ABSTRACTS

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Abstracts

Plenary Lectures

MedSci Plenary Lecture 1

Lung diseases: Should we be thinking about sex?

Prakash, Y.S.

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The physiological and pathophysiological impact of inherent sex differences in lung anatomy vs. the modulating effect of sex steroids (estrogens, progesterone and testosterone) are being increasingly recognized. While the importance of sex steroids in cardiovascular, musculoskeletal, and neuronal function is better established, epidemiological, clinical and bench research data highlight sex differences in frequency, morbidity and mortality of pulmonary diseases such as asthma, COPD, pulmonary fibrosis, cancer, and pulmonary hypertension. Accordingly, it becomes important to ask: 1) What are some relevant, inherent sex differences in lung anatomy and physiology that could contribute to lung diseases in males vs. females? 2) How do sex steroids affect different components of the lung under normal circumstances? 3) How does sex steroid signaling change in or contribute to lung disease. The fundamental, and perhaps overarching question becomes: Are sex steroids detrimental or beneficial in the context of lung disease? As our understanding of this topic improves, it is important to consider whether such information can be used to develop new therapeutic strategies to target lung diseases, in both sexes or in a sex-specific manner. In this talk, I focus on these important, and emerging issues, highlighting basics of sex steroid signaling, the current state of knowledge regarding how they influence structure and function of specific lung components across the life span and how they could play a role in some important lung diseases. I then raise the potential for sex steroids as useful biomarkers and therapeutic targets in lung diseases as a basis for future translational research in the area of gender and individualized medicine.

MedSci Plenary Lecture 2

Deciphering brain connectivity and function with rabies virus and light

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To understand the mechanisms by which neural circuits process information, it is necessary to resolve connectivity with high resolution, to correlate connectivity with function, and to manipulate the activity of defined circuit components. Recent advances in the development of molecular, genetic and viral based tools are now making this possible at the level of resolution of specific cell types and even single neurons. I will describe recent progress in my lab, developing and using rabies virus-based systems for tracing neural circuits and linking them to function. Because rabies virus spreads trans-synaptically, exclusively in the retrograde direction, and only between connected neurons, it is a very powerful tool for studies of neural circuits. Our new tracing systems are based on rabies viruses whose glycoprotein gene has been deleted, making it possible to both control the trans-synaptic spread of the virus and to also select specific neurons or neuron types for primary infection. These viruses also express transgenes, such as fluorescent proteins, at very high levels allowing clear visualization of

detailed neuronal morphology. Building on these viruses we have developed protocols and reagents that make it possible to label neurons in vivo that are directly presynaptic to a single targeted neuron or to label the direct inputs to a population of neurons of genetically defined type from a targeted brain region. Because the rabies virus leaves cells viable for weeks, it is possible to combine rabies labelling of connectionally-defined neuronal populations with studies monitoring or manipulating their activity. This is facilitated by the production of rabies viruses that express transgenes such as genetically expressed activity indicators or channelrhodopsins. I will present data illustrating how genetic approaches for restricting gene expression to specific cell types in the mouse visual cortex can be combined with optical methods for monitoring and controlling activity. This allows us to identify the connectivity of specific cell types using rabies tracing, and then relate connectional and functional differences to understand the unique contributions of cell types to visual function.

Symposia

Symposium 1A: Arcuate Nucleus Regulation of Neuroendocrine Systems

S1A.1

The integrated arcuate nucleus - Regulation of growth hormone release

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The production and release of growth hormone (GH) is regulated by numerous feedback mechanisms, converging at the level of the hypothalamus and anterior pituitary gland. Within this network, stimulatory Growth Hormone Releasing Hormone (GHRH)- and inhibitory somatostatin-expressing neurons are thought to predominantly modulate the characteristic patterned release of GH. This pattern of GH release (referred to as pulsatile GH release) is conserved across all species characterised to date. Modulation of GH release via these mechanisms ensures that the release of GH closely matches physiological requirements that are central to optimal growth, metabolic and reproductive needs.

While mechanisms that control GH patterning are seemingly well defined, our understanding of the integration of mechanisms that control of GH release and those that regulate appetite and reproduction are poorly understood. Using the mouse as a model, we are currently assessing the integrative role of neuronal and peripheral regulators of food-intake and reproductive function in modulating the patterned release of GH. I will highlight key considerations that form the premise for an extended view of the GH axis. I will highlight key interactions between orexigenic Neuropeptide-Y (NPY) expressing neurons and hypothalamic neurons that are central in the control of GH release. While emphasizing the fundamental role of NPY-expressing neurons in regulating GH release relative to meal-provision, I will discuss further physiological adaptations that may override this interaction. It is thought that selective modulation of these mechanisms ensure that the physiological needs of GH are met, even in the absence of optimal nutritional supply. Observations demonstrate a high level of complexity and plasticity within the GH axis, providing new insights to help understand intricacies associated with the patterning of GH release.

S1A.2

The role of arcuate kisspeptin neurons in reproduction and metabolism

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Kisspeptin is the endogenous product of the Kiss1 gene, which is vital for the neuroendocrine regulation of gonadotropin-releasing hormone (GnRH) secretion. Kisspeptin neurons are now recognized as a central pathway responsible for conveying key homeostatic information to GnRH neurons. This pathway has proven to be important for the well-established link between energy balance and reproductive function. Thus, in states of severely altered energy balance (either negative or positive) fertility is compromised, as is Kiss1 expression in the arcuate nucleus. A number of metabolic modulators have been proposed as regulators of kisspeptin neurons including leptin, ghrelin, pro-opiomelanocortin (POMC) and neuropeptide Y (NPY). Whether these regulate kisspeptin neurons directly or indirectly will be discussed. Moreover, whether the stimulatory role of leptin on reproduction is mediated by kisspeptin will be questioned. Furthermore, in addition to being expressed in GnRH neurons, the kisspeptin receptor (Kiss1r) is also expressed in other areas of the brain, as well as in the periphery, suggesting kisspeptin may have additional functions outside of governing reproductive status. Interestingly, arcuate kisspeptin neurons are anatomically linked to, and can directly excite, anorexigenic POMC neurons and indirectly inhibit orexigenic NPY neurons. Thus, kisspeptin may have a role in energy balance, though this possibility has not been closely examined. Although previous data from young Kiss1r knockout (KO) and wild type (WT) mice found no genotype-driven differences in body weight, our observations indicated that Kiss1r KO females displayed later onset obesity. Thus, in addition to regulating reproduction, kisspeptin signaling may also be an important regulator of metabolism and body weight.

S1A.3

Generation of pulsatile luteinizing hormone secretion by selective optogenetic activation of arcuate kisspeptin neurons

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Normal reproductive functioning in mammals depends upon gonadotrophin-releasing hormone (GnRH) neurons generating a pulsatile pattern of gonadotrophin secretion. The neural mechanism underlying the episodic release of GnRH is not known however recent studies have suggested that the kisspeptin neurons located in the arcuate nucleus (ARN) may be involved. In the present study we targeted channelrhodopsin (ChR2) to the ARN kisspeptin population to test directly whether synchronous activation of these neurons would generate pulsatile luteinizing hormone (LH) secretion *in vivo*. Characterization studies showed that this strategy targeted ChR2 to 70 % of all ARN kisspeptin neurons and that these neurons were activated by 473 nm blue light with high fidelity up to 30 Hz. *In vivo*, the optogenetic activation of ARN kisspeptin neurons at 10 and 20 Hz for 5 min evoked high amplitude, pulse-like increments in LH secretion in anaesthetized male mice. The minimal effective activation time for generating an LH pulse was 2 min and could be used to generate repetitive LH pulses. In

diestrous female mice, only 20 Hz activation generated significant increments in LH secretion. In ovariectomized mice, 5, 10, and 20 Hz activation of ARN kisspeptin neurons were all found to evoke LH pulses. Part of the sex difference, but not the gonadal steroid dependence, resulted from differential pituitary sensitivity to GnRH. Experiments in kisspeptin receptor-null mice, showed that kisspeptin was the critical neuropeptide underlying the ability of ARN kisspeptin neurons to generate LH pulses. Together these data demonstrate that synchronized activation of the ARN kisspeptin neuron population is sufficient to generate pulses of LH.

Supported by a grant from the RSNZ Marsden Fund

S1A.4

Arcuate nucleus GABA neurons and the regulation of fertility

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Successful fertility is dependent upon a complex network of neurons in the brain that ultimately regulate the gonadotrophin-releasing hormone (GnRH) neurons. GnRH neurons sit at the top of the hypothalamo-pituitary gonadal axis and direct downstream pituitary and gonadal function. Circulating gonadal steroid hormone levels, and a variety of other cues about the environment, must be appropriately conveyed to GnRH neurons through this large, synaptically connected network of neurons for them to function properly. However, the location, identity, relative contribution and significance of the individual neuronal components within this connectome remain largely unknown. We have recently made anatomical discoveries in a pre-clinical model of a common infertility disorder that highlight the importance of specific circuits originating within the arcuate nucleus (1).

Polycystic ovarian syndrome (PCOS) is the leading cause of infertility in premenopausal women characterised by a failure to ovulate and hyperandrogenism. Despite its name, PCOS may result from impaired neuronal circuits in the brain that regulate steroid hormone feedback to GnRH neurons. Women diagnosed with PCOS have elevated release of pituitary gonadotropins, suggestive of increased GnRH pulse frequency and impaired hormone feedback through this neuronal network. Utilizing a prenatal androgen treated (PNA) mouse model of the syndrome, we have recently identified a specific neuronal circuit that may relay disrupted progesterone signalling to GnRH neurons. Imaging of GnRH neurons has revealed that PCOS-like mice possess GnRH neurons with greater dendritic spine density and increased putative GABAergic, but not glutamatergic input. Mapping of steroid hormone receptors throughout the brain identified dramatically reduced (59%) progesterone receptor (PR) expression in the arcuate nucleus (ARN) of PNA mice. To address whether increased GABA innervation to GnRH neurons originates in the ARN, a viral-mediated Cre-lox approach was taken to trace the projections of GABA neurons residing specifically within the ARN *in vivo*. Surprisingly, ARN GABAergic neurons were found to heavily contact and even bundle with GnRH neuron dendrites. The density of fibres apposing GnRH neurons was even greater in PNA mice (56%) and this ARN GABA population showed significantly reduced co-localisation with PR in PNA animals compared to controls. The functional relevance of this circuit has been demonstrated in preliminary work employing selective optogenetic stimulation of ARN GAGA neurons. Together, these data provide compelling support for disordered progesterone-

sensitive GABAergic input to GnRH neurons, originating specifically within the arcuate nucleus, in prenatal androgen induced forms of PCOS, and highlight the likelihood that the arcuate nucleus is a critical brain region for the steroid hormone feedback control of fertility.

1. A. M. Moore, M. Prescott, C. J. Marshall, S. H. Yip, R. E. Campbell, Enhancement of a robust arcuate GABAergic input to gonadotropin-releasing hormone neurons in a model of polycystic ovarian syndrome. Proc Natl Acad Sci U S A 112, 596-601 (2015)

Symposium 1B: Looking to Rio: the Science of Elite Performance

S1B.1

The psychology of rising to the occasion: The role of challenge and threat appraisals

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Competitive sport is characterized by highly pressurized situations that place individuals under extreme stress before, and during, performance. However, individuals often respond to this stress differently: While one athlete might wilt under competitive pressure, another may thrive. One theoretical framework that offers a potential explanation for individual differences in this stress response is the biopsychosocial model (BPSM) of challenge and threat (Blascovich, 2008). The BPSM suggests that how individuals respond in a motivated performance situation is determined by their evaluations of situational demands and personal coping resources. When personal coping resources are evaluated as sufficient to meet or exceed situational demands, a challenge state occurs. Conversely, when personal coping resources are evaluated as insufficient to meet situational demands, a threat state ensues.

Individuals who exhibit a challenge state (indexed by increased heart rate and cardiac output, and decreased total peripheral resistance) outperform individuals who display a threat state (marked by increased heart rate, and no or small fluctuations in cardiac output and total peripheral resistance). Several underlying mechanisms have been proposed to explain how challenge and threat states influence performance including those related to emotions, attention, and physical functioning (Moore et al., 2012). The first part of this talk will discuss research from our lab which has provided support for the predictions of the BPSM in domains as varied as sport, aviation and surgery (e.g., Moore et al., 2012, 2013a).

However, a key role of a sport psychologist is to support athletes in dealing with the stress of performing when it matters most – i.e. when demands are highest. So, what can be done if an individual experiences a threat state? The second part of the talk will explore some interventions that have been shown to help performers develop more productive stress evaluations. These include reframing instructions (Moore et al., 2013a); providing arousal re-appraisal instructions (Moore et al., in press); and quiet eye training (Moore et al., 2013b).

References

Blascovich, J., (2008a). Challenge and threat. In: Elliot, A.J. (Ed.), *Handbook of Approach and Avoidance Motivation.* Psychology Press, New York, pp. 431–445.

Moore, L.J., Vine, S.J., Wilson, M.R., Freeman, P., (2012). The effect of challenge and threat states on performance: an examination of potential mechanisms. *Psychophysiology, 49*, 1417–1425.

Moore, L.J., Vine, S.J., Freeman, P., & Wilson, M.R. (2013a). Quiet eye training promotes challenge appraisals and aids performance under elevated anxiety. *International Journal of Sport & Exercise Psychology, 11(2),* 169-183.

Moore, L.J., Wilson, M.R., Vine, S.J., Coussens, A.H., Freeman, P., (2013b). Champ or chump? Challenge and threat states during pressurized competition. *Journal of Sport & Exercise Psychology, 35,* 551–562.

Moore, L.J., Wilson, M.R., Vine, S.J., Freeman, P., (in press). Reappraising threat: How to optimize performance under pressure. *Journal of Sport & Exercise Psychology.*

S1B.2

Nutrition for elite performance: Translating substrate metabolism science and supplementation to practice

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Sport Nutrition for Elite Performance is a wide and complex topic. However, the matrix tree of evidenced-based recommendations, guidelines, and practice by-and-large is rooted within the foundation of the science of energy-substrate metabolism. In the time allotted I will provide an evidenced-based snapshot of current understanding of base nutritional requirements and the ergogenic efficacy of current supplement practice for elite athletes. Topics covered will include: dietary carbohydrate guidelines for based on energy expenditure (e.g. low energy turnover sports, such as ,throwing and Rugby Union to high energy sports, such as, marathon and endurance cycling); protein requirements, benefits, timing, quantity, and use in functional pre-competition weight loss; manipulating carbohydrate availability (acute and chronic) to accentuate training adaptation.

In addition to diet, key micronutrients and supplements are widely used with some likely to benefit performance in some cases. There is physiological justification and good evidence to support the use in strength and power sports of creatine, caffeine, protein. For intermittent high-intensity (most sports) and endurance, caffeine, exogenous carbohydrate (sports drinks,), buffers (β-alanine, bicarbonate, sodium phosphate), an analgesic and antipyretic (paracetamol) are likely ergogenic, but come with some side-effects. While promising for sub-elite, dietary nitrate (e.g. beetroot juice) appears of negligible benefit and may harm elite performance. Athletes are more likely harmed by pharmaceutical does of endogenous anti-oxidants than benefit; however, effects on training adaptation of natural anti-oxidants found in foods in athletes eating an insufficient diet suggests benefit.

Elite athletes must go out of their way to reduce of risk of accentual doping via education and informed on inadvertent use of drugs in sport contaminated in supplements and food.

S1B.3

Physiology of elite performance: 'Big Rocks' vs. 'Marginal Gains'

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The sports science research literature is extensive. The elaborate number of reported performance enhancing effects over a multitude of possible interventions (i.e., cold water immersion, hydration, fluid temperature, various nutritional supplements, etc), can cloud a physiologist's ability to determine where (s)he should appropriately invest time and resources within an applied sport setting, so that the largest impact can be made on performance enhancement. Sport scientists have previously termed these potential interventions, 'Marginal Gains'.

The largest potential of all such modifiable actions within sport science, our 'Big Rocks', involve ways of maximizing training and subsequent adaptation aligned with the individual and targeted event. Thus, planning and programming of specific training, monitoring the training completed (i.e., distance, power, speed) to ensure it is specific and consistent, and monitoring the individual physiological response (i.e., heart rate and autonomic nervous system function), are the activities we mostly focus on. Additional marginal gains that may augment our 'big rocks', include heat, altitude and substrate availability.

Symposium 2A: Biological Basis for Obesity

S2A.1

FTO as a brain nutrient sensor

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GWAS indicate that SNPs in intron 1 of *FTO* are robustly associated with BMI. *FTO* loss of function mutations in humans and mice result in severe growth retardation and mice over-expressing Fto become obese. FTO is an amino acid (AA) sensor and couples AA levels to mTORC1 signaling, thereby playing a key role in regulating growth and translation. This was confirmed in adult specific deletion of FTO, which resulted in rapid loss of lean mass. In addition, Fto deficient mice are resistant to high-fat diet (HFD) induced obesity, a condition that leads to leptin resistance. Unlike WT mice, *Fto* KOs on a HFD remain sensitive to the anorexigenic effects of leptin. We analysed NFκB signalling, a known pathway activated by HFD and found that genes for the NFκB pathway were down-regulated in *Fto* KOs on a HFD. When the NFκB pathway is activated in *Fto* KO mice, they become resistant to leptin, similar to WT mice. TRIP4, a transcriptional coactivator of NFκB, is an FTO binding partner and we show that FTO is necessary for TRIP4 transactivation of NFκB. Thus, FTO is required for HFD induced leptin resistance through hypothalamic NFκB signalling.

S2A.2

Leptin resistance and its implication in body weight and glucose homeostasis

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Obesity is one of the most common medical problems of the 21st century and represents a critical risk factor for the development of type II diabetes. Both metabolic derangements are associated with central leptin resistance, a phenomenon that might be either caused by hyperleptinemia or by consumption of a diet rich in saturated fatty acids.

We established that central leptin sensitizes insulin action, which was a critical process for a healthy glucose metabolism in mice. This sensitization occurred via activation of the WNT pathway in the hypothalamus, the neuronal centre for the regulation of body weight. This highly conserved pathway that is involved in embryogenesis and tumorigenesis had not yet been linked to leptin signalling or neuroendocrine regulation of glucose homeostasis. Inhibition of this pathway in the hypothalamus, via pharmacotherapy and viral gene therapy led to profound derangements in whole body glucose homeostasis in mice. Corroborating the importance of Wnt signalling in metabolic control, we subsequently established that Wnt signalling is also involved in seasonal body weight regulation. Wnt target gene expression was furthermore tightly controlled by the light/dark cycle suggesting that this pathway might play an important role in circadian timing.

To investigate whether hyperleptinemia or high fat diet is the cause for leptin resistance we artificially induced hyperleptinemia by chronic delivery of leptin into the brain of hypersensitive leptin deficient mice. Despite superimposed hyperleptinemia these mice revealed a striking loss in body weight which was arrested by feeding a high fat diet, suggesting that the diet and not hyperleptinemia is the cause of leptin resistance. Intriguingly, high fat diet led to a very rapid loss of leptin sensitivity in the arcuate nucleus but not in the ventromedial hypothalamus suggesting differential processing and access of the leptin signal in the hypothalamus.

Taken together these findings reveal novel insights into the pathogenesis of obesity, type II diabetes and associated diseases and might lead to novel therapeutic intervention strategies.

S2A.3

Understanding obesity – mechanisms and translation

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The physiological control of body weight involves several hormones. A promising pharmacological approach to treating obesity is to mimic the effects of combinations of hormones to more closely represent physiology and restore energy balance. The pancreatic hormone amylin is a key example, which works synergistically with leptin to reduce body weight in human clinical studies. Recent data on the molecular understanding of amylin and its receptors, and novel amylin analogues will be presented. This is moving us closer towards combination therapies that could make an impact on the clinical control of body weight.

S2A.4

Mechanisms of weight loss in animal models of bariatric surgery

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Obesity and its related comorbidities can be detrimental for the affected individual, and challenge public health systems worldwide. Currently, the only available treatment options leading to clinically significant and maintained body weight loss and reduction in obesity related morbidity and mortality are based on surgical interventions. This talk will focus on two main clinical effects of Roux-en-Y gastric bypass (RYGB), namely body weight loss and change in eating behavior. Animal experiments designed to understand the underlying physiological mechanisms of these post bypass effects will be discussed. While caloric malabsorption and mechanical restriction seem not to be major factors in this respect, alterations in gut hormone levels (GLP-1; PYY; CKK; amylin) are invariably found after RYGB. However, their causal role in RYGB effects on eating and body weight and in improvement of glucose homeostasis has recently been challenged. Other potential factors contributing to the RYGB effects include increased bile acid concentrations and an altered composition of gut microbiota. RYGB is further associated with remarkable changes in preference for different dietary components such as a decrease in the preference for high fat or sugar. It is important to realize, however, that in many cases, the question about the necessity of these alterations for the success of bariatric surgery procedures remains unanswered.

1. Lutz, T.A., M. Bueter (2014). The physiology underlying Roux-en-Y gastric bypass – a status report. American Journal of Physiology 307: R1275-R1291. doi: 10.1152/ajpregu.00185.2014.

Symposium 2B: Respiratory Diagnostics and Therapies

S2B.1

The Audible Human Project: Developing a comprehensive model of sound and vibration in the lungs for diagnosis and therapy

Royston, T.J.[1], Mansy, H.A.[2,3], Dai, Z.[1], Peng, Y.[1], Henry, B.[1], Kearney, S.[1], Paltnikar, H.[1], Sandler, R.H.[2,4], Balk, R.A.[3]

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The Visible Human Project (VHP) of the National Library of Medicine, which provides anatomically detailed, 3-dimensional medical image sets of the normal male and female human bodies, has been a tremendous asset for both education and research. The VHP has catalyzed the development of advanced visualization software that has aided in anatomy education. The VHP data sets, themselves, have been invaluable to biomedical researchers in improving imaging technology, simulating surgical procedures and developing enhanced diagnostic techniques that utilize simulations based on VHP anatomy. We are developing a comparable Audible Human Project (AHP), whose goal is to accurately simulate the production, transmission and noninvasive measurement of naturally-occurring sounds associated with pulmonary function (with plans to expand to other organs/systems/function) and to simulate the propagation of sound and vibration introduced from outside the body,

e.g. through the mouth into the airways or through direct excitation at the skin surface (percussion). Response to both internal and external stimulation is of interest in emerging noninvasive elastographic imaging modalities whose optimal interpretation and utility relies on an accurate understanding and reconstruction of the mechanical wave motion (sound and vibration) that is imaged. Elastographic modeling and imaging of the lungs is particularly challenging and also has tremendous potential as, due to the unique structure of the lungs, we expect that both shear and compression wave types in the parenchyma, as well as other wave types along the major airways which act as wave guides, could all provide a rich source of diagnostic information. Response to internal and external stimulation is also of interest in developing novel therapeutic technologies that utilize sound and vibration as a part of disease or injury treatment. In this talk, an overview of the Audible Human Project is provided. See http://acoustics.mie.uic.edu/AHP/htdocs/default.php for the latest version of a downloadable executable program, AHP.exe. [Supported by NIH Grant # EB012142]

1. Mansy, H.A., R.A. Balk, W.H. Warren, T.J. Royston, Z. Dai, Y. Peng, and R.H. Sandler (2015). Effect of pneumothorax on pulmonary acoustic transmission. J. Applied Physiology. doi: 10.1152/japplphysiol.00148.2015.
2. Dai, Z., Y. Peng, H.A. Mansy, R.H. Sandler, and T.J. Royston (2015). A Model of Lung Parenchyma Stress Relaxation Using Fractional Viscoelasticity. Med. Engin. Phys. doi: 10.1016/j.medengphy.2015.05.003.
3. Dai, Z., Y. Peng, H. A. Mansy, R. H. Sandler, and T. J. Royston (2015). Experimental and computational studies of sound transmission in a branching airway network embedded in a compliant viscoelastic medium. J. Sound Vib. 339, 215–229. doi: 10.1016/j.jsv.2014.11.026.
4. Dai, Z., Y. Peng, B. Henry, H. A. Mansy, and T. J. Royston (2014). A Comprehensive Computational Model of Sound transmission through the Porcine Lung. J. Acous. Soc. Am. 136 (3), 1419 - 29. doi: 10.1121/1.4890647.
5. Peng, Y., Z. Dai, H. A. Mansy, R. H. Sandler, R. A. Balk, and T. J. Royston (2014). Sound transmission in the chest under surface excitation: an experimental and computational study with diagnostic applications. Med. Biol. Engin. Comp. 52, 695–706 doi: 10.1007/s11517-014-1172-8.
6. Dai Z., Y. Peng, H. A. Mansy, R. H. Sandler and T. J. Royston (2104), Comparison of Poroviscoelastic Models for Sound and Vibration in the Lungs. ASME J. Vib. Acoust. 136(5), 051012. doi: 10.1115/1.4026436 (2014).

S2B.2

State-of-the-art methods of measuring lung function: alternatives to spirometry.

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Spirometry is *de rigueur* in all standard pulmonary function laboratories, and is invaluable for the diagnosis and clinical follow-up of lung diseases such as asthma and chronic obstructive pulmonary disease. However, the test requires the patient to undertake maximal effort breathing manoeuvres, which means that results are highly dependent on patient effort and ability to follow instructions. Consequently, spirometry is often difficult or impossible to perform on infants, young children, the elderly or patients with severe lung disease.

Many state-of-the-art techniques are currently used in research or are at the cusp of clinical application to measure different aspects of lung function. For example, the raised volume rapid thoraco-abdominal compression technique is adapted from spirometry to obtain similar

measures in infants. Descriptors of the highly variable breathing pattern in infants can also reveal considerable information about pathology.

The forced oscillation technique and interrupter technique measure passive respiratory mechanics without need for complex breathing manoeuvres, as data can be collected during normal breathing. The forced oscillation technique involves superimposing small-amplitude mechanical waves at specific frequencies on the airway opening as the subject breathes, and using the resultant pressure and flow to calculate respiratory resistance and elastance. The interrupter technique deduces respiratory resistance and compliance during relaxation in response to a step interruption in flow at the airways.

Multiple breath washout tests have been around for decades but are enjoying a resurgence with the advent of higher resolution equipment and anatomical models to help interpret washout data. These tests can be used to measure functional lung volume as well as heterogeneity in ventilation, particularly in the small airways where early disease is thought to originate in many lung disorders.

Finally, novel imaging techniques such as single-photon emission computed tomography and electrical impedance tomography can provide additional insight into lung structure and function.

S2B.3

SensAwake™ - Responsive Pressure Relief

Whiting, D.R.

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Although Continuous Positive Airway Pressure (CPAP) is an extremely effective treatment of Obstructive Sleep Apnea, patients often struggle to consistently use the therapy. SensAwake™ is a pressure relief technology that aims to improve tolerance of CPAP be detecting when a patient is awake and reducing the CPAP to a more comfortable awake pressure. SensAwake™ was developed on the basis that regularity of respiration is a characteristic of stable sleep and that the appearance of respiratory irregularity may be an indicator of wakefulness[1].

Using the respiratory airflow signal alone from 20 CPAP titration polysomnograms, periods of irregularity were visually identified by multiple scorers. Each study was scored by at least two scorers and then differences were reconciled. EEG was used to formally identify sleep vs awake which was then compared to the visually identified periods of irregular respiration. In the 20 studies a total of 314 runs of wake lasting greater than 2 minutes were found. Of these, 164/315 (52%) were associated with manually marked periods of respiratory irregularity within the first two minutes of the run. The mean positive predictive value of irregular breathing to identify wake was 0.89.

Based on the ability of human scorers, using an airflow signal, to detect wakefulness with a high positive predictive value, a neural network classifier was developed. Features of the neural network were based on the respiratory airflow signal and were designed to capture respiratory irregularity. The features consisted of 8 parameters measuring average breath timing and amplitude and 17 parameters measured variability of breath timing and

amplitude. These features formed 22 inputs to a single hidden layer, 100 hidden nodes, one output neural network.

The neural network was trained against 50 respiratory airflow traces and validated against 24 respiratory airflow traces. Each flow tracing had periods of irregular respiration manually identified and reconciled by multiple scorers. In the validation set, 524 irregular respiratory events were identified by the neural network. Of these, 246 (66%) were associated with EEG defined awake, 104 (20%) were associated with arousal, 39 (7%) were associated with NREM sleep and 35 (7%) were associated REM sleep. The mean positive predictive value of the neural network identified respiratory irregularity to predict the transition from sleep to wake was 0.66 and 0.86 for transition from sleep to wake or arousal.

1. Ayappa, I., et al., Irregular respiration as a marker of wakefulness during titration of CPAP. Sleep, 2009. 32(1): p. 99-104.

S2B.4

Clinical studies of SensAwake Pressure Relief Technology

Cheung, I.C.

Fisher & Paykel Healthcare, Auckland, New Zealand

Reducing the pressure during wakefulness may improve therapy comfort and potentially adherence. SensAwake™ is a unique pressure relief technology developed by Fisher & Paykel Healthcare which detects irregularity in the flow signal indicative of the transition from sleep to wake and reduces the pressure when these transitions are detected. The purpose of this presentation is to compare efficacy, compliance and preference in patients treated by CPAP with and without SensAwake technology from four clinical papers that are published or in preparation for publication.

The four clinical studies[1-4] are reviewed in terms of study design and methods, and the outcomes measured. The effect of SensAwake on treatment efficacy, sleep quality, compliance and patient preference is discussed.

No significant differences were found in both PSG and CPAP data with the Apnea Hypopnea Index (AHI) comparing SensAwake to no SensAwake except for one study[4] (SensAwake AHI = 5.182; No SensAwake AHI = 3.563, p = 0.004), however this was not clinically significant. The Arousal Index (AI) was similar between the two treatments in all of the studies. No significant differences were found with the compliance comparing SensAwake to no SensAwake. However a sub-analysis of patients with high Insomnia scores revealed a trend towards higher compliance with SensAwake compared to no SensAwake of 66 minutes longer[4], however this did not reach the customary level of statistical significance (p=0.15).The preference for SensAwake by participants was shown to be higher with SensAwake compared to no SensAwake[2] (SensAwake preference = 12; No SensAwake = 3, p = 0.039).

SensAwake does not negatively impact CPAP therapy in terms of treatment efficacy and sleep quality. Users have shown a preference for SensAwake compared to no SensAwake, though this has not resulted in an increase in compliance. There is a potential that sub-group of patients with Insomnia could benefit from increased treatment compliance with SensAwake, however further study is required.

1. Dungan GC et al. A randomized crossover trial of the effect of a novel method of pressure control (SensAwake) in automatic continuous positive airway pressure therapy to treat sleep disordered breathing. *Journal of Clinical Sleep Medicine* 2011; 7(3):261-267.
2. Cumin D et al. Randomized crossover evaluation of a novel implementation of pressure relief technology – SensAwake and fixed pressure CPAP. *Sleep Medicine* 2011; 12 (Suppl.1): S75.
3. Powell ED et al. Interim analysis of long-term patient feedback on a novel automatic ramp feature in fixed pressure CPAP. *Sleep Medicine* 2011; 12 (Suppl 1): S72.
4. Bogan et al (TBD) – A long term in-home randomized crossover trial evaluating fixed pressure CPAP with and without SensAwake. [Unpublished raw data]

Symposium 3A: Endocrine-related Cancers: Progress and Prospects

S3A.1

Determinants of resistance to endocrine therapy in breast cancer

Dunbier, A.K.[1,2], Hazlett, J.A.[1,2], Hunter, B.L.[1,2], Buchanan ,S.T. [1,2], Bundock, A.S. [1,2], Wise, L.M.[3], Kemp, R.A.[1,3], Dowsett, M. [4]

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Breast cancer is the most common malignancy in women, accounting for more than 400,000 deaths per year worldwide. Approximately 80% of human breast carcinomas present as oestrogen receptor alpha-positive (ER+ve), which are typically sensitive to hormone deprivation. Oestrogen deprivation, induced by treatment with aromatase inhibitors (AIs) has been identified as the most effective therapy for ER+ve breast cancer in postmenopausal women. Despite this, up to half of patients eventually develop resistance to AIs and understanding of their precise molecular effects and causes of resistance is limited. Using molecular investigations of tumours from post-menopausal breast cancer patients we have identified features of the gene expression in the tumour, stromal microenvironment and hormonal milieu of the tumour that contribute to resistance to treatment.

To better characterise the mechanisms of resistance to oestrogen deprivation, we examined gene expression in 104 patients treated with the AI anastrozole in the neoadjuvant setting. Surprisingly, analyses revealed that pretreatment expression of an inflammatory signature correlated with poor response. Poor response was also associated with higher levels of lymphocytic infiltration in the tumour, suggesting that infiltrating immune cells may play a role in response to aromatase inhibitors. These findings contrast with chemotherapy-treated breast cancers where high levels of infiltration are associated with a good response. Expression of chemokines including *CCL5*, *CXCL16*, and *CCL22* also increased in response to treatment and this was replicated *in vitro* in an MCF7 cell model of oestrogen deprivation. In addition, a significant increase in the total number of peripheral blood mononuclear cells migrating to oestrogen deprived cells compared to cells with normal levels of oestradiol ($p < 0.0001$) was observed in a transwell immune cell migration assay. Furthermore, FACS analysis revealed a significant increase in the number of CD4+ cells and a decrease in the number of CD11+ cells migrating to deprived cells ($p<0.05$). This migration was blocked by

addition of a broad specificity chemokine-binding protein and to a lesser degree by a CCL5-specific protein.

These data suggest that oestrogen deprivation-induced chemokine production induces recruitment of immune cells towards ER+ve breast cancer cells and this response may contribute to resistance to anti-oestrogen therapy. Targeting this inflammatory response could be a future direction for therapy.

S3A.2

Multimodal assessment of oestrogen receptor status, expression and signalling activity in breast tumours

Muthukaruppan, A.[1], Lasham, A.[2], Woad, K.J.[3], Black, M.A.[4], Blenkiron, C.[2], Miller, L.D.[5], Harris, G.[6], McCarthy, N.[7], Findlay, M.P.[8], Shelling, A.N.[1], Print, C.G[2]

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Assessment of oestrogen receptor (ER)-α protein expression using immunohistochemistry (IHC) is used to stratify breast cancer patients for endocrine-based therapy. However, ER-α IHC provides no information regarding the functional status of the ER signalling pathway and it is estimated that up to 20% of ER status assessments may be inconsistent. Genomic indicators of ER activity have been proposed, however, these genomic indicators proposed to reflect ER signalling (usually represented by genes sets) are highly divergent, and the genomic consequences of ER pathway signalling remain incompletely understood.

We identified ER-α associated gene expression patterns in two complimentary ways. Firstly we used a simple well-controlled cell culture model of siRNA-mediated down-regulation of ESR1 (the gene encoding the ER-α protein) in ER positive MCF7 breast cancer cells, to capture the transcriptomic changes in the cells using microarrays. ESR1-dependent genes were significantly enriched for molecular pathways known to be associated with ESR1, CCND1, MYC and NFKB. Secondly, the expression patterns of ESR1 and ER-α associated genes were mapped, along with ER IHC status and 11 previously published ER-associated gene sets, across 1034 primary breast tumours of multiple subtypes. This analysis identified a continuous range of ESR1 mRNA expression across breast tumour subtypes, including low ESR1 expression in some luminal tumours and high ESR1 expression in some basal-like tumours. Using this data, we were also able to generate an inferred ER pathway activity using principal component analysis, which provided a putative measure of ER signalling activity.

We show that there is a continuous range of both ER expression and transcriptional targets of ER signalling in breast tumours. We propose that a combination of ER-α IHC, ESR1 mRNA expression, and bioinformatic inference of ER pathway activation can provide a multi-modal

assessment of breast tumour ER pathway activity, useful for both research and treatment stratification.

S3A.3

The link between oestrogen exposure, inflammation, and prostate cancer

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Prostatitis (inflammation of the prostate) is the most common prostatic condition worldwide and afflicts men of all ages. It is a condition that causes substantial morbidity to male sufferers through the associated constellation of urinary symptoms, sexual dysfunction and pelvic pain. Significantly, prostatitis is believed to contribute and lead to the development and/or progression of prostate cancer (PCa), similar to the role that inflammation plays in the development of malignancy in other organs. Despite this, the underlying causes of prostatitis remain largely unknown, with 90-95% of all prostatitis cases having no evidence of infection and an unknown aetiology.

Several causes of prostatitis have been postulated, however, of particular interest is a link between oestrogen exposure and the development of inflammation. Oestrogens, in addition to androgens, play multiple and important roles in the prostate, with aberrant oestrogen exposure associated with the development of prostatitis and also shown to play a role in the development of PCa. The microenvironment is also a critical mediator of PCa, with specific cell interactions, local oestrogen synthesis and the action of oestrogen receptors, particularly ERα, driving the disease. This microenvironment consists of multiple cell populations, particularly cancer-associated fibroblasts (CAFs) and immune cells, with the latter including mast cells (MCs), a resident prostate stromal population that we have shown to be increased in oestrogen driven inflammation and expanded in the peri-tumoural microenvironment of PCa patients.

To explore the role of CAFs and MCs we have recently developed a bioengineered multi-cellular 3D co-culture model to assess specific cell interactions and their impact on epithelial transformation. Using this system we showed that CAFs induce an invasive phenotype in benign epithelia independent of the Gleason grade of their tumour of origin. Significantly, when MCs were included there was further and significant potentiation of CAF effects on epithelial phenotype, with the effects of MCs mediated by their activation, tryptase production, and remodelling of the extracellular matrix. Further mechanistic studies also revealed that oestrogen, via ERα, mediates the cooperation between CAFs and MCs. Human MCs express ERα, and oestradiol directly stimulates MC proliferation, migration, activation, as well as altered cytokine/chemokine expression. Androgen signalling is reduced in CAFs while ERα transcriptional activity is not, allowing oestrogen to dictate hormone action in the tumour microenvironment. Gene microarray analyses also identified CXCL12 as a major oestrogen driven target gene in CAFs, and CAFs recruit MCs via CXCL12 in a CXCR4-dependent manner.

Overall, these data demonstrate that oestrogen signalling is associated with the development of prostatitis and PCa, with discrete effects mediated via ERα through specific multicellular

interactions that include MCs and CAFs. Our ongoing work defining the role of oestrogen in the prostate microenvironment will ultimately provide new insight into the aetiology of prostatitis and PCa and may identify new factors, such MCs, as novel targets for the development of new diagnostics and therapies.

S3A.4

FOXL2 and granulosa cell tumour of the ovary

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Abstract not available.

Symposium 3B: From Physiology to Pathophysiology of Diseased Hearts

S3B.1

Role of circumventricular organs in determining the excessive cardiac sympathetic nerve activity in heart failure

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Heart Failure (HF) is associated with increased cardiac sympathetic nerve activity (CSNA), but the mechanisms causing this are unclear. We have shown that intracerebroventricular infusion of the angiotensin type 1 (AT-1) receptor antagonist losartan significantly reduced the high level of CSNA in HF. We have investigated possible central nuclei at which losartan causes this effect by determining the response to selective lesion of nuclei that contain AT-1 receptors. We have previously shown that lesion of the paraventricular nucleus of the hypothalamus, which plays a critical role in stimulating renal SNA in HF, does not reduce the high level of CSNA in HF. The area postrema (AP) is a circumventricular organ that contains AT-1 receptors and plays an important role in controlling SNA. We hypothesized that lesioning the area postrema would reduce CSNA in HF and that this reduction in CSNA would attenuate the decline in cardiac function.

In sheep, HF was induced by rapid ventricular pacing for 8-12 weeks. When ejection fraction had fallen to ~50%, lesion or sham lesion of the AP was performed (n=6/group). Subsequently, when HF had developed (ejection fraction <40%), blood pressure, heart rate and CSNA were recorded in conscious sheep. Sheep with HF had a large increase in CSNA compared with healthy sheep (89 ± 3 vs. 34 ± 4 bursts/100 heartbeats, respectively). In sheep with lesions of the area postrema, the increase in CSNA was significantly less (45 ± 10 bursts/100 heartbeats, $P < 0.01$). In rats, HF was induced by myocardial infarction; occlusion of the laft anterior descending coronary artery. Lesion of the AP, or sham lesion, (n=18/group) was performed before myocardial infarction. Eight weeks later HF had developed as indicated by increased left ventricular end-diastolic pressure and reduced ejection fraction in the sham lesion group. In the AP lesion group, left ventricular end-diastolic pressure was significantly lower than in the sham lesion group (9 ± 2 vs 16 ± 2 mmHg, respectively, $P<0.05$) and ejection fraction was

higher. These findings suggest that the AP plays a critical role in setting the high level of CSNA in HF and indicate that lesion of the AP reduces the decline in cardiac function post-myocardial infarction, possibly due to the reduction in CSNA.

S3B.2

How do natriuretic peptides alter sympathetic control to the heart?

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The reported effects of natriuretic peptides (NP's) on sympathetic nerve activity (SNA) are variable, dependent on concomitant haemodynamic actions and likely to be regionally differentiated. There are few reports of the effect of B-type NP (BNP) on SNA and none have measured cardiac SNA (CSNA) by direct microneurography. Infusion of low dose ANP and BNP in sheep induced small but non-significant falls in arterial pressure and cardiac output but a significant rise in heart rate. ANP had no significant effect on any CSNA parameters but BNP induced a rise in CSNA burst frequency and burst area but not in burst incidence (bursts/100beats) and burst area/100 beats.

This is a classic example of SNA bursts being entrained to heart rate, but provides no evidence for inhibition of sympathetic traffic directed to the heart. Studies of the effect of adrenomedullin also show that CSNA is entrained to heart rate with significant increases in heart rate, CSNA burst frequency but not burst incidence. Urocortin peptides consistently show potent inhibition of CSNA in sheep. However, urocortin II infused into man shows no evidence of inhibition of muscle SNA. This may be an example of the effects of vasoactive hormones on SNA being regionally differentiated. Recent studies from the lab show that the classic vasoconstrictor angiotensin II administered systemically to at low-moderate doses does not increase CSNA but rather results in baroreceptor mediated reduction in CSNA. These studies demonstrate that it is not easy to predict responses based on published data from other species and SNA responses from other tissue beds. It does provide clear evidence to confirm that SNA is usually entrained to heart rate and that SNA responses are often regionally differentiated.

S3B.3

Altered relaxation of the human diabetic heart

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Diastolic dysfunction is a key factor in the development and pathology of cardiac dysfunction in diabetes, however the exact underlying mechanism remains unknown, especially in humans. I will present data from studies that used right atrial (RA) appendages and epicardial left ventricular (LV) biopsies collected from patients undergoing coronary artery bypass grafting with preserved ejection fraction, and with or without type 2 diabetes. Experiments in isolated RA trabeculae muscles will reveal differences in contractile function and relaxation,

whereas protein expression of β_1-adrenoreceptor, the sarcoplasmic reticulum calcium ATPase (SERCA2a), and its inhibitor phospholamban (PLB) will provide valuable information on differences in underlying signalling mechanisms. The results will provide novel information regarding chamber-specific effects of type 2 diabetes on calcium-handling proteins and β_1-adrenergic signalling, which may underlie the diabetes-associated dysfunction in cardiac relaxation in humans.

S3B.4

Reflections on Cardiac Muscle

Loiselle, D.S.[1,3], Han, J.C.[3], Tran, K.[3], Johnston, C.M.[3], Pham, T.[1,3], Mellor, K.M.[1,3], Cheuk, M.[3], Anderson, A.J.[3], Nielsen, P.M.F.[2,3], Taberner, A.J.[2,3]

Departments of [1]Physiology and [2]Engineering Science and [3]Auckland Bioengineering Institute, University of Auckland

The heart is a thermodynamic machine. With each beat, it develops force, shortens, performs pressure-volume work (W), and consumes a volume of oxygen (VO_2). Mechanical contraction is triggered by the release of Ca^{2+} from the sarcoplasmic reticulum (SR) and is subsequently effected by relative sliding of the contractile filaments. The beat is terminated by re-uptake of Ca^{2+} into the SR by its resident Ca^{2+}-pump (SERCA). Both Ca^{2+} sequestration by SERCA and the cycling of actomyosin cross-bridges are funded by the Gibbs Free Energy (ΔG_{ATP}) of hydrolysis of ATP. The mechanical efficiency of the heart is given by the ratio of W to the enthalpy of VO_2: $\varepsilon = W/\Delta H$. We mimic these *ex vivo* events by studying the behaviour of ventricular trabeculae undergoing force-length work-loops in a microcalorimeter[1]. But whether in the whole-heart or in a trabecula, the thermodynamic efficiency of capturing ΔG_{ATP} is imperfect. Hence, the performance of microscopic work is accompanied by the liberation of heat (Q). By summing the work performed and the heat evolved we have an independent measure of afterload-dependent enthalpy generation: $\Delta H = W + Q$ so that, once again, mechanical efficiency is given by: $\varepsilon = W/\Delta H$.

We thus have two independent estimates of mechanical efficiency of the myocardium: one arising from the pressure-volume work of a heart consuming oxygen and another from an isolated trabecula performing force-length work while liberating heat. We have exploited these dual technologies to study cardiac energetics of both healthy and pathologically hypertrophied hearts. A particularly revealing result presents in streptozotocininduced Type 1 diabetic cardiomyopathy. Whereas the peak pumping efficiency of the rat whole heart (approximately 15%) is shifted to a reduced afterload[2], that of its isolated trabeculae[3] remains unchanged – a multi-scale reflection on the energetic performance of cardiac muscle.

1. Taberner AJ, Han J-C, Loiselle DS & Nielsen PMF (2011) An innovative work-loop calorimeter for in vitro measurement of the mechanics and energetics of working cardiac trabeculae. Journal of Applied Physiology 111: 1798-1803.

2. Han J-C, Goo S, Barrett CJ, Mellor KM, Taberner AJ & Loiselle DS (2014) The afterload-dependent peak efficiency of the isolated working rat heart is unaffected by streptozotocin-induced diabetes. Cardiavascular Diabetology 13.

3. Han J-C, Tran K, Nielsen PMF, Taberner AJ & Loiselle DS (2014) Streptozotocin-induced diabetes prolongs twitch duration without affecting the energetics of isolated ventricular trabeculae. Cardiovascular Diabetology 13:79: 1-16.

Societies' Free Communications

Session 1A: PSNZ Bullivant Prize Finalists

1A.1 Bullivant Prize Contestant 1

CaMKII inhibition improves cardiac muscle contractility in the Zucker diabetic fatty rat

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Background- Calmodulin-dependent protein kinase (CaMKII) is a multifunctional serine-thereonine kinase that modulates ion channels and Ca^{2+} handling proteins involved in cardiac excitation-contraction coupling. Excessive CaMKII activation in the myocardium promotes hypertrophic cardiomyopathy and apoptosis, ultimately leading to reduced mechanical performance and heart failure. Recent studies show that diabetic patients and mouse models of diabetes have an up-regulation of CaMKII activity. Therefore we hypothesised that inhibition of CaMKII activity would improve myocardial contractility in the Zucker diabetic fatty rat (ZDF) heart. *Methods*- 20-week old type 2 diabetic ZDF (*n*=10) and control (CTRL) rats (*n*=10) underwent echocardiography to assess *in vivo* cardiac function. Cardiac muscles (trabeculae) were subsequently isolated from the right ventricle and myocardial force measurements were performed in the presence of an inhibitor of CaMKII activity (KN-93) or a peptide analogue with no CaMKII inhibitory effects (KN-92). Sections of heart tissue from the right and left ventricle were snap frozen for subsequent analysis of CaMKII expression in the diabetic heart. *Results*- After 20 weeks, fasted blood glucose was 25.8 ± 1.8 mmol/L for the ZDF diabetic rats and 8.2 ± 1.8 mmol/L for the CTRL rats. The E:A ratio was significantly higher in the ZDF rats (2.3 ± 0.1) compared to the CTRL rats (1.85± 0.2, $p<0.05$), indicating early stage diastolic dysfunction in the diabetic animals *in vivo*. CaMKII expression was elevated in the right ventricle of 20 week old ZDF rats (2.3 ± 0.7) compared to the CTRL rats (1.45 ± 0.2). Trabeculae isolated from ZDF rats had reduced contractile force (F_{dev} and dF/dt_{max}) across all stimulation frequencies, alongside impaired relaxation (RT90% and dF/dt_{min}). Inhibition of CaMKII in the diabetic trabeculae significantly improved contractile force, but had no significant effect on relaxation kinetics. *Conclusion*- The heart is predisposed to diastolic dysfunction as diabetes develops, an effect accompanied by increased activation of CaMKII. More importantly, inhibition of CaMKII activity improved myocardial contraction but did not have any effect on relaxation. Our results indicate that CaMKII contributes to the functional changes in the diabetic heart and, moreover, suggest a potential therapeutic role for CaMKII inhibitors in improving cardiac myocardial function in the diabetic heart.

1A.2 Bullivant Prize Contestant 2

Human amniotic epithelial cells: The effects of intranasal cell therapy on chronic hypoxic ischemic brain damage in the preterm fetal sheep.

van den Heuij, L.[1], Miller, S.L. [2], Jenkin, G.[2], Fraser, M.[1], Gunn, A.J. [1], Bennet, L.[1]

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Introduction: Preterm infants have a high risk of perinatal asphyxia and brain injury. Presently therapeutic options are limited to symptom management. Stem cell therapy is a promising option that may improve neural outcomes after brain ischemia. Human amnion epithelial cells (hAECs) may be safer than other stem cell approaches and can attenuate cerebral inflammation. In this study we investigated whether intranasal administration of hAECs could improve recovery from asphyxial brain injury in preterm fetal sheep.

Methods: Preterm fetal sheep (103-4 days gestation; term is 147 days) were continuously monitored before, during and for 21 days after 25 min umbilical cord occlusion. Intranasal (IN) boluses of either hAECs ($30*10^6$ cells/2ml) or vehicle were given at 1 d, 3 d and 10 d post insult. Blood samples were taken for fetal blood gas values. Brains were histologically assessed after post-mortem.

Results: hAEC treatment did not affect any physiological parameters although there was an apparent trend to better EEG recovery. Histologically, surviving hAECs were identified in the white matter tracts. There were no differences in numbers of olig-2+ve oligodendrocytes between sham, asphyxia only and treatment groups. In contrast, hAEC treatment was associated with greater numbers of more mature, CNPase and MBP+ve oligodendrocytes than asphyxia only ($p<0.05$) as well as reduced microglial infiltration and astrogliosis.

Conclusion: These findings strongly suggest that delayed intranasal administration of hAECs is associated with intracerebral migration of the cells, and can help to reduce white matter inflammation and associated maturational arrest after severe asphyxial brain injury.

1A.3 Bullivant Prize Contestant 3

Dexamethasone induced hyperglycaemia during asphyxia is associated with severe cystic white and grey matter brain injury in preterm fetal sheep

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Introduction: Antenatal glucocorticoids improve outcomes among preterm babies but are also associated with hyperglycaemia. In human pregnancy hyperglycaemia is associated with adverse neonatal outcomes; however, it is unclear whether this link is causal. In newborn rodents, both glucocorticoids and hyperglycaemia before hypoxia-ischaemia are highly neuroprotective, but there is little evidence from large animal studies. In this study we investigated whether glucocorticoids modulate asphyxial brain injury through induction of hyperglycaemia.

Methods: At 0.7 of gestation, chronically instrumented singleton sheep fetuses were exposed to maternal injection of 12 mg DEX i.m. (n=7), saline (n=8), or a fetal i.v. infusion of glucose dissolved in saline (2 mmol/ml, Glucose group, n=7), titrated to increase fetal plasma glucose levels to those observed in the DEX group. After 4 hours fetuses received 25 minutes of complete umbilical cord occlusion. Post-mortems were performed after 7 days recovery for cerebral histology.

Results: DEX and glucose treatment increased fetal blood glucose levels before asphyxia (DEX: 2.0±0.2 and Glucose: 2.4±0.3 *vs.* saline: 1.0±0.1 mmol/l, $p<0.05$). Occlusion with saline was associated with subcortical neuronal loss ($p<0.05$) and loss of mature oligodendrocytes ($p<0.05$) without cystic lesions. DEX and Glucose were associated with increased grey and white matter injury compared to saline treatment, including severe cystic infarcts in the thalamus and periventricular white matter in all DEX and Glucose fetuses ($p<0.001$, Fisher exact test). Within the DEX and Glucose groups higher peak plasma glucose values were correlated with more extensive injury, including cystic damage of the striatum and sagittal gyrus.

Conclusions: Maternal DEX injection and fetal hyperglycaemia were associated with dramatic, dose-related exacerbation of neural injury after subsequent fetal asphyxia, including severe cystic infarction. These data strongly suggest that the clinical association of perinatal hyperglycaemia with adverse outcomes is causal.

1A.4 Bullivant Prize Contestant 4

Maternal obesity compromises the blood-brain barrier in the developing fetus

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Maternal obesity during pregnancy is associated with various metabolic and neurobehavioural diseases in the offspring. Our research investigates how altered maternal environment could differentially program the offspring brain. During mid-gestation onwards, the blood-brain barrier (BBB) is formed, with the formation of tight junctions and down-regulation of fenestrations in endothelial cells, and interaction between glial cells and brain vasculature.

Our recent studies on the BBB have revealed that in the arcuate nucleus of the hypothalamus (ARC), the fenestrations in the endothelial cells persist longer than nearby hypothalamic regions. Furthermore, immunochemical analysis and RT-qPCR showed a significantly higher levels of expression of fenestrated endothelial cell markers (MECA-32 and dysferlin) in the postnatal day 0 (PN0) ARC of offspring from the maternal high-fat diet (mHFD) group compared to the normal weight control group. The increase in expression of fenestration markers in mHFD group appeared to result from an increase in the proportion of blood vessels containing fenestrated endothelial cells, rather than a generalised increase in the number of blood vessels.

We then used intraperitoneal injection of Evans blue dye and quantified its diffusion into the ARC as a measure of BBB permeability in the offspring of control and mHFD groups. Consistence with our findings of increased fenestrated endothelial cells, Evans blue diffusion was significantly higher in mHFD group than the control.

Our data indicate that maternal obesity can compromise the formation of the BBB in the developing fetal brain, leading to an increase in fenestrated endothelial cells and reduced BBB function. Future work will define the physiological consequences of this altered BBB permeability.

1A.5 Bullivant Prize Contestant 5

The role of cardiomyocyte organisation in the cardiac structure-function relationship

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Cardiac function is reliant on a process known as excitation-contraction (EC) coupling, and in cardiomyocytes many of the key proteins involved in EC coupling are localised to junctions. Junctions are areas of close contact between invaginations of the plasma membrane, which form the transverse tubules (t-tubules), and terminal regions of the sarcoplasmic reticulum (SR). In addition to the SR calcium release channel, the ryanodine receptor (RyR), cardiomyocyte junctions contain a protein called junctophilin-2 (JPH2) which has been implicated in junctional formation and maintenance. In human and animal models of heart failure, there is a loss of cardiac function associated with impairment of EC coupling, and changes to t-tubule and protein organisation. Currently, the link between cardiomyocyte reorganisation and the loss of cardiac function remains unclear. We have investigated different aspects of this relationship using a combination of JPH2 transgenic mice and cardiac trabeculae from failing human hearts.

JPH2, RyR and t-tubule immunolabelling was performed with confocal and super-resolution microscopy. The nano-scale organisation of junctional proteins was examined in JPH2 transgenic mice using super-resolution imaging. Results show that RyR cluster and t-tubule organisation is altered in response to JPH2 expression levels, contributing potential mechanisms for changes observed in calcium handling properties. These results indicate that JPH2 expression directly influences RyR cluster organisation in cardiomyocytes. In addition, we obtained trabeculae from explanted human hearts with end-stage failure and assessed force development and protein organisation. Confocal microscopy revealed a high degree of variability in function and trabecula macroscopic and microscopic structure, with trabeculae showing poor contractile function often exhibiting low cardiomyocyte content or containing myocytes with severe protein disorganisation. Our findings indicate a clear link between trabecula structure and function in the diseased human heart. In conclusion, together these findings provide novel insights into the multi-scale influence of cardiomyocyte structure on cardiac function.

1A.6 Bullivant Prize Contestant 6

Kisspeptin does not affect excitatory or inhibitory synaptic transmission in magnocellular neurosecretory cells from virgin or late-pregnant rats.

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Magnocellular neurosecretory cells (MNCs) of the hypothalamic supraoptic nucleus (SON) and paraventricular nucleus project to the posterior pituitary gland where they release the hormones oxytocin and vasopressin into the circulation. Oxytocin is important in parturition where it facilitates birth by causing uterine contraction. However, the mechanisms that lead to oxytocin neuron activity at parturition are poorly understood. We have found that fibres in the perinuclear zone (PNZ) around the SON, which contains glutamate and GABA neurons that project to MNCs, show higher kisspeptin expression in late pregnant rats compared to virgin rats. Furthermore *in vivo* electrophysiology results show that central kisspeptin administration increases oxytocin neuron firing rate in late pregnant rats, but not virgin rats.

We hypothesised that kisspeptin neurons excite SON oxytocin neurons via an indirect mechanism involving PNZ neurons. To test this hypothesis, we used patch clamp recordings of SON MNCs in slices from virgin and pregnant rats to determine the effect of kisspeptin on excitatory post-synaptic currents (EPSCs) and inhibitory post-synaptic currents (IPSCs). If the hypothesis were true we would expect that kisspeptin would increase excitatory transmission and / or decrease inhibitory transmission in MNCs in pregnant but not virgin rats. However, kisspeptin did not affect the frequency or amplitude of EPSCs or IPSCs in MNCs from virgin or pregnant rats, suggesting that kisspeptin does not affect the activity of local glutamatergic or GABAergic inputs onto MNCs. Finally, kisspeptin did not affect the baseline holding current during the recording of MNCs from virgin or pregnant rats, suggesting that kisspeptin does not act directly on MNCs. Overall the results suggest that kisspeptin does not mediate its excitatory effects on oxytocin neurons in pregnancy via local inputs onto MNCs.

1A.7 Bullivant Prize Contestant 7:

Cardiovascular microRNAs in diagnosis and therapeutic intervention of diabetic heart disease

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Diabetic heart disease (DHD) is often unrecognized in subclinical stage due to absence of pathognomonic signs, thereby restricting timeous diagnosis and management of disease. Recently, microRNAs (miRs) are gaining popularity as diagnostics and key regulators in the pathophysiology of several diseases including cardiovascular diseases. However, the diagnostic potential and pathophysiological role of miRs in DHD is still unknown.

RNA was extracted from plasma (n=14) of people with diabetes and age-matched non-diabetic volunteers with no history of heart disease. QPCR analyses revealed marked dysregulation of target-miRs (miR-1,-126,-132,-133 and -499) in diabetic plasma which was also dependent on duration of diabetes ($p<0.05$). To further answer, whether modulation of circulating miRs has a correlation with etiology of DHD, miR expressions were studied in cardiac tissues (n=10) of 8-32 weeks old type 2 diabetic (Db/db) and non-diabetic mice. Remarkably, all investigated miRs and their target proteins were dysregulated in diabetic myocardium, starting from 8-weeks of age ($p<0.05$). Importantly, echocardiography and

immunohistochemical analyses did not reveal any noticeable changes in diabetic mice until 20-weeks of age ($p<0.001$). These findings suggest that miRs are early modulators of DHD and can be explored as therapeutic interventions for prompt management of DHD. In line with these results, we elicited *in vitro* modulation of two of my target-miRs (miR-126,-132) to explore their therapeutic potential in diabetic state. It was demonstrated that restoration in expression of both miRs in HUVECs abrogated the deleterious effects against high-glucose-induced impairment in angiogenesis, proliferation and cell survival ($p<0.05$). Current studies aim to determine the therapeutic potential of other miRs using HL-1 cardiomyocytes.

Overall, these findings provide the first evidence that miRs can be used as a novel diagnostic tool for early detection of DHD. It also opens up intriguing ways to develop miR-based therapies for management of DHD.

1A.8 Bullivant Prize Contestant 8:

Altered baroreflex control of cardiac sympathetic nerve activity and heart rate during renovascular hypertension

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Globally, hypertension affects one in three adults. The sympathetic nervous system has been implicated in the development of hypertension. In this context, increased sympathetic drive to the heart promotes arrhythmias and sudden death in patients, but the level of cardiac sympathetic nerve activity (CSNA) in hypertension has been assessed only by indirect methods. We tested the hypothesis that directly recorded CSNA is increased in renovascular hypertension. Renovascular hypertension was induced by surgical clipping of one renal artery. Following three weeks post-clip, electrodes were surgically implanted into cardiac sympathetic nerve fascicles of adult ewes (n=4). Following recovery from surgery, resting levels of mean arterial pressure, heart rate and CSNA were recorded. Baroreflex control of heart rate and CNSA was assessed using intravenous infusions of phenylephrine and sodium nitroprusside. The same protocol was repeated in sham clip ewes (n=5).

Renal clipping resulted in a significant increase in resting levels of arterial pressure (110 ± 5 vs. 84 ± 7 mmHg; $p<0.05$) but no change in heart rate (89 ± 5 vs. 93 ± 5 beats/min). Contrary to our hypothesis, there was no difference in the resting levels of CSNA between the groups (39 ± 4 vs. 32 ± 5 bursts/100 heartbeats). However the baroreflex control of CSNA at lower pressures was impaired (upper plateau of 226 ± 23 vs 386 ± 64 % of control). This was also accompanied by an impaired baroreflex control of heart rate (140 ± 5 vs 158 ± 7 beats/min for the upper plateau). Our data indicate that the increased arterial pressure in renovascular hypertensive animals is not mediated by an increase in CSNA levels. The reduction in baroreflex control of heart rate in renovascular hypertensive animals is mediated in part by impaired baroreflex control of CSNA.

Session 1B: Biomed Tech Prize Finalists and Free Communications

1B.1 Biomed Tech Prize Contestant 1

Factors influencing Blood Flow induced Impedance changes in human limbs

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The estimation of blood flow using a contemporary technique like Bioimpedance Plethysmography can provide an efficient diagnosis comparable to that of ultrasonography and echocardiography. The blood flow dynamics are reflected in the form of electrical impedance variations which can be used to estimate the flow waveform. The analysis of impedance due to blood is contributed by the compositional and dynamic characteristics, which are further interdependent due to clustering and de-clustering of the red blood cells (RBCs) as blood flows. The major contributors are the volumetric changes and the shear profile which are reflective of complex blood dynamics. Also, the acquisition of the impedance variations are affected by the type and size of electrodes and the frequency of operation.

To analyse the factors affecting the blood dynamics induced impedance variations, a basic model of human forearm has been modelled using Ansys, with layers of fat and muscle constituting the arterial blood flow. The blood flow instants were realised using different dimensions of arterial segment width and analysing the change in impedance due to the same. The electrical response was obtained using Ansys HFSS with different positions of electrodes and different frequencies of operation. The obtained data clarifies the significance of electrode placement and operation frequency. Higher sensitivity distribution was obtained with minimum spacing between the input and output electrodes placed along the direction of blood flow.

1B.2 Biomed Tech Prize Contestant 2

Effect of Skin's elasticity on motion artefact reduction in ambulatory ECG monitoring

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The quantification of skin stretch for estimating the motion artifacts induced during an ECG measurement is an effective measure to increase the efficiency of the obtained readings. The present work highlights the design of a patch sensor for motion artefact estimation in different conditions of body movements. Skin is composed of different layers of tissues that contribute to its overall elasticity, which varies with different locations on the body as well as the methods of measurement. The well-established methods for measurement of skin's elasticity include tensile testing, indentation, torsion and suction tests. The aim of this research is to measure skin stretch in terms of strain components which can be transduced into equivalent electrical signals using piezoelectric sensor realization. Also, the significance of the elasticity of patch sensor has been foreseen since it has to highly sensitive and accurate for detecting small strain components.

Hence, different methods for estimating the Young's Modulus of skin have been analysed to determine its optimum value at the chest region. The torsion and the suction tests prove be

adequate for deciding on skin's modulus of elasticity as their mechanics relate most closely to skin stretch. The designed sensor is a PDMS patch which is 0.1" thick, for which the sensitivity have been decided on the basis of skin's elasticity values. The artifact estimation has been carried out by motion tracking of designated points on the patch and using the displacements to compute the corresponding strain values.

1B.3 Biomed Tech Prize Contestant 3

Human upper airway collapse in OSA patients

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Obstructive sleep apnoea (OSA), a common upper airway (UA) respiratory system sleep disorder, is considered as one of the most threatening diseases to the quality of life worldwide. OSA occurs due to obstruction in the UA region, and is characterized by repeated obstruction and collapse of the pharyngeal airway during sleep. The collapse occurs when the forces of the airway muscles are less than those generated from the airway negative pressures during respiration. The tendency for an UA obstruction to occur increases when the patient sleeps in a supine position. In this position, gravitational forces pull the soft palate tip (uvula) and tongue downwards, which in turn reduces the gap between those tissues and airway wall. The chances for airway obstruction and collapse thus increase. Within this narrowed environment, additional concerns arise as structural deformations of the UA soft tissues (particularly the uvula and tongue) further increases the tendency of the upper airway to be obstructed and/or collapsed. Computational fluid dynamics (CFD) has been used successfully for many years in modelling the UA respiratory system, as well as describing the flow parameters and characteristics. In this work 3D UA models are constructed for apneic patients from magnetic resonance images (MRI) and simulated using ANSYS to identify the fluid-structure interaction (FSI) between the air and the soft tissues. The main objective of this research is to identify the conditions of UA collapse associated with apneic events and attempt to determine some structural modifications to reduce the possibility of OSA occurrence.

1B.4

A cell culture model of ion transport in the human alveolar epithelium

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The thickness and composition of the alveolar surface fluid in the human lungs is tightly regulated by ion channels, transporters and junctional proteins. In this study we evaluated the potential of two human lung epithelial cell lines, NCI-H441 and A549, to serve as useful in vitro models to study alveolar fluid and ion transport. Both cells lines were cultured with the apical surface exposed to air and the basolateral surface exposed to culture medium. The

expression of junctional and ion/water transport proteins were examined by RT-PCR, Western blotting, and immunofluorescence. Barrier properties were assessed by measuring transepithelial electrical resistance and fluorescein permeability. The contributions of sodium and chloride channels to ion transport was assessed by measuring transepithelial potential difference in the absence and presence of agonists and inhibitors. NCI-H441 cells exhibited higher levels of junctional proteins and α_1-Na^+-K^+-ATPase expression, higher electrical resistance (529 ± 178 $\Omega \cdot cm^2$ vs 28 ± 4 $\Omega \cdot cm^2$), higher potential difference (11.9 ± 4 mV vs 0 mV) and lower permeability ((178 ± 21) $\times 10^{-8}$ cm/s vs (610 ± 16) $\times 10^{-8}$ cm/s) compared to A549 cells. Treatment of NCI-H441 cells with amiloride, CFTR(inh)-172 and forskolin showed that sodium is absorbed through epithelial sodium channels (ENaC) under baseline and agonist-stimulated conditions while chloride moved through the paracellular pathway. We conculde that NCI-H441 cells cultured under an air-liquid condition are a suitable human model for investigating ion and water transport in the alveolar epithelium.

1B.5

Impedance and targeted image investigation of oral squamous cancer cells using folate conjugated gold nanoparticles

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Mercaptosuccinic acid-coated gold (GM) nanoparticles were prepared and characterized by transmission electron microscopy and dynamic light scattering. Folic acid (F) was then conjugated to the GM to preferentially target oral squamous cancer (KB) cells with folate receptors expressed on their membranes and facilitate the transit of the nanoparticles across the cell membrane. Finally, a fluorescence dye (Atto) was conjugated to the nanoparticles to visualize their internalization into KB cells. After culture of the cells in a medium containing GM and folate conjugated GM (GF), the interaction of surface-modified gold nanoparticles with KB cells was studied using impedance measurements.

1B.6

Microstructural remodelling and mechanics of hypertensive heart disease

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In many forms of heart failure (HF), left ventricular (LV) remodelling has been identified as the leading cause of ventricular dysfunction. Altered haemodynamic loading can lead to changes in LV size, wall thickness, and remodelling of myocardial tissue constituents (e.g. fibrosis). Myocardial fibrosis involves an accumulation of connective tissue (collagen) in the interstitial space, which has been shown to disrupt the organisation of the laminar microstructure within the heart wall. This can lead to altered ventricular chamber mechanical properties (e.g. elevation of chamber stiffness), and thus the mechanical function of the heart. The combined effects of changes in heart geometry and microstructural remodelling of myocardium on ventricular function remain poorly understood.

We have developed an image-driven constitutive modelling framework, which integrates subject-specific geometric data and microstructural organisation of the myocardial tissue, in order to investigate the mechanisms of heart function in health and disease. In this study, we investigated the effect of myocardial microstructural remodelling on passive mechanical function of the LV during the progression of hypertension-induced HF using spontaneously hypertensive rat (SHR) and Wista-Kyoto (WKY) rat as controls. The SHR develops hypertension with age, which induces HF with similar characteristics to those observed in failing human hearts, making it an effective animal model for studies of HF. We constructed biophysical models of the LV using geometric data derived from in vivo magnetic resonance images of healthy and failing rat hearts at both 14-months and 24-months of age. By incorporating subject-specific LV geometries and parameters that directly reflect the tissue microstructure, we demonstrate that the differences in LV geometry and proliferation of endomysial and perimysial collagen must both be accounted for in order to explain the observed differences in LV chamber compliance with age and disease. This study highlights the important role that remodelling of myocardial microstructure plays in the mechanics of the failing heart.

1B.7

Peripheral changes in blood flow as indicators of blockages in central cardiovascular system.

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Cardiovascular disease is one of the leading causes of death in the world, accounting for 30% of all deaths worldwide and 40% of those occurring in New Zealand. In recent years, engineers and scientists have collaborated with the medical community to find new methodologies and approaches for assessing, investigating and understanding the development of cardiovascular diseases. Elements such as computational models developed with fluid dynamic elements (CFD/FE) have become excellent tools for this purpose. One of the important approaches is developing devices for investigating the central blood flow and pressure, and correlating the results to different heart diseases. Higher central blood changes in flow and pressure mean that the heart must work harder. Using an animal model (Rats), we simulated an unhealthy condition (thrombosis like) inducing three different degrees of blockages (severity) at the level of their right carotid artery (central system) and measurements of blood flow were determined non-invasively using an ultrasound system for rodents at the right subclavian artery (periphery system). As the pulse waves travel in the arterial system, the propagation and reflection of these waves through a particular medium (e.g. the artery walls) carries information about the physical characteristics of that medium. The aim of this study is to determine whether changes in blood flow occurring in different vessels, such as the carotid due to arterial blockage (experimentally induced in rat) can be detected in a peripheral location of the vascular system, such as the right subclavian artery.

Session 1C: SESNZ Free Communications

1C.1

The effects of acute ketone supplementation on cycling performance.

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The purpose of the present study was to examine the effects of oral ketone supplementation on endurance cycling performance and metabolism. Using a double-blind, placebo-controlled, randomised, crossover design, 12 highly-trained cyclists (mean ± SD: age; 35 ± 8 y, mass; 74.5 ± 7.6 kg, VO2peak; 68.0 ± 6.7 ml.min^{-1}.kg^{-1}) were supplemented with 60 mL ketone salt (β-hydroxybutyrate in sodium and potassium form) or placebo (3g table salt) during 90 min of cycling at 80% of second ventilatory threshold (VT2) power output before performing a 4 min maximal cycling performance test (4PT). β-hydroxybutyrate (BHB) concentration increased more than two-fold between trials upon ingestion of the supplement (ES = 3.02; *very large*). The increase in BHB resulted in a 2.2% ±1.9% (mean ±90% confidence interval, CI) increase in RER during the submaximal exercise phase (ES = 0.51; *moderate*). VO2 increased 2.4% ± 3.3 during the 4PT in the ketone trial (ES = 0.24; *small*), however differences between VO2 during the submaximal exercise bouts were *unclear* (ES = -0.21). A clear *trivial* (ES = 0.16) performance increase of 2.3% ±4.8% was shown for the ketone trial compared to the PLA. In conclusion, ketone supplementation altered BHB concentrations, RER and VO_2 values during exercise, but had *trivial* effects on cycling performance.

1C.2

Performance and physiology of elite and highly-trained triathletes during simulated racing in cool and hot environments

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New Zealand elite triathletes have performed poorly during international competitions when ambient temperatures exceeded 30°C. This study investigated causes that may contribute to performance decrement in hot conditions. Elite and highly-trained triathletes performed a 60-minute cycling race simulation in cool and hot environments to assess performance power and the associated physiology. Twelve triathletes (8 male and 4 female, 23.9 ± 5.2 years, 176.1 ± 8.1 cm, 68.4 ± 8.4 kg, 58.6 ± 3.6 mL.kg^{-1}.min^{-1} $\dot{V}O_2$ peak) performed a step-incremental cycling test to determine ventilatory thresholds, lactate thresholds, W_{max}, and $\dot{V}O_2$ peak. Three days later each performed a 60-minute cycle race simulation in an environmental chamber in COOL conditions (18°C, 40% RH, 4.5 m/s air velocity), and two days later in HOT conditions (33°C, 60% RH). Exercise was performed using a fixed intensity profile for 40 minutes (1:50 at VT1 power followed by 0:10 at 200% W_{max}, repeated 20 times) immediately followed by self-selected effort for 20 minutes (1:50 at similar power to VT1 followed by 0:10 maximum effort sprint, repeated 10 times), on a Velotron cycle ergometer. Average and peak

brain blood flow velocities were measured at the middle cerebral artery using Doppler Ultrasound. The cerebral oxygenation and the volume of oxyhaemoglobin, deoxyhaemoglobin and total haemoglobin were measured in the right prefrontal cortex, and in the contracting skeletal muscle at the Vastus lateralis using near infra-red spectroscopy. Ventilation and $P_{ET}CO_2$ were measured by gas analysis, peripheral oxygen saturation by pulse oximetry, and T_{Core} by rectal thermistor. Data were averaged over the 60-minute race simulation, and COOL vs. HOT conditions were compared using paired t-tests and two-way RM ANOVA. Power output was 9.7 ± 5.7% lower in HOT (-0.34 ± 0.21 W/kg FFM, p = 0.0008 (mean ± SD)). Physiological responses were significantly influenced by HOT conditions despite the reduced power output; brain oxyhaemoglobin volume (-72.3 ± 88.6 $\mu M.cm^{-1}$, p = 0.03), $P_{ET}CO_2$ (-2.0 ± 1.0 mm Hg, p = 0.0001), SpO_2 (-0.4 ± 0.6%, p = 0.006), and oxygen pulse (-2.6 ± 2.2 $mL.beat^{-1}$, p = 0.02) were lower than in COOL, while brain deoxyhaemoglobin volume (71.5 ± 58.3 $\mu M.s^{-1}$, p = 0.01), heart rate (5 ± 4 $beats.min^{-1}$, p = 0.02), and T_{Core} (0.313 ± 0.308°C, p = 0.002) were higher. Brain blood flow velocities, cerebral TOI and skeletal muscle TOI were not significantly altered (p > 0.05). The lower oxyhaemoglobin and higher deoxyhaemoglobin volumes in HOT indicate greater oxygen extraction that may have inhibited motor cortex output and therefore performance power[1,2].

1. Nybo, L. (2010). *Cycling in the heat: performance perspectives and cerebral challenges.* Scandinavian Journal of Medicine & Science in Sports. 20 (Suppl. 3) 71-79.
2. Abbiss, C. R., Burnett, A., Nosaka, K., Green, J. P., Foster, J. K., Laursen, P. B. (2010). *Effect of hot versus cold climates on power output, muscle activation, and perceived fatigue during a dynamic 100-km cycling trial.* Journal of Sports Sciences. 28 (2): 117-125.

1C.3

Is thirst too late to begin drinking in dehydration?

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Thirst is one of the primary homeostatic mechanisms supporting fluid balance. Physiological signals driving thirst are primarily a rise in plasma osmolality (P_{osm}) and secondarily a decreased blood volume [5]. P_{osm} is considered to show a threshold above which thirst is stimulated. Numerous studies report that P_{osm} does not rise rapidly until at least 2-3% loss of body mass (ΔBM) has been incurred, which is indicative of mild/moderate dehydration. Similarly, hypertonic saline infusion studies show that thirst is not stimulated until P_{osm} rises >5 mOsmol/L [3]. For these reasons it is concluded that thirst is too insensitive to detect or restore fluid balance in the early stages of dehydration. That is, thirst is 'too late' to prevent dehydration, given that negative physiological and performance effects have been shown at such levels of dehydration [4]. These beliefs underpinned the hydration guidelines during exercise changing from "drink to thirst" to "stay within a 2% change in body mass (ΔBM)" [2]. However these claims and changes to the guidelines assume that a significant change in thirst is induced solely by P_{osm}, and disregards the fact that thirst can also be driven by numerous factors including dryness of the mouth and throat [1]. Therefore we investigated the

relationship between thirst and P_{osm} in response to different forms of dehydration, partly to determine whether an "osmotic threshold" or rise P_{osm} is required to elicit a significant change in thirst during dehydration.

Methods: Eight participants (2 females) were dehydrated via passive heat stress or exercise, in randomised and counterbalanced order, with at least 7 days apart for males and 4 weeks for females. Exercise involved 5-min interval exercise bouts in warm conditions (29˚C, 40%RH), and passive heat stress involved sitting sedentary in hot conditions (40˚C, 60%RH) until they incurred a ΔBM of 3-4%. Plasma Osmolality (P_{osm}), change in plasma volume, and thirst sensation (range: 1 = not thirsty, to 9 = very thirsty) were measured at baseline, 1%, 2%, 3% dehydration, and 1, 2 and 24 hours following rehydration onset. Rehydration was using recommended guidelines; 120% ΔBM as soon as possible.

Results: Thirst was stimulated substantially (3.9±1.8) by 1% ΔBM in both conditions, and progressed linearly and equivalently, reaching (7.0±1.8) at 3.5% ΔBM. Furthermore, thirst increased in the absence of a rise in ΔP_{osm}, and did not correlate significantly with P_{osm} in either passive (r=0.48) or exercising (r=0.56) dehydration.

Discussion/conclusions: These results indicate that thirst is stimulated early in dehydration (by 1%, in active and passive dehydration), and before measurable rise in P_{osm} or reduction in plasma volume. Therefore, thirst may not be 'too late' for optimal maintenance of fluid balance during either exercise or ambient heat stress.

1. Cannon, W. B. (1918). Croonian Lecture: the physiological basis of thirst. Proceedings of the Royal Society of London. Series B, Containing Papers of a Biological Character, 283-301.
2. Noakes, T. D. (2010). Is drinking to thirst optimum? Annals of Nutrition and Metabolism, 57(1), 9-17.
3. Phillips, P. A. (1985). Osmotic Thirst and Vasopressin release in humans: a double-blind crossover study. Am. J. Physiol, 17(1), 645-650.
4. Sawka, M. N. (2007). American College of Sports Medicine position stand. Exercise and fluid replacement. Medicine and science in sports and exercise, 39(2), 377-390. (pp. 386).
5. Thornton, S. N. (2010). Thirst and hydration: physiology and consequences of dysfunction,. Physiology & behavior, 100(1), 15-21.

1C.4

Flexible perception-action strategies when keeping distance

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Regulating distance is a core task of daily life and many (interactive) sports. For example, activities such as catching or throwing a ball, or defending a goal each requires some form of distance regulation. In rugby, interpersonal distance has been identified as a key control parameter in the 1-vs.-1 sub-phase [1]. However, it is poorly understood how humans can accurately regulate interpersonal distance in sport.

In a series of studies we examined how people use visual information when regulating distance in a "follow-the-leader" task [2]. We manipulated the appearance of pre-recorded

leaders in virtual reality to show more 'local' information, as a point-light display (i.e., providing primarily segmental motion information), more 'global' information, as a uniform shape (i.e., a cylinder providing expansion-retraction information only), and other visual variations. In the first study, the task consisted of back- and forwards walking, aiming to maintain the same (virtual) interpersonal distance (i.e., ΔIPD = 0 *m*). Temporal synchrony was analysed using response times (RT) to each direction change. Participants displayed tighter temporal synchrony in the point-light condition (RT = 101 ± 3.3 *ms*) in comparison to a static cylinder condition (RT = 113 ± 3.2 *ms*). In contrast, spatial synchrony deteriorated in the point-light condition (ΔIPD = -0.21 ± 0.14 *m*) in comparison to the cylinder condition (ΔIPD = 0.01 ± 0.14 *m*). A follow-up study looked at side-to-side follow-the-leader coordination. Preliminary analysis indicates that the point-light condition (19 ± 0.51 *ms*) again resulted in significantly faster response times than the static condition (22 ± 0.45 *ms*). However, spatial synchronization appeared to be negotiated differently as no significant difference between conditions was found for interpersonal distance.

To sum, participants applied flexible strategies when presented with different visual information to regulate interpersonal distance. These findings inform about how perception-action strategies emerge, which could help identifying key processes in skill acquisition and coaching. Overall, it can be argued that being able to select the most adaptable strategy for a given situation may underpin an individual's "interact-ability" [3].

1. Passos, P., Araújo, D., Davids, K., Gouveia, L., Milho, J., & Serpa, S. (2008). Information-governing dynamics of attacker-defender interactions in youth rugby union. *J Sports Sci, 26*(13), 1421-1429.
2. Meerhoff, L.A., De Poel, H.J., & Button, C. (2014*)*. How visual information influences coordination dynamics when following the leader. *Neurosci Lett, 582,* 12-15.
3. Meerhoff, L.A. & De Poel, H.J. (2014). Asymmetric interpersonal coupling in a cyclic sports-related movement task. *Hum Movement Sci, 35,* 66-79*.*

1C.5

Preparing to take the field: a temporal exploration of stress, emotion, and coping in cricket

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Contemporary research focusing on competition stress and emotion has been informed by Lazarus and Folkman's[5] transactional perspective of stress and the cognitive-motivational-relational (CMR) theory of emotions[2-4]. Whilst sport psychology researchers have explored the various coping strategies used by athletes in response to numerous stressors[1,6,7], few studies have: (a) explored the entire stress, emotion, and coping (SEC) process through an approach that encapsulates each component as an interdependent transaction; and, (b) highlighted the coping strategies that are used to manipulate the stress and emotion experience to enable helpful behaviors to be prevalent. Thus, the purpose of this study was to explore the SEC experiences of elite cricketers during the lead-up to the first competitive fixture of the season. Four elite male cricketers (*M* = 21.25, *SD* = 1.5) completed Stress and

Emotion Diaries (SEDs) for a 7-day pre-competition period and on the day of the first competitive fixture of the season. We then used semi-structured interviews to explore the content of the SEDs in more detail and gain more insight into the individual components of the SEC process (e.g., stressors, appraisals, emotions, coping strategies, and behaviors). Through combining inductive and deductive content analysis, the data provided a holistic and temporal exploration of SEC underpinned by the CMR theory of emotions[3]. Specifically, this study adopted innovative means to portray the players' SEC experiences over a prolonged and significant period of time that coincided with approaching competition. The results highlighted the ongoing and continuous nature of the SEC process whilst illustrating the coping strategies (e.g., pre-performance routines, social support, self-talk, and humor) that cricketers use in the lead-up to competition.

1. Devonport TJ. Lane AM. Biscombe K. *Exploring coping strategies used by national adolescent netball players across domains*. *Journal of Clinical Sport Psychology*. *7*(2):161-177, 2013.
2. Lazarus RS. *Emotion and adaptation.* New York: Oxford University Press, 1991.
3. Lazarus RS. *Stress and emotion: A new synthesis.* London: Free Association, 1999.
4. Lazarus RS. *How emotions influence competition in competitive sports*. *The Sport Psychologist. 14*:229-252, 2000.
5. Lazarus RS. Folkman S. *Stress, appraisal, and coping*. New York: Springer, 1984.
6. Thelwell RC. Weston NJV. Greenless IA. *Batting on a sticky wicket: Identifying sources of stress and associated coping strategies for professional cricket batsmen*. *Psychology of Sport and Exercise*. *8*(2):219-232, 2007.
7. Weston NJV. Thelwell RC. Bond S. Hutchings NV. *Stress and coping in single-handed round-the-world ocean sailing*. *Journal of Applied Sport Psychology. 21*(4):460-474, 2009.

1C.6

Chipping in on the role of working memory in children's golf performance

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Little is known about the role of instructions when children acquire skills; however, their ability to process explicit information is a function of working memory capacity[2] that continues to develop throughout childhood[1]. We therefore asked whether children who are instructed with large amounts of information during skill acquisition learn explicitly, and whether their performance is subsequently affected by dual tasking[3]?

Thirteen year old golf novices learned a golf chipping task using one of 3 sets of explicit movement-related rules. Each set of rules was an expert-approved chipping technique. Participants performed two identical sets of post-tests, containing normal retention tests and a dual-task test with concurrent tone-counting. Performance and video data were collected.

Instead of breaking down in the dual task condition, most children benefited from its introduction. Also, technique changed visibly when the dual task was introduced, indicating that children reverted to a simpler movement pattern.

The results indicate that children can be instructed to learn explicitly, but when working memory is constrained they return to a more implicit form of movement control. The change in technique is generally beneficial for dual-task performance. These results are consistent with Hernandez et al.'s (2011) findings that age of acquisition affects the manner in which learned movements are represented in memory.

1. Hernandez, A. E., Mattarella-Micke, Redding, R. W. T., Woods, E. A., & Beilock, S. (2011). *Age of acquisition in sport: Starting early matters*. The American Journal of Psychology, *124,* 253-260.
2. Newell, A., & Rosenbloom, P. S. (1980). *Mechanisms of skill acquisition and the law of practice.*
3. Maxwell, J. P., Masters, R. S. W., & Eves, F. F. (2003). *The role of working memory in motor learning and performance*. Consciousness and Cognition, *12*(3), 376–402.

Session 2A: PSNZ Hubbard and Early Career Prize Finalists

2A.1 Hubbard Prize Contestant 1

Reversal of morphine tolerance by modulating the neuropeptide FF receptor system

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Agonists of the neuropeptide FF receptors (NPFFR1 and NPFFR2) have been generically termed “anti-opioids” for their putative ability to block opioid function. However *in vivo* evidence for this has been limited to nociceptive tests, which are confounded by the pronociceptive effects of the NPFFR ligands. To elucidate the functions of the NPFFRs, we first identified and characterised a true, potent, and selective antagonist, called GJ14. Next, we used the vasopressin neurons of the supraoptic nucleus as a model to examine the anti-opioid function of the NPFFR ligand, RFamide related peptide-3 (RFRP-3). In extracellular single-unit recordings from urethane-anaethetised rats, the spontaneous firing rate of vasopressin neurons was significantly reduced by morphine (i.v. 30 ug/kg). This inhibition was virtually abolished by pretreatment with RFRP-3 (i.c.v. 12 nmol) and morphine sensitivity was recovered 10 min after RFRP-3 treatment. Control rats receiving 3 consecutive morphine treatments alone did not show any change in morphine sensitivity. RFRP-3 alone had no effect on vasopressin neuron firing rate. A challenging notion is that chronic opioid treatment triggers the upregulation of these anti-opioid systems, which in turn attenuates the effect of morphine, thereby producing tolerance. To test this hypothesis, rats were given a continuous dose of morphine (10 mg/kg/day) via osmotic mini pumps for 6 days. Vasopressin neuron reponses to morphine (i.v. 30 ug/kg) were virtually absent in morphine-infused rats, confirming morphine tolerance. Pretreatment with GJ14 (i.c.v. 50 nmol) increased the sensitivity to morphine in vasopressin neurons of tolerant rats. In summary, this is the first evidence demonstrating an anti-opioid function *in vivo* using electrophysiology. Furthermore using our novel antagonist, we report convincing evidence that the NPFFRs are an important part of a genuine anti-opioid system that regulates opioid sensitivity.

2A.2 Hubbard Prize Contestant 2

Divergent regulation of cardiac ryanodine receptor by proteins

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The cardiac ryanodine receptor (RyR2) is the key Ca2+ release channel in the heart. Accumulating evidence indicates that RyR2 interacts with and can be regulated by a large

number of proteins, making the effect of each protein on RyR2 function difficult to discern. Dysregulation of RyR2 can lead to abnormal Ca2+ release, otherwise known as store overload-induced Ca2+ release (SOICR), which can trigger arrhythmia. The molecular mechanisms for dysregulation of RyR2 by proteins are not fully elucidated. This thesis aimed to investigate the regulation of RyR2 by two protein families within the RyR2 complex: a recently identified RyR2 regulator called histidine-rich Ca2+ binding protein (HRC) and its arrhythmogenic HRC S96A mutant form, and a highly controversial family, FK 506 binding proteins (FKBPs) 12.0 and 12.6.

Using a single cell Ca2+ imaging approach, I found that HRC wild type (WT) significantly suppressed the propensity for SOICR by buffering store free Ca2+ and inhibiting store Ca2+ uptake. Interestingly, the S96A mutation within HRC blunted the Ca2+ buffering and Ca2+ uptake inhibitory function, leading to an enhanced SOICR. These findings not only reveal the novel regulatory mechanism by which HRC regulates RyR2, but also offer the mechanism underlying HRC S96A related arrhythmia. Additionally, I found that both FKBP 12.6 and FKBP12.0 regulate RyR2 by facilitating the termination of SOICR without changing the activation of SOICR, leading to a reduced magnitude of SOICR. Importantly, these regulatory functions of FKBPs were abolished by RyR2 catecholaminergic polymorphic ventricular tachycardia (CPVT) mutations (V4653F and R4496C), despite a conserved interaction with RyR2, suggesting that FKBPs play a critical role in regulating RyR2.

Taken together, this thesis has improved the current understanding of regulation of RyR2 by proteins within the RyR2 complex. More importantly, it sheds light on how dysregulation of RyR2 by these proteins can give rise to SOICR and arrhythmia.

2A.3 Early Career Prize Contestant 1

Novel foundations and clinical translation of high-resolution mapping for gastric dysrhythmia

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Gastric contractions are controlled by an underlying electrical event termed 'slow waves', generated by interstitial cells of Cajal (ICC). Gastric slow wave dysrhythmias have been associated with major motility disorders, however, despite a century of investigations, the understanding of gastric dysrhythmia has been inadequate to inform pathophysiology or clinical diagnosis.

This challenge was critically addressed in a targeted program of novel devices, signal processing and software tools, and animal and clinical experimentation. Flexible printed circuit arrays (256 electrodes at 4 mm intervals) were developed and validated for slow wave mapping. Automated algorithms were validated for slow wave event detection, wave clustering, and mapping of activation patterns, velocity and amplitude fields, and these were incorporated into online and offline software packages. A weaner pig model was introduced, and applied in validation studies as well as pre-clinical trials.

These methods were collectively applied in intra-operative first-in-man studies defining baseline human gastric slow wave propagation, including novel descriptions of the gastric pacemaker and regional activity variations.[1] Translation was then progressed in two significant motility disorders of uncertain aetiology: gastroparesis, and 'chronic unexplained

nausea and vomiting'.[2,3] Unlike controls (1/21), patients with gastroparesis (11/12) and CUNV (9/9) routinely demonstrated heterogenous dysrhythmias, which were defined and classified within a new spatiotemporal scheme. Novel human patterns included initiation disorders (stable and unstable ecoptic pacemaking), and conduction disorders (slow wave re-entry and conduction blocks). ICC counts revealed a gradient of cellular depletion from CUNV to gastroparesis; means: 3.5 vs 2.3 bodies/field (vs 5.6 in controls; $P<0.05$). Anisotropic velocity was discovered to accompany dysrhythmia, due to bidirectional ICC coupling within layered networks.

This work represents a new era for gastric dysrhythmia interpretation and diagnosis, through high-resolution mapping. These advances are being applied to develop diagnostic and therapeutic strategies.

1. Am J Physiol 2010;299:585-92.
2. Gastroenterology 2012;143:589-98.
3. Gastroenterology 2015; 149:56-66

2A.4 Early Career Prize Contestant 2

Improving treatment of perinatal hypoxic-ischaemic brain injury

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Moderate to severe hypoxia-ischaemia before or around the time of birth occurs in approximately 2/1000 live births and is associated with death or disability. Hypothermia is the only currently available clinical treatment for these infants, but is only partially effective. We investigated ways to improve hypothermia, either by giving a longer period of hypothermia (five days instead of three days) or giving hypothermia with another potentially neuroprotective agent (blockade of connexin hemichannels, membrane channels that release toxic molecules such as ATP and glutamate after ischaemia).

Chronically instrumented fetal sheep (0.85 gestation) received 30 minutes of bilateral carotid artery occlusion. Hypothermia was induced from three hours after ischaemia and continued until three or five days. Connexin hemichannel blockade was induced with an intracerebroventricular infusion of Peptide 5 from three hours after ischaemia (50 µM for the first hour followed by 50 µM over the next 24 h) with or without simultaneous hypothermia for three days.

Three days of hypothermia was associated with a significant improvement in neuronal survival and recovery of EEG power as well as a significant reduction in seizure activity and inflammation ($p<0.05$). Five days of hypothermia was not associated with any additional neuroprotective effects and was in fact associated with a slight reduction in neuronal survival in the cortex and dentate gyrus ($p<0.05$). Hemichannel blockade started three hours after ischaemia had no effect on cell survival or EEG recovery ($p>0.05$), although seizure activity and secondary cell swelling were attenuated ($p<0.05$). When hemichannel blockade was combined with hypothermia no synergistic effects on cell survival, recovery of EEG power or seizure activity were seen ($p>0.05$).

In conclusion, the neuroprotective effects of hypothermia were not improved by prolonging the duration of treatment or with combination treatment with connexin hemichannel blockade, potentially due to overlapping mechanisms of action.

Session 2B: NZSE Prize Finalists

2B.1 NZSE Prize Contestant 1

Role of prolactin in mediating the hyporesponsiveness of the stress axis during pregnancy and lactation

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Stress during pregnancy and lactation is associated with increased postpartum maternal anxiety, impaired lactation, and the development of an anxiety phenotype in the offspring. To avoid these outcomes, the activity of the maternal hypothalamic-pituitary-adrenal (HPA) axis is attenuated at these times[1]. The mechanism generating this change is unknown; however, the anterior pituitary hormone prolactin may play a significant role. This project aimed to investigate basal HPA axis activity during pregnancy and lactation in the mouse, focussing upon the corticotropin-releasing hormone (CRH) neurons. *In situ* hybridisation was used to characterise *Crh* mRNA expression in the hypothalamic paraventricular nucleus (PVN) of pregnant (Day 18; n=7), lactating (Day 7; n=7) and pup-deprived (24 h) lactating (Day 7; n=7) mice in comparison to virgin controls (n=6). Quantification of *Crh* mRNA-expressing neuron number in the PVN revealed significant reductions in both pregnant (49.6 ± 9.3) and lactating (53.6 ± 4.9) mice in comparison to controls (158.2 ± 21.5, $P<0.0001$), while pup removal, and thus the associated suckling-induced prolactin secretion, partially restored CRH neuron number (107.6 ± 9.4, $P<0.05$ versus lactation). The prolactin receptor has previously been shown to be expressed within the PVN[2]. To determine whether prolactin might be acting on CRH neurons, we used dual-label immunohistochemistry for pSTAT5 (a marker of prolactin action) and tdTomato (a marker of CRH neurons in a CRH-Cre reporter mouse line). While prolactin-induced pSTAT5 could be readily detected in the PVN, there was no colocalisation of prolactin-induced pSTAT5 and tdTomato immunoreactivity, suggesting prolactin does not directly regulate CRH neurons. These data show that basal HPA axis activity is suppressed in late pregnant and lactating mice and suggest a potential role for prolactin in mediating this suppression through an indirect mechanism. Future studies aim to determine the cellular target and precise role of prolactin in mediating maternal HPA axis suppression.

1. Douglas, A.J., P.J. Brunton, O.J. Bosch, J.A. Russell and I.D. Neumann (2003). *Neuroendocrine responses to stress in mice: hyporesponsiveness in pregnancy and parturition.* Endocrinology. 144: 5268-76.

2. Brown, R.S, A.E. Herbison, D.R. Grattan (2011). *Differential changes in responses of hypothalamic and brainstem neuronal populations to prolactin during lactation in the mouse.* Biology of Reproduction. 84: 826-36.

2B.2 NZSE Prize Contestant 2

Decreased permeability of the median eminence in response to acute prolactin elevation

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Prolactin is a multifunctioned hormone, that peaks in the minutes following onset of acute stress. We have previously shown that neuronal processes within the mouse median eminence (ME) respond rapidly to either acute stress or administration of exogenous prolactin through the phosphorylation of Signal Transducer and Activator of Transcription (STAT)5. The ME is a circumventricular organ, responsible for the secretion of hypophyseal hormones into portal blood to regulate pituitary output. Modification of the blood-brain-barrier allows the transport of hypophyseal hormones across this structure. In this study, we examined whether acute administration of exogenous prolactin changes the permeability of the ME. Adult male C57BL/6 mice were treated with bromocriptine over 24h in order to decrease endogenous prolactin. Either ovine prolactin ($2mgkg^{-1}$) or saline was given intraperitoneally, together with 0.1mL 1% Evans Blue for 1h prior to perfusion with 4% paraformaldehyde transcardially. Brains were excised and 16µm cryostat sections prepared. Sections were imaged on a confocal microscope. The perfusion of Evans Blue through the tissue was measured densitometrically in 10µm increments from the superficial vessels on the ventral surface of the ME, to the tanycytic cell bodies on the dorsal surface. Significant reduction in Evans Blue perfusion was observed in the prolactin treated tissue when compared with controls ($p<0.05$). Decreased permeability of the ME in response to elevated prolactin indicates that it may be liable to adaptation and that environmental signals can modify the blood-brain-barrier. As prolactin reduces the accessibility of the ME, circumstances where prolactin is elevated – such as in stress – may affect its permeability to other bloodborne signals, and could effect hypothalamic secretory pathways regulating the stress axis.

2B.3 NZSE Prize Contestant 3

Effects of mesterolone and growth hormone on penis growth in postpubertal Sprague-Dawley rats

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About 45% of men are reported to be unsatisfied with penis size. The effects of a variety of penis enlargement pills and penis enlargement surgeries are often overstated and may have potential health risks. In this study, we investigated the effects of an androgen named mesterolone and recombinant human growth hormone (rhGH) on penis growth of Sprague Dawley rats in postpubertal period. Mesterolone was administrated by oral gavage into 10-week-old rats at doses of 0, 25, 50 or 75 mg/kg/d for 2 weeks. Under non-stress conditions, a high dose of mesterolone (75 mg/kg/d) moderately, but significantly, increased penile length from 3.30±0.04 cm to 3.63±0.06 cm ($p<0.01$). Since exercise stress can cause hormone imbalance, we investigated whether mesterolone has an effect on penis growth under a stress condition by swimming. Interestingly, in comparison to the non-stress conditions, the stress of forced-swimming (10-minute, twice a week) delayed the penile length growth by 31% (2.52±0.05 cm *vs* 3.30±0.04 cm, $p<0.001$). All three doses of mesterolone treatment rescued

swim stress-induced penis growth defects (3.46±0.04, 3.40±0.06 and 3.70±0.08 cm, respectively, all $p<0.001$). Treatment of rhGH injection (3IU/d for two weeks), which is known to promote tissue growth and shorten recovery time, also reversed the stress-induced inhibition of penis growth (3.48±0.02cm, $p<0.001$). No additive effect was observed on penile length when mesterolone and rhGH were co-administered. The pathological examination of rat organs showed that neither mesterolone nor rhGH had visible damage to the heart, liver and testicle cells, but mesterolone treatment led to a slight degeneration of tubular epithelial cells, slight vacuolization of cells in pituitary glands and a slightly thickened aortic vascular wall. However, co-administration of mesterolone and rhGH caused irreversible and serious damage to tubular epithelial cells and pituitary cells. Preliminary gene expression analysis by RT-PCR revealed that mesterolone (75mg/kg/d) mildly increased the expression of growth-related genes, such as *Vegf 110, Vegf 164* and *Androgen receptor (AR)* in penile tissue under non-stress condition, suggesting that mesterolone may promote penis growth through regulating the expression of these genes. Therefore, our results demonstrate that mesterolone or rhGH alone potentially promoted penis growth in postpubertal rats to gain a larger penis size, and without inducing significant pathological changes in various organs. However, combination treatment with mesterolone and rhGH had no additive effect on penis growth but induced serious pathological damage in pituitary glands, raising a safety concern of combination drug-endocrine treatment.

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2B.4 NZSE Prize Contestant 4

Leptin receptor signalling in AgRP neurons modulates puberty

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The adipose-derived hormone leptin is required to communicate metabolic information to hypothalamic gonadotropin releasing hormone (GnRH) neurons, which are the central drivers of reproduction. Metabolic signals provided by leptin are integrated with the reproductive system so that fertility can be closely linked with metabolic status. GnRH neurons do not possess leptin receptors, indicating that leptin must act through intermediate leptin responsive neurons to exert its effects[1]. Research has also shown that the neurons which are critical for leptin-to-GnRH signalling are GABAergic, which narrows the pool of candidate populations involved in this transfer of information[2]. The arcuate nucleus (ARC) of the hypothalamus contains two main leptin-responsive neuronal populations; agouti related peptide (AgRP)/neuropeptide Y (NPY) neurons and proopiomelanocortin (POMC) neurons. AgRP/NPY neurons are an attractive candidate population for control of reproduction by leptin as they are GABAergic and possess leptin receptors, and NPY is known to negatively modulate GnRH function. We investigated whether leptin actions on AgRP/NPY neurons are required for normal fertility using cre-lox transgenics. Transgenic female mice that did not express leptin receptors specifically on AgRP/NPY neurons exhibited a 3 day delay in the onset of first estrous compared to littermate controls ($P<0.05$). However no deficits were observed in adult fertility data when compared to control females. No significant differences were

observed between male control and male AgRP/NPY leptin receptor knock outs when considering puberty onset and adult fertility. This provides evidence that AgRP/NPY neurons are involved in leptin's effects on development of reproductive function in female mice. A follow-up experiment is using leptin receptor null mice in which the receptor is 'rescued' only in AgRP/NPY neurons to determine whether leptin signalling in this neuronal population is sufficient for normal fertility.

1. Quennell, J. H., et al. (2009). "Leptin indirectly regulates gonadotropin-releasing hormone neuronal function." Endocrinology 150(6): 2805-2812.

2. Zuure, W. A., et al. (2013). "Leptin signaling in GABA neurons, but not glutamate neurons, is required for reproductive function." The Journal of Neuroscience 33(45): 17874-17883.

2B.5 NZSE Prize Contestant 5

Ablation of hypothalamic RF-amide related peptide (RFRP) neurons with diphtheria toxin: effects on anxiety behaviours and LH pulses

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RFRP-3 is a neuropeptide known for inhibiting central regulation of fertility. Recently it has been shown that central RFRP-3 infusions in rodents stimulate stress axis hormone secretion and anxiety-related behaviours. These findings may not reflect physiological RFRP-3 fluctuations since central concentrations of this peptide are unknown. This study aims to demonstrate a role for endogenous RFRP-3 in such responses by characterising the resulting behavioural phenotype in RFRP-3 deficient mice using a novel transgenic technique to specifically ablate RFRP neurons. A new transgenic mouse line in which the *Rfrp* gene also produces Cre recombinase was crossed with a line that enables Cre-dependant expression of the diphtheria toxin receptor. Consequently, injecting the offspring with diphtheria toxin resulted in apoptosis of cells expressing *Rfrp* (1.5±0.33 vs. 9.25±1.7 RFRP neurons/brain section in RFRP-Cre and control mice respectively; $P<0.05$).

We hypothesised that RFRP neuron ablation would have an anxiolytic effect. RFRP deficient mice (13 male and 14 female) were compared against non-cre expressing controls (10 male and 10 female) for anxiety behaviour (elevated plus maze [EPM] and light/dark box tests), obsessive-compulsive behaviour (marble-burying test) and depression (forced swim test) 4 weeks post-diphtheria toxin treatment.

RFRP deficient mice spent similar times in aversive areas compared to controls in the EPM (18.3±2.4 vs. 21.2±2.7%, respectively $P=0.43$) and light/dark box (21.8±2.2 vs. 29.8±4.6% respectively, $P=0.13$). Similarly, RFRP-3 ablation had no significant effect on the marble burying ($P=0.97$) and active swimming duration in the forced swim test ($P=0.48$).

These findings suggest that endogenous RFRP neurons are not required for the acute anxiety responses modeled here, although they may still be involved in chronic affective disorders. Current experiments are looking at the effect of acute stress on LH pulsatility in RFRP neuron ablated mice, results of which may reveal RFRP neurons to be a link between stress and fertility.

Session 2C: SESNZ Keynote Lecture and Free Communications

2C.1 SESNZ Keynote Lecture

When the fastest rider doesn't win: exploring the influence of opponents on performance in cycling races

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In order to provide cycling coaches with information that can be used to improve athlete performance, it seems pertinent to establish the factors underlying success in race environments. Researchers have tended to examine the performance of athletes in simplified environments, often through lab-based testing or in non-interactive competition formats. By examining the components of performance independent of the race environment, the dynamics that result from direct-interaction between opponents are often overlooked and an incomplete understanding of the factors affecting performance is formed[1,2,3,4]. In cycling it is not necessarily the most powerful rider, or the one who has the best aerodynamics that will win the race, instead it is the rider who knows how to use those factors to their advantage that will succeed[5]. I will present research exploring the relationships between time-trial (non-interactive) and mass-start (interactive) race performances of riders in various cycling disciplines, supporting the assertion of Jeukendrup & Martin (2001) that the fastest athlete does not always win. The direct interaction that occurs between opponents in mass-start events appears to have a strong influence on the performances of elite cyclists, resulting in higher values of performance variability and reduced predictability in finish rankings, suggesting riders are able to mitigate physiological disparities and gain tactical advantages over their opponents in mass-start races. I will explore potential approaches for identifying the mechanisms underlying the changes observed in elite cyclists performances in direct-interaction race formats, and whether these mechanisms can be trained, constrained or manipulated to improve athlete performance.

1. Glazier, P. S. (2010). *Game, Set and Match ? Substantive Issues and Future Directions in Performance Analysis.* Sports Med, 40(8), 625–634.
2. Gréhaigne, J. F., Bouthier, D., & David, B. (1997). *Dynamic-system analysis of opponent relationships in collective actions in soccer.* Journal of Sports Sciences, 15(2), 137–149.
3. McGarry, T. (2009). *Applied and theoretical perspectives of performance analysis in sport: Scientific issues and challenges.* International Journal of Performance Analysis in Sport, 9, 128–140.
4. Vilar, L., Araújo, D., Davids, K., & Button, C. (2012). *The role of ecological dynamics in analysing performance in team sports.* Sports Medicine, 42(1), 1–10.
5. Jeukendrup, A. E., & Martin, J. (2001*). Improving Cycling Performance: How Should We Spend Our Time and Money.* Sports Med, 31(7), 559–569.

2C.2

Recovery strategies in elite athletes: Do they help or hinder performance?

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As the training requirements for elite athletes increase, the role of adequate recovery becomes an integral component of improving athletic performance between training sessions and competitions.[1, 2] It is thought that incorporating recovery strategies following exercise will enhance subsequent training quality, improve competition performance, reduce the risk of developing overtraining syndrome and reduce the risk of acquiring an injury.[1] However, recent research would suggest that over-using recovery strategies in a training environment may actually blunt the muscular adaptation to training, leading to performance decrements.[3] This presentation will outline what some of the latest literature is saying about the commonly-used recovery strategies, [1, 2, 4, 5] including what works and what doesn't and will pose the question of whether using recovery strategies is even worthwhile for elite athletes.[6]

1. Rattray B, Argus C, Martin K, Northey J, Driller M. Is it time to turn our attention toward central mechanisms for post-exertional recovery strategies and performance? Frontiers in Physiology. 2015;6:79.
2. Driller M,Halson S. The effects of lower-body compression garments on recovery between exercise bouts in highly-trained cyclists. Journal of Science and Cycling. 2013;2.
3. Fröhlich M, et al. Strength training adaptations after cold-water immersion. Journal of Strength and Conditioning Research. 2014;28:2628-2633.
4. Argus C, Driller M, Ebert T, Martin D, Halson S. The effects of 4 different recovery strategies on repeat sprint-cycling performance. International Journal of Sports Physiology and Performance. 2013;8:542-548.
5. Northey J, Driller M, Argus C, Etxebarria N, Rattray B. Vascular Occlusion and Sequential Compression for Recovery Post Resistance Exercise. Journal of Strength and Conditioning Research. 2015;In Press.
6. Halson SL, et al. Does hydrotherapy help or hinder adaptation to training in competitive cyclists. Medicine and Science in Sports and Exercise. 2014;46:1631-1639.

2C.3

Gradual modification of task constraints in the environment causes implicit motor learning

Masters, R.S.W.[1,2], Poolton, J.M.[2,3], Gao, R.[2]

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Implicit motor learning occurs when a skill is acquired without conscious access to the knowledge that underpins effective performance of the skill [1]. Advantages of implicit motor learning include stable performance under psychological pressure and physiological stress [2]. We examined whether subtle modification of constraints in the environment can be used to cause implicit motor learning by producing movement adaptations of which the learner has no conscious awareness. Participants were asked to learn a line-out throwing task in which they threw a ball over a horizontal bar to a target. The height of the bar was subtly increased in each block of trials until the participant became aware of the change in height. Post-testing was conducted without a bar.

The range of increments at which changes in the height of the crossbar (relative to the previous height) went undetected was extreme, ranging from one training session (a single 4.5cm increment) to nine training sessions (nine 4.5cm increments, 40.5 cm). On average, most participants became consciously aware of a change in crossbar height only after the

crossbar was raised by a staggering 22.5 cm. Kinematic analysis suggested that the trajectory of throws became more elevated as the height of the bar increased and remained elevated during the post-test, despite the absence of a bar over which to throw. The findings suggest that subtle modification of task constraints in the environment can cause implicit motor learning.

1. Masters, R.S.W. (1992). Knowledge, knerves and know-how: The role of explicit versus implicit knowledge in the breakdown of a complex motor skill under pressure. *British Journal of Psychology*, 83, 343-358.
2. Masters, R.S.W. & Poolton, J. (2012). Advances in implicit motor learning. In N.J. Hodges & A.M. Williams (Eds.), *Skill Acquisition in Sport: Research, Theory and Practice* (2nd ed) (pp. 59-75). London: Routledge.

2C.4

Nonlinear pedagogy: A constraints-led approach to teaching movement skills

Button, C[1]., Lee, M.C[2]., Tan, C.W[3]., Komar, J[4,5] & Chow, J-Y[2].

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Historically, physical education pedagogy has been dominated by linear approaches in which the teacher is espoused with the responsibility of instructing groups of learners how to move more effectively. However, nonlinearity in human movement systems is omnipresent and must be accounted for in the philosophy and design of pedagogy (1). Emerging theoretical concepts from ecological dynamics have important implications for how PE teachers plan lessons, deliver instructions, structure tasks and provide informational constraints to learners. Nonlinear pedagogy specifies an individualized approach to learning, focusing on how each learner is able to satisfy the interacting constraints that are present in particular learning situations. In Singapore, the Ministry of Education has recently invested in a schools-based research programme aimed at examining the relative benefit of nonlinear pedagogy in contrast to a traditional, linear approach. The results indicate that children can learn to perform movement skills as effectively when taught with a nonlinear approach as a linear approach (2). Importantly, the nonlinear approach helped to develop important characteristics of skilled behaviour such as skill transfer, creativity, and individual movement solutions, which are not the primary emphasis of a traditional PE teaching approach.

1. Chow, J. Y., Davids, K., Button, C., Shuttleworth, R., Renshaw, I., & Araujo, D. (2007). The role of Nonlinear pedagogy in physical education. *Review of Educational Research, 77*(3), 251-278. doi: 10.3102/003465430305615
2. Lee, M. C., Chow, J. Y., Komar, J., Tan, C. W., & Button, C. (2014). Nonlinear Pedagogy: An Effective Approach to Cater for Individual Differences in Learning a Sports Skill. *PloS One, 9*(8). doi: 10.1371/journal.pone.0104744.

Session 3A: PSNZ Triennial Medal and Free Communications

3A.1

Molecular synergy between microtubule-stabilising agents given in combination

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Microtubule-stabilising agents (MSAs) cause mitotic block by preventing spindle breakdown during mitosis. Taxanes and epothilones are MSAs that are used clinically to treat solid tumours of the breast, lungs, and ovary. Most MSAs bind to the □-tubulin subunit of □□-heterdimers which form the protofilaments of microtubules. There are two known binding sites for MSAs, the taxoid site and the laulimalide/peloruside site. If two MSAs, one that binds the taxoid site and one that binds the laulimalide/peloruside site, are added in combination, a synergistic effect on cell growth is usually observed. For example, paclitaxel and peloruside A, which differentially bind the two sites on □-tubulin, can synergise to cause a greater stabilization than the additive effects of the two compounds on their own; whereas, paclitaxel and epothilone, which bind the same site, do not show synergy when added in combination. Synergy between MSAs has relevance to treatment in the clinic because the concentration of each MSA can be decreased while achieving a greater anti-tumour response. Recent crystallographic analysis has identified the drug-tubulin interactions at the two main binding sites for the MSAs zampanolide and epothilone (taxoid site) and laulimalide and peloruside (alternative site). Epothilone co-occupies the same □-tubulin subunit as laulimalide or peloruside, thus providing a molecular basis for the observed synergistic interactions between these compounds. In addition, both laulimalide and peloruside directly interact with the adjacent protofilament in the microtubule, indicating a biochemically different mechanism of stabilization that might contribute to the synergy with taxoid site MSAs. The possible use of combination therapy of two MSAs in cancer treatment has the potential to increase anti-tumour effects in the clinic and possibly prevent development of resistance to the drugs.

3A.2

Functioning of Ishikawa cancer cells is dependent on the physical microenvironment, which can modify genetic activities

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Although contemporary treatments provide particular instances of improvements in cancer survival, overall, successes are very modest and patients often suffer disabling side effects. The drugs' efficacies can be contrasted with the effects of antibiotics on infectious diseases.

Here, our studies provide evidence that the physical microenvironment is fundamental in the behaviour of cancers, and could therefore be considered as a target of therapies. Mechanical

forces in the form of physical exercise were recognised more than a half century ago to enhance health (1) and later also to reduce mortality in cancer patients (2).

Effects of forces of the biomechanical nano/microenvironment were studied using polystyrene moulds (both positive-convex and negative-concave) of endometrial cancer cell line cultures as substrates for another culture of the cancer cells. We investigated behaviours of cells grown on the cell-like topography compared to cells grown on traditional flat substrates.

We observed differences in expression of proteins that were involved in the direct interaction between cells and the microenvironment (higher integrin and FAK, lower cytokeratin-18) and, using iTRAQ, different protein expression in six cell functional compartments (nuclear activity, cell adhesion, ECM components, cell cytoskeleton, progression behaviours and energy generation). Additionally morphological area was less in cells on imprinted substrate and, importantly, growth was less.

Thus, altering the physical topographical nano/microenvironment affected functional activities of the cancer cells, in the absence of drugs and in the absence of genetic variation. Our results are consistent with the idea that the physical nano/microenvironment can have higher status than genes in cell function, and that "exercise normalises the workings of the body" (3) whereas "corruption of mechanics" underlies onset of diseases (4).

1. Ballard-Barbash et al *JNationalCancerInstitute* 2012;104:815.
2. Morris et al *Lancet* 1953;265:1053.
3. Kuper & Morris *Financial Times* 2009, Sep 12.
4. Jonietz & Weaver *Nature* 2012;491:S56.

3A.3

Active maintenance of the gradient of refractive index is required to sustain the optical properties of the lens

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As a transparent optical element in the eye, the lens allows light rays to pass through it with minimal scattering, while its curved surfaces and the presence of an inherent gradient of refractive index allows the lens to focus light onto the retina. But the lens is not a passive optical element and possesses a unique cellular physiology that generates circulating ionic and fluid fluxes that actively maintain its transparent properties. In this study we show that these circulating fluxes also contribute to the refractive properties of the lens and that inhibition of these fluxes can impair overall visual quality. Using MRI techniques we have extracted the 3D surface geometry and refractive index profiles from bovine lenses organ cultured in solutions that either preserve or inhibit these circulating fluxes. Then using optical modelling software we have calculated the effects inhibiting circulating fluxes have on the optical properties of the lens and overall vision quality in an optical model of the bovine eye. Our results show that inhibiting circulating ionic and fluid fluxes causes changes to lens water

content, the water to protein ratio and surface geometry that manifest as an increase in optical power and a decrease in negative spherical aberration. In particular inhibition of the Na^+ pump creates a marked myopic shift which caused images to be formed in front of the retina. This experimentally induced change in the optical properties of the lens resembles the myopic shift observed clinically in patients who go on to develop lens cataract.

Supported by the Marsden Fund

3A.4

Cushing's mechanism is blunted in conscious hypertensive but not normotensive rats

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In 1901, Cushing described a 'simple and definite law' where experimentally increasing intracranial pressure (ICP) produces matching increases in blood pressure (BP), in order to maintain cerebral perfusion. In the ensuing years, the characteristic hypertension, bradycardia and respiratory irregularity known clinically as 'Cushing's Triad' has been largely viewed as a last ditch protection for the severely ischemic brain. We propose that Cushing's Mechanism may be an important but overlooked physiological regulator of BP[1], and that it may contribute to chronic hypertension.

Conscious normotensive (Wistar; n=4) and spontaneously hypertensive (SH; n=4) rats were instrumented to record BP and ICP via telemetry, and allowed to recover for at least seven days. On the day of the experiment, ICP was increased via successive 2, 5 & 10 µl/min icv infusions of artificial cerebrospinal fluid (20 minutes each). Cerebral perfusion pressure (CPP) was calculated in real-time, as the difference between BP and ICP.

Although baseline ICP was similar between groups (7.8±0.8 vs 7.9±1.0 mmHg; Wistar vs SH), the infusion-driven elevation in ICP tended be higher in SH (+6.3±0.5 mmHg) compared to Wistar rats (+4.2±0.4 mmHg). This increase in ICP was matched with a similar increase in MAP in Wistar rats (+3.3±1.0 mmHg from 95±1 mmHg baseline), while in SH rats despite the larger rise in ICP, MAP *decreased* (-5.6±2.9 mmHg from 147±6mmHg baseline). Thus CPP fell in SH (-12±2 mmHg) but not Wistar rats (-1±1 mmHg).

The blunted pressor response to increased ICP in SH rats may suggest that Cushing's Mechanism is already engaged and supporting arterial hypertension. This may leave SH rats more vulnerable to perturbations in cerebral perfusion. Further experiments will explore the nature of this interaction.

1. Paton *et al*. (2009) *Harvey Cushing and the regulation of blood pressure in giraffe, rat and man: introducing 'Cushing's mechanism'*. Experimental Physiology. *94(1):11-7.*

3A.5 Triennial Medal Lecture

Physiological lies and other fetal tales

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"It is a lie to suggest that any fetus, never mind the preterm fetus, can be exposed to asphyxia *in utero* and survive! To suggest that preterm fetuses can survive for longer than term fetuses frankly beggars belief. It is well established that the preterm fetus is far too immature to cope with such insults, Dr Bennet!"

Cleary the reviewer to my first paper on the preterm fetal responses to asphyxia had a particular view of fetal life. To be fair, at the time he was not alone in believing that life before birth was fragile and even more so for the preterm fetus. After all, babies born preterm are at significantly greater risk of mortality and morbidity. Despite evidence to the contrary it stood to reason that prematurity equals physiological immaturity and thus exquisite vulnerability to such insults. This talk will demonstrate why this conclusion is, however, a physiological lie, at least in part

Why do we care? Simple. If we do not understand the fundamental physiology then we cannot hope to determine mechanisms mediating injury or develop effective treatments. Conservatively, 50% of all preterm babies will have impaired neurodevelopment, in large part due to fetal exposure to adverse events such as infection and hypoxia. Currently there are no specific treatments to prevent injury or to facilitate normal brain development, and no effective biomarkers for the detection of the at-risk infant. This talk will discuss research from our lab and others on the preterm fetal physiological adaptation to such events, why boys are at a greater disadvantage, how standard clinical treatments given during preterm birth such as steroids must be factored into understanding about mechanisms of injury, and finally how all of this informs our current approach to the development of treatments and biomarkers.

1. Stuffrein-Roberts, S., Allelic expression patterns in psychatric candidate genes. PhD Thesis in Pathology. 2008, University of Otago: Christchurch. p. 216.
2. Kikin, O., L. D'Antonio and P.S. Bagga (2006). QGRS Mapper: a web-based server for predicting G-quadruplexes in nucleotide sequences. Nucleic acids research. 34: W676-82.

Session 3B: NZSE Nancy Sirett Lecture and Free Communications, and MedSci Infoblitz

3B.1 Nancy Sirett Memorial Award Lecture

Heart hormones: Physiology as the key link between discovery and translation

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The heart has been recognised as an endocrine organ for more than 3 decades with the discovery of atrial and B-type natriuretic peptides (ANP and BNP respectively) during the 80's. Early studies by our group in large experimental animal models (sheep) and man showed ANP infused at physiologically relevant doses played important roles in volume and pressure homeostasis. The natriuretic peptides (NP's) also demonstrate an array of hemodynamic, renal and hormonal effects that are beneficial in heart failure. Discovery of a number of circulating forms of the NP's by our group and concurrent development of sensitive and specific assays for these peptides led to foundational studies underpinning the world wide use of NP's as biomarkers for diagnosis, prognosis and hormone guided treatment of heart failure. NP's are cleared by a combination of a specialised clearance receptor (NPR-C) and

enzymatic degradation by neutral endopeptidase (NEP) 24.11. With the development of suitable antagonists/inhibitors studies in sheep showed both pathways contributed equally to clearance and the compounds were shown to be effective in raising the levels and bioactivity of NP's, thus offering potential as therapeutic agents. Whilst pre-clinical and early phase clinical trials showed promise, phase III studies with one combined NEP/ACE inhibitor (omapatrilat) showed little benefit along with unwanted side-effects. Results from a recent trial with a combined NEP inhibitor/ATR antagonist (PARADIGM-HF) has re-opened the possibility that manipulation of NP levels may prove an effective therapeutic option in heart failure.

3B.2

The role for cGP in autocrine regulation of IGF-1 in obesity and hypertension

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Background: Impaired Insulin-like growth factor-1 (IGF-1) function is associated with obesity and hypertension, but the correlation of circulating IGF-1 with these conditions is weak. As a metabolite of IGF-1, the ratio of cyclic Gly-Pro (cGP)/IGF-1 which regulates IGF-1 bioavailability may be a more accurate biomarker of IGF-1 function in obesity and HT.

Methods: 40 women were selected from a longitudinal study of women since their first pregnancy, grouped as obese (OB) + hypertensive (HT); OB + normotensive (NT); non-obese (NO) + HT; NO + NT status at both 15 weeks gestation and 6 years post-partum. The 20 women with HT had only their 6 year post-partum samples analysed, and the other 20 women had samples from both time points analysed (OB-OB, NO-NO). A further 20 women were selected on the basis of change in OB status between first pregnancy and 6 years post-partum [(OB-NO and NO-OB) with samples from both time points analysed. Plasma samples were analysed for IGF-1, IGFBP-3 and cGP using ELISA and HPLCms.

Results: At 6 years post-partum: plasma IGF-1 levels were significantly lower among the OB (p=0.001) group; cGP was significantly lower among the HT group (p=0.043) as was IGF-BP3 (p=0.046); cGP/IGF-1 ratio was not different among HT, but significantly higher among OB (p=0.0055) groups. In the paired samples at 15 weeks gestation and 6 years post-partum: the change in plasma IGF-1 was significantly lower in the OB-NO (p=0.0049) and OB-OB (p=0.018) groups compared to NO-NO; change in cGP was not different among the 4 groups; change in cGP/IGF-1 ratio was greater in the OB-NO (p=0.01) and OB-OB (p=0.006) groups than NO-NO; change in IGFBP3 was lower in the NO-OB (p=0.03and OB-NO (0.0001) groups compared to NO-NO.

Conclusions: Increase in cGP/IGF-1 ratio is observed in obesity but not hypertension. The collective responses of reduced IGFBP-3 and increased cGP/IGF-1 ratio may be essential to weight loss rather than weight gain.

3B.3

Flavonoid inhibition of Glucose Transporter 2 (GLUT2) mediated glucose transport in a HEK293-GLUT2 inducible cell line

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Glucose transporter 2 (GLUT2) is a low-affinity, high-capacity carrier protein that facilitates glucose transport across cell membranes. GLUT2 is found in the cellular membranes of pancreatic β and liver cells as well as the basolateral and apical membranes of the gut epithelium. Rapid insertion of GLUT2 into the apical membrane of gut epithelial cells occurs in the fed state when luminal glucose concentrations become elevated (>20 mM), enhancing glucose uptake capacity and the potential for hyperglycaemia [1]. Obesity and Type 2 diabetes mellitus are associated with dysregulation of apical GLUT2 mediated glucose uptake [2].

To identify plant-derived dietary components that may modulate GLUT2-mediated glucose transport, we developed a GLUT2-expressing, inducible cell line (HEK293-GLUT2). Using this cell line, we have quantified the effect of plant compounds on GLUT2-mediated transport by measuring the uptake of [^{14}C]-2-deoxy-glucose, a non-metabolisable glucose analogue. Structure function relationships were investigated using a range of flavonoids e.g. quercetin IC_{50} 5.9 µM, luteolin IC_{50} 9.3 µM and phloretin IC_{50} 10.1 µM, phloridzin no inhibition. Key structural determinates were the planar orientation of the molecule and the presence of hydroxyl groups on the 3' and 4' position of the B ring. Using this screening tool, we have also identified a number of proprietary plant extracts with GLUT2-inhibitory activity as low as IC_{50} 9.7 µg/mL. The potential for these extracts to reduce post-prandial hyperglycaemia is currently under investigation.

1. Kellett, G.L. and P.A. Helliwell, The diffusive component of intestinal glucose absorption is mediated by the glucose-induced recruitment of GLUT2 to the brush-border membrane. Biochem J, 2000. 350 Pt 1: p. 155-62.
2. Ait-Omar, A., et al., GLUT2 accumulation in enterocyte apical and intracellular membranes: a study in morbidly obese human subjects and ob/ob and high fat-fed mice. Diabetes, 2011. 60(10): p. 2598-607.

3B.4

The role of CaMKII activation in atheroma formation in the ApoE-null mouse

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Atherosclerosis is a progressive condition characterised by the formation of plaques and lesions along the arterial lumen[1]. Critically, atherosclerosis is a key precursor to the development of stroke and heart failure, and thus is the leading cause of death in New Zealand and the World. It is now well recognized that reactive oxygen species (ROS) are initiators of the inflammation that underlies the atherogenic process. However the molecular agents through which ROS trigger and maintain this chronic inflammation remain unclear. A potential transducer of pathological ROS is calcium/calmodulin kinase II (CaMKII). CaMKII is a multifaceted enzyme expressed in vascular smooth muscle cells and involved in vascular

homeostasis. The production of ROS has been suggested to be dependent on CaMKII expression in the vasculature. More recently, post-translational modification of CaMKII by ROS has contributed to its pathological signalling in cardiac hypertrophy and heart failure. This project aims to define the role of CaMKII in early atheroma formation. We will examine whether CaMKII activity and expression is modified in the atherosclerotic milieu. Using a mouse model of atherosclerosis (ApoE-null), we will measure expression levels and modification status of CaMKII within the atherosclerotic vessels. We hypothesise that, in the atherosclerotic environment, CaMKII activity and post-translational modification will be increased. Our data will contribute to the current understanding of signalling processes that underlie atherogenesis.

1. Ross R & Glomset JA. (1976). *The pathogenesis of atherosclerosis (first of two parts).* The New England journal of medicine **295,** 369-377.

3B.5

Role of arcuate nucleus GABA neurons in female fertility and the pathophysiology of polycystic ovary syndrome

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Neural networks inside the hypothalamus orchestrate the control of fertility. Gonadotropin-releasing hormone (GnRH) neurons are the central regulator cells of reproduction in the brain of vertebrates. During fetal development, disruption of those circuits can result in infertility as we can observe in the pathophysiology of Polycystic Ovary Syndrome (PCOS). Using prenatal androgen (PNA) exposure in mice we can model PCOS features. Dr. Campbell's research group has revealed a novel hypothalamic pathway from GABA neurons in the arcuate nucleus of the hypothalamus (ARN) to GnRH neurons that may sustain the neuroendocrine abnormalities of PCOS. Projections from ARN GABA to GnRH neurons are increased in PNA mice, with GnRH neuron cell bodies and dendrites receiving approximately 30% greater innervation [1]. However, we still lack functional information about the relevance of ARN GABA-GnRH network controlling fertility and how/when, the androgen imprinting during development could trigger PCOS features. In my PhD project I will investigate whether the ARN GABA-GnRH circuitry abnormalities of PNA mice are hard-wired during embryonic development or established following pubertal development; trying to reverse the circuitry phenotype using flutamide (an androgen receptor antagonist). The next step is to evaluate whether ARN GABA neurons are required for GnRH/LH pulsatility and fertility. We will assess this question with channel-rhodopsin 2 (ChR2) optogenetic activation of ARN GABA neurons and its ablation with GABA cell apoptosis via genetically engineered Caspase 3 technique.

1. Moore AM, Prescott M, Marshall CJ, Yip SH, Campbell RE: Enhancement of a robust arcuate GABAergic input to gonadotropin-releasing hormone neurons in a model of polycystic ovarian syndrome. Proc Natl Acad Sci U S A 2015 Jan 13;112:596–601.

3B.6

Investigating GABAergic input to GnRH neurons at the time of the preovulatory surge

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The hypothalamic-pituitary-gonadal axis is a hormone feedback loop that is essential for fertility in mammalian species. Located at the top of this loop in the hypothalamus are the gonadotropin releasing hormone (GnRH) neurons. Pulsatile GnRH release stimulates pulsatile release of the gonadotropins from the pituitary, luteinizing hormone (LH) and follicle-stimulating hormone (FSH), which act on the gonads to produce sex steroid hormones. Females exhibit a surge in GnRH/LH release necessary for ovulation. At the time of the LH surge, a specific subpopulation of activated GnRH neurons exhibit a robust increase in somatic and dendritic spine density. Spines are small membranous protrusions and are believed to be indicative of excitatory input to a neuron. This plasticity suggests an increase in excitatory input to activated GnRH neurons at the time of the LH surge. Previous work in the Campbell laboratory found no differences in glutamatergic input to activated GnRH neurons, suggesting that, unexpectedly, the increase in spine density does not correlate with increased glutamatergic input. Interestingly, the typically inhibitory neurotransmitter GABA can have excitatory effects on GnRH neurons. My aim is to determine if the increase in spine density observed in activated GnRH neurons at the time of the preovulatory surge is associated with increased GABAergic input. In order to assess this we have collected brain tissue from GnRH-GFP transgenic female mice at the time of the preovulatory surge. Brain sections have undergone immunohistochemistry to identify cFos, a marker of cell activation, the vesicular GABA transporter, to identify GABAergic terminals, and GFP, to visualize GnRH neurons. Quantification of the density of GABAergic inputs to GnRH neurons will determine whether increased GABA inputs could be responsible for increased GnRH neuron plasticity and activation at the time of the preovulatory surge.

3B.7

Modulation of GABAergic synaptic input to CRH neurons by oxytocin

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The stress response is controlled by corticotropin-releasing hormone (CRH) neurons which are located within the paraventricular nucleus (PVN) of the hypothalamus. The excitability of CRH neurons is controlled by glutamate and GABA synapses which relay stress-relevant information from other brain centres. Oxytocin (OT) neurons are located in close proximity to the CRH neurons and previous research suggests that OT locally released within the PVN regulates stress axis excitability. We hypothesised that OT may act by modifying GABAergic inhibitory synaptic input to CRH neurons.

To study CRH neuron excitability, we have used patch-clamp recordings from GFP expressing CRH neurons in acute coronal brain slices from male and female mice. To isolate GABAergic

synaptic inputs, excitatory glutamate neurotransmission was blocked with 6-cyano-7-nitroquinoxaline-2,3-dione (CNQX).

Bath application of 1μM OT for 5 minutes had no effect on the frequency or amplitude of spontaneous inhibitory postsynaptic currents (sIPSCs; $p>0.05$, $n = 8$). Furthermore, application of the OT and vasopressin antagonist, Manning Compound (5μM), had no significant effect on sIPSC frequency or amplitude ($p>0.05$, $n = 6$) indicating that there is no endogenous action of either peptide in the brain slice.

To determine if OT modifies action potential dependent GABA transmission we used electrical stimulation to evoke GABA release onto CRH neurons. Interestingly, our results show a trend for enhanced amplitude of GABAergic synaptic currents and a decreased paired-pulse ratio.

These findings indicate that OT may regulate GABAergic synaptic inhibition onto CRH neurons under certain conditions. Ongoing experiments are determining the mechanisms by which OT regulates GABA synapses.

3B.8

Moderate aerobic exercise prevents the onset of diabetic heart disease through modulation of cardiovascular miRNAs

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Diabetes mellitus is a serious risk factor for the onset and development of heart disease. Exercise has been shown to be beneficial in diabetic patients with heart disease, although the high intensity level is often unsustainable. Heart specific microRNAs (miRs) appear to be adversely altered long before the heart disease is well-established, implicating miR's as a potential diagnostic biomarker for the onset of heart disease. Therefore, we hypothesize that the use of miR's as an effective biomarker for the early detection of cardiac dysfunction will allow the initiation of a moderate and sustainable exercise regime that will effectively prevent the progression of heart disease in diabetes.

To test this hypothesis, we will subject age-matched obese and lean diabetic (*db/db*) mice to one of three different exercise intensities; 1) low, 2) moderate or 3) high intensity, before or after the onset of cardiac dysfunction. Non-exercise obese and lean db/db mice act as controls. Each mouse is subjected to one hour of exercise, 5 days/week for 8 weeks. Each exercise protocol consists of 10 bouts of 5 min run, interspersed by 2 min of rest. Plasma samples will be collected and echocardiography will be done before the exercise regime, and then at week-2, -4, -6 and -8 of exercise so as to assess whether exercise prevents or reverses cardiac dysfunction. We have previously verified several cardiac-specific miRs in the regulation diabetic heart disease. Therefore, at the end of the study, we aim to assess 1) the role of these cardiac-specific miRs in the early detection of diabetic heart disease and, 2) whether the early intervention of 'moderate' exercise has a cardio-protective effects in terms of cardiac dysfunction, based on remodeling, angiogenesis/collateral growth and regenerative capacity (using immunohistochemistry and western blot techniques).

In conclusion, this study serves to provide important data identifying miRs as a novel predictor of heart disease in diabetes and, thus, allowing the early intervention of a moderate exercise regime as part of a healthy lifestyle.

Session 3C: SESNZ Free Communications and Debate

3C.1

Cerebrovascular effects of exercise; sprint exercise is a missing piece of the puzzle

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Introduction. *Why is cerebral blood flow (CBF) important?* The brain requires both adequate and relatively constant perfusion; acutely, too much CBF can cause aneurysm whereas too little causes syncope, and oscillating perfusion may increase redox and oedematous stress. Chronically, insufficient CBF or its poor control may impair neurovascular coupling and neural tolerance to stress, thereby affecting executive functions (e.g., short-term memory), quality of life and the risk for dementia (esp. Alzheimer's disease). *What determines brain blood flow?* Cerebral metabolism governs perfusion requirements, but the localised matching of perfusion to requirements (i.e., neurovascular coupling) depends on local factors (e.g., NO bioavailability, CO_2 reactivity, vascular density and compliance) and factors upstream in the cerebrovasculature or systemically (esp. arterial PCO_2, arterial compliance, arterial pressure and its profile, cardiac output, and sympathetic outflow). *Exercise acutely and chronically impacts all of these determinants of CBF and its control.* And, because different forms of exercise may have markedly different effects on each determinant, understanding the acute and chronic effects of different forms of exercise is important. What seems particularly surprising is that the effect of maximal-intensity cycling exercise on CBF and its control remains unknown, yet is highly relevant to both health and performance contexts, both acutely and chronically. While rapid increases in arterial pressure and cardiac output might raise CBF at the outset of exercise, cerebral autoregulation, hypocapnia, SNS outflow and reduced TPR might be counteractive thereafter.

Aim. To further examine effects of exercise parameters on CBF during exercise and recovery; maximal-intensity sprint cycling exercise (Wingate), and recovery posture.

Methods. In this ongoing study, nine healthy adults are undertaking three exercise sessions of Wingate exercise, in randomised order (7+ d apart); one 30-s Wingate test with upright or supine recovery, or three Wingate tests, 50 min apart. Cerebrovascular function is assessed from the CBF velocity in the middle cerebral artery (2-MHz Doppler) and prefrontal cortex oxygenation (Near-Infrared Spectroscopy), concomitant to systemic factors (Arterial Pressure and $P_{ET}CO_2$), as continuously as possible during exercise and recovery.

Results. This presentation will summarise research by ourselves and others on the acute and chronic effects of exercise on CBF and its control, before briefly presenting findings from this study on the acute effects of maximal-intensity cycling.

3C.2

Stemming the tide: will compulsory physical education classes have any effect on childhood obesity?

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The body weight of New Zealand children continues to increase unabated, resulting in a high prevalence of obesity in our young people ranging from 10% in boys to 11% in girls[1]. These figures are even worse for Maori (17%) and Pacific children (23%)[1]. Obesity is associated with a number of health problems in adults but also in children[2]. Because of the overall reach schools have in most children's lives, schools and in particular physical education within schools, have been suggested as an ideal place to influence children's physical activity and thereby energy expenditure levels. Such interventions are particularly relevant in New Zealand primary schools which, since 1987, have removed the directive statements within the school curriculum requiring compulsory time allocation for physical education. We hypothesized that the re-introduction of compulsory 30 min physical education classes given 3 times per week would help to increase energy expenditure sufficiently to reduce the energy imbalance gap and consequently reduce body mass gains in children. In this presentation we will mathematically model the latest available data to test this hypothesis.

1. Ministry of Health. The Health of New Zealand Children 2011/12. Key findings of the New Zealand Health Survey. Wellington: Ministry of Health, 2012.
2. Thompson D, Edelsberg J, Colditz GA, et al. Lifetime health and economic consequences of obesity. Arch Intern Med 1999;159(18):2177-2183.

3C.3

Energy expenditure associated with prolonged sitting, regular activity breaks, and physical activity

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Sedentary behaviour brings about a unique set of physiological mechanisms associated with an increased risk of cardio-metabolic disease independent to those related with a lack of physical activity. Regular activity breaks from sedentary behaviour impart acute metabolic benefits in terms of postprandial glycaemia and insulinaemia (Peddie et al., 2013). However, it is unknown whether regular activity breaks elicit a cumulative effect on post exercise metabolism thereby increasing energy expenditure compared to a similar amount of exercise conducted in a single bout. Therefore the aim of this study was to compare the energy expenditure of prolonged sitting with regular activity breaks and recommended levels of physical activity. Six male and 18 female (n=24) participants, aged 18-34 years, completed a randomised-controlled crossover study with four separate two day (12 h total) interventions: (1) Prolonged sitting; (2) Sitting with regular activity breaks (2 min of moderate intensity

walking every 30 min); (3) Prolonged sitting with 30 min of moderate intensity walking at the end of day 1; (4) Sitting with both regular activity breaks and 30 min of moderate intensity walking at the end of day 1. All walking was undertaken on a treadmill at a speed and incline to elicit 60% VO_2 max. Indirect calorimetry was used to estimate energy expenditure. Participants consumed weight based standardised meals during the intervention and an ad libitum meal was fed at the conclusion of day 2. Preliminary results of the mixed model regression showed that when compared to prolonged sitting energy expenditure was 781 kJ (95% CI 426 kJ to 1135 kJ; p<0.001) greater for the physical activity, 1808 kJ (95% CI 1458 kJ to 2157 kJ; p<0.001) greater for regular activity breaks, and 2812 kJ (95% CI 2463 kJ to 3161 kJ; p<0.001) greater for the combined intervention. The energy expenditure associated with the regular activity breaks intervention was 1027 kJ (95% CI 673 kJ to 1382 kJ; p<0.001) greater than that associated with the physical activity intervention. Regular activity breaks from sedentary behaviour can have an important effect on cumulative daily energy expenditure which may be beneficial to energy balance and overall health.

1. Peddie, M. C., Bone, J. L., Rehrer, N. J., Skeaff, C. M., Gray, A. R., & Perry, T. L. (2013). Breaking prolonged sitting reduces postprandial glycemia in healthy, normal-weight adults: a randomized crossover trial. Am J Clin Nutr, 98(2), 358-366.

3C.4

Exercise-induced increase in serum zinc level is higher following aerobic exercise involving maximal intensity, running or untrained individuals – a systematic review and meta-analysis

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The majority of zinc is found within the musculoskeletal system, providing enzymatic activities for metalloenzymes, such as lactate dehydrogenase. Zinc depletion leads to reductions in cardiorespiratory function and muscle endurance. Zinc losses during exercise, especially through sweat, are well documented. However, conflicting results have been reported for changes in circulating and tissue zinc concentrations following exercise. The present systematic review aims to quantify the acute effects of aerobic exercise on markers of zinc status in humans. We conducted a systematic review of peer-reviewed papers published up to December 2014 for studies that investigated the acute effects of exercise on zinc biomarkers. Meta-analyses were conducted to determine the changes in serum zinc concentration following exercise. Forty-five studies were included in the systematic review. Sufficient data were available from 34 studies (46 comparisons) to quantify the change in serum zinc following exercise. Serum zinc concentration significantly increased immediately after exercise (0.45 ± 0.12 µmol/L, *P*<0.001; mean ± SE). Serum zinc level was higher after exercising maximally (0.77 ± 0.20 µmol/L, *P*<0.001), running (0.71 ± 0.26 µmol/L, *P*=0.006) and in untrained individuals (0.65 ± 0.19 µmol/L, *P*=0.001). During exercise recovery, serum zinc concentration was lower than pre-exercise values (-1.31 ± 0.22 µmol/L, *P*<0.001). This review shows greater disturbances in serum zinc level following high intensity exercise in

previously inactive individuals; this has clinical implications for exercise prescription and dietary management in chronic diseases, where suboptimal zinc status may exist.

Posters

MedSci Posters

P1

Optogenetic activation of RP3V kisspeptin neurons stimulates luteinizing hormone release in mice

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Ovulation is a process that is critical for fertility in all mammalian species. However, the mechanism though which rising levels of estrogen activate the gonadotropin-releasing hormone (GnRH) neurons to drive the pre-ovulatory surge of luteinizing hormone (LH) remains unknown. Recent studies have suggested that kisspeptin neurons in the rostral periventricular nucleus of the third ventricle (RP3V) may be important in mediating estrogen positive feedback to the GnRH neurons. Using an optogenetic approach, we aimed to investigate whether the direct activation of RP3V kisspeptin neurons could alter the secretion of LH in ovariectomized (OVX), estrogen-treated female mice.

The blue light-activated cation channel: channelrhodopsin-2 (ChR2) was targeted to RP3V kisspeptin neurons by injecting a Cre-dependant adeno-associated virus (AAV) bilaterally into the RP3V of OVX *Kiss1*-IRES-*Cre* mice. Following this, mice were placed on a gonadal steroid-replacement regimen that reliably generates an LH surge. On the afternoon of the day that mice would exhibit an LH surge, they were anaesthetized with isoflourane, which blocks the LH surge, and implanted with an optic fibre to enable the optogenetic activation of RP3V kisspeptin neurons *in vivo*. RP3V kisspeptin neurons were then activated with pulses of blue light (5ms in duration) at a frequency of 10Hz for 15 minutes. Blood samples were collected via tail tip before, during and after optogenetic stimulation and were later assayed for LH concentrations using an ELISA.

In ovariectomized, estrogen-treated *Kiss1*-IRES-*Cre* mice, the optogenetic activation of RP3V kisspeptin neurons at 10Hz for 15 minutes significantly increased LH (ng/mL) levels (n=5, pre: 1.66 ± 0.45, post: 7.32 ± 1.54; $p<0.05$). These results provide the first direct evidence that RP3V kisspeptin neurons can regulate the secretion of LH in mice *in vivo*, and lend support to the hypothesis that RP3V kisspeptin neurons drive the activation of GnRH neurons at the time of the pre-ovulatory GnRH/LH surge.

P2

Abstract "Photoperiodic regulation of Wnt signalling in the arcuate nucleus of the Djungarian hamster, *Phodopus sungorus*"

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The Wnt pathway, well characterized in cellular development, was shown to play an important role in the adult central nervous system. We previously identified the Wnt pathway as a novel integration site of the adipokine leptin in mediating its neuroendocrine control of metabolism in obese mice. Here, we investigated whether Wnt signalling plays an important role on seasonal body weight regulation and in the hypothalamus of the Djungarian hamster (*Phodopus sungorus*), a seasonal mammal that exhibits profound annual changes in leptin sensitivity. We furthermore investigated whether crucial components of the Wnt pathway are regulated in a diurnal manner. We first examined mRNA expression of key components of the Wnt pathway in the arcuate nucleus of hamsters acclimated to either long day (LD) or short day (SD) photoperiod by *in situ* hybridization. We detected elevated expression of the genes WNT-4, Axin-2, Cyclin-D1 and SFRP-2 during LD compared to SD, as well as a diurnal regulation of the genes Axin-2, Cyclin-D1 and DKK-3. Next, we investigated the effect of photoperiod as well as leptin on the activation of the Wnt co-receptor LRP-6 by immunohistochemistry. The number of phosphorylated (activated) LRP-6-(Ser1490)-immunoreactive cells in the arcuate nucleus was elevated during LD relative to SD, as well as in animals from both photoperiods that were treated with leptin (2 mg/kg body weight) compared to controls. These findings suggest that differential Wnt signalling is associated with seasonal body weight regulation and is partially regulated in a diurnal manner in the adult brain. Furthermore, they provide further evidence that this pathway plays a key role in the neuroendocrine regulation of body weight and integration of the leptin signal.

P3

Defining the neuropeptide expression of GABA neurons in the arcuate nucleus of the mouse

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Fertility is controlled by a small population of neurons that reside in the basal forebrain known as the gonadotropin-releasing hormone (GnRH) neurons. These neurons control the release patterns of gonadotrophins from the anterior pituitary, which drive gametogenesis and steroidogenesis. Circulating steroid hormone levels provide feedback to the GnRH neurons via a complex upstream neural network, that is essential for mediating appropriate GnRH neuron activity. Recent work has defined a previously unknown, robust neural circuit between a population of steroid hormone-sensitive GABAergic neurons in the hypothalamic arcuate nucleus (ARN), and GnRH neurons residing in the preoptic area. This circuit has functional relevance, as it is enhanced in a common syndrome causing infertility. While GABAergic input to GnRH neurons is thought to be predominantly excitatory, the activity of GABA on GnRH may be modulated by release of co-expressed neuropeptides that are known regulators of GnRH neuron activity. We therefore aimed to quantify the co-expression of

relevant neuropeptides with the ARN GABAergic population, specifically neuropeptide Y (NPY) and kisspeptin neurons.

Immunohistochemistry for NPY (n=10) or kisspeptin (n=4) was performed on fixed brain slices from colchicine-treated adult female VGAT-Cre$^{(+,-)}$;floxed-stop-tdTomato$^{(+,-)}$ mice. Confocal z-stacks were collected throughout the ARN, co-expression of ARN GABA neurons with NPY or kisspeptin was calculated. Among neurons expressing GABA, 35.3 ± 0.8% co-expressed NPY, while just 1.3 ± 0.3% expressed kisspeptin. Among NPY neurons, 94.2 ± 0.4% expressed GABA, while 13.3 ± 1.3% of kisspeptin neurons expressed GABA.

These results indicate that over one-third of ARN GABA neurons express NPY, a neuropeptide with known regulatory effects on GnRH neurons. By comparison, very few ARN GABA neurons express the important regulatory neuropeptide, kisspeptin. This highlights the importance of defining this neural population to inform future studies aimed at understanding the functional significance of this robust circuit.

P4

Prolactin Signalling in the Arcuate Nucleus of Pregnant and Lactating Mice

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The pleiotropic anterior pituitary hormone prolactin has multiple functions throughout the body, including its well-known lactogenic action. Prolactin regulates its own release through a "short-loop" negative feed-back system mediated by tuberoinfundibular dopaminergic (TIDA) neurons located in the arcuate nucleus of the hypothalamus. When stimulated by prolactin these neurons release dopamine, which inhibits further prolactin release from the anterior pituitary. During lactation prolactin levels must however be allowed to rise to meet the physiological demands of motherhood. Data from our own and other laboratories, indicate that while the TIDA neurons remain responsive to prolactin during this time they switch from dopamine to enkephalin production.

This current study used qPCR to determine changes in the mRNA levels of the dopamine synthesizing enzyme tyrosine hydroxylase (TH) and the enkephalin precursor during late-pregnancy and lactation. Using hypothalamic micropunches we showed that TH mRNA was markedly decreased (approx. 4-fold $P<0.01$) while enkephalin mRNA increased (approx. 11-fold, $P<0.001$) during pregnancy. These alterations were largely maintained during lactation. In a second series of experiments a transgenic mouse, lacking prolactin receptors on forebrain neurons, was used to determine if neuronal prolactin receptors were required for this increased enkephalin expression in the TIDA neurons. Immunohistochemistry showed that while the number of enkephalin-positive cells in the arcuate nucleus was significantly increased in late-pregnancy (compared to diestrus controls $P<0.001$), this did not occur in the prolactin receptor deleted animals. These studies have shown that the previously reported changes in TIDA neuron behaviour in TIDA neurons during late-pregnancy and lactation is mirrored by alternation in mRNA expression. Furthermore this plasticity appears to be mediated by prolactin receptors located on neurons.

P5

The murine adrenal gland is responsive to immune signals *in vivo*

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The acute stress response, often termed fight or flight, is largely facilitated by the activity of the adrenal medulla. The chromaffin cells of the adrenal medulla produce catecholamines and neuropeptides in response to various stressors. These stressors can be physical or psychological in origin, and there is evidence that immune challenge may also be recognised by the adrenal glands as a form of stress. Earlier studies have shown that the adrenal medulla is responsive to signals from the immune system, such as interleukin-6 (IL-6), interleukin-1, tumour necrosis factor alpha and histamine. Research from our lab has previously demonstrated an increase in phosphorylated Signal Transducer and Activator of Transcription 3 (pSTAT3) phosphorylation in isolated bovine chromaffin cells treated with the pro-inflammatory cytokine IL-6. The current study aims to investigate the murine adrenal gland response to inflammatory signals from the immune system *in vivo*, using lipopolysaccharide (LPS) to induce an endogenous cytokine cascade. Male mice were administered 10µg/kg LPS by i.p injection, and were deeply anaesthetised after 3h, before perfusion with 4% paraformaldehyde. The adrenal glands were removed, and 10µm sections cut and processed for immunohistochemistry to examine the phosphorylation of STAT3, a transcription factor activated by various cytokines including IL-6. Dual-label immunofluorescence was also performed using anti-pSTAT3 alongside tyrosine hydroxylase (TH) as a marker of chromaffin cells. LPS treatment induced a dramatic increase in pSTAT3 in the adrenal medullary chromaffin cells compared to saline only controls ($p<0.005$). A pSTAT3 response could also be seen in the cortex ($p<0.005$), the bulk of immunoreactivity seen in the zona glomerulosa, and the staining decreasing in the zona fasciculata. Further experiments are currently underway using LPS alongside an IL-6 blocking antibody to determine whether this increase in pSTAT3 can be attributed to IL-6.

P6

A model of mechanical stress in airway smooth muscle.

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Several in vitro studies have investigated the effect of imposing mechanical length oscillations equivalent to those occurring in tidal breathing on isolated, contracted airway smooth muscle (ASM), and established that these oscillations cause a substantial reduction in force and muscle stiffness. Our Institute has demonstrated that this force reduction can be enhanced with higher frequency oscillations superimposed on tidal breathing. Additional studies have investigated the interaction between the force reduction effect caused by tidal stretch oscillations and those resulting from bronchodilating agonists administered at therapeutic concentrations.

ASM crossbridge disturbance may be considered the primary mechanical process responsible for airway relaxation in this clinically-important mechanism. This paper focuses on analysis of

the combined effects of a bronchodilator in conjunction with Super-Imposed Length Oscillations (SILO), applied mechanical oscillations alone, and applied mechanical oscillations in conjunction with SILO, in order to investigate and determine characteristic ASM mechanical loss due to perturbation of the actinomyosin crossbridges.

Modeling the exponential decay of mechanical stress in the tissues proposes a novel characterization method for ASM mechanics. Constants and terms are defined which are unique to applications of mechanical and pharmaceutical treatment of ASM tissue. From this model, an empirical relationship between force, stress, strain and the rate constant of ASM activity is generated. The characteristics are proposed indicators of perturbation of the ASM mechanical crossbridge elements relative to those processes which define parameters for normal tidal breathing oscillations.

P7

Developing a novel synthetic muscle system with peristaltic actuations using counter-pulsation to assist heart function

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Congestive Heart failure (CHF) presently affects 5 million people in America with approximately 550,000 of new cases diagnosed each year [1]. CHF is a term that describes various complications of heart diseases that reflects on the abnormal functionality of the human heart whereby the heart lacks pumping power to move oxygenated blood around the body. It affects all ages and genders and more than half of the diagnosed patients die within five years of diagnosis [1].

The aim is to produce a synthetic muscle that binds around the descending aorta (DA) and by applying the concept of counter-pulsation with peristaltic movement to the synthetic muscle; increase the coronary blood flow and decrease the cardiac afterload during a cardiac cycle. The study is based on adapting an idea from Sunshine Heart where they have produced a heart assisting device called C-Pulse. Their device uses pneumatic balloon cuff that wraps around an ascending aorta (AA) where the cuff pumps in rhythm of a natural heartbeat; producing a thumbprint like depression on to an AA wall [2].

The synthetic muscle would use a two-layer material that pneumatically actuates with peristaltic movement in a multi chamber air cavity. The peristalsis of the muscle is determined by the cardiac pressure, flow and pulse wave velocity (PWV) output in collaboration with counter-pulsation; to efficiently move blood in a DA by inflation and deflation of the muscle. An artificial aorta with near realistic features has been fabricated for testing the theory. The synthetic muscle is to reduce cardiac afterload and increase aortic pressure and flow to reduce stress on the heart. The significants of this study should provide not only an operational heart assisting prototype but also a better understanding of how modelling aortic pressure, flow and PWV can potentially diagnose or even predict CHF.

Physiological Society of New Zealand Posters

P8

BDNF and TrkB expression are not changed in the hypothalamic supraoptic and paraventricular nuclei during the development of angiotensin II-dependent hypertension

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Arginine vasopressin (AVP) magnocellular cells of the hypothalamic paraventricular nucleus (PVN) and supraoptic nucleus (SON) secrete AVP into the bloodstream, causing vasoconstriction and reabsorption of water from the kidneys. These actions increase arterial blood pressure. Normally, AVP neuron activity is inhibited by a tonic GABAergic input that is activated by a relay of afferent inputs that are, in turn, activated by arterial baroreceptors. Low blood pressure decreases this inhibition of AVP neurons, permitting AVP release to return blood pressure towards normal.

Paradoxically, AVP neuron firing rate is increased during the development of angiotensin II-dependent hypertension in rats to a similar degree to that evident during salt-loading. Increased AVP neuron activity induced by salt-loading is driven by increased brain-derived neurotrophic factor (BDNF) activation of TrkB receptors on AVP neurons. Hence, we hypothesised that increased BDNF signalling through TrkB receptors on AVP neurons increases AVP neuron activity during the development of hypertension. We used the Cyp1a1-Ren2 transgenic rat model in which angiotensin II-dependent hypertension can be induced through the addition of indole-3-carbinol to the diet.

We carried out western blotting on lysates from hypertensive and non-hypertensive rats to determine whether there is increased phosphorylated TrkB (a marker of TrkB activation) and BDNF expression in the PVN and SON of hypertensive rats. There was no difference between the relative expression of pTrkB in the PVN of non-hypertensive rats (0.178) and hypertensive rats (0.282; $P = 0.60$, unpaired t-test; $n = 7 – 8$) or the SON of non-hypertensive rats (0.037) and hypertensive rats (0.015; $P = 0.32$, $n = 5 – 8$). Likewise, there was no difference in the relative expression of BDNF in either of the nuclei. In conclusion, BDNF-TrkB signalling in the SON and PVN does not appear to drive the increased AVP neuron activity evident during the development of angiotensin II-dependent hypertension.

P9

Extract of *Houttuynia cordata* Thunb. improves fat accumulation and dyslipidemia in rats fed with high-fat diet

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Obesity is a significant health problem and has been increasing continuously around the world[1]. Obesity is associated with dyslipidemia and fat accumulation in liver and adipose tissue. Extract of *Houttuynia cordata* Thunb. (HE), a herb that had the action of anti-oxidant,

anti-inflammation, anti-bacteria, and anti-obesity[2]. However, it is still unclear about the effects of HE on fat accumulation in liver and adipose tissue, and dyslipidemia in high-fat diet-induced obese rats. Therefore, we examined the effect of HE by dividing Sprague-Dawley rats into three groups. Each group was fed with different diet for 12 weeks. The first group was control group, which was fed with normal standard rat chow diet. The second group was fed with high-fat diet (HFD) and the third group was fed with high-fat diet containing 1%HE. Body weight and food intake were measured throughout the study. Fasting blood samples were collected to measure lipid profiles and histology of liver and mesenteric adipose tissue was done after the treatment. HFD rats showed a significant increase in body weight. After the HE treatment, body weight was significantly decreased with no significant difference in food intake. Moreover, cholesterol, triglycerides, and low density lipoprotein were significantly decreased after the HE treatment. However, high density lipoprotein did not change after the HE treatment. In addition, HE attenuated fat accumulation in liver and mesenteric adipose tissue. These results suggest that HE may be useful for alternative treatment for fat accumulation and dislipidemia in obesity.

1. Nguyen, D.M., and El-Serag, H.B. The epidemiology of obesity. Gastroenterol Clin North Am. 2010; 39(1): 1–7.

2. Miyata, M., Koyama, T., and Yazawa, K. Water extract of Houttuynia cordata Thunb. leaves exerts anti-obesity effects by inhibiting fatty acid and glycerol absorption. J Nutr Sci Vitaminol 2010; 56(2): 150–6.

P10

Changes in brain N-acetylaspartate after transcranial direct current stimulation in patients with spinal cord injury and neuropathic pain: A pilot study

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Research has shown that anodal transcranial direct current stimulation (tDCS) reduces neuropathic pain (NP) in individuals with spinal cord injury (SCI).[1] Research has also found lower levels of N-acetylaspartate (NAA) in the primary motor cortex (M1) and thalamus in individuals with NP, relative to those without NP, and that NAA levels in these areas are negatively associated with pain intensity [3]. Moreover, lower levels of NAA has also been found in the anterior cingulate cortex (ACC) in individuals with NP [4]. These findings suggest the possibility that the analgesic effects of tDCS may be associated with changes in NAA concentrations. To test this hypothesis, 10 individuals with SCI and NP were given 20 minutes of 2 mA anodal tDCS over the left M1 for 5 consecutive days, and NAA were measured at left M1, left thalamus and left ACC before and after treatment. We found significant pre- to post-treatment increases in NAA/Cr levels in the left M1 cortex and ACC ($p = 0.022$ and $p = 0.005$, respectively), although we observed no significant changes in left thalamus NAA/Cr levels (p=

0.798). The findings are consistent with the possibility that anodal tDCS may be effective, at least in part, because of its effects on M1 cortical excitability[1, 6-8], as reflected by changes in NAA levels. These changes in M1 activity may produce an analgesic effect via M1's influence on (1) subcortical (thalamus) activity (i.e., a cortico-subcortical pathway) and (2) cortical (ACC) activity (i.e., a cortico-cortical pathway) [9,10]. Future research in larger groups of individuals with NP is needed to evaluate the reliability and generalizability of these findings, and to determine if the effects of tDCS on NAA levels are merely incidental to, or reflect the specific mechanisms of, the analgesic effects of tDCS.

1. Ngernyam N, Jensen MP, Arayawichanon P, Auvichayapat N, Tiamkao S, Janjarasjitt S, Punjaruk W, Amatachaya A, Aree-uea B, Auvichayapat P.The effects of transcranial direct current stimulation in patients with neuropathic pain from spinal cord injury. Clin Neurophysiol. 2015 Feb;126(2):382-90.
2. Fukui S1, Matsuno M, Inubushi T, Nosaka S. N-Acetylaspartate concentrations in the thalami of neuropathic pain patients and healthy comparison subjects measured with (1)H-MRS. Magn Reson Imaging. 2006 Jan;24(1):75-9. Epub 2005 Dec 19.
3. Pattany PM1, Yezierski RP, Widerström-Noga EG, Bowen BC, Martinez-Arizala A, Garcia BR, Quencer RM. Proton magnetic resonance spectroscopy of the thalamus in patients with chronic neuropathic pain after spinal cord injury.AJNR Am J Neuroradiol. 2002 Jun-Jul;23(6):901-5.
4. Chang L1, Munsaka SM, Kraft-Terry S, Ernst T. Magnetic resonance spectroscopy to assess neuroinflammation and neuropathic pain. J Neuroimmune Pharmacol. 2013 Jun;8(3):576-93.
5. Simmons ML1, Frondoza CG, Coyle JT. Immunocytochemical localization of N-acetyl-aspartate with monoclonal antibodies. Neuroscience. 1991;45(1):37-45.
6. Mori F, Codecà C, Kusayanagi H, Monteleone F, Buttari F, Fiore S, Bernardi G, Koch G, Centonze D. Effects of anodal transcranial direct current stimulation on chronic neuropathic pain in patients with multiple sclerosis. J Pain. 2010 May;11(5):436-42.
7. Fregni F, Boggio PS, Lima MC, Ferreira MJ, Wagner T, Rigonatti SP, Castro AW, Souza DR, Riberto M, Freedman SD, Nitsche MA, Pascual-Leone A. A sham-controlled, phase II trial of transcranial direct current stimulation for the treatment of central pain in traumatic spinal cord injury. Pain. 2006 May;122(1-2):197-209. Epub 2006 Mar 27.
8. Sakrajai P, Janyacharoen T, Jensen MP, Sawanyawisuth K, Auvichayapat N, Tunkamnerdthai O, Keeratitanont K, Auvichayapat P. Pain reduction in myofascial pain syndrome by anodal transcranial direct current stimulation combined with standard treatment: a randomized controlled study. Clin J Pain. 2014 Dec;30(12):1076-83.
9. Polanía R, Paulus W, Nitsche MA. Modulating cortico-striatal and thalamo-cortical functional connectivity with transcranial direct current stimulation. Hum Brain Mapp. 2012 Oct;33(10):2499-508. doi: 10.1002/hbm.21380. Epub 2011 Sep 16.
10. Yoon EJ1, Kim YK, Kim HR, Kim SE, Lee Y, Shin HI. Transcranial direct current stimulation to lessen neuropathic pain after spinal cord injury: a mechanistic PET study. Neurorehabil Neural Repair. 2014 Mar-Apr;28(3):250-9.

P11

Identifying the functional role of microrna-34a in diabetic cardiac stem cells

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Diabetes mellitus is a chronic metabolic disorder hallmarked by an increase in blood glucose levels. Type 2 diabetes patients have been associated with a greater risk of developing heart

disease, a phenomenon referred to as diabetic heart disease (DHD). DHD is characterised by changes in the structure and function of the myocardium, including increased left ventricular mass, fibrosis and ventricular dilation. At present, treatment for ischaemic heart and subsequent heart failure include drugs, angioplasty, thrombolytic therapy and heart transplantation. Recent studies on stem cell transplantation to the injured myocardium present the potential to improve functioning of the diseased heart. Recent research has shown this therapy is not effective in diabetic patient's post-MI.

Cardiac stem cells (CSCs) which are resident in the heart, possess typical characteristic of stem cells such as self-renewal, clonogenicity and multi-potency. They are believed to play a crucial role in the maintenance of heart functionality and cardiac repair. CSCs are currently used in cell therapy to treat the patients following MI who are resistant to conventional treatment regime and will develop cardiac failure. Among type 2 diabetics, there is marked modulation of microRNAs (miRs) before the development of structural and functional changes. miRs are short, non-coding single-stranded RNA molecules that modulate both physiological and pathological pathways by adversely regulating the gene expression.

The aim of this study is to determine the role of miR-34a in diabetic cardiac stem cells in both acute and chronic diabetic states. Firstly, the expression of miR-34a in these cells will be measured which is hypothesised to be upregulated. Consequently, miR-34a will be knocked down to determine the effect of miR-34a on diabetic stem cell survival, proliferation and senescence. Ultimately, modulating miR expression within diabetic CSCs to restore their proliferation and differentiation ability could help produce sustained effects during cell therapy; thus improving cardiac function, proliferation and survival of cardiomyocytes.

P12

Withdrawn

P13

COMMD10: A novel regulator of the protein trafficking pathway?

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Protein trafficking encompasses the synthesis and targeting of proteins, such as ion channels and lysosomal hydrolases, to their appropriate cellular destination.

Two vesicular populations, COPI and COPII, are crucial for trafficking between the ER and Golgi, for transport through the Golgi as well as protein delivery and are, thus, crucial for this pathway. COMMD10 (Copper Metabolism Murr1 Domain Containing protein 10) is a member of the COMMD family of proteins and has no known function. The family's founding member, COMMD1, has a number of cellular functions including the regulation of copper homeostasis, regulation of sodium uptake through ENaC and the inhibition of NF-κB. Preliminary data has suggested that COMMD10 interacts with COPI-associated proteins including Arf1, a small GTP binding protein crucial for COPI-mediated trafficking from the Golgi to the ER, which also has various other functions throughout the trafficking pathway. Our work aims to identify

whether COMMD10 is a novel regulator of protein trafficking. Initial findings from this study suggest co-localisation of COMMD10 and Arf1, both in its wild-type form as well as a constitutively active form and a constitutively inactive form. However, no co-localisation was observed between COMMD10 and other Arf family members (Arf4 and Arf5) suggesting an Arf1 specific function for COMMD10. Using a cell-line in which COMMD10 is stabily knocked down we have identified a change in localisation of the active form of Arf1 suggesting a potential role for COMMD10 in the recruitment of Arf1 to the Golgi membrane or in keeping Arf1 at the Golgi membrane.

P14

Mechanotransduction of ENaC and the extracellular matrix

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Epithelial Na^+ channels (ENaCs) belong to a highly conserved protein family whose members were found to be mechanosensitive. From *Xenopus* oocytes it is known that shear force (SF) sensation of ENaC depends on an interaction with the extracellular matrix (ECM). The present study characterizes whether or not mammalian expression systems could provide a good alternative allowing investigations of the mechanism of how ENaC senses SF involving the ECM. Human αβγ ENaCs were transfected in HEK293 cells. The activity of ENaC was measured as transmembrane currents by the whole cell patch clamp technique. For SF application (0.01 dyn/cm^2) a flow chamber in combination with a flow rate controlled perfusion system was used. High flow rates (30 dyn/cm^2) were generated by a perfusion through a pipette placed in front of the cell of interest. Transmission electron microscopy (TEM) was applied to visualize the ECM. SF increased membrane currents in just about 30% of the experiments independent from the SF intensity, in which membrane currents increased from -993 ± 256pA in absence of SF to -1305 ± 264pA during SF application ($p<0.001$; n=10). TEM pictures revealed a well-established ECM of HEK293 cells. Furthermore, it was observed that the thickness of the ECM decreased from 30µm to 18µm as cell passage number increases. The activation of ENaC in HEK293 cells by SF varies strongly which can be reasoned by changes of the ECM as observed by electron microscopy. Therefore, it can be concluded that HEK293 cells are not an ideal expression model for SF examinations on ENaC, unless further research establishes cultivation conditions that do not affect the composition/formation of the ECM of HEK293 cells.

P15

The effect of remote ischemic preconditioning on cardiac specific microRNAs in the diabetic heart

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Diabetes mellitus is a chronic metabolic disorder which is becoming increasingly prevalent throughout the world, with cardiovascular disease (CVD) being the leading cause of death in

diabetes. Remote ischemic preconditioning (rIPC) is a procedure in which short bouts of sublethal ischemia, followed by reperfusion, is applied in a remote region of the body (e.g. in the arm with a blood pressure cuff) and is able to produce cardioprotective effects in the heart. However, the mechanisms behind the protective effects of rIPC are still elusive. microRNAs (miRs) are short, non-coding, RNA molecules which are known to be involved in the post-transcriptional regulation of gene expression. miRs are rapidly gaining interest, as they have been shown to be implicated in the pathogenesis of various diseases, including many cardiovascular complications. This study aims to look at the effect of rIPC on the diabetic heart, and whether it is able to prevent/delay the onset of cardiac disease through the modulation of miRs which are known to be expressed in the heart (miR-1, miR-34a, miR-15a, and miR-15b). Diabetic (n=6) and non-diabetic (n=6) mice were subjected to weekly rIPC protocol, consisting of four cycles of 5 minutes of hindlimb blood flow occlusion and 5 minutes of reperfusion, over an 8 week period. Age matched sham animals that did not undergo rIPC protocol were used as controls. Cardiac function was assessed using echocardiography and peripheral blood samples were collected fortnightly over the duration of the study. Peripheral blood samples were used to measure the expression of the miRs of interest using RT-PCR analysis. The study is currently ongoing with all the experimental protocols being optimised. After 8 weeks, hearts will be excised and cardiac tissue will be used to evaluate the expression of miRs and the protective effect of rIPC on the diabetic heart.

P16

Central modulation of cardiac sympathetic nerve activity following acute myocardial infarction

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Acute myocardial infarction (MI) is a global health problem costing around 7.4 million lives every year. One of the main contributing factors to the high mortality associated with acute MI is an adverse increase in cardiac sympathetic nerve activity (SNA). Once established, the sustained increase in cardiac SNA is essentially irreversible, even with the use of sympathetic beta receptor blockers. The increased drive for SNA is most likely central in origin. However, the regions (or nuclei) of the brain involved in the generation of increased SNA immediately after MI are unknown. Therefore, this study aimed to assess activation of specific brain nuclei associated with SNA immediately following MI, which might contribute to the increased cardiac sympathetic nerve activity.

We first established a robust time course of changes in cardiac SNA following acute MI (achieved by ligation of left anterior descending coronary artery) by using a standard multi fiber direct nerve recording technique. Cardiac SNA began to increase immediately following acute MI and became significantly elevated (by 37.44 ± 8.27%) at 16 min post-MI (P = 0.022, one way ANOVA) and remained elevated throughout the four hours of recording. We next determined which specific regions of brain become activated in the early stages following acute MI. Rats were transcardially perfused under anesthesia 90 min following the induction of MI. Immunohistochemistry for Fos protein was performed on brain sections to identify specific localized neuronal activation. Acute MI was associated with a significantly higher (P=0.0002, unpaired t-test) number of Fos-positive cells in the paraventricular nucleus (PVN)

(397 ± 37) compared to sham operated rats (163±19), which was attributable to significantly greater increases in neuronal activation in both parvocellular division (161 ± 15) and magnocellular division (236±26) of PVN compared to sham operated rat. The supraoptic nucleus (SON) which only contains the magnocellular neurons, a significantly higher ($P<0.0001$, unpaired t-test) number of Fos-positive neurons (248 ± 7) were identified in response to acute MI compared to sham operated rat (158 ± 11). As the parvocellular PVN neuron population contains pre-autonomic neurons (1), these results suggest that the activation of these pre-autonomic neurons can be the potential target for driving the cardiac SNA immediately following acute MI. Ongoing research will also investigate the neuronal activation in other brain areas (subfornical organ, nucleus of the tractus solitarious and rostral ventro lateral medulla) in response to acute MI.

1. Stern JE (2001) Electrophysiological and morphological properties of pre-autonomic neurones in the rat hypothalamic paraventricular nucleus. The Journal of physiology 537: 161-177

P17

Dexamethasone elevates C-type natriuretic peptide (CNP) levels in cerebrospinal fluid and plasma: a dose-response study in sheep

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Glucocorticoids have potent actions within central nervous tissues, affect mood and memory and when given acutely reduce cerebral oedema associated with brain tumours. Whereas sustained parenteral injections of dexamethasone reduce plasma CNP peptides in lambs[1], the response of CNP within the CNS is unknown. Accordingly we have studied both the systemic (plasma) and central (cerebrospinal fluid, CSF) dose response in CNP peptides to a single intravenous bolus of dexamethasone (0.025-0.25 mg/kg live weight) in 9 - 14 month-old female sheep (n = 4 per dose). Samples of blood and CSF (cisterna magna) for assay of CNP and amino terminal proCNP (NTproCNP) were collected at -1, 0, 4, 8, 12, 16 and 24 h post dose and responses to dexamethasone were compared with responses to saline (3 ml saline i.v.). CNP and NTproCNP levels increased in plasma and CSF after dexamethasone dose-dependently ($P < 0.05$ for both) to reach peak values at 4-8 h (plasma) and 8-16 h (CSF). Percentage change above baseline in CNP was greater than observed for NTproCNP, and responses in plasma exceeded those in CSF. No consistent change in plasma or CSF levels occurred after saline. This is the first report showing that CSF concentrations of CNP peptides are increased by dexamethasone. Since we have shown previously that plasma CNP products do not access CSF[2], the findings indicate that glucocorticoids acutely stimulate CNP production within CNS tissues, possibly in cerebral micro capillaries or glial tissue where CNP is strongly expressed.[3,4] The effect of sustained dexamethasone administration (which reduces systemic CNP) on CSF levels of CNP remains to be determined.

1. Prickett, T.C., M. Wellby, G.K. Barrell, A.M. Richards and E.A. Espiner (2014). *Differential response of C-type natriuretic peptide to estrogen and dexamethasone in adult bone.* Steroids. 87: 1-5.

2. Wilson, M.O., G.K. Barrell, T.C.R. Prickett and E.A. Espiner (2015). *Sustained increases in C-type natriuretic peptides fail to increase concentrations in cerebrospinal fluid: Evidence from pregnant sheep.* Peptides. 69: 103-108.

3. Vigne, P. and C. Frelin (1992). *C-type natriuretic peptide is a potent activator of guanylate-cyclase in endothelial cells from brain microvessels.* Biochemical and Biophysical Research Communications. 183: 640-644.

4. Yeung, V.T., A.S. Mak, Y.L. Chui, S.K. Ho, K.N. Lai, M.G. Nicholls and C.S. Cockram (1996). *Identification of C-type natriuretic peptide gene transcripts in glial cells.* Neuroreport 7: 1709-1712.

P18

The vascular responses to modulation of flow, but not pressure, are dependent on vascular ENaC function in carotid, femoral and mesenteric arteries from mice.

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The vascular network requires mechanotransduction processes in order to respond to local changes in pressure and flow. The epithelial sodium channel (ENaC) is a mechanosensitive ion channel [1] that is activated by shear stress (flow) in cellular expression systems [2, 3]. Recently, ENaC has been detected in the microvasculature (e.g. resistance arteries) [4], as well as in the larger conduit arteries [5]. Therefore, vascular ENaC is perfectly placed to act as a mechanosensor, although its exact role in vascular function is unclear.

This study aimed to assess the effect of ENaC inhibition on the response of different types of arteries to changes in intraluminal pressure and flow. Male C57Bl/6 mice were euthanised with sodium pentobarbitone (200 mg / kg) and carotid, femoral and mesenteric arteries (n = 5) were isolated, mounted in a pressure myograph, and extended to 80% of *in vivo* length. Vessels were incubated in oxygenated Krebs-Henseleit buffer at 37 °C. Following equilibration at 60 mmHg and assessment of vessel viability, arterial internal diameter was recorded in response to changes in intraluminal pressure (20 – 160 mmHg) and flow (0 – 300 µL / min), in the presence and absence of 10 µM amiloride (ENaC inhibitor). Larger percentage changes in diameter were observed in carotid *cf.* femoral / mesenteric arteries with increasing pressure. Intraluminal flow included a small (<5%) amount of vasodilation in all arteries. Data shows that amiloride had no effect on the response to changing pressure. In contrast, ENaC inhibition resulted in modulation of the response to changes in flow. In conduit (carotid and femoral) arteries the vasodilatory response was enhanced, where as in mesenteric arteries, the response was reduced. Therefore, ENaC has a role in the mechanosensation of vascular flow that is specific to the type of vascular beds.

1. Shi, S., et al., ENaC regulation by proteases and shear stress. Curr Mol Pharmacol, 2013. 6(1): p. 28-34.

2. Althaus, M., et al., Mechano-sensitivity of epithelial sodium channels (ENaCs): laminar shear stress increases ion channel open probability. FASEB J, 2007. 21(10): p. 2389-99.

3. Fronius, M., et al., Epithelial Na+ channels derived from human lung are activated by shear force. Respir Physiol Neurobiol, 2010. 170(1): p. 113-9.

4. Perez, F.R., et al., Endothelial epithelial sodium channel inhibition activates endothelial nitric oxide synthase via phosphoinositide 3-kinase/Akt in small-diameter mesenteric arteries. Hypertension, 2009. 53(6): p. 1000-7.

5. Wang, S., et al., Functional ENaC channels expressed in endothelial cells: a new candidate for mediating shear force. Microcirculation, 2009. 16(3): p. 276-87.

P19

Effects of renal denervation on left ventricular function and the cardiac sympathetic nervous system in established heart failure

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Elevated sympathetic nerve activity (SNA) to the heart and kidneys drives heart failure progression. Renal denervation removes the actions of SNA on the kidney and is a possible new intervention for treating heart failure. We tested the hypothesis that renal denervation in established heart failure improves cardiac function by attenuating adverse changes in the cardiac sympathetic nervous system.

Myocardial infarction (MI) or sham MI was performed in male Wistar rats and 4 weeks later renal denervation or sham surgery was performed. The animals were placed in metabolic cages 3 and 6 weeks post-MI. 7 weeks post-MI, left ventricle function was assessed before and following the acute intravenous infusion of the β1 adrenergic receptor (β1AR) antagonist metoprolol. Brain tissue was collected for immunohistochemical and western blot analysis.

Renal denervation in MI animals improved fluid balance. In animals with MI, renal denervation improved left ventricular contractile (dp/dt max.) and relaxation (dp/dt min. and tau) properties. In both MI groups, acute β1AR antagonism resulted in greater decreases in cardiac output compared to sham MI groups. In response to β1AR antagonism there were no differences in the change in heart rate, stroke volume, and cardiac output between MI groups with either intact or denervated renal nerves. Neuronal nitric oxide synthase, superoxide dismutase and cFOS in the paraventricular nucleus of the hypothalamus were decreased in MI groups compared to sham MI groups and there were no effects of renal denervation on these variables.

The current findings show that renal denervation in established post-infarction heart failure has positive effects on left ventricle contractile and relaxation properties. Furthermore, the results suggest that renal denervation in established heart failure does not significantly alter the actions of cardiac SNA in mediating left ventricle function via the β1AR in the acute setting.

P20

MS1/STARS is a target of the JNK signalling pathway in cardiac myocytes

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Myocyte Stress Protein 1(MS1)/Striated muscle activator of Rho Signalling and Serum Response Factor dependent transcription (STARS) is a stress-responsive regulator of gene expression in both cardiac and skeletal muscle. It is a myofibrillar protein upregulated during myogenic differentiation and in cardiac myocytes by hypoxia and pressure-induced left ventricular hypertrophy[1,2]. MS1/STARS likely plays a role in regulating the growth, development and adaptations to stress in myocytes, although the signalling pathways involved are not well-characterised.

To determine if MS1 were responsive to other stresses relevant to cardiac function we tested if it could be induced by the metabolic stresses associated with ischaemia/reperfusion injury. In cardiac myocytes, metabolic stress increased MS1 expression, both at the mRNA and protein level. This occurred concurrently with activation of the JNK signalling pathway, a major stress-responsive pathway activated during ischaemia and reperfusion in the heart[3,4].

MS1 induction by metabolic stress was blocked by both the transcription inhibitor actinomycin D and a JNK inhibitor, suggesting that activation of the JNK pathway during metabolic stress in cardiac myocytes leads to transcriptional induction of MS1. MS1 was also found to co-precipitate with JNK and be an efficient JNK substrate in vitro. Taken together these data identify MS1 as a transcriptional and post-translational target for the JNK pathway in cardiac myocytes subjected to metabolic stress.

1. Arai, A., Spencer, J. A. & Olson, E. N. STARS, a striated muscle activator of Rho signaling and serum response factor-dependent transcription. J Biol Chem 277, 24453-24459 (2002).
2. Mahadeva, H., Brooks, G., Lodwick, D., Chong, N. W. & Samani, N. J. ms1, a novel stress-responsive, muscle-specific gene that is up-regulated in the early stages of pressure overload-induced left ventricular hypertrophy. FEBS Lett 521, 100-104 (2002).
3. Hausenloy, D. J. & Yellon, D. M. Survival kinases in ischemic preconditioning and postconditioning. Cardiovasc Res 70, 240-253 (2006).
4. Harding, S. J., Browne, G. J., Miller, B. W., Prigent, S. A. & Dickens, M. Activation of ASK1, downstream MAPKK and MAPK isoforms during cardiac ischaemia. Biochim Biophys Acta 1802, 733-740 (2010).

P21

Signalling regulation of glycogen autophagy in the heart

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Autophagy disturbance and glycogen mishandling in the heart play a role in metabolic stress settings such as diabetes. We have recently demonstrated that an autophagy process specific for glycogen ('glycophagy'), which is distinct from macro-autophagy, is modulated by metabolic stress and is an important regulator of glycogen content in the heart. The aim of this study was to elucidate β-adrenergic and AMPK signalling regulation of glycogen handling and autophagy in the heart.

Excised hearts (male Sprague Dawley 8 weeks) were perfused with 10^{-6}M isoproterenol (β agonist) or control buffer for 5 or 60 minutes, snap frozen, homogenised and protein extracted. Neonatal rat ventricular myocytes (NRVMs) cultured in 5mM or 30mM glucose

were exposed to AICAR for 30 minutes, lysed and frozen. Protein expression was assessed by western blot and glycogen content was assessed by amyloglucosidase assay.

Isoproterenol-induced β-adrenergic activation was evidenced by an increased phospho(Ser14)- to total glycogen phosphorylase ratio after 5min of isoproterenol perfusion (62% increase $p<0.05$). Glycophagy markers GABARAPL1 and acid α glucosidase were markedly increased by β-adrenergic signaling activation (3-fold and 1.5-fold increase respectively, $p<0.05$) consistent with depletion of glycogen content (71% lower after 5min and fully depleted after 60min Isoproterenol perfusion, $p<0.05$). Macro-autophagy markers, LC3BII:I ratio and p62 protein expression were not changed in the isoproterenol perfusion groups. Inactivation of glycogen synthase (phosphorylation-Ser641) was only evident after 60min isoproterenol perfusion. AICAR-induced activation of AMPK attenuated high glucose-induced glycogen accumulation in NRVMs with no change in phosphorylase activation, suggesting a role for glycophagy in this setting.

This is the first study to show that β-adrenergic signaling positively regulates glycophagy. These findings suggest that β-adrenergic regulation of glycophagy is distinct from macro-autophagy, demonstrating that autophagy sub-types are influenced differentially by signalling modalities. Indication of AMPK-induced glycophagy activation is evident and further analysis is underway.

P22

Auditory Long Term Potentiation (LTP) with Users of Cochlear Implants

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Problem: Long Term Potentiation (LTP) is accepted as a neural mechanism underlying hippocampal memory (Lomo & Bliss, 1973). Clapp, Hamm, Shephard & Taylor (2005) show rapid pure-tone auditory stimulation induces LTP-like effects on N1 of obligatory cortical auditory evoked potentials (CAEP's). Wilson (2011) demonstrates auditory LTP (aLTP) occurs only at 13HZ stimulation rate. Zaehle, Clapp, Hamm, Meyer, & Kirk (2007) present fMRI evidence supporting aLTP induction. These studies suggest aLTP could have implications for objective measurement of auditory plasticity and hearing rehabilitation.

Aims: Replicate Clapp et al. (2005) using clinical EEG equipment. Examine P2 responses of CAEP's for aLTP. Investigate whether aLTP induction requires binaural stimulation. Investigate if tetanic stimulation works as passive auditory rehabilitation therapy for cochlear implant (CI) recipients.

Method: Twenty-eight normal hearing (NH) participants; 12 using binaural stimulation, 16 using monaural. Eight cochlear implant recipients were assessed on divided auditory attention (Brief Test of Attention) and sentence recognition in noise (50% SRT), as well as EEG. Age- and sex-controlled methodologies are used.

Results: No evidence for aLTP at N1 or P2 found for any group. N1 amplitude found to have decreased post-intervention; however, baseline shift for N1 amplitude is evident for all groups. P2 amplitude was significantly larger for CI than NH, but latency was non-significant.

N1 amplitude correlates with speech recognition in noise, for the CI group. BTA scores correlates with length of time using a CI (r=0.708, p=0.049).

Conclusions: Clapp et al's (2005) binaural findings could not be replicated, nor was aLTP observed with monaural stimulation. Passive exposure to tetanizing auditory stimuli did not induce aLTP for people who use CIs. Attending to the tetanizing stimulus, or longer therapy, may be required for reliable aLTP induction. N1 baseline shift supports published concepts of passive learning during baseline recording; which may compromise aLTP detection.

P23

The effect of TNFα blockade on the cardiovascular responses to intrauterine inflammation in preterm fetal sheep

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Background: Intrauterine inflammation during preterm life is associated with low blood pressure and blood flow leading to increased morbidity and mortality. Mechanisms mediating this cardiovascular instability are poorly understood.

Objective: To examine the hypothesis that up-regulation of the pro-inflammatory cytokine Tumour Necrosis Factor-α (TNF-α) mediates cardiovascular responses during inflammation induced by lipopolysaccharide (LPS), and that TNF-α blockade inhibits these responses.

Methods: Blood pressure (BP), fetal heart rate (FHR), carotid blood flow (CaBF) and femoral blood flow (FBF) were continuously monitored in fetal sheep in utero (0.7 gestation) randomly assigned to receive either: LPS infusion (100 ng/kg i.v. over 24h followed by 250 ng/kg/24h for a further 96h) plus 1μg LPS boluses at 48, 72 and 96h, n=5), LPS protocol plus two i.v. boluses of TNF-α antagonist (Enbrel; 5mg) given immediately before LPS infusion and first LPS bolus (n=3), or saline only (n=8). Fetuses were recovered for 5 days.

Results: LPS caused cerebral hyperperfusion and peripheral hypoperfusion. LPS boluses were associated with transient tachycardia, hypotension and vasodilatation. During recovery FHR and FBF were lower, and BP and CaBF higher. Enbrel did not alter FHR or BP during infusion or boluses, and prevented the fall in FHR during recovery but caused hypotension on day 1, with pressure reduced by ~15%. CaBF and FBF fell during infusion (15 and 25% respectively), did not differ during boluses, and flows normalised during recovery, except for a transient period of femoral vasodilatation during day 1.

Discussion: For the first time we show that TNF-α plays a role in mediating preterm fetal cardiovascular responses to inflammation. TNF- α inhibition, however, did not normalise all responses. Hypoperfusion occurred during early LPS+Enbrel exposure, potentially due to reduced TNF-α mediated release of vasodilators such as nitric oxide. Hypotension occurred during early recovery, likely mediated by transient peripheral vasodilatation.

P24

Withdrawn

P25

The dynamic cardiovascular responses to ischemic stroke: temporal relationships between blood pressure, intracranial pressure and cerebral perfusion pressure

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Over 80% of ischemic stroke patients show an abrupt increase in blood pressure (BP) in the hours and days following stroke; yet whether post-stroke hypertension is beneficial or harmful remains controversial. This may be because the physiological basis underlying the cardiovascular response to stroke response is unclear. We hypothesize that post-stroke hypertension may occur in order to overcome high intracranial pressure (ICP), and thus prevent a fall in cerebral perfusion.

Wistar rats (n=4, 393±34g) were instrumented with radio telemeters to record BP and ICP. After a 1-week recovery period, ischemic stroke was induced via middle cerebral artery occlusion on Day 0; recordings continued for 10 further days. Cerebral perfusion pressure was calculated as the difference between BP and ICP.

Within 36 hours after stroke, BP increased rapidly from baseline (108±9mmHg) to a peak of +44±7mmHg above baseline, remaining slightly elevated at Day 10 (+4±3mmHg). In contrast, ICP increased more gradually from baseline (5±1mmHg), to a peak of +25±8mmHg on Day 3, and remaining +4±2mmHg above baseline at Day 10. This is consistent with the formation of cerebral oedema. Cerebral perfusion pressure increased 24-48 hours after stroke (+27±11mmHg), then decreased below baseline (-13±7mmHg) during Days 3-4, subsequently returning to baseline. As is commonly clinically and experimentally, body weight decreased in the days immediately following the infarct (-8±5%), recovering to baseline by Day 10.

These findings suggest that the increase in BP immediately after ischemic stroke initially increases cerebral perfusion pressure. However, the observed delayed rise in ICP does not elicit a matched increase in BP, thus cerebral perfusion pressure falls, before recovering to baseline. These results indicate that elevated ICP may not be the primary trigger for the initial post-stroke hypertension.

Sport and Exercise New Zealand Posters

P26

Verbal overshadowing in surgical laparoscopy influences neural co-activation and movement kinematics

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It has been shown that verbally describing, overshadowing, a procedural movement induces a shift from holistic to analytical processing, potentially interfering with automatic skill execution. People with a high propensity to consciously control movements (reinvestment) should be less affected by the detrimental effects of verbalization, because they are more likely to be accustomed to verbal processing. This study aimed to examine the underlying mechanisms of verbalization on motor performance. More specifically, we caused verbal overshadowing in a fine motor skill (laparoscopic peg transfer) and examined its effect on performance, neural co-activation between verbal-analytical (T3) and motor planning (Fz) regions of the cortex, and movement kinematics in people with high or low propensity for reinvestment.

Twenty-three young adults were categorised as high or low reinvestors based on their scores on the Movement Specific Reinvestment Scale (MSRS)[1]. They were trained to expert-derived levels of proficiency on a Fundamental Laparoscopic Skill – peg transfer task[2]. Transfer test one and two required participants to perform three trials of peg transfer during which their performance (time), neural co-activation (T3-Fz) and movement kinematics (number of adjustments, speed, path length) were measured. During intervention participants were given four minutes to either describe their movements in as much detail as possible (verbalization) or list as many animals as they could think of (control). The results revealed increased neural co-activation and changes in movement kinematics after verbalization in low reinvestors. Verbalization had no effects on people with high propensity to reinvest.

To conclude, verbalizing movements has acute effects on people with low propensity for conscious verbal involvement in movement execution, possibly, because they are not used to processing information in a declarative manner.

1. Ritter, E.M., & Scott, D.S. (2007). Design of a proficiency-based skills training curriculum for the fundamentals of laparoscopic surgery. *Surgical Innovation, 14,* 107-112

2. Masters, R.S.W., Eves, F.F., & Maxwell, J. (2005). *Development of a movement specific Reinvestment Scale.* In T. Morris, P. Tery, S. Gordon, S. Hanrahan, L. Ievleva, G. Kolt, & P. Tremayne (Eds.) Proceedings of the ISSP 11th World Congress of Sport Psychology, Sydney, Australia

P27

Effects of acute dietary nitrate supplementation on slope estimations, blood pressure and exercise economy in the elderly

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Recent research has shown the benefits associated with dietary nitrate (NO_3^-) ingestion in young, healthy individuals. Decreased blood pressure and increased oxygen efficiency have been reported and there is some evidence of improved physiological and cognitive performance. However, these effects have not been as thoroughly investigated in elderly populations. The current double blind crossover study investigated the effects of NO_3^- in 19 elderly participants (10 female/9 male; 72±5 yrs.) when given an acute 70ml dose of nitrate-rich beetroot juice (BEET; ~4.8mmol NO_3^-) compared to a placebo (nitrate depleted beetroot juice – PLA; ~0.005mmol NO_3^-). Participants performed two separate randomised trials, BEET and PLA, separated by ≥ 7 days. Following ingestion of the supplement, participants had their resting blood pressure and resting heart rate measured followed by cognitive and

physiological tests. Participants performed a number of slope estimation measures as well as a walking economy test where VO_2, RPE and HR were measured during a 5 minute walk at 3km.h^{-1}. There were no significant differences in any of the slope estimation or physiological measures ($P > 0.05$) between the BEET and PLA trials. As expected the participants' haptic (proprioception based) judgements were overall significantly less than conscious or verbal estimates ($P < 0.05$). This study suggests that NO_3^- may not be effective in improving exercise economy or reducing slope estimations in elderly participants.

Low-load high repetition resistance training in combination with vascular occlusion or hypoxia can increase muscle hypertrophy, but the effect of such training on cardiovascular response is less clear. This study aimed to investigate the cardiovascular response to resistance training combined with either hypoxia or venous occlusion. In a randomised controlled trial, 23 well-trained netball athletes took part in a 5-week training of knee flexor/extensor muscles in which low-load resistant exercise (20% 1-RM) was combined with either a), an occlusion pressure of ~230 mmHg around the upper thigh (KT, n = 8), b), breathing hypoxic air to generate an arterial blood oxygen saturation of ~80% (HT, n = 7), or c), no additional stimulus (CT, n = 8). All athletes underwent similar resistance training which included 3 sets of knee extensors follow by 3 sets of knee flexors, 3 times per week for 5 weeks. Systolic pressure (SP), diastolic pressure (DP),mean arterial pressure (MAP), heart rate (HR), stroke volume (SV), cardiac output (CO), total peripheral resistance (TPR) and rate pressure product (RPP) were measured immediately after the final set of knee extension exercises at week 1 and week 5. Compared to CT, HT showed a substantial decrease in SP (11.7±11.3%, mean ±90% CL) over the training period and unclear differences in all other parameters. In contrast, compared to CT, the KT group, as a result of training, showed substantial increases in DP (9.8±10.8%), MAP (5.7±6.5%), and TPR (68.8±40.4%), but decreases in SV (17.2±19.5%) and CO (18.0±21.9%). The reduction of SP after hypoxic training also resulting in a substantial decrease in the RPP by 15.6±9.6%, while unclear differences were found in the KT group (3.9±14.3%), compared to CT. Our results indicate that low load resistance training in hypoxia has a greater cardiovascular benefit than similar resistance training with venous occlusion.

P28

The effects of intermittent sequential pneumatic compression on recovery between exercise bouts in well-trained triathletes

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Purpose*:** To evaluate the effectiveness of intermittent sequential pneumatic compression (ISPC) on the recovery between exercise bouts in well-trained triathletes. ***Methods: Ten highly-trained male triathletes (mean ± SD; age = 29 ± 9 y, mass = 72kg ± 11kg) completed a familiarisation trial and two experimental trials in a randomized, cross-over design. Participants performed a 40-minute high-intensity interval session on a cycle ergometer, followed by a 30-minute recovery period where participants completed either passive recovery (CON) or ISPC recovery. Following the recovery period, participants performed a 5km run time-trial on a treadmill (5kmTT). Blood lactate concentration, 5kmTT time and total quality recovery (TQR) were used to examine the effect of ISPC compared to CON. ***Results***: The 5kmTT resulted in a non-significant difference ($P = 0.31$, ES = 0.07) between groups of 8.2

± 23.7 seconds in favour of the ISPC trial (ISPC; 1189.7 ± 94.9 and CON; 1197.9 ± 101.9). There were no significant differences between trials for blood lactate concentrations or TQR. ***Conclusion***: The current study reports that ISPC was not effective in improving recovery between a cycling and running bout in highly-trained triathletes.

P29

MOTIVATION AND MINDFULNESS: PSYCHOLOGICAL FLEXIBILITY AND AUTONOMOUS MOTIVATION FOR PHYSICAL ACTIVITY

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Self-Determination Theory (SDT) is a theory of motivation that provides a viable framework for developing ways to increase levels of physical activity (PA) within the general population. SDT focuses on the underlying reasons for a given behaviour, positing that autonomous motivation (i.e., emanating from within an individual, such as that based on enjoyment or valued outcomes) leads to increased psychological wellbeing and behavioural persistence. According to SDT, satisfaction of the three basic psychological needs of autonomy, competence, and relatedness results in the increased likelihood of autonomous motivation for that behaviour. SDT-based interventions therefore emphasise support for basic need satisfaction to facilitate autonomous motivation, an approach that has proved efficacious in increasing PA [2]. esearch suggested that the mindfulness-based construct of psychological flexibility a potential important support autonomous motivation [3]is

The first phase of the current research project the relationships between psychological flexibility, psychological need satisfaction, and autonomous motivation, all within a PA context. 18-64 year-old male and female participants, who a battery of questionnaires . Using SEM-based mediational analyses, it is hypothesised that psychological flexibility will predict autonomous motivation for PA, and that this relationship will be mediated by psychological need satisfaction. Dependent on the results of the study, an intervention will be developed that combines a basic need satisfaction intervention and psychological flexibility training to facilitate autonomous motivation for PA.

1. Deci, E. L., & Ryan, R. M. (2002). *Overview of Self-Determination Theory: An Organismic Dialectical Perspective*. In E. L. Deci & R. M. Ryan (Eds.), *Handbook of Self-Determination Research* (pp. 3-33). Rochester, NY. University of Rochester Press.
2. Hayes, S. C., Strosahl, K. D., & Wilson, K. G. (1999). *Acceptance and Commitment Therapy: An Experiential Approach to Behavior Change*. New York: Guilford Press.
3. Teixeira, P. J., Carraça, E. V., Markland, D., Silva, M. N., & Ryan, R. M. (2012). Exercise, physical activity, and self-determination theory: A systematic *review. Int J Behav Nutr Phys Act, 9(1), 78-107.*

P30

Effects of strenuous exercise on cardiovascular function

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Introduction: Blood volume drops during exercise, but recovers within the first few hours after exercise [1, 3] and is typically expanded at 24 hours [3, 5], whereas blood pressures usually do the opposite. Post exercise hypotension (arterial and central venous) appears to be an important mediator of the hypervolaemic response (blood volume expansion) to exercise [3, 4]. High blood volume is advantageous to athletic performance and functional capacity; it increases aerobic capacity and helps to reduce exercise heart rate [5] and sympathetic nervous system activity at rest. However, the profiles of these responses to high intensity exercise are unclear, as is the most efficient volume or pattern of exercise necessary to induce them. The purposes of this ongoing study are to determine the dependence of the hypervolaemic response on post-exercise hypotension following high intensity exercise and to examine the effectiveness of widely-separated, brief bursts of exercise in achieving these responses.

Methods: Two of eight participants have thus far completed three cycling exercise trials (randomised order): (i) three 30-s maximal exercise bouts (Wingates) interspersed with 60 minutes rest in a seated position, and (i) one 30-s maximal exercise bout with seated recovery or with (ii) supine recovery. Haematocrit, [haemoglobin] and arterial pressure were measured before exercise and across the following 48 hours.

Results: A single 30 second intense exercise bout induced neither a hypotensive (MAP or DBP) nor a hypervolemic (ΔPV) response in either recovery condition. Supine recovery was associated with elevated systolic blood pressure (SBP) at 25 minutes (ΔSBP=8±3 mm Hg) and 48 hours post-exercise (ΔSBP=4±2 mm Hg). Plasma volume, MAP, SBP and DBP were all unchanged at all time points after 3 bouts of intense exercise, at this stage of the study progression.

Conclusions: The results so far indicate that single short high intensity exercise bouts do not provide a stimulus strong enough to induce hypotension or subsequent plasma volume expansion known to occur following multiple high-intensity or prolonged moderate-intensity exercise.

1. Boulay, M. R., Song, T. M., Serresse, O., Theriault, G., Simoneau, J. A., & Bouchard, C. (1995). Changes in plasma electrolytes and muscle substrates during short-term maximal exercise in humans. Can J Appl Physiol, 20(1), 89-101.
2. Convertino, V. A. (1983). Heart rate and sweat rate responses associated with exercise-induced hypervolemia. Med Sci Sports Exerc, 15(1), 77-82.
3. Gillen, Lee, Mack, G. W., Tomasell, Nishiyasu, T., & Nadel, E. R. (1991). Plasma volume expansion in humans after a single intense exercise protocol .Journal Appl Physiol, 71(5), 1914-1920.
4. Hayes, P. M., Lucas, J. C., & Shi, X. (2000). Importance of post-exercise hypotension in plasma volume restoration. Acta Physiol Scand, 169, 115-124.
5. Nagashima, K., Mack, G. W., Haskell, A., Nishiyasu, T., & Nadel, E. R. (1999). Mechanism for the posture-specific plasma volume increase after a single intense exercise protocol. J Appl Physiol, 86(3), 867-873.

P31

Research findings from a successful application of Hellison's Teaching Personal and Social Responsibility model in a New Zealand primary school. Implications and considerations for the development of children through physical education in the New Zealand school curriculum

Smith, M.

Web Wonks

Abstract

This research examined Hellison's (2003) Teaching Personal and Social Responsibility model in a New Zealand primary school. The model comprises five levels of personal and social responsibility with social goals for each. The intervention was a forty week training programme. The sample consisted of two scholastically equivalent schools; intervention (*n* = 36), and control (*n* = 49. A time series empirical approach was used and psychometrically reliable and valid instruments were administered at six equal-distant intervals where four self-reporting measures were completed by the child participants. A separate measure was additionally completed each by the participant's parent, and the participant's class teacher. Statistical analysis using regression model fitting demonstrated that scores increased for the intervention participants. Multivariate repeated analysis of the four child self-reporting measures demonstrated that the mean positive change was greatest for the intervention group. Equality of means analysis also confirmed that the intervention group had the highest level of improvement in positive behaviour, as reported by the parents and teachers. Futher analysis using Guttman (1947, 1950) scaling examined the model's stage-like progression. Scalograms were constructed at each interval to produce a Coefficient of Reproducibility, one each for the intervention and control groups. A mean Coefficient of Reproducibility ≥ .90 was demonstrated. The results supported the Hellison (2003) model of stage progression. Further, participants in the intervention group demonstrated that they progressed along a single continuum as the Hellison (2003) model claimed. However, the goals in the current study developed in a differing order than those proposed by the Hellison (2003) model.

P32

The relationship between neck strength and head impact kinetics in rugby union players

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Introduction: Concussions are one of the most prominent medical concerns in contact sports at all ages and levels of competition. This is due to the increasing concern about the susceptibility of the concussed player towards future injuries and the potential for long-term health related problems[1,2]. As rugby is a contact based sport examination of head impact exposures will help to improve understanding of the head injury mechanisms, establish reliable methods to predict injury risk and ultimately reduce the incidence of head injury in sports[3]. Currently, the only strategies employed to reduce concussions are modifications to

the game, limiting contact sessions and/or the use of protective helmets[4]. For rugby where helmets are not an option, prevention strategies to minimize concussions are limited to reducing exposure by not playing. Therefore the identification of a feasible prevention strategy such as the adoption of neck exercises may provide a simple, inexpensive and practical solution to reduce the incidence of concussions. Thus the aim of this investigation is to examine the potential role neck musculature may play in modulating the forces associated with concussive and subconcussive impacts recorded in the head region during rugby training sessions and matches. **Methods:** Participants will be recruited from the Otago Rugby ITM team. Prior to the start of the season an isometric neck strength assessment and a baseline Sport Concussion Assessment Tool3 (SCAT3) will be conducted[5]. Pre-season neck strength testing will be conducted using a device that requires participants to adopt a simulated contact position, which has previously been validated[6]. A single maximal isometric contraction will be performed for flexion, extension, left and right lateral flexion. If during the season a player is suspected of sustaining a concussion, a SCAT3 will be conducted and New Zealand Rugby return to play protocols will be followed. At the end of the season all participants will be asked to complete a post-season SCAT3 regardless of concussion injury history, to assess whether or not there is a cumulative effect of sustaining these subconcussive impacts. During the season head impact acceleration and rotational forces will be collected in real-time using a CSx player cell that is adhered to the skin behind the ear. This device will transmit impact forces recorded from the head to locators on the field that feed into a tablet which will display in real time the impact forces experienced by the players. Monitoring of these impacts will provide the research team with an understanding of the number/magnitude of impacts experienced by players in different positions. **Analysis:** Data will be analysed using regression models to determine how neck strength contributes to the number and/or severity of impacts experienced at the head. **Outcomes**: The results will contribute to understanding the impact forces experienced at the head in different positions in rugby and the relationship between impact forces and neck strength. These findings will form the foundation work to explore whether the provision of neck specific exercises poses a feasible prevention strategy to reduce the frequency and/or severity of head impacts.

1. Benson BW, McIntosh AS, Maddocks D, Herring SA, Raftery M, Dvořák J. What are the most effective risk-reduction strategies in sport concussion? Br J Sports Med. 2013;47(5):321-326.
2. Lisman P, Ie JFS, Del Rossi G, et al. Investigation of the slow isoinertial cervical strength training on dynamic stabilization of the head and neck during football tackle. Int J of Sports Sci Engineering. 2012;6(3):131-140.
3. Cobb B. Measuring head impact exposure and mild traumatic brain injury in humans. Paper presented at: Brain Injuries and Biochanics2013.
4. Collins C, Fletcher E, Fields S, et al. Neck strength: A protective factor reducing risk for concussion in high school sports. J Prim Prev. 2014:1-11.
5. Abrahams S, Fie SM, Patricios J, Posthumus M, September AV. Risk factors for sports concussion: an evidence-based systematic review. Br J Sports Med. 2014;48(2):91-97.
6. Salmon DM, Handcock P, Sullivan SJ, Rehrer N, Niven B. Reliability of repeated isometric neck strength and endurance testing in a simulated contact posture. J Strength Cond Res. 2015;29(3):637-646.

P33

Does the low-load resistance training under hypoxic conditions mimic high-load resistance training?

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High-load resistance exercise (80% 1RM) has been shown to be an effective strength training paradigm, but often injury results. Less is known about whether low resistance exercise combined with hypoxia can replace the conventional training paradigm. The aim of this study was to identify the effectiveness of two different resistance–training loads (30% and 50% of 1RM) combined with hypoxic training compared to a conventional resistance training (80% 1RM). Thirty athletes (20 ± 1.7 y) were divided into 3 resistance training groups; hypoxic 30%1RM (HT_{30}), 50%1RM (HT_{50}) and a normoxic control group 80% 1RM (CT_{80}). The resistance training program included knee extensions of 15 repetitions per set, 3 sets per day, 1 minute rest between sets, 3 days a week of for 5 weeks. Hypoxic conditions were set at FiO_2=14%. A 6-s maximum voluntary contraction (MVC_6), 1RM, number of reps (#reps) and fatigue rate were measured before (1-3 days) and after (1-3 days) the five week resistance training program. There was a significant increase ($p<0.05$) in MVC_6 in all groups (CT_{80} =21.0% ± 14.0, HT_{50} = 16.7% ± 7.9, HT_{30} = 18.5% ± 12.9) compared with their baseline values, but no significance difference ($p>0.05$) between the three groups. The 1RM increased significantly in HT_{50} (24.4 ± 3.8%) compared to HT_{30} (5.0% ± 2.5) but was not significantly different to CT_{80} (23.7% ± 10.8). The percent changes of fatigue rates during concentric contractions was significantly lower after training in hypoxic groups (HT_{30}: 12.6±8.8%, HT_{50}: 13.3±12.1%) but not in the normoxic group (CT_{80}: 4.5±13.3%). The authors conclude that both low-load resistance (30% and 50% 1RM) training under hypoxic condition improve muscular performance and resistance to fatigue, however the higher load hypoxic training (HT_{50}) showed the most promise as an alternative resistance paradigm to the traditional high load training.

P34

Living and training at 825 m incorporated with simulated altitude improves blood parameters in soccer players.

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Much of the research on altitude training for athletes has focused on haematological variables; with inconclusive results. The lack of consistent findings may due to the dose and forms of altitude training and the iron status of the individual athletes. This research aimed

to investigate the effects of natural altitude training supplemented with intermittent hypoxic training (IHT) and iron supplementation on erythropoietin (EPO), red blood cells (RBC) and serum iron concentration in soccer players. Forty university soccer athletes were divided into 4 groups; Sea-level training (ST; N=10), sea-level training with iron supplementation (SI; N=10), supplemented altitude training (AT; N=10), supplemented altitude training with iron supplementation (AI; N=10). All athletes were matched on their soccer ability and followed the same soccer training program for 8 weeks. The altitude groups stayed and trained at 825 m with the addition of 15 min simulated altitude training daily on bike. All athletes performed a pre-test (1-2 days prior to training) and two post tests on day 1 and day 14 after the training camp. By day 1 post camp, compared to the baseline values, EPO concentration and RBC numbers increased substantially in the AI group (14.5 ± 6.6% and 5.3 ± 0.2% respectively, mean ± SD), however only RBC numbers were substantially improved in the AT group (5.7 ± 0.3%). By day 14 post camp, compared to baseline, RBC numbers had increased in both altitude training groups (5.3 ± 0.3%, 5.6 ± 0.3%, AI and AT groups respectively), along with a substantial increase in serum iron concentration (144.7 ± 16.8%, 139.2 ± 32.7%, AI and AT groups respectively). Supplementing 8 weeks of living and training at low altitude with 15 min daily of IHT improves haematological variables important to aerobic performance. These changes may prove beneficial for soccer players.

P35

Reliability of skeletal muscle blood flow and oxygen consumption measurements during incremental exercise using near infrared spectroscopy

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Near infrared spectroscopy can readily report changes in skeletal muscle blood volume and oxygenation. By use of rapid venous occlusions (VO) and arterial occlusions (AO) skeletal muscle blood flow (mBF) and oxygen consumption (mVO_2) can be assessed. Using a Biodex Dynamometer to control workload, we developed a new protocol to assess mBF and mVO_2 responses to incremental exercise.

Purpose: To determine the between-day reliability of mBF and mVO2 responses to incremental exercise using continuous wave near-infrared spectroscopy.

Methods: Thus far 4 healthy and physically active adults were tested on three non-consecutive occasions over 10 days. The NIRS probe was placed on the lower vastus lateralis. After a 10 minute rest, VO and AO were used to determine resting mBF and mVO_2. Using isotonic knee extensions on a Biodex dynamometer, participants performed one knee extension every three seconds for three minutes to achieve steady state. Immediately following knee extension the leg was rested and a VO or AO applied for 15 seconds. Knee extensions resumed for 45 seconds to maintain steady state before another VO or AO. Each workload consisted of three VO and two AO. Workloads were set at 5, 10, 15, 20, 25, and 30% of 1 RM.

Results: The mean data is shown in figure 1. The intra-class coefficient (ICC) values for resting measurements were poor-moderate for mBF (0.39) and excellent for mVO2 (0.83). However,

the ICC values for mBF were excellent for each stage of exercise (0.88-0.94). Similarly, the ICC values for mVO2 were excellent for each stage of exercise (0.91-0.98). The mBF was also plotted against mVO2 for each participant in order to calculate the dose-response (slope); however, the reliability for this method was moderate (ICC: 0.68)

Conclusion: These data confirm that continuous wave near-infrared spectroscopy devices can reliably assess muscle blood flow and oxygen consumption during exercise of various intensities.

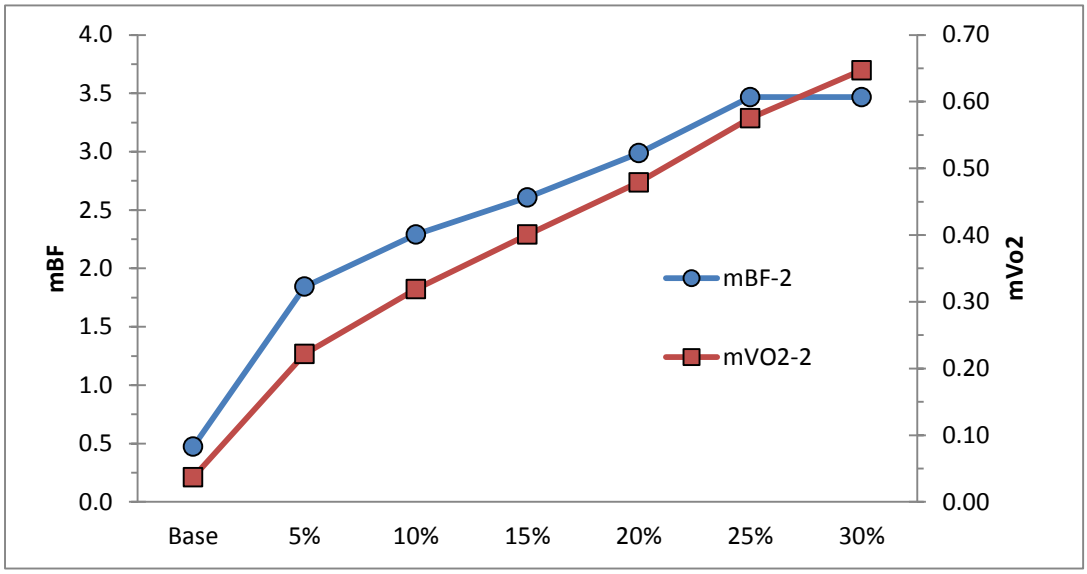

Figure 1. Mean (n=4) muscle blood flow (mBF) and muscle oxygen consumption at rest and for each exercise intensity

P36

Effects of elastic taping versus stretching on delayed onset muscle soreness

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Kinesio taping (KT) has recently been included as a strategy aimed at preventing or reducing the effect of delayed onset muscle soreness (DOMS). However, the effect of KT on DOMS compared to traditional methods (e.g. stretching) has not been studied. In a randomized controlled trial we divided participants into 3 groups (19 participants per group), Kinesio tape (KT), Placebo tape (PT) and Stretching groups (SG). Thirty minutes prior to exercise, Kinesio tape (KINESIO®TEX™, USA) was applied parallel to the dominant quadriceps. Participants in the PT group, had three short pieces of KT applied loosely around the dominant thigh. In both tape groups, the tape remained on the muscles throughout the 4 day post-training. Participants in the SG group completed stretches (10 repetitions held for 30 s with 10 s rest) on the quadriceps immediately after exercise and 3 times per day for the next 4 day. Muscle

soreness was induced by performing 4 sets of 25 maximal isokinetic (60°.s^{-1}) eccentric contractions of dominant quadriceps on an isokinetic dynamometer. Prior to and each day after the eccentric exercise for 4 days the following variables were measured muscle strength, thigh circumference, range of motion, jump performance, pain pressure threshold and creatine kinase levels.

The KT group increased isometric strength by 18.9% (95%CI 3.4-34.4%) at post-exercise day 3 and eccentric strength by 29.6% (3.2-54.8%) at post-exercise day 2 compared to placebo. In addition the KT group reduced muscle soreness at post-exercise day 2 by 23.8% (0.1-47.2%) compared to stretching. However, there was little effect of KT on thigh circumference, jump performance, range of motion, pain pressure threshold or creatine kinase levels throughout the recovery period. In conclusion, the application of KT increased muscle strength recovery after intensive exercise compared to placebo tape and reduced perceived muscle soreness compared to stretching.

P37

Is the test of gross motor development sensitive to intervention across different nations? A meta-analysis

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The Test of Gross Motor Development (TGMD) is an age-normed assessment for fundamental movement skills (FMS) of children aged 3 to 10 years. The test was developed, standardised and enjoying popularity in U.S.A. However, the usefulness of the test outside U.S.A. has not been collectively appraised. This study seeks to determine if the TGMD is sensitive to detect intervention across different nations. We performed a systematic literature search for motor skill intervention studies which had used the TGMD as an outcome measure across EMBASE, MEDLINE, SportsDiscus, and Web of Science. Our inclusion criteria were children aged 3-10 years suitable to be assessed with the TGMD, randomised controlled trials (RCT) or quasi-randomised trials, English language, and reported means and SDs of pre and post-intervention TGMD scores. Risk of bias and quality of studies were assessed by both authors independently, and discrepancies were resolved by discussion.

A total of 7 identified studies were conducted in Australia, Belgium, Brazil, Greece, Iran, Netherlands and USA, were submitted to a meta-analysis. All studies reported statistically significant findings. The random effects model was employed due to large heterogeneity amongst studies. Meta-analysis revealed statistically significant intervention effects for overall TGMD score (SMD = 0.40, 95% CI = 0.19-0.60, $Z = 3.83$, $P < 0.0001$), locomotor subtest scores (SMD= 1.20, 95% CI = 0.50-1.90, $Z = 3.34$, $P < 0.0008$) and object-control subtest scores (SMD = 1.30, 95% CI = 0.62-1.98, $Z = 3.75$, $P < 0.0002$). Quality rating for reported outcomes of TGMD is *moderate* for the overall TGMD, *low* for both locomotor and object-control subtests. Six of the seven studies had a high risk of bias. The present meta-analysis provides evidence of TGMD's sensitivity to intervention across the nations. However, this finding needs to be interpreted with caution due to high risk of bias.

P38

The effect of dynamic and static stretching in the warm-up phase on power output, agility, sprint time and muscular strength; a meta-analysis

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Background: The warm-up process prior to exercise performance is a well-established component of a training programme and stretching is generally an integrated aspect of this process. Static stretching was previously widely implemented but several studies indicated that this method of stretching can actually have a negative effect on subsequent performance outcomes. Research into dynamic stretching indicates that there are no negative consequences on performance when employing this stretching method. Despite this, static stretching is still widely incorporated into the warm-up process.

Objective: The purpose of this study was therefore to review previous research on the effects of static and dynamic stretching on power output, agility, sprint time and muscular strength performance outcomes to determine which stretching method should be incorporated into the warm-up process.

Methods: A search of recent literature (2005 – 2014) was undertaken where only studies that included performance means and standard deviations were selected so that effect sizes could be established. Cohen's "d" was used to calculate effect sizes for relevant variables in each article. Subsequently, mean effect sizes of the 15 articles were calculated to demonstrate any trends. A coding scheme rating each article on 12 criteria on a scale of 0-3 (maximum score of 36) was used to ensure that a high level of research quality was achieved.

Results: The review included 15 studies, from which some conflicting information emerged. The majority of the evidence suggests that dynamic stretching influences performance enhancements when compared to static stretching. Some of the data however indicates that an increased duration of static stretching can enhance performance when compared to shorter durations. However, other components of the warm-up could have influenced these outcomes. The effect size when comparing static and dynamic stretching is commonly low to moderate although an occasional large effect size did occur.

Conclusion: Dynamic stretching predominantly leads to an enhanced performance outcome when compared to static stretching which therefore generally makes this the recommended method of stretching to include in the warm-up process before performance. However, static stretching retains its validity for activities requiring an increased range of motion, intense power, agility and sprinting.

1. Samson, M., Button, D., Chaouachi, A., and Bhem, D. (2012). *Effects of dynamic and static stretching within general and activity specific warm-up protocols.* Journal of Sport Science and Medicine, 11, 131-148.
2. Tramdadia, H. and Jadav, M. (2012*). Effects of static and dynamic stretching on agility performance in tennis players*. Indian Journal of Physiotherapy and Occupational Therapy, 6(1), 36-39.

P39

Improvements in Aerobic Capacity are Associated with Increased Mental and Physical Health in T2DM

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Background: Type-2 Diabetes Mellitus (T2DM) is associated with impaired physical and mental health, which may be improved with exercise.

Purpose: The purpose of the current study was to determine whether a10 week high-intensity exercise intervention in middle-aged men with T2DM improves: (i) mental health, and (ii) whether there's an association between improved physical fitness and mental health.

Methods: 24 middle-aged non-insulin dependent males withT2DM (55.8±5.4y, BMI 28.1±3.3, fasting blood glucose 9.4±3.5) completed high-intensity cycling and resistance training for 10 weeks. Mental and physical health was assessed via the SF-36 Health Survey and a peak aerobic capacity (VO_2peak) test on a cycle ergometer.

Results: The Physical and Mental components of the SF-36 substantially improved by 42±14 (95%CI: 11, 73) and 35±13 points (95%CI: 0.67, 69) respectively. VO_2peak increased significantly by 5.7±4.2 mL/kg/min (95%CI: 1.1, 10). There were moderate likely correlations between mental and physical components of the SF-36 and VO_2peak (r=0.43, 95%CI: 0.01 to 0.72; r=0.33, 95%CI: -0.11 to 0.66) respectively.

Conclusion: These findings indicate that chronic high-intensity exercise in T2DM middle-aged men improves mental health and that these improvements may be associated with aerobic capacity.

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P40

A qualitative examination of a mothers' swim program: What keeps them coming back and how does it improve their psychological wellbeing?

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Exercise is widely accepted as an effective activity for alleviating the psychosocial impact of challenges faced by mothers, however our current understanding of how to help mothers adhere to exercise and how it affects such positive outcomes is lacking. This investigation employed interviews to qualitatively examine what aspects of a mother-focused exercise program (swimming) that participating mothers considered most influential in supporting their continuing exercise adherence as well as positively influencing their psychological wellbeing. The first finding from the 19 mothers interviewed was that their perceptions of the factors supporting their adherence to the swim program were inherently intertwined with

factors they considered positively influenced their mental health. Thematic content analysis of the interviews regarding mothers' experiences of the swim program highlighted three higher order themes associated with supporting continued participation and positive psychological outcomes: environmental factors; social support factors; and health promoting factors. These findings of what appear to be important ingredients for a successful mothers' exercise program to enhance participation and wellbeing should aid the construction of effective interventions based around any sport.

P41

Effects of muscle heating on hypertrophy and strength responses to resistance training

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Heat is known to be a major form of stress caused by exercise, though its value in driving physiological function acutely or chronically is not well understood. There may be potential for greater adaptations in muscle from resistance training with supplemental heating of active muscle mass. Acutely, different aspects of muscle function appear to respond differently to higher muscle temperature, e.g. increased speed of muscle contraction and relaxation, but also more rapid fatigue [1]. Chronically, increased core and muscle temperatures play a role in upregulation of heat shock proteins (HSP). This can lead to muscle regeneration, primarily through facilitation of muscle protein synthesis from enhanced phosphorylation of upstream molecules signaling mTOR (mammalian target of rapamycin) [2].

Through a contralateral-limb control study we aim to examine physical and functional adaptations in muscle to a 12-week resistance exercise programme specifically targeting the knee extensors (quadriceps femoris). One of the participants' limbs will be randomly selected to have mild, external heating of the active muscle mass, using a custom-made heat pad eliciting muscle temperatures of 38-39.5 °C during knee extensor training. Muscle temperature will be measured from the vastus lateralis at rest, immediately after, and 20-minutes after exercise. Anthropometric measures (dual-energy x-ray absorptiometry [DXA], bio-impedance analysis [BIA], thigh girth and skinfolds) will be taken to assess physical changes in muscle mass, and muscle function testing using an isokinetic dynamometer ($60°.s^{-1}$) will be used to measure changes in peak torque and total work. It is hypothesised that the limb subjected to supplemental heating throughout the training programme will produce greater hypertrophy and an improved functional profile. A pilot study is currently being undertaken to investigate the acute effects of local muscle heating on function (strength and work).

The results of this study can provide information that will help determine whether adding passive heating to resistance training protocols may increase the hypertrophic and/or strength response. This will help inform exercise prescription guidelines for healthy and clinical populations seeking to maintain or enhance muscle mass.

1. Ball, D., Burrows, C., & Sargent, A.J. (1999). Human power output during repeated sprint cycle exercise: the influence of thermal stress. Eur J Appl Physiol, 79, 360-366.

2. Kakigi, R., Naito, H., Ogura, Y., Kobayashi, H., Saga, N., Ichinoseki-Sekine, N., Yoshihara, T., & Katamoto, S. (2011). Heat stress enhances mTOR signaling after resistance exercise in human skeletal muscle. J Physiol Sci, 61, 131-140.

P42

Reliability of oscillometric central blood pressure responses to submaximal exercise

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Central blood pressure responses to exercise may provide clinicians with a superior diagnostic and prognostic tool. However, in order to be of value in a clinical setting these assessments must be simple to conduct and reliable. **Purpose**: Using oscillometric pulse wave analysis (PWA), determine the upper limit for between-day reliability of central systolic blood pressure (cSBP) and central pressure augmentation (AIx) responses to three progressive stages of submaximal exercise in cohort of young, healthy participants. **Methods:** Fifteen healthy males (25.8 y (SD 5.7), 23.9 kg/m^2 (SD 2.5)) were tested on 3 different mornings in a fasted state, separated by a maximum of 14 days. Central hemodynamic variables were assessed on the left arm. Participants underwent three progressive stages of submaximal cycling at 50W (low), 100W (moderate) and 150W (moderate-hard). **Results:** During low- and moderate-intensity exercise the ICC values for cSBP (0.79-0.80) and AIx (0.81-0.85) indicated excellent reliability (ICC >0.75). For the moderate-hard intensity AIx could not be computed, and the ICC for cSBP was adequate (0.72). **Conclusion:** Findings from this study suggest that, at least in a young health cohort, oscillometric PWA can be used to reliably assess central blood pressure measurements during exercise, up to a moderate intensity. These measurements offer potential for providing clinicians with a practical option for obtaining important hemodynamic information beyond that provided by resting peripheral blood pressure.

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Exercise intervention in overweight and obese adolescents: Meta-analysis and implications for New Zealand

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Background: The global rise in the prevalence of childhood and adolescent obesity has been linked to modifiable lifestyle factors, including lack of physical activity. However, no known meta-analysis has been conducted on the effects of exercise intervention on weight loss and metabolic risk factors in overweight and obese adolescents.

Objectives: (i) To investigate whether exercise intervention improves body composition and cardio-metabolic risk factors in overweight and obese adolescents. (ii) To discuss the implications of the findings in terms of primary healthcare and public health policy in New Zealand.

Data Sources: Two researchers systematically searched electronic databases (PubMed, Web of Science SPORTDiscus, Google Scholar) from inception up to May 2015. The reference lists of eligible studies and relevant reviews were also checked.

Study Selection: Two reviewers used the following criteria to select studies for inclusion: (i) the study was a randomized controlled trial; (ii) use of a structured exercise intervention, alone or combined with any other kind of intervention; (iii) the control group received no structured exercise control or behavioural modification designed to increase physical activity; (iv) the participants were overweight or obese (BMI $\geq 85^{th}$ percentile); (v) the participants were aged between 10 and 19 years.

Appraisal and Synthesis Methods: Initially, 1667 studies were identified. After evaluation of study characteristics and quality and validity, data from 13 studies (15 trials) involving 554 participants (176 male; 193 female; 187unknown) were extracted for meta-analysis. Fixed effects meta-analyses were utilised for the 5 body composition parameters, and 10 cardio-metabolic parameters. Effect sizes are reported as mean differences.

Results: Following exercise intervention there was a significant reduction in BMI (2.04, CI: 1.54, 2.53), body weight (3.70 Kg, CI: 1.65, 5.75), body fat percentage (3.14 %, 95% CI: 2.15, 4.13), and waist circumference (3.02 cm, CI: 1.25, 4.79), which lean mass significantly increased (1.57 Kg, 95% CI: 0.53, 2.61). There a significant decrease in systolic blood pressure (7.08 mm Hg, CI: 3.49, 10.67), HOMA (1.02, 95% CI: 0.66, 1.39), and following an oral glucose challenge a significant improvement in area under the curve for glucose (39.01 mg/dl, 95% CI: 9.40, 68.61) and insulin (162.02 μU/ul, 95% CI: 93.28, 230.75). This was a non-significant change in fasting glucose (-1.30 mg/dl, 95% CI: -2.78, 0.18), fasting insulin (0.72 μU/ul, 95% CI: -0.89, 2.33), total cholesterol (5.79 mg/dl, 95% CI: -2.16, 13.73), triglycerids (9.18 mg/dl, 95% CI: -2.85, 21.22), HDL (0.20 mg/dl, 95% CI: -1.18, 1.57) and LDL (5.83 mg/dl, 95% CI: -1.20, 12.86).

Limitations: Most included trials were short term (8 to 6 months) and 7 had important methodological limitations. Additionally, the meta-analyses for some of the secondary outcomes had a small number of participants or substantial statistical heterogeneity.

Conclusions: The current evidence suggests that exercise intervention in overweight and obese adolescents improves body composition, including decreased body fat and increased lean muscle mass. The limited available evidence further indicates that exercise intervention improves cardio-metabolic risk factors.

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The effect of low-load high repetition resistance training combined with vascular occlusion or hypoxia on cardiovascular response

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Low-load high repetition resistance training in combination with vascular occlusion or hypoxia can increase muscle hypertrophy, but the effect of such training on cardiovascular response is less clear. This study aimed to investigate the cardiovascular response to resistance training combined with either hypoxia or venous occlusion. In a randomised controlled trial, 23 well-trained netball athletes took part in a 5-week training of knee flexor/extensor muscles in which low-load resistant exercise (20% 1-RM) was combined with either a), an occlusion pressure of ~230 mmHg around the upper thigh (KT, n = 8), b), breathing hypoxic air to generate an arterial blood oxygen saturation of ~80% (HT, n = 7), or c), no additional stimulus (CT, n = 8). All athletes underwent similar resistance training which included 3 sets of knee extensors follow by 3 sets of knee flexors, 3 times per week for 5 weeks. Systolic pressure (SP), diastolic pressure (DP),mean arterial pressure (MAP), heart rate (HR), stroke volume (SV), cardiac output (CO), total peripheral resistance (TPR) and rate pressure product (RPP) were measured immediately after the final set of knee extension exercises at week 1 and week 5. Compared to CT, HT showed a substantial decrease in SP (11.7±11.3%, mean ±90% CL) over the training period and unclear differences in all other parameters. In contrast, compared to CT, the KT group, as a result of training, showed substantial increases in DP (9.8±10.8%), MAP (5.7±6.5%), and TPR (68.8±40.4%), but decreases in SV (17.2±19.5%) and CO (18.0±21.9%). The reduction of SP after hypoxic training also resulting in a substantial decrease in the RPP by 15.6±9.6%, while unclear differences were found in the KT group (3.9±14.3%), compared to CT. Our results indicate that low load resistance training in hypoxia has a greater cardiovascular benefit than similar resistance training with venous occlusion.

P45

Effect of Zingiber cassumunar ROXB (Plai cream) in the treatment of delayed onset muscle soreness

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Plai (Zingiber cassumunar ROXB) is a popular herb in Asia used for relieving pain and inflammation in musculoskeletal disorders. There are currently two commercially available Plai creams on the market, a lower cost, but lower concentration cream (7%), and a more expensive but higher concentration brand (14%). Little is known about the effectiveness of either cream in the reduction of delayed onset muscle soreness (DOMS). Seventy-five untrained healthy volunteers performed 4 sets of 25 eccentric repetitions (100 total) of the dominant leg's quadriceps muscle on an isokinetic dynamometry machine. Participants were then randomized into 3 groups; 14% Plai cream, 7% Plai cream and placebo cream. All groups immediately applied 2 grams of cream (strips of 5 cm long) and gently massaged this into the quadriceps muscles following the exercise and every 8 hours thereafter for 7 days. DOMS, muscle strength (MVC), muscle power (jump height), muscle swelling (thigh circumference),

and muscle damage (creatine kinase) were measured pre and post eccentric exercise in all groups.

Compared to the placebo cream the 14% Plai cream substantially reduced muscle soreness over the 7 days by -82% (95%CI = -155 to -6%, p = 0.03), but had similar muscle soreness effects to 7% Plai cream (-34%, -96 to 27%, p = 0.2). Compared to the placebo cream the 7% Plai cream resulted in a small non-significant reduction in muscle soreness levels over the following 7 days (-40%, -116 to 36%, p = 0.3). Compared to placebo cream there was little effect of Plai cream (7% or 14%) on muscle strength, jump height, thigh circumference or creatine kinase concentration. In conclusion, using 14% Plai cream over a 7 day period substantially reduced DOMS compared to 7% Plai cream or a placebo cream. The 14% Plai cream is a useful alternative for the management of DOMS.

P46

A study of the relationship and influences between leisure and technology in Saudi Arabia society in the city of Riyadh

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The enjoyment of particular technologies during leisure time gives users an opportunity to identify with their devices (Poser, 2011). Leisure is one activity that has captured the interest of man since the Golden Ages. Interestingly, there is almost a universal agreement on the importance of recreational activities to the well-being of mankind (Spracklen, 2009). There is also universal agreement that human beings derive entertainment from a very wide variety of sources depending on many variables, but technology has, in recent days, become one of the most important sources of leisure in the leading cities in the developed and developing world (Leung and Lee, 2005; Tacken, Marcellini, Ruoppila, & Szeman, 2005; Wiggins, 2011; Wajcman, 2008; Aguiar & Erik, 2006; Kaufman, 2006; Vandelanotte, Sugiyama, Gardiner, & Owen, 2009; Biddle, Marshall, Gorely, & Cameron, 2009; Polzien, Jakicic, Tate, & Otto, 2007; Plowman, McPake, & Stephen, 2010; Sonnentag, 2012; Kautiainen, Koivusilta, Lintonen, Virtanen, & Rimpela, 2005). Technology can be defined as the use of scientific know-how to generate practical solutions for the world (Spracklen, 2009). It could also mean any item or machinery produced from application of scientific know how (Spracklen, 2009). The last three decades have seen major advancement within the technology sector with all forms of gadgets coming into being all over the world (Kautiainen, Koivusilta, Lintonen, Virtanen, & Rimpela, 2005; Leung & Lee, 2005; Kaufman, 2006). This has also caused a major shift in the way people utilize their leisure time and the leisure sector continues to be appreciated worldwide for its social-economic contribution.

Nowhere has this shift in the allocation of leisure time been more pronounced than in Saudi Arabia. According to Jakovljevic (2014), more than anywhere else on the globe Smartphone infiltration is highest in the Gulf Cooperation Council, with the average Saudi Arabian resident recording 50% of their view time from mobile gadgets. This statistic implies that the number of people using smartphones in the country is high and the average amount of time people are spending on their smartphone is also high. The statistic indicates that a large percentage of the individuals spending elevated periods of time on their smartphones are from Riyadh Jakovljevic (2004).

The city of Riyadh happens to be the capital of Riyadh province with a population record to the tune of seven million making it the largest city in Saudi Arabia. Being majorly an Islamic society with deep rooted cultures followed to this day, Saudi's people happen to be peculiar in all ways including their way of spending leisure time. It is also vital to note that freedom is expensive in this society, and there exists massive segregation of people on the basis of gender, social class and even religion. However, the Kingdom of Saudi as a whole has marked major strides in increasing the literacy levels with an adult literacy index of 87% by the end of the year 2013 (Index Mundi, 2013). The literacy factor is important in gauging the ability of an individual to use technology.

With this kind of background information about the Riyadh society, we can proceed to identify the searchable fields of knowledge with regard to leisure and technology in Riyadh. Therefore, research on this topic can be carried out on the following angles:

- Availability of technology in the average home in Riyadh
- Contribution of the age factor, economic status, literacy, social class and gender factor in the choice of entertainment technology
- Types of technology available in the Riyadh market
- Play habits among the people of Riyadh
- Motivation behind leisure participation
- The degree of generational gap in children versus adults in terms of technology
- Mobile phone ownership and use as a multi-purpose gadget
- Internet use
- Commonly desired items within the populace
- Over-reliance on technology for leisure as an effect of embracing technology

Summary of Abstracts for the MedSci 2015 Poster Session

No.	Title	Presenter	Institutions
P1	Optogenetic activation of RP3V kisspeptin neurons stimulates luteinizing hormone release in mice	Timothy McLennan	University of Otago
P2	Photoperiodic regulation of Wnt signalling in the arcuate nucleus of the Djungarian hamster, Phodopus sungorus	Alisa Boucsein	University of Otago
P3	Defining the neuropeptide expression of GABA neurons in the arcuate nucleus of the mouse	Christopher Marshall	University of Otago
P4	Prolactin signalling in the arcuate nucleus of pregnant and lactating mice	Eloise Williams	University of Otago
P5	The murine adrenal gland is responsive to immune signals in vivo	Danielle Tranter	University of Otago
P6	A model of mechanical stress in airway smooth muscle	Kevin Roos	Auckland University of Technology
P7	Developing a novel synthetic muscle system with peristaltic actuations using counter-pulsation to assist heart function	Parn Jones	Auckland University of Technology
P8	BDNF and TrkB expression are not changed in the hypothalamic supraoptic and paraventricular nuclei during the development of angiotensin II-dependent hypertension	Aaron Korpal	University of Otago
P9	Extract of Houttuynia cordata Thunb. improves fat accumulation and dyslipidemia in rats fed with high-fat diet	Orathai Tunkamnerdthai	Khon Kaen University
P10	Changes in brain N-acetylaspartate after transcranial direct current stimulation in patients with spinal cord injury and neuropathic pain: A pilot study	Paradee Auvichayapat	Khon Kaen University
P11	Identifying the functional role of microrna-34a in diabetic cardiac stem cells	Sophie Gandhi	University of Otago
P12	Withdrawn		
P13	COMMD10: A novel regulator of the protein trafficking pathway?	Adam Ware	University of Otago
P14	Mechanotransduction of ENaC and the extracellular matrix	Daniel Barth	University of Otago
P15	The effect of remote ischemic preconditioning on cardiac specific microRNAs in the diabetic heart	Langi Vehikite	University of Otago

P16	Central modulation of cardiac sympathetic nerve activity following acute myocardial infarction	Ranjan Roy	University of Otago
P17	Dexamethasone elevates C-type natriuretic peptide (CNP) levels in cerebrospinal fluid and plasma: a dose-response study in sheep	Michele Wilson	Lincoln University
P18	The vascular responses to modulation of flow, but not pressure, are dependent on vascular ENaC function in carotid, femoral and mesenteric arteries from mice	Zoe Ashley	University of Otago
P19	Effects of renal denervation on left ventricular function and the cardiac sympathetic nervous system in established heart failure	Max Pinkham	University of Auckland
P20	MS1/STARS is a target of the JNK signalling pathway in cardiac myocytes	Martin Dickens	Massey University
P21	Signalling regulation of glycogen autophagy in the heart	Kimberley Mellor	University of Auckland
P22	Auditory long term potentiation (LTP) with users of cochlear implants	Nathan Barlow	University of Auckland
P23	The effect of TNFα blockade on the cardiovascular responses to intrauterine inflammation in preterm fetal sheep	Joanna Tse	University of Auckland
P24	Withdrawn		
P25	The dynamic cardiovascular responses to ischemic stroke: temporal relationships between blood pressure, intracranial pressure and cerebral perfusion pressure	Yasemin Sabanli	University of Auckland
P26	Verbal overshadowing in surgical laparoscopy influences neural co-activation and movement kinematics	Liis Uiga	University of Waikato
P27	Effects of acute dietary nitrate supplementation on slope estimations, blood pressure and exercise economy in the elderly	Luke Thomson	University of Waikato
P28	The effects of intermittent sequential pneumatic compression on recovery between exercise bouts in well-trained triathletes	Shannon O'Donnell	University of Waikato
P29	Motivation and mindfulness: Psychological flexibility and autonomous motivation for physical activity	Matthew Jenkins	University of Otago
P30	Effects of strenuous exercise on cardiovascular function	Tasha Bamford	University of Otago

P31	Research findings from a successful application of Hellison's Teaching Personal and Social Responsibility model in a New Zealand primary school. Implications and considerations for the development of children through physical education in the New Zealand school curriculum	Michael Smith	Web Wonks
P32	The relationship between neck strength and head impact kinetics in rugby union players	Danielle Salmon	University of Otago
P33	Does the low-load resistance training under hypoxic conditions mimic high-load resistance training?	Worrawut Thuwakum	Khon Kaen University
P34	Living and training at 825 m incorporated with simulated altitude improves blood parameters in soccer players	Preetiwat Wonnabussapawich	Khon Kaen University
P35	Reliability of skeletal muscle blood flow and oxygen consumption measurements during incremental exercise using near infrared spectroscopy	Adam Lucero	Massey University
P36	Effects of elastic taping versus stretching on delayed onset muscle soreness	Dissaphon Boobpachat	Khon Kaen University
P37	Is the test of gross motor development sensitive to intervention across different nations? A meta-analysis	Jonathan Ng	Khon Kaen University
P38	The effect of dynamic and static stretching in the warm-up phase on power output, agility, sprint time and muscular strength performance: A meta-analysis	Michael Mann	Universal College of Learning
P39	Aerobic capacity is associated with mental and physical health in T2DM	Kim Gaffney	Massey University
P40	A qualitative examination of a mothers' swim program: What keeps them coming back and how does it improve their psychological wellbeing?	Geoff Lovell	University of the Sunshine Coast
P41	Effects of muscle heating on hypertrophy and strength responses to resistance training	Antony Stadnyk	University of Otago
P42	Reliability of oscillometric central blood pressure responses to submaximal exercise	Lee Stoner	Massey University
P43	Exercise intervention in overweight and obese adolescents: Meta-analysis and implications for New Zealand	Lee Stoner	Massey University

P44	The effect of low-load high repetition resistance training combined with vascular occlusion or hypoxia on cardiovascular response	Apiwan Manimmanakorn	Khon Kaen University
P45	Effect of Zingiber cassumunar ROXB (Plai cream) in the treatment of delayed onset muscle soreness	Nuttaset Manimmanakorn	Khon Kaen University
P46	A study of the relationship and influences between leisure and technology in Saudi Arabia society in the city of Riyadh	Khalid Alghenaim	King Saud University