometric handgrip exercise, followed by brachial circulatory occlusion during cycle ergometry exercise. Four healthy adults (males=4, age: 20.5 ± 2.1 years, peak $\text{VO}_2 = 41.8 \pm 6.0$ ml/kg/min) performed square-wave exercise transitions from a power output that elicited a HR of 80-105 bpm in stage 1 to 110-120 bpm in stage 2. The control (CTL) condition was compared to an MMA condition with isometric handgrip exercise at 40% maximal voluntary contraction (MVC) followed by circulatory occlusion. HR (ECG) and mean arterial pressure (MAP; Finometer) kinetics were measured. Data were analyzed using paired sampled t-tests. $P < 0.05$ was considered significant.

Results:

There was a non-significant speeding of HR kinetics, where the time constant, tau, for MMA (20 ± 5 s) was faster when compared to CTL (33 ± 11 s, $P = 0.108$). All four participants demonstrated a speeding in HR kinetics during the MMA condition; specifically, the four participants demonstrated a 1 s, 10 s, 11 s, and 28 s speeding in tau during MMA compared to CTL. There was a significant effect of occlusion on pre-transition MAP, where MAP was higher for MMA (121 ± 10 mmHg) than for CTL (107 ± 4 mmHg $P = 0.027$). Post-transition MAP was also significantly higher during MMA (126 ± 13 mmHg) than CTL (113 ± 8 mmHg, $P = 0.037$). Pre-transition HR was significantly lower during MMA (95 ± 7 beats/min) compared to CTL (100 ± 6 beats/min, $P = 0.013$).

Conclusion:

Our findings show that increasing SNA via the muscle metaboreflex may be important for speeding HR kinetics during low-moderate intensity exercise. Our findings also suggest that MMA increases MAP during pre-transition and post-transition cycle ergometry exercise, suggesting that SNA was elevated during MMA. This observation warrants further investigation for a better understating of the effects the muscle metaboreflex has on heart rate kinetics.

Keywords:

Muscle metaboreflex, heart rate kinetics, autonomic nervous system

30. OSMOTICALLY-INDUCED TRPV1 TRANSLOCATION IN RAT SUPRAOPTIC NEURONS

Presenter: Kirk Haan
College: Anatomy, Physiology, and Pharmacology
Supervisor: Dr. Thomas E. Fisher

Background:

Osmoregulation is a crucial homeostatic process in mammals. Defects in osmoregulation can lead to clinical issues such as dehydration. This project aims to identify key mechanisms involved in central osmoregulation in mammals.

Methods:

Live-cell immunocytochemistry experiments were performed on supraoptic neurons isolated from male Long Evans rats (aged 8-14 weeks). Microscopy was completed using a Zeiss LSM700 confocal microscope. ImageJ was used for all image analyses. GraphPad PRISM 7 was used for all statistical analyses.

Results:

An osmotically-induced increase in membrane TRPV1 occurs in rat MNCs and is mediated by: phospholipase C, protein kinase C, and exocytotic membrane fusion. This increase is reversible, and the reversal requires dynamin-mediated endocytosis.

Conclusion:

Osmotically-induced TRPV1 translocation occurs in rat supraoptic neurons, and could be part of a larger response of MNCs to sustained increases in osmolality (i.e. dehydration). An enzyme shown in this project to be required for translocation, phospholipase Cdelta1, could be a key player in mediated multiple osmoregulatory processes in mammals, and defective PLCd1 could lead to potential dysfunctional systemic osmoregulation.

Keywords:

Osmoregulation, TRPV1, translocation, phospholipase C.

31. INCREASING CELLULAR LONGEVITY IN BUDDING YEAST BY ACTIVATING THE ANAPHASE PROMOTING COMPLEX

Presenter: Rachel Harris
College: Medicine
Supervisor: Dr. Troy Harkness

Background:

Canada's population is currently in the midst of a fundamental shift: seniors are a rapidly growing proportion of our population, and are living longer and healthier lives than previous generations. Our current understanding of the biological causes of aging remains poorly understood, yet extensive research suggests that many age-related pathologies may be mitigated by focusing on the aging process itself. Healthy cellular functions can be efficiently studied utilizing the budding yeast *Saccharomyces cerevisiae*, one of the best studied model organisms and a powerful system for genetic analysis. Our enzyme of interest, the Anaphase Promoting Complex (APC), is a highly conserved E3 ubiquitin ligase that is a key regulator ensuring genetic integrity throughout the mitotic cell cycle. By researching the structure and function of conserved proteins, as well as the specific protein-protein interactions that occur, it will allow for our further understanding of the complex cellular mechanisms that govern the aging process.

Methods:

The aim of this research project is to study molecular mechanisms which affect cellular longevity. Understanding changes in function of the Anaphase Promoting Complex (APC) and how they can be optimized may lead to increased cellular longevity. By utilizing direct biological activation of the APC rather than indirect, commercially available activators (such as M2I-1), I hope to identify potential therapeutic agents which can increase APC activity and extend lifespan, utilizing *Saccharomyces cerevisiae* as a model organism. It is hypothesized that the APC loses function with age, and that the introduction of biological activators may aid to rescue these effects to improve the overall health of the cell and extend longevity. A library of random peptides that reproducibly interact with the APC were screened, and thus far a small number of them were found to improve growth under stressed and normal conditions in wild type cells and could rescue mutant phenotypes.

Results:

Preliminary results suggest that the APC loses activity in aging cells, and that as cells age, the binding of select peptides rescues APC activity and extends cellular lifespan. Our current chronological life span (CLS) assays have been showing that the APC loses activity in aging wild type (WT) cells, and that introduction of a specific peptide increases APC activity beyond a hormetic response. In replicative life span (RLS) assays, a commercial inhibitor (M2I-1) increased APC activity and was found to increase cellular lifespan in WT strains.

Conclusion:

The abundance of orthologous genes and pathways between eukaryotes allows for rapid advancement of research by deciphering gene functions in yeast to predict human disease and aging. Using budding yeast as a model organism, our aim is to develop a mechanistic characterization of how these APC-binding peptides work to improve cell health and lifespan, and to provide insight into further understanding the function of the APC and its role in vital cell processes.

Keywords:

Anaphase Promoting Complex, APC, aging, lifespan

Basic Science 3

32. THE ROLE OF HNRNP A1 DYSFUNCTION AND STRESS GRANULE FORMATION IN OLIGODENDROGLIA CELLS IN THE PATHOGENESIS OF MULTIPLE SCLEROSIS MODELS

Presenter: Ali Jahanbazi Jahan-Abad
College: Medicine
Supervisor: Michael C. Levin

Background:

Multiple sclerosis (MS) is a chronic inflammatory demyelinating disease of the central nervous system (CNS). In MS, demyelination is caused by oligodendrocyte damage and death, but our knowledge of the molecular mechanisms of demyelination in MS is still lacking. Recent data suggests that dysfunctional RNA binding proteins (RBPs), features of which include nucleocytoplasmic mislocalization and stress granule (SG) formation in neuronal and glial cells, may contribute to the pathogenesis of autoimmune mediated neurological diseases of the CNS. Using MS tissue and relevant MS models, our lab has shown that neuronal dysfunction of the RBP heterogeneous nuclear ribonucleoprotein A1 (hnRNP A1) and its colocalization to cytoplasmic SGs, correlates with neurodegeneration and disease progression. Interestingly, other studies have indicated that hnRNP A1 regulates myelin gene expression, such as myelin-associated glycoprotein, which is critical for oligodendrocyte myelination. However, it is unclear whether hnRNP A1 dysfunction contributes to oligodendrocyte biology in MS and relevant MS models. We hypothesized that there might be evidence of dysfunction of the RBPs, including hnRNP A1 and SG formation in oligodendrocytes under inflammatory conditions in mice oligodendrocyte in vitro and in experimental autoimmune encephalomyelitis (EAE), an animal model of MS.

Methods:

Mice neural stem cells were isolated from the brain of E16 embryos using a neurosphere assay, and differentiated into oligodendrocytes. Cells were plated and treated with the following cytokines (2.5 μ g/mL, 24h): IFN- γ , TNF- α , and IFN- γ / TNF- α . Immunocytochemistry was used to determine hnRNP A1 localization and SG formation by stress granule assembly factor 1 (G3BP), a marker of SG formation. C57BL/6 female mice were immunized with myelin oligodendrocyte glycoprotein (MOG35-55) to induce EAE. Spinal cord tissues (n=4 each EAE and naïve control) were harvested at the peak of EAE for detection of the RBP hnRNP A1 and SG formation by immunohistochemistry and western blot.

Results:

In primary mice oligodendrocytes, cytokines (IFN- γ , TNF- α , and IFN- γ / TNF- α) caused hnRNP A1 mislocalization from the nucleus to the cytoplasm, SG formation and hnRNP A1 colocalization with SGs. EAE animals showed a higher percentage of oligodendrocytes with mislocalization of hnRNP A1 and formation of SGs ($p < 0.05$, t-test) as compared to naïve animals. There was a significant increase in hnRNP A1 expression, but not G3BP, in spinal cords of mice with EAE ($p < 0.05$) by western blot.

Conclusion:

These data indicate that hnRNP A1 dysfunction and cytoplasmic SG formation contribute to oligodendrocyte biology in EAE, which might also apply to the pathogenesis of MS.

Keywords:

Multiple Sclerosis, Experimental autoimmune encephalomyelitis, Oligodendrocyte, Heterogenous nuclear ribonucleoprotein A1, Stress granule

33. THE ROLE OF CREB3L1 IN THE REGULATION OF EPITHELIAL-TO-MESENCHYMAL TRANSITION IN BREAST CANCER CELLS

Presenter: Anish Kandel
College: Medicine
Supervisor: Deborah Anderson

Background:

Breast cancer affects roughly 1 in 8 women and is accountable for 13% of all cancer mortalities in Canadian women. Unfortunately, patients that go on to develop metastatic breast cancer have a much lower chance of survival. Epithelial-to-mesenchymal transition (EMT) is a process in which primary epithelial cancer cells can acquire mesenchymal phenotypes. This transition can facilitate invasion, migration and eventual metastasis of cancer cells. Of the many pathways that can induce activation of EMT, a key enabling pathway is the TGF β -SMAD pathway. TGF β can lead to the expression of EMT-inducing transcription factors such as TWIST1/2, SNAI1/2, and ZEB1/2. These transcription factors regulate expression of many genes via promoter activation or repression. Epithelial and mesenchymal genes such as E-Cadherin (CDH1) and Fibronectin (FN1) respectively, are regulated by the transcription factors. Other genes subject to regulation include genes involved in extracellular matrix degradation, cell movement, and cell survival. A common feature of metastatic breast cancers is the loss of expression of cAMP responsive binding element protein 3 like 1 (CREB3L1). Forced expression of HA-CREB3L1 reduces cell migration, cell invasion and anchorage-independent growth of these cells in vitro and blocks tumor growth and metastasis in mouse xenografts. CREB3L1 expression is downregulated by epigenetic silencing and treatment with histone deacetylase (HDAC) inhibitors such as trichostatin A (TSA) can induce expression of endogenous CREB3L1. The mechanism of CREB3L1 action in its metastasis suppressing activity is still unclear and must be further investigated. In order to better understand CREB3L1 activity, differential gene expression analysis of several breast cancer cell lines \pm HA-CREB3L1 was completed by the Anderson Lab. Using Ingenuity Pathway Analysis (IPA), EMT and TGF β signalling were strongly activated in highly metastatic CREB3L1-deficient breast cancers, in comparison to the poorly metastatic HA-CREB3L1 expressing cells. ChIP on chip data also highlights that CREB3L1 directly binds to promoter regions of TWIST1 and SNAI1 genes which suggests a role for CREB3L1 in the regulation of EMT inducing transcription factors.

Methods:

1) Evaluate TGF β responsiveness in several \pm HA-CREB3L1 breast cancer cell lines treated with TGF β . This will be done by assessing the activation of downstream TGF β targets and the regulation of TGF β target genes and EMT markers. SMAD2/3 knockdown (directly involved in TGF β signalling pathway) will be performed to determine whether CREB3L1 requires the TGF β pathway, or if it acts more directly. 2) Characterize the regulation of TWIST1 and SNAI1 genes by CREB3L1 using luciferase reporter assays in \pm HA-CREB3L1 cells. Mutational analysis of the predicted CREB3L1 binding sites within the promoter regions of the TWIST1 and SNAI1 genes will be completed as well. 3) Evaluate the impact of HDAC inhibitors such as TSA, panobinostat, and entinostat on re-expression of endogenous CREB3L1, TGF β responsiveness and the ability to induce MET to restore the epithelial phenotype and block metastasis. Since HDAC inhibitors act broadly to alter gene expression, these experiments are going to be repeated in CREB3L1 knockdown cells to block the re-expression of CREB3L1 and better evaluate the impact of CREB3L1 specifically.

Results:

We expect that TGF β will induce SMAD2/3 and regulate several target genes that lead to the increase in expression of EMT inducing genes and subsequent mesenchymal phenotypes in the absence of HA-CREB3L1. In the presence of HA-CREB3L1 we expect that these effects will be blocked due to the expression of CREB3L1. As well, we suspect that since CREB3L1 can bind to the promoter regions of both TWIST1 and SNAI1, that it will regulate both genes to reduce cell migration, invasion and tumor progression. Lastly, we anticipate that one or more of the HDAC inhibitors will restore endogenous CREB3L1 expression and that this will block the effects of TGF β , shifting the phenotypes of the cells to a less mesenchymal, more epithelial phenotype.

Conclusion:

No conclusions have been reached yet.

Keywords:

EMT, Breast cancer, CREB3L1, TGF β , Metastasis

34. CARTILAGE PGS INHIBIT BMP SIGNALING THROUGH THE CANONICAL SMAD PATHWAY, BUT NOT THE NON-CANONICAL P38 PATHWAY, DURING ENDOCHONDRAL OSSIFICATION

Presenter: Elham Koosha
Collaborators: E. Koosha, C. Brenna, N. Jain, and B.F. Eames
College: Medicine
Supervisor: Brian Eames

Background:

The involvement of the extracellular matrix (ECM) in cell signaling is not fully understood, but it may hold secrets relating to human pathologies of the skeleton. During endochondral ossification, which produces most bones in the human body, chondrocytes secrete a proteoglycan (PG)-rich ECM in which growth factors can travel to induce maturation and perichondral bone formation. Mutation in *fam20b*, encoding a xylose kinase that phosphorylates xylose residue in PGs, leads to lower levels of chondroitin sulfate PGs, early *ihh* expression, and initiation of perichondral bone formation earlier. Given BMP's known role in endochondral ossification and promoting *ihh* expression, we hypothesize that cartilage PGs normally inhibit BMP signaling pathway. To evaluate changes in the canonical and non-canonical BMP signaling pathways, immunocytological staining of cartilage sections was performed for phospho-Smad (p-Smad) and phospho-p38 (p-p38), respectively. Also, the hypothesis was tested functionally by determining changes in endochondral bone formation and chondrocyte maturation gene expression, *col10a1* and *ihh*, using skeletal histology and in situ hybridization techniques in *Tg(hsp70l:dnXla.Bmpr1a-GFP)*, *Tg(hsp70l:dnXla.Bmpr1a-GFP)/fam20b* mutant, and DMH1-treated zebrafish embryos. Mutant *fam20b* zebrafish chondrocytes had up-regulated p-Smad signaling, but not p-p38. *Tg(hsp70l:dnXla.Bmpr1a-GFP)* and DMH1-treated zebrafish embryos both had downregulated p-Smad signaling, decreased expression of chondrocyte maturation genes including *col10a1* and *ihh*, and less perichondral bone compared to wild-type fish. Also, early perichondral bone formation in *fam20b* mutants was phenotypically rescued by the BMP loss-of-function transgene and DMH1 treatment, establishing a clear relationship between BMPs and proteoglycans. Through these in vivo analyses, we propose a novel role of ECM proteoglycans as inhibitors of BMP signaling molecules that control bone formation.

Methods:

Results:

Conclusion:

Keywords:

Proteoglycans, BMP Signaling Pathway, Perichondral bone formation

35. ARE DETOXIFICATION ENZYMES INDUCED SIMILARLY ACROSS HONEY BEE CASTES IN RESPONSE TO NEONICOTINOID EXPOSURE?

Presenter: Ivanna Kozii
Collaborators: Sarah Wood, Colby Klein, Michael Zabrodski
College: Veterinary Medicine
Supervisor: Elemir Simko

Background:

Neonicotinoid insecticides are implicated in decreasing honey bee health. Regulatory toxicity assays in honey bees focus on the worker caste, possibly overlooking toxicity to the queens and drones. Our previous study demonstrated that neonicotinoid toxicity is highly caste-specific. The objective of this study was to determine if there is a correlation between detoxification enzyme activity and the caste-specific susceptibility of honey bees (workers, drones and queens) to a commonly used neonicotinoid, thiamethoxam (THI), in response to larval, adult or combined larval and adult exposure.

Methods:

We tested the induction of enzyme activity in bees in response to larval and/or adult THI exposure. Age-matched honey bee larvae received either water (control) or 25ng THI through larval food contamination. At emergence, adult bees in these groups were further subjected to contact exposure of incremental doses of THI (control, low and high concentration). Activity of esterase, glutathione S-transferase (GST), and acetylcholine esterase (AChEst) were determined at emergence and 48 hours post contact exposure.

Results:

We found that enzyme activity is highly caste-specific; however, THI exposure during larval and/or adult stages did not have a significant effect on enzymes activity. Enzyme activity was highest in worker bees, followed by drones, and then queens. Esterase, GST and AChEst activity of queens was 20x, 5x and 70x lower, respectively, compared to workers. Similarly, esterase and AChEst activity was 5x and 70x lower in the drones compared to workers, whereas their GST activity was similar.

Conclusion:

Accordingly, enzyme activity of esterase, GST and AChEst does not correlate with the differential caste survival in response to THI exposure observed in our previous studies. However, our findings highlight that enzyme activity is highly variable between castes, which may affect their susceptibility to insecticide toxicity and should be considered in future toxicity studies.

Keywords:

Apis mellifera, caste, enzymes, thiamethoxam

36. DISCOVERING THE LINK BETWEEN VIDEO GAMING AND READING: PERIPHERAL DEMANDS ARE ASSOCIATED WITH ATTENTIONAL CUING AND LEXICAL READING

Presenter: Shaylyn Kress
Collaborators: Josh Neudorf, Braedy Borowsky, Chantal Chabot
College: Arts and Science
Supervisor: Ron Borowsky

Background:

Video games continue to increase in popularity as a past-time among Canadians (Entertainment Software Association of Canada, 2018). As more people play video games, it becomes increasingly critical to understand the implications of this activity on cognitive processes. Research spanning back to the early 2000s (e.g. Green & Bavelier, 2003) has identified a relationship between action video game experience and visual-spatial attention, and more recent research (e.g. Franceschini et al., 2015) found action video games improved reading ability in children with dyslexia. It may be the case that video games impact reading ability via attentional mechanisms, as previous research has identified neurobiological links between visual-spatial attention and reading processes (Ekstrand et al., 2019). The current study seeks to identify what components of video games may be related to reading and attentional processes in a hybrid attention-reading task.

Methods:

Twenty-three participants completed an 8-location hybridized attention-reading task. The attentional location cue (e.g. NW) with 75% cue validity was followed by a target that required either lexical reading (exception word; EXC; e.g. 'yacht') or phonetic decoding (pseudohomophone; PH; e.g. 'yawt'). Participants reported their most frequently played games and the time spent playing these games. Brief gameplay videos from each reported game were analysed for the frequency of visual-spatial changes. Central graphical (CG) and central text (CT) changes (CG) were the average number of graphical and text changes that occurred per minute within a 3.5 cm radius at the screen centre, while peripheral graphical (PG) and peripheral text (PT) changes were the average number of graphical and text changes that occurred per minute outside of this radius.

Results:

Fifty-one games were reported by participants. The "Weighted Scores" for each of the four visual-spatial change measures were calculated for each participant as $\Sigma(\text{monthly hours for each reported game} * \text{visual change score for each reported game})$. PT Weighted Score was positively correlated with the attentional cuing effect during exception word reading ($r = .558, p = .006$), and PG Weighted Score was also positively correlated with the attentional cuing effect during exception word reading ($r = .508, p = .013$).

Conclusion:

These results suggest that the quantity of peripheral visual-spatial demands in a video game may drive the previously observed relationship between video game experience and both reading and attentional processes. These findings have implications in the field of video game development, where game developers, researchers, and educators could work together to design video games with

peripheral demands tailored to improve lexical reading skills. Future research should examine automatic attention, given the overlap between exception word reading and automatic attentional processes (e.g. Ekstrand et al., 2019).

Keywords:

Video games, lexical reading, phonetic decoding, attention

37. TISSUE FACTOR PATHWAY INHIBITOR AND THE DEVELOPMENT OF MULTIPLE DRUG RESISTANCE IN BREAST CANCER

Presenter: Mathew Labachowski
College: Medicine
Supervisor: Troy Harkness

Background:

Chemotherapeutics are an effective form of cancer treatment on which many patients rely. However, for any given patient chemotherapy will eventually lose its effectiveness due to the development of multiple drug resistance (MDR). Given enough time MDR occurs almost universally, and once resistance to one chemotherapeutic is developed this resistance then applies in a non-specific manner to a wide range of other drugs. The coagulation regulator tissue factor pathway inhibitor (TFPI) is elevated in many MDR cancers, where it localizes to the nucleus instead of its normal location on the cell surface, and is believed to drive development of MDR. We believe a large ubiquitin ligase the anaphase promoting complex (APC) can target nuclear TFPI for degradation helping to prevent MDR.

Methods:

We examine the abundance and localization of TFPI within drug sensitive and MDR human MCF7 breast cancer cells, as well as cells undergoing development of resistance. We use commercially available tamoxifen, an estrogen receptor modulator, resistant MCF7 cells, as well as generate our own drug resistant cells using exposure to the chemotherapeutic doxorubicin. An APC activator known as M2i, and small peptides developed in our lab, are used to activate the APC, and observe the effect of APC activation on TFPI and drug resistance. APC inhibition is also performed using an inhibitor known as APCIN.

Results:

We have shown that TFPI abundance is increased in drug resistant MCF7 breast cancer cells, and becomes elevated early in response to doxorubicin exposure. This elevation of TFPI occurs before the development of MDR markers. APC substrates are also elevated within drug resistant MCF7 cells, and cells undergoing exposure to doxorubicin.

Conclusion:

TFPI is elevated in response to chemotherapeutic exposure before increased MDR markers are observed. This is compatible with TFPI playing a driving role in the development of MDR. Cancer cells displaying increased TFPI abundance, also show an increased abundance of APC substrates. This observation suggests that APC activity is impaired in these cells, and provides a possible explanation for TFPI accumulation. Future work will further explain what is occurring.

Keywords:

TFPI, Multiple Drug Resistance, Breast Cancer, Cancer, APC

38. ANTIBODIES TO THE RNA BINDING PROTEIN HNRNP A1 CONTRIBUTE TO NEURODEGENERATION IN AN IN VITRO MODEL OF MULTIPLE SCLEROSIS

Presenter: Cole Libner
Collaborators: Dr. Hannah Salapa
College: Medicine
Supervisor: Dr. Michael Levin

Background:

Multiple sclerosis (MS) is an autoimmune and neurodegenerative disease of the central nervous system. Neurodegeneration, death and damage of neurons, has been identified to underlie permanent disability in persons living with MS, yet its cause remains poorly understood. MS patients make antibodies to the RNA binding protein heterogeneous nuclear ribonucleoprotein A1 (hnRNP A1). We have previously identified that anti-hnRNP A1 antibodies enter neurons and exacerbate hnRNP A1 dysfunction and neurodegeneration in models of MS. Dysfunctional RNA binding proteins (including hnRNP A1) have become a pathogenic hallmark of many neurodegenerative diseases including MS and have been demonstrated to result in mislocalization of the protein from the nucleus to the cytoplasm along with the formation of cytoplasmic stress granules. Although dysfunctional hnRNP A1 is a feature of MS, it is unknown whether or not this dysfunction triggers or occurs as a result of neurodegeneration. Therefore, we hypothesize that the addition of anti-hnRNP A1 antibodies to neuronal cultures will result in an exacerbation of hnRNP A1 dysfunction preceding neurodegeneration.

Methods:

Embryonic mouse cortical neurons were cultured and treated with anti-hnRNP A1 or control IgG antibodies (20 ug/mL) for 6, 12 or 24 hours. A separate group of cultures received no treatment and were left as controls. Neurons were analyzed quantitatively for antibody uptake, hnRNP A1 mislocalization, stress granule formation, and neurodegeneration with markers of necroptosis, a cell death pathway, and neurite length.

Results:

By immunocytochemical analysis we found that compared to controls, anti-hnRNP A1 antibodies were preferentially taken up by neurons at 6, 12 and 24 hours ($p < 0.01$) resulting in (i) increased hnRNP A1 mislocalization at 6 and 12 hours ($p < 0.001$), (ii) increased stress granule formation at 12 and 24 hours ($p < 0.05$), (iii) increased markers of necroptosis at 12 hours ($p < 0.001$), and (iv) a reduction in neurite length at 24 hours ($p < 0.05$).

Conclusion:

In contrast to controls, neurons treated with anti-hnRNP A1 antibodies showed that hnRNP A1 dysfunction, including hnRNP A1 mislocalization and stress granule formation, occurred prior to increased markers of necroptosis and reduced neurite length. This is indicative of hnRNP A1 dysfunction triggering rather than occurring as a result of neurodegeneration. These data reveal a novel mechanism of neurodegeneration involving autoimmunity to an intraneuronal target (hnRNP A1), which may be targeted to inhibit permanent disability in MS.

Keywords:

Multiple Sclerosis, RNA binding protein dysfunction, heterogenous nuclear ribonucleoprotein A1, neurodegeneration, necroptosis

39. EXPLORING THE INFLUENCE OF SETTINGS ON SPATIOTEMPORAL STRIDE PARAMETERS DURING WALKING AT DIFFERENT SPEEDS IN YOUNG ADULT MALES AND FEMALES

Presenter: Jackson Lordall
Collaborators: Alison Oates, Joel Lanovaz
College: Kinesiology
Supervisor: Alison Oates
Co-supervisor(s): Joel Lanovaz

Background:

Wearable technology allows quantitative examination of walking outside of laboratory settings. Past research suggests there can be differences in stride parameters between settings; however, studies differ in methodology and no studies have compared more than two settings. This study explored how stride parameters are influenced across multiple settings for young adult males and females during walking at different self-selected speeds.

Methods:

In a block randomized design, participants walked in four settings (laboratory, hallway, indoor open, outdoor pathway) at three speeds (slow, preferred, fast) following standardized instruction. An inertial-based full body kinematic data collection system was worn; collecting stride velocity, stride length, and cadence for the middle strides of each trial. A 4 x 3 x 2 (setting x walking speed x participant sex) RM ANOVA was conducted for each dependent variable. Significant interaction effects were further investigated using multiple RM ANOVAs with adjusted pairwise comparisons.

Results:

A total of 14 males (age=23+/-4yrs; height=181+/-7cm; mass=79+/-1kg) and 15 females (age =22+/-4yrs; height=170+/-7cm; mass=70+/-2kg) participated. Statistical analysis indicated significant setting x speed interactions for stride velocity ($p=.021$), stride length ($p<.001$), and cadence ($p=.002$). There were significant main effects of participant sex: females had greater cadence ($p=.013$) and males had larger stride lengths ($p=.023$).

Conclusion:

The effect of setting depended on walking speed. There were greater effects of setting on stride parameters at slow and preferred speeds. Generally, the lab and hallway were similar, and the indoor open and outdoor pathway were different. These findings suggest that laboratory-based assessments of walking may not reflect walking outside of laboratory settings. The sex-based differences highlight the importance of considering sex as an independent factor to improve walking data interpretation. Further research in different settings for older adult and clinical populations is important to assess the ecological validity of laboratory-based walking assessments.

Keywords:

Walking biomechanics, motor control, wearable sensors, ecological validity

Basic Science 4

40. UNDERSTANDING THE ROLE OF ATP IN CEREBRAL BLOOD FLOW REGULATION FOR CLINICAL EXERCISE PRESCRIPTION

Presenter: Adam Luchkanych
Collaborators: Dr. T. Dylan Olver
College: Kinesiology
Supervisor: Dr. Corey Tomczak

Background:

Competing influences regulate blood flow control in the brain. In the skeletal muscle vasculature, purinergic signaling attenuates α 1-adrenergic and peptidergic-induced vasoconstriction (i.e., phenomenon referred to as functional sympatholysis). Whether this occurs in the cerebrovasculature remains unknown. The purpose of this study was to determine the influence of ATP on α 1-adrenergic and peptidergic-mediated vasoconstriction in cerebral arteries. We hypothesized that ATP would attenuate the α 1-adrenergic- and peptidergic-mediated vasoconstriction in isolated pial arteries.

Methods:

Female pigs (n=5) were euthanized and their brains were harvested. Thereafter, 1a branches (mean ID: 319 μ m) of the middle cerebral artery (MCA) were dissected for wire-myography. Dose-response curves for the α 1-adrenergic agonist phenylephrine (PE) (1e-10-1e-4 M) and for the peptidergic agonist NPY (1e-12-1e-6M) were performed in the absence or presence of ATP (1e-6 M). A two-way repeated measures ANOVA and paired, one-tailed t-tests were performed where appropriate.

Results:

The overall magnitude (area under the curve) of PE mediated cerebral vasoconstriction was attenuated by ATP (p=0.03). However, reductions in the maximal response to PE in arteries pre-treated with ATP were not significantly different (p=0.10). The overall magnitude as well as maximal NPY mediated cerebral vasoconstriction was attenuated by ATP (p \le 0.05).

Conclusion:

ATP attenuates PE- and NPY-mediated cerebral vasoconstriction. Therefore, similar to the skeletal muscle vasculature, purinergic signaling attenuates vasoreactivity to α 1-adrenergic and peptidergic receptor activation in the cerebrovasculature. Functional sympatholysis may assist in coupling cerebral blood flow to brain metabolism in the setting of heightened sympatho-excitation.

Keywords:

Cerebral Blood Flow, Functional Sympatholysis, Adenosine Triphosphate, Adrenergic, Peptidergic

41. FACING RESUSCITATION HEAD ON: REVISITING CPR GUIDELINES TO IMPROVE NEUROLOGICAL OUTCOMES

Presenter: Rory Andrew Marshall
College: Veterinary Medicine
Supervisor: Dr. T. Dylan Olver

Background:

Introduction: Cardiopulmonary resuscitation (CPR) is a standard treatment for cardiac arrest. CPR only produces ~30% of normal blood flow, which is insufficient to perfuse the brain adequately. The standard chest compression (SCC) location is over the mid-sternum, which is not over the largest area of the heart. Adopting a left ventricle chest compression (LVCC) location, directly over the largest area of the heart, has been shown to improve blood pressure during CPR. We hypothesized that, consistent with improved blood pressure, LVCC will promote greater cerebral blood flow (CBF) than standard chest compressions (SCC).

Methods:

Methods: Female pigs (N=32; 35±2 kg) were randomized to receive either SCC (n=14) or LVCC (n=18) following 2 minutes of untreated asphyxiated cardiac arrest. Transthoracic echocardiography was used to identify and externally mark the aortic root and midpoint of the left ventricle for mechanical chest compressions (LUCAS III). ETCO₂ (surrogate for cardiac output), arterial blood pressure (BP, arterial catheter line), and CBF velocity (CBFv; transcranial Doppler) were measured at baseline, during cardiac arrest, and through 3 rounds of Basic Life Support (BLS) CPR. Data were analyzed using a Mixed Model ANOVA.

Results:

Results: All baseline hemodynamics were similar between the SCC and LVCC groups ($P \geq 0.224$). During CPR, ETCO₂ (SCC=24±10 vs. LVCC=36±6 mmHg, $P < 0.001$), systolic BP (SCC=45±10 vs. LVCC=61±10 mmHg, $P < 0.001$), diastolic BP (SCC=33±10 vs. LVCC=41±8 mmHg, $P < 0.001$), mean BP (SCC=33±9 vs. LVCC=49±9 mmHg, $P < 0.001$), systolic CBFv (SCC=19±6 vs. LVCC=32±6 cm/s, $P < 0.001$) and mean CBFv (SCC=5±2 vs. LVCC=11±5 cm/s, $P < 0.001$) were significantly elevated in the LVCC vs SCC group.

Conclusion:

Conclusion: LVCC improved ETCO₂, BP, and the index of CBF throughout BLS CPR in a porcine model of cardiac arrest. **New and Noteworthy:** This is the first study to provide evidence that compared with mechanical compressions performed over the middle of the chest, compressions performed over the left ventricle promote greater CBF during BLS CPR. Compressing a larger area of the heart may be an effective technique to improve CBF in a clinical setting. **Funding:** This work was funded by the Canadian Resuscitation Outcomes Consortium Young Investigator Award RAM & TDO, the Western College of Veterinary Medicine Devolved Scholarship RAM, and the Saskatchewan Health Research Foundation TDO.

Keywords:

CPR, brain, left ventricle, chest compression

42. CANNABINOID RECEPTORS AND REGULATION OF BRAIN BLOOD VESSELS

Presenter: Cameron J Morse
Collaborators: Jude S Morton, Zeyad El-Karsh, Rory A. Marshall
College: Western College of Veterinary Medicine
Supervisor: T. Dylan Olver
Co-supervisor(s): Darrell D Mouddeau

Background:

Cannabinoid receptors 1 & 2 (CB1 & CB2) are present throughout the cardiovascular system and evidence indicates that CB1 activation causes vasodilation in peripheral vascular beds. However, it remains unclear what the direct effects of CB1 or CB2 activation are in cerebral arteries. The present study tested the hypothesis that CB1 and not CB2 receptor activation elicits vasorelaxation in the cerebrovasculature.

Methods:

Female pigs (age=2 months; n=16) were euthanized, their brains were harvested, and pial arteries branching from the middle cerebral artery were isolated for wire myography (Multi-Wire Myograph System; DMT). Vessels were pre-contracted with a prostaglandin analogue (U46619; 1e-6M to 1e-4M). Thereafter, vasorelaxation in response to a CB1 & CB2 receptor agonist CP55940 (3e-12M to 1e-6M; half log doses) was examined under the following conditions: 1) untreated; 2) CB1 receptor blockade (AM251; 1e-7); or 3) CB2 receptor blockade (AM630; 1e-7). To determine whether CB1-mediated vasomotor responses occur through an endothelial-dependent pathway, vasoreactivity in response to CP55940 was examined during CB2 blockade + endothelial removal (denudation). To further examine the mechanism through which CB1-dependent relaxation occurs, vasorelaxation in response to CP55940 under the following conditions: 1) CB2 blockade + nitric oxide synthase (NOS; L-NAME, 3e-4M) inhibition; 2) CB2 blockade + cyclooxygenase (COX; naproxen, 3e-4) inhibition; 3) CB2 blockade + combined NOS and COX inhibition.

Results:

The data reveal that CP55940 elicits a CB1-dependent relaxation in cerebral arteries and this effect is blunted significantly by removal of the endothelium. The data shows that CB1-mediated vasorelaxation was attenuated, but not abolished, by NOS inhibition, COX inhibition, and the combination of NOS + COX inhibition.

Conclusion:

Overall, these data indicate CB-1 acts on the endothelium to cause vasorelaxation through a combination of nitric oxide, prostaglandins and endothelial hyperpolarizing factor. The effects of cannabinoids on brain vascular function are not established. Therefore, this information may be leveraged to study new therapeutic applications of cannabinoids and be important when evaluating the physiological effects and safety of cannabinoid use.

Keywords:

Cannabinoid, Vascular function, Physiology

43. EFFECTS OF CIRCADIAN DYSREGULATION ON SALIVARY GLAND MORPHOLOGY AND FUNCTION

Presenter: Helya Mortazavi
Collaborators: Raed Said, Liubov Lobanova, Silvana Papagerakis
College: Dentistry
Supervisor: Petros Papagerakis
Co-supervisor(s): Silvana Papagerakis

Background:

The sympathetic nerve activation from the suprachiasmatic nucleus rhythmically controls salivary gland function. This rhythmicity is controlled by the circadian clock, a biochemical oscillator that determines the sleep and wake patterns and regulates behavior, electrophysiological, and metabolic activities via transcriptional-translational feedback loops. Objectives: To assess the function of circadian clock genes in salivary gland morphology and function.

Methods:

We assess the salivary gland function and rate of saliva production in four clock genes knock-out (KO) mice models: Aryl hydrocarbon receptor nuclear translocator-like protein 1 (ARNTL) KO/Arrhythmic, Period 2 (Per2)-KO and Cryptochrome (Cry1)-KO/shortened circadian period, and Cry2KO/elongated circadian period and their corresponding wild-type siblings. We used gross inspection, histological analysis, immunohistochemistry, qRT-PCR, and proteomics. We assess the rate of saliva secretion by using pilocarpine for parasympathetic stimulation at morning versus night in young (6-weeks), mature adult (12-weeks), and middle age (7-months) mice.

Results:

Circadian dysregulation results in noticeable differences in the salivary gland morphology and structure particularly in the middle age mice with the most prominent changes observed in the Cry1KO and Per2KO. Our data demonstrate that Cry1KO salivary glands present an increase in fat and connective tissue, and more basophilia implying a reduced rate of salivary protein production while Per2KO show enhanced hypertrophy. Furthermore, the expression of multiple salivary functional biomarkers (ductal and acinar) was altered in knock-out mice models compared to wildtypes. Interestingly, circadian ablation did not result in significant changes in the volume of saliva induced; however, the volume of saliva was lesser at night compared to the morning.

Conclusion:

Collectively, the data presented here, strongly suggest that the circadian clock may play an important role in regulating salivary gland development and function. Understanding the circadian controls of salivary glands will provide the basis for a better understanding of salivary gland pathologies such as Sjogren's syndrome and sialadenitis.

Keywords:

Circadian Clocks, Sjogren's syndrome, Salivary glands

44. NMR FECAL METABOLOMICS: A NOVEL TECHNIQUE FOR MONITORING STRESS IN WATERFOWL

Presenter: Breanne Murray
College: Veterinary Medicine
Supervisor: Dr. Karen Machin

Background:

Waterfowl populations are expected to decline because of anthropogenic and environmental changes that act as stressors to wild birds (such as altered habitat and food supply, climate change, etc.). These stressors can trigger the hypothalamic pituitary adrenal (HPA) axis to release stress hormones (corticosterone, CORT) which triggers a myriad of physiological processes that provide energy to deal with the stressor, restore homeostasis and increase survival. Corticosterone has been used to monitor the impacts of stressors in many species. However, as CORT can be highly variable (necessary for normal bodily function and fluctuating amongst life history stages) and is impacted by acute stressors, such as handling during blood sampling, it may not be a reliable indicator. A better approach is to examine multiple measures of stress and physiological responses to evaluate these impacts. Metabolomics is a novel tool that involves a systems approach to studying small, endogenous metabolites that participate in metabolic reactions including response to stressors

Methods:

The objective of this study was to investigate the use of fecal metabolomics to identify metabolites related to stress in waterfowl. We hypothesized that metabolomics can be used to differentiate between ducks that were subjected to a stressor (restricted feed) from unstressed (baseline) duck. Captive mallard ducks (*Anas platyrhynchos*) were subjected to a six-day restrictive food trial (25% food restriction based on weight per bird, treatment, n=9). Fecal samples were collected from ducks prior to (baseline) and during feed restriction (stressor). H1 Nuclear Magnetic Resonance (NMR) spectroscopy was performed to analyze metabolites.

Results:

We found that fecal metabolite profiles could be used to distinguish ducks subjected to restricted feed from baseline.

Conclusion:

Fecal metabolomics shows promise as a non-invasive novel tool in identifying and characterizing physiological responses associated with stressors in wild birds.

Keywords:

Stress physiology, wildlife, metabolomics

45. SYNTHETIC OLIGODEOXYNUCLEOTIDES CONTAINING CPG MOTIFS INCREASE SYSTEMIC ANTIMICROBIAL MECHANISMS AND IMMUNE CELL METABOLISM IN BROILER CHICKENS

Presenter: Iresha Subhasinghe
Collaborators: Susantha Gomis, Khawaja Ashfaque Ahmed, Betty Chow-Lockerbie
College: Veterinary Medicine
Supervisor: Dr. Susantha Gomis

Background:

Bacterial diseases of the poultry industry associated with increased mortality and decreased production are the major economic burden of the commercial poultry industry. Preventative use of antibiotics will soon be discontinued to minimize the development of antimicrobial resistant bacteria. Therefore, development of control strategies using alternatives to antibiotics is crucial in controlling bacterial diseases in the poultry industry to improve poultry health. Cytosine phosphodiester guanine oligodeoxynucleotides (CpG-ODNs) is a proven immune stimulant in chickens and provides protection against bacterial diseases following different delivery routes such as intramuscular (IM) and intrapulmonary (IPL). Our objective was to investigate antimicrobial mechanisms and associated cellular metabolic pathways of immune cells responsible for immunoprotection following delivery of CpG-ODN.

Methods:

CpG-ODN (TCGTCGTTGTCGTTTTGTCGTT2007) was used in all animal experiments at the dose of 50µg/bird and the control group received saline by the intramuscular (IM) route in 2-3 week old broiler chickens. We have modified assays developed for mammalian species and measured oxidative burst, phagocytosis. A novel degranulation assay was developed to measure antimicrobial activities of heterophils using lysosomal specific anti-LAMP-1, CD107 antibody. Besides, a novel assay using Agilent Seahorse XFP analyzer was optimized to quantify real-time measurement of glycolysis and mitochondrial respiration of birds.

Results:

Birds received CpG-ODN increased their oxidative burst activity of heterophils 1250-1400 mean fluorescent intensity (MFI) compared to the control group 750-900 MFI. Furthermore, phagocytosis of heterophils in CpG-ODN treated birds (35-40%) was higher compared to the control birds (20-25%). An elevated degranulation was detected in birds received CpG-ODN (60-75 %) compared to the control group (40-58%). Birds received CpG-ODN had increased glycolytic capacity, compensatory glycolysis of leukocytes [extracellular acidification rate (ECAR)], 150-250 (pmol/min) compared to the control group [40-60 (pmol/min)]. Furthermore, birds received CpG-ODN had increased mitochondrial respiration [oxygen consumption rate (OCR)] 75-80 (pmol/min) compared to the OCR of the control group 20-40 (pmol/min).

Conclusion:

Results of our study demonstrated that CpG-ODN activated antimicrobial activities of broiler chickens via increased energy production and metabolic activities of immune cells. Novel assays that we developed will be resourceful in our ongoing studies measuring immunoprotective activities of immune cells activated with CpG-ODN in our infectious disease models of broiler chickens. Our results demonstrated the utility of CpG-ODN as an alternative to antibiotics in the broiler chicken industry.

Keywords:

CpG-ODNs, Antimicrobial Mechanisms, Immune Cell Metabolism, Broiler Chickens

46. IN VITRO EFFECTS OF FUNGICIDES ON THE SUSCEPTIBILITY OF HONEY BEE (APIS MELLIFERA) LARVAE TO EUROPEAN FOULBROOD

Presenter: Jenna Thebeau
Collaborators: Dana Liebe, Sarah Wood, Larhonda Sobchinshin
College: Veterinary Medicine
Supervisor: Elemir Simko

Background:

Canada is the world's second largest producer of blueberries, honey bees (*Apis mellifera*) contributing 90% of pollination services required by blueberry crops each year. This symbiotic relationship and commercial blueberry pollination is threatened by the increased incidence of bacterial infections colloquially referred to as European foulbrood disease (EFB). *Melissococcus plutonius* is the causative agent of EFB with infection resulting in higher mortality rates in honey bee larvae in colonies under environmental and nutritional stress. Pesticide exposure has been implicated in the immunosuppression of honey bees and is suspected to increase susceptibility to EFB. The effects of exposure to formulated fungicide products commonly used in blueberry production on the susceptibility of honey bee larvae to EFB during blueberry pollination is currently unknown.

Methods:

Using an in vitro larval infection model of EFB, we tested the effects of chronic larval exposure to field-relevant concentrations of two formulated blueberry fungicides, Captan® and Kenja®, on larval mortality from *M. plutonius* infection.

Results:

We found that larvae chronically exposed to Captan®, Kenja®, or a combination of these two products, did not experience a significant decrease in larval survival relative to infected control larvae that were not exposed to fungicides. Instead, chronic exposure to Captan® or Kenja® during development significantly increased larval survival against EFB by 33% compared to infected control larvae ($P < 0.01$).

Conclusion:

These in vitro results suggest that chronic exposure of honey bee colonies to these two formulated fungicide products during blueberry pollination should not predispose these colonies to EFB, although colony-level studies are necessary to verify the field-relevance of these in vitro results. Further in vitro experiments are underway to test larval survival during *M. plutonius* inoculation and subsequent exposure to additional fungicidal product combinations commonly used during commercial blueberry production.

Keywords:

Honeybees, fungicides, European foulbrood disease (EFB), mortality, blueberries

47. NOVEL NON-INVASIVE WAY TO DRIVE ROBUST REPAIR IN AN MS PRECLINICAL MODEL

Presenter: Nataliya Tokarska
Collaborators: Hannah E. Salapa, Michael C. Levin, Bogdan F. Popescu
College: Medicine
Supervisor: Valerie M.K. Verge
Co-supervisor(s): Sarah J. Donkers

Background:

Multiple Sclerosis (MS) is an inflammatory disease of the central nervous system (CNS) characterized by immune-mediated segmental demyelination and variable degrees of axonal and neuronal degeneration. Efficient repair of demyelinated lesions is a major challenge of MS. Conventional therapies tend to focus on immune response modulation responsible for the generation of these lesions. While this alleviates symptoms and mitigates damage, it alone does not address the fundamental problem of efficiently remyelinating damaged areas of the CNS. In early MS, demyelination can be followed by efficient remyelination, supporting that endogenous repair mechanisms exist. Our lab focuses on therapies that enhance these intrinsic repair mechanisms following nervous system injury. We find acute intermittent hypoxia (AIH; intermittent periods of reduced oxygen), a non-invasive therapy, improves outcomes in spinal cord and peripheral nerve injured animals. But its potential for repair in MS is unknown. The aim of this research was to investigate the effects of AIH treatment on repair of the demyelinated CNS and disease progression in the myelin oligodendrocyte glycoprotein 35-55 (MOG35-55) experimental autoimmune encephalomyelitis (EAE) mouse preclinical model of MS.

Methods:

EAE was induced by immunization with MOG35-55. EAE mice received either AIH (10 cycles of 5min 11% O₂ alternating with 5min 21% O₂) or Normoxia (control; 21% O₂ for same duration) treatment once daily for 7d at near peak EAE disease (score = 2.5), with mice followed for an additional 7d post-treatment. Clinical scores were recorded daily to examine changes in animals. Spinal cord tissue was processed and analyzed quantitatively to assess the impact that AIH has on multiple indices of repair, including degree of myelination, axon protective phenotype, oligodendrocyte precursor cell (OPC) recruitment, and immune response modulation.

Results:

Quantitative analysis showed that 7 days of daily AIH significantly improved clinical scores when treatment was started at near peak EAE disease. Compared to Normoxia, AIH resulted in significantly more myelin basic protein (MBP) and elevated levels of axon protective phosphorylated neurofilaments, reorganization of node of Ranvier Caspr⁺ paranodes and OPC recruitment. A quicker resolution of the inflammatory response and the polarization of macrophages/microglia towards an M2 pro-repair phenotype was also observed.

Conclusion:

AIH treatment started at near peak disease shows a remarkable impact on improvement of clinical scores and drives robust repair in EAE mice. Collectively, these findings support a role for AIH treatment as a non-invasive therapeutic strategy to enhance CNS repair following demyelination in an

MS preclinical model. Further investigations confirming these results and providing additional insight into the mechanisms and benefits of AIH treatment will allow for translation into a pilot clinical study in MS patients.

Keywords:

Acute Intermittent Hypoxia, AIH, Experimental Autoimmune Encephalomyelitis, EAE, Multiple Sclerosis, Repair

48. CPG-RECODING IN ZIKA VIRUS GENOME CAUSES HOST-AGE-DEPENDENT ATTENUATION OF INFECTION WITH PROTECTION AGAINST LETHAL HETEROLOGOUS CHALLENGE IN MICE

Presenter: Daniel Udenze
Collaborators: Ivan Trus
College: Public Health
Supervisor: Uladzimir Karniychuk

Background:

Frequent outbreaks of emerging pathogens emphasize the need for safe vaccines and rapid vaccine manufacturing. Experimental increase of CpG dinucleotides in an RNA virus genome may represent such an approach. While CpG recoding is an emerging and promising vaccine approach, little is known about the infection phenotypes caused by recoded viruses in vivo and in different population and age groups.

Methods:

In the present study, we generated several Zika virus (ZIKV) variants with increased CpG content and compared genetic stability of recoded variants in vitro and in vivo, infection phenotypes in vitro, and safety and efficacy of potential vaccine candidates in validated mouse models.

Results:

In vitro (ten passages on VERO cells) and in vivo (ZIKV sequencing in mouse brains) assays demonstrated the stability of de novo introduced CpG dinucleotides in all recoded ZIKV variants. Increasing the ZIKV genomic CpG content reduced infection kinetics in mammalian cell lines and human dendritic cells; and the reduction was consistently dependent on the CpG content in recoded ZIKV variants. Increasing the CpG content also caused host-age-dependent attenuation of infection with considerable attenuation in neonates and high attenuation in adults during pregnancy. Expression of the zinc-finger antiviral protein (ZAP)—the host protein targeting viral CpG dinucleotides—was also age-dependent. Similar to the wild-type virus, ZIKV variants with the increased CpG content evoked robust cellular and humoral immune responses and protection against lethal challenge

Conclusion:

The host age should be accounted for in future studies on mechanisms targeting viral CpG dinucleotides and applications of CpG-recoded vaccines. In the future, safe and efficient CpG-recoded vaccines may reduce the social and economic burden associated with viral infections.

Keywords:

Zika virus, CpG, dinucleotides, Vaccines, mouse

49. SARS-COV-2 REPLICATION MODELS AND THERAPEUTIC DISCOVERY THROUGH GENETIC SCREENS

Presenter: Juveriya Qamar Khan
Collaborators: Darryl Falzarano, Franco Vizeacoumar,
College: Medicine
Supervisor: Joyce Wilson

Background:

SARS-CoV-2 is a novel betacoronavirus, that emerged in late 2019 and is the causative agent for COVID-19, an acute respiratory disease which may lead to death. In our study, we have used a genome wide CRISPR screen to identify host factors and pathways usurped by the virus which may prove to be effective targets for antiviral therapeutic design. Additionally, we have developed novel tools useful to screen antiviral drugs, characterize viral variants and identify virus-host dependencies.

Methods:

In preparation of the CRISPR screens, we have established human lung and kidney cell lines that support SARS-CoV-2 infections with high cytopathology. 8 human lung cell lines derived from squamous cell carcinomas and adenocarcinomas and HEK293/T derived from human embryonic kidney cells were transduced to stably express Angiotensin-converting enzyme 2 (ACE2). Using reverse genetics, we have also generated a molecular BAC (bacterial artificial chromosome) clones of wild-type SARS-CoV-2 Wuhan1 and a reporter virus that expresses NanoLuciferase (NLuc).

Results:

6 of the 10 cell lines we tested support SARS-CoV-2 infections with 95-100% cell killing. Two of these cell lines, HEK293T_ ACE2 and NCI-H23_ ACE2 have been used for the genome wide CRISPR knockout screens to identify hits that will allow us to choose an array of drugs that can be potentially repurposed as effective treatments for COVID-19. As for the replication tools, we have successfully rescued the wild-type and reporter virus by transfecting the in-vitro transcribed RNA from the BAC clones. The NLuc expression kinetics shows that the reporter virus can rapidly generate high luciferase values within the first 24-48 hours of infection. Both the viruses also induced titres and cytopathic effect similar to lab isolated wild type SARS-CoV-2. These virus clones will be used to generate and assess SARS-CoV-2 variants as well as carry out anti-viral drug screens.

Conclusion:

Keywords:

COVID-19, SARS-CoV-2, CRISPR, Nanoluciferase reporter

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50. PERSISTENT DYSPNEA, REDUCTION IN QUALITY OF LIFE, FUNCTIONAL STATUS, AND MODERATE TO VIGOROUS PHYSICAL ACTIVITY FOLLOWING MILD COVID-19 INFECTION.

Presenter: Hussain Aslan
College: Medicine
Supervisor: Scotty Butcher
Co-supervisor(s): Corey Tomczak

Background:

The purpose of this study was to explore the effects of COVID-19 on select physical, functional, and psychological variables among survivors compared to age matched healthy participants, and their implications for rehabilitation programs in this population.

Methods:

Seventy-eight (female, male age 30-70 yrs.) participants (39 COVID-infected, CI and 39 age-matched healthy controls, HC). Four questionnaires were used to assess the variables in this study: dyspnea scale of the Modified Medical Research Council (mMRC), International Physical Activity Questionnaire (IPAQ), Functional Status Questionnaire (FSQ), and the RAND-36 measure of health-related quality of life. A Mann Whitney test was used to compare the variables data between HC and CI.

Results:

Dyspnea scores in CI group were significantly higher than in HC group (mean = 1.77 vs 0.13). Scores of IPAQ, FSQ and RAND-36 HRQoL questionnaires were also significantly lower in CI than in HC group. However, sitting and walking activity scores of IPAQ were not significantly different between both groups.

Conclusion:

The results of the CI group were significantly different than the HC group in all parameters of the questionnaires used in this study. Scores for sitting and walking activity in IPAQ were not significantly different between the two groups.

Keywords:

Dyspnea, functional status, physical activity, quality of life, COVID-19

51. AN INNOVATIVE AND HIGHLY SPECIFIC APPROACH TO THE DETECTION OF COVID-19 SALIVARY BIOMARKERS

Presenter: Lina Marin
Collaborators: George Katselis, Paulos Chumala
College: Dentistry
Supervisor: Walter Siqueira

Background:

The detection of SARS-CoV-2 in the saliva of COVID-19 individuals has provided a strong rationale to propose saliva as the most reliable tool to detect SARS-CoV-2. Thus, saliva has a pivotal role in COVID-19 pathogenesis and human-to-human transmission, providing foundations to develop a non-invasive and fast diagnostic platform for COVID-19 through saliva. Considering the recent advances in clinical proteomics for the identification of multiple protein biomarkers for viral infections and the shedding of SARS-CoV-2 through saliva, we expected that multiple SARS-CoV-2 proteins and peptides could also be detected in saliva by means of a mass spectrometric-based proteomics. Therefore, in this study we assessed the translational applicability of mass spectrometry-based proteomic approaches to identify SARS-CoV-2 proteins in saliva from individuals with COVID-19.

Methods:

This study was approved by the USask Research Ethics Board (#1911), and obtained an Operational Approval within the Saskatchewan Health Authority (OA-UofS-1911). Stimulated whole saliva was collected from male and female individuals diagnosed with COVID-19 by a test performed by the Saskatchewan Health Authority (COVID-19 group) and from healthy individuals (control group). Saliva samples were self-collected by each participant using a salivary collection kit (SimpLOFy™, Oasis Diagnostics® Corporation, USA). Immediately after collection, saliva samples were placed on ice and transported to the Salivary Proteomics Research Laboratory (USask), where viable viral particles were inactivated at 60 °C for 30 min. Samples from the control group were also heat-treated. Whole saliva was centrifuged to separate “pellet” containing bacteria, host cells and other debris, from “whole saliva supernatant” containing host and viral soluble proteins/peptides. Proteins from both “whole saliva supernatant” and “pellet” fractions were extracted and digested with trypsin and then subjected to mass spectrometry analysis (LC-ESI-MS/MS). The acquired MS/MS spectra were queried against a customized SARS-CoV-2 and human saliva database (SwissProt/TrEMBL) using SEQUEST algorithm.

Results:

Whole saliva was obtained from 32 COVID-19 individuals, 13 female and 19 male; and from 6 healthy individuals, 2 female and 4 male. The mean age of the individuals in the COVID-19 group was of 39.6 (± 14.8) and 41.1 (± 16.5) years for female and male participants, respectively. The mean age in the control group was of 34.0 (± 1.4) and 34.3 (± 12.7) for female and male participants, respectively. Our technology allowed us to identify 82 tryptic peptides from 12 SARS-CoV-2 proteins among COVID-19 individuals. From the identified proteins, three correspond to structural proteins (spike glycoprotein, nucleoprotein, and membrane protein), two to non-structural proteins (replicase polyprotein 1a and replicase polyprotein 1ab), and seven to accessory proteins (ORF3a, ORF3b, ORF3d, ORF6, ORF7a, ORF8a, ORF9b). The most frequent viral proteins identified were replicase polyprotein 1ab (100%) and replicase polyprotein 1a (90.6%), followed by nucleoprotein (50%), ORF3b protein (50%), and spike

glycoprotein (28.1%). Membrane protein (15.6%), ORF7a protein (9.4%), and ORF3a (6.3%) were among the less frequent proteins identified (Table 1). Regarding the tryptic peptides identified, the most frequent were those originated from replicase polyprotein 1ab, replicase polyprotein 1b, nucleoprotein, spike glycoprotein and ORF3b protein (Table 2), being the most abundant peptides those derived from replicase polyprotein 1ab/a (VVSTTTNIVTRCLNR) and nucleoprotein (NSSRNSTPGSSRGTSPPAR). No SARS-CoV-2 proteins were detected in saliva samples obtained from healthy individuals.

Conclusion:

In this study, we characterized SARS-CoV-2 proteome in saliva from positive COVID-19 individuals, exploring a novel area of COVID-19 diagnosis through the combined use of saliva and proteomics, based on mass spectrometry. Considering that the total time required to collect and analyze each saliva sample by mass spectrometry is only of 3.5 h, the results from this study reinforce the advantages of using mass spectrometry for the diagnosis of COVID-19 over real-time RT-PCR which results are obtained after more than 24 hours. Based on the results of this ongoing study and on the exciting data here presented, our innovative approach is reliable for the identification of SARS-CoV-2 proteins biomarkers in saliva of positive COVID-19 individuals, indicating that our MS technology per se might be used as a simple and effective diagnostic test of COVID-19 in saliva.

Keywords:

COVID-19, saliva, proteomics, mass spectrometry, diagnosis

52. BALANCE AND WALKING INTERVENTIONS FOR CHILDREN LIVING WITH CEREBRAL PALSY THROUGH THE LENS OF THE SYSTEMS FRAMEWORK FOR POSTURAL CONTROL: A SYSTEMATIC REVIEW

Presenter: Valerie Caron
Collaborators: Christa Falaye
College: Rehabilitation Sciences
Supervisor: Dr. Sarah Donkers
Co-supervisor(s): Dr. Alison Oates

Background:

Cerebral palsy (CP), caused by a brain injury prior to, during, or shortly after birth, is the most common neurological condition to limit gross motor function in childhood. Postural control is a primary concern for children living with CP and impairments limit independent walking and impact participation in peer-groups and community engagement. The Systems Framework for Postural Control (SFPC) describes six individual domains of postural control including biomechanical constraints, orientation in space, movement strategies, control of dynamics, sensory strategies, and cognitive processing. The evidence for rehabilitation interventions targeted at balance and walking for children living with cerebral palsy is vast and diverse, but how these interventions address the components of postural control remains unclear. The aim of this review is to explore which components of the SFPC are targeted in balance and walking interventions for children living with CP.

Methods:

A systematic review following the PRISMA guidelines was conducted Jan 2021. MEDLINE, CINAHL and EMBASE databases were searched. Inclusion criteria: English/French; full-text research articles (not review articles); intervention for balance and/or walking; children ages 6-18 years; with CP; ≥ 1 outcome measure for function and/or walking and/or balance. Two researchers independently screened and extracted data, a third was used for consensus. Data were extracted into a standardized template. Interventions were classified into five types of rehabilitation for clearer analysis. Further descriptive analysis categorized intervention types using the six domains of the SFPC.

Results:

3223 studies were identified: 969 removed with deduplication, 1955 excluded at title/abstract screening, 299 underwent full-text review, 139 were included. In terms of 'types of rehabilitation' 39% were classified as gait, 26% as exercise, 13% as balance, 13% as technology, and 9% as 'other' rehabilitation (e.g. hippotherapy, task-oriented training). In terms of the SFPC domains, only 21% of included interventions addressed all domains of the SFPC (3 were gait interventions, 9 'other' rehabilitation, 8 technology and 9 sports-based exercise). All interventions addressed the biomechanical constraints and 94% addressed movement strategies domains; the least represented domains were orientation in space (42%), and cognitive processing (34%). Interestingly, gait-style interventions were most represented (39%) but were the least comprehensive regarding SFPC domains. 65% of all interventions addressed 3 or less SFPC domains. 'Other' rehabilitation interventions were least represented (9%), but contained interventions most comprehensive of SFPC domains - 69% in the 'other' addressed all six domains of postural control.

Conclusion:

These results identify that according to the SFPC rehabilitation interventions for walking and balance in children living with cerebral palsy mainly target biomechanical constraints and movement strategies. Many do not include orientation in space or cognitive processing thereby limiting the comprehensiveness of the intervention design. Combining task-oriented practice with walking interventions would be a more comprehensive approach to treating postural control domains. This information informs the design of future rehabilitation interventions to better address the complexities of postural control in this population.

Keywords:

Child; cerebral palsy; neurological rehabilitation; postural balance; walking

53. CAN ENZYMES KEEP FAILING KIDNEYS WORK LONGER?

Presenter: Sana Daneshamouz
College: Engineering
Supervisor: Amira Abdelrasoul

Background:

Protein bound uremic toxins (PBUTs) are poorly removed using hemodialysis (HD) treatment as they tightly bind to the vital human serum proteins like human serum albumin (HSA). The p-Cresol, one of the well-studied uremic toxins, is generated by the partial breakdown of tyrosine and phenylalanine by intestinal obligate or facultative anaerobes. The p-Cresol exists mainly as p-cresyl sulfate in blood because most of it undergoes conjugation with sulfates in the submucosal tissue via the action of sulfotransferases. Thus p-cresyl sulfate is accumulated via organic anion transporters and enhances the production of reactive oxygen species in renal tubular cells resulting in cytotoxicity. The average levels of p-cresyl sulfate in patients undergoing HD are 10 times the normal level.

Methods:

Molecular docking will be used as an assistant to have depth understanding of the interaction between p-cresol and different biocompatible enzymes. The results of the interactions of p-cresol binds in different protein chains of HSA with p-cresol will be discussed. The competitive affinity of interactions between HSA-p-cresol and the selected enzymes will be comprehensively analyzed

Results:

Results showed that hydrogen bonds play more important role in the interactions for p-cresol removing. Common functional group of sulfone in PCS is responsible for the interaction with the enzymes.

Conclusion:

Keywords:

Chronic kidney disease, Protein Bound Uremic toxins, P-cresol sulfate, Enzymes, Polar interactions

54. SEPARATING TRABECULAR AND CORTICAL BONE IN PEDIATRIC IMAGES OF DISTAL RADIUS: COMPARISON BETWEEN AUTOMATED AND MANUALLY MODIFIED CONTOURING METHODS

Presenter: Imanma Tiffany Egeonu
Collaborators: Zahra Ghafouri, JD Johnston, Saija Kontulainen
College: Engineering
Supervisor: Saija Kontulainen
Co-supervisor(s): JD Johnston

Background:

High resolution peripheral QCT (HR-pQCT) imaging is a non-invasive imaging technique used to monitor cortical and trabecular bone development in children and youth. In prior research, HR-pQCT-derived density and microarchitectural measures were considered precise when analyzed using manually modified contours to separate cortical and trabecular bone at the distal radius in children. In studies with large sample sizes, however, an automated method of contouring may be required. Therefore, it is important to assess if bone outcomes and related precision errors would differ between manually modified and automated endosteal contouring methods in pediatric scans. Study objectives were to: 1. Compare bone microarchitecture and density mean outcomes at the distal radius obtained with modified or auto contouring methods 2. Characterize precision errors for bone outcomes using modified and auto contouring methods at the distal radius

Methods:

Participants were scanned at two time points approximately 1 week apart using HR-pQCT (Kawilalak et. al, 2017). Endocortical contours were defined using manually modified and automated contouring methods to define cortical and trabecular bone properties at the distal radius of 25 children. We used paired t-test to compare bone outcomes between the automated and the modified contouring methods. We calculated CV%RMS precision errors for repeated bone outcomes analyzed using the automated and modified contouring methods.

Results:

Cortical pore volume and porosity at the distal radius were 65% and 50% smaller, respectively, when analyzed using the automated contouring method. Cortical total volume, bone volume, area, apparent thickness, and pore diameters outcomes were 2.5 – 13.7% smaller when analyzed with the automated contouring method, while cortical bone mineral density, tissue mineral density, fine-structured thickness, and trabecular area were 0.3 – 3.3% greater with the automated contouring method ($p < 0.001$). The precision errors appeared 3 – 27% lower when analyzed using the automated contouring with the exception of the cortical pore diameter being 39% higher. Precision errors for the fine-structured cortical thickness, cortical tissue density, and total bone area were comparable between the modified and automated contouring methods.

Conclusion:

Endosteal contouring methods appeared to influence cortical bone outcomes in children. The automated contouring method appeared more precise than the manually modified contouring

method when assessing bone microarchitecture and density at the distal radius in children. Automated contouring provides an attractive option for pediatric bone studies using HR-pQCT imaging. Future studies are needed to assess accuracy of contouring methods to define cortical and trabecular bone properties

Keywords:

Pediatrics, High resolution peripheral QCT, HR-pQCT, imaging, bone

55. DEFINING TRABECULAR AND CORTICAL BONE IN PEDIATRIC DISTAL TIBIA SCANS: COMPARISON BETWEEN AUTOMATED AND MANUALLY MODIFIED CONTOURING METHODS

Presenter: Zahra Ghafouri
Collaborators: Imanma Tiffany Egeonu, Saija Kontulainen
College: Kinesiology
Supervisor: Saija Kontulainen

Background:

Introduction: Separation of cortical and trabecular bone by endocortical contouring is important when assessing clinically important bone details, such as cortical porosity, at long bone ends. In mature adult bone, automatic contouring provided comparable results to manual contouring (Kawalilak et al 2016). It is unknown, if immature bone outcomes and related precision errors would differ when analyzed using automated versus manually modified contouring. **Objectives:** Our first objective was to compare bone size, density and microarchitectural outcomes between automated and manually modified contouring methods in the distal tibia scans of typically developing children. Our second aim was to estimate precision errors in bone outcomes between the methods.

Methods:

Methods: We re-analyzed previous acquired distal tibia (8% of tibia length) images, from 32 children (age range 8–13 years). Images were obtained twice (1 week apart) using high resolution peripheral QCT (HR-pQCT). We compared bone outcomes between automated and manual contouring methods using paired t-test (Objective 1). We calculated root-mean-squared coefficients of variation (CV%RMS) to estimate precision errors with both methods (Objective 2).

Results:

Results: Automated contouring method provided 4-6% lower cortical volume and area, 1-2% greater cortical density and trabecular area when compared to manually modified contours ($P < 0.001$). Cortical porosity outcomes were 18-21% lower with automated contouring ($P < 0.001$). Precision errors across all bone outcomes ranged between 1-6% for both methods.

Conclusion:

Conclusion: Modifying endocortical contours seemed to emphasize cortical bone size and contributing to lower cortical porosity than automated contouring. Precision errors appeared comparable between the methods. Future studies are needed to identify most accurate analysis method for pediatric HR-pQCT images.

Keywords:

Trabecular and cortical bone, pediatric bone, HR-pQCT automatic & modified contouring methods

56. USE OF ANTIBACTERIAL ENVELOPES FOR PREVENTION OF INFECTION IN NEUROMODULATION

Presenter: Amit Persad
Collaborators: S Uzair Ahmed, Rosalie Mercure-Cyr, Karen Waterhouse
College: Medicine
Supervisor: Aleksander Vitali

Background:

Neuromodulation unit placement carries a historic infection rate as high as 12%. Treatment requires surgical removal and a long course of systemic antibiotics. TYRX antibacterial envelopes (Medtronic Inc., Minneapolis, MN), which are absorbable mesh envelopes that elute minocycline and rifampin, have been used in implantable cardiac devices with substantial risk reduction for infection. At our center, one surgeon uses these envelopes with all implanted neuromodulation units.

Methods:

We conducted a retrospective cohort study of consecutive implantable pulse generator (IPG) and intrathecal pump unit implantation with a TYRX antibacterial envelope[®] at our center between October 2014 and December 2019. We collected demographic data, including postoperative infections, reoperations, and complications associated with the devices. This cohort was then compared to a historical cohort of consecutive patients undergoing IPG or pump placement or revision prior to the use of the envelopes (between October 2007 and April 2015) in order to assess the rate of infection associated with envelope use.

Results:

In the pre-envelope cohort of 151 IPGs placed in 116 patients, there was a culture-confirmed infection rate of 18/151 (11.9%). In the antibacterial envelope cohort of 233 IPGs placed in 185 patients, there were 5 cases of culture-confirmed infection (2.1%). The absolute risk reduction with the use of the antibacterial envelope was 4.6% (95% CI, 0.045-0.048), with a relative risk reduced by 77% (odds ratio, 0.23; 95% CI 0.05-1.08; P=0.065). The NNT was 21 (95% CI 20.8-22.4) envelope uses to prevent one IPG infection. The pre-envelope cohort of 41 pumps placed in 39 patients, there was a culture-confirmed infection rate of 6/41 (14.6%). In the antibacterial envelope cohort of 59 pumps placed in 54 patients, there was 1 culture-confirmed infection (1.7%). The absolute risk reduction with the use of the antibacterial envelope was 12.9% (95% CI 1.6-24.3), with a relative risk reduction of 88% (odds ratio, 0.13; 95% CI, 0.02-1.11; P=0.04). The NNT was 7.7 (95% CI 4.4-32.3) antibacterial envelope implantations to prevent one confirmed infection.

Conclusion:

Usage of an antibacterial envelope with device placement for neuromodulation therapy has resulted in a lower infection rate at our center. Based on these results, we can recommend the use of envelopes for infection prophylaxis. More follow-up is needed to fully understand the impact of this intervention.

Keywords:

Neurosurgery, neuromodulation, infection, prevention, antibiotic

57. COMPARISON OF TWO APPROACHES TO CERVICAL PARAVERTEBRAL NERVE BLOCK IN CANINE CADAVERS.

Presenter: Maria Podsiedlik
College: Veterinary Medicine
Supervisor: Dr. Tanya Duke–Novakovski

Background:

The cervical paravertebral block (PVB) targets the cervical sixth (C6), seventh (C7), eighth (C8) and first thoracic (T1) spinal nerves as they exit the vertebral foraminae before forming the brachial plexus. The technique for the cervical PVB block was described earlier using a dorsoventral (DV) approach. Finding landmarks for this approach is difficult in obese or heavily muscled dogs. An alternative craniocaudal (CC) approach was developed which may be more accurate where the dorsal approach landmarks are difficult to palpate. The CC approach can provide analgesia for many thoracic limb procedures, including scapula-removal limb amputation. The primary objective was to compare the accuracy of the craniocaudal (CC) and dorsoventral (DV) approaches to the cervical paravertebral block (PVB) in canine cadavers. The secondary objective was to compare time and ease of performance of each approach in the hands of a novice.

Methods:

The operator was initially trained to perform both approaches by experienced clinicians on five cadavers. For the main study, a CC or DV approach to the PVB on both thoracic limbs of 10 cadavers (10 for each approach) was performed. Methylene blue dye was diluted in saline and equally divided into four aliquots to stain the sixth cervical to first thoracic spinal nerves. The time to perform the approaches was recorded and ease of performance was subjectively scored using a numerical scale (1 'easy' to 4 'difficult'). Successful staining of nerve trunks (stain > 1 cm) was assessed following dissection. Data were analyzed using Wilcoxon Signed Rank test. Significance was set at $p < 0.05$.

Results:

There was a significant difference between groups for the number of successfully stained nerves between the CC approach (median 3; range 2–4) and the DV approach (median 2; range 0–4) ($p = 0.047$). The median [interquartile range] time to perform the CC approach 118 [102] seconds was not significantly different than the DV approach 145 [105] seconds ($p = 0.106$). The ease of performance score for the CC approach was 1.5 (1–4) and was not significantly different from the DV approach which scored 3 (2–4) ($p = 0.063$).

Conclusion:

In the hands of a novice, the CC approach to the cervical PVB is similar to the DV approach with respect to speed and ease of performance, but might be more accurate.

Keywords:

Cervical paravertebral, dog, forelimb, nerve block, regional anesthesia, technique

58. DEFICITS IN BONE MICRO-ARCHITECTURE AND LOWER BONE STRENGTH IN CHILDREN AND ADOLESCENTS WITH TYPE 1 DIABETES: A SYSTEMATIC REVIEW AND META-ANALYSIS

Presenter: Mahdi Rostami Haji Abadi
Collaborators: Yuwen Zheng, Zahra Ghafouri, Suelen Meira Goes, J.D. Johnston, Munier Nour, Saija Kontulainen
College: Kinesiology
Supervisor: Saija Kontulainen

Background:

The elevated risk of fracture in children and adolescents with type 1 diabetes (DM1) might be related to a weaker bone structure. A previous systematic review reported lower bone mass in children with DM1; however, no systematic reviews or meta-analyses have synthesized the evidence of bone micro-architecture and strength differences between children with DM1 and typically developing children (TDC). We aimed to systematically review studies comparing bone micro-architecture and strength between children with DM1 and TDC using quantitative meta-analysis and qualitative synthesis.

Methods:

We searched articles published until July 2020 through a comprehensive search in MEDLINE, Embase, CINAHL, Web of Science, Scopus, Cochrane Library databases. We report standardized mean differences (SMD) from the meta-analyses comparing bone outcomes reported in 3 \geq studies and assessed heterogeneity using I-square. We evaluated bone outcomes reported in 1-2 studies using qualitative synthesis.

Results:

We included 11 studies in the systematic review which assessed 675 children and adolescents with DM1. Nine studies were included in the meta-analysis. Children with DM1 had lower trabecular bone mineral density (SMD = -0.51; 95% CI, -0.81 to -0.21) and trabecular bone volume fraction (BV/TV) (-0.34; -0.58 to -0.11) at the distal radius as well as lower BV/TV (-0.39; -0.61 to -0.16) and trabecular thickness (-0.42; -0.68 to -0.15) at the distal tibia ($p < 0.05$). There was no evidence of heterogeneity between the studies ($p > 0.05$). Our qualitative synthesis suggested that children with DM1, when compared to TDC, had 8-17% lower bone strength (density-weighted polar section) at the radius and tibia shafts, 7-11% lower BV/TV and trabecular number with 13% greater trabecular separation at the proximal tibia. Cortical density was 3% lower at the lumbar spine when compared to TDC.

Conclusion:

This meta-analysis indicated that children with DM1 have deficits in trabecular bone micro-architecture at the distal radius and tibia. Evidence (albeit limited) also suggested that children with DM1 have lower bone strength at the radius and tibia shafts as well as deficient trabecular micro-architecture at the proximal tibia. Importantly, bone micro-architecture and strength deficits may contribute to the elevated risk of fracture in children with DM1. Future studies, with advanced imaging, are warranted to monitor bone development and develop evidence-based therapies for the prevention and treatment of bone fragility in children with DM1 as well as inform updates of clinical guidelines to optimize bone health in children with DM1.

Keywords:

Type 1 Diabetes, Bone micro-architecture, Bone strength, Risk of fracture, Meta-analysis

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59. EVALUATION OF THE MODIFIED BARIUM SWALLOW STUDY CONDUCTED WITH AND WITHOUT RADIOLOGIST SUPERVISION: A PRE- AND POST- OBSERVATIONAL STUDY

Presenter: Yang, Luhe MD.CM.
Collaborators: Leswick, David MD, FRCPC, Butler, Michael MSc, MD, CCFP
College: Medicine
Supervisor: Ellchuk, Tasha BSc, MD, FRCPC, CAQ Neuroradiology

Background:

The modified barium swallow study (MBSS) is one of the most commonly performed swallowing assessments and has been validated with published evidence-based guidelines. Although many MBSS are still performed with radiologist supervision, several facilities are now performing the procedure without the radiologist present with study review and reporting at a later time. A recent change at our institution, from radiologist supervised to non-radiologist supervised MBSS, presents the opportunity to clarify the impact on quality metrics. The objective of this study is to assess the quality and safety of MBSS performed pre- and post-institutional.

Methods:

Retrospective review of MBSS performed on adult inpatients at a tertiary care hospital 6-months pre- and post-institutional change from having to not having a radiologist present during the examination. Factors assessed include: fluoroscopy time; study duration; number of cine loops; number of images; efficiency of collimation (using a 5-point scoring system); and time to final report. Differences in outcomes were analyzed using Welch's t-test and a test of proportions for continuous and count data under the normal approximation.

Results:

106 and 119 MBSS were analysed from the radiologist present and radiologist absent periods, respectively. No statistically significant differences were found for: the average fluoroscopy time (116.1s vs. 126.9s; $p=0.161$); study duration (400.4 s vs. 417.3 s; $p=0.453$); number of cine loops (9.3 vs. 10.2; $p=0.075$); and number of images (620.5 vs. 581.1; $p=0.350$). There was improved performance without the radiologist present for collimation (1.92 vs. 1.43; $p=0.003^*$) and fewer nondiagnostic images (6.5 vs. 4.5; $p=0.001^*$). Time to final report was longer with the radiologist absent due to several reports with significant delays in the radiologist absent group.

Conclusion:

MBSS performed by technologists without radiologist supervision is not inferior to those performed with radiologist supervision on multiple performance measures. This supports technologist operated MBSS without radiologist supervision, while acknowledging a need to further address radiologist report time delay.

Keywords:

modified barium swallow study, MBSS, video fluoroscopic swallowing exam, patient safety, speech language pathology, radiation technologists

60. IMPROVING METHODS OF CONTROL OF AMERICAN FOULBROOD IN HONEY BEES IN SASKATCHEWAN

Presenter: Michael Zabrodski
Collaborators: Geoff Wilson, Antonio Ruzzini, Tasha Epp
College: Veterinary Medicine
Supervisor: Elemir Simko

Background:

American foulbrood (AFB) is a devastating disease of newly hatched honey bee larvae caused by the spore-forming bacterium, *Paenibacillus larvae*, which parallels *Bacillus anthracis* (anthrax) in its extreme infectivity, prolificity, and spore resiliency. Clinical disease often results in colony death by either natural disease progression or destruction by the beekeeper to limit the spread of spores to other colonies. North American beekeepers rely heavily on routine antimicrobial metaphylaxis to prevent disease, but treatment fails to eliminate infectious spores. As a result, beekeepers have developed a dependency on antimicrobials to prevent AFB. With the emergence of antibiotic-resistant strains of *P. larvae*, there is a need for alternative, evidence-based management tools to effectively reduce the use of antibiotics while maintaining sustainable beekeeping operations.

Methods:

Province-wide surveillance of *P. larvae* spores in honey may be a proxy for evaluating yard-level AFB risk. Accordingly, we analyzed the spore content of pooled, extracted honey from 50 large-scale and 72 small-scale Saskatchewan beekeepers, representing over 70,000 of the province's 110,000 honey bee colonies. Pasteurized honey samples were cultivated on enhanced, semi-selective MYPGP media for 7 days, and colony forming units of *P. larvae* were used to determine the number of spores per gram of honey. These concentrations were correlated with subsequent incidence of AFB disease in the following year. These results, in conjunction with data from an accompanying AFB questionnaire, will establish prognostic reference ranges for honey to identify the immediate risk of AFB outbreaks in antibiotic-dependent management systems. Overall, this will improve the ability of beekeepers to implement evidence-based antimicrobial use in the prevention of AFB.

Results:

To date, spores have been detected in 47% of large-scale honey samples at either low (60.5%), medium (29.5%), or high (9.9%) concentrations. A smaller proportion (26%) of small-scale samples have detectable spores at low (95.7%), medium (3.4%), or high (0.9%) concentrations. Subsequent incidence of AFB was observed in 1/1 small-scale and 3/6 large-scale beekeepers with high spore concentrations, and 3/14 large-scale beekeepers with medium spore concentrations. Consistent with our current risk criteria, AFB has not been observed in large- or small-scale beekeepers with low spore concentrations.

Conclusion:

The concentration of *P. larvae* spores in pooled honey is a prognostic indicator of the risk of AFB disease within honey bee yard. Beekeepers assigned a low risk of AFB disease may be able to temporarily cease antimicrobial metaphylaxis if done in conjunction with the implementation of other integrative pest management strategies.

Keywords:

American foulbrood, *Paenibacillus larvae*

61. LOWER BONE MINERAL MASS AND AREAL BONE MINERAL DENSITY IN CHILDREN WITH TYPE 1 DIABETES – A SYSTEMATIC REVIEW AND META-ANALYSIS

Presenter: Yuwen Zheng
Collaborators: Mahdi Rostami Haji Abadi, Zahra Ghafouri, Suelen Goes, Munier Nour
College: Kinesiology
Supervisor: Saija Kontulainen

Background:

Higher fracture risk in children and adolescents with type 1 diabetes (DM1) may relate to deficits in bone mineral mass and density. There are no up-to-date meta-analyses comparing bone mineral mass (BMC) and areal bone mineral density (aBMD) between children with DM1 and typically developing children (TDC). Therefore, our 1st objective was to perform a systematic review and meta-analysis comparing BMC and aBMD between children and adolescents with DM1 and TDC. Our 2nd objective was to assess if diabetes related factors (e.g., disease duration) would explain differences in bone outcomes.

Methods:

We identified and included studies in this systematic review and meta-analysis through a comprehensive search in MEDLINE, Embase, CINAHL, Web of Science, Scopus, Cochrane Library (inception to July 9, 2020) databases. Search terms included children OR adolescents AND type 1 diabetes AND bone. For the current analyses, we identified studies comparing DXA-derived BMC and aBMD outcomes between children with DM1 and typically developing controls. We report significant ($p < .05$) standardized mean differences (SMD) from the meta-analysis (1st objective). We also report significant ($p < 0.05$) β -coefficients between diabetes related factors (disease duration and HbA1c level) and the pooled SMD between-group total body and lumbar spine aBMD from meta-regression analyses (2nd objective).

Results:

We included 33 studies in systematic review with 2073 children and adolescents with DM1 and 2606 TDC. Children with DM1 had lower aBMD in total body, lumbar spine and femoral neck (SMD = -0.2 to -0.3, $p < .05$), and lower BMC in total body and lumbar spine (SMD = -0.2, $p < .05$). Longer disease duration was associated with a larger between group difference in total body aBMD ($\beta = 0.3$, $p < .05$).

Conclusion:

This meta-analysis indicated deficits in BMC and aBMD in children and adolescents with DM1. Longer DM1 duration contributed to the larger deficit in total body aBMD in children with DM1. Bone deficits associated with DM1 may contribute to the increased risk of fracture and require attention in both clinical research and guidelines to optimize bone development in children with DM1.

Keywords:

Type 1 diabetes, children, bone mineral density, bone mass

62. FEMALE PREGNANCY AFTER FIXED-TIME ARTIFICIAL INSEMINATION USING SEX-SORTED SPERM IN WOOD BISON

Presenter: Eric M. Zwiefelhofer
Collaborators: Gabriela F. Mastro Monaco, Clara González-Marín
College: Veterinary Medicine
Supervisor: Gregg P. Adams

Background:

In mammals, the sex chromosome of the sperm (X-female, Y-male) determines the sex of the offspring. Sex-sorted sperm technology has been used to produce offspring of the desired sex with >90% accuracy in domestic cattle; however, fixed time artificial insemination (FTAI) using sex-sorted sperm has not yet been reported in bison. Female calves are desired in bison conservation and zoological herds, as a male can produce multiple calves per year while a female only produces one. Therefore, there is a need to produce female sex-sorted sperm which can be used in advanced reproduction techniques in these herds. The objective of this experiment was to determine the efficacy of sex-sorted sperm used in a FTAI protocol in bison.

Methods:

Semen was collected via electroejaculation from wood bison bulls (n=3) at the Native Hoofstock Centre (NHC; Saskatoon, SK) and sent to a commercial laboratory (Sexing Technologies, Calgary, AB). At the lab, the ejaculate of the bull with the best semen quality underwent sperm sorting (X-chromosome bearing [female]) via flow-cytometry and the sorted semen was cryopreserved. In late January, wood bison females (n=31) were synchronized for FTAI at the NHC. On Day 0, transvaginal ablation of follicles ≥ 5 mm was done and a progesterone-releasing intravaginal device (PRID) was inserted. On Day 6, the PRID was removed and bison were given 500 ug cloprostenol im to induce luteolysis. On Day 9, bison were given 2500 IU human chorionic gonadotropin (hCG) im and ranked based on the diameter of the dominant follicle. The bison of similar rank were assigned randomly in replicate to be inseminated with a single unit of either sexed or conventional semen 18 h later. Insemination was done in the uterine horn ipsilateral to the dominant follicle. Transrectal ultrasonography was done on Day 6 and 9 to assess the diameter of the dominant follicle, and on Day 10.5 to confirm ovulation. Pregnancy diagnosis and fetal sexing was done by transrectal ultrasonography 30- and 60-days post-insemination, respectively. Statistical analyses were done by ANOVA or chi-square test.

Results:

There was no difference in the diameter of the dominant follicle (mean \pm SEM) between the sexed and conventional groups on Day 6 (10.0 ± 0.5 mm vs. 9.6 ± 0.4 mm; $P=0.59$) or 9 (13.3 ± 0.5 mm vs. 12.9 ± 0.7 mm; $P=0.66$). A total of 26/31 [83.9%] bison ovulated following hCG, and there was no difference between groups ($P=0.57$). The 5 bison that did not ovulate after hCG were removed from pregnancy data. There was no difference ($P=0.21$) in pregnancy per ovulation in the sexed (1/14; 7.1%) vs. conventional (3/12; 25%) group. The single pregnancy in the sex-sorted group was a female fetus, and all three pregnancies in the conventional group were male fetuses.

Conclusion:

In summary, sex-sorted sperm in a FTAI protocol can be used to produce pregnancies in bison. Results warrant future studies to confirm the effectiveness of sex-sorted sperm for in vitro production of embryos and for large FTAI trials to confirm the increased proportion of embryos/calves of the desired sex produced in bison. Funding provided by Sexing Technologies, Mitacs, Toronto Zoo, and NSERC.

Keywords:

Bison, wood bison, sexed semen, artificial insemination

63. PRODUCTION OF LIVE CALVES AFTER TRANSFER OF IN VITRO- PRODUCED EMBRYOS IN SYNCHRONIZED WOOD BISON (BISON BISON ATHABASCAE)

Presenter: Miranda Zwiefelhofer
Collaborators: Gabriela Mastromonaco
College: Veterinary Medicine
Supervisor: Gregg Adams

Background:

Wood bison (*Bison bison athabascae*) are a threatened subspecies native to Canada. They are culturally significant to the First Nations peoples and a keystone species in the ecosystem. As part of an overall effort to develop reproductive technologies to establish a functional germplasm biobank for bison conservation, the objective of the study was to identify factors that influence post-implantation embryo viability. We compared pregnancy rates after the transfer of in vitro produced (IVP) embryos 1) vitrified at different stages of development (morula, early blastocyst, blastocyst and expanded blastocyst) and on different days post-fertilization (7-8 days; Exp. 1), and 2) vitrified, frozen in glycerol or fresh (Exp. 2).

Methods:

The study was completed in two consecutive years (Exp. 1 & 2). Embryos were produced from wood bison oocytes collected by transvaginal ultrasound-guided follicular aspiration subjected to in vitro fertilization with frozen-thawed wood bison semen. Female bison between 3 and 16 years of age were used as surrogates in October (n=28 & 26; Exp. 1 & 2, respectively). A single embryo was transferred into the uterine horn ipsilateral to the corpus luteum 7 days post-ovulation. Transrectal ultrasonography was done at 30- and 60-days post-ovulation to diagnose pregnancy. Data were analyzed by Fisher's exact test.

Results:

In Exp. 1, there was no difference among the 4 embryo stage groups for pregnancy per embryo transferred (P/ET) at 30 days post-ovulation (P=0.26), but P/ET tended to be greater among morula-stage embryos than blastocyst stage embryos (3/7 [42.9%] vs 2/21 [9.5%]; P=0.08). The day the embryo was frozen (i.e., days 7 to 9 post-fertilization) had no effect on P/ET at 30 or 60 days. At the 60-day pregnancy check, 2 of the 5 previously confirmed pregnancies were no longer pregnant. The transfer of morulae resulted in a higher P/ET at 60 days than the other groups combined (3/7 [42.9%] vs 0/21 [0%]; P=0.01). Three calves were carried to term and were born in July 2020; however, one calf died at birth as a result of dystocia. In Exp. 2, pregnancies were produced after the transfer of either fresh and vitrified embryos, but embryos frozen in glycerol produced no pregnancies. The Day 30 pregnancy rate was 4/9 [44.4%] vs 3/8 [37.5%] vs 0/9 [0%], respectively (P=0.20) and the Day 60 pregnancy rate was 2/9 [22.2%] vs 2/8 [25%], 0/9 [0%], respectively (P=0.50). There are four ongoing pregnancies, due in July 2021.

Conclusion:

In conclusion, the vitrification method of cryopreserving embryos resulted in a pregnancy rate similar to that after the transfer of fresh embryos. Results also suggest that cryopreservation at the morula

stage will yield the best outcome for the purpose of biobanking bison embryos. Future efforts should focus on the in vitro system to create better quality embryos.

Keywords:

Bison, species conservation, embryo transfer, in-vitro embryo, vitrification

64. UNIMANUAL FATIGUING HANDGRIP CONTRACTIONS INCREASE CORTICAL FUNCTIONAL CONNECTIVITY AND MOTOR PERFORMANCE IN THE CONTRALATERAL HAND

Presenter: Justin W. Andrushko
Collaborators: Jacob Levenstein, Catharina Zich, Charlotte Stagg
College: Kinesiology
Supervisor: Dr. Jonathan P. Farthing

Background:

In humans, learning of motor skills is underpinned by changes in functional connectivity across a wider network of inter-connected brain areas (Sampaio-Baptista et al., 2015; Sugata et al., 2020). A putative route to develop interventions to improve function might therefore be to modulate this connectivity. However, it is not currently clear how best to do this. Unilateral fatiguing exercise has been found to increase contralateral motor cortex (cM1) and ipsilateral M1 (iM1) cortical excitability and descending neural drive, which together may aid in overcoming peripheral fatigue (Benwell et al., 2006). Further, unilateral fatiguing exercise has been shown to increase iM1 functional connectivity within the wider sensorimotor network, including the supplementary motor area (SMA) bilaterally (Jiang et al., 2012). The SMA has been identified as an important sensorimotor network node involved in changes in contralateral limb motor performance with unilateral motor training (i.e., cross-education of motor behaviour). This acute enhancement in functional connectivity with the iM1 after a fatiguing bout of exercise may present a 'window of opportunity' to improve neural plasticity, making motor training with the non-fatigued limb during this enhanced neural state a putative therapeutic tool to enhance motor learning and therefore motor rehabilitation (Maruyama et al., 2012).

Methods:

Fifteen participants took part in a within-subject cross-over design research study at the University of Oxford over two separate sessions. During each session participants performed a response time test with each hand and received a resting-state functional magnetic resonance imaging (fMRI) brain scan before and after performing a nine-minute repeated 0.5 Hz right-handgrip motor task at either 5% or 50% of their maximum voluntary contraction (MVC). The 50% MVC condition was intended to result in motor fatigue, whereas the 5% MVC condition served as a non-fatiguing control motor task.

Results:

The handgrip contractions at 50% MVC resulted in a motor performance decline, with the area under the curve for each contraction decreasing over time (as determined by a linear slope/Beta fitted to these data) compared to the 5% MVC condition (50% MVC: $\beta = -0.912 \pm 1.070$; 5% MVC: $\beta = -0.022 \pm 0.107$; $p = 0.006$, $\text{hedges } g = 0.801$). Response times were found to improve in the opposite left hand for the 50% MVC condition only (50% MVC: $-5.8 \pm 7.1\%$; 5% MVC: $0.1 \pm 6.0\%$, $p = 0.037$, $g = 0.574$), with no other improvements observed for either condition or hand. An increase in functional connectivity was observed between the right iM1 and the right orbitofrontal cortex ($z\text{-max} = 5.12$, $p = 0.03$). Importantly, there was a significant interaction with the changes in functional connectivity between the motor areas in each hemisphere, whereby the M1-M1 connectivity decreased and the

SMA-SMA connectivity increased after the right handgrip contractions in the 50% MVC condition ($F(1,14) = 11.970$, $p = 0.004$, $\eta p^2 = 0.461$).

Conclusion:

Right fatiguing handgrip contractions augmented response time motor performance in the contralateral non-fatigued hand. This change in motor performance was accompanied by changes in cortical resting-state functional connectivity between network nodes that are likely contributing to the contralateral motor enhancement. These results have important clinical implications, whereby unilateral fatigue may augment motor rehabilitation in individuals with unilateral impairments.

Keywords:

Resting-state functional connectivity, MRI, response time, contralateral motor performance, fatigue

65. "METAGENOMIC STUDIES ON CLOSTRIDIUM PERFRINGENS MEDIATED DYSREGULATION OF INTESTINAL MICROBIOTA IN BROILER CHICKENS DEVELOPING NECROTIC ENTERITIS"

Presenter: Hemlata Gautam
College: Veterinary Medicine
Supervisor: Dr. Susantha Gomis

Background:

Necrotic enteritis (NE) is an economically important disease in the broiler chicken industry, caused by *Clostridium perfringens* (*C. perfringens*) associated with predisposing factors such as high protein diet, immunosuppression and coccidiosis. Pathogenesis of NE is not fully understood and no effective preventive measures or vaccines are available. The objective of this study was to understand the pathogenesis of NE to develop effective control strategies. In order to explore this objective, we studied intestinal microbiome of broiler chickens when birds develop clinical and subclinical NE following *C. perfringens* exposure.

Methods:

We have successfully developed a subclinical and clinical NE disease model by increasing the dietary protein to promote colonization of *C. perfringens* in broiler chickens. Birds challenged with *C. perfringens* developed classical gross and histopathological lesions of NE. Intestinal contents were collected (n=8/category) from healthy birds, and birds with clinical and subclinical disease to conduct metagenomics of the intestinal microbiome. Next generation 16S amplicon sequencing was performed to assess the degree of dysbiosis. Genomic DNA was isolated from the Jejunum using a commercial kit (Qiagen Inc., Germany). Nextera XT DNA Library Preparation Kit (24 samples) from Illumina was used and microbial 16S amplicon genes were amplified with indexed and adaptor-linked universal primers targeting the V3-4 region. Amplicon libraries were sequenced using Illumina MiSeq system (Illumina, San Diego, US) for paired-end reads of 300 bp. Metagenomics data were analyzed using Geneious prime software 2020.

Results:

Normal intestinal flora consisted primarily with Lactobacillaceae, Cyanobacteriaceae and Peptostreptococcaceae, with a small amount of Clostridiaceae. Birds with NE had considerably decreased Lactobacillaceae, and increased Clostridiaceae and Enterobacteriaceae. The degree of dysbiosis was severe in birds with clinical disease compared to subclinical infection.

Conclusion:

The results of this study will provide the opportunity to study preventative measures of NE associated with *C. perfringens* infection

Keywords:

Next generation sequencing, microbiome dysbiosis, clinical and subclinical necrotic enteritis, preventive methods

66. IMPAIRED AUTONOMIC CONTROL OF HEART RATE IN PHYSICALLY ACTIVE CHILDREN WITH CONGENITAL HEART DEFECTS

Presenter: Ramlah Iqbal
Collaborators: Ramlah Iqbal, Natasha Boyes, Marta Erlandson
College: Kinesiology
Supervisor: Dr. Corey Tomczak

Background:

Children with congenital heart disease (CHD) have evidence of autonomic dysfunction as indicated by a reduction in heart rate variability (HRV) and delayed post-exercise heart rate (HR) recovery compared to healthy age-matched controls. Children with CHD may also have more sedentary lifestyles and thus be less physically active as compared to healthy controls. Several studies have found that physically active adults have better autonomic modulation. It is not known whether the phenomenon of autonomic dysfunction would persist in physically active children with CHD. We tested the hypothesis that physically active children with CHD will have reduced HRV at rest, slower HR recovery kinetics following 6-minute walk testing (6MWT) compared to healthy controls and there will be a relationship between HRV and HR kinetics.

Methods:

Eighteen children with CHD (11±2 years; males=11; females=7) were matched for age, BMI, and physical activity (using the Physical Activity Questionnaire for Older Children, PAQ-C) with healthy controls (11±3 years; males=8; females=10). CHD diagnoses included Tetralogy of Fallot (n=5), pulmonary or aortic stenosis (n=3), hypoplastic left or right heart syndrome (n=3), Ebstein's anomaly (n=1), ventricular septal defect (n=1), transposition of the great arteries (n=1), double inlet right ventricle (n=1), tricuspid atresia (n=1), coarctation of the aorta (n=2). HRV standard deviation of R-R intervals (SDRR) was determined following 10 min supine rest using a 5 min surface ECG recorded epoch. Post-exercise HR kinetics were determined over a 4-min period following the 6MWT using telemetry-based HR. Mono-exponential modeling was used to derive a HR recovery time constant, tau (time to reach 63% change). Analyses were completed using un-paired t-tests with $P < 0.05$ being significant. Data are mean ± SD. Correlation regression analysis was also done between HR kinetics and HRV different time domain and frequency domain measures of HRV.

Results:

Children with CHD had a lower 6MWT distance (513±75 vs. 599±81 m; $P < 0.001$) and lower average exercise HR (122±15 vs. 139±18 beats/min; $P = 0.001$) compared to controls. HRV SDRR was lower in children with CHD (55.9±40.4 ms) compared to controls (92.1±24.5 ms, $P < 0.01$). Post-exercise HR kinetics were slower in children with CHD (tau = 34±15 s) compared to controls (tau = 24±8 s; $P = 0.01$), indicating a longer recovery time for HR. There was also a negative correlation between SDNN and tau ($r = -0.35$, $P = 0.036$).

Conclusion:

Children with CHD have autonomic dysfunction as measured by a reduction in HRV. The slower HR kinetics may be due to decreased parasympathetic activity or increased sympathetic activity in

patients with CHD during the post-exercise recovery period. Our findings suggest that autonomic dysfunction functionally alters HR control during or immediately following exercise in physically active children with CHD.

Keywords:

Congenital heart disease (CHD), heart rate variability (HRV), post-exercise heart rate (HR) recovery, 6-minute walk testing (6MWT), HR kinetics, HRV standard deviation of R-R intervals (SDRR).

67. THE EFFECT OF INTERFERON-ALPHA SUBTYPES ON HIV-1 ASSOCIATED CD8+ T CELL HYPERACTIVATION AND DYSFUNCTION

Presenter: Saurav Saswat Rout
Collaborators: Yunyun Di, Kathrin Sutter, Ulf Dittmer
College: Medicine
Supervisor: Kerry J. Lavender

Background:

Different interferon-alpha (IFN- α) subtypes have been shown to elicit distinct control of different viral infections. Along with its direct antiviral effects, IFN- α also strongly modulates host innate and adaptive immune responses. Our previous work showed that IFN- α subtypes differentially control HIV-1 infection and mediate distinct effects on immune function. Clinical use of the IFN- α 2 subtype has not been highly effective in reducing viral or proviral HIV-1 and high levels of endogenous IFN- α 2 has been associated with CD8+ T cell hyperactivation and dysfunction in HIV-1 patients. Our prior study with the IFN- α 14 subtype suggested that some IFN- α subtypes may be beneficial in HIV-1 infection.

Methods:

We infected humanised TKO-BLT mice that are susceptible to HIV-1 infection and treated them with IFN- α 14 or IFN- α 2. We isolated splenocytes from the spleens of mice either immediately after treatment or 6 weeks post-treatment withdrawal. We analysed the splenocytes for different marker of exhaustion using multi coloured flow cytometry and also stimulated them ex-vivo to determine their functionality.

Results:

We demonstrated that after 3 weeks of treatment IFN- α 14 significantly reduced markers of CD8+ T cell-related dysfunction such as hyperactivation, exhaustion and apoptosis and, unlike ART, these low levels were maintained even after the treatment was withdrawn. IFN- α 14 treated mice also maintained a more naïve CD8+ T cell profile as opposed to the development of the larger effector memory subset observed in HIV-1 infected and IFN- α 2 treated mice. Although IFN- α 14 reduced the activation profile and proliferative capacity of CD8+T cells, it did not change their ability to secrete cytokines or degranulate upon stimulation ex vivo.

Conclusion:

IFN α 14 treatment did not exacerbate disease progression and may have therapeutic potential to alleviate CD8+ T- cell hyperactivation and exhaustion during HIV-1 infection.

Keywords:

HIV-1, Interferon-alpha, humanized mice, CD8+ T cell

68. IMPROVING HEMODIALYSIS CLINICAL PRACTICE BASED ON MODELING AND OPTIMIZATION OF PROTEIN ADSORPTION

Presenter: Heloisa Westphalen
Collaborators: Dr. Amira Abelasoul, Dr. Ahmed Shoker
College: Engineering
Supervisor: Dr. Amira Abelasoul

Background:

Chronic kidney disease (CKD) leads to a gradual loss of kidney function and affects almost 700 million people worldwide. In Canada, 1 in 10 Canadians has a diagnose of kidney disease and millions are at risk. To compensate for the loss of renal function, patients rely on renal replacement therapies with hemodialysis (HD) being the most prescribed option. HD consists of a membrane-based treatment that allows the removal of metabolic wastes and excess fluid by diffusive and convective transport. Although this treatment is life-sustaining for many patients, the contact between the patient's blood and the membrane filter triggers a series of biochemical cascades associated with protein adsorption, promoting a chronic state of inflammation, and increased thrombotic response. Additionally, the adsorption and deposition of proteins of the membrane surface hinder the filtration by limiting diffusion and convection mechanisms that reduce the treatment effectiveness in a phenomenon called fouling. In clinical practice, the HD operating conditions (blood flow rate, dialysate flow rate, treatment time) are manipulated to clear uremic toxins, but without a real understanding of the limitations and biological consequences of its changing, it can lead to back-filtration, significant loss of vital blood proteins and patient deaths. Furthermore, HD treatment represents a financial burden for many patients and costs the Canadian healthcare system approximately \$310 Million/year. By improving clinical practices, the frequency of hospitalizations of hemodialysis patients can be reduced, and consequently, a reduction in financial costs is expected.

Methods:

The goal of the present study is to investigate correlations between protein adsorption and inflammatory response experienced by HD patients as a consequence of the interaction between blood and membrane materials. We performed in-vitro adsorption of fibrinogen (FB) - which is a highly abundant blood protein - to polyaryl ether sulfone-polyvinylpyrrolidone (PAES-PVP) clinical membrane. Utilizing the response surface methodology, we modeled how the adsorption of FB is influenced by the operating conditions. Additionally, we used in-situ Synchrotron-based X-ray micro-tomography (SR- μ CT) to evaluate the occurrence of fouling across microscopic layers of the polymeric membrane. This allows us to understand how the morphology of the membrane influences the adoption process. To correlate the in-vitro results with the clinical response, we collected blood samples from HD patients from Saint Paul's Hospital in Saskatoon before, during (30 and 90 min), and after (240 min) treatment and analyzed the extend of inflammatory biomarkers released. Utilizing Human Magnetic Luminex assays we measured the concentration of Serpin/ Antithrombin-III, Properdin, complement component (C) 5a, interleukin (IL)-1 α , IL-1 β , IL-6, TNF- α , and vWF. Then we compared the inflammatory profile pre- and post-dialysis of patients treated under different operating conditions.

Results:

The results from this study demonstrated how the operating conditions of HD treatment affect the adsorption of FB in-vitro as well as the inflammatory and thrombotic response of HD patients. We were also able to observe in which parts of the membrane structure proteins tend to adsorb. Our results indicate that when operating at high flow rates, the adsorption of FB occurs faster but a lower cumulative amount is adsorbed due to the hydrodynamic conditions developed inside the membrane fibers. With that higher blood flow rates are expected to lead to lower activation of inflammatory and thrombotic responses. On the other hand, when operating at low flow rates, the residence time of the blood in the membrane filter is prolonged. With that, the contact between the blood component and membrane surface is prolonged, which can lead to more activation. These observations corroborate with our clinical observations where we compared the levels of the biomarkers pre- and post-dialysis. The results showed that patients treated with lower blood flow rates presented an overall more inflammatory profile and stronger thrombotic tendencies.

Conclusion:

With the present study, we demonstrated the influence of hydrodynamic conditions established by the clinical operating conditions of HD treatment on protein adsorption and activation of biochemical cascades. This study demonstrates that we can optimize the clinical operating conditions of HD treatment based on the adsorption of proteins to reduce activation of complement and coagulation systems. With that, we can improve HD patients' response and quality of life.

Keywords:

Protein adsorption, membrane fouling, hemodialysis, inflammatory biomarkers, Synchrotron imaging

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69. A COMPARATIVE ANALYSIS OF MACHINE LEARNING APPROACHES FOR PREDICTION OF FREQUENT EMERGENCY DEPARTMENT VISITS

Presenter: Razieh Safaripour
College: Medicine
Supervisor: Dr. Hyun J. "June" Lim

Background:

Emergency department (ED) visits due to infectious-disease and mental health have increased drastically during the pandemic. This experience has shown that healthcare systems need to minimize the burden on EDs by prevent unnecessary frequent visits. Accurate and timely prediction of frequent emergency users, and adopting interventions accordingly, will not only increase the quality of care for patients who need it most but also reduces the spread of an infectious disease such as COVID-19. This study aims to assess and compare the predictive ability of machine learning (ML) models for predicting frequent ED users.

Methods:

Korean Health Panel data from 2008 to 2015 were used for this study. Individuals with at least one ED visit were included, among whom those with four or more visits per year were considered as frequent ED users. Patients' demographic and ED-related factors were included in the analysis. Logistic Regression, Random Forest, Support Vector Machine (SVM), as well as two ensemble models, Bagging and Voting, were trained and tested to examine their predictive performance.

Results:

The significant predictors of ED frequent visits included sex, age, day and season of visit, and reason for visit. The ML classification algorithms identified frequent ED users with high precision (90% - 98%) and sensitivity (87% - 91%), whereas logistic regression showed fair precision (65%) and sensitivity (67%). The ML classification algorithms showed high area under the curve (AUC) values from 89% for SVM to 96% for Random Forest, while logistic regression showed the lowest AUC (65%). The classification error varied among algorithms; logistic regression had the highest classification error (34.9%) while random forest had the least (3.8%).

Conclusion:

Results show that ML classification algorithms are robust techniques to accurately predict frequent ED users, which contribute to designing interventions that prepare healthcare systems for inevitable situations in the future.

Keywords:

Machine learning (ML), emergency department (ED), health services, big data

70. THE IMPACT OF FACE MASKS ON PERFORMANCE AND PHYSIOLOGICAL OUTCOMES DURING EXERCISE: A SYSTEMATIC REVIEW AND META-ANALYSIS

Presenter: Keely Shaw

Collaborators: Dr. Scotty Butcher, Dr. Leandy Bertrand, Jongbum Ko

College: Kinesiology

Supervisor: Dr. Philip Chilibeck

Co-supervisor(s): Dr. Gordon Zello

Background:

Face masks are promoted for preventing the spread of viruses; however, it has been suggested that wearing a mask during exercise might increase CO₂ rebreathing, decrease arterial oxygenation, and decrease exercise performance.

Methods:

A systematic review and meta-analysis was conducted on the impact of wearing a mask during exercise. Data sources included SPORTDiscus, PubMed, and Medline. Eligibility criteria included all study designs comparing surgical, N95, or cloth masks to a no mask condition during any type of exercise where exercise performance and/or physiological parameters were evaluated. Healthy and clinical participants were included. Mean differences (MD) or standardized mean differences (SMD) with 95% confidence intervals were calculated and pooled effects assessed

Results:

Twenty-two studies involving 1,573 participants (620 females, 953 males) were included. Surgical, or N95 masks did not impact exercise performance (SMD -0.05 [-0.16,0.07] and -0.16 [-0.54,0.22], respectively) but increased ratings of perceived exertion (SMD 0.33 [0.09,0.58] and 0.61 [0.23,0.99]) and dyspnea (SMD 0.6 [0.3,0.9] for all masks). There were small effects for increased end-tidal CO₂ (MD 3.3 [1.0, 5.6] and 3.7 [3.0,4.4] mmHg), and heart rate (MD 2 [0,4] beats/min with N95 masks)

Conclusion:

Face masks can be worn during exercise with no impacts on performance and minimal impacts on physiological variables.

Keywords:

Physical Activity; Surgical Mask; COVID-19; N95; Heart Rate

Self-declaration of research alignment with additional themes (optional)

COVID-19 Pandemic Research, Response, and/or Outreach

71. EXPLORING THE EXPERIENCES OF INDIGENOUS FAMILY CAREGIVERS OF CHILDREN WITH LIFELIMITING/LIFE THREATENING ILLNESSES WHEN PARTICIPATING IN SYMBOL-BASED INTERVENTION

Presenter: Aliya Abbasi, RN
College: Nursing
Supervisor: Jill Bally PhD, RN
Co-supervisor(s): Meredith Burles, PhD

Background:

Largely influenced by Canada's long history of European colonization, a multitude of social and health disparities between the Indigenous and non-Indigenous populations exist (Wilmot, 2018). In Saskatchewan, Indigenous caregivers of children with life threatening and life-limiting illnesses (LTIs/LLIs) face many complex healthcare inequities and their experiences have not been fully explored. In 2015, the Truth and Reconciliation Commission of Canada (TRC) developed "94 Calls to Action" to advance Canadian reconciliation. The 19th call to action (TRC, 2015), calls for the federal government to consult with Indigenous peoples and establish measurable goals to identify and close the gaps in health outcomes between Indigenous and nonIndigenous communities. Additionally, the Canadian Pediatric Society (2014) has issued a call to address systemic barriers that negatively impact Indigenous children and enhance cultural safety in health care and support. Addressing these calls to action is imperative for increasing integration of cultural knowledge and practices into pediatric healthcare.

Methods:

This proposed research will support the exploration and development of this topic using a narrative approach aligned with Indigenous methodologies. Through qualitative research, study participants are given a voice as it focuses on their attitudes, beliefs, experiences, and understanding (Austin & Sutton, 2014). Narrative research is based on the premise that by listening to the stories of others, the researcher can make sense of an individual's experience and understand how they construct meaning within a broader social context

Results:

Conclusion:

In collaboration with family and cultural advisors, our research team aims to pursue collaborative, patient-orientated research. Together, our priority is to engage Indigenous families to identify priorities for health care and support that is inequity-responsive, culturally safe, and trauma-informed. As one part of a two-phase study, the purpose of this qualitative study is to explore the experiences of Indigenous family caregivers navigating healthcare for their child with LLIs/LTIs. The findings will, in part, inform the development and testing of a symbolbased support intervention. Indigenous culture utilizes symbol-based arts such as visual art, drumming, storytelling, and journaling, to promote healing in all realms of wellness (Wright et al., 2016). Therefore, this research aligns with Indigenous research principles and employs a trauma-informed approach to produce awareness of Indigenous families' experiences. The knowledge obtained will support development of a meaningful culturally-based support intervention to promote safe, holistic pediatric healthcare.

Keywords:

Healthcare experience, determinants of health, Indigenous health, Indigenous children, life-limiting/life threatening illness

72. ORAL HEALTH SUPPORT NEEDS FOR INDIGENOUS CHILDREN IN NORTHERN SASKATCHEWAN: A REALIST REVIEW

Presenter: Maniza Abedin Chowdhury
College: Public Health
Supervisor: Dr. Gary Groot

Background:

Early childhood caries is a growing public health concern in Canada and oral Health inequalities in Indigenous children of great concern. It poses a significant obstacle to the development of a fair health care policy. Despite numerous initiatives and interventions of the government and non-government organizations to address Indigenous children's oral health inequalities, the situation remains the same. This study aims to understand how we can improve Indigenous children's oral health living in northern Saskatchewan through a realist lens.

Methods:

At first, I will conduct a realist synthesis of the literature to develop an initial program theory around Indigenous children's oral health that can be further tested and refined, using the program theory as the unit of analysis. By analyzing the relationship between mechanism, context, and outcome, realist reviews provide an approach to uncover the underlying theories of why a programme works, for whom and when. Subsequently, I will identify additional facts after stakeholder and patient family advisors confirmation by searching different databases to refine our initial theory into a middle-range programme theory. Data extraction will be based on the contextual factors at the individual, community, and system-level that result in positive (or negative) oral health amongst Saskatchewan Indigenous children and the mechanisms behind that.

Results:

Conclusion:

This middle-range theory will help us to understand how oral health programmes for indigenous children living in northern Saskatchewan can work and in what context and why. It will serve as a basis for the design and delivery of successful and context-specific oral health services to local settings through the exploratory nature of this realist analysis. It will also guide policymakers to decide on the type of intervention that should be implemented for Indigenous children. This will be the first study in Saskatchewan that will explore an in-depth exploration of the individual, community, and policy level barriers to uncover the impact of what works for whom, in what context and how.

Keywords:

Early childhood caries, Oral health inequalities, Context, Mechanism and Outcome.

73. ENGAGING INDIGENOUS OLDER ADULTS WITH TECHNOLOGY USE TO RESPOND TO HEALTH AND WELLBEING CONCERNS AND NEEDS

Presenter: Cari McIlduff
Collaborators: Victor Starr
College: Medicine
Supervisor: Carrie Bourassa

Background:

Increased access to technology can promote independent living, stimulate cognitive functioning, relieve caregiver stress, access telehealth, increase overall wellbeing and be used to share cultural resources such as Indigenous language applications. Many Indigenous older adults would like to learn more about technology and recognize the value of technology in supporting healthy aging; however, as Morning Star Lodge has previously found, accessibility and readiness were key factors in the use of this technology (Starblanket et al., 2019a).

Methods:

Utilizing the guiding principles of the Model of Engaging Communities Collaboratively (MECC, McIlduff et. al., 2020) and the Ethical Engagement Training Module (Bourassa, 2020), Morning Star Lodge partnered with Star Blanket Cree Nation to support five Indigenous older adults to support a healthy lifestyle by increasing their access to and engagement with culturally safe technology solutions individual to their specific health and lifestyle needs. These co-researchers are provided with tablets and MiFis (mobile internet access) and learning workshops and were interviewed prior to the workshops to assess their comfortability with the device and information relevant to their needs. Following the completion of their individual workshops, another interview will assess their level of comfort with the device and the benefit of the applications provided to them.

Results:

Currently all co-researchers have gone through their first interview and several workshops from which, from observation, their confidence has grown using the technology to access health information. However, this is still preliminary data as there are a few more workshops the co-researchers have requested and the post interviews and data analysis have yet to be completed.

Conclusion:

Particularly given the need during the COVID-19 pandemic to continue to stay semi-isolated at this time due to Indigenous older adults being a very high-risk population; the information gained through this work will support Indigenous communities in Canada and globally in using technology to respond to Indigenous older adults' health and wellbeing. There is also significant need for pandemic preparedness work to be done with Indigenous communities and this work could inform this in part.

Keywords:

Indigenous health, Older adults, Technology

74. BODY APPRECIATION OF CHILDREN WITH CONGENITAL HEART DISEASE COMPARED TO HEALTHY PEERS

Presenter: Yekeen Abu-Shiraz
Collaborators: Dr. Margo Adams, Mr. Matthew Chapelski, Dr. Corey Tomczak
College: Kinesiology
Supervisor: Dr. Marta Erlandson

Background:

Despite significant advances and rising survival rates, children with congenital heart disease (CHD) face many physical, emotional, and behavioral challenges. As a result, these challenges can have an impact on how a child feels about themselves and how others perceive them. Although this challenge has often been assumed, there are a limited number of studies examining body image and body appreciation in children with CHD. Body appreciation refers to an individual's acceptance of, positive feelings toward, and respect for their bodies. Therefore, understanding the body appreciation of children with congenital heart diseases will help us better understand aspects of their well-being. As such, this study aims to evaluate the body appreciation of children with CHD compared to age and sex matched healthy peers.

Methods:

Twelve children with CHD (age = 13.6 ± 2.1 , n= 3 females) and nine healthy children (age = 12.6 ± 2.7 , n= 4 females) completed the Body Appreciation Scale - 2 (BAS-2). This scale consists of 10 fundamental questions that can be given a score of 1 (Never) to 5 (Always) that best characterizes the child's attitude or behavior. A higher score on the BAS-2 represents a higher degree of positive feelings towards one's body. Body appreciation scores, age, height, weight and physical activity levels between CHD and control groups were assessed using independent t-tests.

Results:

No significant difference between groups for age, height, weight and physical activity level were found ($p > 0.05$). For each question on the BAS-2 scale, as well as the overall score, no differences ($p > 0.05$) were found between the groups. When comparing males to females for the entire sample (CHD and controls combined), there was no significant difference between sexes. However, when analyzing sex differences in the CHD group alone, there was a significant difference in the feelings of respect that each group had towards their body, with females being less likely to always have respect for their bodies ($p < 0.05$).

Conclusion:

Our preliminary findings suggest that there is no difference in body appreciation of children with CHD and their healthy counterparts. Future studies should focus on increasing the sample size, as this might influence the significance between groups. Furthermore, focusing on sex differences within the CHD group could also have important implications.

Keywords:

Congenital Heart Disease, Body Appreciation, Body Appreciation Scale - 2

75. EXPLORING THE INFLUENCE OF SOCIAL ECOLOGICAL FACTORS ON THE PHYSICAL ACTIVITY BEHAVIOURS OF SOUTHEAST ASIAN YOUTH WHO ARE NEWCOMERS TO CANADA

Presenter: Emily Harwood-Johnson
College: Medicine
Supervisor: Dr. Louise Humbert

Background:

The term newcomer refers to people who have immigrated within the past ten years and are still adjusting to the culture and customs of their new country. Many youth who are newcomers report having a unique experience with settlement that requires them to settle in the society of their new country while undergoing the psycho-social development associated with adolescence. Physical activity may be beneficial to newcomer youth because it provides an opportunity to experience language and culture in a setting not dominated by verbal communication. The physical activity levels of Canadian newcomer youth are lower than that of immigrants who have lived in Canada longer as well as Canadian born youth. Among young newcomers in Canada, those arriving from Southeast Asian countries have the lowest physical activity levels. The purpose of this research was to measure the physical activity levels of Southeast Asian youth who are newcomers and to understand the individual, social, community, and policy factors that influence the physical activity behaviours of Southeast Asian youth who are newcomers to Canada.

Methods:

Using an explanatory sequential mixed methods research design, this study collected data in two phases. The first phase was quantitative and used questionnaires and pedometers to measure physical activity levels among the participants (N = 8). The second phase used focus groups and a semi-structured interview guide based on McLeroy et al.'s (1988) ecological model of health promotion (EMHP) to explore the social ecological factors that influence the participants' (N = 8) physical activity behaviours.

Results:

Results from Phase One revealed that either 0% or 12.5% of participants were physically active enough to meet Canadian physical activity guidelines of 60 minutes of MVPA per day depending on the operationalized definition. Additionally, there were no significant differences in physical activity levels when compared by gender or time since immigration. In Phase Two, participants identified factors in every level of the EMHP (e.g. intrapersonal, interpersonal, institutional, community, and policy) that influenced their physical activity behaviours.

Conclusion:

The findings of this study support previous research that has found that Southeast Asian youth who are newcomers have low physical activity levels. Upon further investigation in the focus groups, the participants identified some factors that enhance or increase their physical activity levels and other factors that make it more difficult for them to be physically active. This study contributes to the growing body of research, by directly measuring physical activity levels of newcomer youth and by providing newcomer youth with an opportunity to share their personal experiences with physical activity in Canada.

Keywords:

Newcomer, youth, physical activity, ecological model, southeast asia, mixed methods

76. PHYSICAL ACTIVITY ON CAMPUS: WHERE DO YOU SIT?

Presenter: Karly J. Anderson
Collaborators: Kevin S. Spink, Sahya A. Bhargava
College: Kinesiology
Supervisor: Kevin S. Spink

Background:

There is growing evidence of increased physical inactivity and sedentarism among university students (Castro et al., 2020; Scarapicchia et al., 2015). This may not be surprising, given how the university environment is structured. From a choice architecture perspective (i.e., the physical or symbolic environment that individuals are confronted with when required to make a decision, Thaler & Sunstein, 2009), the default option for students on campus is more likely to favour being less active or more sedentary. When required to make decisions about activity on-campus, students are likely to be confronted with environments consisting of physical (e.g., class layouts) and symbolic (e.g., need to study) barriers. This makes the university environment an important factor for targeting inactivity and sedentarism in this population. As humans are social beings (Baumeister & Leary, 1995) and universities are social settings, it is plausible that using the influence of other on-campus students could counter the maladaptive default activity decisions that might result from the existing choice architecture. In terms of the influence of others, results have established a positive relationship between social norms and physical activity (Crozier & Spink, 2017). Using social norms theory (Cialdini et al., 1990), the purpose of this exploratory study was to examine the effects of two specialized norms (i.e., trending minority norms and dynamic norms) on university students' reported on-campus physical activity and sedentary behaviours.

Methods:

Using an experimental online design, 156 university students (73% aged 18-24) were randomly assigned to receive one of four messages: trending minority norm (i.e., minority norm that physical activity on campus is increasing from one time period to the next, n=46), dynamic norm (i.e., minority norm that physical activity on campus is starting to change, n=39), descriptive norm (i.e., minority norm about physical activity on campus, n=30), and attention control (no reference to physical activity, n=41). Condition specific messages outlined behaviours being performed by other university students to be active and less sedentary while on campus. Participants completed pre- and post-message online surveys that assessed on-campus physical activity and sedentary behaviours. A MANCOVA was used to examine the effects of the message conditions on reported on-campus physical activity (i.e., stair use on campus and briskly walking between classes) and sedentary behaviours (i.e., intentionally standing up when sitting too long and standing up to stretch while on campus), while controlling for baseline physical activity. Responses to all dependent variables were made on 7-point Likert scales ranging from 1= not at all to 7 = very often.

Results:

MANCOVA results revealed a significant main effect for message condition, $F(4, 147) = 3.36, p = .01$. Follow-up univariate comparisons revealed standing up when seated for long periods was the only significant on-campus behaviour, $F(3, 148) = 3.32, p = .02, \eta^2 = 0.06$. Post hoc tests, using a Bonferroni correction, indicated that those who received the trending minority norm message reported significantly more standing up when seated for an extended period than those in the attention control message condition ($p = .01$). All other relationships were not significant.

Conclusion:

The current findings provide initial support that exposure to trending minority norm messages may present students with the incentive to overcome barriers presented by choice architecture and decrease their sedentary behaviours while on campus.

Keywords:

Physical inactivity; sedentary behaviour; trending minority norm; dynamic norm

77. EXPLORING THE DEVELOPMENT OF PLAYFULNESS AMONG YOUTH WITH DISABILITIES IN THE HB FIRST ROBOTICS® PROGRAM

Presenter: Sunny Bui
Collaborators: Sally Lindsay
College: Kinesiology
Supervisor: Alison Oates (PhD)
Co-supervisor(s): Sally Lindsay (MSc)

Background:

Play amongst youth with disabilities and their peers are critical in the development of life skills (i.e. social, problem solving, attention). Among typically developing youth, robotics programs have the potential to improve STEM-related skills, teamwork, self-confidence and social and communication skills. Although there is growth in literature on the potential role of robotics programs, such as LEGO therapy, little is known about the impact of an adapted, group-based robotics program specifically for youth with disabilities. The objective of this study was to determine to what extent does the HB FIRST® Robotics Program impact the development of playfulness amongst youth with disabilities.

Methods:

A total of 27 youth (aged 9-14) were recruited with varying disabilities (e.g. autism, cerebral palsy) and each youth was video recorded for six sessions (2 hours each) while enrolled in the program. The Test of Playfulness (ToP) was used to assess play in sessions one and six through observational coding. The first and last 10 minutes of the sessions underwent observational coding (four ToP scores) using the master coder method. ToP scores from session one and six were then averaged to have one score for each session.

Results:

Interrater reliability was deemed moderate ($k=0.6247$) and internal consistency was high ($\alpha=0.89$). Paired sample t-tests were performed to assess the difference between time 1 and time 2. Results were statistically significant using a significance level of 0.05.

Conclusion:

The adapted robotics program improved the playfulness scores of youth with disabilities while enrolled in the program. These findings suggest that youth with disabilities can improve their playfulness through recreational and/or leisurely means.

Keywords:

Children, youth, disability, development, pediatrics, play, playfulness

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78. APPLICATION OF SEMIPARAMETRIC, GROUP-BASED TRAJECTORY MODELS TO DEPRESSION AND ANXIETY IN GERIATRIC POPULATION

Presenter: Yanzhao Cheng
College: Public Health
Supervisor: Dr. Hyun J. “June” Lim

Background:

The traditional method for trajectory analysis usually focuses on the trajectory of the overall mean or individual variation. Group-based trajectory modeling (GBTM) as an extension of the finite mixture model was developed to generate heterogeneity from the population. In this study, trajectories are built with two longitudinal outcomes (depression and anxiety) using GBTM from Korea Health Panel Data Survey (KHPDS). Risk factors are also found for each outcome of trajectories.

Methods:

Unlike other trajectory analysis using covariance structure methods, GBTM can detect unobserved subgroups in the overall population using the multinomial logit function. The trajectory paths of each subset can be identified with polynomial distributions. Since the outcome of our study is binary, each trajectory should follow a logistic polynomial function. Risk factors are selected based on the baseline characteristics using Multivariate Logistic Regression Analysis.

Results:

KHPDS is a survey data having 3,983 elderly participants with up to 8 years of follow-up. From GBTMs, four trajectory groups for depression were identified with “low-flat (86.6%)”, “low-to-middle (9.2%)”, “low-to-high (1.3%)” and “high-curve (2.9%)”, respectively. Also, four groups of trajectories are identified for anxiety with “low-flat (94.4%)”, “low-to-middle (3.2%)”, “high-to-low (1.8%),” and “high-stable (0.6%)”, respectively. Gender females, age more than 80, having more than three chronic diseases, and homeownership are significant risk factors of depression trajectory groups. For anxiety trajectory groups, gender female is the only substantial risk factor.

Conclusion:

Due to its sizeable reliable differentiation of trajectory groups can be made from this sample, with our findings supporting previously published results. Our findings will also assist health policy decision-makers in addressing, monitoring, and planning intervention programs targeting those most likely to experience persistent depression to improve psychological well-being in the Korean elderly.

Keywords:

Depression, Anxiety, Trajectory analysis, Elderly

79. DOES EXPOSURE TO RECREATIONAL GYMNASTICS INFLUENCE BONE ACCRUAL FROM 6 TO 16 YEARS OF AGE: THE YOUNG RECREATIONAL GYMNASTS STUDY

Presenter: Brendan Ernst
Collaborators: Matthew S. Chapelski, Marta C. Erlandson
College: Kinesiology
Supervisor: Dr. Adam D.G. Baxter-Jones

Background:

Bone development during the growing years is important because the size, content and strength of bone that is accrued during this time period has a profound impact on bone health across the life span. Bone responds to mechanical loading and stress from factors, such as athletic training, that promote adaptations to ensure that the bone can withstand the same stresses in the future. Gymnastics is a unique form of athletic training that creates forces to the bone at different locations and with different magnitudes. The Young Recreational Gymnastics Study (YRGS) was initiated in 2006 and followed 4–6-year old's for 6 years. YRGS found that gymnastics exposure independently increased Total Area (ToA) and Total Content (ToC) in the distal radius by 12 years of age. The purpose of this study was to examine the effects of exposure to recreational gymnastics, over 10 years in the YRGS cohort, on bone accrual and strength development within the distal and shaft locations of the radius and tibia between 6 and 16 years of age.

Methods:

This mixed-longitudinal study design recruited 3 age cohorts (4,5- and 6-year old's) from recreational gymnastics programs within the city of Saskatoon and non-gymnasts from University of Saskatchewan sports camps. Between 2008 and 2016 one hundred and twenty-five participants were measured on up to 4 occasions. Cross-sectional slices of the left radius (4% and 65% locations) and tibia (4% and 66% locations) were measured by peripheral quantitative computed tomography (pQCT). Scans were analyzed for cross-sectional bone area (ToA, mm²), volumetric density (ToD, mg/cm³), bone content (ToC, mg/mm), trabecular bone density (TrD, mg/cm²), muscle area (mm²), and a bone strength index was calculated (BSIc, mg/mm⁴). Individual bone parameter growth curves were constructed using multilevel random effect models. Fixed effects included age, weight, sex, muscle area and gymnastic exposure, with alpha set at 0.05.

Results:

Age was centred around 9 years. For most models age centre random variance coefficients were significant and indicated that bone parameters were increasing significantly within individuals with age (Level 1). The between-individuals variance matrices (Level 2) indicated that individuals, in most models, had significantly different growth curves in terms of intercepts (at 9 years) and slopes. The fixed part of the models showed that gymnastics exposure produced a significant time dependant independent effect at the distal radius (4%) for ToA ($25.43 \pm 6.95\text{mm}^2$), ToC ($9.58 \pm 2.42\text{mg/mm}$), ToD ($14.19 \pm 6.46\text{mg/cm}^3$), TrD ($13.07 \pm 6.21\text{mg/cm}^2$), and BSIc ($3.17 \pm 1.07\text{mg}^2/\text{mm}^4$) when the confounders of age, sex and size were controlled. Gymnastics exposure had no time dependant independent significant effect at the radial shaft or any locations on the tibia ($p>0.05$).

Conclusion:

In this cohort exposure to recreational gymnastics, at any age between 4 and 16 years, produced bone health benefits to the distal radius but not the tibia. Since wrist fractures are an early indication of poor bone health, these results suggest that exposure to weight bearing activities at a young age have long lasting effects on radius strength into adolescence.

Keywords:

80. PARENTS, TEACHERS, AND COMMUNITY: A DREAM TEAM APPROACH TO DEVELOPING PHYSICAL LITERACY IN CHILDREN

Presenter: Matthew Chapelski
Collaborators: Louise Humbert, Amanda Froelich Chow, Adam Baxter-Jones
College: Kinesiology
Supervisor: Marta Erlandson

Background:

Higher physical literacy has been linked to greater physical activity engagement which in turn is linked to improved health. Physical literacy is a multidimensional term that encompasses a person's motor competence, knowledge, confidence, and motivation; all of which influence their physical activity levels. Previous physical literacy interventions have generally targeted only one setting where children are active, like school. However, Saskatchewan in Motion's 30-30-30 model promotes engaging in 30 minutes of physical activity with the family (parents), at school, and in the community and highlights the shared responsibility these settings have to offer physical activity opportunities. Therefore, the purpose of our study was to utilize the 30-30-30 model to assess the effectiveness of a 12-week home, school, and community-based physical literacy intervention on motor competence of children in kindergarten and grade one.

Methods:

Four schools matched for demographics were either assigned to receive the intervention (n=2) or continue with their regular practice (n=2) (controls). The intervention was implemented in eight kindergarten and grade one classes and involved a 12-week physical literacy intervention at home, school, and in the community. Weekly activities were sent home in a physical literacy backpack to be practiced with the family, curricula based physical education classes were provided by a trained facilitator twice a week and biweekly physical literacy community nights were held. Physical literacy was assessed pre- and post-intervention in 103 intervention (41 female) and 83 control (36 female) kindergarten and grade one students using an age-appropriate adapted version of the PLAYfun tool. This adapted version of the PLAYfun tested 10 different fundamental motor skills in the movement domains of run, locomotor, object control, and balance. Group differences were assessed with repeated measures ANOVA to evaluate change in physical literacy with alpha set at $p < 0.05$.

Results:

Both intervention and control children significantly improved their overall motor competence after the intervention but children in the intervention group had significantly higher total motor competence when compared to controls ($p < 0.05$) after the intervention. Children in the intervention significantly improved their motor competence for seven skills: skip, gallop, hop, throw, catch, kick, and balance ($p < 0.05$). Children in the control group also significantly improved their jump, throw, catch, kick, and balance ($p < 0.05$) motor competence from pre to post test. Children in the intervention group had higher motor competence for skip, gallop, throw, kick, and balance ($p < 0.05$) when compared to controls after the intervention. On the other hand, children in the control group had higher motor competence for balance at baseline and jump post-intervention when compared to children in the intervention ($p < 0.05$). Confidence and comprehension significantly improved in the control group but not the intervention group ($p > 0.05$). Additionally, confidence and comprehension were not different between intervention and control ($p > 0.05$).

Conclusion:

A 12-week multi-setting intervention was found to improve the motor competence of kindergarten and grade 1 children. Future research is needed to evaluate if an intervention can also influence confidence, comprehension, and motivation.

Keywords:

Physical Literacy, Young Children, Physical Activity, Motor Competence

81. GROWTH RETARDATION AND SEX DIFFERENCE IN BONE DENSITY AMONG GUATEMALAN AND MEXICAN

Presenter: Michele Monroy-Valle
Collaborators: Ginny Lane, Hassan Vatanparast
College: Public Health
Supervisor: Hassan Vatanparast
Co-supervisor(s): Ginny Lane

Background:

Child malnutrition is a leading health problem worldwide, encompassing a broad range of nutritional deficiencies and excesses. Reducing the prevalence of malnutrition is the focus of Sustainable Development Goal (SDG) second goal. Stunting is the result of chronic malnutrition that prevents a child from growing or developing properly, and is associated with compromised development, decreased neurocognitive skills, and increased risk for nutrition-related chronic diseases in early adulthood. In stunted children, bone development may be affected by nutritional deficiencies resulting in increased bone stiffness that can lead to frailty in adulthood. The study objective is to explore possible associations between stunting and bone growth among Guatemalan preschool children.

Methods:

This cross-sectional study of children aged 2 to 5 years living in Chichicastenango (n=156), Guatemala took place between February and October 2020. Community leaders assisted with participant recruitment and preparation of data collection sites that met COVID-19 biosecurity requirements. We measured height with a stadiometer and collected date of birth from the health card. We measured bone density with Speed of Sound (SOS) using the quantitative trans-axial ultrasound method (Sunlight MiniOmni Ultrasound Bone Sonometer) thrice from dual-site measurement at the left distal radius and midshaft tibia anterior bone.

Results:

Of the 156 children measured, 46.8% (n=73) were girls and 53.2% boys (n=83) with a mean age of 44 months (11.6 SD). According to anthropometric data 50.6% of girls (n=37) and 55.4% of boys (n=46) were stunted (height for age < -2 SD of the WHO Child Growth Standards). Compared to their age matched Mexican peers, the radial SOS of Guatemalan boys aged 2 and 3 years was significantly lower [3370.5 (SD184.5) and 3454.6 (SD170.1) correspondingly]; while for Guatemalan boys 4 and 5 years old, had significantly higher bone density (SOS) than Mexican counterparts [3590.2 (190.0 SD) and 3711.3 (85.5 SD) correspondingly]. For girls aged 2 years, the radial SOS was significantly higher than their Mexican peers [3247.6 (192.4 SD)]. Among 5-year-old girls, only the tibial SOS was significantly higher [3427.8 (SD95.6)] than Mexican girls of the same age.

Conclusion:

Child growth is internationally recognized as an important population indicator of nutritional and health status. The prevalence of growth retardation is considerably high among Guatemalan children. The sex difference in bone density in Guatemala and Mexican children disregarding the high prevalence of growth retardation warrants further investigation.

Keywords:

Stunting, malnutrition, bone health

82. NEW ZEALAND'S CASE FOR A WELLBEING BUDGET: WHAT CAN OTHER COUNTRIES LEARN?

Presenter: Stephanie Ortynsky
College: Johnson Shoyama Graduate School of Public Policy
Supervisor: Dr. Haizhen Mou
Co-supervisor(s): Dr. Marwa Farag

Background:

Budgeting is a key process of any government. Even with efforts to make budgeting more productive, decisions are incremental and outcomes are difficult to measure. Economies are losing steam, financial resources are strained, and global leaders will face the policy implications of COVID-19 for years to come. Therefore, the importance of health and social policy is clear. These crises can no longer be combatted individually. Governments are reacting to problems rather than setting an objective such as wellbeing. An outcome-based approach directs funds and policies to support people and the environment to flourish.

Methods:

Wellbeing as a policy outcome was rarely considered before the early 2000s. New Zealand made history in 2019 when it released its Wellbeing Budget. A case study on this budget can provide lessons for other nations. This thesis explores how a wellbeing budget was adopted and implemented in New Zealand. I am interviewing three groups of budget actors to determine what worked and if the budget is achieving its outcomes.

Results:

In the first part of this study, with budget officers in Canada, I found that most jurisdictions use incremental budget approaches. Yet, the majority of respondents agree on the overarching outcomes of the public programs and services they fund. How to tie assigned funds to specific outcomes remains to be better understood.

Conclusion:

As current systems and institutions are tested, it is an opportune time for governments to examine how they can make large jumps towards wellbeing rather than small, incremental changes.

Keywords:

Wellbeing policy; budgets; governments; environment

83. THE VOICES OF MOTHERS OF TWICE-EXCEPTIONAL CHILDREN: A NARRATIVE INQUIRY

Presenter: Elyse Proulx-Cullen
College: Medicine
Supervisor: Dr. Anne Leis

Background:

Twice-exceptional (2e) children manifest both giftedness and disabilities and are defined as high-potential, talented individuals with neurological disorders (ADHD, learning disabilities, social impairments). As a result of the lack of adapted and biometric diagnostic tools, the paucity of expert resources and societal stigmas related to the condition, 2e children are often diagnosed too late, misdiagnosed or even undiagnosed. As research has shown, this results in potentially devastating consequences to their well-being from increased risk of mental illness and education failure to self-medication and addiction. In our society, mothers typically experience the atypical behaviours and warning signs of their 2e child first-hand. However, little is known about how mothers become aware of their child's exceptionalities, an experience mostly dismissed and marginalized in the traditional health care system.

Methods:

Purpose: Considering the mounting evidence about the importance of early screening in contributing to a successful life journey for 2e children, this qualitative health research project aims to elicit the lived experiences of mothers of 2e children and to listen to these critical steps in their journey.

Results:

Methods: This study will be realized through a narrative inquiry design. The patient-parent expert will be at the core of this inquiry. Using snowball and later purposive sampling, mothers of 2e children will be recruited and invited to share their story. Interviews will be audio recorded and transcribed. Field notes will also be kept. Critical feminist and intersectionality theories will provide a lens through which to conduct the inductive analysis. At this time, the study is awaiting approval from the Behavioural Research Ethics Board.

Conclusion:

The significance of the project is to uncover the acquired knowledge of the mothers in raising their 2e children and to inform the delivery of services and resources mothers will need to access. This narrative inquiry project will also act as the building block of a subsequent research project about providers and related systems designed to support these children and their families. Furthermore, this study aims to build on seven of the 17 Sustainable Development Goals (#3-4-5-8-9-10-17) by developing a model of sustainable engagement whereby the dyad child-mother would become a key partner and decision-maker as well as a bridge between the education sector and the health care system.

Keywords:

Twice-exceptionality, early screening, patient-parent expert, mothers of twice-exceptional children, narrative inquiry, acquired knowledge of mothers, learning disabilities, giftedness, Sustainable Development Goals.

84. ATTITUDES AND KNOWLEDGE OF DIETITIANS AND ORAL HEALTH PROFESSIONALS REGARDING NUTRITION AND DENTAL CARIES: A SCOPING REVIEW

Presenter: Amanda Vanzan
Collaborators: Dr. Petros Papagerakis - College of Dentistry, University of Saskatchewan, Dr. Silvana Papagerakis - College of Medicine, University of Saskatchewan
College: Pharmacy and Nutrition
Supervisor: Dr. Jessica Lieffers - College of Pharmacy and Nutrition, University of Saskatchewan

Background:

Dental caries are the most common chronic disease in the world. Nutrition and dental caries have a closely connected and complex relationship that goes beyond sugar. Despite the strong relationship between nutrition and dental caries, studies have found that nutrition care provided by oral health professionals and dietitians regarding dental caries is limited. This review will seek to investigate and understand the knowledge and attitudes of dietitians and oral health professionals regarding nutrition and dental caries.

Methods:

A scoping review was designed and developed using the PRISMA-ScR (PRISMA extension for Scoping Reviews). A search was conducted in February-March 2020 in three different databases (Medline, EMBASE and CINAHL) using specific index terms and keywords. Survey or qualitative interview/focus group studies conducted from 2000-2020 that captured information on the knowledge and attitudes of dietitians and oral health professionals regarding nutrition and dental caries were eligible for inclusion.

Results:

Twenty studies met the inclusion criteria and were included in the review (two were qualitative studies; 18 were quantitative studies). In total, three studies included information on dietitians/nutritionists and 17 studies included information on oral health professionals. Six articles assessed knowledge. The types of knowledge that was assessed could be categorized into two themes: a) food and dental caries; and b) feeding young children and dental caries. Overall, the studies found that dietitians and oral health professionals had strong knowledge in these areas, but they focused mostly on sugar. In total, 15 articles assessed attitudes regarding nutrition and dental caries; the types of attitudes assessed varied focused on nutrition as a risk factor for dental caries, sugar consumption and dental caries, and attitudes regarding providing advice/counselling regarding nutrition and dental caries. These studies found that professionals felt that nutrition was important to prevent tooth decay, that sugar frequency was considered more important than amount, and that nutritional advice/counselling was important for reducing dental caries. Barriers identified to providing assistance in this area included: not enough time, financial compensation, lack of knowledge, lack of education, and lack of referrals.

Conclusion:

This review highlights significant gaps in the literature on attitudes and knowledge of dietitians and oral health professionals regarding nutrition and dental caries. Additional research in this area may help to reduce the burden of dental caries and achieve better results in practice.

Keywords:

Dietitians, Oral health professional, Dental caries, Nutrition, Attitudes, Knowledge

85. WHEN CULTURES CLASH: AN EXAMINATION OF HEALTHCARE PROVIDERS' EXPERIENCES WITH HYMENOPLASTY AND THE DEVELOPMENT OF A CULTURALLY SENSITIVE MODEL TO IMPROVE THE PROVISION OF HYMENOPLASTY IN CANADA

Presenter: Somayyeh Zare
College: Arts and Science
Supervisor: Dr. Melanie Morrison

Background:

Hymenoplasty (HP) or hymen reconstruction surgery is intended to produce bleeding at the first sexual intercourse after the operation to mimic virginity. There has been an increase in the demands for this procedure in western societies including Canada. The requests come from young women who belong to cultures that place considerable importance on female premarital virginity, which is reduced to having an "intact hymen." Prior to marriage, a woman is obliged to prove her virginity either through demonstrating a blood-stained sheet or a virginity certificate issued by a doctor. A women's failure in meeting these expectations may lead to monumental ramifications, varying from stigma to honour killing. Having originated from cultural value systems different from that of western societies, HP has been surrounded by many debates: The proponents highly censure this procedure, considering HP as medically unindicated, ethically wrong, and a violence against women; the opponents, in contrast, highly encourage it, arguing that it is necessary for women's social and psychological well-being, and it will empower women to negotiate cultural suppressions. Despite the significance of this procedure, in almost all western countries, including Canada, there are no clear guidelines for healthcare professionals as to how to respond to the requests for HP, leaving them in a highly dilemmatic situation. The absence of guidelines and the controversies surrounding the procedure along with many other factors including legal ambiguities surrounding HP, lack of cultural information, lack of required medical knowledge and expertise have resulted in the arbitrary provision of effective healthcare for these women, leaving them at a huge risk of stigma, violence, suicide, or honour killing. These complexities, however, have not been a barrier to the provision of HP in the private healthcare sector. With the increasing rate of requests for HP, this procedure has become a new source of revenue for private cosmetic surgery clinics in different western countries. In Canada, in particular, these clinics are openly advertising and providing this procedure at a wide range of costs. Despite the increasing popularity of this procedure in Canada, no empirical study has been done on HP to date and there is no information on how HP is practiced in Canada.

Methods:

Thus, my PhD research aims to develop a program to improve the provision of HP in the public healthcare sector in Canada. To this aim, a two-phase study will be conducted. In Phase I, a qualitative study (Grounded Theory method) will be conducted to explore the diverse dimensions of how HCPs experience and approach to the requests for HP. In Phase II, the findings generated from the qualitative phase, will be used to develop a model to address the gaps in the provision of HP.

Results:

Research is in progress.

Conclusion:

Research is in progress.

Keywords:

Hymen, virginity, hymenoplasty, hymen reconstruction surgery, women, culturally sensitive health, sexual norms, immigrant women

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Thanks to their commitment to supporting the next generation of health professionals, the expo has been able to continue its mission of bridging disciplinary gaps and enhancing discovery while championing efforts that can improve the health of people across Saskatchewan, Canada, and the world.

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