The 10th Annual

BPK RESEARCH DAY

SFU Burnaby
Leslie & Gordon Diamond
Family Auditorium

Friday, April 5th, 2019
8:30 am - 5:00 pm
Social at Club Ilia
5:00 pm - 6:30 pm
Dear all,

We are excited to welcome you to the 10th Annual Biomedical Physiology and Kinesiology Research Day! We have a full program of events in store, including four student oral presentations, a keynote address from Dr. Holly Andersen, a three-minute thesis competition, 47 poster presentations, an image contest, lunch, and a social following the event to celebrate our successes.

We hope you share our excitement about what promises to be an excellent day. Today is a chance to highlight and celebrate the breadth and quality of research being conducted in our Department by our talented BPK trainees.

We would like to thank the companies that have generously donated door prizes – make sure you get your ticket for a chance to win! To make this day possible, funds were also generously donated by the BPK Department, Graduate Student Society, BPKSA, and BPKGSA. The committee would also like to thank the BPK office staff, specifically Zhanna Yelyubayeva, Nicole Yoo and Maisie Morsara, for their dedication, effort, and time to help with event organization, promotion, and the creation of this program booklet.

Please enjoy the day!

Sincerely,

The BPK Research Day 2019 Organizing Committee
Vera-Ellen Lucci (Graduate Chair), Dawn Mackey (Faculty Chair), Olivia Aguiar, Amanda Bakkum, Javier Domínguez-Zamora, Matthew Dorton, Natalie Heeney, Brooke Hockin, Evan Hutcheon, Nicole Whittle, Erin Williams
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<td>9:00 am - 9:15 am</td>
<td>Welcome &amp; Introductions</td>
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<td>9:15 am - 9:30 am</td>
<td><strong>Amanda Bakkum</strong>, J. Maxwell Donelan, Daniel S. Marigold: Learning during whole-body movements leads to the construction of a more generalizable model</td>
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<td>9:30 am - 9:45 am</td>
<td><strong>David S Ryan</strong>, Norman Stutzig, Tobias Siebert, James M. Wakeling: Passive and dynamic muscle architecture during transverse loading for gastocnemius medialis in man</td>
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<td>9:45 am - 10:00 am</td>
<td><strong>Kaveh Rayani</strong>, Glen F. Tibbits: Challenging the status quo: A study on the role of cellular magnesium in regulating cardiac contractility</td>
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<td>10:00 am - 10:15 am</td>
<td><strong>Matthew C Dorton</strong>, Sonja de Groot, Marcel Post, Victoria E. Claydon: Establishing a cardiovascular disease risk profile for individuals with spinal cord injury</td>
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<td>10:15 am - 10:45 am</td>
<td>Break</td>
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<td>10:45 am - 11:45 am</td>
<td>Keynote: <strong>Dr. Holly Andersen</strong> Using Mechanisms and Causation</td>
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<td>11:45 am - 12:30 pm</td>
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<td>12:30 pm - 2:00 pm</td>
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Dr. Holly Andersen will discuss the idea of mechanisms and causation from the perspective of philosophy of science. The focus will be on how thinking about mechanisms, especially their structure and organization, can help with experimental research. Abstract conceptual tools like mechanisms facilitate thinking about experimental procedures, including how to set them up, how to draw justified inferences from the results, and in giving effective explanations. She will provide some useful distinctions from philosophical discussions of causation, causal modelling, and mechanisms, to show how these ideas can be used.

Dr. Holly Andersen is an Associate Professor in the Philosophy Department at Simon Fraser University. She works in philosophy of science, especially on causation, causal modeling, and explanation in the sciences.
1. AMANDA BAKKUM, J. Maxwell Donelan, Daniel S. Marigold

*Learning during whole-body movements leads to the construction of a more generalizable model*

The ability to transfer or generalize learned behaviours to novel contexts is an important component of learning. Limited generalization is often seen across different arm movements. However, most of these studies focus on isolated movements where participants are typically in a seated position, such that balance is not a concern. Yet balance challenges are inherent to everyday reaching and walking tasks, where the ability to complete these tasks depends critically on the control of the whole body. Generalization across different walking tasks appears more robust, suggesting that task dynamics may dictate the extent to which learned sensorimotor mappings can be transferred to new situations. We propose that balance challenges encountered during whole-body movements require the nervous system to use a more complete internal model of the body’s dynamics, and a more complete model may be a more generalizable model. Here we determined how challenging balance during standing-based reaching and walking tasks (i.e., whole-body movements) affects generalization. Four groups (n=12 each) of participants adapted to a new visuomotor mapping induced by prism lenses while performing either a standing-based reaching or precision walking task, without any additional balance manipulation or with inflatable rubber hemispheres (radii: 8.5cm) attached to the soles of their shoes. This manipulation increased effort (muscle activity: p=3.8e-5), instability (trunk acceleration variability: p=5.7e-6), and motor variability (limb-endpoint error variability: p=1.2e-6). To assess generalization, participants performed a single trial of each of the other group’s tasks (i.e., the non-adapted tasks) with non-prism lenses after the adaptation phase. Both the walking and reaching groups generalized within their respective non-adapted tasks (e.g., reaching balance-unchallenged generalized to reaching balance-challenged and vice versa). However, the balance-challenged groups showed greater generalization (reaching, p=0.008; walking, p=0.017). These results support the idea that challenging balance may lead to the construction of a more generalizable internal model.

2. DAVID S. RYAN, Norman Stutzig, Tobias Siebert, James M. Wakeling

*Passive and dynamic muscle architecture during transverse loading for gastrocnemius medialis in man*

External forces from our environment translate to transverse loads on our muscles. Studies in rats showed that transverse loads affect muscle
force in the longitudinal direction, where increases in transverse load decreased maximum longitudinal force. Changes in muscle architecture during contraction may contribute to the observed force decrease. The aim of this study was to quantify changes in pennation angle, fascicle dimensions, and muscle thickness during contraction under external transverse load. Electrical stimuli were elicited to evoke maximal force twitches in the right calf muscles in man. Trials were conducted with transverse loads of 2, 4.5, and 10 kg. An ultrasound probe was placed on the medial gastrocnemius in line with the transverse load to quantify architectural muscle characteristics during muscle twitches. Ultrasound images were enhanced and quantified using manual digitization and image transformations. Transverse loading of the muscle resulted in a decrease in the initial muscle thickness and pennation angle, with higher loads causing greater decreases. During twitches the muscle belly and fascicles transiently increased in thickness and pennation angle. The increase in muscle thickness was reduced with greater transverse load, and the increases in pennation angle and fascicle thickness were also reduced. Maximum twitch force decreased with increased transverse loads. The 2, 4.5, and 10 kg of transverse load showed a 9, 13, and 16% decrease in longitudinal muscle force, respectively. Transverse load impacts muscle deformation and contraction dynamics. This study showed that increased transverse loads caused a decrease in ankle moment, muscle thickness, pennation angle, and deformation of the fascicles.

3. KAVEH RAYANI, Glen F. Tibbits

Challenging the status quo: A study on the role of cellular magnesium in regulating cardiac contractility

Binding of cellular calcium (Ca\(^{2+}\)) to troponin C (cTnC) with the contractile apparatus is the precursor to force production. Factors which alter this interaction have significant implications for the ability of the heart to pump blood. The current dogma in the field posits that magnesium (Mg\(^{2+}\)) does not play a direct role in contractile regulation through cTnC. However, cellular Mg\(^{2+}\) (~1000 µM) is at least 1000x more prevalent than Ca\(^{2+}\) (~0.1 – 1 µM), therefore binding, even if governed by significantly lower affinities could have major physiological consequences. To establish a baseline, we used high precision calorimetry (ITC) to titrate cTnC with Ca\(^{2+}\)/Mg\(^{2+}\). The dissociation constant (Kd) is the concentration of titrant which half-saturates the ligand and is inversely proportional to binding affinity. Ca\(^{2+}\) was found to bind cTnC (Kd = 22.7 ± 0.5 µM) with 18x higher affinity than Mg\(^{2+}\) (Kd = 406.1 ± 7.9 µM). To further explore these binding interactions, two single amino acid changes (D67A/D73A) were made in the regulatory Ca\(^{2+}\) binding site; these changes significantly reduced the binding affinity of both cations to cTnC. Moreover, preincubation of cTnC
with increasing concentrations of Ca$^{2+}$ decreased Mg$^{2+}$ binding affinity in a graded manner, and the opposite was also seen ($p<0.001$). Taken together, these results suggest that both cations interact with the same binding site within cTnC. We further explored a series of cardiomyopathy-associated cTnC mutations (A8V, L29Q, A31S, L48Q, Q50R, and C84Y) known to affect changes in the Ca$^{2+}$ binding interaction with cTnC. We found that at cellular concentrations, Mg$^{2+}$ significantly reduced the binding of Ca$^{2+}$ to each mutant ($p<0.05$). Pending further studies, our findings suggest that Mg$^{2+}$ may reduce Ca$^{2+}$ binding to site II of cTnC, thus affecting changes in the force production capabilities of heart tissue in health and the diseased state.

4. MATTHEW C DORTON, Sonja de Groot, Marcel Post, Victoria E Claydon

Establishing a cardiovascular disease risk profile for individuals with spinal cord injury

Cardiovascular disease (CVD) is the leading cause of morbidity and mortality in individuals with spinal cord injury (SCI). Obesity, injury characteristics and impaired autonomic function may influence the increased CVD risk following SCI. We aimed to further understand the role of these variables and establish cut-points for CVD risk for individuals with SCI. We performed a multicentre cross-sectional study of individuals with traumatic SCI ($n=257$, 61 females, aged 47±9 years, duration of injury [DOI] 23±9 years). CVD risk was determined from the 10yr Framingham risk score (FRS). Risk factors for CVD included: waist circumference (WC); body mass index (BMI); waist-to-height ratio (WHtR); DOI, level, and completeness of injury; resting blood pressure; and peak heart rate (HRpeak) response to exercise ($n=126$). Most lesions were cervical (45%) or thoracic (50%); 71% were motor/sensory complete and 78% had lesions that could affect cardiovascular autonomic control. Based on the FRS, 34% had moderate-high CVD risk; men (12±8%) had a higher risk than women (5±3%; $p<0.0001$). WC was the most strongly correlated anthropometric measure with FRS ($r=0.439$; $p<0.0001$). The area under the receiver operating characteristic curve was significantly higher ($p<0.05$) for WC (0.69) than WHtR (0.66) and BMI (0.65). The optimum WC cut-off for males was 96cm. Due to low numbers ($n=3$) of at-risk females, specific WC cut-off criteria could not be determined. Akaike information criteria identified important predictors for CVD risk: DOI (importance 1.0, estimate 0.30±0.06); chronotropic incompetence (HRpeak≤125bpm) (importance 0.89, estimate -4.26±2.38), WC (importance 0.83, estimate 0.12±0.08), and HRpeak (importance 0.81, estimate -0.06±0.03). DOI, WC, and the ability to regulate HRpeak (a marker of severity of injury to cardiovascular autonomic pathways) are important variables for CVD risk following SCI. WC provides a convenient predictor of CVD risk after SCI. For men with SCI, a healthy WC is smaller than in the able-bodied.
THREE-MINUTE THESIS

1 Abeline Watkins | BSc
Cannabidiol’s mechanism of interaction with cellular targets

2 Bader Al-Zeer | BSc
Cardiac excitation-contraction coupling in zebrafish: The role phospholamban

3 Shivani Rana | BSc
Improvement techniques that work to reduce blood pressure in hypertension individuals

4 Olivia Aguiar | MSc
Circumstances of head impact in ice hockey

5 Natalie Heeney | MSc
Pediatric Syncope: Diagnostic Dilemmas

6 Erin Williams | BSc
Relax... blood vessel stiffness is a marker of heart disease risk

7 Bisman Dhaliwal | BSc
The importance of resiliency in the maintenance of physiological health: As seen in super seniors vs. non-super seniors

8 Gaby Jensen | MSc
Neuroregulation of vascular tone

IMAGE CONTEST
Image Contest Poll:
https://www.surveymonkey.ca/r/RDimagepoll
# POSTER PRESENTATIONS

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<td>3  Nataliya Shishov</td>
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<td>5  Kim Hoang Tran (Henry)</td>
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<td>7  Kyle Simpson &amp; Shoaib Faizi</td>
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<td>15  Jasmine Gill</td>
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<td>17  Linden Lechner</td>
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<td>27  Amanda Zacharuk</td>
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<td>33  Kyle Dumont</td>
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<td>35  Adonay Nunes</td>
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<td>37  Taylor McColl</td>
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<td>39  Bisman Dhaliwal</td>
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<td>41  Carly Johnston</td>
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POSTER ABSTRACTS

1. MADELINE C. ANGUS, and Peter C. Ruben

Voltage gated sodium channels in prostate cancer

Prostate cancer is the most common cause of mortality due to cancer in men. Traditional treatments include radiotherapy and hormone therapy, however in some cases cancer can become unresponsive to treatment and continue to spread to other tissues. Our research attempts to target the movement and spread of prostate cancer cells by targeting voltage gated sodium channels, which are believed to play a role in invasiveness of cancer cells. Our research shows that voltage gated sodium channels are found in the leading edge of cancer cells where we believe they are key for forming invasive structures that enable the cells to invade surrounding tissues. Further, drug studies we have done have shown that inhibiting this channel drastically reduces invasiveness in prostate cancer. Sodium channels may offer a new therapeutic target for late stage prostate cancers, where there are currently not very many treatment options.

2. BRAEDEN CHARLTON, and David C. Clarke

Effectiveness of a relative energy deficiency syndrome and female athlete triad education module

The Female Athlete Triad (FAT) is a condition that has been researched since the early 1990’s. This condition, most commonly seen in female athletes, is the presentation of low bone mineral density, hormonal dysfunction leading to irregular menstruation, and low energy availability (LEA); the symptoms can occur in isolation or in combination. Recently, it has been seen that male athletes can also present with these symptoms, except for irregular menstruation. As such, researchers have introduced a more inclusive term: Relative Energy Deficiency in Sport (RED-S). The underpinning issue of both RED-S and FAT is LEA. Since the discovery of FAT, few research groups from the United States have sought to elucidate the quality of knowledge of FAT or RED-S among healthcare professionals, coaches, and athletes, while no studies in Canada have taken place. As a means of primary prevention, it has been suggested by the International Olympic Committee, among other sport related organizations, that coaches should be well-informed of behaviours that put athletes at risk of FAT and RED-S. To our knowledge, the efficacy of coach education programs, with a focus on FAT and RED-S, have yet to be studied. The goal of our study is to understand the quality of coach knowledge of FAT and RED-S in a sample
The use of Kinovea software for kinematic analysis of real-life falls

Falls cause up to 80% of traumatic brain injuries (TBI) in older adults (Fu et al., 2017). In long-term-care (LTC), over one-third of falls result in head impact, which most often occurs during backward falls (Yang et al., 2017). In such events, TBI risk depends, in part, on the impact velocity of the head. In this study, we measured the accuracy of Kinovea open-source digitization software in determining head velocities during falls in the lab, and then applied Kinovea to measure head velocities in real-life falls in older adults. In laboratory experiments, the participant was instructed to fall backwards (n=21). Head velocities were calculated with 3D motion capture (Qualisys, 600Hz), and with Kinovea from a single camera (Cisco, 30Hz) oriented perpendicular to the plane of the fall. We then applied Kinovea to calculate head velocities from sagittal-view videos of LTC falls with (n=6) and without head impact (n=6). Mean percent differences between Qualisys and Kinovea in peak values of resultant, vertical and horizontal velocities were 3.94%, 9.31%, and 5.23% respectively. RMSE was 0.18m/s for peak resultant velocity. In LTC falls with head impact, different movement patterns were displayed. In most cases, we observed two peaks in head velocity, which closely aligned with the perceived instants of pelvis and subsequent head impact. The first peak was often the largest (n=3), but the second peak was highest in another case indicating rapid descent of the head and torso after pelvis impact. In other cases, we observed near-simultaneous impact of the pelvis and head or a gradual decrease in head velocity after pelvis impact, leading to low contact velocity. Our results demonstrate the accuracy of Kinovea in measuring head velocities during falls from standard sagittal-plane video. We also demonstrate how Kinovea allows kinematic analysis to quantify head impact severity during real-life falls.
The impact of strain pressure and posture on cardiovascular responses to the Vasalva Manoeuvre

The Valsalva Manoeuvre (VM) is a respiratory strain that produces a specific, phasic, reproducible blood pressure (BP) and heart rate (HR) response in healthy individuals. Abnormal responses reflect impairments in cardiovascular autonomic control; thus, the VM is commonly used clinically to evaluate baroreflex function and diagnose autonomic disorders. During a clinical VM, the participant lays supine and exhales into a tube, maintaining a pressure of 40mmHg for 20s. However, many individuals are unable to reach and/or sustain 40mmHg for the full 20s, and it may be that smaller strains evoke smaller responses. Furthermore, in some individuals (for example wheelchair users) it is preferred to conduct the VM seated, but the addition of the orthostatic stimulus may enhance the responses obtained. We examined the effect of VM intensity and position on BP and HR responses. Healthy participants (n=19; 9 male; age 26±5 years) performed 3 VM in both seated and supine positions at pressures of 20, 30 and 40mmHg. Starting position and VM pressure order were randomized. Beat-to-beat BP and HR (Finometer) were recorded continuously and non-invasively throughout. Blood pressure decreases during phase IIA, eliciting compensatory reflex responses. The compensation in systolic, diastolic, and mean arterial pressure was larger in the seated position than when supine (p<0.016, main effect of position), and showed dose dependence (p<0.0027, main effect of strain pressure). Compensatory heart rate responses are expressed clinically as the Valsalva ratio – the relative increase in heart rate in phase IIB compared to the decrease in heart rate in phase IV. This response also exhibited main effects of position (p<0.05) and dose dependence (p<0.05). These data illustrate that cardiovascular responses to the VM exhibit dose dependence and are sensitive to posture. These factors should be taken into consideration when interpreting VM in those unable to perform VM to the clinical standard.

Combining electrical stimulation, electromyography, and muscle synergy to create a more informative map of the rat motor cortex

The motor cortex is a critical brain region responsible for regulating goal-directed movements and generating the motor commands that are sent to muscles. Much of our understanding about the motor cortex comes from experiments in which intracortical (electrical) microstimulation (ICMS)
stimulation was performed at different sites to evoke movements of the body. These reveal that motor cortex contains a fractured somatotopic representation of the body, meaning that many cortical regions of the motor cortex overlap with one another. Moreover, ICMS at one site can produce movements in multiple parts of the body, called synergies. Several lines of evidence suggest that ICMS synergies provide useful information about motor control. First, they are similar to natural synergies whether they are analyzed at the level of individual muscles or at the level of complex movements such as flinching and eating. Second, the area of cortex from which ICMS evokes a synergy related to a specific behavior expands after training on that behavior. However, most previous mapping studies focused on only parts of the motor cortex and did not collect data on muscle synergies. As a result, most of the motor maps available in the literature are incomplete. The goal of this study is to collect data on the representation of muscle synergies in cortex. We will create a map of muscle coactivations using an accelerated automated electromyographic (EMG) mapping apparatus, which we are developing to enable us to collect EMG data at a faster rate and automatically discriminate spontaneous and ICMS-induced movements. These data can be utilized for future studies that aim to investigate individual brain variation regarding skill learning and resilience against neurological disorders.

6. NICOLE K. WHITTLE, Emaan Abbasi, Dawn C. Mackey

**Steps for change: A systematic review about the impact of financial incentives on physical activity in older adults**

Nearly 90% of older Canadians (65+ years) do not meet the Canadian Physical Activity Guideline of 150 mins/week of moderate-to-vigorous aerobic physical activity, placing them at risk of declining mobility and chronic disease. Behavioural economics proposes that individuals are more likely to make decisions that favour immediate benefits (e.g., being sedentary) over long-term benefits (e.g., being physically active). Offering financial incentives for the uptake and adherence to a behaviour attaches tangible short-term benefits to that behaviour. Therefore, financial incentives may motivate physical activity behaviour more effectively than the inherent long-term benefits of physical activity. However, it remains unclear whether financial incentives are effective for increasing physical activity among older adults. We conducted a systematic search of 10 academic databases to identify randomized controlled trials that used financial incentives to promote physical activity in older adults. Two reviewers screened 1094 articles for eligibility and extracted data from five studies that met eligibility criteria (n=309). Two studies that examined the proportion of days that step goals were achieved, and one study
that tracked daily aerobic minutes, produced significant increases in physical activity using assured financial rewards that allowed for gradual increases in physical activity levels over time. These studies used a range of incentive values; thus, the magnitude of the reward did not appear to determine its effectiveness. Two studies found no change in physical activity following intervention with financial rewards. Three studies included a post-intervention follow-up period and found that physical activity levels declined after the financial rewards were withdrawn. In conclusion, financial rewards have potential to promote short-term uptake of physical activity in older adults. Future studies are needed to determine how to promote long-term adherence to healthy levels of physical activity once financial rewards are removed, and to test the acceptability and effectiveness of financial losses.

7. KYLE SIMPSON, SHOAIB FAIZI, Thomas Claydon

Optimization of precise CRISPR-Cas9 editing of the zebrafish cardiac zERG gene to create a model of Long-QT syndrome

Individuals with Long-QT syndrome present delayed repolarization in the cardiac action potential that is reflected by an extended QT interval on an ECG, creating a substrate for cardiac arrhythmias. hERG potassium channel dysfunction is a major contributor to Long-QT syndrome. Testing and development of therapeutics to restore hERG channel function requires examination in a translatable complex system to account for system-wide effects and interactions. Zebrafish have been shown to provide such a model, partially due to strong similarity in their cardiac electrophysiology with humans. Here, we describe initial optimization of a gene-editing strategy to generate inherited hERG mutations in zebrafish hearts to model Long-QT syndrome. We used adult fish for breeding, and collected one-cell stage embryos for micro-injection of CRISPR-Cas9 components. These include Cas-9 endonuclease to create double-stranded breaks in the DNA of the embryo, guide RNAs to target the Cas-9 to a precise location in the zERG gene, and DNA containing the mutation of interest, serving as a template for repair of the Cas-9 induced cleavage. We designed this template DNA to include a reporter gene, which upon incorporation turns the eyes of the fish green. Embryos were analyzed 3-5 days post-injection for presence of green eyes. In four separate experiments, we found green eyes in 2/19, 1/27, 1/12, and 9/43 embryos (12.8%). We then delivered the mutated template DNA in a plasmid that can be linearized by Cas-9 within the embryo, since this may enhance efficiency. We found green eyes in 2/26, 1/12, and 5/25 embryos (12.7%), suggesting no improvement. Future work will examine editing efficiency in conjunction
A human iPSC-derived cardiomyocyte (hiPSC-CM) model for catecholaminergic polymorphic ventricular tachycardia (CPVT)

Background: CPVT is a devastating heritable arrhythmia and leading cause of sudden cardiac death, with a prevalence of 1 in 10 000 and an estimated mortality of 30-50% by age 35. Type one CPVT is caused by genetic variants in the cardiac ryanodine receptor (RyR2), and the arrhythmia may be triggered by catecholamine release in response to physical exertion and/or emotional responses. The RyR2 functions to gate Ca$^{2+}$ release from the sarcoplasmic reticulum (SR), however mutated RyR2s may be susceptible to inappropriate Ca$^{2+}$ release causing delayed after depolarizations as a trigger for arrhythmia. This phenomenon can be studied using novel platforms such as hiPSC-CMs which carry RYR2 variants.

Objective: The objective of this study is to use an hiPSC-cardiomyocyte platform to model the disease phenotype caused by novel CPVT-associated variant, RYR2 R417L.

Methods: An hiPSC line harbouring the RYR2 R417L variant was created using CRISPR/Cas9 genome editing technology. This mutant line, along with an isogenic control line, was differentiated into a monolayer of beating cardiomyocytes using small molecule modulation of the canonical Wnt pathway. Increased propensity for inappropriate calcium release and delayed-after-depolarizations was characterized by simultaneous recordings of membrane voltage (Vm) and Ca$^{2+}$ transient via optical mapping on a functional monolayer of hiPSC-cardiomyocytes. Furthermore, single cell Ca$^{2+}$ dynamics were analyzed via confocal microscopy.

Results: An hiPSC line carrying a heterozygous RYR2 R417L variant has been established. Phenotyping results indicate that the R417L variant increases the propensity for inappropriate Ca$^{2+}$ release events, which may lead to increased delayed-after-depolarization frequency in a monolayer of hiPSC-CMs.

Conclusion: Use of hiPSC-cardiomyocytes provides a compelling and informative method to model heritable cardiac diseases. An hiPSC-derived cardiomyocyte model reveals the R417L mutation may be arrhythmogenic, provides a molecular substrate for deadly CPVT and a sophisticated tool for developing precise methods of life saving interventions.
Can the Valsalva maneuver serve as a biomarker for syncope diagnoses?

Syncope or fainting is ultimately caused by a reduction in cerebral blood flow. Previous research identified that impaired cerebral autoregulation contributes to increased fainting susceptibility. The Valsalva maneuver (VM) challenges cerebral autoregulation and may reveal impairments in individuals who are susceptible to syncope. Seated VM elicit exaggerated blood pressure responses, and may further unmask cerebrovascular impairments, and so better identify syncope disorders. We hypothesized that both cardiovascular and cerebrovascular responses to the VM would be exaggerated in the seated position and would serve as biomarkers for syncope susceptibility. In a randomized order, healthy participants (N=19; 9 males; 26±5 years) performed a standard 40mmHg, 20s VM in both supine and seated positions. This was followed by a graded 60° head-up-tilt test with combined lower body negative pressure continued to pre-syncope, to determine orthostatic tolerance (OT; susceptibility to syncope) in minutes. Beat-to-beat cardiovascular responses were determined using finger plethysmography, and transcranial Doppler ultrasound was used to measure systolic cerebral blood flow velocity (sCBFv). Systolic arterial pressure (SAP) responses to the VM were greater when seated in phases 2A (p=0.023), 2B (p<0.001) and 4 (p=0.004), compared to supine. sCBFv responses were not greater in seated VM, because these healthy participants effectively buffered the larger pressure changes with greater cerebrovascular resistance responses (p<0.013). The magnitude of phase 4 sCBFv overshoot (p=0.003) was greater in seated VM, compared to supine. In the seated position, the magnitude of the phase 2B sCBFv recovery was predictive of OT (R=0.615, p=0.0065), this relationship was not seen in supine VM (R=0.191, p=0.448). We postulate that, in seated VM, cerebral responses to the 2A reduction in cerebral perfusion better replicate cerebral responses to reduced cerebral perfusion associated with orthostasis, and thus are related to OT. Cardiovascular and cerebrovascular responses to seated VM may provide attractive biomarkers for susceptibility to syncope. 1.Claydon VE, Hainsworth R. Clin Auton Res. .2003. 13:321-329 2.Perry BG et al. Physiol Rep. 2014. 10;2(2):e00233

Arterial tonometry: Differences with recording site, sex, and stress

Arterial stiffness is a positive risk factor for cardiovascular disease and
mortality, and is a common screening tool for cardiovascular risk. Arterial applanation tonometry is a simple, non-invasive, reproducible means to measure arterial stiffness; however, it is unclear whether factors such as recording site, sex, and stress levels impact the quality of measurement. Recordings at the femoral artery are currently regarded as the “gold standard”; however, this measurement is taken in a sensitive area that is of limited accessibility in some patients (e.g., spinal cord injury), and may evoke an emotional pressor response or “white coat effect” that could impact blood vessel tone. We aim to: (i) evaluate factors affecting tonometry measurements including sex, and mental stress; (ii) consider the equivalency of measurements taken at the carotid, femoral, and radial sites. Arterial compliance will be determined using Tonometry (PulsePen arterial tonometer) measures of augmentation index (Alx) and pulse wave velocity (PWV) in 40 healthy men and women. Beat-to-beat blood pressure will be measured using finger plethysmography. A three lead ECG will be used to detect heart rate, and rhythm. We anticipate that arterial stiffness will be greater in males than females, reflected in increased PWV and lower Alx in men. We expect that vasoconstriction secondary to mental stress will increase both stiffness indices. We expect that central measures (carotid-femoral) will agree with those taken peripherally (carotid-radial). This exploration will provide important clinical insight as to the use of tonometry to accurately evaluate arterial stiffness, and thus better serve as a predictor of cardiovascular mortality.

11. F. JAVIER DOMÍGUEZ-ZAMORA, and Daniel S. Marigold

Changes in motor cost affect gaze-limb coordination

Frequent gait modifications are often required to navigate our world. These can involve long or wide steps, or changes in direction. People generally prefer to minimize the motor cost (or effort) of a movement, though with changes in gait, this is not always possible. The decision of when and where to shift gaze is critical for controlling motor actions, since vision informs the brain about the available choices for movement—in this case, where to step. Here we asked how motor cost influences the allocation of gaze. To address this, we had participants walk and step to the center of sequential targets on the ground. We manipulated the motor cost associated with controlling foot placement by varying the location of one target in the lateral direction on a trial-to-trial basis within environments with different numbers of targets. Costlier steps caused a switch from a gaze strategy of planning future steps to one favoring visual feedback of the current foot placement when participants had to negotiate another target immediately after. Specifically, costlier steps delayed gaze shifts away from the manipulated target. We show that this relates to the cost of moving
the leg and re-directing the body’s center of mass from target-to-target. Overall, our results suggest that temporal gaze decisions are affected by motor costs associated with step-to-step demands of the environment. Moreover, they provide insight into what affects the coordination between the eyes and feet for the control of stable and accurate foot placement while walking.

12. RAVICHANDRA VENKATESHAPPA, Jake Kemp, Thomas Claydon

*The hERG channel activator, RPR260243, rescues loss of hERG protective current in early cardiac repolarization induced by an inherited mutation*

hERG is a cardiac delayed rectifier potassium channel that is a major player in the cardiac ventricular repolarization process. hERG channels provide a protective role against premature stimuli late in repolarization and early in diastole. Inherited loss of function mutations in hERG are responsible for type 2 long QT syndrome (LQT2), a disorder associated with lethal cardiac arrhythmia. Restitution of the protective function of hERG channels by activator molecules may provide a method of treating LQT2. RPR260243 is one such activator which is known to increase hERG currents by slowing deactivation. We tested the effect of RPR260243 on WT hERG channels, expressed in HEK-293 cells, using the patch clamp technique, at 37°C. We found that RPR260243 produced a concentration dependent slowing of deactivation and an increase of peak protective currents during premature stimuli. To test the ability of RPR260243 to restitute the peak protective current in an arrhythmic condition, we used the hERG-R56Q mutant. This LQT2-causing variant has accelerated deactivation kinetics, which we show significantly reduced peak protective currents during premature stimulation. RPR260243 showed a concentration dependent recovery of deactivation in hERG-R56Q mutant channels and was also able to restitute hERG peak protective currents during premature stimulation in the mutant. This study shows that hERG activator molecules, like RPR260243, which increase hERG current by slowing deactivation kinetics of the channel, can restitute the peak protective currents and restore the function of hERG during ventricular repolarization. These findings suggest a novel potential therapeutic role for similar hERG activator compounds.

13. AKSEL H. B. SMIT-ANSEEUW, and Dawn C. Mackey

*Using activity monitors to quantify changes in daily walking following intra-articular injections for knee osteoarthritis in older adults*

Background: Knee osteoarthritis (OA) is a common, chronic, non-curative
disease that is a leading cause of walking disability in older adults around the world. Studies suggest that the best intervention strategy follows a progressive approach beginning with non-operative treatment such as intra-articular (IA) injection to reduce symptoms and restore the lived-experience of patients. IA corticosteroid (CS) and hyaluronic acid (HA) injections reduce inflammation, boost intra-capsular synovial fluid, and improve the symptomology of OA in older adults. However, past studies have been limited to clinic-based, in-person assessments conducted intermittently after injection, which may not properly capture the variability of the patient’s day-to-day experience. Consumer-grade activity monitors may be a valuable tool in guiding OA treatment by allowing clinicians to observe daily walking patterns following IA injection. Methods: Participants will be community-dwelling older adults (65+ years) who are seeking IA knee injection of either CS or HA at the White Rock Orthopedic Surgery Center. We will use a hip-worn Fitbit Zip to track daily step counts for 1 week before injection, and 3 weeks after. During this 4-week observation period, participants will also complete weekly WOMAC symptom questionnaires to quantify their knee pain, stiffness, and disability. Data Analysis: We will use step count data to describe and compare the impacts of CS and HA injection. We will quantify mean daily step count before and after injection and calculate the percent change in mean daily step count following injection. We will examine associations between changes in step count and self-reported symptoms following injection. Significance: This pilot study may provide evidence that supports the use of activity monitors in treatment plans for knee OA in older adults. The results might also provide a greater understanding of the different effects of two common types of IA injection for OA treatment.

14. EVAN HUTCHEON, and Sherri Ferguson

The effect of oxygen and nitrogen on nitrogen narcosis severity

Nitrogen narcosis (NN) is a cognitive impairment similar to alcohol intoxication that occurs when gases are breathed at a pressure greater than 3 ATA. The exact mechanism of NN is unknown, and the exact role of N₂ and O₂ in regards to NN severity is still being researched. We hypothesize that the partial pressure of O₂ will have a greater impact on nitrogen narcosis than N₂. We had participants’ complete cognitive tasks while breathing air at pressures and O₂ concentrations equivalent to submersion under 45m and 57m of water, and also a normoxic gas mixture at 45m. A fixed effect ANOVA was then performed on least square means. Participants had significantly more correct responses with a simple digit math task in the 45m air condition than in the 57m air condition. Participants performed
Assessment of the effect of a phospholamban gene knock-out on cardiac parameters in adult zebrafish using high resolution echocardiography

Zebrafish (ZF) have gained popularity as a model for human cardiac function due to their shared cardiac characteristics and fully sequenced genome that can be manipulated using genome editing techniques such as CRISPR. The transparency of ZF embryos allows them to easily be studied in vivo using techniques such as common light microscopy. However, as the ZF reach adulthood, they lose their transparency making it difficult to study adult cardiac function in vivo: high resolution echocardiography (HRE) has been employed to overcome this caveat. The contribution of the sarcoplasmic reticulum (SR) in activation of contraction in ZF hearts is controversial as ZF cardiomyocytes lack T-tubules and exhibit a less developed sarcoplasmic reticulum (SR) and lower expression of ryanodine receptors (RyR). Therefore, Ca\(^{2+}\) induced Ca\(^{2+}\) release (CICR) may play a limited role in ZF hearts compared to mammals. Phospholamban (PLN), regulates the SR Ca\(^{2+}\) pump (SERCA) that allows Ca\(^{2+}\) uptake in the SR. The dephosphorylated form of PLN inhibits the pump while PLN phosphorylation mediated by β-adrenergic stimulation results in disinhibition. To examine the role of PLN on SR function, the effect of knocking out the PLN gene [both heterozygote (PLN+/-) and homozygote (PLN -/-) KOs] in the hearts of ZF will be studied and compared to wild-type (WT) ZF using HRE (70 MHz). Cardiac parameters such as ejection fraction, end-diastolic volume and stroke volume will be determined in the presence and absence of the β-adrenergic agonist isoproterenol. In addition, as ZF must cope with temperature changes, studying ZF heart responses at physiologically relevant temperatures may be crucial in unmasking any potential temperature dependence. Therefore, ZF will be studied at temperatures of 18°C, 23°C and 28°C to determine how contractile function changes to cope with diverse environment conditions.
Noisy vestibular stimulation improves lateral stability in balance-challenged standing tasks but not in walking tasks

Our vestibular system is essential for providing detailed information about head motion, which is important for maintaining an upright posture. The effects of age and injury on this system can disrupt balance. Researchers have recently found novel techniques using electrical vestibular stimulation to potentially mediate this problem. Stochastic resonance is a phenomenon whereby the capacity to detect a weak signal or process information may be enhanced with the addition of noise or random interference. Recent studies show that low-level stochastic vestibular stimulation (SVS) is associated with improved balance function. However, the results varied depending on the task, degree of challenge in balance, and with methods for determining the appropriate stimulation threshold. Here, we determined how the application of SVS affects challenged and unchallenged standing and walking balance. Additionally, we compared two common stimulation thresholding protocols (cutaneous and sinusoidal). Thirteen healthy university-aged participants performed balance-challenged and balance-unchallenged standing and walking tasks with SVS or sham stimulation. For the balance-challenged condition, we attached inflatable rubber hemispheres (radii: 8.5cm) to the soles of participant’s shoes. We found no effect of SVS on balance for the walking tasks (p > 0.05). Similarly, we found no effect of SVS on the unchallenged standing tasks. However, SVS significantly decreased mediolateral trunk velocity variability for the balance-challenged standing task (p = 0.036). These observations were consistent across both cutaneous and sinusoidal stimulation levels. These results indicate that enhancing vestibular sensitivity using SVS may have beneficial effects on stability; however, this appears to be task dependent. We propose that the extent to which SVS is beneficial may be dictated by the degree of postural control required to perform the task.

Comparison of percussion power massagers on range of motion and subjective muscle soreness

Self myofascial release (SMR) has become a common practice among athletes of all levels and recreational sport enthusiasts. Research is lacking on the more expensive, vibrating therapeutic tools such as the Theragun and Hyperice Hypervolt. Research has, however, accredited the
benefits of these SMR modalities to the placebo effect and increasing input to the nervous system. The proposed research experiment is a blind study comparing these commercial percussion massagers to a regular vibrating object to see if the vibration has a positive therapeutic effect. By varying the vibrational levels of the massagers and our sham treatment, we may explore how the severity of vibration reflects changes in range of motion (ROM) and subjective muscle soreness. Overall, if there is no difference in our variables, we further support the hypothesis SMR is most beneficial by placebo and varying nervous system stimulation.


**Forearm vascular resistance responses to the Valsalva Maneuver**

In response to orthostatic reductions in blood pressure (BP), intact baroreflex-mediated vasoconstriction is crucial for effective autonomic BP control and the prevention of syncope, or fainting. The Valsalva maneuver (VM) induces BP changes that provide a stimulus for baroreflex-mediated vasoconstriction that may identify individuals who are susceptible to syncope. We aimed to evaluate forearm vascular resistance (FVR) responses to the VM in healthy men and women, and their association with syncope. We hypothesized that: (i) individuals with smaller vascular resistance responses would be more susceptible to syncope; (ii) males would mount larger FVR responses and be less syncope-prone than females. Healthy participants (N=37; 18 males; age 26.5±4.6 years; 19 females; age 25.1±4.5 years) performed a standard supine 40mmHg, 20s VM. This was followed by a graded 60° head-up-tilt test with combined lower body negative pressure continued to presyncope to determine orthostatic tolerance (OT) in minutes (susceptibility to syncope). Beat-to-beat BP and heart rate (Finometer Pro) were recorded continuously and non-invasively. FVR was calculated as mean arterial pressure divided by brachial blood flow velocity (Doppler ultrasound) relative to baseline. The VM produces a distinctive FVR pattern that peaks (+82±11%) in phase 2B (15.3±0.7 sec) as the baroreflex responds to low pressure perturbations. The peak FVR response and timing was not significantly different between men (86.3±15.6%) and women (78.5±14.7%, p=0.71). The maximum FVR (r=-0.383, p=0.03) and area under the curve of the FVR (r=-0.406, p=0.02), when normalised for the magnitude of the BP decrease in phase 2A, were correlated with OT. This is the first study to characterize FVR responses to the VM. The VM elicits a large baroreflex mediated increase in FVR in response to the BP dip in phase 2A. FVR responses to the VM may be a useful tool to identify individuals who are susceptible to syncope.
19. TAMARA K. PHU, Karam Elabd, Vicki Komisar, Nataliya Shishov, Stephen N. Robinovitch

**Kinematic analysis of real-life backward falls in older adults leading to head impact**

Introduction: Falls are the number one cause of traumatic brain injuries (TBI) in adults over age 65. Improved understanding of the dynamics of head impact in falls should help to inform prevention strategies. This study aims to: (1) determine, based on video analysis of real-life backward falls in older adults, the time-varying positions and velocities of the body segments during the initiation, descent, and impact stages of falls; and (2) identify the kinematic factors that separate falls with and without head impact. Methods: We reviewed a database of over 2500 videos of falls in long-term care residents, to identify cases that satisfied the following inclusion criteria: (1) primarily backward landing, (2) the camera captured a sagittal view of the fall, and (3) clear view of the body throughout the fall. 74 falls met these criteria. In 30 falls, the head impacted the floor or another object; in 44 falls, head impact did not occur. We also validated our approach for kinematic analysis of videos through lab-based falling experiments (21 falls). We found that Kinovea digitization software was 96% accurate in estimating peak head impact velocity, when compared to 3D motion capture. Efforts are ongoing to characterize the dynamics of the falls from videos. We will quantify the time-varying velocities and configurations of the trunk, lower limbs, and upper limbs, to extract features that reflect fall severity and landing strategy. We will then test whether these variables associate with the probability for head impact. Expected Impact: This study will provide new and valuable insight on the dynamics of real-life falls in older adults that result in head impact. The results should inform the development of more realistic methods for evaluating and optimizing the design of fall injury prevention methods, including helmets, flooring, and exercise.

20. JACOB KEMP, Raj Johal, Zhao Kai Pang, Thomas Claydon

**A hERG channel activator compound restores loss of protective currents in the early action potential refractory period induced by the LQTS-causing variant V535M**

hERG K+ channels underlie the rapid delayed rectifier current of the cardiac action potential. Contributing to repolarization of cardiac tissue, loss-of-function of hERG channels due to mutations or drug block results in action potential prolongation and Long QT Syndrome 2 (LQTS2), which is associated with the potentially lethal arrhythmia, Torsade de Pointes. As such, there is significant interest in identifying compounds that
activate hERG channels as potential therapeutics. One such compound, RPR260243, slows deactivation (closing) of hERG channels, which would be expected to increase repolarizing hERG current. Although RPR260243 has little effect on action potential duration, we recently showed that RPR260243 increases hERG protective current that flows early in the refractory period in response to premature stimulation and hypothesize that this may be antiarrhythmic. Here, we have studied the effects of RPR260243 on a hERG-channel variant, V535M, which is associated with LQTS2. We show that the mutation altered inactivation gating and dramatically reduced the protective current in response to premature stimulation. Application of RPR260243 slowed deactivation kinetics in the mutant channel and increased the protective currents in a concentration-dependent manner. These data show that an LQTS2-causing mutation reduces hERG protective current in early refractory, which may establish a substrate for early afterdepolarizations. Furthermore, hERG activator compounds targeting deactivation gating, such as RPR260243, enhance protection against after depolarizations and premature excitation suggesting a novel therapeutic potential for this class of activator molecules, even in cases of apparently unrelated gating defects.

21. PATRICK MAYERHOFER, Matt Jensen, David C. Clarke, James M. Wakeling, J. Max Donelan

System identification of a mathematical model to predict cycling power as part of a pacing control system

Our long-term goal is to maximize athlete performance by tightly regulating pacing using closed-loop feedback control. We hypothesize that this regulation of pacing will improve performance by preventing athletes from exceeding or wasting their energy capabilities. Our lab recently demonstrated that effective closed-loop control of running speed can be accomplished through the real-time adjustment of commanded step frequency. Here we seek to accurately control mechanical power output in outdoor cycling. Our first step is to identify a dynamic model of the relationship between commanded cadence and mechanical power. Our participants cycle on an outdoor bike while a metronome commands step changes in cadence. A microcontroller controls the metronome frequency of the participant’s earphones, and measures mechanical power. We treat participants as dynamic systems that can be identified by providing controlled inputs (commanded cadence) and measuring dynamic output (measured power). We derive a model from first principles in which power is a function of cadence and gear ratio, and use non-linear optimization to identify the single unknown parameter, drag, that best fits the predicted power to the measured power. A simple parameterized point-mass model
of athlete and bike, driven forward by the athlete’s force, and backward by air resistance, captures 82% of the measured power variance with an optimized drag parameter of 0.3. Literature wind-tunnel tests find values around 0.2 depending on the magnitude of the reference area of the athlete, the air density, and the drag coefficient. We expected our value to be slightly larger as our drag parameter partially subsumes unmodeled losses, such as rolling resistance. Towards our long-term goal, we will next leverage this model to design and test a closed-loop feedback system to control power in cycling. This will provide athletes with stroke by stroke control over their power through more precise pacing and optimal energy consumption.

22. OLIVIA M. G. AGUIAR, Brigitte M. Potvin, Tim R. Chow, Stephen N. Robinovitch

Association between situational factors and severity of head impacts in men’s varsity ice hockey

Among varsity sports, ice hockey has the highest rates of concussions. In this study, we examined situational factors associated with the frequency and severity of head impacts in men’s varsity ice hockey. Over 42 home games, we collected video and helmet sensors data of 409 head impacts experienced by players of the SFU Men’s Ice Hockey team. We used ANOVA (subject code as a covariate) to examine whether sensor measures of head impact severity (peak linear head acceleration (amax) and angular velocity (ωmax)) associated with the body part striking the head, puck possession, and whether the struck player was visibly affected (“shaken up”) by the impact. In 50% of cases (n=203), the head was struck by the upper extremity of an opposing player. Of these, 25% of cases (n=51) involved the shoulder and 45% (n=92) involved the hand. When compared to other upper limb contact sites, shoulder-to-head impacts generated 41% greater amax (39 g (SE 5) versus 28 (SE 2);p=0.006) and 29% greater ωmax (955 rad/s (SE 82) versus 743 (SE 32);p =0.004). In 13% of cases (n=52), the struck player had puck possession when receiving the head impact, and in 87% of cases, they neither had nor were seeking puck possession. Puck possession had no effect on amax (p=0.347) nor ωmax (p=0.119). Players were visibly shaken by the impact in 13% of cases (n=55), and these cases involved 31% greater amax (41 g (SE 4) versus 32 (SE 1);p=0.011) and 28% greater ωmax (989 rad/s (SE 69) versus 772 (SE 21);p =0.0004). Our findings suggest that hand-to-head impacts are more frequent but less severe than shoulder-to-head impacts; most head impacts occur without puck possession and are just as severe as those with possession; and that visible signs of players being shaken up associate with head impact severity.
Physiological models of velocity-duration data

Team-sports athletes often wear GPS devices, from which their velocity is calculated. These devices produce thousands of data points over the course of a practice/game. A major challenge in sports analytics is to develop methods for synthesizing such data ("big data") into models for predicting and optimizing performance. The long-term goal of this research is to develop and validate physiologically interpretable models of velocity-duration data from GPS in team-sport athletes, and compare them with empirical models and traditional fitness tests measures. While the relationship between the duration of movement and maximal power output (or velocity) has been successfully modeled in individual and endurance sports, it is yet to be modeled in team sports. To date, models used to describe GPS-based velocity-duration data do not allow for inference of physiological variables, such as aerobic/anaerobic fitness. However, the Critical Velocity model is comprised of these physiologically attributes, where critical velocity represents the maximum velocity that can be sustained by aerobic energy alone, and D' is the distance that can be covered at speeds that exceed critical velocity (i.e. anaerobic capacity). Thus, successful implementation of this model in team-sports would eliminate the need for dedicated testing sessions to assess fitness, and coaches would be able to optimize practice planning, monitor fatigue, and inform tactical planning. In this analysis, we compare the ability of three versions of the critical velocity model to quantify and predict anaerobic and aerobic fitness, versus other empirical models and traditional fitness tests.

Effects of cannabidiol on lipid membrane fluidity

Cannabidiol (CBD) is a non-psychoactive component of Cannabis sativa. CBD is relatively underrepresented in the scientific literature compared to its now-legalized and popular counterpart, trans-Δ⁹-tetrahydrocannabinol (THC). CBD interacts with a host of different cellular targets, apparently without specificity, including: GPCRs, TRP channels, K+ channels, Ca+ channels, and Na+ channels; however, its mechanism of action has yet to be discovered. An amphipathic molecule, CBD is similar in structure to cholesterol - a molecule that readily inserts into biological membranes. Due to CBD affecting membrane channel properties similar to the changes seen in more fluid membrane environments, we hypothesize...
that CBD inserts itself into cellular membranes, increase membrane fluidity, and thereby indirectly affect membrane protein properties. We will investigate the interaction between CBD and membranes using deuterium nuclear magnetic resonance (2H NMR) spectroscopy. Fluidity will first be measured in a control sample of POPC (a glycerophospholipid containing a glycerol backbone, two fatty acid chains, and a phosphocholine head group). Then, membrane fluidity will be measured in a POPC/CBD mixture. We predict that the 2H NMR spectra width will decrease in the presence of CBD, compared to the POPC control, indicating an CBD-induced increase in membrane fluidity. Our results will help us to further understand the interactions between CBD and the cells it affects and elucidate mechanism of action of CBD in pathophysiological conditions with altered membrane channel function such as Dravet syndrome or neuropathic pain. Further projects may include analysing 2H NMR spectra with cholesterol and membrane proteins incorporated into the synthetic membranes to reproduce a more physiological environment for CBD interactions, as well as developing dose-response curves for CBD within membranes. Co-localization fluorescence microscopy could also be done to localize where CBD inserts and determine whether it targets close to the membrane channels themselves.

25. SNEHA RALLI, Samantha Jones, Stephen Leach, Amy Williams, Joe Connors, Henry T. Lynch, Angela Brooks-Wilson

An exome-based strategy for hereditary cancer gene identification in a five-generation family with 28 early onset cases of lung, sarcoma, breast, adrenal, brain and lymphoid malignancies

We are studying an unusual family having 8 members with early onset of lymphoid cancers and 20 members with other early onset malignancies including lung (1), brain (8), breast (4), sarcoma (5) and adrenal (2). This spectrum of cancers is reminiscent of Li-Fraumeni syndrome, an autosomal dominant hereditary cancer syndrome caused by mutations in TP53. Our family pedigree is consistent with autosomal dominant inheritance of a single genetic factor that increases susceptibility to multiple early onset cancers. Mutation of TP53 exons 5-8 and 10 (mutated in Li-Fraumeni syndrome) were excluded by targeted sequencing. Our goal is to identify a hereditary cancer gene in this family. We hypothesize that a gene other than TP53, potentially a gene in the TP53 pathway, is involved. We have generated exome sequences of one family member who developed lymphoma at age of 14, and two obligate carriers (who are parents of family members who developed lung and breast cancer at age 32 and 35 respectively and lymphoma at age 24). Genetic variants identified in exome
data were filtered for variant quality using VQSR. We are using RefineIBD to
detect chromosomal segments that are identical-by-descent (IBD), as
we expect the locus harbouring the causative mutation to be IBD amongst
affected family members. Genotypes that are shared by all 3 exomes within
such IBD regions will be identified and prioritized. Prioritization involves
removing variants with minor allele frequency (MAF) < 0.01, and predicted
deleteriousness by at least four of six dbNSFP algorithms. MAF is applied
using ExAC, TOPMed and 1000 genomes databases. Variants that fail to
be annotated by these databases are retained. In an initial screen of one
chromosome, we identified a rare variant in NOTCH2NL. Analysis of the
entire exome is expected to produce a small number of variants of interest
for further prioritization and study.

26. SABRINA ABRAM, Jessica Selinger, J. Max Donelan

*Understanding how the nervous system defines the dimensionality of energy optimization in walking*

People prefer to move in ways that minimize metabolic energy use during
walking. Our lab has recently demonstrated that this preference arises not
just through evolution and development, but that people can continuously
optimize step frequency and step width to minimize energy. We tested for
energy optimization by manipulating the relationship between either step
frequency or step width and energetic cost to create a new cost landscape.
In this new cost landscape, people can minimize energy by simply adjusting
the relevant gait parameter. However, adjusting step width, for example,
may be more complex within the nervous system as it can coordinate
thousands of motor units to achieve a particular width. Our findings that
people can optimize energy within minutes suggest that the nervous
system may have efficient ways for managing the high-dimensionality of
walking. I hypothesize that the nervous system reduces the dimensionality
of energy optimization to be along the relevant gait dimensions. Our lab
has recently demonstrated that simple reinforcement learning models
can predict features of energy optimization in human walking. To design
experiments that test my hypothesis, I have developed this model to
include both a low- and high-dimensional representation of the new cost
landscape. In the nervous system’s energy optimization algorithms, a low-
dimensional representation may be if it reduces the dimensionality along
the gait dimensions, whereas a high-dimensional representation may be if
it considers all combinations of motor units. I simulated my experimental
protocol and found that only the low-dimensional representation was
influenced by changes in the dimensionality of the new cost landscape—
the rate of adaptation increased from 30 seconds to 10 minutes for one- and two-dimensional cost landscapes, respectively. For a high-dimensional representation, the rate of adaptation was 26 and 24 minutes for one- and two-dimensional cost landscapes, respectively. My next step is to test my hypothesis by determining people’s rate of adaptation in one- and two-dimensional new cost landscapes and comparing this to my model predictions.

27. AMANDA D. ZACHARUK, and Dawn C. Mackey

Characteristics of falls in long-term care: Differences between bedrooms and common areas

Background: Falls are the leading cause of injury-related death among older adults, making fall prevention a public health priority. Fall prevalence is especially high in long-term care (LTC). The characteristics of falls in LTC are not well understood, especially for falls that occur in private resident bedrooms. The purpose of this study was to investigate fall characteristics in LTC and examine how they differ based on location. Methods: Resident falls were monitored at New Vista Society Care Home in Burnaby from September 2013 through August 2017. New Vista staff completed an incident form within 24 hours of each resident fall. Trained research assistants reviewed incident forms to ascertain fall characteristics. Pearson Chi-square tests were used to compare differences in fall characteristics between bedrooms and common areas (e.g., dining rooms, hallways, lounges). Results: There were 4263 reported falls during follow-up. Most falls occurred in bedrooms (68%). Falls were more frequently unwitnessed in bedrooms than common areas (94% vs. 63%, p<0.001). Falls in bedrooms were more likely to be experienced by men than falls in common areas (35% vs. 31%, p=0.018). Falls in bedrooms were more likely to occur overnight compared to falls in common areas (27% vs. 7%, p<0.001). Cause of the fall was more often unknown in bedrooms (63% vs. 52%, p<0.001). The most commonly reported activities at the time of the fall were getting up/sitting down (26%) in bedroom falls compared to walking (36%) in common area falls (p<0.001). Conclusions: This study provides evidence of differences in fall circumstances based on fall location in LTC. Falls were more common in bedrooms than common areas; however, falls were frequently unwitnessed in bedrooms. Improved monitoring of private spaces is vital to understanding circumstances of falls in LTC. Interventions to prevent falls should focus on the bedroom.
28. SHIVANI RANA, Leanne Ramer, Bushra Khokhar, Doreen Rabi, Norman Campbell, Birinder K. Mangat

**Quality improvement strategies for blood pressure management in low and middle-income countries**

Background: Hypertension management control remains inadequate for patients in low- and middle-income countries. Purpose: The objective of this study was to evaluate the effectiveness of various forms of interventions to lower blood pressure in hypertension and/or diabetic patients in low- and middle-income countries. Data Sources: The Cochrane, Campbell, MEDLINE, and Joanna Briggs Institute databases were searched to select articles to be included in the study. Study Selections: Trails evaluating interventions that were targeting hypertension control and reporting pre and post blood pressure outcomes were included in the study. Data Extraction: Two reviewers assess 2000 articles to select a subset population that was in line with the inclusion criteria. The selected studies were classified into the following categories and data was extracted regarding: provider education, provider education, facilitated relay of clinical information, patient education, self-management, patient reminders, audit and feedback, team change and financial intervention. Data Synthesis: Statistical analysis was conducted on the extracted data for the intervention and control group to evaluate the effectiveness of the interventions. Conclusion: Data will be evaluated to assess which form of intervention is most effective in low- and middle-income countries to help lower blood pressure in hypertensive patients.

29. MISHAA A. KHAN, Tory Frizzell, Lukas A. Grajauskas, Sujoy G. Hajra, Caressa Liu, Irene Vavasour, Erin MacMillan, Xiaowei Song, Ryan C. N. D'Arcy

**Assessment of motor learning related neuroplasticity in white matter using myelin water imaging**

Motor training has been shown to cause structural and functional changes in the brain, in a phenomenon known as neuroplasticity. This is evidenced by studies that have used magnetic resonance imaging (MRI) sequences, such as diffusion tensor imaging (DTI) and functional MRI, to show anatomical and functional changes in cortical and subcortical structures caused by motor training, respectively. Though the majority of work has focused on gray matter, changes within the white matter have been reported, and it is speculated that changes in myelination may underly this. While DTI has shown structural changes in white matter tracts, little work has directly tested for myelin changes. To detect these changes in myelination, we are investigating myelin water imaging (MWI), an MRI
sequence that detects water between myelin sheath layers. MWI therefore allows for the quantification of myelination changes within specific tracts. We will be using the Philips 3T MRI (Ingenia CX) at the SFU ImageTech Lab to conduct our scans. In the experiment, participants were trained on a fine motor task over the course of a week and myelination changes were measured within the descending corticospinal tract. Using a repeated measures crossover design, all participants received baseline MRI scans together with a week of the motor learning with a follow-up scan and a matched control task with follow up scan (with the order of motor learning and control tasks switched for half the sample). Myelination changes were assessed using myelin water fraction to evaluate motor learning differences across whole brain white matter networks. The goal of the research is to better understand the fundamental mechanisms of plasticity in distributed neural networks and apply this knowledge to improve clinical rehabilitation application in motor function recovery following neurological disorders (e.g., acquired brain injury).

**30. RAYMOND SIDHU**, Ben Minaker, Leanne Ramer

*Heterotopic ossification in the interosseous membrane of the tibia and fibula: A case study and review of the literature*

Heterotopic ossification (HO) is characterized by unusual bone formation occurring in soft tissue structures. Here we review the literature describing the incidence, etiology, and the available evidence on treatment approaches for this rare condition. In addition, we report an unusual case of myositis ossificans circumspecta (MOC), a sub-category of HO, where new bone growth occurs post-trauma. A university-aged athlete presented with severe pain in the lower lateral third of the right leg with no history of severe traumatic injury. CT scan revealed a calcified mass in the interosseous membrane between the tibia and fibula. A conservative therapeutic approach of physiotherapy, shockwave therapy, and laser therapy was prescribed to alleviate the pain; we describe the effects of these treatments on symptoms and tumour mass documented by imaging.

**31. TSE NING CHEUNG**, Samrat Thouta, Thomas Claydon

*Restoration of ion channel function in neurological disease-causing Kv7.5 mutations by XE991*

Voltage-gated Kv7.5 potassium channels are expressed widely throughout the central and peripheral nervous systems and are thought to contribute to the M-current, which plays a crucial role in regulating neuronal excitability by preventing repetitive action potential firing during long-
lasting depolarizing inputs. Inhibition of the M-current leads to enhanced neuronal excitability associated with neurological disorders. We recently identified a de novo missense Kv7.5 mutation, P369R, associated with intellectual disability and epilepsy. This mutation causes a left-shift in the voltage dependence of activation, acceleration of activation kinetics, and slowing of the channel closure. These findings suggest that P369R is a gain-of-function mutation, which would be expected to increase suppression of excitability, thus leading to pathophysiology. To further investigate the physiological consequences of this mutation, the P369R mutant was heterologously expressed in Xenopus oocytes, and membrane currents were recorded using the two-electrode voltage clamp technique.

A standard M-current protocol was used to examine the phenotype of this mutant in a more physiological context. The data showed that unlike wild-type Kv7.5 channels, P369R channels remain open at physiological resting membrane potentials. In addition, the mutant channels pass a larger persistent current during periods of excitation. XE991 is a selective blocker of Kv7 channels, known to modify both activation and deactivation gating. We hypothesized that XE991 may restore function in gain-of-function mutant P369R channels. We tested the effect of XE991 on P369R at two different concentrations (100 nM and 300 nM). XE991 resulted in reduced currents at resting membrane potential, upon initial excitation, and upon sustained depolarization input. XE991 also right-shifted the voltage-dependence of activation in P369R mutant channels, with no effect on activation threshold of wild-type channels. These data show the ability of XE991 to restore function in gain-of-function Kv7.5 mutations, thus providing a potential therapeutic target for the treatment of neuronal excitability disorders.

32. **DAVE BORREL**, Brett H. Shaw, Kimiya Sabbaghan, Colton Kum, Yijian Yang, Stephen N. Robinovitch, Victoria E. Claydon

*Relationships between orthostatic hypotension, frailty, falling and mortality in elderly care home residents*

Orthostatic hypotension (OH; profound falls in blood pressure when upright) is a common deficit that increases in incidence with age, and may be associated with falling risk. Deficit accumulation results in frailty, regarded as enhanced vulnerability to adverse outcomes. We aimed to evaluate the relationship between OH, frailty, falling and mortality in elderly care home residents. From the Minimum Data Set (MDS) document, a frailty index (FI-MDS) was generated ranging from 0 (no deficits) to 1.0 (58 deficits). OH was evaluated from beat-to-beat blood pressure and heart rate (finger plethysmography) collected during a 15-minute supine-seated orthostatic
stress test. Retrospective and prospective falling rates (falls/year) were extracted from facility falls incident reports. All-cause 3-year mortality was determined. Data are reported as mean±standard error. Data were obtained from 116 older adults (aged 84.2±0.9 years; 44% males) living in two long term care facilities. The mean FI-MDS was 0.36±0.01; FI-MDS was correlated with age (r=0.277; p=0.003). Those who were frail (FI≥0.27) had larger Initial (-17.8±4.2 vs -6.1±3.3 mmHg, p=0.03) and Consensus (-22.7±4.3 vs -11.5±3.3mmHg, p=0.04) orthostatic reductions in systolic arterial pressure. Frail individuals had higher prospective and retrospective falling rates and higher 3-year mortality. Receiver operating characteristic curves evaluated the ability of FI-MDS alone to predict prospective falls (sensitivity 72%, specificity 36%), Consensus OH (sensitivity 68%, specificity 60%) and 3-year mortality (sensitivity 77%, specificity 49%). Kaplan Meier survival analysis show significantly higher 3-year mortality in those who were frail compared to the non-frail (p=0.005). Frailty can be captured using a frailty index based on MDS data in elderly individuals living in long term care, and is related to susceptibility to orthostatic hypotension, falling risk and 3-year mortality. Use of the MDS to generate a frailty index may represent a simple and convenient risk assessment tool for older adults living in long term care.

33. KYLE DUMONT, and David C. Clarke

**Signaling dynamics underlying skeletal muscle cell adaptations to exercise**

Skeletal muscle comprises ~40% of total body mass and is therefore a primary contributor to whole-body metabolic health. It is known that exercise induces many stressors on muscle cells including increased energy demand, mechanical forces, oxygen and temperature changes, among many others. The adaptations to these stressors enhance fitness and health. A classic unresolved question in the field of exercise physiology is how skeletal muscle cells sense and integrate these stressors to coordinate fitness-promoting adaptations. Several biochemical signaling pathways such as AMPK, VEGF and PGC-1α, translate the stressors into chemical signals, which in turn cause changes to gene expression. These pathways are interconnected as part of a broader network; however, the structure and dynamic behaviours of this network are poorly understood. The goal of my research is to understand the dynamics between signaling pathways caused by exercise. Accordingly, I aim to develop an in vitro model of exercise in which I will treat cultured skeletal muscle cells with stressors both alone and in combination. I will then apply antibody-
based proteomics to study the responses of the signaling pathways to the stressor combinations. At various time points, I will measure levels of key post-translationally modified intramuscular signaling proteins (e.g., AMP-activated protein kinase, hypoxia-inducible-factor-1α, heat shock protein 72) using antibody-based proteomic techniques. The signaling network and its dynamics caused by exercise are poorly understood. Successful implementation of the proposed project will further our understanding of how fitness-promoting adaptations result from signaling network dynamics.

34. PAWEL KUDZIA, Stephen N. Robinovitch, J. Max Donelan

**Characterizing the force and position control performance of the human leg**

 Humans are remarkably agile. We can move at fast speeds while rapidly executing motor control strategies that redirect body motion and reposition our limbs. The central goal of our research is to understand the neuromechanical mechanisms that enable such agility, as well as the factors that limit it. When navigating the environment, our legs interact with the ground by producing external forces that either maintain or change our state of motion. For example, by altering the magnitude and the point of application at which our legs apply external force, we can selectively shift our state of motion from walking, to jumping and or to sprinting. In previous work, we proposed a model of the legs performance limits during maximum height vertical jumping. Here, we extend on that work by studying the legs force and position control capabilities in producing external force. To study this, we have developed a purpose-built apparatus where subjects use their legs to push against a force platform while presented with real-time feedback on the magnitude and the point of application of the external force that they are applying. To test the legs control capabilities, we rapidly present subjects with pre-defined force and center of pressure traces and ask them to match these, as best as possible, to what they are doing in real-time. We compute the error between the pre-defined and measured signals, how rapidly forces and positions can be adjusted, and the variability of the applied force and position signals to describe the control performance of the leg. Subsequently, we will use this data to further develop and characterize our mathematical model. Quantitative agreement between our model and empirical data will not only identify potential limits to agility but also help with the design principles for augmentative exoskeletons that may improve agility.
Preterm birth is associated with a higher prevalence of cognitive, behavioural and motor difficulties even in the absence of major brain injury. It has been reported that children born very preterm (≤ 32 weeks) present abnormal thalamic volume, indicating alterations in thalamocortical system. The thalamus is a sensory and cortical relay that regulates cortical activity in different frequency bands, and is critical for cognitive functions and their alterations in numerous neurological conditions. In the present study, we hypothesised that decreased thalamic volume in children born very preterm is associated with altered resting spectral power. Resting state magnetoencephalography data were recorded from participants at the age of 7 years from 3 groups: extremely low gestational age (ELGA, 24-28 weeks, N = 24), very low gestational age (VLGA, 28-32 weeks, N = 34), and full-term (N = 37). From 76 cortical areas the relative power was calculated. Thalamic volume was obtained from a subsample of 14, 24, and 13 participants due to limited availability of individual MRI scans. Statistical analysis was performed to assess the association between cortical power and thalamic volume. Significant differences were found in spectral power between the three groups, with increased relative power at delta and theta frequencies in the ELGA, but decreased power at alpha and beta frequencies, compared to VLGA and fullterm groups. Thalamic volume was positively correlated with gestational age and with lower power in delta and theta and with higher power in the alpha and beta frequencies. This study provides evidence that thalamic volume is associated with altered resting state activity. Increased delta and theta activity together with reduced relative alpha and beta activity is consistent with slowing of spontaneous cortical oscillations, and suggests that the disruption of thalamic development in the very preterm affects the thalamic modulation of cortical power at school age.
Does autonomic dysreflexia increase the incidence of arrhythmia in individuals with SCI?

Approximately 2.5 million people are living with the devastating consequences of spinal cord injury (SCI). Although SCI is traditionally associated with motor deficits, cardiovascular autonomic function may also be affected by damage to the spinal cord, with cardiovascular diseases being the leading causes of morbidity and mortality in those living with SCI. Autonomic dysreflexia (AD) is a common condition seen in individuals with SCI above T6, and is characterized by profound acute hypertensive episodes that may give rise to cardiac arrhythmias. AD is initiated by peripheral afferent stimulation below the SCI, with visceral stimuli such as bladder and bowel distension being particularly potent triggers for AD. We aimed to: (i) document whether the incidence of arrhythmia increases during visceral stimulation (bowel care) in individuals with SCI; (ii) examine whether use of lidocaine lubricant, which is thought to decrease the afferent stimulus and therefore the magnitude of AD, ameliorates arrhythmia during bowel care. We measured beat-to-beat electrocardiograms (ECG) and blood pressure during at-home bowel care in 13 individuals (age 44±12 years) with high-level SCI (C4-T4) on two days, in which they used either placebo or lidocaine lubricant, in a randomised, double-blind fashion. Arrhythmia symptoms were obtained by self-report. ECG were visually inspected and mean heart rate (HR), incidence of sinus bradycardia (<60 bpm) or tachycardia (>100 bpm), as well as numbers of atrial, ventricular, or junctional ectopics (alone or in runs) calculated during three phases: baseline, after insertion of placebo or lidocaine lubrication, and throughout the bowel routine. The results of this study will provide a clearer picture of the incidence of cardiac arrhythmia during AD and the potential impact of lidocaine use during bowel care in individuals living with SCI.

Mathematical modeling of mammalian target of rapamycin following leucine ingestion

Introduction: The mammalian target of rapamycin complex 1 (mTORC1) is a regulatory protein for several cell processes and is critical in the control of muscle protein synthesis and hence muscle size. Its activity is primarily regulated by nutrition (i.e., protein) and growth factors (i.e., insulin); however, how the whole-body dynamics of these factors translate into
protein translational signaling in skeletal muscle cells is poorly understood. Purpose: The purpose of this study was to develop and analyze a simple mathematical model of the signaling controlling protein translation in human skeletal muscle following leucine ingestion. Methods: The model was expressed as a system of ordinary differential equations (ODEs) incorporating the signaling proteins involved in the control of protein translation (e.g., IR/PI3K/AKT/mTOR axis). Intracellular biochemical reactions were represented by mass-action kinetics. We constructed the model by modifying amalgamated published models of mTOR signalling [Pezze et al. (2012) Sci Signal] and skeletal-muscle leucine kinetics [Tessari et al. (1995) Am J Physiol]. The Pezze model was specific to HeLa cells, so we calibrated the kinetic parameters using signaling data from human skeletal muscle following leucine ingestion. The ODEs were solved using the ODE23s solver in MATLAB. Results: The model outputs qualitatively agreed with published time-course data for plasma leucine, plasma insulin, and phosphorylation of AktS473, mTORC1S2448, and p70S6KT389 following the ingestion of a single leucine bolus or multiple, pulsatile leucine doses. Parameter sensitivity analysis determined that mTORC1 activity was most sensitive to total mTORC1 concentration and highly sensitive to the rate of leucine transamination to alpha-ketoisocaproate. Conclusion: Our model represents a working quantitative hypothesis of the dynamics of protein translational control in skeletal muscle by nutritional and hormonal factors.

38. KARAM ELABD, Vicki Komisar, Brigitte M. Potvin, Stephen N. Robinovitch

Examining how the dynamics of backward falls affect head impact severity with a falling dummy

Introduction: Traumatic brain injury (TBI) is a frequent and debilitating consequence of falls in older adults. From videos of real-life falls in long-term care, we found that backward falls caused most head impacts. Further, leg raise after pelvis impact reduced head impact risk. In this study, we developed a falling dummy to recreate backward falls, and examine how torso shape and lower limb dynamics affect head impact severity. Methods: The dummy includes a 50th percentile Hybrid III head-and neckform secured to torso and lower limb segments that matched the anthropometry of a typical 83-year-old woman (1.6m height, 55.8kg body mass). The headform included a 3-2-2-2 linear accelerometer array for quantifying peak resultant linear and angular accelerations. We considered a curved torso versus flat torso, and freely rotating versus fixed hips with metal and plywood floorings. The dummy was dropped from a seated position via electro-magnet tether, with an initial head height of 73cm. We collected three trials per configuration. Effect of torso shape,
hip stiffness and flooring on head impact severity were quantified via 3-way ANOVAs and post hoc Tukey HSD tests. Results and Discussion: Peak head accelerations were higher with rotating hips than with fixed hips (p<.001). Mean acceleration values for the rotating hip conditions consistently exceeded concussion thresholds of 100g and 5krad/s/s. Torso shape did not affect linear acceleration (p=0.246), while angular acceleration was lower with the curved torso than with the flat torso (p<.001). Hip stiffness and torso shape interacted significantly for both linear (p=0.046) and angular (p<0.001) accelerations, reflecting lower impact severity for the curved torso versus the flat torso with rotating hips. Metal flooring led to higher linear acceleration (p<.001) than plywood. Flooring did not affect angular acceleration (p=0.509).

39. BISMAN DHALIWAL, Amy Williams, Bader Al-Zeer, Mike Park, Monique Sekhon, Olivia Aguiar, Angela Brooks-Wilson

The role of resiliency in healthy aging

The Healthy Aging Study examines ‘Super-Seniors’, individuals 85 or older who have had no prior diagnosis of cancer, cardiovascular disease, diabetes, dementia, or pulmonary disease, to study factors associated with healthy aging. Data collected include a medical and family history questionnaire, with physiological assessments, blood samples and geriatric tests. A Phase two recruitment initiated in 2015 added a resiliency questionnaire, the Wagnild and Young 1987 Resiliency Scale. Resiliency (RS) is the ability to maintain baseline physiological functioning despite the biological stressors that constitute aging. It is influenced by genetic and psychosocial factors such as self-efficacy and intrapersonal relationships. A decline in physiological resiliency is inherent to aging and may underlie the onset of frailty, chronic diseases and multimorbidity. This decline is due to increased cellular damage and impaired interaction between physiological regulatory mechanisms that further impairs restoration of homeostasis. Physiological resiliency may be impacted by surgical stress, metabolic syndrome, immobility and obesity. Exercise is a proposed mechanism for maintaining resiliency, as it may enhance tissue and cellular resistance, bone density and also enables the organism’s physiological systems to respond to acute stressors with higher vigour and shorter duration. Based on the literature, we hypothesize that Super-Seniors have higher RS scores than others their age. I will conduct interviews of seniors aged 85 and older who have multiple chronic conditions and compare their RS scores to those of the Super-Seniors. I will also compare their scores to literature reports of individuals of various ages and circumstances, for whom RS was measured using the same tool. I will also test for association between the
RS scores of Super-Seniors with those of two geriatric rests: The Timed Up and Go Test and the Mini Mental State Exam. Studying Super-Seniors may help discern strategies to promote resilience and help to avoid diseases.

40. MATIAS RASKI, Charles Krieger, Nicholas Harden, Simon Wang

*Adducin at the mouse neuromuscular junction: A new lead in the pathophysiology of amyotrophic lateral sclerosis*

Impaired nerve-muscle connections are an early and possibly initiating event in the development of the neurodegenerative disease amyotrophic lateral sclerosis (ALS). Loss of adhesion between the neuron and muscle fiber at the neuromuscular junction (NMJ) is thus implicated as a precursor to the eventual denervation and progressive weakness that characterize ALS. Previous work suggests that dysregulation of adducin, a plasma membrane-associated protein that stabilizes cytoskeletal elements at both inter-neuronal synapses and NMJs, plays a role in the loss of these contacts. When phosphorylated, adducin dissociates from and destabilizes the cytoskeleton, thus serving as a ‘switch’ capable of regulating plasticity. Phospho-adducin is dramatically elevated in ALS patients’ spinal cords as compared to controls, it is elevated in the spinal cords of the mSOD mouse model of ALS as compared to wildtype controls, and knockdown of adducin increases longevity and neuronal survival in both in vivo and in vitro models of neurodegeneration. Our previous work also shows that the adducin homolog, Hts, organizes adhesion molecules at the NMJ in Drosophila melanogaster. Here, we present new findings demonstrating adducin’s presence presynaptically, postsynaptically, and in glial cells at the mouse neuromuscular junction. Preliminary findings show hyperphosphorylation of adducin at the NMJs of mSOD mice as compared to wildtype controls, mirroring previous findings in the spinal cord. Given adducin’s situation as a regulator of synaptic stability, its demonstrated role in mediating neurodegeneration in model systems, and the primacy of impaired nerve-muscle connections in ALS, these findings raise the possibility that adducin dysregulation at the NMJ plays a causal or mediating role in ALS denervation and illness.

41. CARLY JOHNSTON, Ben Minaker, Leanne Ramer

*Confidence-weighted multiple choice questions for formative and summative assessment*

Standard multiple choice (MC) testing is inherently limited by a lack of insight into student learning: a correct guess is indistinguishable from a
correct answer determined by reason or understanding, and a silly mistake (e.g., reading a question incorrectly) is indistinguishable from a lack of knowledge or understanding. Based on student feedback in BPK 426, we have developed a novel (to our knowledge) approach to confidence-weighted (CW) testing. Our aim is to identify if this novel format can provide more nuanced feedback for instructors and students of student performance, while maintaining student grades. We envision this version of CW multiple choice testing providing feedback that divides a students’ response into four categories – informed, misinformed, uninformed, or guess - for each question/topic. This is based on their correctness and confidence indicated (high confidence (75%-100%); low confidence (0%-75%)). University students (n=59) in Functional Anatomy (BPK 326) were asked to fill out both formats simultaneously during their unit tests. Students will be awarded a portion of the potential 2 points according to their level of confidence and correctness (ie a 75% confident correct response will yield a score of 1.5 out of 2). We hypothesize that (i) CWMC performance will have a greater correlation than Standard MC performance when correlated to written scores; (ii) CWMC will have a smaller mean difference than Standard MC when each are compared to written scores. These analyses will provide a greater insight into student performance and the effectiveness of CWMC as an assessment tool. CWMC potentially can improve course design and studying strategies for instructors and students, respectively.

42. NATALIIA KOZHEMIAKO, Adonay Nunes, Vasily A. Vakorin, Cecil M. Y. Chau, Alexander Moiseev, Urs Ribary, Ruth E. Grunau, Sam M. Doesburg

Sex differences in brain connectivity and male vulnerability in very preterm children

Background: Accumulating evidence indicates better cognitive and behavioural outcomes for females born very prematurely (≤ 32 weeks gestation) compared to males, but the neurophysiology underlying this apparent resiliency of the female brain remains poorly understood. It has been shown that atypical interregional brain connectivity may underlie the relationship between adverse neonatal experience and long-term outcome in preterm children. Here we test the hypothesis that very preterm males express more pronounced connectivity alterations as a reflection of higher male vulnerability. Methods: Resting state magnetoencephalography (MEG) recordings, neonatal and psychometric data were collected from 100 participants at the age of 8 years: very preterm males (n=27), very preterm females (n=34), full-term males (n=15) and full-term females (n=24). Neuromagnetic source dynamics were reconstructed at 76 cortical brain regions. Functional connectivity estimated as interregional phase-
synchronization was quantified at frequencies between 4 and 50Hz. We also quantified deviations in functional connectivity in very preterm males and females with respect to averaged full-term connectivity, separately for each sex. We performed a series of multivariate analyses to test for differences across experimental groups as well as to explore correlations between deviations in functional connectivity and psychometric and neonatal scores for preterm cohorts. Results: Very preterm males expressed significantly higher absolute deviation from average connectivity of same-sex full-term group, compared to very preterm females. In the connectivity comparison between very preterm and full-term groups separately for males and females, significant group differences were observed for males, but not females. Sex differences in connectivity were observed in very preterm children but not in full-term groups. Conclusions: Our findings indicate that very preterm males having stronger alterations in resting neurophysiological network communication than females. Such uneven brain communication disruption provides first evidence of neurophysiological bases of male vulnerability in long-term behavioural and cognitive outcome.

43. JESSICA LEAVER, and Leanne Ramer

The gut microbiome and Alzheimer’s disease

The gut-brain axis has become a widely-appreciated physiological phenomenon, with data rapidly accumulating implicating the gut microbiome in almost every aspect of brain health and disease. The role of the intestinal microbiome in Alzheimer’s disease (AD) has recently emerged as a hot topic, with recent animal data suggesting that there is a role for gut microbiota in modulating host cognition and AD-related pathogenesis. Intriguingly, bacteria in the gut produce large amounts of amyloid. Here, we review the available date on the gut microbiome and AD, with a focus on putative mechanisms linking the bacteria populating the digestive tract to onset and progression of cognitive symptoms of AD.

44. BADER AL-ZEER, and Glen F. Tibbits

Zebrafish model in cardiac physiology: Investigating sarcoplasmic reticulum calcium role in excitation-contraction coupling using phospholamban knockout

Zebrafish (Danio rerio) is a popular model used in comparative cardiac development and function research. This is due to its ease of accessibility, small size, fast growth rate and large number of offspring. Furthermore,
the zebrafish and human share similar action potential (AP) morphologies and operate at similar heart rates indicating potential electrophysiological similarities. Ion channel expression and Ca\textsuperscript{2+} handling are two intertwined differences between zebrafish and human cardiac physiology. Overall, Ca\textsuperscript{2+} handling differs between the two as extracellular Ca\textsuperscript{2+} plays the main role in the zebrafish cardiomyocyte as it enters using L-type Ca\textsuperscript{2+} channel, T-type Ca\textsuperscript{2+} channel, and the sodium-Ca\textsuperscript{2+} exchanger, while most of the Ca\textsuperscript{2+} that is involved in the human myocyte contraction comes from the sarcoplasmic reticulum (SR). One way to study SR Ca\textsuperscript{2+} in ZF is to investigate the role of phospholamban (PLN), which inhibits the sarco/ endoplasmic reticulum Ca\textsuperscript{2+} pump (SERCA) and, therefore, not allowing SR Ca\textsuperscript{2+} loading. This inhibition is alleviated once PLN is phosphorylated at the Ser(16) residue, or Thr(17) residue by activated protein kinase A or CaMKII, respectively. ZF hearts express PLN, and have the ability to release Ca\textsuperscript{2+} from the SR in an unclear mechanism. To test the role of PLN, we will investigate Ca\textsuperscript{2+} handling in phospholamban knockout ZF (PLN-KO ZF) and compare their beta adrenergic agonist responses to wild type ZF. Our hypothesis is that PLN-KO will produce a significant effect in the response to catecholamines. Optical mapping will be utilized to study different elements of cardiac electrophysiology like conduction velocity, transmembrane action potential, and the interplay between Vm and Ca\textsuperscript{2+} transients simultaneously in the heart. Variable rate stimulation will also be done to investigate any potential rate-dependent effect in PLN-KO. Recordings will also be done at 18°C, 23°C and 28°C to unmask any potential temperature-dependent effect in the PLN-KO.

45. ZHAOKAI PANG, Yu Patrick Shi, Marvin Gunawan, Eric Lin, Sanam Shafaattalab, Shoab Faizi, Kaveh Rayani, Glen Tibbits, Thomas Claydon

Demonstration of Torsade de Pointes (TdP) arrhythmia risk in a whole hearts exposed to acute external acidosis

Ischemic heart disease is the leading cause of death worldwide and is associated with heart failure, myocardial infarction, and arrhythmias including Torsades de Pointes (TdP), a rare but lethal polymorphic ventricular tachycardia. One consequence of myocardial ischemia is extracellular acidosis, which we have previously shown inhibits cardiac voltage-gated Kv11.1 potassium channels encoded by the human ether-a-go-go related gene (hERG). The hERG channel passes current critical in the repolarization phase of the cardiac action potential and its loss of function has been shown to be associated with increased TdP risk. However, the associated TdP risk in acute acidosis remains unknown. Here, we measured the electrical restitution curve (ERC), which describes
how action potential duration (APD) adapts as a function of the diastolic interval, as a useful surrogate parameter in evaluating TdP risk. We studied the effect of acute extracellular acidosis (pH 6.5 for 1 min) on the ERC in zebrafish whole hearts, since this species models human cardiac electrophysiology remarkably well. Acute acidosis shifted the ERC upwards (maximum APD increased from 134 ± 7 ms in pH 7.4 to 154 ± 7 ms in pH 6.5 (n=6, p<0.01, paired t-test)) and reduced the maximal slope of the ERC from 0.78 ± 0.13 in pH 7.4 to 0.50 ± 0.10 in pH 6.5 (n=6, p<0.01, paired t-test). Both indicate reduced ability to adapt to rate changes. In addition, acute acidosis reduced the effective refractory period from 59 ± 7 ms in pH 7.4 to 46 ± 4 ms in pH 6.5 (n=6, p<0.01, paired t-test) indicating increased cardiac excitability. Taken together, these data demonstrate that acute external acidosis increases TdP risk in a whole heart translatable model. Furthermore, the protocols established in the zebrafish system can be used to assess the TdP liability of novel pharmacological agents, mutations, and pathophysiological states.

47. NATALIE D. HEENEY, Brooke C. D. Hockin, Victoria E. Claydon

Are Quantab® chloride test sticks accurate in determining urine sodium concentration?

Syncope diagnosis is challenging and often requires numerous tests and visits to multiple physicians before a diagnosis can be confirmed. One aspect of this diagnosis includes measuring urinary sodium, as individuals with syncope tend to have low sodium levels, and benefit from increases in dietary sodium intake; however, urine sodium measurements are often difficult and inconvenient, particularly in children, as they are completed through a 24-hour urine collection. Use of a spot urine sample has been investigated as an alternative to 24-hour urine collections, but the accuracy of a single spot sample is poor. The gold standard for urine sodium analysis is flame photometry, which may not always be accessible. It is unknown whether at-home test strips provide acceptable accuracy for determination of urine sodium compared to flame photometry. Since sodium and chloride are present in equal concentrations in urine, chloride test strips may provide a suitable proxy for urine sodium concentration. We aim to determine if: (i) chloride test strips provide a reliable measure of urinary sodium compared to flame photometry; (ii) multiple spot samples provide an accurate estimate of 24-hour urine sodium. We recruited 10 participants (5 males) aged 23.6±1.5 (range 19-35) years to complete five consecutive morning urine spot samples, with a 24-hour urine sample on the third day. No significant difference was found between flame photometry (107±14mmol/day) and chloride test strips (104±14mmol/day, p=0.513) for 24-hour measurements. Bland-Altman plots found a bias for these two
measurements of -3.2±14.9 mmol/day. Bland-Altman plots were used to determine the accuracy of the five-spot sample mean compared to the 24-hour urine sample (0.20±36.4 mmol)/day. Chloride test strips provide a simple alternative to flame photometry for assessment of urinary sodium, but some caution should be applied when determining a 24-hour urine sodium estimate from multiple spot samples. Chloride sticks provide a comfortable and feasible opportunity for patients with syncope to monitor dietary sodium supplementation for the treatment of syncope.

49. VERA-ELLEN LUCCI, Rhonda Willms, Maureen S. McGrath, Chris McBride, Heather L. Gainforth, Victoria E. Claydon

Barriers and facilitators to changing bowel care routines in individuals with chronic spinal cord injury

Changes to autonomic processes such as bladder, bowel, and sexual function have been prioritised over improvements to movement and sensation in the spinal cord injury (SCI) community. Individuals with SCI rely on bowel care programs (lifestyle management) and routines (methods employed) to empty their bowels. Bowel care is associated with high levels of dissatisfaction and markedly decreased quality of life. Bowel care is also a potent trigger for cardiovascular complications in high-level SCI. Despite dissatisfaction, 71% of individuals report using the same bowel care routine for at least the past five years. This suggests a disconnect between dissatisfaction with bowel care and ability to make changes to bowel care routines. Why is it that many individuals with SCI don’t change their bowel care even though they are unhappy with it? The aim of this study is to investigate the barriers and facilitators to making change to a bowel care routine. This study will use the Theoretical Domains Framework (TDF) to understand these barriers and facilitators. Semi-structured interviews will be conducted with individuals living with SCI (target n=13; collected to date n=6; age=55.7±11.4 years) and transcribed verbatim. Barriers and facilitators will be extracted using a two-stage deductive and inductive analytical approach, whereby barriers and facilitators will be deductively coded using TDF domains and inductively analyzed for themes within each domain. Relevant domains will then be linked to a comprehensive, evidence-based framework for developing knowledge translation interventions. Our findings will inform current bowel care guidelines, as well as assist the systematic development of future interventions to target factors shown to be barriers to making change to bowel care. Future directions will include conducting similar interviews with SCI clinicians and caregivers to gain a more holistic view of the challenges posed by bowel care after SCI.
CONTACT BPK

Graduate Program Chair
Dr. Will Cupples
Phone: 778-782-9084
Email: william_cuples@sfu.ca

Graduate Program Assistant
Phone: 778-782-4061
Email: bpk_programs@sfu.ca

Undergraduate Program Assistant
Nicole Yoo
Phone: 778-782-3573
Email: bpkasst@sfu.ca

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