Submissions Abstract Book - Submission And Contributor New Document Abstract Book (Included Submissions)

OC01

Movement and heart rate in the Scandinavian brown bear (*Ursus arctos)*

Leslie Blanchet[1], Boris Fuchs[1], Ole-Gunnar Støen[2], Audrey Bergouignan[3], Andrés Ordiz[4], Timothy G. Laske[5], Jon M. Arnemo[1, 6], Alina L. Evans[1]

[1]Department of Forestry and Wildlife Management, Faculty of Applied Ecology and Agricultural Sciences, Inland Norway University of Applied Sciences, Koppang, Norway [2]Norwegian Institute for Nature Research, Trondheim, Norway [3]Institut Pluridisciplinaire Hubert Curien, CNRS, University of Strasbourg, Strasbourg, France [4]Faculty of Environmental Sciences and Natural Resource Management, Norwegian University of Life Sciences, Ås, Norway [5]Department of Surgery, University of Minnesota, B172 Mayo, MMC 195, Minneapolis, The United States of America [6]Department of Wildlife, Fish and Environmental Studies, Swedish University of Agricultural Sciences, Umeå, Sweden

Background: Understanding animal movement facilitates better management and conservation (Ordiz *et al*., 2016). The link between movement and physiology holds clues to the basic drivers of animal behaviours (Ropert-Coudert *et al*., 2012). In bears, heart rate increases with the metabolic rate during the active phase (Laske *et al*., 2018). Their movement and heart rate change at seasonal and daily scales and can also depend on environmental factors (Ditmer *et al*., 2015). Their behaviour is therefore flexible in activity patterns with high individual variations (Hertel *et al*., 2017). The aim of this study was to establish the relationship between heart rate and distance travelled, and test whether this relationship was influenced by environmental (e.g., time of year and time of day) and biological (e.g., reproductive status, sex, body mass and age of the bears) factors.

Methods: We analysed data of distance travelled and heart rate of 15 GPS-collared brown bears, both males and females, equipped with cardiac loggers in the south of Sweden in 2014 to 2017. For chemical immobilization, the bears were anesthetized with medetomidine, tiletamine-zolazepam and ketamine with doses ranging from 1.5 - 17.1 mg/kg.

Results: Heart rate increased with distances travelled exceeding 50m in an hour (long distances) (Fig. 1), but this correlation depended on the day-of-year with higher heart rate in August than in May (Fig. 2). Bears accompanied by cubs had lower heart rate (59.6±18 (mean±SD) beats per minute, n=5) than solitary bears (66.6±21 beats per minute, n=18), especially in May (Fig. 3). When movement was minimum (<50m in an hour, short distances) (Fig. 1), heart rate was not related to distance travelled and was very variable, regardless of the months (Fig. 4).

Conclusions: Our findings suggest that heart rate increases with long distances travelled, but varies with day-of-year and reproductive status, depending on the metabolic rate. Studying the change in heart rate in bears can help to evaluate their seasonal rhythms and how different factors affect them. This study illustrates the usefulness of combined bio-logging proxies, i.e., movement and heart rates in our case, in animal ecology.

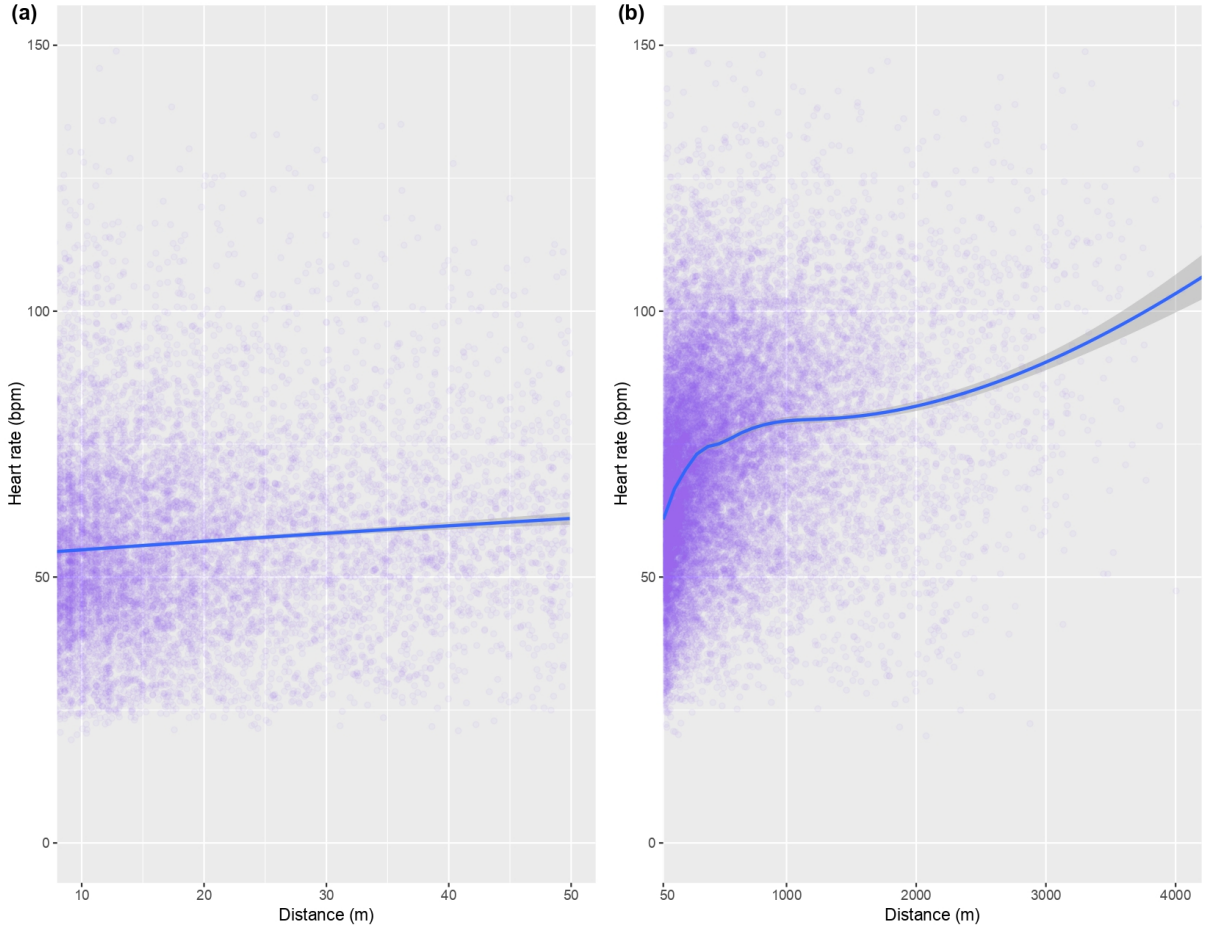
Figures' legend:

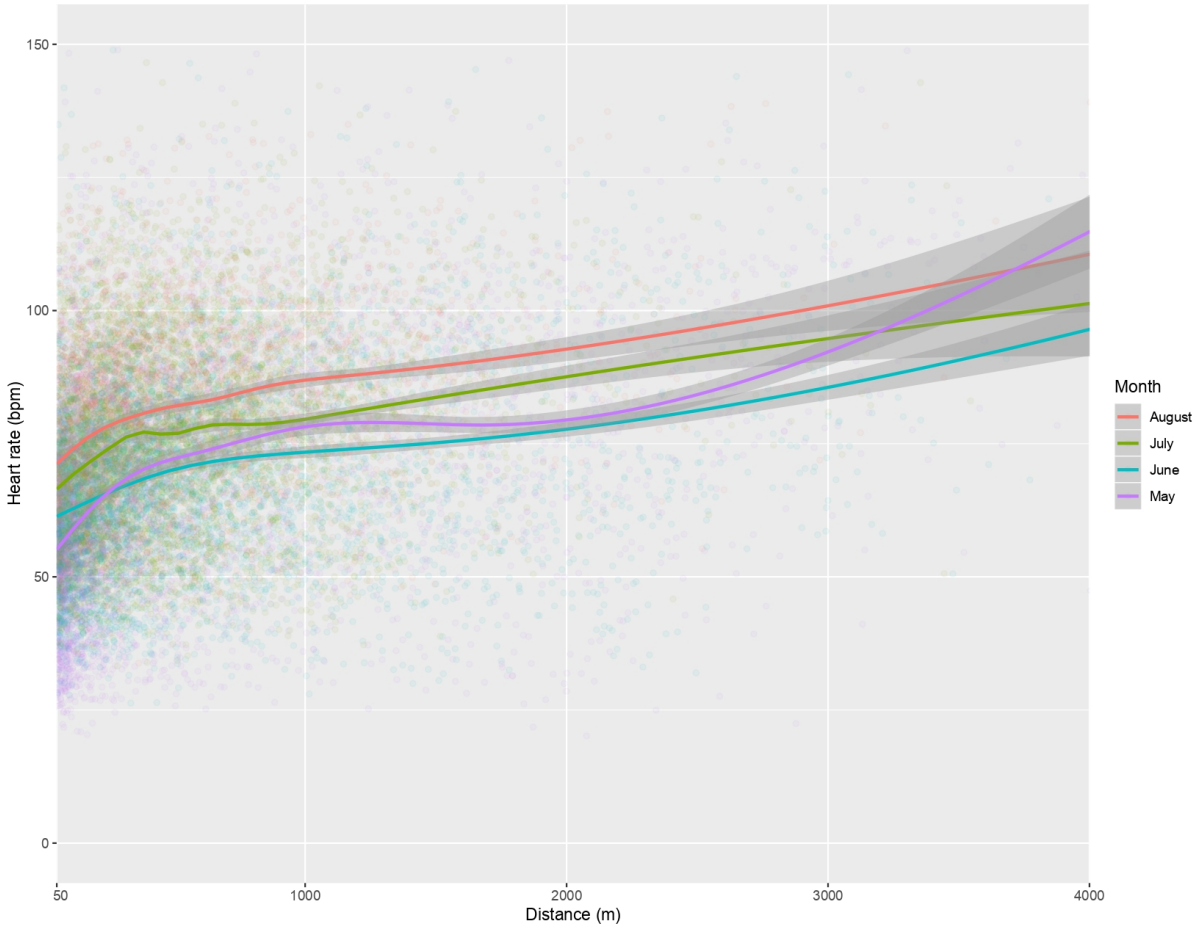
Fig. 1 Scatter plots of distance travelled (m) against heart rate (bpm) during (a) short distances and (b) long distances in brown bears in southcentral Sweden (n=15) (Pearson, P<0.001).

Fig. 2 Scatter plot of long distances travelled (>50m) against heart rate (bpm) grouped by months in brown bears in southcentral Sweden (n=15) (Linear mixed effect, P<0.001).

Fig. 3 Scatter plot of day-of-year against heart rate (bpm) grouped by reproductive status (accompanied bears (A, n=5) and solitary bears (S, n=18)), in brown bears in southcentral Sweden (Linear mixed effect, P<0.001).

Fig. 4 Scatter plot of short distances travelled (<50m) against heart rate (bpm) grouped by months in brown bears in southcentral Sweden (n=15) (Linear mixed effect, P=0.70).

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Distance (m)
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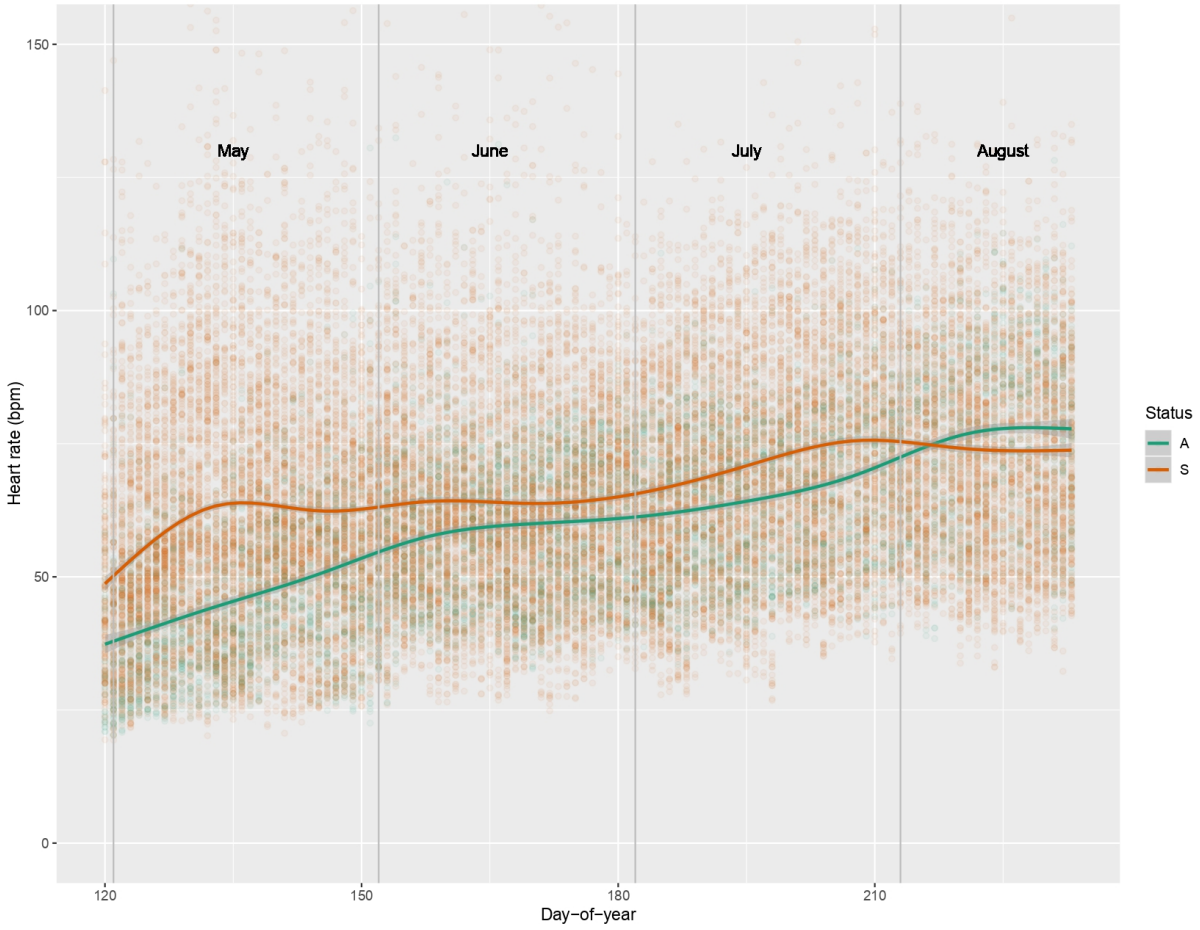
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Heart rate (bpm)
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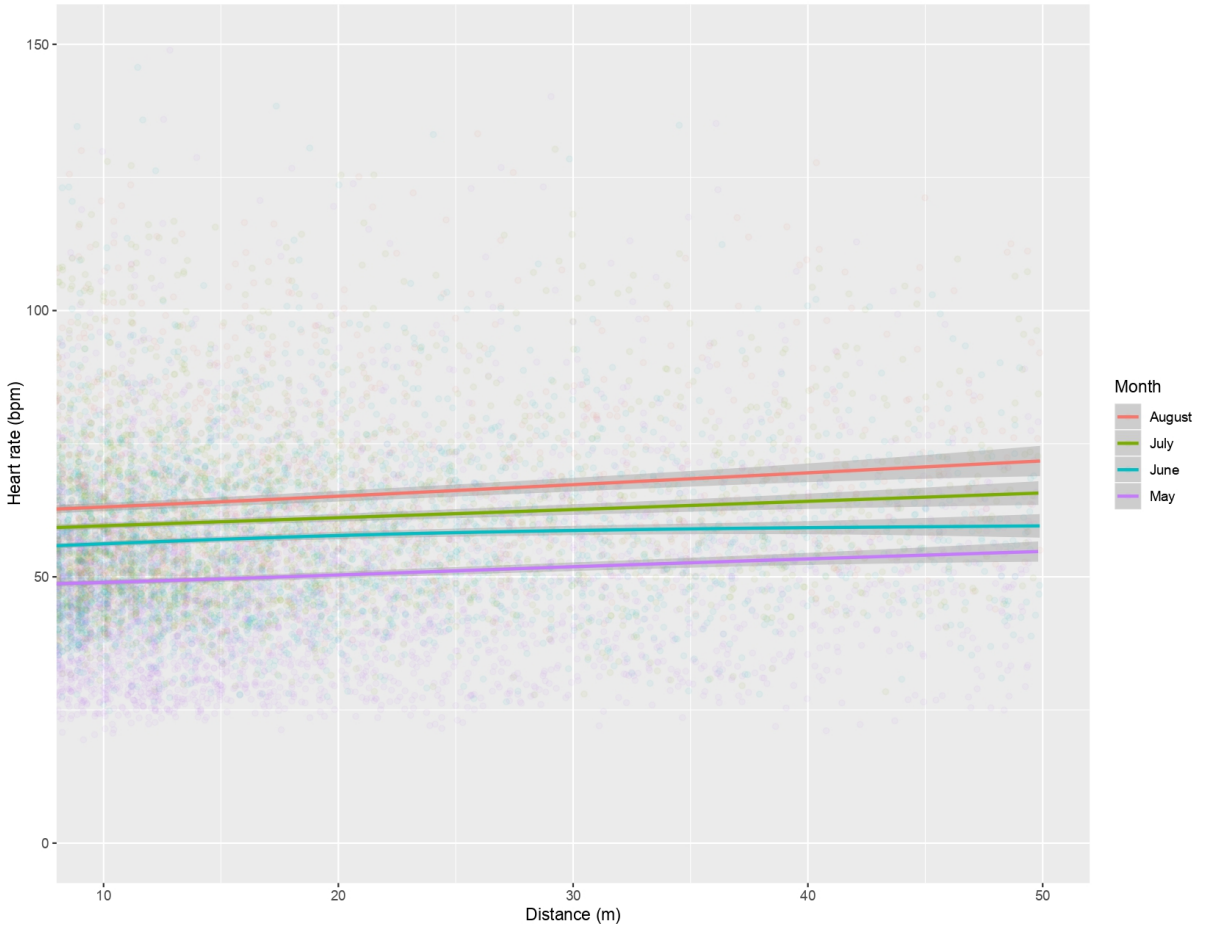

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OC02

Mitochondrial respiration in adipose tissue following long-term diet-induced obesity

Paula Darwin[1], Alice Sowton[1], Julian Griffin[1, 2], Andrew Murray[1]

[1]University of Cambridge, Cambridge, United Kingdom [2]Imperial College London, London, United Kingdom

Obesity is defined by the World Health Organization as an excessive accumulation of fat, such that it becomes a health risk. It is a growing global problem, with 29% of adults in the UK classed as obese in 2017, and is a burden to health services with the NHS reporting that obesity-related illnesses account for more government spending than the police or fire service. It has been linked to changing human behaviour within an obesogenic environment, including more sedentary lifestyles and greater availability of high-fat and high-sugar foods.

Most fats are stored in white adipose tissue (WAT), acting as a fuel store which can be mobilized in times of need. WAT is greatly expanded during obesity, whilst changes are observed in tissue morphology and function. The remodelling of WAT during the progression of obesity is, however, incompletely understood. In particular, it is not known whether changes in mitochondrial function are associated with WAT expansion, and whether this affects the balance between lipid synthesis and oxidation.

We therefore aimed to investigate mitochondrial respiration in the adipose of C57BL/6J mice fed a high-fat high-sucrose (HFHS) diet or standard laboratory chow for 12 months. Clark-type Oxygen electrodes and a substrate-uncoupler inhibitor assay were used to assess different components of respiration in three types of adipose tissue; inguinal (iWAT) and epididymal (epiWAT) WAT, and intrascapular brown adipose tissue (BAT).

Initially, succinate (10 mM) was added to stimulate mitochondrial respiration. This was followed by a titration of the protonophore carbonyl cyanide-4-phenylhydrazone (FCCP; 0.25 µM increments), to uncouple ATP synthase from the electron transfer system. After a peak rate was reached with FCCP additions, antimycin A (10 µM) was added to inhibit complex III and sodium azide (100 mM) added to inhibit complex IV. O_2 consumption rates were recorded at baseline and following each addition, whilst the peak rate of O_2 consumption following FCCP titration was taken. Rates were corrected to tissue mass.

Compared with chow-fed controls, iWAT from HFHS mice had a 57% higher rate of mitochondrial respiration upon activation with succinate ($p<0.01$), and when FCCP was added O_2 consumption was 56% higher in iWAT from HFHS mice ($p<0.01$). EpiWAT from HFHS-fed mice showed a 35% higher O_2 consumption rate in the uncoupled state ($p<0.05$) compared with controls. BAT from HFHS mice showed 19% lower O_2 consumption following antimycin A ($p<0.05$) compared with controls, whilst in iWAT, complex III-inhibited O_2 consumption rate was 42% higher in HFHS mice ($p<0.05$).

This preliminary data highlights that adipose tissue mitochondrial function is altered in diet-induced obesity, with increased respiratory capacity seen in WAT, and non-mitochondrial respiration decreased in BAT but increased in WAT. Lipidomic analysis is ongoing, whilst future work will investigate how alterations in the lipid profile impact on signalling and function of subcellular organelles.

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OC03

A zebrafish model of embryonic growth disruption reveals an ongoing impact on metabolic and cardiac phenotype

Bridget Evans[1]

[1]*University of Manchester, Manchester, United Kingdom*

As climate change continues to pose a global problem, the need to understand organisms immediate and ongoing responses to the changing environment is essential. Temperature modulation and altered access to nutrition have been shown to impact embryonic growth trajectory in a diverse range of animal models[1-3]. The ability of an organism to respond to such changes during embryogenesis is known as developmental plasticity and can heavily influence embryonic growth trajectory. There is significant that altered embryonic growth trajectory has a lasting negative impact on metabolic and cardiac health, with early life growth disruption correlating strongly with increased adiposity, cardiac dysfunction, and metabolic disorder[4,5]. The coordination of these diverse pathways is not fully understood. Grb10 is a negative regulator of the insulin signalling pathway, the main coordinator of embryonic growth and development. While studies have revealed that Grb10 disruption in mammals alters insulin sensitivity and body mass and size, the long-term impact has not been investigated. To address this issue, this study validated the transient disruption of *grb10a* expression in *Danio rerio* by antisense- oligonucleotide-mediated knockdown. The impact on embryonic growth was measured in terms of total body length, while the impact on metabolism was measured in terms of rate of yolk consumption and glucose uptake. Heart rate was also measured to assess cardiac health. The persistent impact on late-juvenile metabolism was measured in terms of

oxygen consumption by stop-flow respirometry. An Affymetrix GeneChip™ Zebrafish Genome Array was used to monitor gene expression over the first 30 days post fertilisation. All data were compared to embryos treated with a standard control morpholino (targeting human beta globin). Phenotypic rescue and reversal were possible through injection of *grb10a* RNA and displayed a dose-dependent effect. Knockdown was sufficient to alter embryonic growth trajectory, respiratory rate, and cardiac function, similar to existing mammalian models. Results are quoted as the mean ± S.E.M., compared by paired t-test. Total body length (3.41 ± 0.02 mm vs 3.16 ± 0.03 mm, $p<0.0001$, n=42), yolk consumption (0.0848 ± 0.009 mm^2 vs 0.0024 ± 0.008 mm^2, $p<0.0001$ n=18), and glucose uptake (55701 ± 2131 AU vs 39811 ±1079 AU, p=0.0002, n=5) were significantly elevated in morphant fish, while heart rate was significantly reduced (79.1 ± 7.3 bpm vs 116.9 ± 2.3 bpm, $p<0.0001$, n=14). Late-juvenile morphant fish continued to present altered metabolic rate (134.40 ± 15.60 $\mu gO_2h^{-1}g^{-1}$ vs 19.00 ± 3.28 $\mu gO_2h^{-1}g^{-1}$, $p<0.0001$, n=5). Transcriptomic data analysed by Qlucore Omics Explorer 2.2 (Lund, Sweden) revealed transient modulation of *grb10a* expression permanently remodelled the transcriptional landscape. Multiple growth factor mediated pathways were highly impacted long after morpholino attenuation. Additionally, expression of key cardiac genes was significantly altered in adult cardiac tissue (*myl7* elevated 20%, $p<0.0001$, n=3, *nppa* down 40%. p=0.0012, n=3). The enduring nature of these changes suggests the zebrafish is a suitable model for longitudinal investigation of the link between embryonic growth disruption, adult phenotype, and later life disease risk. This also provides a predictive example of the impact the rapidly changing environment can have on adult health and phenotype.

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OC04

Maximum voluntary torque and rate of torque development are not effected by whole-body hyperthermia or ten consecutive days of isothermic heat acclimation

Ralph Gordon[1], Christopher Tyler[1], Ceri Diss[1], Neale Tillin[1]

[1]*University of Roehampton, London, United Kingdom*

Maximal voluntary torque (MVT) can be impaired by hyperthermia due to a reduction in the central nervous system's capacity to voluntarily drive (neural drive) the available force capacity of the muscle (1). Rate of torque development (RTD) is a functionally relevant measure of neuromuscular function, with neural drive and the intrinsic contractile properties of the muscle key determinants of RTD (2). Heat acclimation (HA) can offer beneficial physiological and performance benefits (3); however, it is unclear whether these benefits are seen in the neuromuscular system, specifically the neural and contractile determinants of RTD.

Ten participants (5 males, 5 females) visited the laboratory on 13 consecutive days to complete two experimental trials pre- and post- 10 days of isothermic HA, to a target T_{re} of ~39 °C. In each experimental trial participants completed a neuromuscular protocol at T_{re} ~37 °C and ~39 °C. The neuromuscular protocol assessed MVT and voluntary RTD. RTD was assessed at 50, 100 and 150 ms from contraction onset (T_{50}, T_{100} and T_{150}). To quantify neural drive, neural efficacy (NE), which is the ratio between voluntary and evoked torque at 50 ms, was compared. Involuntary Octets (300 Hz) were evoked at rest to assess peak torque (PT), peak RTD (pRTD) and time to peak to tension (TPT). Both experimental trials and HA sessions were conducted in the same environmental conditions (50 °C, 50 % relative humidity). The mean ± SD of each data set were determined and compared by Two and One-way repeated measures ANOVA.

All neuromuscular assessment data are presented in Table 1. HA decreased resting T_{re} (-0.5 °C; $p<0.005$), mean HR (-6 beat/min; $p<0.005$) and increased sweat rate (+0.6 L/hr; $p<0.005$) between HA 1 vs. 10. MVT was unaffected by T_{re} ($p=0.69$) or HA ($p=0.84$) with no interaction effect ($p=0.82$). Similarly, voluntary RTD at all time-points was not effected by T_{re} ($p>0.05$) or HA ($p>0.05$) and did not have an interaction effect ($p>0.05$). Participants produced similar neural drive, evidenced by NE, at both T_{re} ($p=0.92$) and this did not change following HA ($p=0.99$), with no interaction effect ($p=0.75$). There was a main effect of T_{re} ($p<0.005$) for Octet PT, pRTD and TPT, but no effect of HA ($p>0.05$) or interaction effects ($p>0.05$) were observed.

These data show that HA elicited physiological changes indicating successful adaptation to the heat. Maximal and rapid torque production were not effected by a rise in rectal temperature and this was similar following 10 days of HA. The intrinsic contractile properties of the muscle were greater when participants were hotter but also did not change following HA. These data suggest the beneficial physiological adaptations associated with HA do not confer any benefit to the neuromuscular system.

Table 1. Maximal voluntary torque (MVT), voluntary rate of torque development (RTD) at 50 (T_{50}), 100 (T_{100}) and 150 (T_{150}) ms from contraction onset, neural efficacy (NE), peak torque (PT), peak RTD (pRTD) and time to peak tension (TPT) in electrically evoked Octet contractions of the knee extensors, pre- and post- 10 days of heat acclimation, at two different rectal temperatures (T_{re}) . Data are mean ± SD. Significant differences are Bonferroni corrected paired comparisons.

Dependant Variable	T_{re}	Pre	Post
MVT ***(N·m)***	37 °C	203 ± 57	197 ± 53
	39 °C	200 ± 52	202 ± 55
T_{50} ***(N·m)***	37 °C	48 ± 25	52 ± 28
	39 °C	55 ± 30	62 ± 31
T_{100} ***(N·m)***	37 °C	115 ± 39	115 ± 40
	39 °C	121 ± 37	121 ± 38
T_{150} ***(N·m)***	37 °C	152 ± 51	139 ± 27
	39 °C	149 ± 36	136 ± 32
NE	37 °C	0.67 ± 0.18	0.69 ± 0.14
	39 °C	0.65 ± 0.29	0.68 ± 0.17
Octet PT (N·m)	37 °C	127 ± 53	134 ± 57
	39 °C	144 ± 56	**146 ± 66** *
Octet pRTD (N·m·s)	37 °C	2651 ± 1469	2940 ± 1368
	39 °C	**3326 ± 1373** **	**3582 ± 1638** **
Octet TPT (ms)	37 °C	147 ± 10	149 ± 11
	39 °C	**127 ± 7** **	**136 ± 11** **

Significant difference from 37 °C is denoted by * ($p<0.05$) or ** ($p<0.005$)

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OC05

Effectiveness of short-term heat acclimation on heat shock protein 70 in a trained female and male population.

E. J. Cole[1], J. Shaw[1], C.J. Walkington[1], R. Burke[1], J. Bray[1], D. O. Gleadall-Siddall[1], R. V. Vince[1], A. J. Simpson[1], A. T. Garrett[1]

[1]*The University of Hull, Hull, United Kingdom*

Introduction: Short-term heat acclimation (STHA) with no fluid intake, initiates physiological adaptations that has been shown to improve heat tolerance and human performance. Heat shock protein 70 (HSP70) is a highly inducible stress protein elevated in response to heat stress, as well as other conditions such as exercise, cellular acidosis and hypoxia. In male participants, it has been reported that after bouts of STHA, there is an increase in basal intracellular HSP70 expression and an attenuation of the HSP70 response to a subsequent heat stress. HSP70 response could be used as a molecular marker of heat adaptation. However, limited data exists on heat shock protein response in female participants. Therefore, the aim of this work was to determine the effect of STHA on HSP70 in a trained female and male cohort.

Methods: Seventeen participants; six females (Mean [SD]; 23 [3] y; stature 164.9 [7.0] cm; body mass 61.0 [9.2] kg; VO_2 max 44.01 [8.94] $mL.kg^{-1}.min^{-1}$) and eleven males (Mean [SD]; 36 [15] y; stature 175.7 [4.5] cm; body mass 79.4 [11.7] kg; VO_2 max 52.40 [11.01] mL.kg-1.min-1) participated in a STHA programme. This consisted of 90 minutes of heat exposure, with permissive dehydration during heat acclimation (39.5°C and 60% relative humidity), using the controlled-hyperthermia technique (~rectal temperature [T_{re}] 38.5°C), for five consecutive days, in females and four days in males. On the first and final day of acclimation venous blood samples were taken from the median cubital vein prior to, and immediately, after acclimation. Serum samples were analysed using a HSP70 high-sensitivity ELISA (Abcam; ab133061). HSP70 data was corrected for total protein (TP), with the no-fluid intake regime during STHA. Differences pre- and post- STHA, on the first and final day were analysed using a Wilcoxon Signed Rank test. Data are median [Q1-Q3].

Results: In females, HSP70/TP increased from 0.092 [0.088-0.093] ng/ml pre-acclimation to 0.539 [0.535-0.542] ng/ml post-acclimation (P=0.03), on day one of STHA. Similarly, on day 5 of acclimation, HSP70/TP increased from 0.096 [0.092-0.097] ng/mL pre-acclimation to 0.576 [0.558-0.584] ng/mL post-acclimation (P=0.03). The magnitude of change in HSP70/TP was no different on the first and last day of heat acclimation (P=0.16). In males, HSP70/TP increased from 0.089 [0.085-0.092] ng/mL to 0.565 [0.549-0.582] ng/mL on day one of heat acclimation (P<0.001). On the final day of acclimation, baseline HSP70/TP decreased to 0.078 [0.077-0.082] ng/mL, compared to day 1 baseline levels (P<0.001). Interestingly, whilst the increase post-acclimation (0.506 [0.481-0.531] ng/mL), remained (P<0.001), the magnitude of change was less on the final day compared to the first day of acclimation (P=0.002).

Conclusion: - Our work suggests that STHA attenuates the heat shock protein response in the male cohort only. Given the limited information regarding the heat shock protein response in females, further research is required to ascertain the kinetics of the extracellular HSP70 response in this population. Furthermore, our data suggests if HSP70 is to be used as a biomarker for heat acclimation, more research is required into the heat shock response in females.

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OC06

Exercise performance of moderate altitude native athletes at varying altitudes

Emma Clare[1], Dr. Azmy Faisal[1]

[1]*Manchester Metropolitan University, Manchester, United Kingdom*

Introduction: Despite a growing interest in altitude training to improve athletes' performance, the impacts of altitude acclimatization and natural hypoxic training on exercise performance in moderate altitude native athletes at sea-level and higher altitudes are not fully understood (Vogt & Hoppeler 2010; Townsend et al. 2016; Park et al. 2016).

Aim: This study aimed to examine the potential performance advantage in moderate altitude native athletes over lowlander athletes at different altitudes, and to shed light on the live high-train high (LHTH) model for competitions at varying altitudes.

Methods: Twelve elite Ecuadorian inline speed-skaters [6 sea level natives (SLN) and 6 moderate altitude natives (MAN) matched for age, height, weight and performance level] completed 3 incremental cycling exercise tests to exhaustion with measurements of heart rate (HR), blood lactate (BLa), and ratings of perceived exertion (RPE), at sea-level (SL), moderate altitude (MOD, 2700 m), and high altitude (HI,4000 m). Resting haemoglobin (Hb) and haematocrit (Htc) levels were measured at the athlete's native altitude. Statistical significance was determined using ANOVAs and

independent sample t-tests. This study was approved by Manchester Metropolitan University Ethics committee (ethics number:15314).

Results: MAN had significantly higher Hb and Htc levels compared to SLN [15.7±0.9 vs. 13.7±0.4 g/dL; 47.2±2.3 vs. 41.3±1.5 %, respectively; $p < 0.05$ (mean±SD)]. Both SLN and MAN showed progressive reductions in maximum exercise power with increased altitude. However, MAN achieved approximately 10% higher maximum power over SLN at all altitudes with a significant difference between groups at MOD (MAN: 355±35 vs. SLN: 315±31 W, $p<0.05$) (Figure 1. A). There were no changes in submaximal BLa in MAN at various altitudes while SLN showed steady increase in submaximal BLa with increasing altitude (Figure 1. B). Maximum exercise BLa was similar between groups at all altitudes, and surprisingly BLa was significantly higher at MOD compared to SL and HI in both groups ($p<0.5$) (Figure 1. C). MAN had significantly lower resting and exercise HRs compared to SLN at all three altitudes ($p<0.05$) (Fifure 1 D-F). SLN reported greater dyspnoea intensity throughout exercise at high altitude compared to MAN (Figure 1. G-I), while leg discomfort was similar between groups and was not affected by altitude.

Discussion & Conclusion: Increased oxygen carrying capacity with altitude acclimatization and hypoxic training as shown by higher Hb and Htc levels and potentially larger stroke volume from lower HR observed in MAN may account for improved exercise performance over SLN (Diebel et al. 2017; Burtscher et al. 2018). Our findings support the LHTH model for improving exercise performance both at altitude and at SL since MAN were able to achieve higher exercise capacity with less physiological perturbation and lower perceived dyspnoea than SLN.

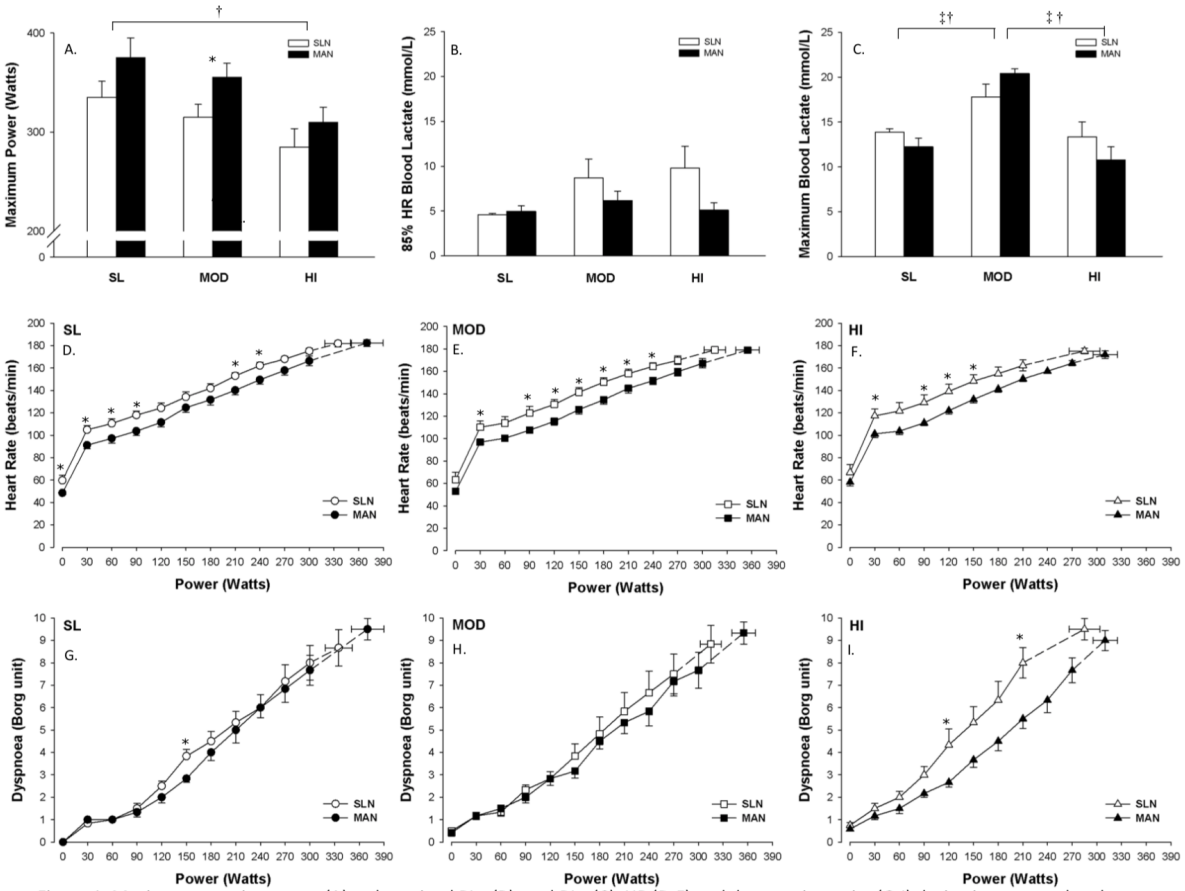

Figure 1. Maximum exercise power (A), submaximal BLa (B), end BLa (C), HR (D-F) and dyspnea intensity (G-I) during incremental cycle exercise to exhaustion in moderate altitude native athletes (MAN, closed symbols) and age-matched sea level control subjects (SLN, open symbols). Values are mean, SE bars. *P<0.05 for MAN versus control SLN; †P<0.05 for differences within MAN; ‡P<0.05 for differences within SLN. Solid line in panels (D – I) represents workloads achieved by all participants.

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OC07

Carbohydrate utilisation during prolonged submaximal exercise is associated with post-exercise *ad libitum* energy intake in healthy adults

Benjamin Narang[1], Javier Gonzalez[1]

[1]*University of Bath, Bath, United Kingdom*

Excessive weight gain is attributed to a chronic positive energy imbalance (1), so an understanding of the interaction between energy expenditure and energy intake is vital. Rodent studies have positively correlated both carbohydrate oxidation rates (2) and liver glycogen content (3) with subsequent energy intake, suggesting a greater utilisation of carbohydrate relative to fat may increase food consumption. More recently, Edinburgh and colleagues (4) observed a moderate positive correlation between hepatically-derived exercising carbohydrate utilisation and energy intake compensation in humans. Whether these observations reflect a causal relationship is currently unclear. Therefore, this study aimed to investigate the interaction between exercising substrate utilisation and post-exercise appetite in healthy adults. An increased utilisation of carbohydrate relative to fat during exercise was hypothesised to increase voluntary energy intake and subjective appetite ratings.

Nine healthy adults (mean ± 95%CI; age 25 ± 4 y, body mass index 23.0 ± 1.7 $kg \cdot m^2$, peak oxygen uptake 45 ± 7 $ml \cdot kg^{-1} \cdot min^{-1}$) volunteered for a two-trial randomised crossover study. Participants cycled for one hour at (mean ± 95%CI) 45 ± 3% $\dot{V}O_2peak$, ingesting 25 $mg \cdot kg$ body $mass^{-1}$ niacin - to suppress fat oxidation - or placebo. Energy expenditure and relative substrate utilisation were quantified using indirect calorimetry and stoichiometric equations (5). Fingertip blood samples were analysed for serum non-esterified fatty acid concentrations using enzymatic colorimetric assays. Subjective appetite ratings were assessed using visual analogue scales. An *ad libitum* lunch was provided in the laboratory before participation continued in free-living conditions. For the remainder of the day participants exclusively consumed the test meal to appetite and replicated their physical activity behaviours between trials.

As niacin did not inhibit lipolysis (**Figure 1A**) or influence whole-body exercising substrate utilisation (**Figure 1B**), inferences regarding the study aims and hypotheses were made using within-individual correlations (*r*) with 95% confidence intervals (lower bound, upper bound). Strong positive associations were observed between exercising carbohydrate utilisation and energy intake at lunch (*r* = 0.79 (0.28, 0.95); **Figure 2A**) and across 24 hours (*r* = 0.74 (0.08, 0.95); **Figure 2B**). However, carbohydrate utilisation did not correlate with increases in subjective appetite (*r* = 0.31 (-0.51, 0.83); **Figure 3A**), and subjective appetite exhibited little association with subsequent energy intake (*r* = 0.28 (-0.53, 0.82); **Figure 3B**).

These data suggest that an upregulation of carbohydrate oxidation relative to fat oxidation during exercise is positively associated with subsequent *ad libitum* food consumption in healthy adults. However, these behavioural responses do not appear to be mediated by subjective appetite perception. Further research is required to establish causality, and to investigate the real world

application of these findings.

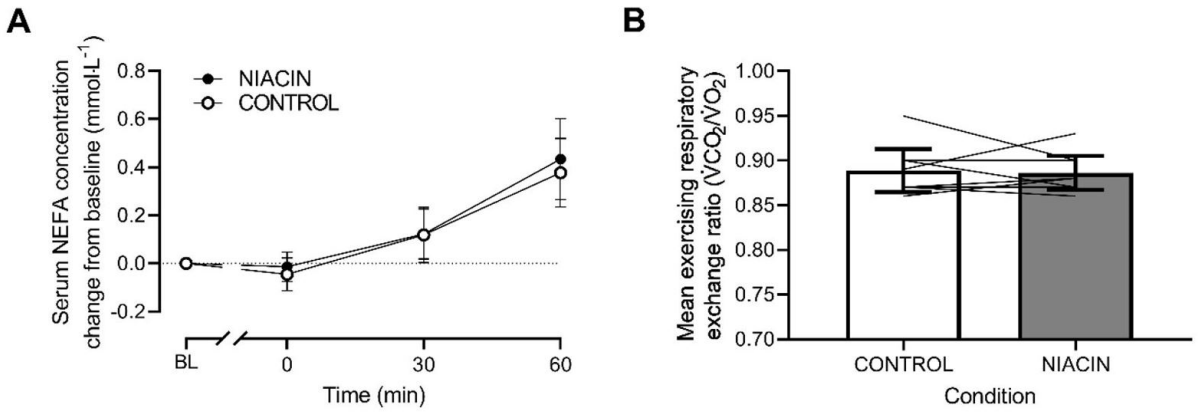

Figure 1. The metabolic effect of niacin during one hour of cycling displayed as change in serum non-esterified fatty acid (NEFA) concentrations relative to baseline (A) and whole-body respiratory exchange ratio (B). Values are means with error bars representing 95% confidence intervals. *n* = 8. $\dot{V}O_2$, oxygen uptake; $\dot{V}CO_2$, carbon dioxide production.

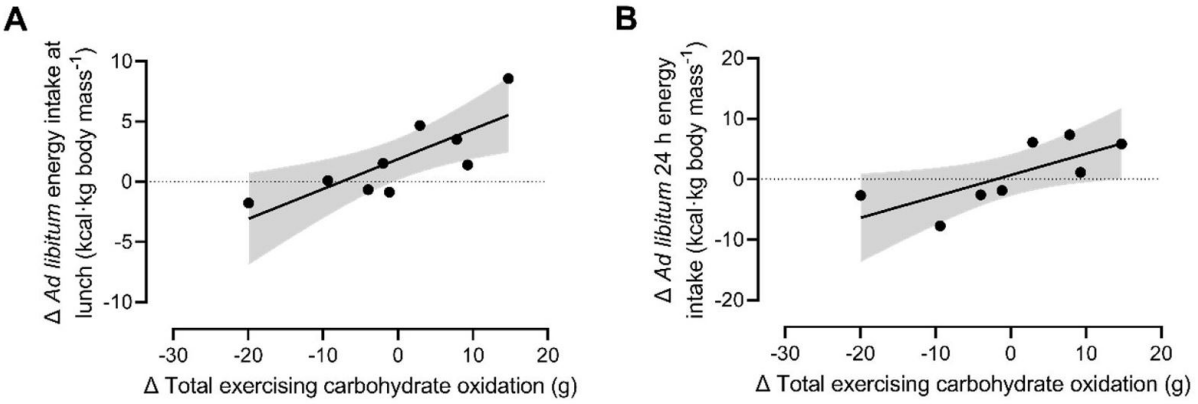

Figure 2. Pearson correlations between within-individual inter-trial differences in total exercising carbohydrate oxidation and energy intake at lunch (A) and across 24 hours (B). Shaded areas represent 95% confidence limits for correlation coefficients. One participant consumed all available food during free-living conditions and was therefore excluded from 24 hour analysis. For panel A, *n* = 9; for panel B, *n* = 8.

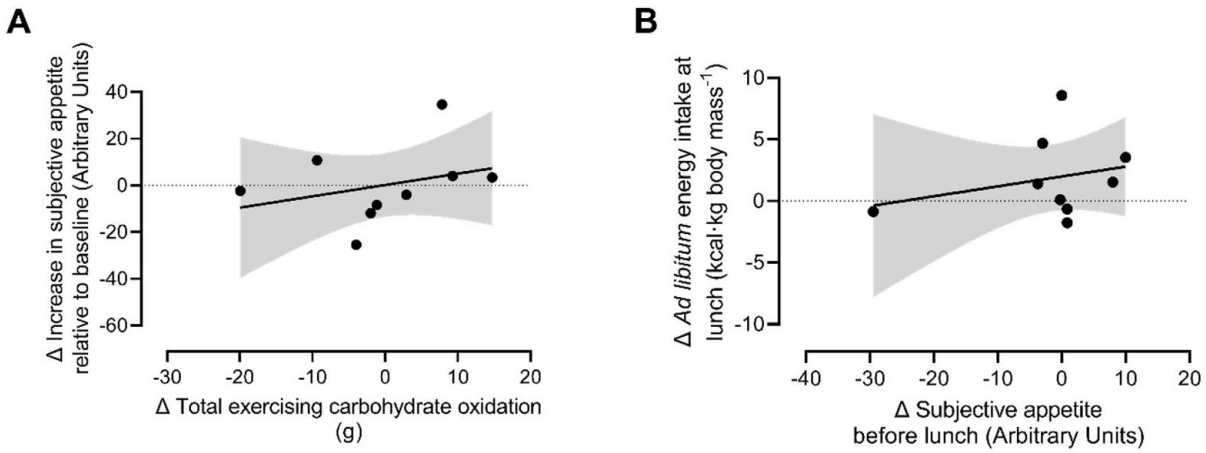

Figure 3. Pearson correlations between within-individual inter-trial differences in total exercising carbohydrate oxidation and increases in subjective appetite ratings from baseline to lunch (A), and inter-trial differences in subjective appetite ratings before lunch and subsequent *ad libitum* energy intake at lunch (B). Shaded areas represent 95% confidence limits for correlation coefficients. *n* = 9.

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Protective effect of co-administration of vitamins C and E on reserpine-induced motor and cognitive impairments and oxidative stress in mice (Mus musculus)

Timothy Danboyi[1], Abdulazeez Jimoh[2], Abdulwahab Alhassan[2], Evelyn Hassan-Danboyi[2]

[1]Kaduna State University , Kaduna , Nigeria [2]Ahmadu Bello University Zaria , Zaria , Nigeria

Introduction: Oxidative stress plays a central role in the pathogenesis of Parkinson's disease (PD). Several antioxidants have been explored but no study have shown the efficacy or benefits of combining vitamins C and E in ameliorating the motor and cognitive impairments associated with PD and there is no existing therapy that halts or slows the progression of PD yet. Aim: This study was aimed at finding out whether combining vitamins C and E confer protection against reserpine-induced motor and cognitive impairments as well as oxidative stress in mice. Methods: Twenty-five mice were randomly assigned into 5 groups of 5 animals each. Group I received distilled water only. Groups II-V received reserpine 0.1 mg/kg intraperitoneally on alternate days. In addition to reserpine, Group III received vitamin E 200 mg/kg/day orally, group IV received vitamin C 250 mg/kg/day orally and group V received combined vitamin E 200 mg/kg/day and vitamin C 250 mg/kg/day orally. All vitamins were given one hour before reserpine administration for 28 days. Neurobehavioral assessment using novel object recognition test (NORT), Y-maze, beam walk and open field test (OFT) was carried out. Thereafter, the mice were humanely sacrificed and brain homogenate made. Values at $P<0.05$ were considered significant. Ethical approval was obtained from the Ahmadu Bello University Committee on Animal Use and Care (Approval No.: ABUCAUC/2020/71). Results: The poor discrimination index noted in group II (-0.35±0.23) was significantly ameliorated in group V (0.59±0.12). There was also significant increase in percentage alternation (66.7±9.25%) but decrease in number of foot slips (0.3±0.25) and time taken to reach the safe box (3.00±0.41s) in group V compared to the other groups. In the OFT, the transfer latency was significantly decreased (10.3±1.45s) while the number of lines crossed was increased (56.0±13.53) in group V compared to the other groups. The malondialdehyde concentrations was significantly decreased in all vitamin-treated groups compared to group II (42.2 ± 028 µmol/L). But a significant increase in superoxide dismutase and catalase levels was observed across all the vitamin-treated groups compared to group II. Conclusion: The co-administration of vitamins C and E confers a protective effect against motor and cognitive impairments and oxidative stress induced by reserpine in mice.
Key words: co-administration, cognitive impairment, motor impairment, oxidative stress, protective, vitamins.

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OC09

The increased sensitivity of Alzheimer's disease patients to antipsychotics such as amisulpride could be linked to changes in solute carrier (SLC) transporters expression at the blood-brain barrier (BBB)

Sevda Boyanova[1], Hao Wang[1], Dr Alice Fleckney[1], Dr Ariana Gatt[2], Dr K. Miraz Rahman[1], Dr Gema Vizcay-Barrena[3], Prof Roland Fleck[3], Dr Suzanne J. Reeves[4], Dr Sarah A. Thomas[1]

[1]King's College London, School of Cancer and Pharmaceutical Science, Institute of Pharmaceutical Science, 150 Stamford Street, SE1 9NH, London, United Kingdom [2]King's College London, Wolfson Centre for Age-Related Diseases, Institute of Psychiatry, Psychology and Neuroscience, SE1 1YR, London, United Kingdom [3]King's College London, Centre for Ultrastructural Imaging, Guy's Campus London Bridge, SE1 1UL, London, United Kingdom [4]University College London, Division of Psychiatry, 149 Tottenham Court Road, W1T 7NF, London, United Kingdom

Amisulpride is an atypical antipsychotic which antagonises dopamine (D2, D3) receptors *in vitro* and *in vivo* [1]. However, there is not enough data for its safe and effective dosage in older people or people with dementia, including Alzheimer's disease (AD) [2]. Importantly, aged patients, and especially older patients with dementia show increased sensitivity to atypical antipsychotics, including amisulpride [2,3]. Studies have suggested that central pharmacokinetic alterations at the blood-brain barrier (BBB) might cause the increased sensitivity [3, 4]. Our present study examines healthy and Alzheimer's disease physiology to further understand this increased sensitivity.

In silico molecular docking studies were used to identify transporters of interest for our model substrate amisulpride. *In vitro* we studied the impact of the solute carrier transporters: plasma membrane monoamine transporter (PMAT), multi-antimicrobial extrusion proteins 1 and 2 (MATE1 and MATE2) on amisulpride transport in human cerebral microvessel endothelial cells/D3 (hCMEC/D3). We incubated the cells with [^{3}H]amisulpride (3.8-7.7 nM) and [^{14}C]sucrose (0.7-1.5 µM) with or without transporter inhibitors. *In vivo*, we investigated the BBB transport of amisulpride in 5xFamilial Alzheimer's mouse model (5xFAD), and in age matched wild type mice (WT, C57/BL6) (12-15 months old). All experiments were performed in accordance with the Animal Scientific Procedures Act (1986) and Amendment Regulations 2012 and with consideration to the Animal Research: Reporting of In Vivo Experiments (ARRIVE) guidelines. All mice were anaesthetised via intraperitoneal injection of a mixture of medetomidine hydrochloride (2 mg/kg, Vetoquinol UK Limited) and ketamine (150 mg/kg, Pfizer, UK, and Chanelle, UK). Once the absence of surrogate indicators of consciousness was confirmed, the mice were perfused with artificial plasma, containing [^{3}H]amisulpride (6.5 nM) and [^{14}C]sucrose (9.4 µM). The presence of amyloid plaques was confirmed in 5 and 12 months old 5xFAD mice by transmission electron microscopy. The presence of PMAT in hCMEC/D3, and in WT and 5xFAD brain capillary samples was studied by Western blot.

Preliminary *in silico* analysis and molecular docking suggested that amisulpride is a substrate of MATE1, PMAT, organic cation transporter 1 (OCT1), and glucose transporter 1 (GLUT1). In hCMEC/D3 cells PMAT inhibition led to a significant increase in [^{3}H]amisulpride cell accumulation ($F(1, 58) = 16.33$, $p=0.0002$). The increase was observed at 20, 30, 60 and 120 minutes by 63.9% ($p=0.0338$); 83.3% ($p=0.0237$); 85.1% ($p=0.0010$); and 68.6% ($p=0.0001$), respectively. MATE1 and MATE2 inhibition did not cause an effect. Compared to WT (n=6), the 5xFAD (n=7) mice had increased [^{3}H]amisulpride uptake in the striatum ($t=1.975$, $df=11$, $p=0.0370$), whereas [^{14}C]sucrose (passive

permeability measure) permeability was not significantly changed. Western blots confirmed PMAT expression in hCMEC/D3 cells. OCT1, MATE1 and MATE2 expression in hCMEC/D3 cells has previously been confirmed by our group [4, 5]. Also, we found that PMAT is expressed in WT and 5xFAD brain capillaries.

PMAT, MATE1, OCT1 and GLUT1 are implicated in the transport of amisulpride at the BBB. The increased brain permeability to amisulpride in 5xFAD mice suggests altered BBB transporter function, possibly due to changes in brain capillary SLC transporter expression with AD [4].

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OC10

NMDA receptors modulate Ca^{2+}-dependent presynaptic activityat multisensory synapses of the dorsal cochlear nucleus

Maša Švent[1], Nick Hartell[1], Martine Hamann[1]

[1]*University of Leicester, Leicester, United Kingdom*

Recent studies have shown that acoustic over-exposure, leading to gap-detection deficits in a rodent model of tinnitus, also increases glutamate release at dorsal cochlear nucleus (DCN) multisensory synapses (1). This activates NMDA receptors (NMDARs) and leads to saturation of long-term potentiation (LTP) (1). The aim of this study was to investigate the role of NMDARs in modulating Ca^{2+}-dependent presynaptic activity and glutamate release in the DCN molecular layer. Whole-cell recordings were used to record miniature excitatory postsynaptic currents (mEPSCs) from DCN fusiform cells in CBA mouse slices. Miniature EPSCs were isolated with tetrodotoxin (1µM) and recorded in the presence of NMDAR agonist (500nM NMDA) with and without antagonist (50µM D-AP5). All values are reported as mean±SD. Unless otherwise stated, Friedman test with Dunn's correction was used for statistical comparisons. In 8 out of 12 fusiform cells, NMDA increased mEPSC frequency (decreasing inter-event intervals from 0.68±0.41s to 0.42±0.31s, $p<0.05$) which was reversed by the addition of D-AP5 (inter-event interval 1.0±0.89s, NMDA vs NMDA+D-AP5 $p<0.05$, control vs NMDA+D-AP5 $p>0.99$, $F=7$, $n=8$). NMDA did not affect mEPSC amplitude ($p=0.2$, $F=1.85$, RM one-way ANOVA with Holm-Sidak's correction, $n=8$) or decay time constant ($p=0.24$, $F=3.3$, $n=8$). Selective effect on mEPSC frequency indicates a presynaptic effect of NMDARs. This was further assessed in transgenic mice expressing SyGCaMP2-mCherry, a ratiometric Ca^{2+} sensor reporting Ca^{2+} level changes in presynaptic boutons (2). Epifluorescence imaging of molecular layer showed that NMDA increased baseline fluorescence compared to control slices ($p_{interaction}<0.001$, $F=3.3$, mixed ANOVA, control $n=5$, NMDA $n=7$) after 12 min of perfusion ($p<0.05$, $F=9.9$, univariate ANOVA). Fluorescence responses evoked by parallel fibre stimulations were recorded in absence and presence of D-AP5. D-AP5 decreased the peak fluorescence compared to control slices (from 101.2±5.9% to 77.1±8.6% F/F_0, p(interaction)<0.01, $F=2.4$, mixed ANOVA, control $n=7$, D-AP5 $n=8$) after 25 min of perfusion ($p<0.001$, univariate ANOVA). Multiphoton imaging showed that D-AP5 decreased the peak F/F_0 per bouton (from 1.4±0.2 to 1.3±0.2 F/F_0, $p<0.0001$, Wilcoxon test, $W=-1281$, $n=57$ boutons, $N=4$ slices) without changing the number of responding boutons (from 62.9±15.9% to 52.3±22.2%, $p=0.06$, unpaired t-test with Welch's correction, $t=1.9$, $n=24$, $N=4$). In conclusion, activation and inhibition of NMDARs lead to an increase and a decrease of presynaptic calcium respectively, at DCN multisensory synapses. This study suggests that the increase of glutamate release observed after acoustic over exposure (1) is likely to be mediated by a presynaptic action of NMDA at those synapses.

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OC11

Artificial intelligence, Bioprinting and Nanotechnology: The role of future Physiologist.

Abdulrahman Olagunju[1]

[1]*The Federal University of Technology, Akure, Nigeria, Akure, Ondo state, Nigeria*

A recent statistics released by Allaboutcareers.com, a leading careers exploration website, reveal that 44% of undergraduates are unable to define the industry that they would like to work in once they graduate. These are worrying statistics that emphasise the need for high quality, free and easy to access careers information for young people that will increase undergraduate awareness with different careers that can be pursued as a physiologist.In this paper, I show how artificial intelligence (A.I), bioprinting and nanotechnology can create employment opportunities for future physiologist by bridging wide gap of knowledge in research, teaching and clinics.The role of physiologist in the advancement of A.I in medicine is critically indispensable. For common diseases, physiological genomic readouts in disease-applicable tissues may be an effective surrogate to measure the effect of genetic and environmental factors and their interactions that underlie disease development and progression. As AI continues to advance, new analytical approaches, including those that go beyond data correlation, are under development. Physiological genomic readouts in disease-relevant tissues, combined with advanced AI, can be a powerful approach for precision medicine for common diseases. Also, deep learning process of A.I analyzes unstructured physiological/medical data (ECG, blood tests, EKGs, genomics, patient medical history) to give doctors better insight into a patient's real-time needs. Moreover, how quick diagnoses can prospectively reach throughout recovering the analysis measures on electrophysiological (EP) or electronic medical record (EMR), imaging and genetic which is a major power of the artificial intelligence (AI) techniques are explained. In another vein, Nanotechnology is another exciting new area in science, with many possible applications in medicine and physiological research. The application of nanotechnology to biosensor design and fabrication promises to revolutionize therapy at the molecular and cellular level. A great example of this is a group of researchers at Worcester Polytechnic Institute who are using antibodies attached to carbon nanotubes in chips to detect cancer cells in the blood stream. The researchers believe this method could be used in simple lab tests that could provide early detection of cancer cells in the bloodstream. Also, applications of nano particles in drug delivery, protein and peptide delivery, cancer are explained. Also, another technology in which physiologist could use to enhance their work and researches is bioprinting. Bioprinting is an emerging technology for constructing and fabricating artificial tissue and organ constructs. This technology surpasses the traditional scaffold fabrication approach in tissue engineering(TE). Currently, there is a plethora of research being done on bioprinting technology and its potential as a future source for implants and full organ transplantation. Recreating tissues and organs requires the recreation of structures and functions within the tissue, including signaling networks, cellular interactions, multiple cell types, and physiological activity; this can be done by physiologist with their understanding of composition of structures and their mechanisms of action. This paper shows how physiologist can apply this exciting technology in their research which will largely help in the field of medicine.

OC12

Enhancing physiology teaching and learning through the use of holograms in health sciences and medicine

Christian Moro[1], Charlotte Phelps[1], Zane Stromberga[1]

[1]*Bond University, Gold Coast, Australia*

Due to increasing demands in the content that needs to be covered in physiology and anatomy, as well as the increased need to dedicate time to clinical skills practice, medical students can benefit from the introduction of effective tools to enhance their level of engagement with learning material while promoting knowledge retention. One of the key aspects of medical education is mastering the terminology, science and clinical application of human anatomy, which some students may perceive as challenging in their pre-clinical years (1). However, there are substantial limitations for students to effectively learn anatomy due to the restrictions regarding the time frame in which they have face-to-face access to a cadaver. Students studying the human body from illustrations or textbooks may find it challenging to understand the complex interactions of organs in 3D space (2). A new disruptive technology, mixed reality through the use of holograms, has been introduced as a tool which can render the human body in a full 3D environment (3). The aim of this study was to investigate and compare the effectiveness of holographic technologies using Microsoft's HoloLens against an identical lesson on a tablet-based augmented reality platform, to assess students' perceptions, experiences, and knowledge acquisition. Thirty-eight participants were randomly allocated to either mixed reality (HoloLens) or augmented reality (AR) group to complete a lesson of the structure and function of the brain. Participants completed a five-question pre-test before the lesson, as well as a post-test questionnaire consisting of 10 questions evaluating the acquired knowledge of the structure and function of the brain discussed in the lesson. After the lesson, participants completed two Likert-style questionnaires evaluating the adverse health effects experienced and the participant engagement with the learning module. A Mann-Whitney U test was undertaken to analyze pre- and post-test scores, as well as the significance between the adverse health effects experienced and enjoyability using the learning tools. At baseline, there was no significant difference in knowledge between the two groups. The average post-test scores for the AR group was 74% and for the HoloLens group was 79%, with no significant differences between knowledge gained. Both augmented reality and holograms resulted in similar adverse health effects experienced during the lesson, however the participants in the holograms group experienced a significant increase in the severity of dizziness. The holograms group rated a higher overall enjoyment with their learning tool and reported a significantly higher rating towards the clearness of instructions and labels in the brain lesson compared to the AR group. Finding ways to improve and optimize learning for the diverse range of learners in today's higher education classrooms can be challenging. Variations in the disruptive technology devices, the introduction of mixed reality, and other new modes provide a range of options for educators wishing to adopt technology-enhanced learning within their curricula (4). This study provided evidence that the HoloLens is as effective as AR-based lessons for learning and engagement within physiology education.

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OC13

Establishing Baseline Physiological Parameters in the Gray Wolf (*Canis lupus*) for Future Environmental Impact Studies

Noelle Laske[1], Roberta Ryan[2], Mark Beckel[2], Rosana Moraes[3], Timothy Laske[4], Peggy Callahan[2]

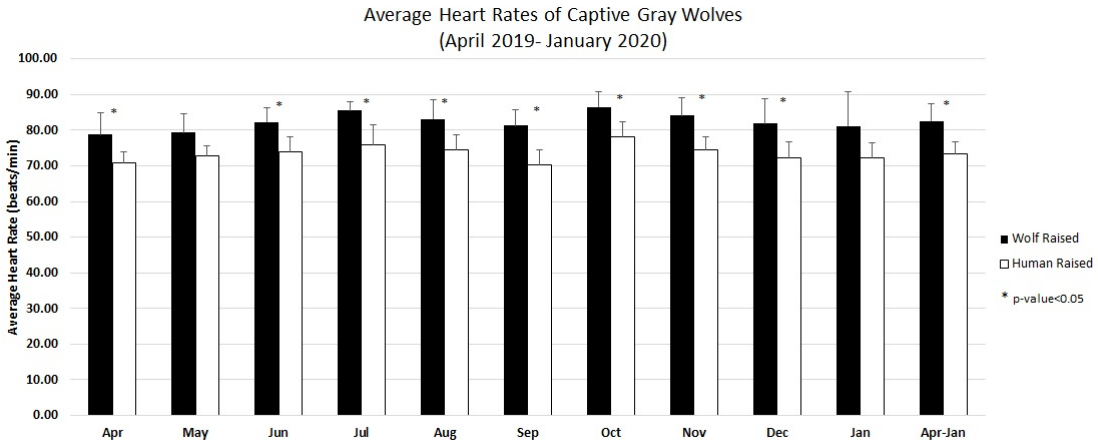
[1]University of St. Thomas, St. Paul, MN, The United States of America [2]Wildlife Science Center, Stacy, MN, The United States of America [3]Smithsonian Conservation Biology Institute, Front Royal, VA, The United States of America [4]University of Minnesota, Minneapolis, MN, The United States of America

Background: In order to characterize the impact of environmental factors on a species, both methods for collecting such information and baseline values are required. Advances in implantable cardiac monitors for human patients provide an opportunity for sophisticated physiologic monitoring in wild species. This study aimed to collect baseline data on cohorts of captive gray wolves housed at the Wildlife Science Center in Stacy, MN. Twelve wolves in four cohorts of wolves were included in this study. Three wolves were wild-born/wolf-raised, three were captive-born/wolf-raised, and two cohorts of three wolves were captive-born/human-raised.

Methods: To collect physiological data, insertable cardiac monitors (ICM; Medtronic Reveal LINQ™) with custom software (B-Ware) were subcutaneously implanted in a left axillary position in 12 sub-adult wolves. The ICM has a 3-year life and records average heart rates (HR) over 2-minute intervals, activity in 15-minute intervals, and subcutaneous impedance, temperature, and posture once every 4 hours. Following implantation, the wolves were handled at least once per year and data downloads were conducted wirelessly (Medtronic CareLink™ programmer).

Results: Several months of high-density physiological data were successfully retrieved from 10 wolves for inclusion in this analysis. Monthly average HR was calculated for each wolf based on two-minute averages (at least 188,026 HR values were available and analyzed per animal). Two-tailed t-tests were performed to determine differences in heart rates among the cohorts. When comparing wolf-raised versus human-raised, it was found that the wolf-raised cohorts had significantly higher HRs overall (82.5 versus 73.4 bpm) and differences were significant in 8 of 10 months ($p<0.05$). The two animals with the highest average heart rates were both wild-born/wolf-raised (87.7 and 87.8 bpm). Four of the five animals exhibiting the lowest heart rates were captive-born and human-raised. See bar graph for details. Additional analyses are in progress, including daily and monthly variations in HR, in addition to an assessment of the other physiological parameters.

Conclusions: Insertable cardiac monitors were successfully deployed in captive gray wolves, capturing long term physiological recordings. Heart rates were characterized in a population of wolves, including wild-/captive-born, and wolf-/human-raised. These methods and results can provide a foundation for future studies on the impact of climate change and/or human interactions on wolf welfare and behavior.



Acknowledgements :- Insertable cardiac monitors donated by Medtronic.

OC14

Small heart revealing big insights: understanding pharmacology of cardiotoxic air pollutant phenanthrene using zebrafish

Shiva N. Kompella[1], Jules C. Hancox[2], Fabien Brette[3], Holly Shiels[1]

[1]Division of Cardiovascular Sciences, The University of Manchester, Manchester, United Kingdom
[2]School of Physiology, Pharmacology and Neuroscience, University of Bristol, Bristol, United Kingdom
[3]IHU-Liryc, Electrophysiology and Heart Modeling Institute, Foundation Bordeaux Université, Pessac-Bordeaux, France

Cardiovascular diseases (CVDs) are one of the leading the cause of deaths globally and in UK, costing an estimated 9 billion pounds to UK's healthcare system. This burden is further amplified with established detrimental health effects of air pollution and its strong correlation with CVDs such as cardiac arrhythmias and stroke (1). Phenathrene (Phe), an important component of air pollution, is a 3 ringed poly-aromatic hydrocarbon (PAH) that binds to the surface of fine particulate matter (PM2.5). Previous studies show proarrhythmic effects of Phe on the heart of various marine fishes via the inhibition of I_{Kr} current leading to action potential (AP) prolongation (2). The rapid delayed rectifier K^+ current, I_{Kr}, participates in phase 3 repolarisation of ventricular APs; it also plays a key protective role against premature stimuli late in repolarization and early diastole by mediating fast transient outward currents in response to premature ventricular beats.

The aim of this study was to investigate the cardiotoxic effects of Phe using whole-cell patch-clamp in zebrafish (*D. rerio*) ventricular cardiomyocytes. Firstly, we show significant potency in inhibition of zebrafish I_{Kr} peak-tail current by Phe with an IC_{50} value of 2.7 ± 0.1 µM and a Hill slope (nH) of 0.6 ± 0.09 (n=6-9; N=3), along with increased channel deactivation kinetics. Further to this, we examined the effects of Phe on the protective I_{Kr} current envelope in zebrafish ventricular cardiomyocytes. A paired ventricular AP-like command waveform protocol was used to elicit transient outward currents in absence and presence of 3 µM Phe. Significant inhibition of approximately 60% of peak transient current was observed in presence of 3 µM Phe (n=7-8; N=3). Surprisingly, when Phe was tested on ventricular action potential (AP) elicited at 0.5 Hz through whole-cell patch current clamp recording, it significantly shortened action potential duration (APD_{90}) at both 3 µM (by 20%; n=4; N=2; $p<0.05$, paired t-test) and 10 µM Phe (by 41% ms; n=4; N=2; $p<0.05$, paired t-test). Phe (10 µM) exhibited significant (40%) inhibition of I_{CaL} currents (n=10; N=4; $p<0.05$, paired t-test) elicited using a double-pulse protocol with potassium free solutions, in the presence of 0.5 µM TTX.

In these experiments Phe abbreviated AP duration, likely due to I_{CaL} inhibition, whilst reducing the protective effect of I_{Kr} to premature stimulation. This combination of effects may abbreviate refractoriness and increase susceptibility to certain arrhythmia triggers such as premature ventricular beats/contractions.

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Acknowledgements :- Supported by British Heart Foundation Grant PG/17/77/33125.

OC15

Faster, warmer, stronger: calcium cycling in avian myocardium

Tatiana Filatova[1, 2], Denis Abramochkin[1, 2, 3], Holly Shiels[4]

[1]Lomonosov Moscow State University, Department of Human and Animal Physiology, Moscow, The Russian Federation [2]Russian National Research Medical University, Department of Physiology, Moscow, The Russian Federation [3]Ural Federal University, Ekaterinburg, The Russian Federation [4]University of Manchester, Faculty of Life Sciences, Manchester, United Kingdom

Birds are an intriguing research object for cardiac physiology: though they, as well as mammalians, developed endothermy and four-chambered high-performance heart, their cardiomyocytes share similar ultrastructure with those in reptilians. Although there are evidences that birds use intracellular Ca^{2+} stored in SR, Ca^{2+} cycling and SR Ca^{2+} storage have not yet been studied in adult avian myocardium. In the present study, we used whole-cell voltage clamp to study sarcolemmal Ca^{2+} flux, SR Ca^{2+} storage and the degree of interplay between these sources of Ca^{2+} in enzymatically isolated cardiomyocytes of Japanese quail (*Coturnix japonica*).

At room temperature, sarcolemmal calcium current (I_{Ca}) was present in atrial and ventricular quail cardiomyocytes. In ventricular cells I_{Ca} was higher than in atrial myocytes and reached -9.9±1.588 pA/pF at 0 mV (here and further the data presented as mean±s.e.m), which exceeds the reported I_{Ca} density in mammalian myocardium (1). According to activation kinetics and the current-voltage curve, I_{Ca} in adult quail myocardium is presented only by L-type calcium current.

We stimulated the cells with 200 ms square pulses applied at 1 Hz frequency to load the SR with Ca^{2+}. SR Ca^{2+} content was estimated as time-integral of inward current generated by Na^{+}/Ca^{2+} exchanger activated by application of caffeine. SR Ca^{2+} accumulation in isolated quail cardiomyocytes was higher than that in mammalian cells (2). In atrial cells the SR content was higher than in ventricular; after 100 pulses it reached 750.6 ± 128.2 µmol l^{-1} in atrial cells and 423.3 ± 47.2 µmol l^{-1} in ventricular cells. As Ca^{2+} was being reaccumulated in SR, sarcolemmal I_{Ca} showed calcium-dependent acceleration of inactivation and at room temperature it reached steady-state configuration within 7-10 pulses. It is faster than that in fish cardiomyocytes (3), suggesting tight interaction between LTCC and SR in avian heart. However, we did not observe similar changes in I_{Ca} kinetics after depletion of SR Ca^{2+} stores in quail atrial myocytes. That could resulting from lower I_{Ca} amplitude in atrial cells at room temperature or from less favorable distribution of ryanodine receptors in atrial SR.

Thus, our study for the first time demonstrates the interaction between large SR Ca^{2+} stores and LTCC in avian myocardium, which would presumably result in a string gain of Ca^{2+} signaling during excitation-contraction coupling. Together with considerably large amplitude of sarcolemmal I_{Ca}, these mechanisms can provide the high rate and contractility of an avian heart.

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Acknowledgements :-

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PC0010

Can mitochondria dynamics in the dorsovagal complex modulate brown adipose tissue activation and recruitment to prevent an obese phenotype?

Arianna Fozzato[1], Bianca Patel[1], Lauryn New[1], Beatrice Filippi[1], Susan Deuchars[1]

[1]*University of Leeds, Leeds, United Kingdom*

Obesity epidemic is rising globally posing a burden on healthcare systems worldwide, and behavioural interventions may not be sufficient to tackle obesity. The recent discovery of brown adipose tissue (BAT) in humans, has been shown to positively regulate energy expenditure, raising new possibilities. BAT activation is driven by the central nervous system (CNS); the Nucleus of the Tractus Solitarius (NTS) in the Dorsovagal complex (DVC) receives information on nutritional status from visceral vagal afferents. An increase in glutamatergic vagal inputs to the NTS, inhibiting the physiological cooling-activation of BAT, exist in high-fat diet (HFD) fed rats (Madden&Morrison, 2016). Moreover, studies have found that HFD causes an increase of mitochondria fission in the DVC, which is regulated by dynamin related protein 1(Drp1) (Filippi et al, 2017). Previous studies within our group have shown that injecting a dominant negative form of Drp1 (Drp1-K138A) to inhibit mitochondria fission in rats NTS decreased food intake, restored insulin sensitivity in the NTS and prevented weight gain in HFD fed-obese rats, while these effects are not seen in HFD-GFP expressing controls. Furthermore, HFD alters astrocytes functionality in the NTS (MacDonald et al, 2019), but the role of mitochondria dynamics is still unknown in this cellular-subset.

We aim to investigate whether the aforementioned beneficial effects are due to a DVC-driven increase in BAT amount and function; We also aim to establish the cellular network involved in this pathway.

An obese model (Yue et al, 2016) (1) and a non-obese model (2) of male Sprague-Dawley rats were anesthetised with 4% isoflurane by inhalation and submitted to stereotactic surgery to implant a bilateral cannula in the NTS (day 0). On day 1 animals were injected with an adenovirus expressing either Drp1K138A or GFAP:Drp1K138A or GFP or GFAP:GFP and kept for 14 days on either HFD(5.51kcal/g) or control diet (3.93kcal/g). On day 15 animals were culled with pentobarbital (60 mg/kg i.p) and BAT dissected and weighted. A pilot PET study (n=3, obese model) was performed before sacrifice. Where applicable, values are mean±SEM, analysed with ANOVA.

(1) The amount of BAT in HFD-K138A (5.8±0.2g/kg) animals was 44% higher ($p<.001$) (n=9) than that of GFP-HFD (3.0±0.1g/kg) and 38%($p<0.01$) higher than normal GFP-RC control rats(3.8±0.2g/kg)(n=9). The PET scan revealed that BAT activity level in HFD-K138A was 46% higher than that GFP-HFD and 16% higher than GFP-RC control. (2) GFAP:Drp1K138A administration produced a decrease in body weight and cumulative food intake in GFAP:Drp1K138A-HFD-fed rats(n=12) which become significant from day 2 and day 3 respectively, compared with GFAP:GFP-HFD expressing controls(n=12). A trend of increase in BAT mass in in GFAP:Drp1K138A-HFD animals was observed, but this was not significant ($p=0.1669$) when compared to GFAP:GFP-HFD controls (n=8 GFAP:Drp1K138A-HFD, n=9 in GFAP:GFP-HFD).

Global inhibition of mitochondria dynamics in the NTS appears to act as BAT recruiter and stimulator. Astrocytes are important to maintain body weight and suppress food intake in HFD, but the effects on BAT recruitment appear modest. Molecular analysis is required to determine effects on BAT activation and functionality upon mutant Drp1 administration to the NTS.

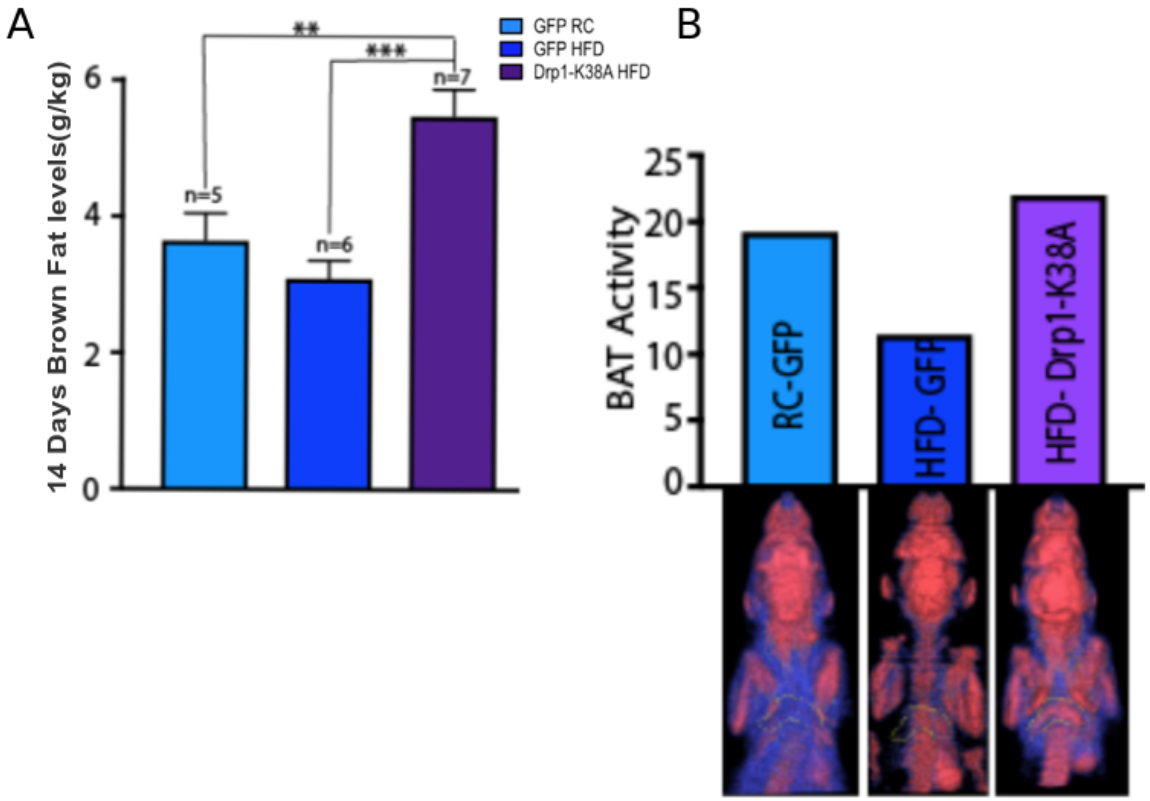

Figure 1: Rats were fed for 28 days with HFD or RC; at day 29 a double cannula was inserted in the brain targeting the NTS and an adenovirus expressing GFP or dominant negative form of Drp1 (Drp1K138A) were injected and brown adipose tissue (BAT) collected. (A) shows BAT weight±SEM.

(B) shows PET scans of n=3 rats performed before sacrifice. A control RC-fed expressing GFP in the NTS (RC-GFP), a HFD-fed rat expressing GFP in the NTS (HFD-GFP) and a HFD-fed rat expressing Drp1-k138a to inhibit mitochondria fission in the NTS. BAT activity is presented as radioactivity of the intrascapular BAT divided by the background radioactivity. Representative PET images with BAT area highlighted (yellow) are shown at the bottom.*p < 0.05, **p <0.01, *** p<0.001.

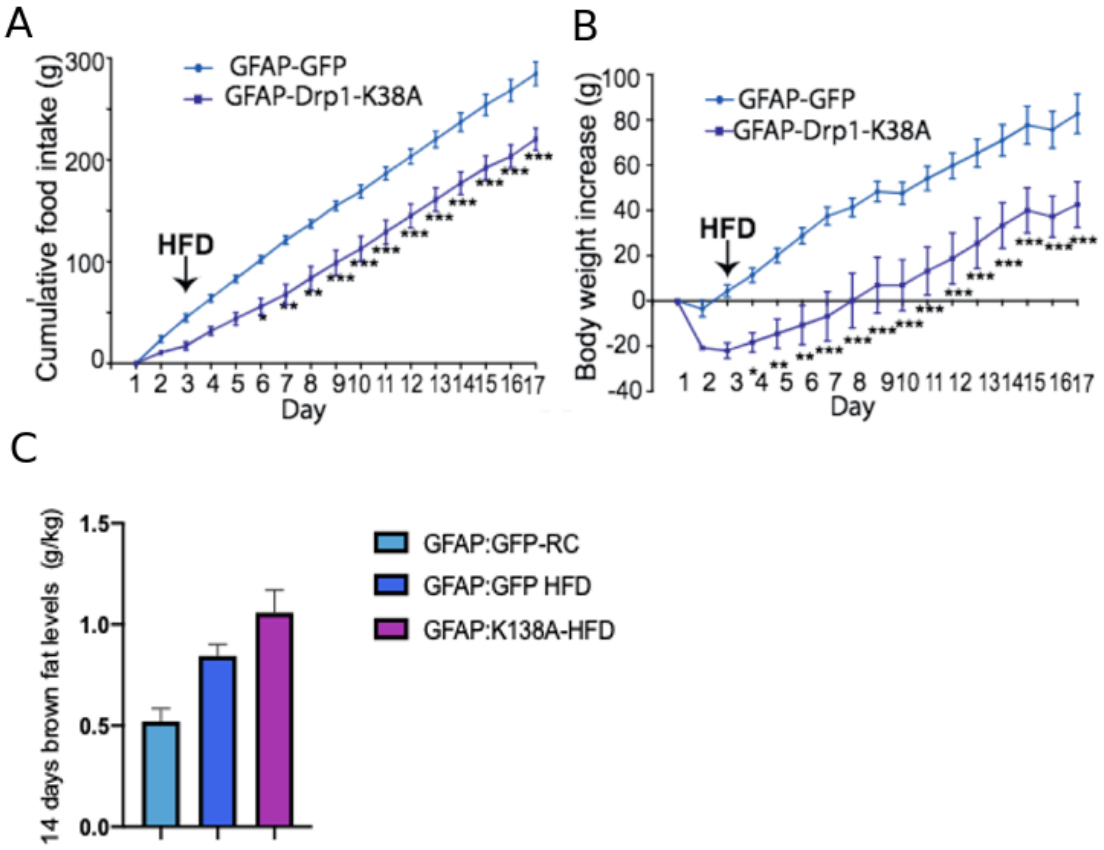

Figure 2: Inhibition of mitochondria fission in astrocytes of the DVC lowers food intake and body weight in HFD-fed male rats but have modest effects on brown adipose tissue mass. (A) Cumulative food intake from day 1. (B) Increase in body weight from day 1. (C) Brown adipose levels in the day of the sacrifice. *p < 0.05, **p <0.01, *** p<0.001.

Reference 1 :- 1 Madden, C.J. and Morrison, S.F. (2016) A high-fat diet impairs cooling-evoked brown adipose tissue activation via a vagal afferent mechanism. *Am. J. Physiol. Metab.* 311, E287–E292 10.1152/ajpendo.00081.2016

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PC0011

Quassia amara stem bark prevent cadmium-induced hepatotoxicity and dyslipidemia in male Wistar rats

Olawale OBEMBE[1], Taofeek USMAN[1], Yinusa Raji[2]

[1]Osun State University, Osogbo, Nigeria [2]University of Ibadan, Ibadan, Nigeria

The liver is one of the primary biorepositories of cadmium and it has been implicated in the pathogenesis of hepatic diseases [1,2]. In this study, cadmium was administered to rats to induce hepatic oxidative damage and derangement of lipid panel. The effects of *Quassia amara* on these markers in cadmium treated rats were thereafter examined.

Rats were divided into 3 groups. Group 1 served as control, Group 2 received cadmium (5 mg/kg) for 4 weeks while Group 3 was pre-treated with *Q. amara* extract (200 mg/kg) for 2 weeks and received *Q. amara* and cadmium concurrently for another 4 weeks. Rats were sacrificed 24 hours after the last treatment by cervical dislocation under sodium pentobarbital (30 mg/kg IP) anesthesia and blood samples were obtained by cardiac puncture. Lipid profile was assayed by colorimetric method from serum obtained while hepatic oxidative stress was assayed spectrophotometrically from liver homogenate using respective commercial available kits [3]. All procedures in this study conformed to the guiding principles for research involving animals as recommended by the Declaration of Helsinki and the Guiding principles in the care and Use of animals (2002).

Cadmium caused significant increase in serum cholesterol (152.96 ± 13.98 *vs* 123.86 ± 9.61 mg/dl) and LDL (102.17 ± 8.08 *vs* 86.85 ± 6.31 mg/dl) and decreased HDL (3.01 ± 0.40 *vs* 5.65 ± 1.02 mg/dl)

when compared with control. Also, hepatic MDA was higher (12.75±2.3 *vs* 4.27±0.56 iμ/ml) while SOD (0.25±0.04 *vs* 0.87±0.16 iμ/ml) was lower in cadmium treated rats compared with the control. However, *Q. amara* prevented cadmium-induced increase in cholesterol (123.83 ± 9.41 *vs* 152.96 ± 13.98 mg/dl) and LDL (84.53 ± 4.31 *vs* 102.17 ± 8.08 mg/dl) and prevented cadmium-induced decrease in HDL (6.66 ± 0.91 *vs* 3.01 ± 0.40 mg/dl). Also *Q. amara* augmented cadmium-induced decline in SOD (0.62±0.13 *vs* 0.25±0.04 iμ/ml) and ameliorated cadmium-induced increase in MDA (6.16±0.87 *vs* 12.75±2.3).

In conclusion, *Quassia amara* stem bark has hepatoprotective properties as it ameliorated cadmium-induced damage to liver by preventing dyslipidemia and oxidative damage in the hepatic tissue.

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PC0015

Larger loads of inertia during flywheel exercise impose a greater burden to the cardiovascular system in normotensive adults

Damir Zubac[1], Vladimir Ivančev[2], Zoran Valić[3], Rado Pišot[1], Cécil J. W. Meulenberg[1], Nandu Goswami[4], Boštjan Šimunič[1]

[1]Science and Research Center Koper, Institute for Kinesiology Research, Koper, Slovenia [2]University of Split, Faculty of Kinesiology, Split, Croatia [3]University of Split, School of Medicine, Department of Integrative Physiology, Split, Croatia [4]Gravitational Physiology, Aging and Medicine Research Unit, Physiology Division, Otto Loewi Center of Vascular Biology, Immunity and Inflammation, Medical University of Graz, Graz, Austria

Introduction:

The variable load exercise model (e.g., the flywheel, FW) is currently considered to be the most effective method for countering muscle-atrophy (Seynnes et al., 2007). However, it is still unknown

to which extent this type of exercise challenges the cardiovascular system. We investigated the effects of the FW exercise (nHance, Barcelona, Spain) on hemodynamics and cardiovascular adjustments in healthy, normotensive participants.

Methods:

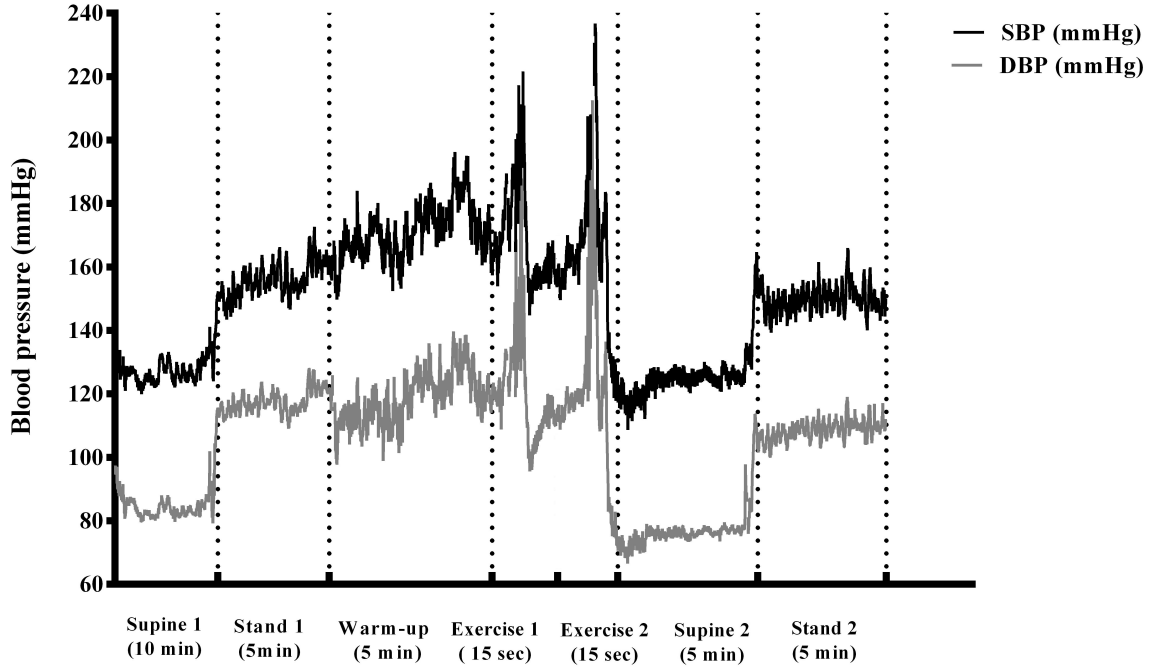
The present study was approved by the Republic of Slovenia National Medical Ethics Committee (approval number: 120-487/2018/21). Thirty participants (age from 20 to 55 y, 37% women) underwent a detailed medical examination and their $V'O_2$ max. was determined. Following preliminary sessions completion, the participants performed three different experimental conditions (in a random order), that is, the FW squat ergometer set at three different (low at 0.025 $kg \cdot m^2$, moderate at 0.050 $kg \cdot m^2$ and high at 0.075 $kg \cdot m^2$) moments of inertia. The hemodynamics response and the heart rate (HR) were continuously monitored (Task force monitor, CNSystems, Graz, Austria) throughout all FW sessions. More precisely, the blood pressure was assessed via photoplethysmograph using a pneumatic cuff, positioned around the middle finger of the left hand, instructed to be held at the level of the heart throughout the session. The cardio-impedance electrodes were positioned according to the manufacturer's guidelines to allow non-invasive insight into the hemodynamics throughout the experimental sessions, while the HR was obtained from the bipolar 3-lead electrocardiograph (Goswami et al., 2015).

Results:

A robust rise in mean arterial pressure (MAP) was observed across all three moments of inertia compared to baseline (p=.001), while MAP had reached the highest values of 179±4 mmHg during high inertial loading. All hemodynamics parameters had a similar response to different FW exercise throughout, while the total peripheral resistance increased by 11% (p=.001) during the high inertial loading. Likewise, an increase in HR was noted during all exercise interventions compared to baseline (p=.001), whereas the HR response was 10 bpm higher (p=.001) at high level compared to readings at low and moderate loading. There were no correlations observed between relative increase in MAP and the age of the participants across different levels of inertial loadings.

Conclusion:

Apparently, larger moments of inertia during FW exercise impose a substantial burden to the cardiovascular system, whereas the study population age-related differences did not modulate a robust rise in MAP following FW exercise. Thus, caution is warranted when prescribing high-load FW exercise to counter muscle-atrophy.



Reference 1 :- Goswami, N., Evans, J., Schneider, S., von der Wiesche, M., Mulder, E., Rössler, A., ... & Blaber, A. P. (2015). Effects of individualized centrifugation training on orthostatic tolerance in men and women. *PLoS One*, 10(5)

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Acknowledgements :- This study was supported by the National Research Agency of Slovenia (ARRS), under the grant number: Z7-9420, head of project dr. Zubac, D.

PC0016

Discovering early markers of diabetic vascular disease

Huda Alfardus[1], Nadira Yuldasheva[1], Karen Porter[1], John Colyer[1], Andrew Smith[1]

[1]*University of Leeds, Leeds, United Kingdom*

Diabetic vascular disease (DVD) is a cause of significant morbidity in individuals with Type 2 diabetes. It is estimated that 50% of patients have already got vascular complications at the time of diagnosis with Type 2 diabetes. It is, therefore, important to develop techniques that may assist in early identifications of possible markers for vascular complications. Our work aims to identify proteins that

can be used as biomarkers to diagnose DVD early in its development, thereby enabling earlier interventions to delay or halt its progression.

We have recently discovered a novel non-destructive method of protein sampling, employing the polymer styrene maleic acid (SMA), to extract nanodiscs (containing membrane-bound proteins) from the membranes of cells without killing them. Our pilot data from liquid chromatography–mass spectrometry (LC-MS) based proteomics analysis of proteins isolated using SMA from intact rat aortic tissue ex vivo will be presented. We can show that we have recovered proteins from plasma membrane, intracellular membranes and cell cytosol without any associated cell death. This serves as proof-of-principle that SMA application is a promising method for non-destructively extracting proteins from vascular endothelial cells. Next, we applied SMA to the aortic tissue of a widely-used model of diabetes in genetically-modified (db/db) mice and their wild-type counterparts, to study the changes in the levels of expression of the SMA-recovered proteins in diabetic mice compared to wild-type mice over the course of early disease development. Preliminary data from our quantitative LC-MS proteomics analysis of samples from mouse aortic tissue will also be presented. We can show that we have successfully identified approximately 300 proteins isolated using our SMA-based method which demonstrates the feasibility of our approach.

By understanding of the molecular changes during DVD development, this project aims to facilitate earlier detection of DVD and thus lead to earlier interventions for patients

Reference 1 :- Smith AJ et al. (2019). Sci Rep. 9: 16408 (available at https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6877624/)

Acknowledgements :- This project is funded by Heart Research UK

PC0021

Relation of Different Components of Climate with Human Pituitary-Thyroid Axis and FT3/FT4 Ratio: A Study on Euthyroidand SCH Subjects in Two Different Seasons

Taha Mahwi[1], Darya Abdulateef[2]

[1]University of Sulaimani, College of Medicine, Medicine Department, Sulaymaniyah, Iraq [2]Physiology Department, College of Medicine, University of Sulaimani, Sulaymaniyah, Iraq

Background. Various changes in thyroid hormones (TH) and thyroid-stimulating hormone (TSH) level were observed in different seasons among euthyroid and hypothyroid subjects living in areas with an extreme temperature difference between summer and winter.

Objectives. This study aims at finding the effect of temperate climate on the seasonal variations of TSH and TH in euthyroid and subclinical hypothyroidism (SCH) subjects and at evaluating if the test season has an effect on the number of subjects diagnosed as SCH. It basically focuses on the relation

of different components of climate with TH and TSH.

Method. In a prospective study on 152 healthy (euthyroid) volunteers and 25 SCH subjects, the serum hormone levels (TSH, FT4, and FT3) were measured in both the summer and winter seasons and correlated with all the climate components using Pearson's correlation coefficient. The effect of duration of outdoor exposure on hormone levels was compared using a paired sample t-test (P < 0 05).

Results. Small but statistically significant increased FT3 level and decreased FT4 level were observed during the winter season in euthyroid and SCH subjects, respectively. There was a significant negative correlation between FT3 and FT3/FT4 ratio with temperature and sunshine duration and a positive correlation with humidity and atmospheric pressure. A positive correlation was found between FT4 and sunshine duration.

Conclusion. The climate components contributed to the slight variance in hormone levels in different seasons, and the effect was mostly on peripheral conversion of FT4 to FT3 rather than the pituitary-thyroid axis leading to slightly higher FT3 in winter. Seasonal variation does not affect the diagnosis of SCH cases.

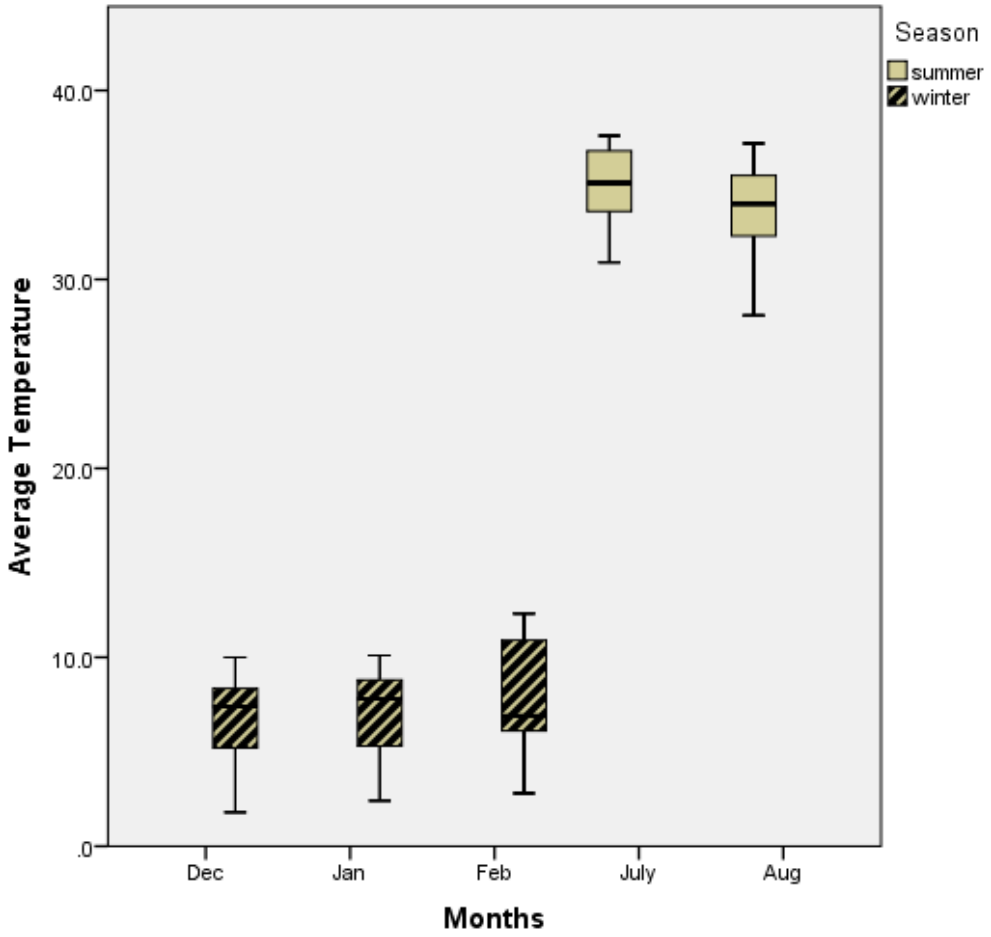


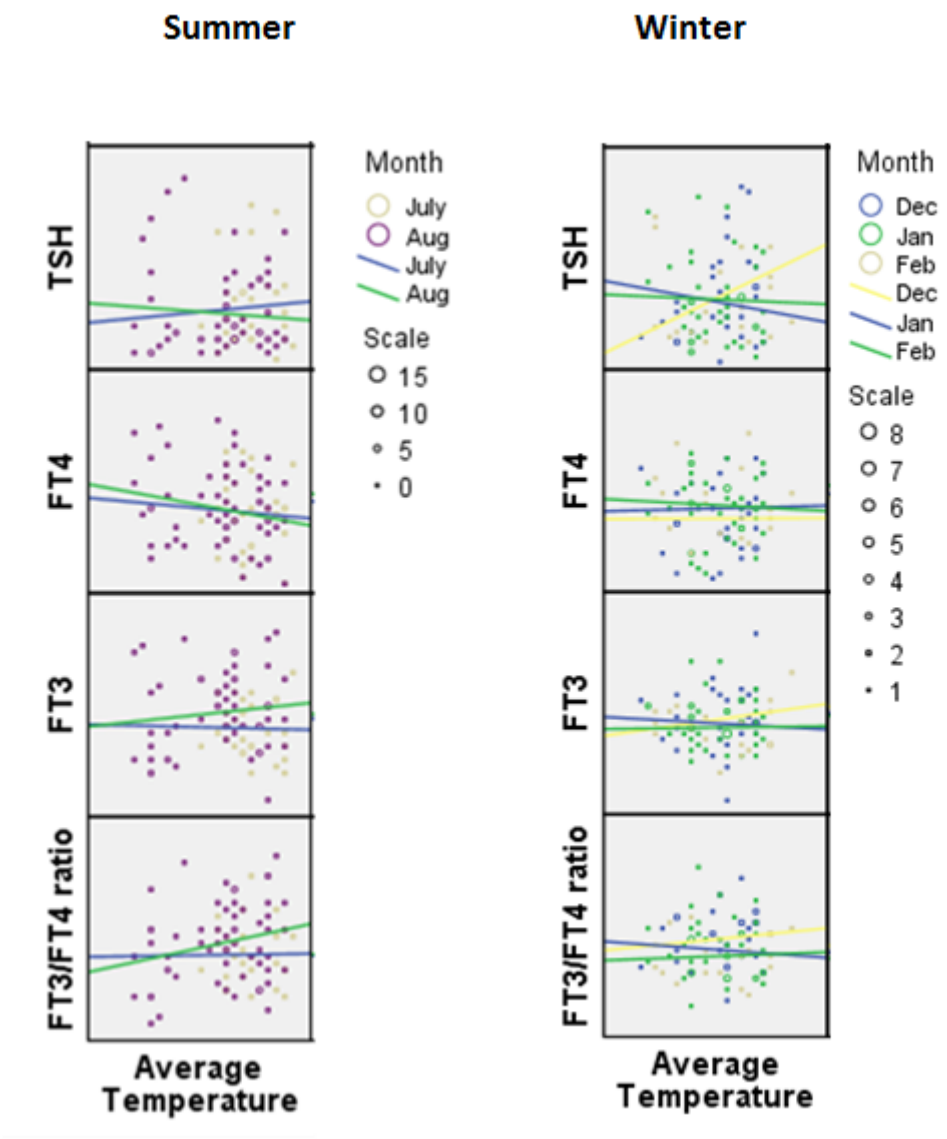
Table 5. Correlations of climate parameters of one day, one week and one month before blood sample collection with the mean TSH, FT3, FT4, FT3/FT4 ratio

Duration from sample taking	Climate parameters	Euthyroid FT3 (pg/ml)	FT4 (ng/dl)	FT3/FT4 ratio	TSH (mIU/L)
One day	Temperature	-0.195*	0.029	-0.193*	0.027
	Humidity	0.204*	-0.032	0.222*	-0.046
	Sunshine duration (Hours)	-0.203*	0.098	-0.264**	0.077
	Cloud cover (Octa)	0.140	-0.136*	0.254**	-0.085
	Atmospheric pressure	0.174*	-0.02	0.151	-0.001
One week	Temperature	-0.220**	0.058	-0.239	0.007
	Humidity	0.227**	-0.050	0.212**	-0.033
	Sunshine duration (Hours)	-0.141	0.033	-0.142	0.07
	Cloud cover (Octa)	-0.041	0.001	-0.042	-0.021
	Atmospheric pressure	0.067	-0.004	0.057	-0.014
One Month	Temperature	-0.143	0.045	-0.172*	0.003
	Humidity	0.124	-0.02	0.136	-0.037
	Sunshine duration (Hours)	-0.127	0.05	-0.202*	0.023
	Cloud cover (Octa)	0.108	-0.021	0.174*	-0.005
	Atmospheric pressure	0.168*	-0.035	0.186*	0.001

Table 3. Comparison of the serum TSH, FT4, FT3and FT3/FT4 ratio between summer and winter season

		Total	P value	EU	P value	SCH	P value
TSH(mIU/L)	Summer	2.93±1.96	0.136	2.34 ±1.25	0.382	6.64±1.60	0.171
	Winter	2.77±1.79		2.25±1.25		6.04±1.17	
FT4 (ng/dl)	Summer	1.23±0.57	**0.007**	1.23±0.15	0.063	1.21±0.15	**0.009**
	Winter	1.20±0.16		1.21±0.16		1.14±0.14	
FT3 (pg/ml)	Summer	3.23±0.44	**<0.001**	3.22±0.44	**<0.001**	3.27±0.45	0.853
	Winter	3.37±0.39		3.39±0.40		3.25±0.32	
FT3/FT4 ratio	Summer	2.68±0.45	**<0.001**	2.65±0.45	**<0.001**	2.81±0.44	**0.037**
	Winter	2.87±0.43		2.84±0.43		2.99±0.43	

The parameters are expressed as mean±SD, and the means are compared using Paired sample t-test



PC0023

LOW DOSE SPIRONOLACTONE PROTECTS EXPERIMENTALLY-INDUCED POLYCYSTIC OVARIAN SYNDROME FROM INSULIN-RESISTANT METABOLIC DISTURBANCES

Oluwaseun Aremu Adeyanju[1], Timothy Falodun[1]

[1]*Afe Babalola University, Ado-Ekiti, Nigeria*

Objective: Polycystic ovarian syndrome (PCOS) is the most common endocrinological disorder in women of reproductive age and hyperandrogenism is a prominent feature of PCOS resulting in infertility and increased risk of developing metabolic disorders including insulin resistance (IR),

abdominal adiposity, glucose intolerance and cardiovascular diseases. Spironolactone (SPL), a non-selective mineralocorticoid receptor (MR) antagonist, has been in wide clinical use for several decades. In this study, we investigated the effects of SPL on IR and metabolic disturbances in letrozole-induced PCOS rats.

Design and method: Eighteen adults female Wistar rats were randomly divided into 3 groups and treated with vehicle, letrozole (LET; 1 mg/kg) and LET + SPL (SPL; 0.25 mg/kg), p.o. once daily for 21 consecutive days.

Results: Results showed that LET treatment induced PCOS characterized by elevated plasma testosterone
and luteinizing hormone (LH) accompanied with increased body weight and visceral adiposity, IR, glucose intolerance, dyslipidemia and altered histomorphological ovaries. Treatment with SPL however attenuated the elevated testosterone in LET-induced PCOS model accompanied with a reversal in all the observed alterations.

Conclusion: Taken together, analysis of the physical, biochemical and histological evidences shows that the
protective effect of this very low dose spironolactone may be through its anti-androgenic mechanism. In conclusion, this study shows for first time, the protective effect of spironolactone at this dose against insulin resistance and metabolic disturbances induced by experimental PCOS. The protective mechanisms appears to be through suppression of elevated circulating testosterone. Therefore, SPL alone at this very low dose might be very effective as against its combination with other known anti-androgenic drugs in the treatment of characteristic features of PCOS.

PC0024

Diaphragm neuromuscular transmission is preserved in 4- and 8-month old mdx dystrophic mice.

Lauren Noonan[1], Ken O'Halloran[1], David Burns[1]

[1]*Department of Physiology, School of Medicine, University College Cork, Cork, Ireland*

Duchenne muscular dystrophy (DMD) is a neuromuscular disorder resulting in impaired skeletal muscle force-generating capacity, with attendant muscle fibre remodelling. Dystrophin deficiency leads to reduced respiratory muscle strength and premature death due to cardiorespiratory failure. DMD has been extensively researched in animal models such as the dystrophin-deficient *mdx* mouse. Alterations to the specialised structure of the neuromuscular junction have been described in *mdx* mice, which may lead to adaptive or mal-adaptive changes in neuromuscular communication. It is unclear if altered neuromuscular transmission contributes to impaired respiratory muscle performance in DMD and *mdx* mice and how this might change over the course of disease progression. We examined the effects of dystrophin deficiency on diaphragm neuromuscular

transmission and diaphragm muscle function *ex vivo* in male wild-type and *mdx* mice.

We assessed diaphragm neuromuscular transmission in wild-type (n=12) and *mdx* (n=12) mice at 4- and 8-months of age using an *ex vivo* nerve-muscle preparation (phrenic-diaphragm). Phrenic-diaphragm preparations were studied in Krebs solution bubbled with 95% O_2/ 5% CO_2 at 35^{o}C. The phrenic nerve was stimulated via a glass suction electrode while the diaphragm muscle was stimulated directly via field stimulation using platinum electrodes. Phrenic-diaphragm preparations were stimulated at 25, 50, 75 and 150Hz to establish force-frequency relationships. Next, neuromuscular transmission for phrenic-diaphragm preparations was examined by repeatedly stimulating the phrenic nerve every 2s and the diaphragm muscle every 15s at 50Hz. Neuromuscular transmission failure was calculated by comparative differences in nerve- and muscle-evoked force. Data were statistically compared using two-way ANOVA with Bonferroni *post hoc* test. $P<0.05$ was considered statistically significant.

Diaphragm specific force was depressed for *mdx* preparations compared to age-matched wild-type at high stimulation frequencies (75-150 Hz). Diaphragm specific force was equivalent in response to nerve and muscle stimulation for both wild-type and *mdx* preparations at both ages, but specific force for *mdx* preparations remained lower compared to wild-type. Repeated stimulation at 50Hz resulted in significant neuromuscular transmission failure for wild-type phrenic-diaphragm preparations, whereas neurotransmission for *mdx* preparations was remarkably preserved at 4- and 8-months of age.

These data demonstrate profound muscle weakness in dystrophin-deficient diaphragm. Neuromuscular transmission data suggests compensatory plasticity is present in *mdx* diaphragm, allowing dystrophic diaphragm to preserve neuromuscular transmission during repeated stimulation at 50Hz albeit in the context of significant muscle weakness. A greater appreciation of neuromuscular communication in dystrophin-deficient diaphragm is essential to understand the neuro-mechanical control of breathing in muscular dystrophy. Examining compensatory mechanisms that act to preserve neuromuscular transmission in DMD may lead to the identification of potential therapeutic targets.

Acknowledgements :- Supported by the Department of Physiology (UCC) and The Physiological Society (Research grant to DPB).

PC0026

Oestrogen Regulation of the Wnt/Beta-Catenin Pathway as a Protective Mechanism Against Colorectal Cancer

Santralega Lingam[1, 2]

[1]Perdana University , Selangor , Malaysia [2]Department of Molecular Medicine, Royal College of Surgeons in Ireland, Dublin , Ireland

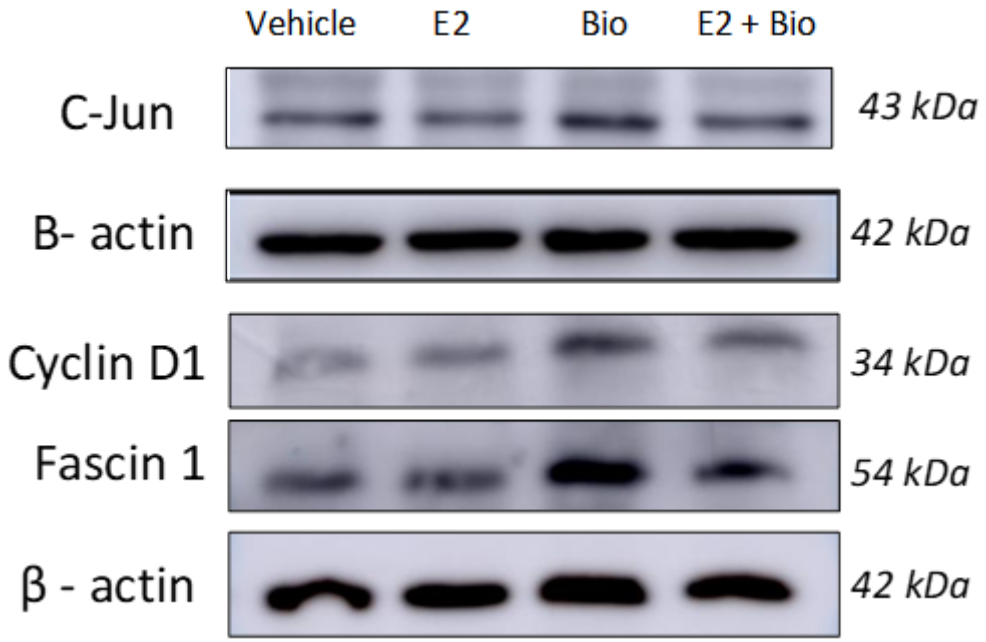
Introduction: Men are more likely to get colorectal carcinoma than women. There is evidence that oestrogen can provide a protective effect against colorectal carcinoma in females, although the mechanisms are not fully elucidated [1]. Over activation of the Wnt/beta-catenin signalling pathway occurs frequently in colorectal cancer and can lead to proliferation of colorectal carcinoma cells [2]. We hypothesise that oestrogen may provide protection by preventing over activation of the Wnt/beta-catenin signalling pathway.

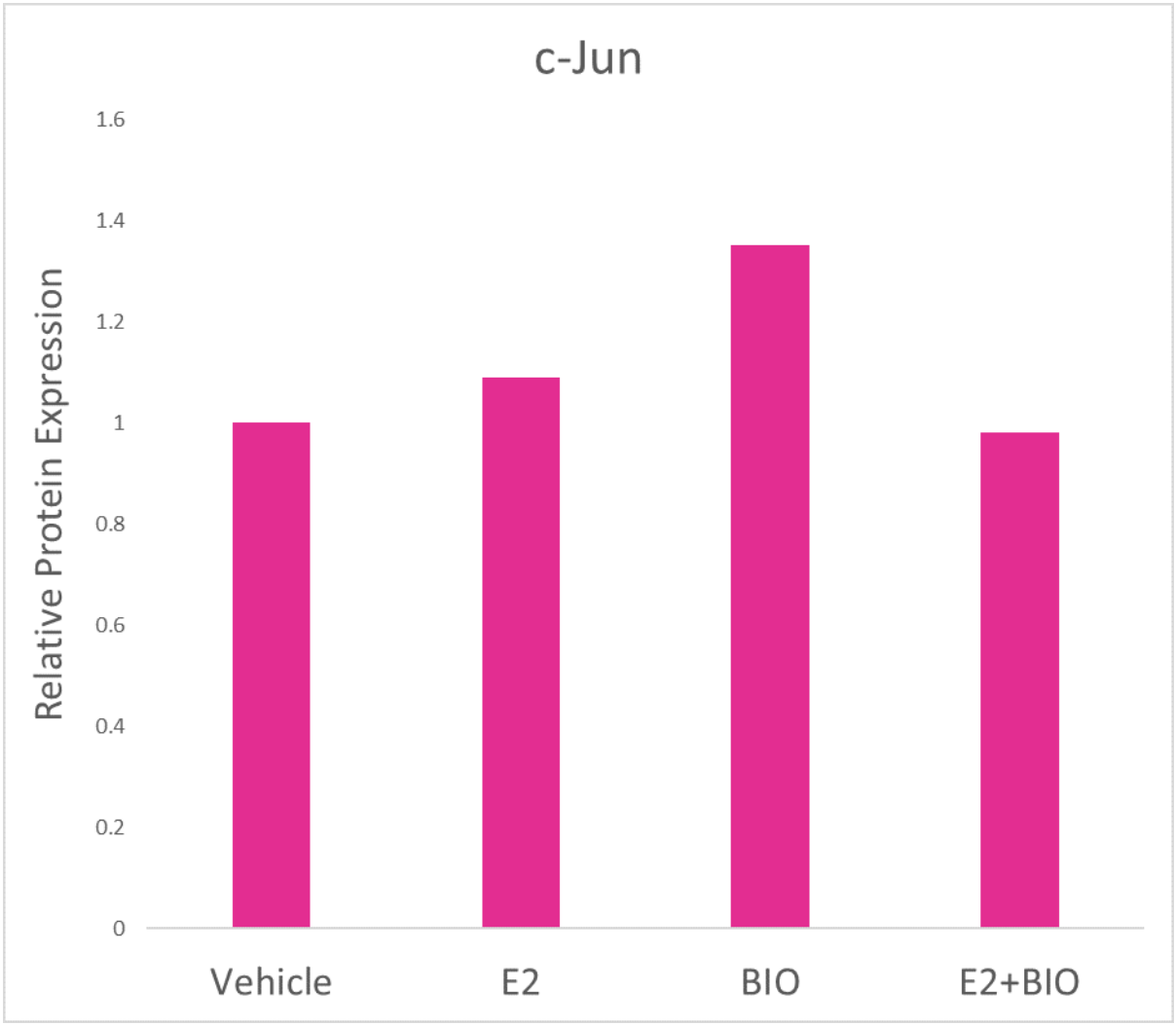
Aim: The aim of this research was to determine the effect of oestrogen on the Wnt/beta-catenin signalling pathway in colorectal carcinoma cells.

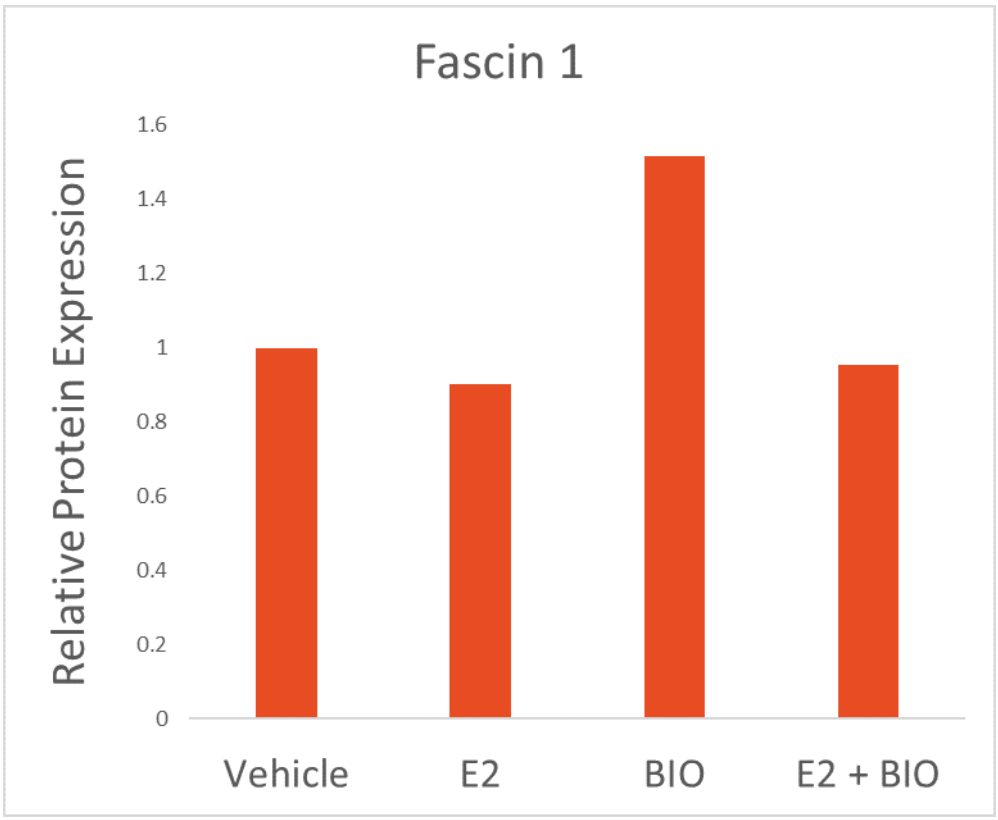
Methods: HT29 colorectal cancer cells were cultured and treated with 100nM oestradiol (E2) or vehicle (ethanol). In order to over-activate the Wnt/beta-catenin pathway, cells were also treated with 0.25µM GSK3-β inhibitor ("BIO") or vehicle (DMSO). Western blotting was performed to assess expression of the Wnt/beta-catenin target proteins, c-Jun, cyclin D1 and fascin1. Protein expression was normalised to β-actin and quantified by densitometry using Image J 1.52 software.

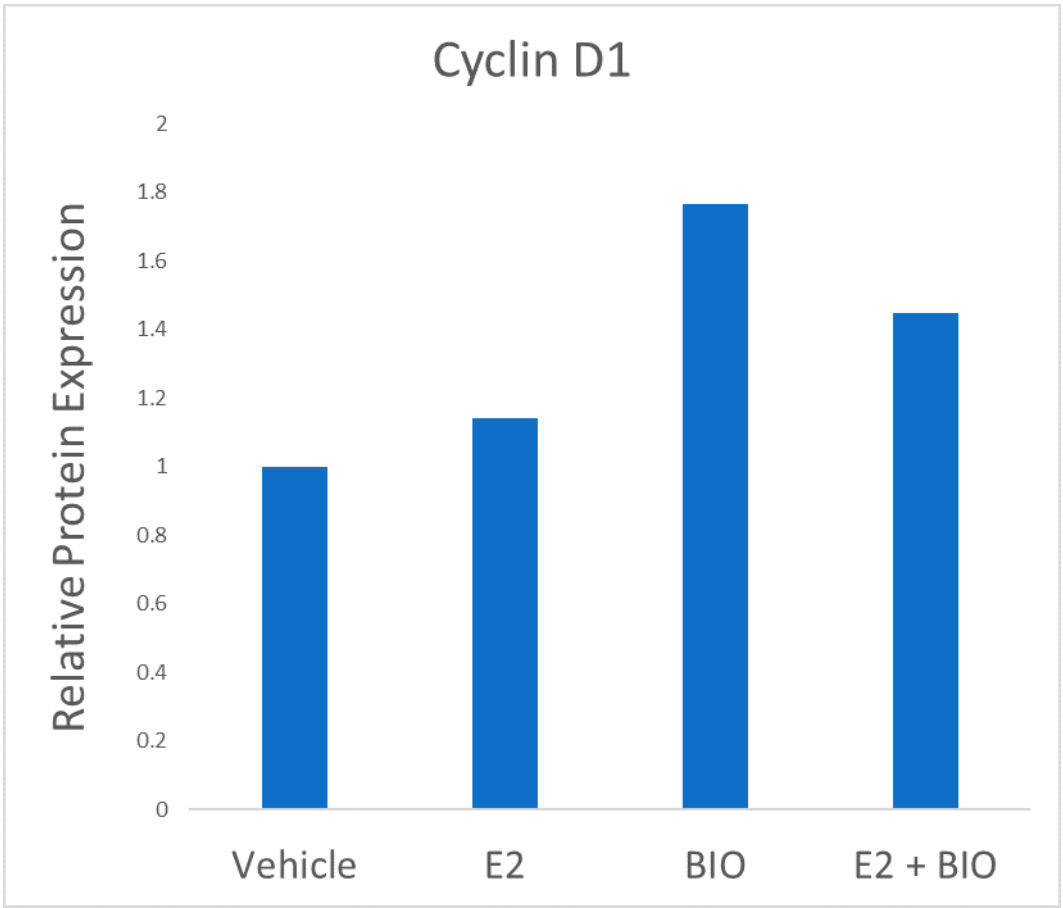
Results: Oestrogen treatment alone did not impact the protein levels of c-Jun, cyclin D1 or fascin1 which are the Wnt/beta-catenin targets in HT29 cells (n=2). Over-activation of the Wnt/beta-catenin pathway, by inhibition of GSK3-β using BIO, resulted in an increase of the protein levels of the Wnt targets as expected. Interestingly, oestrogen co-treatment with BIO prevented the increase in c-Jun (n=2), cyclin D1 (n=1) and fascin1 (n=1) induced by BIO alone.

Conclusion: Oestrogen does not inhibit the Wnt signalling pathway under basal conditions but it may exert a protective effect against colorectal carcinoma by preventing Wnt/beta-catenin over-activation.


Vehicle
E2
Bio
E2 + Bio
C-Jun
43 kDa
B- actin
42 kDa
Cyclin D1
34 kDa
Fascin 1
54 kDa
β - actin
42 kDa


c-Jun
Relative Protein Expression
1.6
1.4
1.2
1
0.8
0.6
0.4
0.2
0
Vehicle
E2
BIO
E2+BIO


Fascin 1
Relative Protein Expression
1.6
1.4
1.2
1
0.8
0.6
0.4
0.2
0
Vehicle
E2
BIO
E2 + BIO


Cyclin D1
Relative Protein Expression
2
1.8
1.6
1.4
1.2
1
0.8
0.6
0.4
0.2
0
Vehicle
E2
BIO
E2 + BIO

Reference 1 :- Williams C, DiLeo A, Niv Y, Gustafsson JÅ. Estrogen receptor beta as target for colorectal cancer prevention. Cancer Lett. 2016 Mar 1;372(1):48-56. Available from: http://www.ncbi.nlm.nih.gov/pubmed/26708506

Reference 2 :- Shang S, Hua F, Hu ZW. The regulation of β-catenin activity and function in cancer: therapeutic opportunities. Oncotarget. 2017 May 16;8(20):33972-33989. Available from: http://www.ncbi.nlm.nih.gov/pubmed/28430641

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PC0027

Cardiac Automonic Tone and its association with stress in medical students

Leeza Shah[1], Shreya Parashar[1], Aishwarya Tandon[1], Rita Khadka[1]

[1]B P Koirala Institute of Health Sciences, Dharan, Nepal

Medical students are always confronted with significant stressors because of their course, hectic schedule, and enormous syllabus, which may affect their cardiac function and well being. A few studies have assessed cardiac autonomic modulation and correlated it with stress level in healthy medical students. We aimed to compare cardiac autonomic modulation and stress level between male and female medical students and correlate their stress levels with their cardiac autonomic modulation.

The study was conducted on 15 healthy male (age 22.2±1.2 years) and 15 female (age 21.0±0.7 years) third year medical students. Their cardiac autonomic modulation was assessed using short-term heart rate variability (HRV) and stress scores were evaluated using medical student stressor questionnaire (MSSQ) which included parameters: academic related stressors, inter and interpersonal related stressors, teaching and learning related stressors (TLRS), drive and desire related stressors and social related stressors (SRS). Data were analyzed statistically. A $P<0.05$ considered statistical significant. Results showed mild to moderate levels of stress in all stressor parameters both in male and female students. There were no significant differences in stress scores between the groups. Markers of sympathetic actvity; LFnu and LF/HF ratio [1.1 (0.8-1.5) vs 0.4 (0.3-0.9), P= 0.007] were higher in male students, whereas, markers of parasympathetic activity; HFnu [46.7 (39.65- 55.9) vs 69 (52.85-75.3), P=0.01], HFpower, RMSSD, pNN50 [28.6 (6.65-39.85) vs 47.4 (26.45-55.85), P= 0.023] were higher in female students. HF power showed negative correlation with TLRS and SRS in male students**,** whereas, in female students none of the HRV variables showed correlation with stress scores.

In the conclusion, similar mild to moderate levels of stress in all the stressor parameters were found in both male and female medical students. However, sympathetic activity was found more in male students, and parasympathetic activity more in female students. Parasympathetic activity was found decreased with increase in teaching and learning related stressors, and social related stressors in

male students**,** whereas, in female students none of the HRV variables showed correlation with stresses scores. It indicates that cardiac autonomic modulation is not affected much with increase in stress level in female medical students.

Key words: Stress, MSSQ, autonomic, heart rate variability, medical students

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Reference 2 :- ´Barikani A. (2008). Stress in Medical Students. *Journal of Medical Education Winter & Spring*, Vol. 11(1,2) P 41-44

Reference 3 :- ´Arnold SV, Smolderen KG, Buchanan DM, Li Y, Spertus JA. (2012). Perceived Stress in Myocardial Infarction Long-Term Mortality and Health Status Outcomes. *Journal of the American College of Cardiology*, Vol 60(18), P 1756-63

Reference 4 :- ´Upadhyay N, Khadka R, Paudel BH. (2014). Impact of educational stress on cortisol, cardiac autonomic drive and academic performance of medical students. *Asian Journal of Medical Sciences*, Vol 5(4), P 73-78

Reference 5 :- ´Sivan S, Rangasubhe P. (2013). Prevalence of stress and its associated factors. *Journal of Evolution of Medical and Dental Sciences*, Vol2(48), P 9386-9394

PC0029

The Effect of Acute Hypoxic Exercise on Calcium Metabolism

Scott Hannah[1], Conor McClean[1], Sonyia McFadden[2], Andrea McNeilly[1]

[1]Ulster University, Sport and Exercise Science Research Institute, Jordanstown, Belfast, United Kingdom [2]Ulster University, Institute of Nursing and Health Research, Jordanstown, Belfast, United Kingdom

Several investigations show exercise induces a decrease of ionised calcium which may be responsible for increased bone breakdown following acute exercise (1-3). While the general mechanism of decreased Ca^{2+}stimulating PTH and subsequent bone resorption has been comprehensively detailed (1-2), what causes Ca^{2+} to decrease remains unknown. We suggest it may be the result of the complex acid-base changes seen during exercise (4) as Ca^{2+} is heavily influenced by pH. We investigated whether pH alterations, achieved by use of exercise and hypoxia, influenced calcium metabolism.

Sixteen healthy physically active males volunteered for our study ([mean ± 1 SD] age 24 ± 5 years, height 1.80 ± 0.08m, body mass ± 78.5 ± 12.6kg), approved by the University's Research Ethics Committee and in accordance with the *Declaration of Helsinki*. Participants were randomly assigned

in a counter-balanced manner to perform two $\dot{V}O_{2max}$ tests on a cycle ergometer in either normoxia (21% FiO_2) or hypoxia (13% FiO_2), one week apart. Participants then completed 60 minutes of cycle exercise at 70% of their respective $\dot{V}O_{2max/peak}$ in both conditions. Venous blood was collected via venepuncture: pre-exercise; immediately post- exercise; and 1h, 4h and 24h post exercise, to measure markers of calcium metabolism. A sub-sample of participants (n = 5) provided additional blood samples during the exercise trials (see Figure 1a) for analysis of Ca^{2+} and pH. Data were analysed using two-way repeated measures ANOVAs and regression.

We observed that exercise caused a transient increase in Ca^{2+} at the onset of exercise and later decrease until cessation (Figure 1a). Ca^{2+} was positively correlated with PTH (Figure 1d: R = -0.82, p < .001) further supporting previous observations. Although hypoxic exercise reduced relative Ca^{2+} to a greater degree, and despite pH being higher during hypoxia (Figure 1c: Condition*Time p = .01), the interaction of time and condition was non-significant. The respiratory alkalosis during hypoxia appeared to reduce competition for albumin binding positions, demonstrated by the positive correlation between pH and albumin (Figure 2b: R = 0.7, p < .001). We speculate that a greater sample size may observe a difference between conditions. The higher total calcium concentration following hypoxic exercise (Figure 3c; MD = 0.04±0.01, p < .001) and the negative correlation between Ca^{2+} and pH (Figure 2c-d: R = -0.57, p < 0.0001) support that Ca^{2+} is bound to albumin during respiratory alkalosis. Hypoxia attenuated the phosphate response to exercise, demonstrated at the post exercise time point (Figure 3d: MD = -0.21±0.02, p < .001), which may be explained by hypocapnia. The reduced CO_2 increased pH (Figure 2a), known to stimulate the glycolytic system and the production of phosphofructokinase (PFK). PFK enhances sugar phosphate production and subsequently stimulates phosphate entry to muscle (5). It is possible that the decrease in phosphate may have been compounded by the hypoxic-induced transcription of fibroblast growth factor 23 (FGF23). FGF23 is known to reduce serum phosphate concentrations and negatively regulate PTH, possibly explaining the lower PTH response post hypoxic exercise (Figure 3f; MD = -0.11 ± 0.05, p < .05).

Figure 1:

Ca^{2+}, pH and PTH response to hypoxic/normoxic exercise

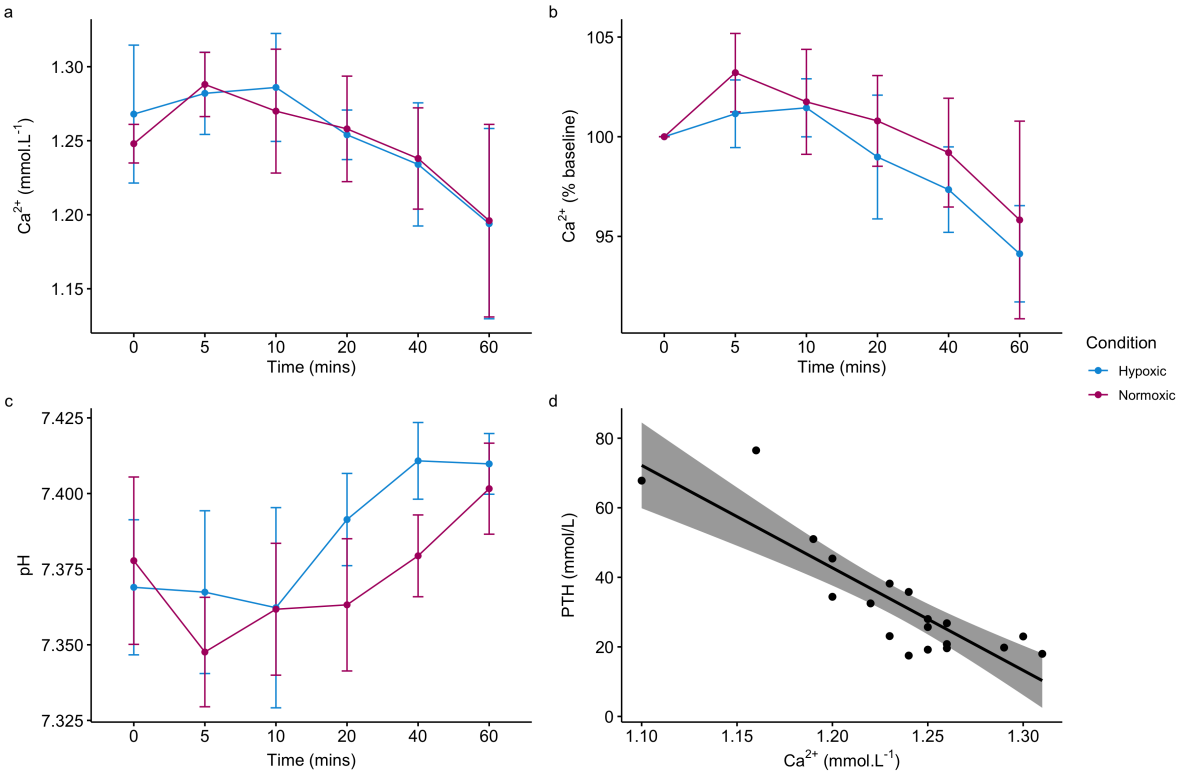

Figure 1: Data are presented as mean ± 1SD. a) Time course response of absolute Ca2+ to both normoxic and hypoxic exercise, no interaction effect was identifiable.
b) Ca2+ presented as a percentage of baseline showing the lower Ca2+ in hypoxia. c) pH response displaying the increased pH during hypoxia.
d) Spearman's correlation showing the signifcant negative correlation bewteen Ca2+ and PTH.

Figure 2:

Does pH regulate Ca^{2+}during exercise?

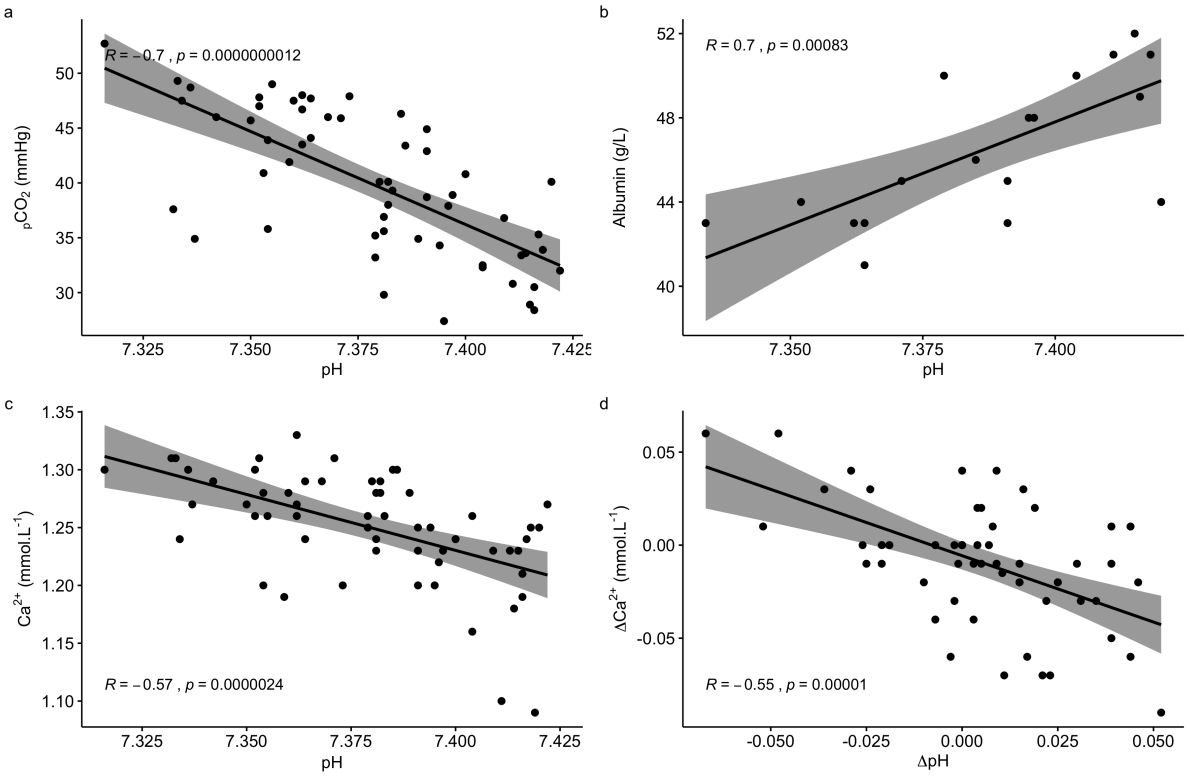

Figure 2: Bold lines represent the regression line whereas the shaded area indicates the 95% confidence interval. a) Significant negative correlation between pCO2 and pH during exercise. b) Relationship between pH and albumin (pre and post exercise pooled sample). c) Negative relationship between Ca2+ and pH suggesting that pH is an important regulator of Ca2+ during exercise

Figure 3:

Hypoxic exercise increases total calcium concentrations but attenuates the PTH increase

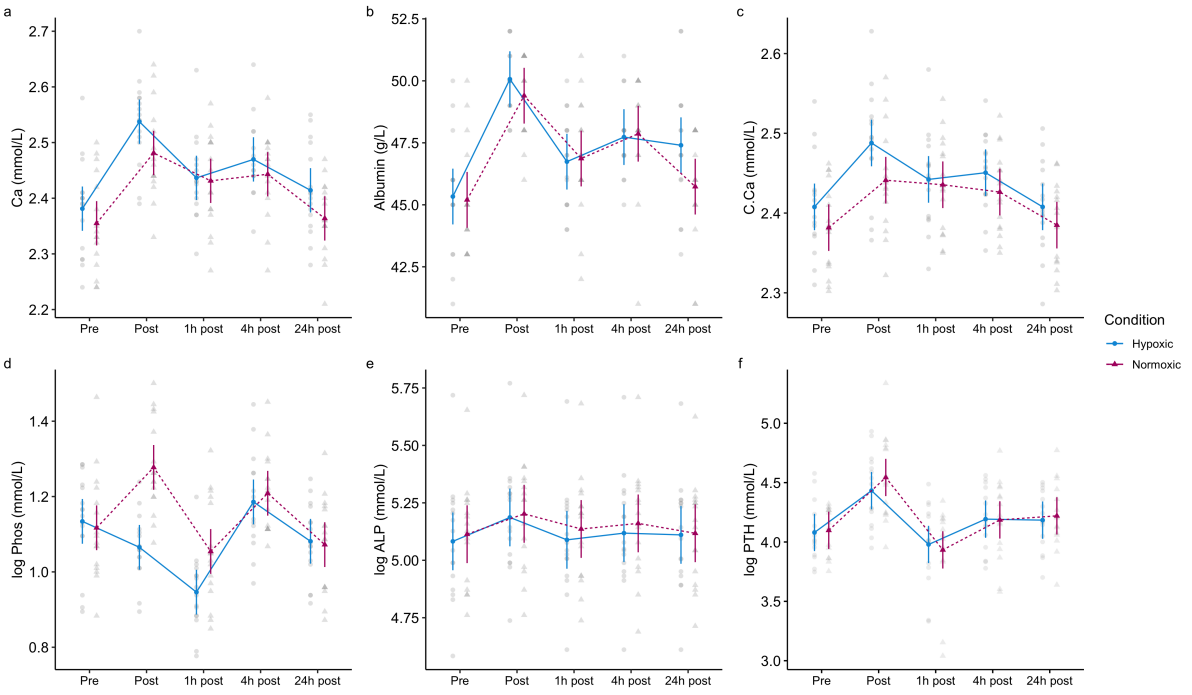

Figure 3: Data shown are estimated marginal means derived from ANOVA models and their 95% confidence intervals.

Reference 1 :- (1) Townsend R, Elliott-Sale KJ, Pinto AJ, Thomas C, Scott JP, Currell K, Fraser WD, Sale C. Parathyroid hormone secretion Is controlled by both ionized calcium and phosphate during exercise and recovery in men. The Journal of Clinical Endocrinology & Metabolism. 2016 Aug 1;101(8):3231-9.

Reference 2 :- (2) Sherk VD, Wherry SJ, Barry DW, Shea KL, Wolfe P, Kohrt WM. Calcium supplementation attenuates disruptions in calcium homeostasis during exercise. Medicine and science in sports and exercise. 2017 Jul;49(7):1437.

Reference 3 :- (3) Kohrt WM, Wherry SJ, Wolfe P, Sherk VD, Wellington T, Swanson CM, Weaver CM, Boxer RS. Maintenance of serum ionized calcium during exercise attenuates parathyroid hormone and bone resorption responses. Journal of Bone and Mineral Research. 2018 Jul;33(7):1326-34.

Reference 4 :- (4) Wasserman K. Lactate and related acid base and blood gas changes during constant load and graded exercise. Canadian Medical Association Journal. 1967 Mar 25;96(12):775.

Reference 5 :- (5) Favus MJ. Intestinal absorption of calcium, magnesium, and phosphorus. Disorders of bone and mineral metabolism. 1992:57-81.

Acknowledgements :- We would like to thank the Ulster hospital for their assistance in our laboratory analyses, with special thanks to Prof. Tom Trinick and Dr. Ellie Dully. We would also like to thank Prof. Craig Sale for his sound advice throughout. Finally, we would like to thank all the participants who volunteered for this study.

PC0031

The effect of standing when cycling on skeletal muscle oxygenation

Marianne Beach[1]

[1]*King's College London, London, United Kingdom*

When cycling uphill, a standing position results in a lower RPE (rating of perceived exertion) compared to a seated position (Hansen and Waldeland 2008). For example, Tanaka et al 1996 found a significantly ($P<0.05$) lower RPE when cycling in a standing position for a 10% grade. This reduction in RPE could be due to increased oxygenation of the skeletal muscles of the leg when in a standing position. NIRS (near infrared spectroscopy) can be used to calculate the TSI (tissue saturation index), and thereby assess skeletal muscle oxygenation (Belardinelli et al 1995). The aim of this study was to investigate the effect of standing when cycling on *vastus lateralis* muscle TSI at different cadences. It was hypothesised that standing when cycling would result in a higher TSI value and therefore greater skeletal muscle oxygenation than seated cycling.

An incremental ramp test was used to determine the ventilatory threshold (VT) of 7 healthy participants (3 male, 4 female, age (years) 24.6 ± 7.9, height (m) 1.71 ± 0.05, weight (kg) 73.9 ± 18.9 (**Table 1**)). The participants then cycled for 5 minutes (3 minutes seated then 2 minutes standing) on

an ergometer at cadences of 40, 50, 60, and 70 rpm (revolutions per minute), in a randomised order, at a work rate matching 75% VT. The participants had a 3 minute warm-up and a 2 minute active recovery period in-between each 75% VT exercise period. *Vastus lateralis* muscle TSI, heart rate, respiratory parameters and RPE were measured.

TSI (%) when standing was not significantly different (P= 0.157) from seated cycling baseline TSI values at 40, 50, 60 or 70 rpm (**Figure 1**), with a mean change of -1.8%. Heart rate (**Figure 2**), $\dot{V}O_2$ (**Figure 3**) and $\dot{V}CO_2$ (**Figure 4**) had mean changes of + 12 bpm, + 0.21 L/min and + 0.36 L/min respectively and were significantly (P< 0.001) greater when participants were cycling in a standing position. There was no significant difference in RPE score (**Table 2**) between positions (P= 0.242).

The oxygenation of the *vastus lateralis* muscle is not significantly different, at a 75% VT work rate, between a seated or a standing cycling position. This concurs with other studies (Harnish et al 2007, Ryschon and Stray-Gunderson 1991). A benefit of standing may depend on the work rate and gradient cycled at, cyclist muscle composition and training level. Future studies should consider using ultrasound, electromyography and muscle biopsies to determine this.

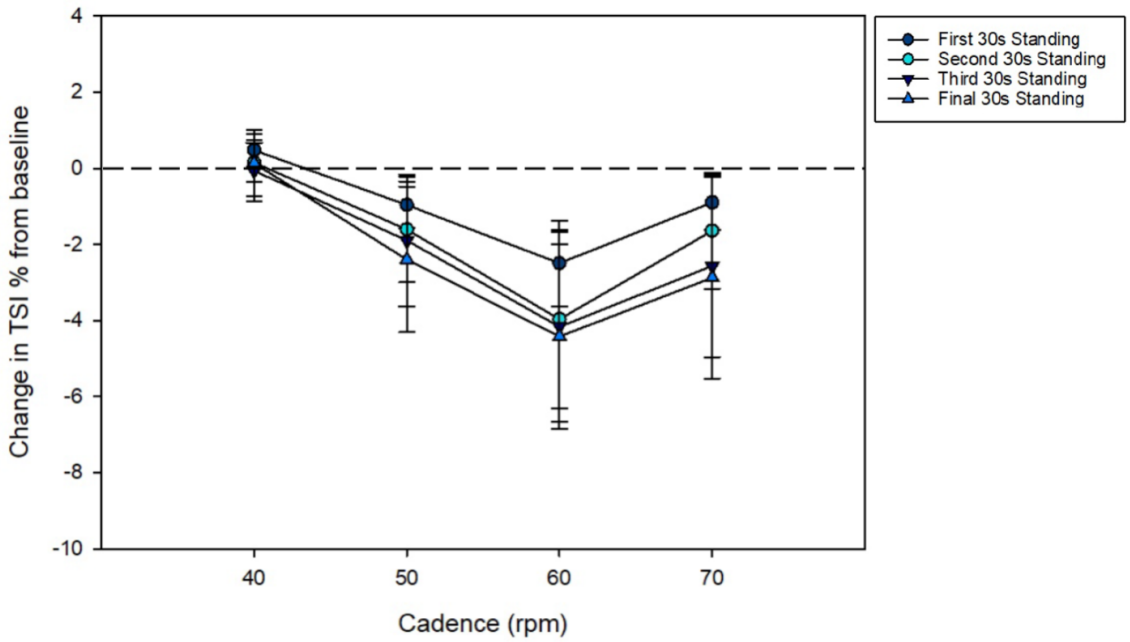

Figure 1 - Changes in TSI (%) when standing compared to seated cycling (baseline) for each cadence and period of standing cycling assessed. These changes were not statistically significant (P=0.157) for any cadence or period assessed (First 30 s P=0.897, Second 30 s P=0.572, Third 30 s P=0.331, Final 30 s P=0.238).

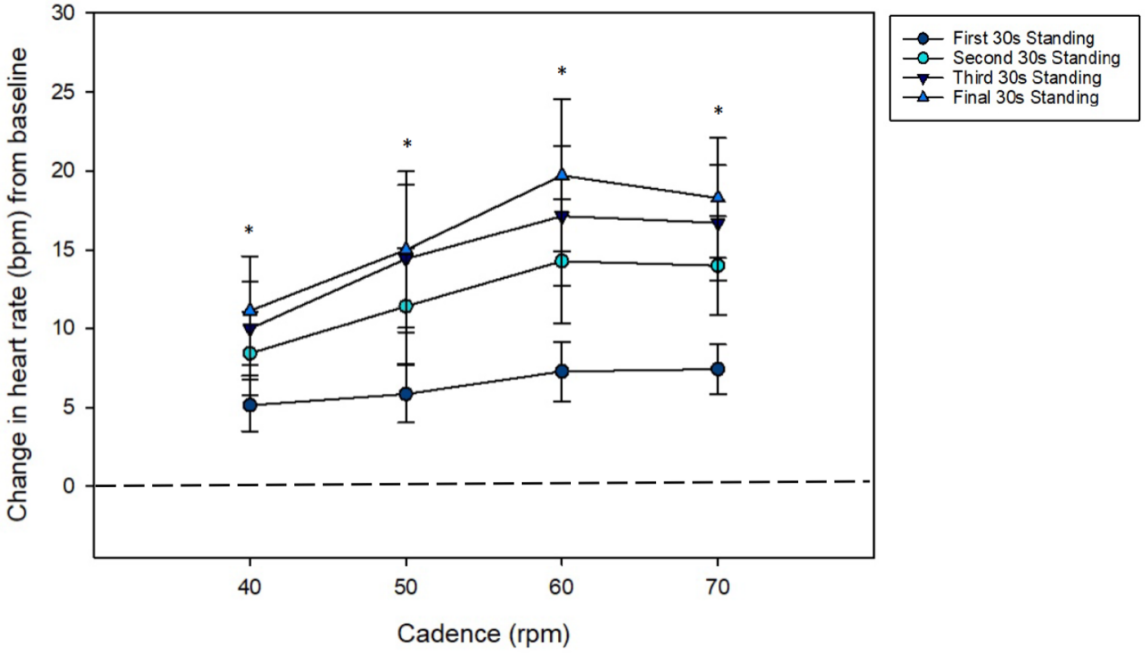

Figure 2 - Changes in heart rate (bpm) when standing, compared to seated cycling (baseline), for each cadence and period of standing cycling assessed. These changes were overall statistically significant ($P<0.001$) with heart rate being higher when standing (First 30 s $P=0.150$, Second 30 s $P<0.001$, Third 30 s $P<0.001$ and Final 30 s $P<0.001$) at all cadences assessed. A statistically significant difference according to calculated p-values, between seated and standing positions at each cadence, is represented by an * symbol.

Characteristic	**Mean ± SD (N=7)**
Age	24.6 ± 7.9
Height (m)	1.71 ± 0.05
Weight (kg)	73.9 ± 18.9
BMI (kg/m^2)	25.2 ± 5.8
Skin Fold (mm)	4.7 ± 1.0
Seat Height (cm)	25.5 ± 4.1
Distance between seat and handles (cm)	44.1 ± 2.5

Table 1 – Mean and standard deviation (SD) data of the characteristics of participants (N=7) used in the statistical analysis for this study. Of these 7 participants, 4 were Female and 3 were male. BMI = Body Mass Index

Cadence	Position	Participant Number						
		1	2	3	4	5	6	7
		RPE Score						
Rest Period	Seated	6	6	6	6	6	6	7
40	Seated	11	15	15	13	13	10	15
40	Standing	13	15	17	11	11	13	14
50	Seated	13	14	13	12	12	7	14
50	Standing	14	11	17	13	11	9	13
60	Seated	13	15	14	10	11	8	12
60	Standing	13	14	15	15	11	13	12
70	Seated	13	15	13	13	11	8	12
70	Standing	12	16	16	14	11	14	12

Table 2 – RPE (rate of perceived exertion) scores for participants in the seated vs standing protocol. RPE was measured at the end of each seated and standing period for each cadence assessed using the Borg Scale. As can be seen, there is a variation in whether RPE increases or decreases when a transition from a seated to a standing position is made.

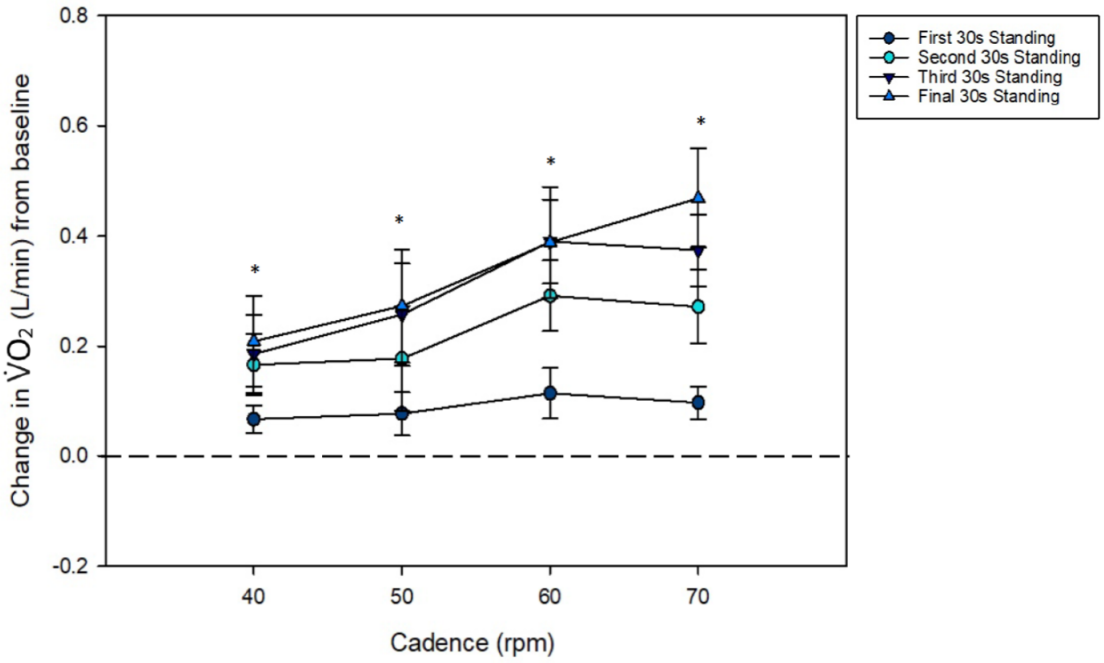

Figure 3 - Changes in $\dot{V}O_2$ (L/min) when standing, compared to seated cycling (baseline), for each cadence and period of standing cycling assessed. These changes were overall statistically significant ($P<0.001$) with $\dot{V}O_2$ being higher when standing (First 30 s $P=0.566$, Second 30 s $P=0.002$, Third 30 s $P<0.001$ and Final 30 s $P<0.001$). A statistically significant difference according to calculated p-values, between seated and standing positions at each cadence, is represented by an * symbol.

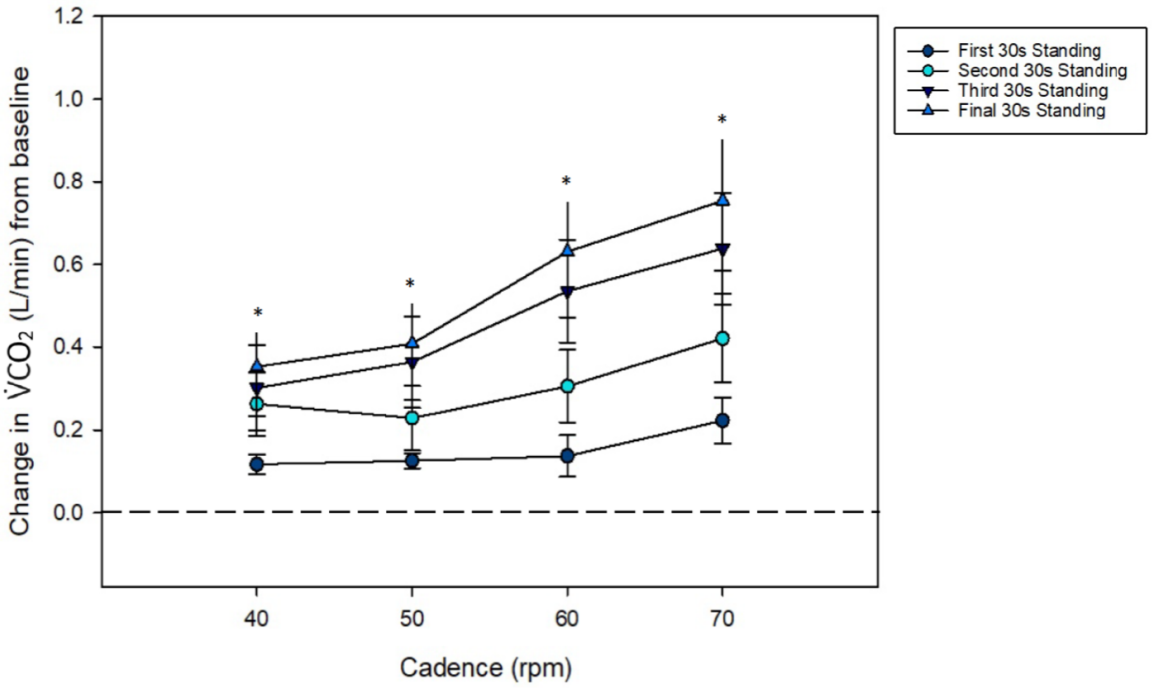

Figure 4 – Changes in $\dot{V}CO_2$ (L/min) when standing, compared to seated cycling (baseline), for each cadence and period of standing cycling assessed. These changes were overall statistically significant (P<0.001) with $\dot{V}CO_2$ being higher when standing (First 30 s P=0.269, Second 30 s P<0.001, Third 30 s P<0.001 and Final 30 s P<0.001). A statistically significant difference according to calculated p-values, between seated and standing positions at each cadence, is represented by an * symbol.

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PC0032

INVESTIGATION INTO THE EFFECT OF A COMBINED ADAPTIVE EXERCISE PROGRAM ON AEROBIC CAPACITY AND MUSCLE STRENGTH IN CANCER SURVIVORS.

Ananya Gupta[1]

[1]*Discipline of Physiology NUI Galway, GALWAY, Ireland*

Cancer is among the leading causes of morbidity and mortality worldwide, with approximately 14 million new cases and an incidence rate expected to rise by 70% over the next two decades. It is well documented that cancer progression and its treatment is associated with adverse physical and physiological changes leading to metabolic and functional modifications, inducing pathologies of the cardiac, pulmonary, neural, bone and skeletomuscular systems. These alterations effect cardiorespiratory capacity (fitness), strength, body composition, and physical function including immune system integrity, peripheral neuropathy, and quality of life. However, it is increasingly becoming clear that prescribing exercise during and post-cancer treatment may mitigate many of these adverse changes.

The aim of the current study was to design and implement an individualized combined exercise program and evaluate its effects on improving cardiopulmonary fitness in cancer survivors. Breast cancer patients who have received a combination of surgery, chemotherapy or radiation therapy as part of their cancer treatment were recruited to the study. All the participants were at least 2-6 months post-treatment. Cardiorespiratory fitness, muscular strength, flexibility and quality of life were assessed at baseline using CPET, 5-RM, sit-an-reach test and SF-36 questionnaire respectively. An exercise program consisting of aerobic exercises, flexibility exercises and resistance exercises based on the American College of Sports Medicine (ACSM) prescribed guidelines for cancer survivors were implemented for 2 months. Patients received a flexible individualized exercise program based on their baseline assessment and PPI feedback received from them.

The program significantly improved the aerobic capacity and muscle strength in most of the participants. The patients also reported a significant increase in all parameters related to well being as assessed using the 36-SF questionnaire including increased energy, reduction in fatigue, emotional well-being, alleviation of pain, improved physical function and general health scores. This study clearly shows that such an intervention is beneficial to patients recovering from cancer treatment and will contribute significantly to improving their quality of life.

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PC0033

A MULTI-COMPONENT EXERCISE PROGRAM CAN IMPROVE MOBILITY IN BREAST CANCER SURVIVORS SUFFERING FROM LYMPHEDEMA

Ananya Gupta[1]

[1]*Discipline of Physiology NUI Galway, GALWAY, Ireland*

Lymphedema is a common side-effect of cancer treatment which involves surgical removal of lymph nodes resulting in disruption of lymph drainage. This leads to swelling and reduced strength and mobility in the effected part. In breast cancer patients this often affects the arms and can be very painful and debilitating. Exercise therapy has been shown to reduce the side-effects of cancer treatment. This study investigates the effects of exercise therapy in improving upper limb mobility and other fitness related variables in breast cancer survivors suffering from lymphedema.

This study was conducted as a non-randomized pilot study. 4 breast cancer survivors clinically diagnosed with lymphedema were assigned to group A (lymphedema group). An additional 4 breast cancer survivors without lymphedema were assigned to group B (non-lymphedema group). All enrolled participants had completed cancer treatment 2-6 months prior to this study. For each outcome baseline characteristic was assessed at the initiation. Both groups participated in a multi-component exercise program, which included aerobic, resistance and flexibility exercises for 8 weeks. Additional lymphedema specific exercises were also prescribed to enhance lymphatic drainage. Outcomes were measured every 4 weeks and included range of motion, flexibility, strength and 1RM on resistance machines, limb circumference, balance and aerobic capacity.

All parameters improved significantly after 8 weeks but there was no significant difference between the two groups. Range of motion of the shoulder was shown to have similar improvements in both. Both groups showed significant progression in balance, flexibility and strength. Evaluation of strength revealed that group B progressed on all upper body machines, while group A showed greater progression in chest-press, shoulder-press and lateral pull-down. Limb circumference measures (lymphedema arm) reported only a small improvement between the initial and final assessment, this may be due to the resistance component of the program resulting in increased muscle tone. Nevertheless, all enrolled participants reported a positive change in their current quality of life on completion of the study. Exercise therapy was shown to improve mobility and strength in cancer survivors suffering from lymphedema. However; a longer interventions (> 8 weeks) is needed to

promote significant improvement in lymphedema status.

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PC0034

Vitamin B12 Deficiency Leads To Fatty Acid Metabolism Dysregulation and Increased proinflammatory cytokine production in Human Adipocytes and in Maternal Subcutaneous and Omental Adipose Tissue.

Jinous Samavat[1], Antonysunil Adaikalakoteswari[2], Joseph Boachie [1], Laura Jackisch[1], Mark Christian [2], Ponnusamy Saravanan[1]

[1]University of Warwick, coventry, United Kingdom [2]Nottingham Trent University, Nottingham, United Kingdom

Vitamin B12 (B12) is an essential micronutrient required for several metabolic reactions. Animal and clinical studies show that B12-deficiency is associated with metabolic syndrome. Given the key metabolic role of adipose tissue, we investigated whether B12 deficiency may affect triglyceride synthesis and lipid metabolism leading to adipose tissue inflammation. The AbdSc pre-adipocyte cell line (Chub-S7)and human AbdSc primary pre-adipocytes were differentiated under different B12 concentrations (25pM,100pM,1nM,500nM). Human Om, Sc- AT and blood samples were collected from 106 pregnant women at delivery.SerumB12 and relevant metabolic risk factors were measured. Gene expression was performed by q-RT-PCR, de novo triglyceride synthesis was quantified by radioactive tracing, ß-oxidation and palmitateinduced oxygen consumption rate was determined using the seahorse-XF analyzer. Adipocytes cultured in low-B12 conditions showed significantly increased expression ($P<0.01$)of triglyceride biosynthesis genes (ELOVL6,SCD,GPAT,LPIN1 and DGAT2), a significantly decreased expression ($P<0.01$) of ß-oxidation genes (FAT/CD36, CPT1-ß, ACADL, ECHS1 and ACAA2) and an increased expression ($P<0.01$) of pro-inflammatory cytokines (IL-1, IL-6,IL- 8,IL-18,TGF-β,TNF-α and MCP-1). These data were also confirmed in the AT of B12-deficient pregnant women. Additionally, real-time fatty acid flux synthesis and fatty-acid-oxidation induced by palmitate were signi□□cantly altered ($P<0.05$) in B12-deficient adipocytes. Our data highlights that B12-deficiency has profound effects on adipocyte dysfunction, opening new insights into the pathogenesis of maternal obesity and the relevance of micronutrient supplementation for pregnant mothers.

Acknowledgements :- Sir Jules Thorn Charitable trust

PC0035

Arts-Based Learning as a complementary educational tool in physiology class.

Edson Rodrigues[1], Suzana da Cunha Lima[2]

[1]UNEB, SALVADOR, Brazil [2]UFBA, SALVADOR, Brazil

In Problem-based learning, students work together to learn subject concepts triggered by an open-ended situation, aiming to develop knowledge in a critical, communicative way. Such student-centered, active teaching and learning methodologies have been used in different fields where multidisciplinary work is characteristic. We describe a teaching and learning activity derived from Problem-based Learning established on collective artistic creation related to human physiology, in the molecular, cellular, and systemic levels, called Arts-based Learning. Undergraduate students of a Physiology course from a Brazilian Public University were stimulated to create acrylic painting panels, aiming to help learning in group with long-term memorization. Art works were produced throughout the academic semester and the participants evaluated the activity by an applied survey. Data shows favorable results pointing to general approval. On average, approximately 70% of students agreed that the method helps in learning, reinforces vocational training, critical aptitude, creativity, and increases the level of academic achievement.

Key words: Teaching, Active methodology, Learning, Arts-based learning, Physiology, Biology, Painting.

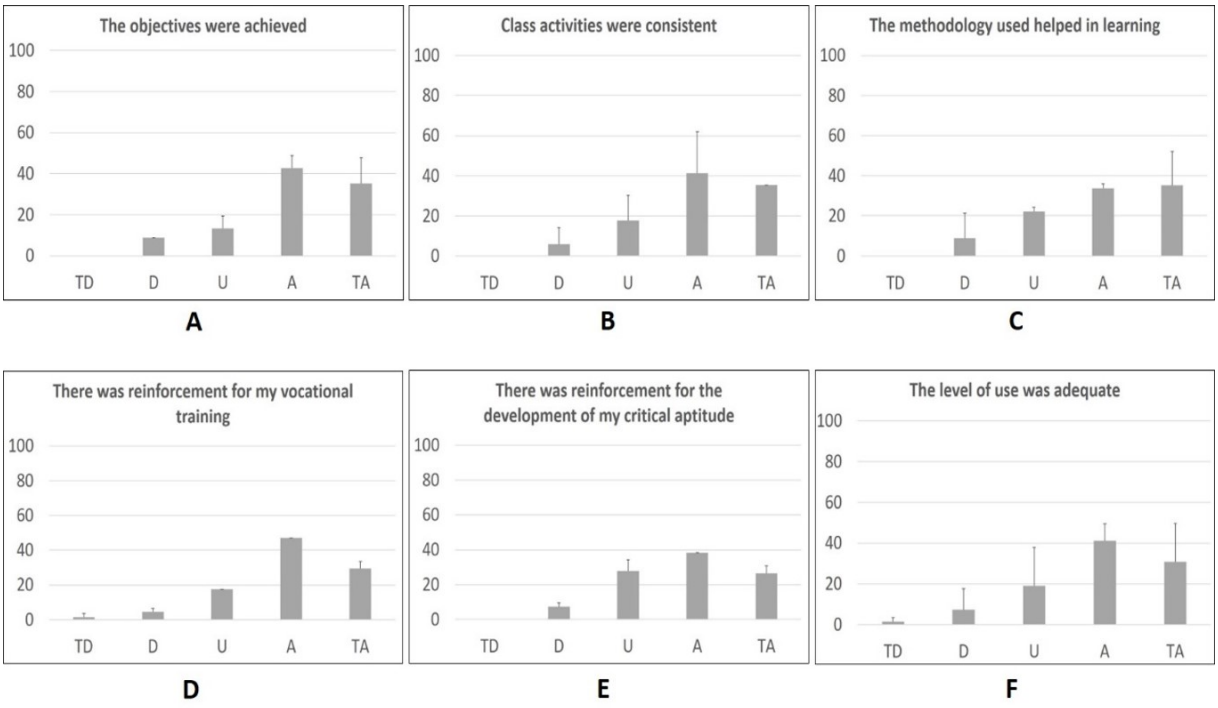

Figure 03 – Evaluation of the ABL activity performed by the students of the CCS016 Physiology class. The numbers show the average between 2018.1 and 2018.2 classes, with responses in percentage on a Likert scale (TD, Totally Disagree; D, Disagree; U, Undecided; A, Agree; TA, Totally Agree).

Figure 02 – Final artwork prepared by nursing, pharmacy, physiotherapy, speech therapy and nutrition students by Physiology ABL tutoring (UNEB, 2018).

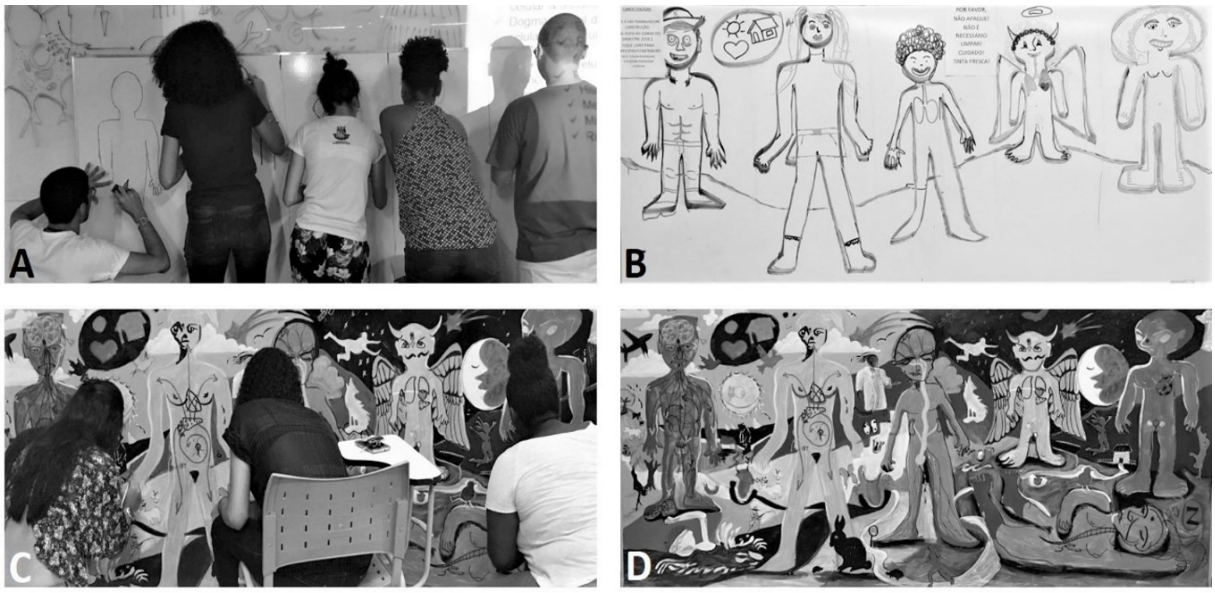

Figure 01 – Sequence of chronological images of the ABL activity. (A) Students draw human figures in anatomical position. (B) Basic draw at the end of the introductory activity. (C) Group of students work on the panel. (D) Base painting elaborated at the end of the activity.

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PC0036

The Role of Carbohydrate Balance in Acute, Exercise-Induced Improvements in Insulin Sensitivity in Healthy Adults.

Drusus Johnson-Bonson[1], James Betts[1]

[1]*University of Bath, Bath, United Kingdom*

The residual improvement in insulin sensitivity (IS) following individual exercise bouts is a key mechanism by which endurance exercise enhances glycaemic control (1). However, it is unclear to what extent this benefit is dictated by a negative carbohydrate (CHO) balance (greater CHO oxidation than ingestion). Supporting a regulatory role of CHO balance, Taylor *et al.* (2) demonstrated that the morning after 90 minutes of treadmill exercise, with or without CHO replacement, whole-body IS was reduced by 25% when CHO was replaced. However, use of a non-exercise control condition alongside CHO replete and CHO deficit exercise conditions is necessary to establish whether elimination of the exercise-induced CHO deficit partially or fully negates the acute-exercise-induced improvement in IS. Therefore, the present study compared IS and glycaemic control the morning after evening treadmill exercise, with or without CHO replacement, versus a non-exercise control.

Seven males and two females (mean ±SD age: 23 ±1 years; body mass index: 24.0 ±2.7 kg/m^2) completed all conditions in a randomised order, preceded by two days diet replication and exercise cessation. Conditions *Ex-Plac* and *Ex-Malt* (beginning ~16:30) involved 90 minutes of identical treadmill exercise (79% ±4% and ±6% age-predicted maximum heart rate), followed immediately by ingestion of either maltodextrin (*Ex-Malt*; 200 or 150 g for males and females, respectively) or taste-matched placebo (*Ex-Plac*). *Rest* involved seated rest with no drink. After evening visits, participants consumed nothing but water and a prescribed low CHO dinner (55, 441 and 178 kcal from CHO, fat and protein, respectively) until an oral glucose (75 g) tolerance test undertaken the following morning (~14 hours after evening visits), to assess glycaemic control and whole-body IS. Plasma glucose and insulin were assessed using a spectrophotometric analyser (Randox Daytona, Crumlin, UK) and enzyme-linked immunosorbent assays (Mercodia AB, Uppsala, Sweden), respectively. Data are: mean Δ (95% confidence intervals).

While there were only minor differences in glycaemic and insulinaemic responses between conditions (**Figure 1**), both the Matsuda insulin sensitivity index (ISI_M [3]) and homeostatic model of insulin resistance (HOMA-IR [4]) were improved in *Ex-Plac* versus *Ex-Malt*, by 21% (2.2. au [0.4, 4.0]) and 13% (-0.11 au [-0.18, -0.03]), respectively (**Figure 2**). Data also suggested improvements in *Ex-Plac* versus *Rest*, but these differences were less clear; +16% (1.8 au [-0.3, 3.9]) in ISI_M and -14% (-0.10 au [-0.22, 0.01]) in HOMA-IR. Outcomes were similar between *Ex-Malt* and *Rest*. Additional glucose and insulin summary statistics are shown in **Table 1**.

Differences between *Ex-Plac* and *Ex-Malt* were similar to those reported by Taylor et al. (2), supporting that CHO replacement attenuates the acute, exercise-induced improvement in IS. The complete absence of improvements in *Ex-Malt* versus *Rest* indicate that any acute, endurance-exercise-induced benefit to IS in healthy populations is likely *fully* dependent on the presence of a negative CHO balance. Thus, extending the post-exercise CHO deficit, via maximising CHO oxidation during exercise or delaying CHO replenishment (by altering type, timing or amount of CHO intake) may reduce glycaemic or insulinaemic exposures, but intervention studies are required to test this hypothesis.

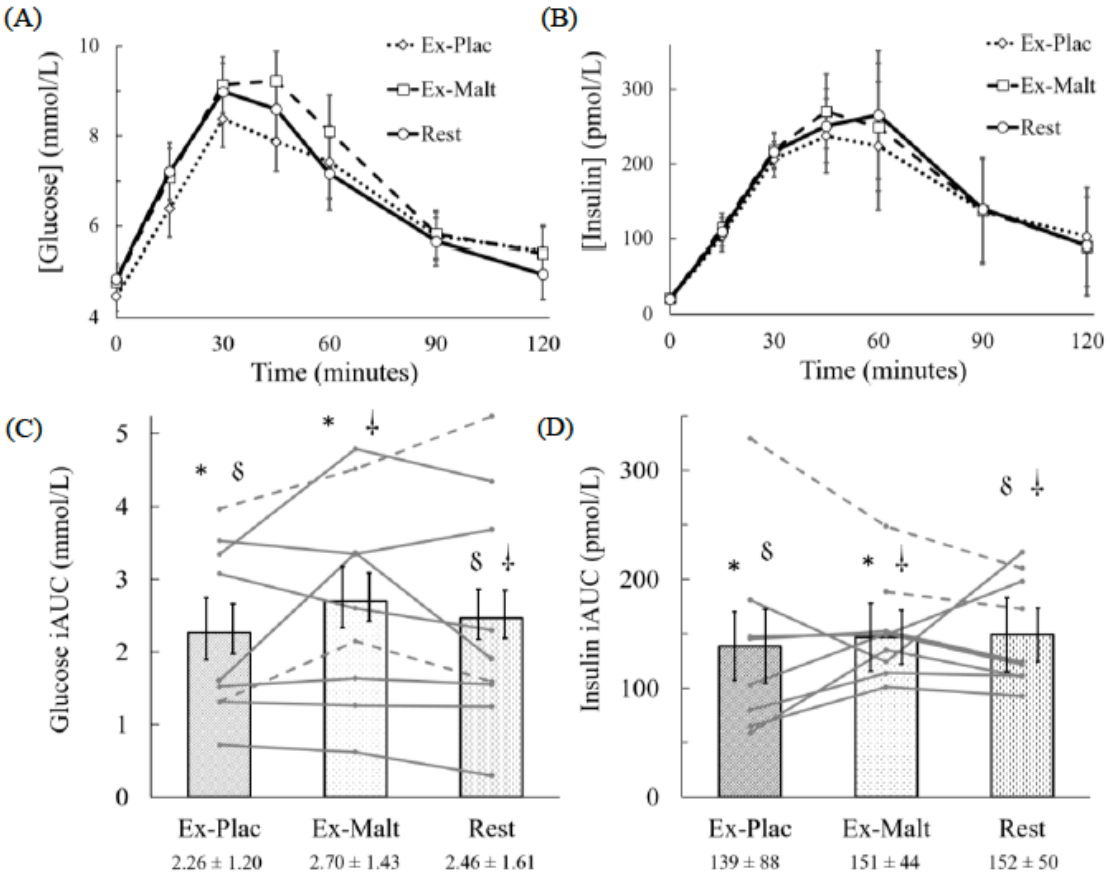

Figure 1. Glycaemic (A) and insulinaemic (B) responses during OGTTs; time-averaged iAUCs (C and D); error bars are 95% normalised CIs (Masson & Loftus, 2003 [5]; matching symbols correspond to between-conditions comparisons; a three level hypothesis test was used for timepoints on line graphs, with Greenhouse Geiser correction, if applicable); n = 8 for *Ex-Plac*; n = 9 for *Ex-Malt* and *Rest*; mean ± SD values are shown under respective columns.

Table 1. Plasma glucose and insulin summary statistics during OGTTs.

	Ex-Plac	*Ex-Malt*	*Rest*
Baseline [glucose] (mmol/L)	4.47 ± 0.34	4.78 ± 0.48	4.85 ± 0.65
Peak [glucose] (mmol/L)	8.70 ± 1.41	9.56 ± 2.06	9.47 ± 1.83
ToP [glucose] (minutes)	38 ± 16	35 ± 13	42 ± 13
Baseline [insulin] (pmol/L)	20.0 ± 1.0	21.8 ± 3.9	20.8 ± 3.2
Peak [insulin] (pmol/L)	254.9 ± 127.6	284.8 ± 104.8	307.5 ± 140.5
ToP [insulin] (minutes)	54 ± 8	47 ± 10	53 ± 11

All values are mean ± SD; ToP = time of peak; square brackets denote concentrations; n = 8 for insulin values; n = 9 for glucose values.

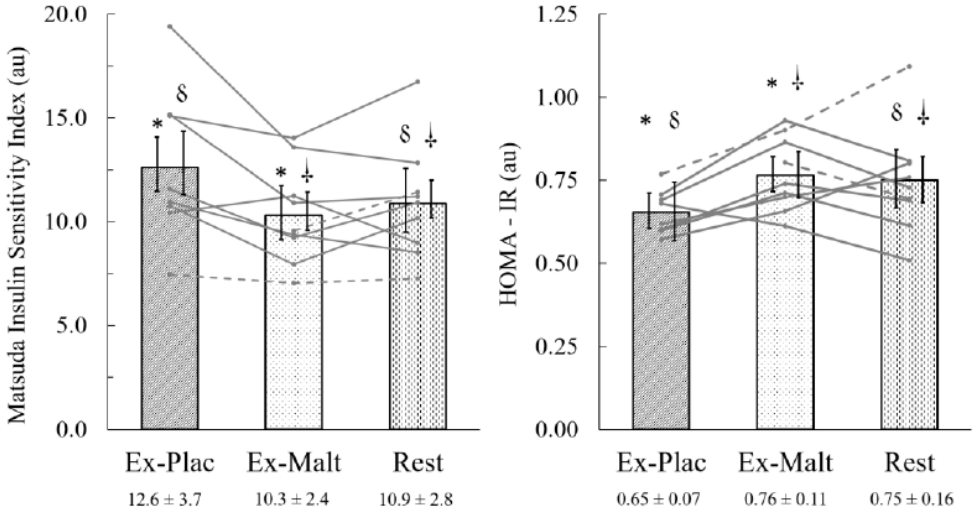

Figure 2. Insulin sensitivity indices; error bars are 95% normalised CIs (Masson & Loftus, 2003 [5]; matching symbols corresponding to between-conditions comparisons); solid and dashed grey lines represent individual male and female participants, respectively; n = 8 for *Ex-Plac*; n = 9 for *Ex-Malt* and *Rest*; mean ± SD values are shown under respective columns.

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PC0038

Nitrate-rich beetroot juice offsets salivary acidity in healthy male runners following carbohydrate ingestion before and after endurance exercise designed to cause mild dehydration

Mia Cousins Burleigh[1], Chris Easton[2], Nicholas Sculthorpe[2], Fiona Henriquez[3]

[1]Univeristy of the West of Scotland, Lanarkshire, Glasgow, United Kingdom [2]University of the West of Scotland, Lanarkshire, Glasgow, United Kingdom [3]University of the West of Scotland , Renfrewshire, Paisley, United Kingdom

Oral disease is prevalent in elite athletes due to carbohydrate ingestion and frequent bouts of dehydration. These factors combine to lower salivary-pH and acidity related diseases such as caries result. Conversely, chronic ingestion of nitrate (NO_3^-)-rich beetroot juice has been shown to increase salivary-pH. The purpose was to determine the effect of a single dose of NO_3^- on salivary-pH following carbohydrate ingestion before and after exercise. Eleven male endurance runners completed a double-blind randomised placebo-controlled study comprising four experimental trials in temperature of 23 ± 1ºC, 40 ± 5% relative humidity. Participants ingested the following fluids one hour before each trial: (a) 140 ml of water (negative-control), (b) 140 ml of water (positive-control), (c) 140 ml of NO_3^--rich beetroot juice (~12.4 mmol NO_3^-) (NO_3^-) or (d) 140 ml NO_3^--depleted beetroot juice (placebo). During the negative-control trial, participants ingested 795 ml of water in three equal aliquots: before, during, and after 90 min of submaximal running. In the other trials they received 795 ml of carbohydrate supplements in the same fashion. One venous blood was collected before and after exercise. At the same time points, saliva was sampled before and repeatedly for 20 min following carbohydrate or water ingestion, area under the curve (AUC) was calculated for these samples. Values are means ± S.D., compared by ANOVA. Exercise resulted in a sweat rate of 1.2 ± 0.2 L/h which, following correction for fluid intake and urine loss, resulted in a 3 ± 1% reduction in body mass. Urine osmolality increased (pre-exercise 366 ± 190 mOsm/kg, post-exercise 595 ± 164 mOsm/kg, P<0.001). The changes in body mass and urine osmolality did not differ between trials (all P>0.05). Stimulated salivary flow-rate reduced from pre to post-exercise in both the positive-control (from 1.35 ± 0.60 ml/min to 0.88 ± 0.43 ml/min, P=0.02) and the placebo trial (from 1.50 ± 0.63 ml/min to 0.95 ± 0.45 ml/min, P<0.001) but did not change in the negative-control (P=0.177) or the NO_3^--trial (P=0.086). As expected, nitrite (NO_2^-) and NO_3^- were highest in the NO_3^--trial (all P<0.001). Salivary-pH followed a similar pattern (NO_3^--trial - Pre-exercise 7.4 ± 0.4 Post-exercise 7.4 ± 0.4, negative-control - Pre-exercise 7.1 ± 0.3 Post-exercise 7 ± 0.2, positive-control - Pre-exercise 7.1 ± 0.3 Post-exercise 6.9 ± 0.2, placebo - Pre-exercise 7 ± 0.3 Post-exercise 7 ± 0.2, all P<0.05). Compared to negative-control, salivary-pH AUC was significantly reduced following carbohydrate in positive-control and placebo (Pre-exercise - positive-control 33 ± 2.9, placebo 33.2 ± 2.7, negative-control 36.3 ± 1.8. Post-exercise – positive-control 32.1 ± 3, placebo 32.7 ± 2.4, negative-control 36.2 ± 1.9, all P<0.05). Conversely, AUC was similar in negative-control and NO_3^- despite ingestion of carbohydrate in the NO_3^--trial (Pre-exercise 34.8 ± 2.5, Post-exercise 34.5 ± 2.6, both P≥0.221). Ingesting NO_3^--rich beetroot juice attenuates the decrease in salivary-pH after carbohydrate supplements and protects against reduced salivary flow-rate following exercise. These results suggest that NO_3^- may protect athletes' teeth from acid erosion caused by frequent carbohydrate ingestion and exercise induced dehydration.

Acknowledgements :- This project was funded by the Hannah Dairy Research Foundation

PC0039

Inflammation-induced skeletal muscle wasting: emerging role of the NLRP3 inflammasome

Moritz Eggelbusch[1, 2, 3], Mariana Vázquez-Cruz[1], Gerard de Wit[1], Bart Everts[4], Richard Jaspers[1], Rob Wüst[1]

[1]Laboratory for Myology, Department of Human Movement Sciences, Faculty of Behavioral and Movement Sciences, Vrije Universiteit Amsterdam, Amsterdam, The Netherlands [2]Department of Nutrition and Dietetics, Amsterdam UMC, location VUmc, Amsterdam, The Netherlands [3]Faculty of Sports and Nutrition, Center of Expertise Urban Vitality, Amsterdam University of Applied Sciences, Amsterdam, The Netherlands [4]Department of Parasitology, Leiden University Medical Center, University of Leiden, Leiden, The Netherlands

Introduction: Systemic low- and high-grade inflammation in various acute and chronic diseases is associated with skeletal muscle mass atrophy and metabolic dysfunction. While the nucleotide-binding oligomerization domain-like receptor family pyrin domain containing 3 (NLRP3) inflammasome is an integral component of the innate immune system, its role in skeletal muscle atrophy and metabolic dysfunction is poorly understood. Complicating factors in understanding molecular mechanisms underlying this loss, are that muscle wasting is a multifactorial process, and human tissue under well-controlled wasting conditions is sparse.

Purpose: Here we studied mechanistically how inflammation induces skeletal muscle atrophy and metabolic dysfunction.

Methods: We treated differentiated C2C12 myotubes with different concentrations of lipopolysaccharide (0,10,100-200 ng/ml LPS), and measured muscle fiber diameter, gene expression and protein concentrations of markers of the NLRP3 inflammasome.

Results: LPS reduced fiber diameter up to 42±6% (at 100 ng/ml LPS) after 24 hrs, which remained smaller up to 72 hrs. NLRP3 and downstream caspase-1 mRNA gene expression increased in a dose-dependent response after 24 hrs. NLPR3 and cleaved (p20) caspase-1 effector protein concentrations increased dose- and time-dependently upon LPS treatment. The addition of 10 ng/ml TGF-β further induced NLRP3 gene expression upon LPS treatment. Using STED fluorescent imaging, NLRP3 colocalized to mitochondria (66±5%), with unknown functional consequences. Treating the C2C12 cells with additional SS31 (to stabilize cardiolipin function) mitigated LPS-induced fiber atrophy.

Conclusions: These data suggest an inflammation-induced priming of the NLRP3 inflammasome in myofibers, independent of immune cell involvement. We show a structural link between the NLRP3 inflammasome and mitochondria in skeletal muscle cells that requires further study to understand the functional role of the NLRP3 inflammasome in the development of skeletal muscle wasting and metabolic dysfunction.

PC0041

Surgical Emergencies during Exploration Class Missions: Considerations of the Extreme Operating Environment, Crew & Payload Preparedness, & the Physiological Deconditioned Status of the Prospective Patient

Nina Purvis[1, 2]

[1]Barts and The London School of Medicine and Dentistry, London, United Kingdom [2]King's College London, London, United Kingdom

Introduction: Crewed missions to Mars are anticipated by the 2040s. Risks include distance and the extreme environment faced. Planning and self-sufficiency are key to success. Stabilisation, transport, and robust telemedicine capabilities are not a feasible model, and further, astronauts will have undergone significant physiological deconditioning with limited payload & training. Considerations of the environment in which such a surgery may take place, the statistically likely surgical emergencies, the deconditioned status of the patient, crew training, and utilising technologies are needed (Hamilton, *et al.*, 2008).

Methods: A systematic literature review and thematic analysis (Laws, *et al*., 2019). Databases searched: PubMed, NASA online archives, ESA online archives, cross-checking of reference lists.

Search terms (1960-2020, papers in English):

*Surgery *AND Spaceflight, *AND Mars, *AND Submarine, *AND Antarctica; Robotic Surgery *AND Spaceflight, *AND Mars;Autonomous Robotic Surgery *AND Spaceflight, *AND Mars; 3D Printing Surgical Instruments *AND Spaceflight, *AND Mars*

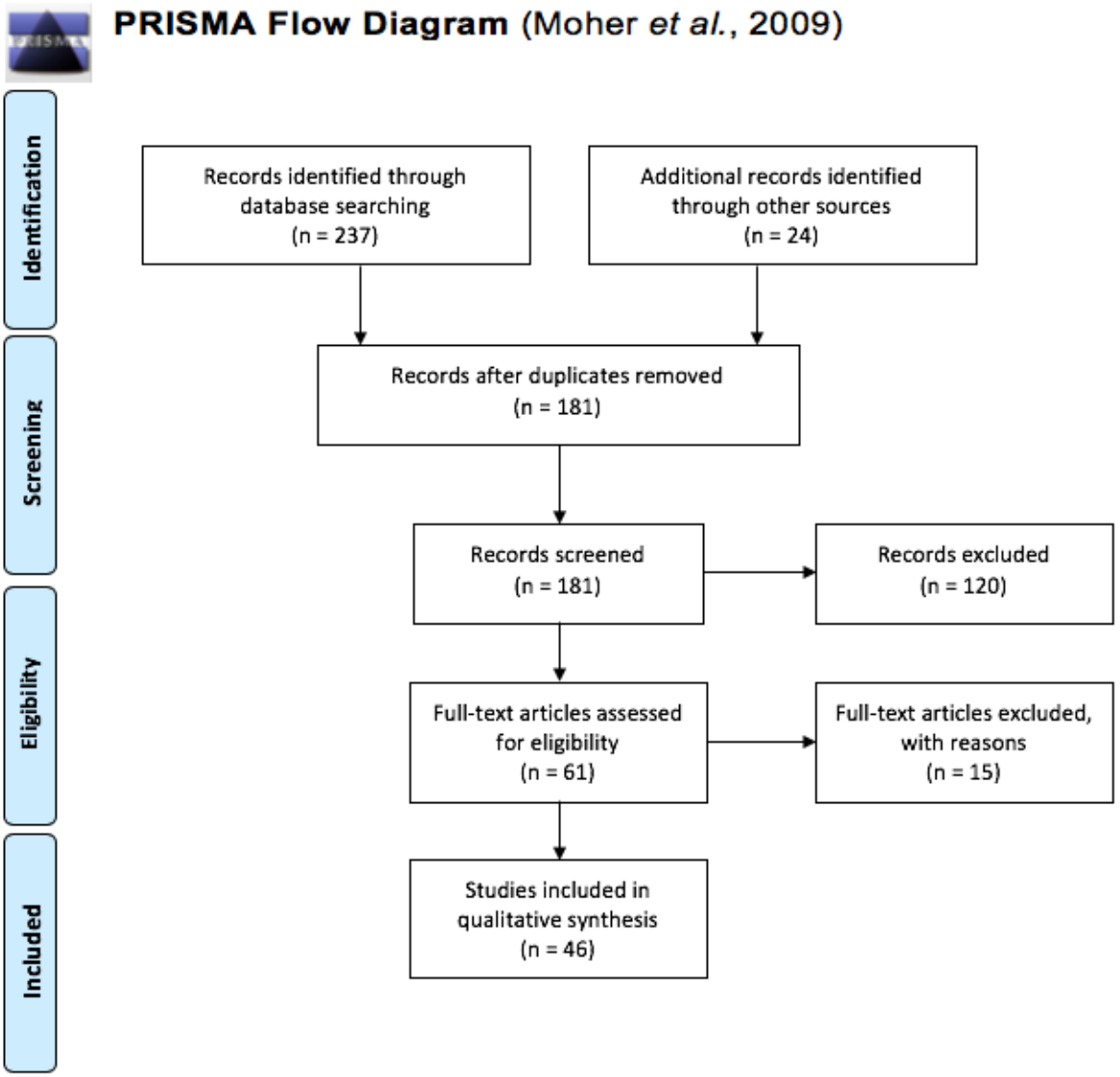
Results: Figure 1 shows 237 abstracts screened resulting in 46 papers to be reviewed using PRISMA (Moher, 2009) and CASP 2018 guidelines.

Discussion: Surgery in space has been considered previously – rat dissection and tail repair were carried out by crew during the Neurolab STS-90, 3D printed surgical instruments have been tested during Mars analogue missions, robotic surgery has been tested during NEEMO missions, and microgravity surgical workstations have been developed ((Campbell, *et al.*, 2002; Panesar & Ashkan, 2018).

Most studies do not consider partial gravity of 0.38 *g*, most evidence is in 0 g or analogues. Anticipated surgical emergencies include trauma, appendicitis, cholecystitis, dental and urological emergencies. Preventative prophylactic surgery is suggested. Astronauts have the potential to be trained in a basic surgical skillset. Surgical techniques such as laparoscopic surgery have been tested in microgravity on animal models. Surgical enclosures of various design exist creating a sterile and adaptable surgical environment. Utilising technologies such as 3D printing instruments and robotics could allow for reduced payload and more complex surgeries. There is a also significant mass, power, volume and training constraint for Mars missions.

In terms of considering astronaut fitness-for-surgery, such a scenario was speculated by comparing known deconditioning to the pre-operative assessment carried out routinely before elective or emergency surgery (ASA, 2019). Astronauts would likely be a higher grade after deconditioning, or an emergency case – surgery would be avoided unless absolutely necessary without alternative medical management. The extent of physiological deconditioning during long-duration missions is not completely known – the best analogue is time spent aboard space stations for extended periods of time. Pertinent to this scenario would be the possible reduction in blood volume, blunted baroreceptor response, blood clot risk, lower exercise tolerance (an indicator for adverse outcomes during anaesthesia), urological dysfunction (stones, infection), and immune system dysregulation. Standard history such as medications, pregnancy status, allergies and inherited disorders such as malignant hyperthermia is also important. Much of this will be documented in advance of the mission.

Conclusion: Ultimately, prevention is better than surgery - healthy crew selection, countermeasures, and crew protection help alleviate a surgical emergency but do not prevent it entirely.



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PC0042

Hypoenergetic diet with reduced protein intake does not impair lean body mass in trained females

Alice G Pearson[1], Lee Alexander[2], Oliver C Witard[3], Tom Coughlin[2], Kevin D Tipton[1], Ian H Walshe[4]

[1]Durham University, Durham, United Kingdom [2]University of Stirling, Stirling, United Kingdom [3]Kings College London, London, United Kingdom [4]Northumbria University, Newcastle, United Kingdom

Increasing protein intake during energy restriction (ER) can attenuate the loss of lean body mass (LBM) in trained males. However, whether this relationship exists in trained females is currently unknown. The present study aimed to examine the impact of higher (35% of energy intake) compared to lower (15% of energy intake) protein intakes on body composition in trained females during 2 wks of severe ER. Eighteen well-trained females completed a 1-week energy balanced diet (HD100), followed by a 2-week hypoenergetic (40% ER) diet (HD60). During HD60, participants consumed either a high protein (HP; 35% protein, 15% fat) or a lower protein (CON; 15% protein, 35% fat) diet. Assessment of body composition by dual energy x-ray absorptiometry (DEXA) and a battery of exercise performance tests were conducted at baseline, pre-HD60, and post-HD60. Participants maintained habitual physical activity throughout the study. There were no significant interactions between time point and dietary condition on exercise performance. Absolute protein intake was reduced from HD100 to HD60 in the CON group (1.6 to 0.9 $g \bullet d^{-1} \bullet kgBM^{-1}$) and maintained in the HP group (~1.7 $g \bullet d^{-1} \bullet kgBM^{-1}$), despite an increase in relative protein intake. No differences in body composition existed between groups at any time point. CON and HP groups decreased body mass equally during HD60 (-1.0 ± 1.1 kg; $p = 0.026$ and -1.1 ± 0.7 kg; $p = 0.002$, respectively). The lack of change in LBM during HD60, irrespective of whether absolute protein intake is maintained or reduced, contrasts with findings in trained males. In trained females, the impact of increased absolute protein intake (>1.7 $g \bullet d^{-1} \bullet kgBM^{-1}$) on LBM change during ER warrants investigation. Future recommendations for protein intake during ER should be expressed relative to body mass, not total

energy intake, in trained females.

Key words: weight loss, body composition, diet composition

PC0043

Insulin Signaling in the Heart Mitochondria and Its Impact on Glucose Oxidation and Cardiac Efficiency

Qutuba Karwi[1], Cory Wagg[1], Tariq Altamimi[1], Golam Mezbah Uddin[1], Gary Lopaschuk[1]

[1]*Cardiovascular Research Centre University of Alberta, Edmonton, Alberta, Canada*

Glucose oxidation is a major contributor to myocardial energy production and its contribution is orchestrated by insulin. While insulin increases myocardial glucose uptake, it can also directly stimulate glucose oxidation, independent of increasing glucose uptake and glycolysis, through activating pyruvate dehydrogenase (PDH), the rate-limiting enzyme of glucose oxidation. However, how insulin directly stimulates mitochondrial PDH is not known. Here, we show that insulin-stimulated mitochondrial translocation of protein kinase B (Akt) plays a prerequisite role in transducing insulin signal to mitochondria to stimulate glucose oxidation. We found that inhibition of mitochondrial Akt completely abolishes insulin-stimulated glucose oxidation, independent of any change in glucose uptake and glycolysis. This was also associated with an increase in myocardial oxygen consumption due to increased reliance on fatty acid oxidation at the expense of glucose that led to a significant decrease in cardiac efficiency. We also revealed a novel role of mitochondrial protein kinase C-delta (PKC-δ) as a negative feedback loop to regulate the insulin stimulation of glucose oxidation. Inhibition of mitochondrial PKC-δ mimics the stimulatory effect of insulin on glucose oxidation via enhancing mitochondrial translocation of Akt. Although it can be translocation following insulin stimulation, inhibition of mitochondrial glycogen synthase kinase-3 beta (GSK-3b) did not affect insulin-stimulated glucose oxidation, suggesting it has a negligible role in mediating the direct stimulation of insulin on glucose oxidation. Thus, we identify insulin-stimulated mitochondrial translocation of Akt as a major transmitter of the insulin signal from to the mitochondrial to directly stimulate glucose oxidation in a glycolysis-independent manner.

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PC0046

Preference of Specialty Selection In MBBS Medical Students in Government and Private Medical Colleges of Pakistan

Qudsia Umaira Khan[1], Farida Hafeez[2], Haleema Anwar[2], Sana Asif[2], Haroon Rasheed[2], Abdul Khaliq Naveed[2]

[1]CMH Lahore Medcial College &IOL, Lahore, Pakistan [2]CMH Lahore Medical College, Lahore, Pakistan

Background: The graduate students of medical colleges comparatively have distinct intentions and certain interests upon whom they decide to enter any specific and specialized practical field of medicine. In fact, career selection of medical students perceived to be very honorable because it provides them an opportunity for serving mankind more than that of any other aspect.

Objectives: To study the trends selection in MBBS Medical students and to compare the preferences in private and government medical colleges .

Methods: The study is cross-sectional observational study that was carried out from July -2019 to Jan- 2020 in first to third year male and female undergraduate (MBBS) medical students at CMH Lahore Medical College of Lahore, Punjab and undergraduate students (MBBS) from Fatima Jinnah Medical University. Data from 588 questionnaires was analyzed using Statistical Package for Social Sciences version 21.0. The normality of the data was analyzed using shipharo wilk test. Modified Schwartz method was used to classify the specialties as having either a controllable or uncontrollable lifestyle. Chi square test was used to evaluate differences between the choice of preference of specialties along with choice of controllable and uncontrollable lifestyle careers among the public and the private medical college students. A p-value≤0.05 was considered statistically significant.

Results: Of the 660 questionnaires administered, 588 (98%) were completed and returned comprising more of females respondents 54% compared to males. The prime most reason for the specialty selection was interest, comprising more than half of the students in all the groups preferred to choose their specialty on their interest basis. Surgery was in the top most of the trend but a statistically significant inclination towards medicine was noted in 3rd year student when compared to 1st year students in both the categories of the colleges p value (0.05). More female students preferring pediatrics, medicine and gynecology p value (p=0.000).

Conclusion: Most students perceive surgery as a very preferred and fascinating specialty when the students enter medical field .As the years advance they are inclined towards medicine. Females prefer pediatrics, medicine and gynecology .

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PC0052

Effect of Rhythmic Breath holding on Baro Reflex Sensitivity- an observational study

Manisha Mavai[1], Bharti Bhandari[2]

[1]Government Medical College, Bharatpur, India [2]Government Institute of Medical Colleges, Greater Noida, India

Background: The baroreflex is one of the mechanisms that regulate acute blood pressure changes via controlling heart rate, contractility, and peripheral resistance. Baroreflex sensitivity (BRS) is an important parameter for the assessment of autonomic control of the cardiovascular system. Impaired baroreflex sensitivity (BRS) is associated with poor cardiovascular prognosis.

Objectives: The study was planned to investigate baroreceptor sensitivity in healthy subjects during episodic inspiratory and expiratory breath holding.

Material and Methods: We investigated baroreflex sensitivity in thirty-five healthy young adults; subjects were instructed to hold their breath repetitively, for 5 minutes, in two patterns, one following maximum inspiration and other following maximum expiration. ECG and continuous blood pressure (BP) were recorded using Biopac MP150 (BIOPAC Systems Inc.,USA,) at rest and during both the maneuver. BRS was calculated by Nevrokard™ BRS analysis/version 6.4.0 (Nevrokard Kiauta, Izola, Slovenia). Cardiovascular parameters like arterial blood pressure and heart rate were also continuously recorded.

Results: Spontaneous sequences were defined as three or more consecutive cycles of either systolic blood pressure elevation (up sequences) or fall (down sequences) coupled with RR interval changes in the same direction. There was rise in blood pressure following breath holding, although significant difference from baseline was observed only during expiratory breath holding ($p<0.05$). The detailed analysis of baroreflex recruitment for up sequences did not show any significant change. There was fall in down sequences BRS-SBP from 12.95±6.29 ms/mmHg at baseline to 11.20±6.19 ms/mmHg

during inspiratory and 9.07±6.85 ms/mmHg during expiratory BH (p<0.01). Similarly, down sequences BRS-MBP decreased from 19.76±10.42 ms/mmHg at baseline to 14.32±6.4 ms/mmHg during inspiratory and 11.60±5.71 ms/mmHg during expiratory BH, respectively (p<0.01). This difference for down BRS-MBP value was statistically significant between baseline and inspiratory BH (p<0.05), baseline and expiratory BH (p<0.001).

Conclusion: The blood pressure changes may be the result of changing intrathoracic pressure induced variations in venous return, pulmonary circulation, right and left ventricular afterload, and finally stroke volume. The activation of sympathetic nervous system has also been observed during breath holding. The sympathetic activation can modify the central and peripheral vagal responses. Sympathetic over activation and modification of vagal responses may lead to significant fall in down sequence BRS-SBP and BRS-MBP during breath-holding.

Keywords: Cardiac Autonomic activity, Baro reflex sensitivity

Table 1. Cardiovascular parameters at rest (baseline) and at the breakpoint of the last episode of inspiratory and expiratory Breath Holding

Parameters	Baseline	Inspiratory BH	Expiratory BH	Overall P	*P*(Within baseline, inspiratory and expiratory breath-holding)
HR (bpm)	82.40 (10.30)	83.20 (10.90)	87.98 (7.90)	df = 1.89, *P = 0.081*	0.89*, 0.06**, 0.13#
SBP (mmHg)	124.40 (10.83)	149.60 (18.10)	137.80 (16.90)	df = 1.85, *P = 0.020*	0.008* 0.255**, 0.060#,
DBP (mmHg)	80.90 (8.90)	95.60(10.20)	92.10 (10.90)	df = 1.81, *P = 0.014*	0.040*, 0.438**, 0.111#
MBP (mmHg)	95.40 (8.30)	113.20 (10.40)	110.70 (10.30)	df = 1.82, *P = 0.018*	0.01*, 0.264**, 0.040#

Note: All values are mean (SD). *P*<0.05 were considered as statistically significant. Inter-group (baseline, inspiratory and expiratory breath-holding) comparisons were carried out by One-way repeated measures ANOVA, with post hoc test. Here * = baseline vs inspiration, ** = baseline vs expiration, # = inspiration vs expiration
Abbreviations : BH: Breath-holding; HR: heart rate; SBP: Systolic blood pressure; DBP: Diastolic blood pressure; MBP: Mean blood pressure.

Table 2. Baroreflex sensitivity (BRS) at rest (baseline) and at the breakpoint of the last episode of inspiratory and expiratory Breath Holding				
Parameter	**Baseline**	**Inspiratory BH**	**Expiratory BH**	**P value**
Up-sequences SBP	14.34±5.57	10.20±4.59	8.72±3.84	<0.01*,NS‡, <0.001†
Up-sequences MBP	11.46±5.97	9.67±2.88	8.66±3.28	NS*‡,<0.05†
Up-sequences DBP	8.29±6.27	9.0±2.97	7.86±3.46	NS*†‡
Up-BRS SBP (ms/mmHg)	12.08±5.88	12.82±6.79	12.11±9.82	NS*‡†
Up-BRS MBP (ms/mmHg)	15.97±8.19	16.13±6.29	12.7±6.63	NS*†‡
Up-BRS DBP (ms/mmHg)	17.49±15.57	14.73±5.28	13.24±7.95	NS*†‡
Down-sequences SBP	14.40±8.36	13.27±5.72	10.83±5.38	NS*‡†
Down-sequences MBP	12.66±7.05	12.87±4.37	12.34±5.87	NS*‡†
Down-sequences DBP	8.46±7.09	11.80±4.8	11.86±7.31	NS*‡†
Down-BRS SBP(ms/mmHg)	12.95±6.29	11.20±6.19	9.07±6.85	NS*‡, <0.01†
Down-BRS MBP(ms/mmHg)	19.76±10.42	14.32±6.4	11.60±5.71	<0.05*NS‡, <0.001†
Down-BRS DBP(ms/mmHg)	18.44±11.38	15.69±12.47	13.09±7.42	NS*‡†
LF alpha (ms/mmHg)	13.51±8.47	14.12±7.41	12.99±9.59	NS*‡†

Note: All values are mean (SD). $P<0.05$ were considered as statistically significant. Inter-group (baseline, inspiratory and expiratory breath-holding) comparisons were carried out by Kruskal-Wallis followed by Dunns multiple comparison test.
*Baseline versus Inspiratory BH, † Baseline versus Expiratory BH, ‡ Inspiratory BH versus Expiratory BH,
Abbreviations : SBP: Systolic blood pressure; DBP: Diastolic blood pressure; MBP: Mean blood pressure; LF alpha, low frequency cross spectral baroreflex gain; ms, millisecond.

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PC0056

Role of Nitric Oxide in Cardiac Performance during Experimental Ischemic Cardiac Arrest and Re-perfusion

Faten Mahmoud[1, 2], Enas AAbdel-Hady[3], Mohamed Abdel-Salam[3], Mohammed Othman[4]

[1]Gulf Medical Univeristy, Ajman, The United Arab Emirates [2]Ain Sham University, Cairo, Egypt [3]Ain Shams university, Cairo, Egypt [4]EL-Markab, Triboli, Libya

Background/Aim:

Re-perfusion strategies are the current standard therapy for acute myocardial infarction, despite the spectrum of re-perfusion-associated pathologies that may contribute to irreversible myocardial injury. The aim of present study is to clarify the alterations in intrinsic cardiac functions in response to cardiac ischemic arrest followed by re-perfusion in isolated hearts perfused with nitric oxide (NO) donor, L-arginine, or NO inhibitor, Nω-Nitro-L-arginine methyl ester hydrochloride (L-NAME), to shed light on the possible role of NO in re-perfusion process.

Methods:

Cardiac activities of hearts isolated from Adult albino rats of both sexes were studied on Langendorff preparation under basal conditions and during 30 min re-perfusion following 30 min of total global ischemia. Rats were randomly allocated into three groups; control and L-arginine or L-NAME infused heart groups. Both L-arginine and L-NAME were infused over 20 min during the baseline activity before induction of total global ischemia. Thereafter, cardiac tissue levels of malondialdhyde, catalase and nitrite were assessed.

Results:

Compared to the control, both L arginine and L-NAME infused hearts showed increased basal chronotropy and myocardial flow rate. Significantly depressed basal inotropic state was only observed in L-arginine group. The three studied groups demonstrated significant deterioration in the inotropic activity and compromised myocardial flow rate during the whole period of reperfusion. L-arginine infused hearts demonstrated depressed inotropy and chronotropy, weak systolic and diastolic functions with compromised myocardial flow at early 5 min of reperfusion, yet with significantly higher myocardial flow rate % recovery by the end of reperfusion (82.7% ±3.01 vs. 56.4% ±2.32 in control and 62.6% ±2.17 in L-NAME). The chronotropic activity was maintained in both the control and L-NAME infused hearts. Cardiac tissue NO showed the highest level in L-arginine group and the lowest level in L-NAME one. Both catalase and MDA were insignificantly changed among the three studied groups.

Conclusion:

Reducing NO availability by L-NAME revealed mild impact on the ischemia re-perfusion induced contractile dysfunction. Excess NO worsens cardiac performance at early re-perfusion. However, it may have potentially protective effect by acquiring higher the myocardial flow rate during the reperfusion.

Keywords: Cardiac arrest, ischemia/re-perfusion, L-arginine, L-NAME, nitric oxide.

PC0059

Severity of Central Sleep Apnea Does Not Improve Sleeping Oxygen Saturation During Ascent to High Altitude

Jordan Bird[1], Anne Kalker[2], Jason Chan[1], Alexander Rimke[1], Garrick Chan[1], Gary Saran[1], Richard Wilson[3], Tom Brutsaert[4], Nick Jendzjowsky[3], Mingma Sherpa[5], Trevor Day[1]

[1]Department of Biology, Faculty of Science and Technology, Mount Royal University, Calgary, Canada [2]Radboud University, Nijmegen, The Netherlands [3]Hotchkiss Brain Institute, Cumming School of Medicine, University of Calgary, Calgary, Canada [4]School of Education, Department of Exercise Science, Syracuse University, Syracuse, NY, USA, Syracuse, The United States of America [5]Kunde Hospital, Khunde, Solukhumbu, Nepal

Central sleep apnea (CSA) is characterized by intermittent periods of apnea (no breathing) and hyperventilation (over breathing) with associated fluctuations in blood oxygen saturation. CSA is universal at high altitude (>3000m), increasing in severity with ascent and/or time spent at high altitude. Although there is a large degree of variability in CSA severity, factors that increase susceptibility to CSA at altitude include: (a) hypoxia, (b) hypoxic ventilatory response-mediated hypocapnia and (c) increases in chemoreflex responsiveness via ventilatory acclimatization. Whether CSA is adaptive or maladaptive at altitude is unknown. Notwithstanding the brief periods of desaturation associated with apnea, the subsequent relative intermittent hyperventilation may increase oxygen reserves during sleep, protecting overall mean saturation. We hypothesized that CSA protects mean sleeping oxygen saturation during acclimatization to high altitude. In two groups of Diamox-free native lowlanders, we characterized the effects of increasing CSA severity on night-time sleeping oxygen saturation during two separate high altitude ascent profiles: (I) incremental ascent to 5160m over 10 days/nights in the Nepal Himalaya (n=21) and (II) rapid ascent to and residing at 3800m over 10 days/nights in the Sierra Nevada mountains, CA, USA (n=21). Using portable polysomnographs and scoring software (ResMed ApneaLink; AASM criteria), we assessed apnea-hypopnea index (AHI), oxygen desaturation index (ODI), and baseline, mean and nadir oxygen saturation (SpO2) during sleep at each altitude. During sleep across both ascent profiles, AHI and ODI increased in severity, and baseline, mean and nadir SpO2 decreased significantly, suggesting both altitude- and sleep apnea-associated hypoxia. During incremental ascent to 5160m over 10 days/nights (Part I), AHI and ODI increased from 3.9±4.1 and 9.8±7.8 (1045m) to 37.5±32.8 and 54.4±24.8 events/hour, respectively ($P<0.001$). In addition, baseline, mean and nadir SpO2 decreased from 96.0±2.0, 94.3±1.6 and 87.1±3.7% (1045m) to 78.9±3.6, 73.5±4.2 and 63.7±6.6%, respectively ($P<0.0001$). After 10 days/nights following rapid ascent to 3800m (Part II), AHI and ODI increased from 3.4±3.5 and 6.8±5.3 (1045m) to 23.2±21.2 and 38.0±24.4 events/hour, respectively ($P<0.001$). In addition, baseline, mean and nadir SpO2 decreased from 95.3±1.9, 93.7±2.1 and 86.0±5.1% (1045m) to 85.6±1.8, 84.0±2.4 and 74.1±6.2%, respectively ($P<0.0001$). There were no significant correlations between AHI nor ODI and mean nor nadir SpO2 during sleep at 5160m (night 9/10; Part I; $r>-0.35$, $P>0.2$) and 3800m (night 9/10; Part II; $r>-0.45$, $P>0.05$). We conclude that the severity of CSA following acclimatization to high altitude does not play a role in improving oxygen saturation. However, the relative hyperventilation between apneas likely protects against the apnea-mediated oxygen desaturations during sleep at altitude.

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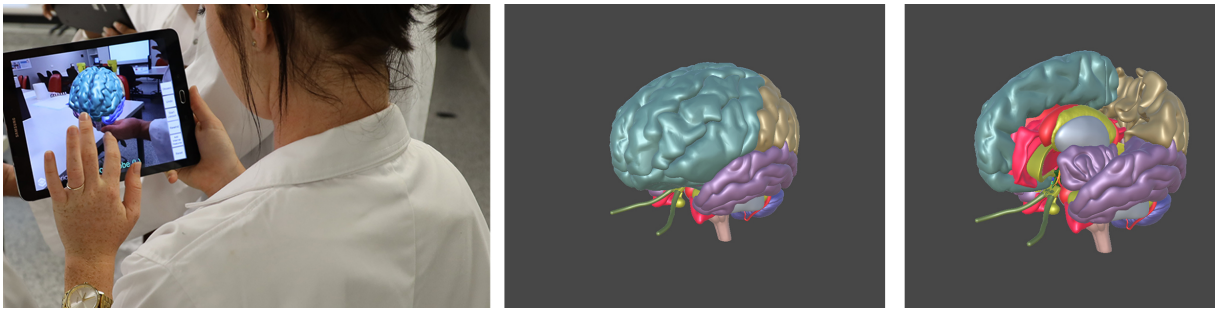
PC0060

Using augmented reality for disease education in health sciences and medical physiology

Christian Moro[1], Jessica Smith[1], Emma Finch[2]

[1]Bond University, Gold Coast, Australia [2]University of Queensland, Brisbane, Australia

59% of adults have been reported to have inadequate health literacy, suggesting a gap in the public understanding of healthcare. Stroke poses a concern in health literacy as it constitutes 6.8% of the total burden of disease, yet remains preventable in many cases. As stroke affects many Australians, it is beneficial to investigate effective ways to provide accessible and understandable information regarding its anatomy and physiology. Modern technologies can assist, such as augmented reality (AR) which allows people to interact with virtual renders of anatomical models, showing great promise in improving the user's understanding of health (1, 2). In addition, the introduction of novel and technology-enhanced learning tools can assist students studying health to better understand concepts covered throughout their course (3, 4). The aim of this study was to assess the effectiveness of AR in contrast with a pamphlet as an educational tool by assessing learning acquired from each, as well as participant perceptions of the two different delivery modes. 59 participants were randomised into two groups, one used AR (n=32, Figure 1) and the latter used a printed pamphlet (n=27) to learn identical content relating to stroke. Participants answered a pre-test multiple choice questionnaire to evaluate knowledge prior to the intervention. A Likert-scale questionnaire was used to determine participant perceptions post-learning intervention, followed by another multiple-choice post-test. A Mann-Whitney U test analysed the significance between pre- and post-test scores. A D'Agostino and Pearson Normality Test found that the Likert-scale data was normally distributed, allowing for a Student's two-tailed unpaired *t*-Test to assess variations in the AR and pamphlet interventions. Pre- and post-test scores suggested that participants learned in both interventions ($p<0.001$), despite no significance between the interventions themselves. Participants reported better learning experiences when using AR ($p<0.001$), perceiving that AR allowed them to better understand anatomy ($p<0.005$) and that AR was a better learning tool ($p<0.001$). Participants also felt AR would help their non-student friends or family to better understand stroke compared the pamphlet intervention ($p<0.001$). Participants preferred AR over pamphlets as a learning tool, with both modes being equally effective for participant learning and stroke education.



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PC0062

Telomere dynamics during hibernation is positively affected by warmer winter temperature and food availability

Julia Nowack[1, 2], Iris Tarmann[2], Marie-Therese Ragger[2], Thomas Ruf[2], Sylvian Giroud[2]

[1]Liverpool John Moores University, Liverpool, United Kingdom [2]University of Veterinary Medicine Vienna, Vienna, Austria

Global climate change is assumed to be a significant threat to biodiversity. The expected increase in average temperature will not only lead to an increase in extreme hot temperatures in summer, but also decrease the number of cold days in winter. A large fraction of temperate zone endotherms is undergoing winter hibernation and therefore are highly sensitive to changes in environmental temperature. Higher hibernation temperatures will increase the number of interbout arousals during hibernation and frequent arousals are expected to increased telomere shortening. We experimentally tested this hypothesis by comparing telomere dynamics and hibernation pattern of garden dormice (*Eliomys quercinus*), a fat-storing hibernator, hibernating at different temperatures with or without access to food. Garden dormice were allowed to hibernate during the winter month in climate chambers set to either 3°C or 14°C and we used recordings of nest temperature as a proxy for body temperature to estimate torpor use, frequency of rewarming from torpor and length of interbout euthermia. Further, we estimated telomere length by a quantitative PCR technique using DNA extracted from the inner cheeks by gently twisting a small brushfor ca 30 s inside each cheek. Our results show that relative telomere length was positively affected by warmer winter temperature, even when no food was available. In contrast, hibernation at cold temperature led to a reduction in telomere length when animals had no access to food, while individuals were able to increase telomere length when food was available. Our data show that hibernation at low body temperatures comes with costs on a cellular level and that hibernators can actively counterbalance

telomere shortening.

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PC0067

Rise of sport and exercise Physiology in Pakistan: a cross-sectional study to assess and compare cardiorespiratoryfitness parameters among bodybuilders and non-bodybuilders

Saqib Javaid[1]

[1]*Services Institute of Medical Sciences (SIMS), Lahore, Pakistan*

INTRODUCTION: Physical fitness and athletic performance can be assessed through parameters like volume oxygen maximum (VO2max), blood lactate levels, respiratory exchange ratio (RER), maximum heart rate (HR) and body fat %. Sedentary or physically active lifestyles can modify these parameters. The study determines and compares these fitness indicators in active bodybuilders and inactive non-bodybuilders.

METHODS: A cross-sectional comparative pilot study was carried at the sport and exercise Physiology Lab at Post-Graduate Medical Institute Lahore, Pakistan. After Ethical board approval, twelve (12) healthy male subjects between age range of 20-30 years were recruited through stratified random sampling. Subjects with history of smoking or drug abuse were excluded. Participants were divided into two (2) equal groups; Group I (n=6): regularly active bodybuilders and Group II (n=6): inactive non-bodybuilders, as defined by ACSM's guidelines for exercise. Exercise pre-participation health screening was done via the Physical Activity Readiness Questionnaire (PAR-Q+). Anthropometric measurements were recorded including age, weight, height and body fat percentage. Bruce protocol was used in which the participant underwent a graded exercise test till exhaustion on a treadmill. HR was recorded continuously using Bluetooth Polar belt. Cortex Metalyzer 3B-R3 was used for breath to breath gas analysis of various cardiorespiratory fitness parameters like VO2, VCO2, RER. Post exercise blood lactate levels were recorded from fingertip using Nova Biomedical Lactate Plus meter. Results were printed as 12-panel plots and quantitative values. SPSSv20 used for analysis.

RESULTS: All 12 participants were in healthy weight BMI range. Values are expressed as mean±SD in active bodybuilders vs inactive non-bodybuilders: age 23.6±1.3 vs 24.2±2.3 years; Body fat % 16.2±1.4% vs 20.0±1.6%; VO2peak 40.2 ±2.8 vs 26.8±3.3 ml/kg/min ($p<0.05$); HRmax 185±3 vs 198±7 beats/min($p<0.05$); Lactatemax 10.6±0.6 vs 12.9±0.9 mmol/L ($p<0.05$); RER: 1.02±0.04 vs 1.14±0.05 ($p<0.05$).

CONCLUSION: A higher VO2peak in active bodybuilders means that physical activity/training improves oxygen uptake. Lower blood lactate and RER values mean that they have more active lipid oxidation metabolism and oxidize a greater proportion of lipids respectively than inactive participants. Comparable results have been found in studies of Milanovic Z et al-1 & Ramos-J et al.

Active bodybuilders showed significant higher VO2peak, lower RER values and lower blood lactate concentrations than inactive non-bodybuilders. The data demonstrate that these parameters can be used to quantitatively assess physical fitness of sport athletes in Pakistan on a larger scale.

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PC0070

Showcasing diversifications of Physiology as a course of study arouse students' interest in the field of science.

Aiyeola Afusat[1]

[1]*Department of Physiology, College of medicine, University of Ibadan., Ibadan, Nigeria*

In the late 1950s, Paul Hurd coined the term “scientific literacy”, which he defined as the ability of the society to understand science and its applications to their daily activities, which can only be achieved through effective science communication. The present study is a science outreach focused on school children and first year undergraduate physiology students, with the aim of imbibing in them the fundamentals of physiology as a course of study and clarifying its diversifications. Professors of different specializations in physiology were invited to share their experiences in the field and expatiate on the various opportunities available for trained physiologists. Data were collected with the aid of questionnaires, which were designed so that we could evaluate the physiological knowledge of the participants before and after the orientation exercise by the professors. The results obtained from the analyzed data showed that the aim of the research was fulfilled. Specifically, the interest of the school children was observed to be escalated after they had learnt about the diversifications of physiology as a field of study. Moreover, the undergraduate students demonstrated an enhanced understanding of the basics of physiology. Conclusively, effective communication of science should be encouraged among prospective young scientists, so as to promote the awareness of scientific research in our society.

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PC0071

THE SPERM ELECTROGENIC PUMP AND BIOCHEMICAL ANALYSIS OF COENZYME Q-10 AND TAURINE IN PREVENTING CHLORPROMAZINE-INDUCED PEROXINITRITE FORMATION IN RATS MODEL

Mega Obukohwo OYOVWI[1], Eze K Nwangwa[2], John C Igweh[2], EMOJEVWE VICTOR[3]

[1]Achiever University, Owo, Ondo State, Nigeria [2]Delta State University, Abraka, Delta State, Nigeria
[3]University of Medical Sciences , Ondo State, Nigeria

Background: Electrogenic transmembrane integrity and its constituents are the basic features of the sperm membrane necessary for spermatogenesis, testicular metabolism and sperm fertilization potential; therefore, it is important to note that membrane surface responsible for ion exchanged and permeability modified upon oxidation and nitrosation. **Objectives:** The present study was designed to investigate the preventive effects of CoQ-10 and taurine supplement on transmembrane proton pump (ATPase) activitiesin CPZ-induced peroxinitrite formation in male wistar rats. **Method:** Thirty-Six male Wistar rats (150-200g) were divided into six groups (n=6) and treated daily for 56 days as follows: group 1 received distilled water (0.5 ml/kg) and served as normal control, group 2 received PG (0.5 ml/kg of 20%) and served as vehicle control, groups 3 had received distilled water (0.5 ml/kg, p.o.), group 4 was pre-treated with CoQ10 (10 mg/kg, p.o./day), group 5 received taurine (150 mg/kg, p.o./day), while group 6 was pre-treated the combination of CoQ10 (10 mg/kg, p.o./day) + taurine (150 mg/kg, p.o./day) However, from days 29 to 56, rats in groups 3-6 additionally received chlorpromazine (30mg/kg, p.o./day) once daily. All treatments were made 30 min between each treatment. The rats were euthanized at the end of 56 days; Samples were collected for analysis. Biochemical parameters were measured by spectrophotometry. Data were analysed using ANOVA and differences in mean values were considered significant at $p<0.05$. **Results:** CPZ treated rats exhibited a significant decreased Na^+/K^+-ATPase, Ca^{2+}-ATPase, Mg^{2+}-ATPase, H^+-ATPase activities and sulphydryl content with corresponding increased in peroxynitrite formation as compared to control group.The reduction in Na^+/K^+-ATPase, Ca^{2+}-ATPase, Mg^{2+}-ATPase, H^+-ATPase activities by peroxynitrite formation may be through possible depletion of sulphydryl content. Decrease in sperm motility, immature sperm and poor sperm function in CPZ can be attributed to these sulphydryl groups of the sperm membrane which plays a very important role in sperm motility and metabolism. Moreover, Pre-treatment with CoQ-10 (10 mg/kg, p.o) and taurine (150 mg/kg, p.o) significantly prevents the alteration observed in CPZ-treated rats. **Conclusion**: In conclusion, CPZ decreases sperm plasma membrane bound proton pump (ATPase) activities and inhibits sperm motiliy. It invokes nitrosative stress by possible mechanisms of peroxynitrite formation and depletion of free thiol content. The result from this study shows that CoQ-10 and taurine supplement has preventive effects on CPZ-induced peroxynitrite formation via its antioxidant and cyto-protectant activities. Hence, CoQ-10 and taurine could be use as therapeutic adjuvants for maintaining ion homeostasis necessary for sperm motility and maturation. Our results suggest potentially beneficial effects of CoQ-10 and taurine, which may be useful in the modified antioxidant approach in chlorpromazine-therapy.

Keywords: CoQ-10, taurine, CPZ, proton pump (ATPase) and sperm motility

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PC0072

Redefining physiological responses of moose (*Alces alces*) to warm environmental conditions

Daniel Thompson[1, 2], John Crouse[1], Perry Barboza[2], Scott Jaques[3]

[1]Alaska Department of Fish and Game - Kenai Moose Research Center, Soldotna, Alaska, The United States of America [2]Department of Wildlife and Fisheries Sciences, Texas A&M University, College Station, The United States of America [3]Applied Biosciences LLC, College Station, The United States of America

We tested the concept that moose (*Alces alces*) begin to show signs of thermal stress at ambient air temperatures as low as 14°C. We determined the response of Alaskan female moose to environmental conditions from May through September by measuring core body temperature, heart rate, respiration rate, rate of heat loss from exhaled air, skin temperature, and fecal and salivary glucocorticoids. Seasonal and daily patterns in moose body temperature did not passively follow the same patterns as environmental variables. We used large changes in body temperature (≥1.25°C in 24hr) to indicate days of physiological tolerance to thermal stressors. Thermal tolerance correlated with high ambient air temperatures from the prior day and with seasonal peaks in solar radiation (June), ambient air temperature and vapor pressure (July). At midday (12:00hr), moose exhibited daily minima of body temperature, heart rate and skin temperature (difference between the ear artery and pinna) that coincided with daily maxima in respiration rate and the rate of heat lost through respiration. Salivary cortisol measured in moose during the morning was positively related to the change in air temperature during the hour prior to sample collection, while fecal glucocorticoid levels increased with increasing solar radiation during the prior day. Our results suggest that free-ranging moose do not have a static threshold of ambient air temperature at which they become heat stressed during the warm season. In early summer, body temperature of moose is influenced by the interaction of ambient temperature during the prior day with the seasonal peak of solar radiation. In late summer, moose body temperature is influenced by the interaction between ambient temperature and vapor pressure. Thermal tolerance of moose depends on the intensity and duration of daily weather parameters and the ability of the animal to use physiological and behavioral responses to dissipate heat loads.

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PC0075

Comparison of acute pressor effects of plain water, oral rehydration solution, and fruit juice in healthy young adults

Mrigendra Amatya[1]

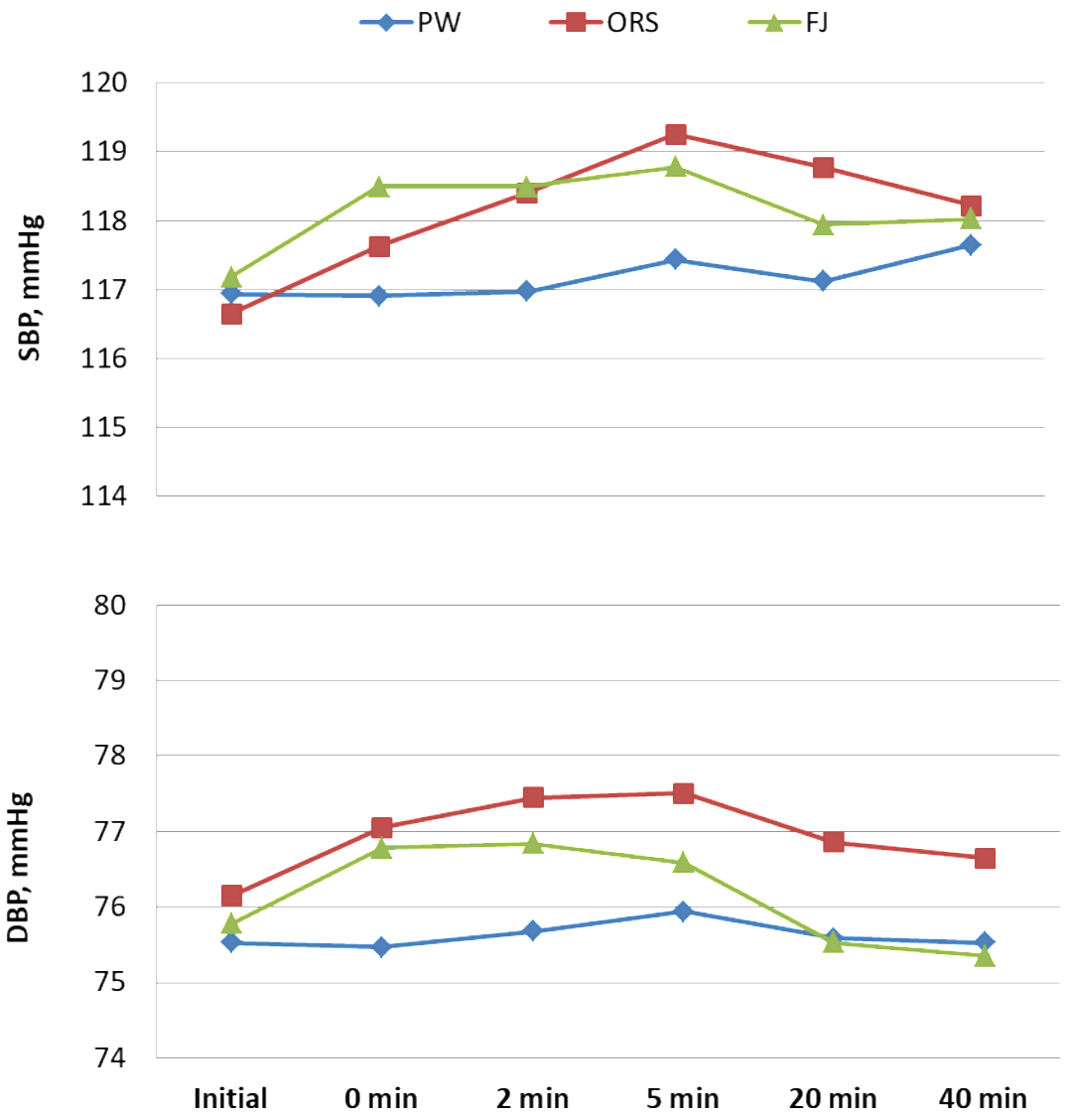
[1]*Department of Physiology, Nepal Medical College, Gokarneswor-8, Kathmandu, Nepal*

Background: Ingestion of about half a liter of plain water raises blood pressure in a few minutes in patients with autonomic failure [1], probably due to elicitation of a sympathetic reflex [2]. In healthy individuals, this pressor response of plain water ingestion is disputed [3,4]. Other types of fluid, such as isotonic banana juice, could have different effects [5].

Materials and Methods: In a cross-over experimental study, young medical students ingested 500 mL of plain water (PW), 500 mL of oral rehydration solution (ORS) or 400 mL of fruit juice (FJ) on separate occasions, at least two days apart. Their heart rate (HR, bpm) and blood pressure (BP, mmHg: systolic, SBP and diastolic, DBP) were recorded immediately after (0 min), and at 2, 5, 20 and 40 min after fluid ingestion and compared with initial (pre-ingestion) values (ANOVA repeated measures).

Results: Sixty nine apparently healthy students (40 males, 29 females; aged 18-24 years) participated. Compared to initial values, SBP and DBP were significantly ($p=0.000$) with ORS and FJ ingestion at 0, 2 and 5 min; then lowered at 20 and 40 min (fig. 1). With PW, the BP changes were not significant at time of measurement ($p>0.1$). In all three experimental set ups, HR increased significantly ($p=0.000$) at 0, 2 and 5 min and lowered to near initial levels then after (fig. 2)

Conclusion: Ingestion of ORS (500 mL) and FJ (400 mL), but not PW (500 mL), is associated with acute rises in BP in healthy young adults. This finding could have implications on the choice of fluid for prophylaxis in hypotensive conditions such as blood donation, postural hypotension, and autonomic dysfunction.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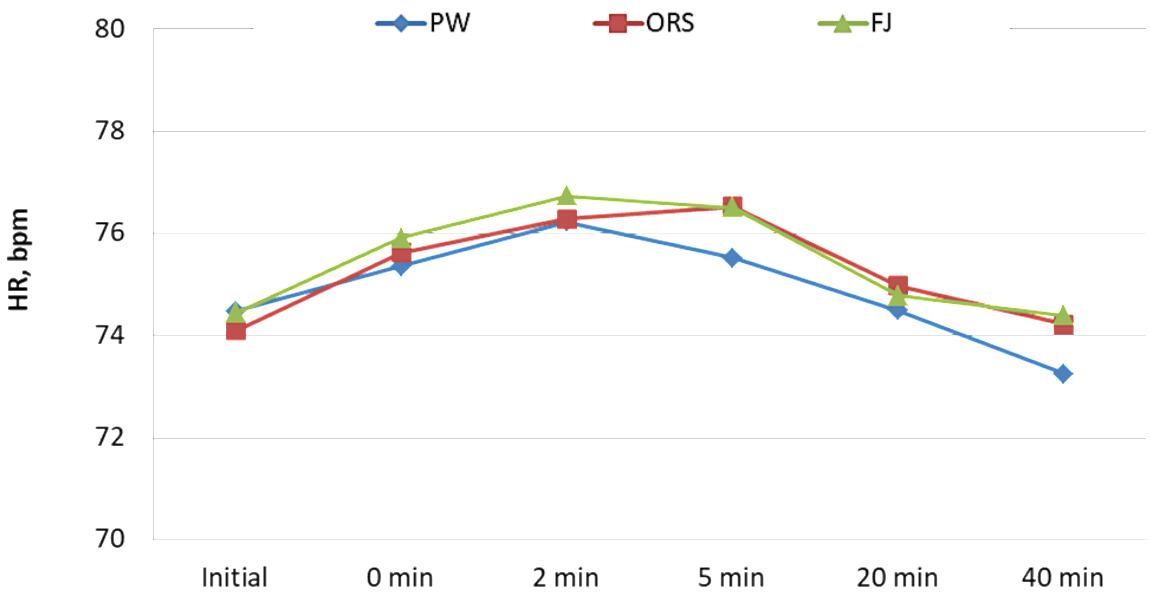

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PC0076

Influences of the mast cell degranulates histamine and prostaglandins on urinary bladder contractile activity

Zane Stromberga[1], Jessica Smith[1], Jonathan Tan[1], Christian Moro[1]

[1]Bond University, Gold Coast, Australia

Urinary bladder inflammation has been observed in various disorders such as overactive bladder (OAB) and interstitial cystitis/bladder pain syndrome (IC/BPS). It is apparent that acetylcholine release is involved, yet other mediators and regulator chemicals may also contribute to modulating bladder function and sensation (1-3). An increased presence of inflammatory cells within the bladder and urine of patients suffering from OAB and IC/BPS may stimulate some dysfunction via the release of inflammatory mediators, known to modulate contractile activity in both the urothelium with lamina propria and the detrusor muscle (4, 5). Therefore, the involvement of immune cells and the various inflammatory mediators released at sites of inflammation is an important avenue to explore. This research aims to determine the effect of histamine on tonic contractions and phasic activity of the urinary bladder. Functional tissue baths containing adjacent strips of porcine urothelium with lamina propria (U&LP) or detrusor smooth muscle were mounted in gassed Krebs-bicarbonate solution at 37°C. Responses to histamine or various prostaglandin agonists in the absence and presence of selective receptor antagonists were examined. Data analysis of the responses was performed using a paired Student's t-tests with $p<0.05$ considered significant. In the absence of any stimulation, strips of U&LP naturally develops spontaneous phasic contractions of 3.34 ± 0.06 cycles per minute (n=223) with an amplitude of 0.53 ± 0.02 grams (n=223). Both the histamine and prostaglandin receptor systems were capable of stimulating tonic and phasic contractions of urinary bladder urothelium with lamina propria and detrusor. The H1 histamine receptor subtype was determined to mediate U&LP increases in tonic contractions and also increase the frequencies of phasic contractions in response to histamine. In the presence of H1 receptor antagonists, increases in tonic contractions were significantly inhibited in both U&LP and the detrusor smooth muscle ($p<0.001$). The H2 receptor enhanced the increases observed to tonic contractions in response to histamine in U&LP but did not affect contractions in isolated detrusor preparations. Neither the H3 nor H4 receptors demonstrated any response or involvement in the mediation of bladder contractions or phasic activity. All five primary prostaglandins were able to mediate contractions in both U&LP and detrusor with a potency of PGE2>PGF2α>TXA2>PGD2>PGI2. Further investigation in the PGE2 receptor subtypes revealed that increases in contractions were not mediated via any of the EP receptors. This response appears to be mediated via the FP receptor in both U&LP and detrusor, suggesting some conversion of PGE2 to PGF2α upon contact with tissue. The preliminary findings of this research suggest that degranulation of mast cells infiltrating the bladder wall might induce increases to both tonic and phasic contractions of the urinary bladder via the actions on histamine and prostaglandin receptors. Future directions for this project aim to investigate the presence, prevalence and distribution of mast cells within the urinary bladder wall in various models of urinary disease and dysfunction. The influence of other infiltrating immune cells, such as lymphocytes, will also be explored generally in the lower urinary tract.

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PC0077

Inflammatory mediators as contributors to age-related urinary bladder dysfunction

Zane Stromberga[1], Russ Chess-Williams[1], Christian Moro[1]

[1]Bond University, Gold Coast, Australia

There is an increased prevalence of urinary bladder dysfunction with ageing. Although the contributing factors underlying this are unknown, it may be related to the actions of inflammatory mediators (1, 2). Treatment with histamine induces significant increases in both the tonic contractions and frequency of spontaneous phasic contractions in both urothelium with lamina propria and the underlying detrusor muscle through the activation of the H1 receptor (3). Additionally, this effect may work in conjunction with other inflammatory-cell released chemicals such as 5-HT (4) or prostaglandins (5). This study aimed to compare urothelium with lamina propria (U&LP) and detrusor responses to histamine and prostaglandin E2 in juvenile and adult tissues. Functional tissue baths containing adjacent strips of porcine U&LP or detrusor smooth muscle were mounted in gassed Krebs-bicarbonate solution at 37°C. Responses to histamine and prostaglandin E2 in the absence and presence of selective receptor antagonists were examined in juvenile and adult tissues. Data analysis of the responses was performed using a paired Student's t-tests with $p<0.05$ considered significant. Addition of histamine (100µM) increased tonic contractions in juvenile U&LP by 47.84±6.52 mN/g ($p<0.001$, n=51) and in adult U&LP by 50.76±4.10 mN/g ($p<0.001$, n=55). Additionally, the frequency of phasic spontaneous contractions increased by 1.29±0.26 cpm ($p<0.001$, n=51) in juvenile tissues and by 1.18±0.16 cpm ($p<0.001$, n=55) in adult. The amplitude of phasic contraction decreased by 5.54±1.60 mN/g ($p<0.001$, n=51) in juvenile tissues and by 10.05±2.06 mN/g ($p<0.001$, n=55) in adult. In detrusor preparations, juveniles showed significantly greater ($p < 0.05$) increases in tonic contractions of 19.10±4.92 mN/g (n=51) when compared to adult tissues exhibiting increases of 8.21±0.89 mN/g (n=56) to histamine (100 µM). In the presence of H1 antagonists, increases in tonic contractions and phasic activity to histamine (100µM) were

significantly inhibited in both juvenile ($p<0.05$ for all) and adult ($p<0.05$) tissues. Treatment with H2 antagonist in U&LP of juvenile tissues caused significant enhancement of tonic contractions when compared to control tissues ($p<0.05$). These increases were not observed in adult U&LP and detrusor of both juvenile and adult tissues. Treatment with H3 and H4 antagonist did not influence contractile responses to histamine (100μM) in the U&LP and detrusor of both age groups. In conclusion, histamine and PGE2 increases the contractile activity of both U&LP and detrusor in juvenile and adult animal models. There was no difference in the contractile responses observed to histamine in the U&LP of juvenile and adult tissues. However, maximal contractions in detrusor were greater in juvenile tissues than in adult samples. The activation of the H2 receptor inhibited tonic contractions in the U&LP of juvenile animals but did not affect adult U&LP or the contractility of detrusor in both age groups. There were no differences in contractile responses in both U&LP and detrusor in response to PGE2 between juvenile and adult tissues. These results suggest that any influence of the inflammatory mediator histamine on the increased prevalence of bladder dysfunction observed in ageing may be related to its influence on the detrusor smooth muscle.

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PC0079

Electroencephalographic characterization in epilepsy patients: a comparative cross-sectional study

Jay Prakash Jha[1], Rita Khadka[1], Priza Subedi[1], Baikuntha Raj Adhikari[1], Bhupendra Shah[1], Bishnu Hari Paudel[1]

[1]*BP Koirala Institute of Health Sciences, Dharan, Nepal*

Introduction: Epilepsy is a chronic neurological disorder that challenges neurologists in diagnosis and treatment. Electroencephalogram (EEG) has adjunctive value in epilepsy diagnosis. Its presentation is usually asymptomatic, where EEG might show characteristic epileptiform discharges. Routine inter-ictal EEG suffers from poor sensitivity, spatial resolution and inter-observer reliability. The seemingly-normal background EEG can be quantitatively analyzed to find marker of the disease. **Objective:** To compare the frequency parameters in background EEG of adult epileptic patients with healthy controls. **Methods:** Twenty-seven epilepsy cases and forty-two apparently healthy controls were selected using convenient sampling method. Comorbidities like encephalopathy were excluded. EEG was recorded by 19-channel scalp EEG machine using 10-20 system. Eleven channels were band-filtered at 1-30 Hz window, and five-second epochs of background waves selected at resting eye-closed and hyperventilated states. Spectral power was computed using Fast Fourier Transform (FFT). Absolute power (AP), relative power (RP) and Shannon spectral entropy (SSE) were compared between cases and controls. **Results**: Anthropometric, cardiorespiratory variables and posterior dominant rhythm frequency were comparable between the groups. On quantitative analysis of background waves in resting state, cases (n=27) had significantly higher AP than controls (n=42) globally, notably in delta [12.06 (7.03-18.08) vs 6.65 (4.17-10.16), p=0.002 at F7; 6.77 (5.42-13.66) vs 5.96 (4.29-7.49), p=0.04 at P4; 10.43 (6.60-16.50) vs 6.16 (4.07-8.92), p=0.002 at Cz]; and theta [4.27 (2.77-13.09) vs 1.77 (1.37-2.50), p<0.001 at F7; 5.65 (2.92-14.99) vs 2.25 (1.36-4.11), p<0.001 at P4; 7.32 (3.11-16.33) vs 3.14 (1.88-4.16), p=0.001 at Cz] (Wilcoxon Rank-sum test). In RP, cases had higher power in theta band globally [e.g., at F7, 0.15 (0.10-0.21) vs 0.09 (0.06-0.13), p<0.001]; whereas it was less at F7 in beta [0.10 (0.05-0.15) vs 0.14 (0.09-0.18), p=0.01] and at Cz in alpha band [0.36 (0.20-0.53) vs 0.47 (0.26-0.66), p=0.04] (Wilcoxon Rank-sum test). Comparison during hyperventillation showed similar differences between the groups [e.g., delta AP of 12.9 (8.50-22.12) vs 7.55 (5.06-11.84), p=0.003 at F7]; except for delta AP at Cz, F3 and P3 (Wilcoxon Rank-sum test). The effect of hyperventillation in resting EEG was a significant increase in spectral power of controls at lower frequency bands compared to resting state, notable in Cz [AP of 7.94 (5.70-10.40) vs 6.16 (4.07-8.92), p=0.004 and RP of 0.30 (0.21-0.42) vs 0.24 (0.15-0.33), p=0.001, in delta]; which was not seen in cases [AP of 9.80 (6.10-19.9) vs 10.4 (6.60-16.5), p=0.46 and RP of 0.31 (0.21-0.37) vs 0.26 (0.17-0.36), p=0.96, in delta] (Wilcoxon Signed-Rank test). In most comparisons, SSE and RP showed similar trend of changes. **Conclusion**: The background EEG of epileptic patients showed higher spectral power at low frequency in most of the scalp sites, along with decrease in relative power at higher frequency; indicating slowing of the brainwaves. The expected effects of hyperventillation in EEG was less in patients than controls. These findings can be utilized for detecting epilepsy from background EEG.

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PC0080

A Potential Universal Mechanism for Axon to Glia Metabolic Signalling

Laura Rich[1], Angus Brown[1]

[1]*University of Nottingham, Nottingham, United Kingdom*

Astrocytes of the central nervous system (CNS) and, more recently, myelinating Schwann cells of the peripheral nervous system (PNS) have been assigned a metabolic role as the result of their unique possession of glycogen and supply of lactate as an energy source to neurones (Brown *et al.*, 2003, 2012). Glutamate was one of the first suggested metabolic signals between neurones and glia when the astrocyte-neuron lactate shuttle hypothesis (ANLSH) was proposed (Pellerin & Magistretti, 1994). However, glutamate is not a universal signal within the nervous system, unlike K^+ which is released from axons of the CNS and PNS. Released during the repolarisation phase of the action potential, the amount of K^+ efflux is a direct indication of neuronal firing frequency and therefore energy demand (Baylor & Nicholls, 1969). Moreover, it is widely considered that glial cell membrane potential, particularly astrocytes, is mediated solely by K^+ (Kuffler *et al.*, 1966). Within the CNS increased extracellular K^+, as the result of increased neuronal activity, has been found to be tightly coupled to increased astrocytic glycolysis (Ruminot *et al.*, 2019). A suggested mechanism involves K^+ induced depolarisation of the astrocyte membrane potential triggering bicarbonate uptake via the sodium bicarbonate cotransporter. Bicarbonate-sensitive soluble adenylyl cyclase becomes activated resulting in an increase in cAMP which stimulates glycogen metabolism and thus lactate efflux (Choi *et al.*, 2012). The aim of this study was to expand upon the role of K^+ as a metabolic signal between axons and glia in both the CNS and PNS.

All procedures were carried out in accordance with the Animals (Scientific Procedures) Act 1986 under appropriate authority of establishment, project and personal licenses. Adult male CD-1 mice were killed by cervical dislocation and decapitated. Optic and sciatic nerves, to represent the CNS and PNS respectively, were dissected and placed in a superfusion chamber, superfused with aerated control aCSF (10mM glucose and 3mM K^+) at 37°C. Lactate biosensors (Sarissa Biomedical) were used to record real-time lactate release from the nerve into the bath solution. Suction electrodes were used to stimulate the nerve during high frequency stimulus (HFS) protocols.

Superfusion of aCSF containing K^+ above and below 3mM increased and decreased, respectively, the steady state concentration of lactate recorded; a relationship that was found to be logarithmic for both nerves (slope= 75.6 and 5.6 µM lactate/mM K^+, optic (n=3) and sciatic (n=5) respectively). HFS

of the optic nerve was then used to induce increased extracellular K^+ directly from axons as the result of increased axonal firing (Connors *et al.*, 1982). Increasing the frequency of stimulation increased the concentration of lactate detected by the biosensor up to ~50Hz, after which further increase in stimulation frequency caused no further rise in lactate release (n=3).

The consistency of this preliminary data between the optic and sciatic nerve in response to changes in extracellular K^+ suggests a promising universal role of K^+ as an axon-glia metabolic signal within both the CNS and PNS. Furthermore, the logarithmic relationship observed implies changes in glial cell membrane potential influence lactate efflux.

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PC0081

Reliability of blood biomarkers of physiological stress at rest and in response to exercise under hot-humid conditions.

Daniel Snape[1, 2], Barney Wainwright[1], John O'Hara[1]

[1]Leeds Beckett University, Leeds, United Kingdom [2]English Institute of Sport , Manchester , United Kingdom

Purpose: Establish the short-term reliability and acute responsiveness of biomarkers of physiological stress to exercise in the heat. As such, informing their prospective application in research and field settings. **Method:** Fourteen male endurance trained cyclists/triathletes completed two heat stress tests (HST), separated by 5-7 days. HST's involved 45-minutes fixed-intensity cycling (2.5W.kg^{-1}) under hot-humid conditions (32^{o}C and 70% relative humidity). Venous blood was drawn pre- and immediately post-HST for the concentration of normetanephrine (NMET), metanephrine (MET), kidney-injury molecule 1 (KIM-1), neutrophil gelatinase-associated lipocalin (NGAL), serum osmolality (S_{osmo}) and copeptin. **Results:** No biomarker displayed systematic trial order bias ($p \leq 0.05$). The majority of biomarkers had acceptable within-participant variation (CV range: 0.9-14.3%). Copeptin had the lowest short-term variation at rest (CV = 0.9%) and post-HST (CV = 1.2%). However, greater variation was evident in biomarkers MET and KIM-1 at rest (CV = 28.6 & 43.2%) and post-HST (CV = 29.9 & 29.6%), respectively. NMET exhibited *very large* increases (trial 1 = Δ1048 ± 461; trial 2 = Δ 1067 ± 408) in response to exertional heat stress (p <0.0001, d = 2.8; p <0.0001, d = 3.8). In contrast, KIM-1 demonstrated *trivial* changes (trial 1 = Δ -3 ± 21; trial 2 = Δ 2 ± 17) in response to exercise in the heat (p = 0.53, d = 0.1; p = 0.60, d = 0.1). **Conclusion:** Each biomarker, except MET and KIM-1 had acceptable reliability at rest and following exercise. In addition, biomarkers NMET, copeptin and NGAL demonstrated large increases in response to exercise in the heat. Thus, these markers can provide accurate and sensitive measurement for wide-spread application in laboratory and field research.

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PC0082

Costs and implications associated with thermal adaptation of fishes on the World's hottest coral reefs

Grace Vaughan[1], Jacob Johansen[2], Matthew Mitchell[3], Dain McParland[3], Holly Shiels[4], John Burt[3]

[1]New York University Abu Dhabi / University of Manchester, Abu Dhabi, The United Arab Emirates [2]University of Hawaii, Hawaii, The United States of America [3]New York University Abu Dhabi, Abu Dhabi, The United Arab Emirates [4]University of Manchester, Manchester, United Kingdom

Tropical coral reefs are predicted to be amongst those most impacted by climate change since they have evolved under relatively thermally stable conditions. Furthermore, it is suggested that many species may already be living close to their upper thermal limits, with little capacity to acclimate to further warming conditions. Current maximum summer temperatures for the majority of coral reefs globally is 32C, with an additional 3-4C heating projected by 2100. However, the hottest coral reefs on Earth (Arabian Gulf) are already experiencing summer maxima above 35^{o}C and an annual thermal range >17^{o}C, creating a present day example of ocean warming impacts. Here, we use the Arabian Gulf reefs as a natural laboratory for climate change to investigate how three species of coral reef fishes (*Scolopsis ghanam, Cheilodipterus novemstriatus* and *Escenius pulcher*) have managed to acclimate and/or adapt to extreme thermal conditions. For each species we compared the metabolic performance (maximum metabolic rate, resting metabolic rate, aerobic scope and excess post-exercise oxygen consumption (EPOC)) across populations from the southern Arabian Gulf, and populations from the thermally more benign reefs in Gulf of Oman (annual temperature fluctuations 22-32C), focusing on five temperatures incorporating the existing seasonal Arabian Gulf thermal range (18, 22, 27, 31.5, 35.5^{o}C). Fishes were caught throughout the year when SST matched that of experimental temperature, allowing an accurate representation of any naturally occurring acclimation. Additionally, as conditions in the Gulf of Oman do not reach the same seasonal extremes, fishes from this region were acclimated for >3 weeks to 18C and 35.5C before experimental procedure. Maximum and resting oxygen consumption rates were then measured for each species and population at each temperature, using static intermittent respirometry. Our results reveal that all three species from the Arabian Gulf displayed a shift in peak aerobic scope to higher temperatures than Gulf of Oman fishes, suggesting thermal adaptation has occurred in order to meet metabolic demands at higher temperatures. However, all three species showed a significantly reduced aerobic scope at both the coolest and warmest temperatures, leaving little additional energy available for enhancing ecological activities. Resting metabolic rate increased exponentially from 18^{o}C to 35.5^{o}C in all species and populations, indicating the importance of maintaining performance to acquire food and fulfill energetic demand. By using Arabian Gulf reef fish populations as a natural proxy for climate change, this study indicates that although there may be capacity for some reef fish species to adapt to survive projected increases in SSTs and thermal fluctuations, this comes at the cost of severely reduced aerobic performance at both ends of the scale.

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PC0084

Exploration of the human rod-driven electroretinogram on different backgrounds in control subjects and selected patients with genetic and acquired retinal disease

Megan Margetts[1]

[1]*Megan Margetts, Loughborough, United Kingdom*

Full-field electroretinograms (ERGs) are a well-characterised method to indirectly study the clinical function of the visual system from the level of the photoreceptors to the ganglion cells. In past research, the a-wave and b-wave components have been studied separately (Thomas and Lamb, 1999; Cameron, Mahroo and Lamb, 2006), however, few sources evaluate them together. In this study, we aimed to address the rod contribution to the full-field ERG response for both the A-wave and B-wave components. This was done by comparing the responses from normal subjects to the responses of subjects with a range of genetic and acquired retinal diseases to dissect the different components of the full-field ERG response.

Patients with Vitamin A deficiency experience night blindness and ERGs typically show abolished rod system responses and preserved cone system responses, two main hypotheses have been put forward to explain this phenomenon:

1. Vitamin A deficiency reduces quantal catch (total number of photons absorbed per unit time) due to lack of chromophore in the outer photoreceptor segment.
2. The presence of significant quantities of free opsin weakly activating the phototransduction cascade, leading to the shut-off of circulating current.

These two hypotheses cannot easily be tested, as the rod driven ERG responses are normally completely abolished in most cases of Vitamin A deficiency. This study used a patient with moderate Vitamin A deficiency where the ERG response is only partially reduced.

According to the first explanation, a response to a flash stimulus in Vitamin A deficiency would be identical to a response to a dimmer flash delivered when Vitamin A levels are normal. In the second case, the flash response would resemble the response obtained in the presence of a light-adapting background (which similarly causes a reduction in photoreceptor circulating current).

In our patient, we found rod-driven responses were more consistent with the second explanation, indicating that loss of rod sensitivity in Vitamin A deficiency is largely a result of shut-off of circulating current due to sustained activation of the phototransduction cascade, probably by free rod opsin.

Acknowledgements :- I would like to thank my supervisors Dr Omar Mahroo and Xiaofan Jiang for their help and guidance on throughout this project. I would particularly like to thank Xiaofan Jiang for helping me to learn how to perform a clinical full-field ERG and how to analyse the a- and b-wave Peak data. I would also like to acknowledge the work of Remi Rufus-Toye who worked with Dr Omar Mahroo on a project, but also assisted me by operating the trials when I was the test subject.

Finally, I would also like to thank all the subjects who participated in my study, and the team at Guy's and St Thomas' Ophthalmology department for all their accommodation and support.

PC0086

Ameliorative effect of resveratrol on kidney function in doxorubucin-induced toxicity in wistar rats

Abdulazeez Jimoh[1], Joseph Olusegun Ayo[2], Ibrahim Binta Umar[3], Adam Abdulhameed[3], Yusuf Tanko[3], Umar Muhammed Bello[4], Ahmed Abubakar[5], Aliyu Mohammed[3]

[1]Faculty of Basic Medical Sciences, Human Physiology Department, College of Medical Sciences, Ahmadu Bello University,, Zaria, Nigeria [2]Faculty of Veterinary Medicine, Department of Veterinary Physiology, Ahmadu Bello University,, Zaria, Nigeria [3]Human Physiology Department, Faculty of Basic Medical Sciences, College of Medical Sciences,Ahmadu Bello University,, Zaria, Nigeria [4]Laboratory of Cell Biology and Histology, Department of Veterinary Anatomy, Faculty of Veterinary Medicine, Ahmadu Bello University,, Zaria, Nigeria [5]Department of Pharmacognosy and Drug Development, Faculty of Pharmaceutical Sciences, Ahmadu Bello University, , Zaria, Nigeria

Abstract: Doxorubicin (DOX) is a broad spectrum antitumor antibiotic widely used clinically as an anti-cancer agent. Doxorubicin (Adriamycin) is measured as one of the most effective anti-cancer drugs. DOX has a sheer and widespread organ toxicity, which makes it to be reconsidered as a chemotherapeutic agent for cancer patients. Although cardiotoxicity is the main side effect for DOX use, renal anomalies have also been seen in patients receiving the drug, Doxorubicin has been found to compromised kidney function as depicted by increased sodium and chloride ions concentration and decreased bicarbonate ion concentration in the blood This project work attempts to evaluate the ameliorative effect of resveratrol on kidney function in doxorubicin-induced toxicity in wistar rats. 28 wistar rats were grouped into four groups of 7 Wistar rats each (n=7). Group A (control group) received only distilled water and normal feed; Group B (positive group) were administered resveratrol only dose of 20 mg/kg at zero hour and 24 hour of the experiment; Group C (Acute rat models of DOX-induced toxicity) were administered 20 mg/kg of DOX. Group D (Treatment group) received DOX (20 mg/kg) simultaneously with resveratrol (20 mg/kg). The experiment lasted 48hrs. The animals were handle according to the principle guiding the use of laboratory animals in Ahmadu Bello University, Zaria, Nigeria. At the end of the experimental protocol, the rats were placed under light anaesthesia of ketamine and diazepam to remain unconscious. The animals were dissected to expose the heart. After which about 4 ml of blood was drawn via cardiac puncture for urea electrolyte analysis. it can be concluded that resveratrol improves the concentration of serum chloride and bicarbonate, improved renal creatinine clearance in doxorubicin induced toxicity in wistar rats. Notably, resveratrol impeded the renal clearance of urea indicating potential kidney damage by resveratrol.

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PC0087

Influence of Low Dose Acute Glutamine on Gastrointestinal Barrier Integrity and Microbial Translocation Following Exertional Heat Stress

Henry Ogden[1], Joanne Fallowfield[2], Robert Child[3], Glen Davison[4], Simon Fleming[5], Simon Delves[2], Alison Millyard[1], Caroline Westwood[1], Joseph Layden[1]

[1]MARJON University, Plymouth, United Kingdom [2]Institute of Naval Medicine, Alverstoke, United Kingdom [3]University of Birmingham, Birmingham, United Kingdom [4]University of Kent, Medway, United Kingdom [5]Royal Cornwall NHS Trust, Truro, United Kingdom

Purpose: Exertional-heat stress adversely disrupts gastrointestinal (GI) barrier integrity and, through subsequent microbial translocation (MT), can have negative health consequences for physically active populations (e.g. military personnel, athletes, laborers). Acute glutamine (GLN) supplementation is a potential nutritional countermeasure (Zuhl et al., 2015; Pugh et al., 2017), although doses previously validated for this purpose can cause symptoms of GI intolerance (e.g. nausea, bloating; Ward et al., 2003).

Method: Ten moderately trained males completed two 80-minute exertional-heat stress tests (EHST) separated by 7-14 days with a double-blind, randomised, counterbalanced, cross-over design. Low

dose oral GLN (0.3 g·kg^{-1} fat free mass) or PLA beverages were ingested one hour before commencing the EHST. Venous blood was drawn immediately pre- and post- EHST. GI barrier integrity was assessed using the serum dual-sugar absorption test (DSAT) and plasma Intestinal Fatty-Acid Binding Protein (I-FABP). MT was assessed using plasma total 16S bacterial DNA and *Bacteroides*/total 16S DNA.

Results: Whole-body physiological and perceptual strain were comparable between the GLN and PLA trials during the EHST (p > 0.05). The GLN bolus was well tolerated, with no evidence of GI intolerance. Serum DSAT responses were similar (p = 0.14) between the GLN (0.029 ± 0.023) and PLA trials (0.023 ± 0.005), though the post-EHST elevation in I-FABP was more pronounced with GLN (Δ = 2.542 ± 1.205 ng·ml^{-1}) than PLA (Δ= 1.374 ± 1.101 ng·ml^{-1}) supplementation (p = 0.01). *Bacteroides*/total 16S DNA responses tended to increase (p = 0.06) following the EHST, but there was no difference between the GLN (Δ = 0.02 ± 0.05) and PLA (Δ = 0.16 ± 0.34) trials.

Conclusion: Acute low-dose (0.3 g·kg^{-1} fat free mass) oral GLN supplementation one hour before exertional-heat stress enhances I-FABP concentrations, but this does not translate to augmented GI MT.

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PC0088

AMELIORATIVE EFFECT OF COMBINED TREATMENT WITH ZINC SULFATE AND N-ACETYLCYSTEINE ON SPERM ACROSOME REACTION, CAPACITAION AND CHROMATIN INTEGRITY IN DEHP-INDUCED REPROTOXICITY IN MALE WISTAR RATS

Victor EMOJEVWE[1], Alexander Obidike NAIHO [2], Eze Kingsley NWANGWA[2], Mega Obukohwo OYOVWI[3]

[1]Department of Physiology, University of Medical Sciences, Ondo, Nigeria [2]Department of Physiology, Delta State University, Abraka, Nigeria [3]Department of Basic Medical Sciences (Physiology Unit), Achiever University, Owo, Nigeria

Di-2-ethylhexyl phthalate (DEHP), as a low molecular weight phthalate has been used as a plasticizer in many products, especially medical devices, food packaging, cosmetics, and personal care products (Sai and Jiaxiang, 2018). Unfortunately, Consistent experimental evidence shows that some phthalates are developmental and reproductive toxicants in animals. Therefore, reduction of these side effects is necessary. The present study was aimed to explore the ameliorative effect of combined treatment with zinc sulfate ($ZnSO_4$) and n-acetylcysteine (NAC) on sperm acrosome reaction, capacitaion and chromatin integrity in DEHP-induced reprotoxicity in male wistar rats. The study included thirty five (35) Male Wistar rats randomly assigned into five groups (n=7). Group A served as untreated control, group B served as treated control and received Phthalate (750 mg/kgbw) only for 21 days, group C received phthalate (750 mg/kgbw) + 0.5mg of Zinc per kgbw for 21 days, group D received phthalate (750 mg/kgbw) + 100mg of N-acetylcysteine per kg bw for 21 days and group E received Phthalate (750 mg/kg/day) + N-acetylcysteine (100mg/kgbw) + Zinc (0.5mg/kgbw) for 21 days. At the end of the experimental period, the animals were fasted overnight and sacrificed by cervical dislocation followed by laparotomy. The epididymis were carefully dissected out and sperm sample was collected by perfusing the caudal epididymis of the rats through the distal end of the vas deferens into a pre-warmed modified sperm capacitation medium (SCM) as modified from the method of Morakinyo *et al*., (2011) for sperm capacitation; and acrosome reaction evaluation was done using Coomassie brilliant blue staining technique (Feng *et al*., 2007) while sperm chromatin integrity was evaluated by toluidine blue method as explained by Talebi *et al*., 2013. Data were analysed using ANOVA and differences in mean values were considered significant at $p<0.05$. The result showed that DEHP significantly decrease the percentage acrosome intact reacted sperm after incubation in sperm capacitation medium when compared to control groups (Fig.1). This was ameliorated in ZnSO4, NAC and Zn+NAC treated groups. Sperm capacitation was also significantly reduced in DEHP treated group but this was significantly ameliorated in NAC and Zn+NAC treated groups when compared with the DEHP treated group respectively (Fig.2*)*. Numbers of abnormal sperm chromatin was seen to be high in DEHP treated group which was also significantly reduced in Zn+NAC treated groups when compared with the DEHP, Zn and NAC treated groups respectively (Fig.3). It was therefore concluded that combination of zinc sulfate and n-acetylcysteine has the capacity to ameliorate the reprotoxic effects DEHP on the examined parameters.

Keywords: Phthalate, DEHP, Sperm capacitation, Acrosome reaction, Sperm chromatin integrity

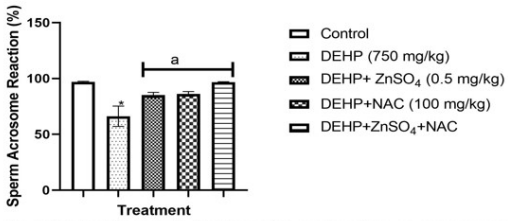

Fig. 1 Effects of treatment with Zinc and N-acetylcysteine on acrosome reaction in DEHP-induced reproductive toxicity in Male Wistar rats

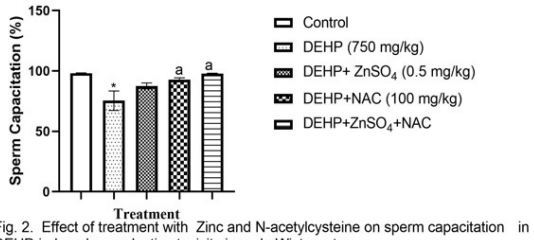

Fig. 2. Effect of treatment with Zinc and N-acetylcysteine on sperm capacitation in DEHP-induced reproductive toxicity in male Wistar rats

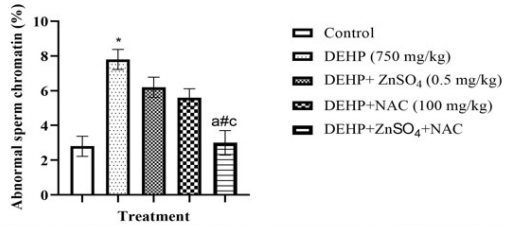

Fig. 3 Effect of treatment with Zinc and N-acetylcysteine on abnormal sperm chromatin condensation of DEHP-induced reproductive toxicity in male Wistar rats

Values are expressed as Mean ± SEM (n=7) (One-way ANOVA followed by Tukey's *post hoc* test). DEHP= Di-2-ethylhexyl phthalate, $ZnSO_4$=Zinc Sulfate, NAC=N-acetylcysteine

*, a, c, # $\alpha_{0.05}$ were considered statistically significant when compared with the Control, DEHP, $ZnSO_4$ and NAC treated groups respectively

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PC0089

FREQUENCY OF ABO BLOOD GROUPS AND BMI CORRELATION WITH BLOOD GROUPS IN FIRST YEAR MBBS STUDENTS OF CMH LAHORE MEDICAL COLLEGE.

Qudsia Umaira Khan[1], Sehrish Zaffar[1], Farida Hafeez[1], Haroon Rasheed[1], Abdul Khaliq Naveed[1]

[1]CMH Lahore Medical College, Lahore, Pakistan

Background: Blood is a significant fluid of the human body that is responsible for the flow of essential nutrients, hormones, enzymes, as well as oxygen in our body. Blood groups are essential for

blood transfusions, organ transplantation. Blood groups antigens can be used in forensic pathology, genetic research and anthropology.

Objective: The objective of this study was to estimate the frequency of ABO blood groups in first year MBBS students of CMH Medical College, Lahore and to find correlation between blood groups and BMI.

Study design: A cross-sectional study

Place &duration: CMH Lahore Medical and Dental College, Physiology Department. 2 months.

Methodology: The study was carried out on undergraduate first year MBBS medical students of CMH Lahore Medical College. After taking consent and filling the proforma ,height and weight were measured using standard method thus BMI was calculated . Blood groups were determined by ABO blood group were determined in a practical in Physiology laboratory by conventional glass slide method.

Results: Blood group B Positive was most predominant blood group (41.2%),No relationship between blood groups and BMI was observed.

Conclusion: Our finding relate that Blood group B is most prevalent in the first year MBBS students of CMH LMDC. There is no relationship between blood groups and BMI**.**

PC0090

The effects of standing whilst cycling on skeletal muscle oxygenation

Molly Bridge[1]

[1]*Kings College London, London, United Kingdom*

Introduction and Aims: The degree of oxygenation in the exercising skeletal muscle may be a factor influencing optimum cycling performance, together with work rate, cadence or position used by the cyclist. Where muscle metabolism is greater, i.e. with increasing work rate or elevated cadence, its oxygenation can decline at a work rate equal to the participant's ventilatory threshold (Tvent) (1,2). Current literature agrees that where work rate and cadence are fixed, standing while cycling increases metabolism (3,4).The present study considered the effect of standing on skeletal muscle oxygenation, during cycling exercise at different cadences at a submaximal work rate equivalent to 75% Tvent.

Methods: Seven healthy human participants, of varying cycling experience, completed a protocol pedalling at 40, 50, 60 and 70 revolutions per minute (rpm) on an electromagnetically braked cycle ergometer. Each cadence was sustained for 5 minutes, subdivided into seated (3 min) followed by

standing (2 min) phases, and interspersed with active recovery periods at 19% of Tvent (5). Near infrared spectroscopy (Portamon, Artinis) was used to determine vastus lateralis oxygenation changes with posture and cadence. Cardiopulmonary data were collected via Metasoft computer system (Cortex). A two-way repeated measures ANOVA and where appropriate Bonferroni's post hoc test were used for analyses. The study was approved by the Research Ethics Committee at King's College London.

Results: Oxygenated haemoglobin was 2.5% lower at 60 rpm compared with 40 rpm ($P = 0.019$) [Fig. 1a]. Total haemoglobin increased over time during standing cycling, where the 60-120s standing values were 1.3% greater than 0-30s values ($P<0.004$) [Fig. 1c]. Tissue saturation index was not significantly different between cycling intervals and cadences [Fig. 1d]. All cardiopulmonary variables studied increased with cadence and time spent in standing position [Fig. 2a-d].

Conclusions: Vastus lateralis oxygenation changes between seated and standing were significant for total haemoglobin, where time of standing phase increased, and for oxygenated haemoglobin at 60pm at 75% Tvent. This study provides a basis for further research into the effect of postural changes during cycling on muscle oxygenation. To consolidate these findings, a greater number of participants must be assessed. Further studies may employ electromyography to investigate how a change in muscle activity may be associated with muscle oxygenation in different positions.

Key Words: Cycling, Position, Cadence, Near Infrared Spectroscopy, Tissue Saturation Index.

Figure 1:

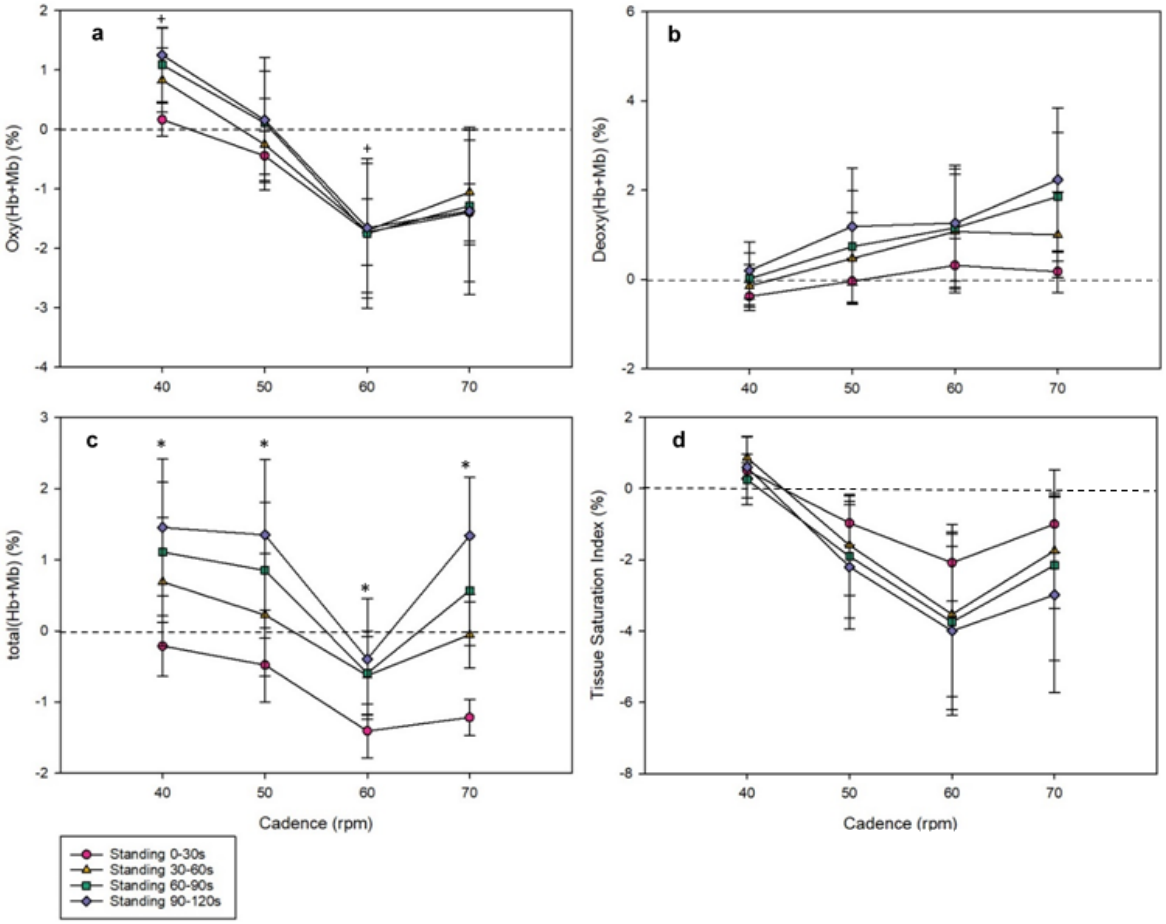

Figure 1: ***Changes in skeletal muscle oxygenation at different cadences and during each 30 second phase of cycling exercise while standing*** *relative to the final 30 seconds of seated cycling). a) Oxygenated Haemoglobin (OxyHb+Mb); a reduction was found between cadences 40 rpm and 60 rpm (P=0.019); b) Deoxygenated Haemoglobin (DeoxyHb+Mb) changes with position and cadence; c) total haemoglobin, (tHb+Mb), increased with time spent in standing position whereby values for 60-120s were greater than 0-30s values (P = 0.004); d) Tissue saturation index (TSI) changes with position and cadence. * statistically significant difference with cadence or * with position (P<0.05).*

Figure 2:

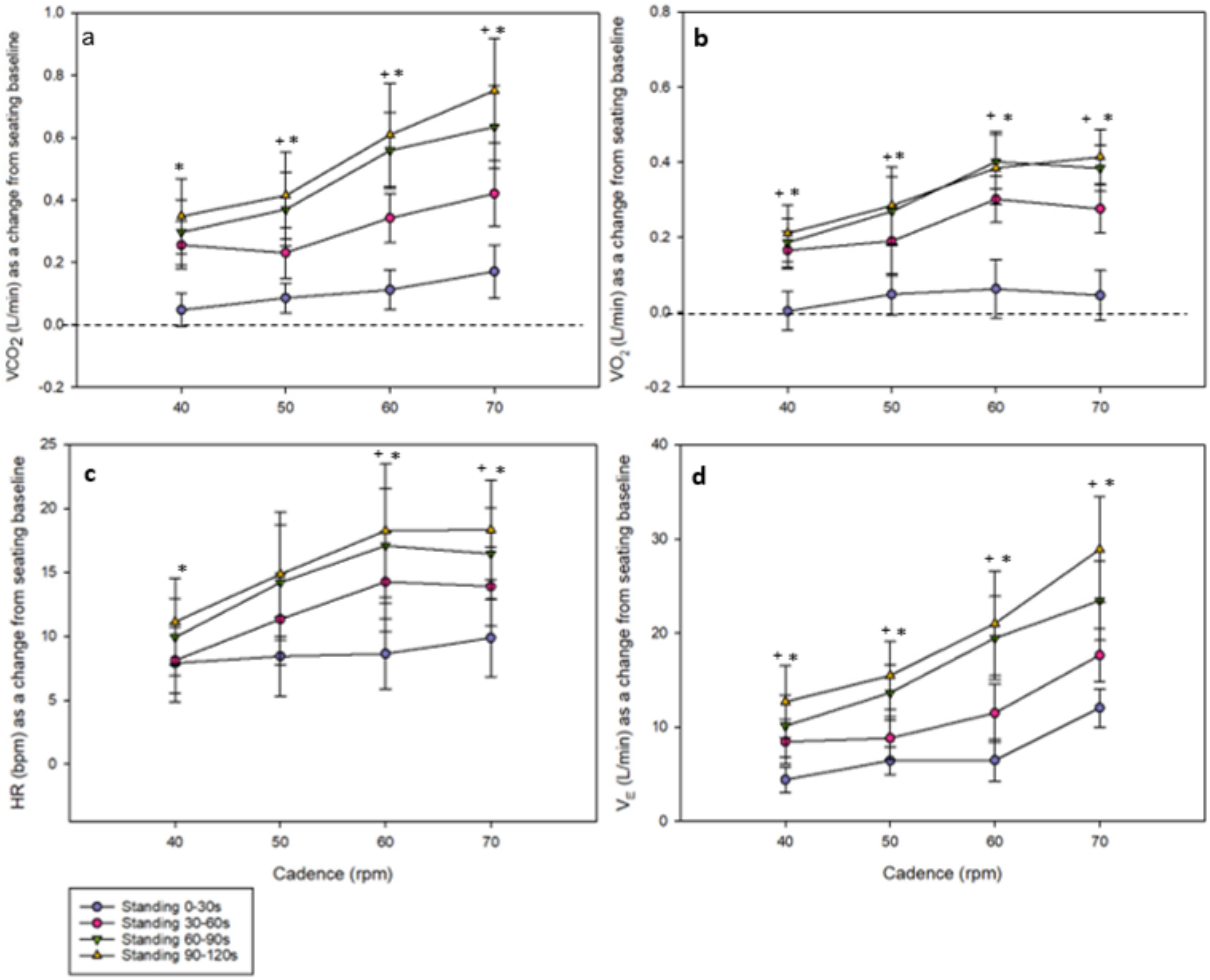

Figure 2: ***Cardiopulmonary responses with changing cadence during each 30 second phase of cycling exercise while standing*** *(relative to the final 30 seconds of seated cycling). a) VCO_2; compared to 0-30s, values were greater at 30-120s for 70 rpm (P<0.001) and 60 rpm (P<0.001) and at 60-120s for 50 rpm (P=0.007). Values for 60-120s increased from 40 to 70 rpm (P<0.001). b) VO_2 values were greater for the standing intervals 30-120s compared to 0-30s at cadences 40 (P=0.005), 50 (P=0.001), 60 and 70 rpm (both P<0.001). Standing values for 60-120s increased between 40 and 70 rpm (P<0.001) c) Heart rate was greater where 0-30s and 90-120s of standing at 60 (P=0.010) and 70 rpm (P=0.029) were compared. 60-120s values increased between 40 and 70 rpm (P=0.002). d) Minute Ventilation (V_E) was greater at 30-120s at 60 and 70 rpm (both P<0.001), at 60-120s for 50rpm (P=0.007) and 90-120s for 40 rpm (P=0.015) when compared to 0-30s. Values for 60-120s increased between 40 to 70 rpm (P<0.001).* statistically significant difference with cadence or ⁺ with position (P<0.05).*

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PC0091

Lung diffusing response to exercise at sea level and high-altitude

Iker García Alday[1, 2], Franchek Drobnic[3], Yinkiria Cheng[4, 5], Victoria Pons[1], Casemiro Javierre[6], Ginés Viscor[2]

[1]Centro de Alto Rendimiento (CAR), Av. Alcalde Barnils s/n, 08173 , Sant Cugat Del Valles, Spain [2]Physiology Section, Department of Cell Biology, Physiology and Immunology, Faculty of Biology, University of Barcelona, Barcelona, Spain [3]Medical Services Shenhua Greenland FC, Shanghai, China [4]Departamento de Fisiología y Comportamiento Animal, Facultad de Biología, Universidad de Panamá, Ciudad de Panamá, Panama [5]Centro de Estudios de Recursos Bioticos (CEREB), Ciudad de Panamá, Panama [6]Exercise Physiology Unit, Department of Physiological Sciences, Faculty of Medicine and Health Sciences, Universitat de Barcelona, L'Hospitalet de Llobregat, Spain

Changes in lung diffusing capacity for carbon monoxide (DL_{CO}) are linked to aerobic performance and lung interstitial disease (1-2), both at sea level (SL) (3) and high-altiude (HA) (4). The aim of this study is to evaluate the changes in lung diffusion capacity for carbon monoxide (DL_{CO}) produced after anaerobic and aerobic exercise at SL and after a rapid exposure and exercise at HA. The participants were 10 healthy active subjects (7 females and 3 males) aged 21 to 26. A study of DL_{CO} was developed under different conditions: The first day, DL_{CO} was obtained basal at SL, post-maximal 30-s exercise at SL (SL-ANA), and post-moderate exercise at SL (SL-ANA). The second day, DL_{CO} was obtained basal at SL, basal at 4,000 m of altitude (HA-R) and post-moderate exercise at 4,000 m (HA-AER). The method used to evaluate DL_{CO} was the single-breath method in a computerized spirometer. There was an increase in DL_{CO} after 30-s maximal exercise at SL. Also there was a direct correlation in basal DL_{CO} at SL and Watts developed during 30-s maximal exercise (R=0.95). Then DL_{CO} was reduced after aerobic exercise at SL. During HA exposure, there was no changes in DL_{CO} or any other pulmonary structural or functional parameter, either after a rapid exposure to 4,000 m, or after moderate aerobic exercise. Large increases in DL_{CO} can occur acutely after anaerobic 30-s maximal exercise in a cycle ergometer. An acute exposure to HA does not elicit any change neither at rest nor at exercise. Therefore exercise intensity may be the most important factor to elicit

modifications in lung diffusing capacity.

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PC0092

Using the mouse as a model to study the cardiotoxicity of air pollutants.

Sana Yaar[1], Holly Shiels[1], Edward Hayter[1], David Bechtold[1], Luigi Venetucci[1]

[1]*University of Manchester, Manchester, United Kingdom*

An estimated 4.2 million premature deaths worldwide are attributed to air pollution, primarily through increased cardiovascular (CV) morbidity and mortality. Studies have found particulate matter (PM), a subgroup of pollutants, are associated most strongly with CV disease (CVD); particularly due to the ability of smaller particles (PM2.5), such as polyaromatic hydrocarbons (PAHs), to cross the alveolar-blood barrier and enter the systemic circulation. Most research on PAHs is done in fish and there is a paucity of experimental evidence in mammalian models. The mouse model could prove a vital experimental tool to elucidate the molecular mechanisms underlying the CV effects of PAHs, such as Phenanthrene. Firstly, the mouse model allows the effect of PAH exposure on whole heart function, both *ex-vivo* and *in-vivo*, to be determined; preliminary studies show a reduction in heart rate from 348.5+/-15.51 bpm under control conditions to 288+/-5.63 bpm after 15 minute Phe exposure ($P<0.022$, $n=3$). Secondly, chronic exposure to PAHs can be studied in mice, this is important due to the ability of PAHs to bioaccumulate in tissue over time. Finally, the availability of mouse CVD models, allows the potential of PAH exposure to exacerbate existing disease to be studied.

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PC0094

Characterization of the spectral profile of transcutaneous oxygen tension signals

Henrique Silva[1, 2], Luis Monteiro Rodrigues[1]

[1]Universidade Lusófona, School of Health Sc & Technologies, CBiOS (Research Center for Biosciences and Health Technologies), Campo Grande 376, 1749-024, Lisboa, Portugal [2]Universidade de Lisboa, Faculty of Pharmacy, Pharmacol. Sc Depart, Lisboa, Portugal

Transcutaneous (tc) gasimetry has been employed for several decades as a technique to noninvasively assess oxygen tension (pO_2) levels. It is valuable for early detection of lower limb ischemia in peripheral artery disease and diabetes, being a predictor for level of amputation. $tcpO_2$ provides a continuous signal whose spectral organization is virtually unknown. Our aim was to assess the spectral organization of $tcpO_2$ signals acquired during two experimental maneuvers destined to challenge circulatory homeostasis. Fifty-seven subjects (23.0 ± 4.0 y.o.) were enrolled in this study after giving informed written consent, and were subjected to two maneuvers while lying supine. Thirty-five subjects were subjected to a passive leg raising (PLR) test while twenty-two were subjected to a leg lowering test destined to evoke the venoarteriolar (VAR) reflex, both with the same structure - 10 min baseline, 10 min challenge, 10 min recovery. $TcpO_2$ levels were collected from a distal region of the foot while LDF signals were acquired on the inferior aspect of the second toe. Both signals were decomposed with the wavelet transform (WT) to obtain the respective frequency spectra. The spectral organization of the LDF signal is well known (cardiac, respiratory, myogenic, sympathetic, endothelial NO-dependent, endothelial NO-independent). $TcpO_2$ suffered opposite significant changes during both protocols – a decrease with PLR and an increase with VAR. In either protocol, $tcpO_2$ spectra revealed three low-frequency spectral regions, partly overlapping the endothelial regions of the LDF spectra. These results suggest that although the $tcpO_2$ signal is mainly from macrocirculatory origin, it might suffer a modest contribution from the endothelium.

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PC0095

Mapping murine hindlimb laser Doppler perfusion with the wavelet transform

Henrique Silva[1, 2], Alain-Pierre Gadeau[3], Luis Monteiro Rodrigues[1]

[1]Universidade Lusófona, School of Health Sc & Technologies, CBiOS (Research Center for Biosciences and Health Technologies), Campo Grande 376, 1749-024, Lisboa, Portugal [2]Universidade de Lisboa, Faculty of Pharmacy, Pharmacol. Sc Depart, Lisboa, Portugal [3]U Bordeaux & INSERM, U1034, Adaptation cardiovasculaire à l'ischémie, F-33600, Pessac, France

Laser Doppler flowmetry (LDF) is a reference technique to assess microcirculation perfusion signals, typically in the skin. It impinges a laser light through an organ and onto flowing red blood cells, which

reflect it back. Flow is estimated through the Doppler shift, i.e., the difference between impinging and reflected laser frequencies. A major factor that influences the penetration depth is skin thickness. Provided the skin is sufficiently thin, light can probably reach large caliber vessels on the dermis/hypodermis. Our aim was to noninvasively characterize the LDF signal of large caliber vessels in murine hindlimb, using microcirculation LDF signals as comparison. Six C57/BL6 male animals (12 w.o.) were anesthetized with a ketamine-xylazine (137.5 mg/kg-11.0 mg/kg) i.p. mixture. All procedures involving animal experimentation were performed in accordance with the current ethical guidelines for the protection of animals used for scientific purposes in the EU. Twenty minutes after induction the animals were placed on a heated plate and LDF probes were attached to skin regions directly above large vessels (region 1 - macroLDF) and free of large vessels (region 2 - macroLDF). After 15 min stabilization, both LDF signals were measured for 30 minutes, after which they were decomposed in their spectral components with the wavelet transform. microLDF is believed to be composed of six spectral bands - cardiac, respiratory, myogenic, sympathetic, NO-dependent endothelial, NO-independent endothelial. macroLDF displayed bands in the same spectral regions although with significantly higher amplitude over the entire spectrum. The cardiac, sympathetic and NO-independent endothelial spectral bands showed higher resolution in the macroLDF, while respiratory and myogenic bands showed poor resolution with both signals. To the authors knowledge this is the first study to attempt to describe the spectral organization of macrocirculation signals. Even considering that macroLDF signals might be partly overlaid with microLDF signals, these results suggest that large caliber vessels display similar spectral organization to microcirculation signals. This opens new possibilities to assess regional perfusion in real time during interventions, i.e., limb ischemia.

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PC0097

Describing the microcirculatory flowmotion reactivity to phentolamine with the wavelet analysis - data from a murine model

Henrique Silva[1, 2], Étienne Roux[3], Alain-Pierre Gadeau[3], Luis Monteiro Rodrigues[1]

[1]Universidade Lusófona, School of Health Sc & Technologies, CBiOS (Research Center for Biosciences and Health Technologies), Campo Grande 376, 1749-024, Lisboa, Portugal [2]Universidade de Lisboa, Faculty of Pharmacy, Pharmacol. Sc Depart, Lisboa, Portugal [3]U Bordeaux & INSERM, U1034, Adaptation cardiovasculaire à l'ischémie, F-33600, Pessac, France

Animal models are of pivotal importance in vascular physiology, allowing the application of different 'challengers' for the in vivo study of regulatory phenomena, for example drugs to modulate vascular function. The effect of these challengers is best observed with noninvasive perfusion assessment techniques. Our objective was to characterize the microcirculatory reactivity to phentolamine (PL). A group of six C57/BL6 male mice (12 w.o.) under a ketamine (K, 137.5 mg/kg) and xylazine (X, 11

mg/kg) mixture received two IP doses of PL (2.5 mg/kg). Animal experiments were performed in accordance with the EU guidelines on animal welfare and complied with principles and standards for reporting animal experiments. Perfusion was assessed with laser Doppler flowmetry (LDF), collected on a random hindlimb and decomposed with the wavelet transform (WT) for the inspection of the respective spectral components - cardiac, respiratory, myogenic, sympathetic, endothelial NO-dependent (NOd) and endothelial NO-independent (NOi). Both PL doses increased perfusion, although without statistical significance. The first PL dose caused the significant decrease of the myogenic activity, together with the significant increase of the sympathetic and NOd activities. The second PL dose increased the myogenic activity and decreased the NOd, although baseline values were not reached. PL acts as an alpha-1 receptor antagonist, which is in line with the observation of perfusion increase. However, this mechanism contrasts with the observed increase in sympathetic activity. Therefore, these results suggest that, under ketamine-xylazine anesthesia, PL administration evokes mainly an indirect vascular effect, resulting from the combined effect of both the myogenic and endothelial activities.

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PC0099

Same-session Concurrent Exercise Training in Overweight and Obesity: A Systematic Review and Meta-Analysis

Jordan Bell[1], Will Evans[1], Morc Coulson[1], David Archer [1]

[1]*University of Sunderland, Sunderland, United Kingdom*

Same-session concurrent training (CT) incorporating high-intensity interval training (HIIT) or continuous aerobic training (AT) alongside resistance training (RT) may be a feasible, efficient and enticing form of exercise to achieve exercise guidelines and improve physiological health and related outcomes in overweight and obesity. The aim of this systematic review and meta-analysis was to: update the current knowledge-base on the effectiveness of otherwise healthy overweight and obese individuals performing same-session concurrent HIIT/AT and RT to improve obesity-related health outcomes. Studies which completed same-session concurrent HIIT/AT and RT in overweight and obese populations were retrieved from 5 electronic databases (PubMed, CINAHL, SPORTDiscus, MedLine, and Web of Science) and systematically reviewed and, where appropriate, evidence was pooled through meta-analysis. 5 studies totalling 193 participants were included, no studies incorporating HIIT into CT programmes were identified. The mean tool for the assessment of study quality and reporting in exercise (TESTEX) score of the five studies was 8/15. Where sufficient data was available pooled evidence revealed standardised mean differences in; body mass -1.7 kg (95% CI -3.6, 0.1; *P* = 0.07; n = 136), body fat percentage -3.7 % (95% CI -6.4, -1.1; *P* = 0.006; n = 136) and waist circumference -2.8 cm (95% CI -4.0, -1.7; *P*< 0.001; n = 115). CT was effective in improving cardiorespiratory fitness (average increase 2.7 $ml{\cdot}kg^{-1}min^{-1}$), as well as secondary outcome measures

including strength, though there was insufficient data to undertake accurate meta-analysis. CT was established as an effective means of improving measures of physiological health and related outcomes including cardiorespiratory fitness, body composition and strength compared to a non-exercise control in overweight and obese individuals. CT may also demonstrate greater improvements (particularly for body fat) than either exercise type (AT or RT) in isolation, due to an amalgamation of the physiological adaptations attained from each. However, a low sample size ensured that making assumptions from the data was difficult. Accordingly, results should be interpreted with caution. CT is a beneficial form of exercise training for overweight and obese individuals, though, further research and confirmatory studies are required, particularly CT research including the use of HIIT.

PC0101

Skeletal muscle oxygen delivery in response to an altitude hypoxia trekking: muscle group and ethnic origin on point

Danilo Bondi[1], Vittore Verratti[1], Gabriele Mulliri[2], Giovanna Ghiani[2], Tiziana Pietrangelo[1], Antonio Crisafulli[2]

[1]University "G. d'Annunzio" of Chieti - Pescara, Chieti, Italy [2]University of Cagliari, Cagliari, Italy

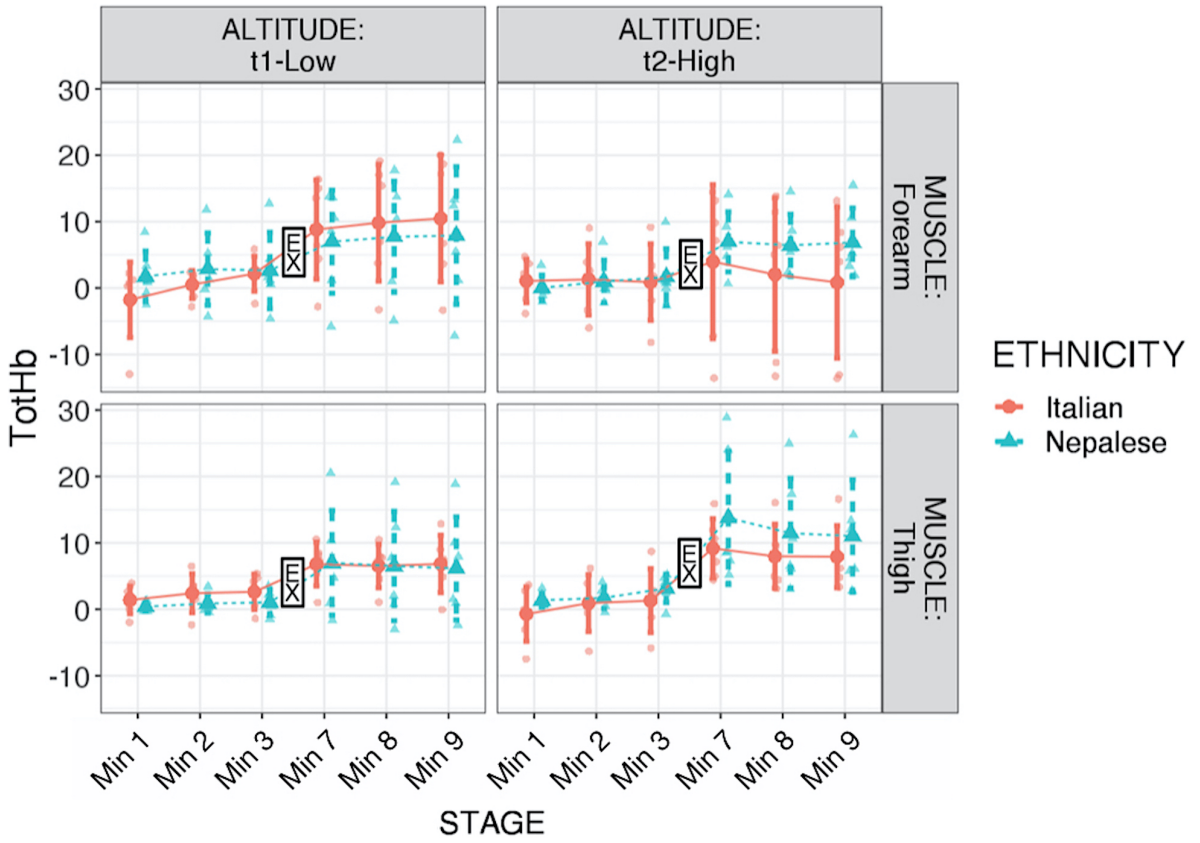
Altitude traveling represents an intriguing experimental model to reproduce physiological and pathophysiological conditions sharing hypoxemia as the denominator, as ageing [1]. Moreover, traveling to high altitude is nowadays very popular, and it appears necessary to provide medical advice in terms of altitude tolerance and acclimatization [2]. The main aim of this study was to investigate oxygen delivery and utilization in response to hypobaric hypoxia and to a submaximal strength exercise, taking into account several factors including muscle group and ethnic origin. As part of the “Kanchenjunga Exploration & Physiology” project, 6 Italian trekkers and 6 Nepalese porters took part in a high-altitude trek in the Himalayas. The measurement was carried out at low (1450 m) and high altitude (4780 m). NIRS-derived parameters (Tot-Hb and TSI) were gathered at rest and after a 3-minutes submaximal resistive exercise, both in quadriceps and forearm muscles. Peripheral saturation (SpO_2), starting from physiological values, decreased from low to high altitude in all the participants (percentage of oxygenated haemoglobin moved from 98±1 to 86±4 in the Italian group, and from 96±1% to 85±3 percent of saturation, in the Nepalese group; $F_{1,10}$=122.50, p<.001, partial η^2=.925), confirming the typical response to high altitude ascents. TSI decreased with altitude, particularly in forearm muscles (from 66.9% to 57.3%), whereas this decrement was less evident in quadriceps (from 62.5% to 57.2%); Nepalese porters had greater values in thigh saturation than Italian trekkers. Tot-Hb was increased after exercise. At altitude, it seemed that this increase was particularly high in quadriceps. The response of diverse muscles to hypoxia, or to hypoxic exercise [3], deserves to be further explored basing of morpho-functional characterization of muscle groups. High altitude may represent a stressor to the oxygen system, capable of entailing beneficial effects in oxygen delivery and utilization: we argue about the long-term adaptive memory due to the frequent exposure to altitude. We further suggest a long-term adaptation of the Nepalese porters due to improved oxygenation in those muscles involved in a hypoxic exercise, possibly through

increasing muscle blood flow. Individual factors, such as age, gender, altitude exposure time, and muscle structure should be taken into account in further investigations on oxygen delivery and utilization in altitude.

Table. Descriptive characteristics of participants and oxygen saturation measured in the same days of NIRS testing; BP is expressed as SystolicBP / DiastolicBP; group values are expressed as mean±SD

	Ethnicity	**Gender**	**Age** (years)	**BMI** (Kg/m^2)	**Basal BP** (mmHg)	**SpO_2-LA** (%)	**SpO_2-HA** (%)
It1	Italian	Female	36	25.07	117 / 76	99	84
It2	Italian	Male	63	28.91	133 / 83	97	84
It3	Italian	Male	59	21.91	139 / 87	98	80
It4	Italian	Male	25	24.31	126 / 68	99	85
It5	Italian	Male	32	24.14	124 / 67	98	89
It6	Italian	Male	48	30.54	136 / 82	97	92
	Italian Group		44 ± 15	25.81 ± 3.25	129±8 / 77±8	98 ± 1	86 ± 4
Ne1	Nepalese	Male	26	26.49	128 / 87	96	85
Ne2	Nepalese	Male	18	17.51	112 / 62	99	90
Ne3	Nepalese	Male	39	22.99	143 / 92	96	88
Ne4	Nepalese	Male	40	28.83	131 / 89	96	85
Ne5	Nepalese	Male	30	29.41	127 / 93	95	82
Ne6	Nepalese	Male	29	20.94	130 / 93	96	82
	Nepalese group		30 ± 8	24.36 ± 4.70	129±10 / 86±12	96 ± 1	85 ± 3

BMI: Body Mass Index; **BP**: Blood Pressure; **SpO2**: oxygen saturation; **LA**: low altitude**;** **HA**: high altitude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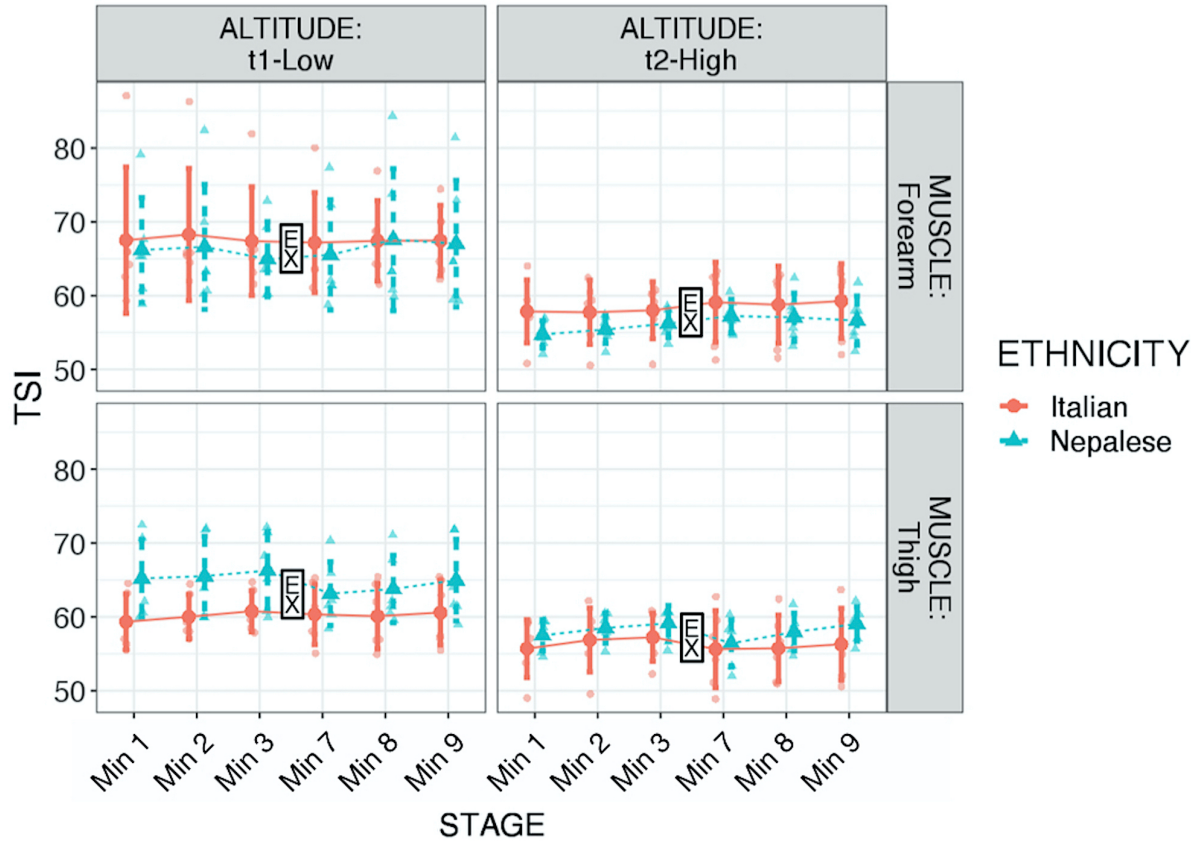
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STAGE
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Nepalese

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PC0103

The effects of carbon dioxide on monocyte differentiation and macrophage activation

Moritz J. Strowitzki[1], Ross Nelson[1], Mario P. Garcia[1], Susan Fitzpatrick[1], Eric Brown[1], David Phelan[1], Alfonso Blanco[1], Eoin P. Cummins[1], Cormac T. Taylor[1]

[1]Conway Institute of Biomedical & Biomolecular research, University College Dublin, Dublin, Ireland

Motivation: Recently, the Mauna Loa Observatory in Hawaii repeatedly measured unprecedented inclines of carbon dioxide (CO_2) levels over the last years. In patients with chronic lung diseases, studies suggest that increased levels of CO_2 reduce macrophage function during inflammatory processes; however, little is known how macrophages might sense CO_2 and adapt upon high levels of CO_2 during differentiation and activation. We, therefore, aimed to elucidate the effects of CO_2 on gene and protein expression during basic inflammatory processes, such as monocyte differentiation and macrophage activation.

Methods: Monocyte differentiation was induced by phorbol 12-myristate 13-acetate (PMA). Primary macrophages (BMDMs) were polarized using different cytokines to induce pro-inflammatory (M1) macrophages (lipopolysaccharides) or immuno-modulatory (M2) macrophages (interleukin-4). Cells were simultaneously subjected to different levels of CO_2. Morphological changes, mRNA and protein expression of markers for cell differentiation and macrophage polarization were determined.

Results: High levels of CO_2 attenuated PMA-induced cell differentiation of human monocytes. mRNA and protein levels of several pro-inflammatory markers of cell differentiation were reduced upon high CO_2 levels. In BMDMs, CO_2 significantly reduced transcript levels of M1-marker and exclusively increased the expression of arginase-1 (M2-marker). Moreover, CO_2 mitigated PMA-stimulated PKC activity. Experiments with buffered medium revealed that changes in pH were responsible for most, but not all, of the CO_2-mediated effects on monocyte differentiation and macrophage polarization.

Conclusion: CO_2 markedly reduces both monocyte differentiation and macrophage activation. A better understanding of CO_2-adaptive molecular pathways and CO_2-sensing mechanisms will have great therapeutic impact on all inflammation-driven diseases characterized by a microenvironment with high CO_2 levels, including chronic lung and tumor diseases.

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PC0104

The Effects of Acute Hypocapnia on Neurovascular Coupling Magnitude

Taylor Bader[1], Anna-Maria Ciorogariu-Ivan[1], Joanna Keough[1], Josh Donald[1], Jack Leacy[2], Ken O'Halloran[2], Trevor Day[1]

[1]Mount Royal University, Calgary, Canada [2]University College Cork, Cork, Ireland

The brain requires well-regulated cerebrovascular perfusion to match metabolic demand. Regional coupling of perfusion to metabolic rate is termed neurovascular coupling (NVC). NVC remains stable during blood gas perturbations upon ascent to altitude, where individuals are exposed to the antagonistic effects of hypoxia and hypocapnia. Few studies have addressed the effects of acute hypocapnia and respiratory alkalosis independently. We aimed to assess the specific effects of acute steady-state hypocapnia on NVC magnitude in a laboratory setting. We recruited 17 healthy participants and instrumented the posterior cerebral artery (PCA) with a transcranial Doppler ultrasound. NVC was elicited using a standardized strobe light stimulus (6 Hz; 5x30sec on/off), and both peak and mean absolute responses from baseline (BL) were quantified. Participants were coached to hyperventilate to reach steady-state hypocapnic steps of Δ-5 and Δ-10 Torr end-tidal (P_{ET})CO_2 from baseline levels. $P_{ET}CO_2$ levels were significantly decreased from 36.7±3.2 (baseline) to 31.6±3.9 Torr (Δ-5) and 26±4.0 (Δ-10) Torr (P<0.001). There was a significant reduction in NVC magnitude (ΔPCAv) from BL during controlled hypocapnia at both Δ-5 and Δ-10 in peak ΔPCAv (P=0.044 and P=0.037, respectively), but no significant decrease in mean ΔPCAv (P=0.193). Our study demonstrates that acute respiratory alkalosis attenuates peak NVC magnitude at Δ-5 Torr $P_{ET}CO_2$, without further attenuation at Δ-10. Although peak NVC magnitude was attenuated, our data suggests that NVC is remarkably stable in acute respiratory alkalosis given (a) the magnitude of reduction in peak NVC was small and (b) NVC was unchanged in mean responses to visual stimulation.

PC0105

Microcirculatory perfusion changes registered in the Inferior limb with static and dynamic position

Sérgio Miguel Loureiro Nuno[1, 2, 3], Margarida Florindo[1, 4], Henrique Silva[1, 5], Luis Monteiro Rodrigues[1]

[1]Universidade Lusófona, CBiOS (Research Center for Biosciences and Health Technologies), Campo Grande 376, 1749-024, Lisboa, Portugal [2]Clínica S João de Deus – CTD, Lisboa, Portugal [3]Lisbon School of Health Technology of the Polytechnic Institute of Lisbon, ESTeSL-IPL, Lisboa, Portugal [4]Department of Physiotherapy, Portuguese Red Cross Superior Health School, ESSCVP, Lisboa, Portugal

[5]*Universidade de Lisboa, Faculty of Pharmacy, Pharmacol. Sc Depart, Lisboa, Portugal*

The adaptation of peripheral microcirculation to body position and, in particular, to movement illustrates the complexity of the multiple mechanisms, central and local, neural, humoral and neurohumoral involved vascular homeostasis. The objective of this study is to explore the impact of different body positions on both legs using non-invasive optical based technology.

Five healthy participants, 3 females and 2 males, previously selected (26.0±6.5 years old; Body Mass Index 22.9 ± 1.1 kg/m^2). Peripheral perfusion was measured in both feet using Laser Doppler Flowmetry (LDF, from Perimed, S) and Polarised Spectroscopy (TiVi System® Wheelbridge AG, S). The experimental protocol involved: (1) Baseline, seated, standup and seated to rest; (2) Standup, squat repetitions and standup to rest; (3) Standup, knee to hip flexion, standup to rest. Descriptive and comparative statistics were applied and a confidence level of 95% adopted.

Significant changes in blood volume (BV) and in the concentration of red blood cells (CRBC) were seen in the orthostatic and functional positions. No statistically significant changes were found between the right and left lower limbs, which means that the microcirculatory homeostasis immediately adjusts the perfusion conditions when body position changes. However the knee to hip flexion demonstrates that the load change evokes a significant change in the perfusion of both limbs, here significantly different. In addition the usefulness of these technologies is well demonstrated. Although sharing different wavelengths, and therefore different penetration capacities, they provide valuable information to better understand the mechanisms behind microcirculatory homeostasis.

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PC0107

The effect of zero glucose on human uterine contractility

Tshikaya Kaleta[1], Susan Wray[1]

[1]*University of Liverpool, Liverpool, United Kingdom*

Uterine contractility issues, such as preterm or dysfunctional labours, remain major obstacles to female reproductive and neonatal health. The mechanisms of uterine contraction and its dysfunction, need to be better clarified. During labour, contractions produce transient ischemia, consequently, glucose supply to the myometrium becomes limited. A direct cause-and-effect relationship between the exhaustion of glucose and impairment of muscle function is still to be established in the myometrium. We explore this and compare effects under hypoxic conditions. Myometrial strips were taken from labouring and non-labouring pregnant women undergoing emergency and elective caesarean sections at Liverpool Women Hospital. Samples were equilibrated in oxygenated physiological saline (pH7.4) at 37°C.Contractile activity was isometrically measured. The effects of zero-glucose, combined zero-glucose and hypoxia (N_2) were tested. N is number of

women. The amplitude of spontaneous contractions declined significantly (t-test) to 87±2% (n=5) of control in labouring women and 82±6% (n=12) in non-labouring. Studied so far in non-labouring samples, this inhibition was significantly greater with hypoxia and zero-glucose 48±6% (n=7).Our results reveal that zero-glucose significantly inhibits uterine contractions. The results suggest that glucose depletion *in vivo* will contribute to the pathway underlying uterine contractility related disorders. The mechanism of its effect needs to be better elucidated

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PC0110

Respiratory Sinus Arrhythmia Reactivity During Acute Exposure to Normobaric Hypoxia and Hyperoxia

Brendan Lazar[1, 2], Stephanie Nguyen[1], Matthew Betton[1], Evan Olar[1], Trevor Day[1, 2]

[1]Mount Royal University, Calgary, Canada [2]Department of Biology, Faculty of Science and Technology, Mount Royal University, Calgary, Canada

Respiratory sinus arrhythmia (RSA) is the normal fluctuation in heart rate (HR) in phase with the respiratory cycle, increasing during inspiration and decreasing during expiration. The underlying mechanisms and potential physiological utility remain elusive. RSA magnitude is thought to be affected by autonomic balance, with sympathetic nervous system (SNS) activation attenuating its magnitude. In addition, RSA is thought to improve ventilation-perfusion (V/Q) matching in the lung, which may protect oxygen saturation in hypoxia. We hypothesized that (a) acute hypoxia would decrease the magnitude of RSA through SNS activation, and (b) those with larger RSA in hypoxia would have improved oxygen saturation. Healthy participants (n=15) were instrumented with a pneumotachometer and instructed to breathe at three percentages (30, 40 and 50%) of their forced vital capacity (FVC) at three levels of randomized inspired gases: (a) room air (21%), (b) hypoxia (~13.5%) and (c) hyperoxia (100%). RSA was quantified via the peak-valley approach, and RSA reactivity (RSA_R) was quantified as the slope of increases in RSA across FVC levels. RSA magnitude was not different at each percentage of FVC with each gas (P>0.05), nor were RSA_R slopes different between gases (P=0.97). There was no relationship between RSA magnitude at 50% FVC in hypoxia, and the improvement in oxygen saturation from baseline breathing (r=-0.011, P=0.71). Our data provides evidence that (a) hypoxic stimulation of the carotid bodies elicits activation of both arms of the autonomic nervous system, maintaining autonomic balance and (b) RSA magnitude plays no role in improving V̇/Q matching in hypoxia.

PC0111

EVALUATION OF CARDIOVASCULAR, ANTHROPOMETRIC AND STRENGTH VARIABLES' RELATIONSHIP IN APPARENTLY HEALTHY MALE SUBJECTS IN FUTA SOUTH-GATE COMMUNITY

Success Ajayi[1], Olusoji Adalumo[1]

[1]*Department of Physiology, School, of Health and Health Technology, Federal University of Technology, Akure, Nigeria*

70 young adults were assessed in FUTA south-gate community, Nigeria, to evaluate the relationship between some cardiovascular, anthropometric and strength variables. These participants were apparently healthy and were assessed by evaluating their electrocardiographic parameters, body mass index, body surface area and maximum voluntary contraction (MVC). The results analysed by descriptive and inferential statistics showed that despite the narrow age range of 15 to 30 years, the age of the subjects had significant relationship with the PR-intervals ($p<0.05$).

Also, the BMI had correlation with the SpO_2 values, mean arterial blood pressure (MAP) as well as their PR-intervals. Furthermore, the BSA had significant influence on the SpO_2 values, MAP and the Rate Pressure Product (RPP) of the subjects. Moreover, the MVC also correlated with weight and may predict left ventricular hypertrophy in young adults. These results advocate that adequate knowledge of differences between people will enhance the methods and strategies of treating associated disorders.

	Mean ± SD	Minimum	Maximum
Systolic BP (mmHg)	117.69 ± 13.241	90	158
Diastolic BP (mmHg)	75.19 ± 9.09	50	92
Pulse Pressure (mmHg)	42.50 ± 11.03	10	74
MAP (mmHg)	89.35 ± 9.30	67.3	114.00
Heart Rate (bpm)	67.5 ± 12.06	44	107
Rate Pressure Product (mmHg)	8002.3 ± 2036.5	4620	14220

Table 4.1.2: Blood Pressure and Its Derivatives

	Mean ± SD	Minimum	Maximum
MVC (kg)	40.96 ± 8.06	26.7	64.5
SpO_2 (%)	96.73 ± 2.06	87	99

Table 4.1.3: Strength and Respiratory Parameters

Variable A	Variable B	P value	Significance
Age (years)	P-R Interval	0.000	Very Significant
BMI (kgm^{-2})	SpO_2	0.042	Significant
BMI (kgm^{-2})	MAP	0.042	Significant
BMI (kgm^{-2})	P-R Interval	0.014	Significant
BSA(m^2)	SpO_2	0.000	Very Significant
BSA (m^2)	MAP	0.014	Significant
BSA (m^2)	RPP	0.042	Significant
MVC (kg)	Weight	0.042	Significant
MVC (kg)	LVH	0.000	Very Significant

Significance Level at $p < 0.05$
BMI = Body Mass Index
BSA = Body Surface Area
MVC =Maximal Voluntary Contraction
SpO_2 = Blood Oxygen Saturation
MAP = Mean Arterial Pressure
RPP = Rate Pressure Product
LVH =Left Ventricular Hypertrophy

Table 4.2.1: Significant relationships Table

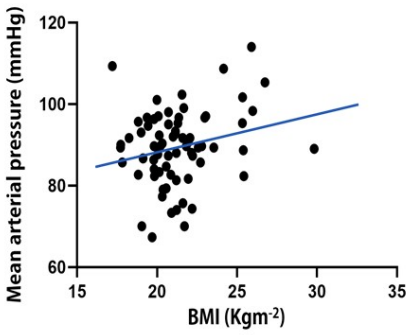

Figure 4.5: Showing correlation of BMI (X-axis) with that of mean arterial pressure (Y-axis) in males. ($P > 0.05$, $Y=0.9384*X+69.35$, $R^2 = 0.054$)

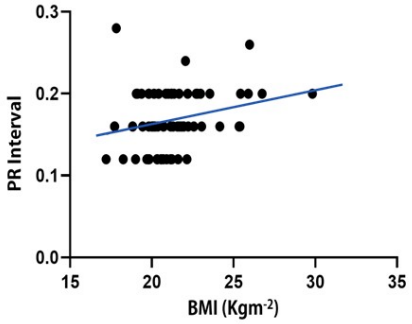

Figure 4.6: Showing correlation of BMI (X-axis) with that of P-R interval in milliseconds (Y-axis) in males. ($Y=0.0042*X+0.0782$, $R^2 = 0.074$)

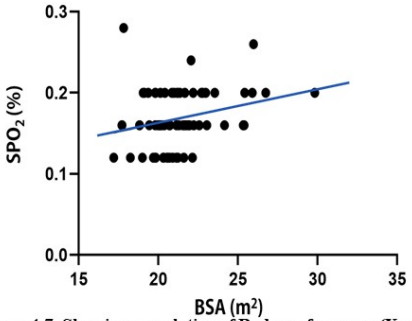

Figure 4.7: Showing correlation of Body surface area (X-axis) with that of Peripheral oxygen saturation (Y-axis) in males. ($P < 0.05$, $Y=4.514*X+88.97$, $R^2 = 0.086$)

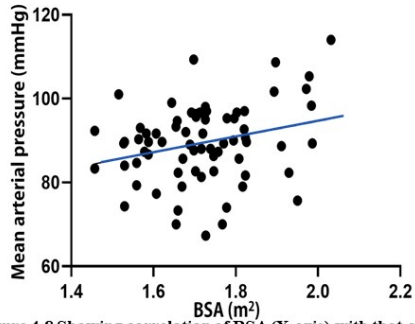

Figure 4.8 Showing correlation of BSA (X-axis) with that of Mean arterial pressure (Y-axis) in males. ($P < 0.05$, $Y=18.73*X+57.17$, $R^2 = 0.073$)

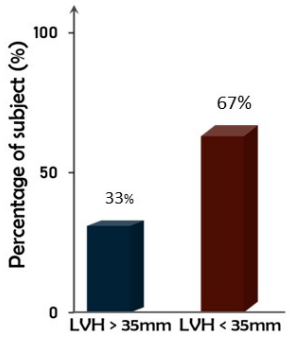

Figure 4.1: The Percentage of Participants that have Left Ventricular Hypertrophy

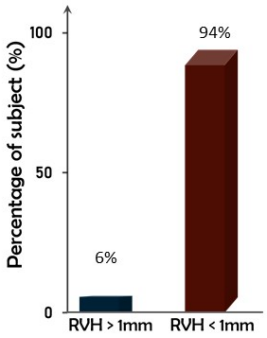

Figure 4.2: The Percentage of Participants that have Right Ventricular Hypertrophy

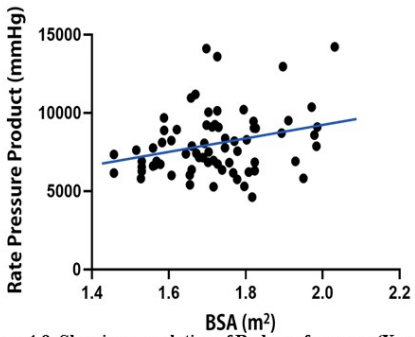

Figure 4.9: Showing correlation of Body surface area (X-axis) with that of Rate pressure product (Y-axis) in males. ($P < 0.05$, $Y=4356*X + 516$, $R^2 = 0.082$)

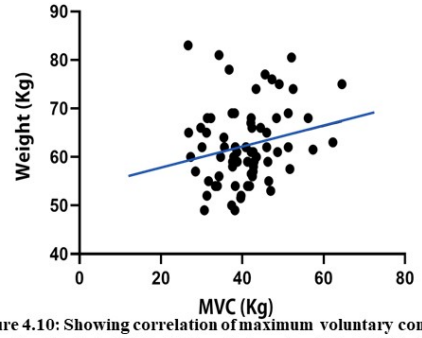

Figure 4.10: Showing correlation of maximum voluntary contraction (X-axis) with that of Weight (Y-axis) in males. ($P > 0.05$, $Y=0.2078*X + 53.87$, $R^2 = 0.043$)

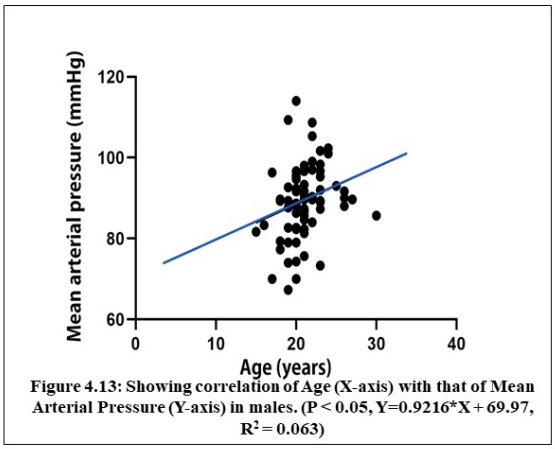

Figure 4.13: Showing correlation of Age (X-axis) with that of Mean Arterial Pressure (Y-axis) in males. ($P < 0.05$, $Y=0.9216*X+69.97$, $R^2 = 0.063$)

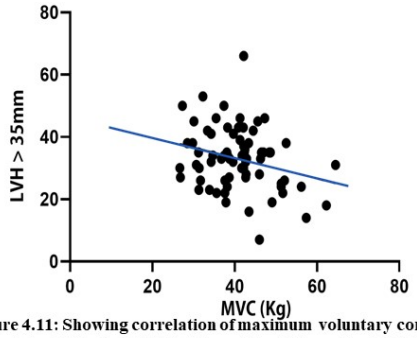

Figure 4.11: Showing correlation of maximum voluntary contraction (X-axis) with that of LVH > 35mm (Y-axis) in males. ($P < 0.05$, $Y=-0.3408*X+47.02$, $R^2 = 0.076$)

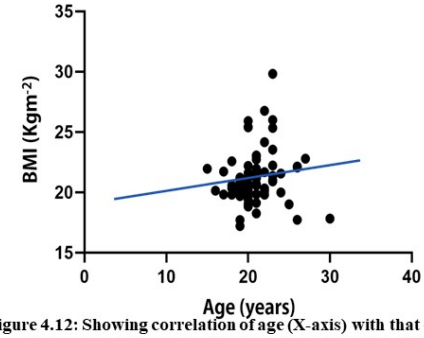

Figure 4.12: Showing correlation of age (X-axis) with that of Body mass index (Y-axis) in males. ($P < 0.05$, $Y=0.0998*X+19.22$, $R^2 = 0.012$)

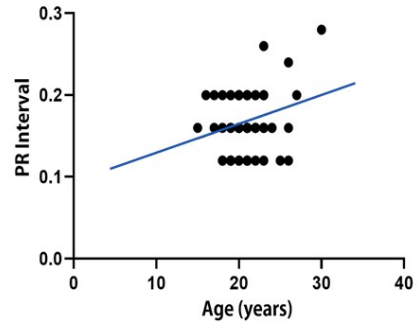

Figure 4.3: Showing correlation of age (X-axis) with that of P-R interval in milliseconds (Y-axis) in males. ($P < 0.05$, $Y=0.0036*X+0.093$, $R^2=0.064$)

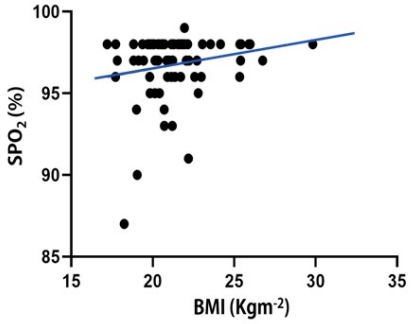

Figure 4.4: Showing correlation of BMI (X-axis) with that of Peripheral oxygen saturation (Y-axis) in males. ($P > 0.05$, $Y=0.1800*X+92.89$, $R^2=0.041$)

	Mean ± SD	Minimum	Maximum
AGE (years)	21.03 ± 2.54	17	26
HEIGHT (m)	1.71 ± 0.07	1.51	1.87
WEIGHT (kg)	62.38 ± 8.07	49	83
BMI (kgm^{-2})	21.32 ± 2.31	17.21	29.82
BSA (m^2)	1.72 ± 0.13	1.46	2.031

Table 4.1.1: Anthropometric Data (N=70). SD=Standard Deviation

	Mean ± SD	Minimum	Maximum
P Wave (secs)	0.1040 ± 0.09	0.06	0.80
P-R Interval (secs)	0.1677 ± 0.36	0.12	0.28
QRS-Complex (secs)	0.0540 ± 0.016	0.04	0.08
RVH=$(R/S)_{V1}$	0.40 ± 0.25	0.06	1.10
LVH=$S_{V1} + R_{V5/V6}$	35.06 ± 9.934	7	66
T Wave Morphology	1.0 ± 0.00	1	3
ST Segment	1.0 ± 0.00	1	2
QT Interval (secs)	0.3507 ± 0.3154	32	48
Cardiac Axis	1.0 ± 0.00	1	3
Rhythm	1.0 ± 0.00	1	1

Abbreviations:

MAP- Mean Arterial Pressure

HR- Heart Rate

RVH- Right Ventricular Hypertrophy

LVH- Left Ventricular Hypertrophy

RPP- Rate Pulse Pressure

BMI- Body Mass Index

BSA- Body Surface Area

SBP- Systolic Blood Pressure

DBP- Diastolic Blood Pressure

PP- Pulse Pressure

MVC- Maximum Voluntary Contraction

Table 4.1.4: ECG Parameters

EVALUATION OF CARDIOVASCULAR, ANTHROPOMETRIC AND STRENGTH VARIABLES' RELATIONSHIP IN APPARENTLY HEALTHY MALE SUBJECTS IN FUTA SOUTH-GATE COMMUNITY

TABLES AND FIGURES

PC0114

Acute Hyperglycemia Attenuates Cerebrovascular Reactivity to CO_2 In Healthy Participants

Anna-Maria Ciorogariu-Ivan[1, 2], Jordan Bird[1, 2], Trevor Day[1, 2]

[1]*Mount Royal University, Calgary, Canada* [2]*The Physiological Society , London, United Kingdom*

Cerebrovascular reactivity (CVR) is one of three regulatory mechanisms to maintain adequate cerebral blood flow (CBF): autoregulation, neurovascular coupling (NVC) and cerebrovascular reactivity (CVR). Autoregulation and NVC have been implicated in blunted responses following an acute glucose load in the context of both healthy individuals and those with metabolic diseases. However, it has yet to be demonstrated if CVR magnitude changes in response to acute glucose loading in healthy participants. The aim of this study was to elucidate the effects of acute hyperglycemia on CVR to increases in carbon dioxide (CO_2). We hypothesized that acute glucose loading would blunt the magnitude of the cerebrovascular response to increases in CO_2 during rebreathing. 23 healthy participants were recruited and subjected to two separate hyperoxic CO_2 rebreathing trials: fasted, and 30-min following ingestion of a standard 300 mL, 75g glucose drink. Blood glucose levels were tested before and after glucose loading, and the difference between these was significant ($P < 0.0001$). CVR was quantified via linear regression during CO_2 rebreathing, with the average CVR slope decreasing from the fasted state (1.37±0.5 cm/s/mmHg) to glucose loaded state (1.04±0.6 cm/s/mmHg; $P=0.005$). This data suggests that relative hyperglycemia significantly blunts the regulatory mechanisms underlying CVR to CO_2, and these results could have implications for those suffering from metabolic disorders like diabetes and populations who regularly consume high carbohydrates diets.

PC0115

Macronutrient Constitution of Parents' Diet Influences Metabolic Enzyme Gene Expression in F2 Generation

Temitope Adedeji[1], Adesoji Fasanmade[2], Emiola Olapade-Olaopa[3]

[1]*Department of Physiology, School, of Health and Health Technology, Federal University of Technology, Akure, Nigeria* [2]*Department of Physiology, College of medicine, University of Ibadan., Ibadan, Nigeria* [3]*Urology Division, Department of Surgery, College of Medicine, University of Ibadan, Ibadan, Nigeria*

Diet has the ability to influence phenotypes, not just in an individual, but also in the progeny. This can be due to developmental programming in the growing offspring *in utero*, especially during critical stages of plasticity during foetal growth and development. Our prior studies have demonstrated that different diets show varying phenotypes, which can be observed in successive generations (Adedeji *et al*., 2019). Thus, we hypothesized that these diets could be causing the early-life programming changes by altering the activity of particular key rate-limiting enzymes of different aspects of metabolism. Eighty (80) Wistar rats of both sexes (F0 generation) were divided into control, high carbohydrate (HCD), high fat (HFD) and high protein diets (HPD) of twenty (20) rats each. They were fed for a period of nine (9) weeks on the diets after which they were mated. F1 sibling pairs from each dietary group were selected randomly (10 males and females respectively from each group) and fed for a period of nine (9) weeks on the experimental diets after a three-week weaning period to give an F2 generation. Liver samples were collected from ten (10) randomly selected weaned pups

from the F2 generation of each dietary group. Real-time qPCR was used to determine enzyme gene expression, in F2 generation not fed the experimental diet. Data obtained were evaluated using analysis of variance (ANOVA) and expressed as mean±SEM. The means (diet vs control) were compared using Tukey-Kramer multiple comparison test. $P<0.05$ was regarded as statistically significant. In F2 generation, HFD (Glucokinase 0.98±0.04 vs 1.49±0.07; Pyruvate kinase 0.88±0.04 vs 1.04±0.02; Glycogen synthase 1.02±0.06 vs 1.33±0.07) and the HPD (Glucokinase 0.54±0.08 vs 1.49±0.07; Pyruvate kinase 0.78±0.08 vs 1.04±0.02; Glycogen synthase 1.03±0.07 vs 1.33±0.07) groups showed a significant decrease ($P<0.05$) in glycolysis and glycogen synthesis gene expression, while the HCD was upregulated (Glucokinase 3.96±0.04 vs 1.49±0.07; Pyruvate kinase 3.64±0.09 vs 1.04±0.02; Glycogen synthase 4.01±0.14 vs 1.33±0.07). HFD (Phosphoenolpyruvate carboxykinase 3.11±0.05 vs 1.02±0.04) and HPD (Phosphoenolpyruvate carboxykinase 3.54±0.09 vs 1.02±0.04) also caused an upward shift in gluconeogenic enzymes gene expression, while HCD (Phosphoenolpyruvate carboxykinase 0.38±0.06 vs 1.02±0.04) reflected downregulation. The HCD (AcetylcoA carboxykinase 3.88±0.06 vs 1.08±0.12; Fatty acid synthase 4.27±0.07 vs 2.00±0.03) and HFD AcetylcoA carboxykinase 3.79±0.06 vs 1.08±0.12; Fatty acid synthase 4.78±0.03 vs 2.00±0.03) reflected significant upregulation ($P<0.05$) in expression of fatty acid biosynthesis gene expression. The HPD (AcetylcoA carboxykinase 0.34±0.05 vs 1.08±0.12; Fatty acid synthase 0.28±0.05 vs 2.00±0.03), on the other hand, showed downregulation. HPD (Carnitine palmitoyltransferase 1.60±0.04 vs 1.28±0.07; acyl CoA oxidase I 0.82±0.06 vs 0.83±0.04) and HFD (Carnitine palmitoyltransferase 1.48±0.04 vs 1.28±0.07; acyl CoA oxidase I 0.45±0.08 vs 0.83±0.04) groups expressed upregulation of β-oxidation genes, while HCD (Carnitine palmitoyltransferase 0.87±0.05 vs 1.28±0.07; acyl CoA oxidase I 0.70±0.07 vs 0.83±0.04) showed downregulation. The results of this study suggest that prenatal parental diet affects the expression of genes rate-limiting enzymes involved in metabolism, with an effect observed in F2 generation.

Reference 1 :- Adedeji TG, Fasanmade AA, Olapade-Olaopa EO.Multigenerational effects of dietary macronutrient intake on the metabolic phenotype of male Wistar rats.Nutrition. 2019; 58:125-133. https://doi.org/10.1016/j.nut.2018.06.008.

PC0116

The membrane cholesterol modulates the 17-βEstradiol effect on the BK channel

Sara T. Granados[1], Yolima Torres[1]

[1]*Departamento de Nutrición y Bioquímica, Facultad de Ciencias, Pontificia Universidad Javeriana, Bogotá, Colombia*

BK channel is ubiquitously expressed. In vascular cells it is expressed with the accessory β1 subunit, where they play an important role in the modulation of arterial tone and blood pressure. Modifications on the cholesterol concentration in the cellular membrane can lead to changes on the BK channel activity, which could affect the interaction of BK channel with other regulatory molecules like 17β-Estradiol (E2). The aim of this research was to evaluate the effect of the changes on cholesterol membrane concentration in the Estradiol-BK channel interaction. HEK 293 cells were

transfected with human BKα (U11058) and/or BKβ1 (U25138) harbored in pcDNA3.1 plasmids. Cholesterol depletion was conducted in transfected cells with MbCD treatment. BK membrane expression was analyzed by flow cytometry and confocal microscopy. Cells were treated with E2-BSA-FITC and binding assays were carried out using confocal microscopy and flow cytometry. Patch clamp recordings in inside out configuration was used to determinate the E2 modulatory effect on BK channel. Cholesterol depletion increased BKα subunit expression in α/β1 co-transfection (from 85±2.3 to 94±1.2%) with any change in the β1 subunit expression alone (from 89±1.5 to 93±1.2) or in co-expression with α (from 92±1.3 to 95±1.0). These results suggest that the BK channel expression is modulated by membrane cholesterol concentration. After cholesterol depletion we found an increase in the E2 binding to the β1 subunit, when it is expressed alone (from 5.5±0.2 to 6.8±0.3. n = 3; $P \leq 0.01$) but not in α/β1 co-transfection. When we evaluated the effect of cholesterol depletion on the E2-BK channel interaction, we observed that the activation kinetics of the BKα/β1 complexes was not affected. However, cholesterol depletion prevents the modulatory effect of E2 on the channel, since the half-maximal activation potential ($V_{0.5}$) remains the same after the E2 stimuli (from 137±4mV to 140±4mV after depletion). These data suggest that changes in membrane cholesterol concentration causes the loss of the modulatory effect of the E2 on the BKα/β1 channels, which is not related with the BKα or β1 subunits expression.

Acknowledgements :- Pontificia Universidad Javeriana, Grant ID5571 (Yolima P. Torres)

PC0118

How intranasal insulin regulates feeding behavior in the mice

Niannian Wang[1]

[1]*Niannian Wang, Leeds, United Kingdom*

In recent years, it is becoming increasingly apparent that insulin signaling regulates neural circuits in the brain, playing roles in the control of appetite, cognition and memory. However, the detailed action of insulin in the brain has not yet been fully explained, especially in respect of food intake. Here, firstly we performed intranasal FITC-insulin to track the distribution of insulin receptor in the mice brain to highlight the areas of the brain that intranasal delivery can reach. In addition, monitored the metabolic changes after delivering intranasal Standard-insulin in mice. Our results show that the insulin receptors distribute many areas of mice brain, including olfactory bulb, nucleus of the horizontal limb of the diagonal band, hippocampus, and brainstem. And the intranasal insulin could reduce food consumed and oxygen consumption, and ambulatory activity. Overall, our data indicates that intranasal delivery of insulin is a good way to target areas of the brain important for controlling energy balance. Due to the metabolic effect that intranasal insulin have both in rodents and humans, further studies are warrant in order to understand the which insulin sensitive neurons are involved in this process.

PC0119

An Investigation of Subtypes of Purinergic-2X Receptors and their effects on Myometrial Contractility in Laboring and non-Laboring Women

Hind Zafrah[1], Susan Wray[2]

[1]Hind Zafrah, Liverpool, United Kingdom [2]Susan Wray, Liverpool, United Kingdom

Objectives: Dystocic labour, also known as slow to progress in labour, represents an important clinical and research challenge (Wiberg-Itzel et al., 2018). The uncoordinated myometrial contractions associated with dystocia cannot dilate the cervix, and thus ultimately end with an unplanned caesarean delivery. Adenosine triphosphate (ATP) is an extracellular signalling molecule regulating numerous physiological and pathophysiological conditions (Burnstock, 2017). The stressful situations associated with each contraction during labour can result in ATP release into the extracellular milieu. Animal model experiments have shown that extracellular ATP increases uterine contractions (Zafrah et al., 2017). Further studies have suggested that ATP stimulate P2X7receptos P2X7R (Miyoshi et al., 2012, Alotaibi, 2018). Therefore, we hypothesized that ATP binding to P2X7Rs could be used for labour augmentation. My study was designed to examine the effect of ATP and its analogues, ATPɣS (a non-hydrolyzing form of ATP) and BzATP (a more potent agonist at the P2X7R) on human myometrial contractility. To further determine P2X7R roles in mediating this action, selective antagonists, A-438079 and A-740003, were used. **Methods**: The responses of human term pregnant myometrium to ATP, ATPɣS, BzATP, the effects of A-438079 and A-740003 were investigated using tissue baths and measuring contractility. **Results:** Agonists caused concentration-dependent contractions with rank order of ATPɣS> BzATP>ATP. The contractions to ATP and BzATP were reduced in response to P2X7 antagonists but these effects were not significant. **In conclusion**; P2X7R appears to be only partially involved in mediating the contractile responses of the tissues to ATP. **Further work:** I have three aims. Firstly, to compare the effect of ATP on myometrial contractions in biopsies from labouring women, some of whom will have been labouring dysfunctionally. Comparing failure to progress vs. fetal distress will test whether reduced responses to extracellular ATP contribute to failure to progress, and our understanding of the underlying mechanism of action of ATP. Secondly, to identify the expression of P2X7 receptors in the myometrium, I will undertake western blot analysis. Thirdly, I will undertake immunohistochemistry to understand the localization of P2X7 receptors in human uterine tissues.

Reference 1 :- WIBERG-ITZEL, E., WRAY, S., ÅKERUD, H. J. T. J. O. M.-F. & MEDICINE, N. 2018. A randomized controlled trial of a new treatment for labor dystocia. 31**,** 2237-2244.

Reference 2 :- BURNSTOCK, G. J. F. I. P. 2017. Purinergic signalling: therapeutic developments. 8**,** 661.

CODDOU, C., YAN, Z., OBSIL, T., HUIDOBRO-TORO, J. P. & STOJILKOVIC, S. S. J. P. R. 2011. Activation and regulation of purinergic P2X receptor channels. 63**,** 641-683.

Reference 3 :- ZAFRAH, H. A., ALOTAIBI, M. F. J. J. O. B., PHYSIOLOGY, C. & PHARMACOLOGY 2017. The effect of extracellular ATP on rat uterine contraction from different gestational stages and its possible mechanisms of action. 28**,** 209-217.

Reference 4 :- MIYOSHI, H., YAMAOKA, K., URABE, S. & KUDO, Y. J. R. S. 2012. ATP-induced currents carried through P2X7 receptor in rat myometrial cells. 19**,** 1285-1291.

Reference 5 :- ALOTAIBI, M. 2018. Changes in expression of P2X7 receptors in rat myometrium at different gestational stages and the mechanism of ATP-induced uterine contraction. *Life sciences,* 199**,** 151-157.

PC0120

Neuromuscular function and motor unit firing following 4 weeks of motor control training

Isabel A. Ely[1], Siobhra Dooley[1, 2], Sarah B. J. Miller[1, 2], Bethan E. Phillips[1], Mathew Piasecki[1]

[1]MRC Versus Arthritis Centre for Musculoskeletal Ageing Research & NIHR Nottingham BRC, University of Nottingham, Derby, United Kingdom [2]School of Agriculture, Food Science and Veterinary Medicine, University College Dublin, Dublin, Ireland

Muscle strength is a function of muscle size and neural mechanisms and is important for the completion of tasks associated with daily living, including walking and standing balance (1). Such tasks are conducted by multiple muscles in unison, meaning intramuscular factors, neural capacity and levels of muscle coordination are all required for efficient and successful movement (1). Muscle strength decreases at a greater rate than muscle mass in older age (2), with a concurrent age-related decrease in the level of motor control (MC; 3), both of which are largely explained by neuromuscular factors including declines in motor unit (MU) number and the influence of MU remodelling (4). Although forms of exercise training, such as resistance exercise, may attenuate these decrements and improve neuromuscular function (5), these are often unachievable for older individuals. We therefore investigated whether targeted motor control training (MCT) could lead to improved muscle functional capacity and control, and alterations of individual MU function.

Six healthy young volunteers (4 females; age, 25.2±5.8 years; BMI, 22.5±4.0 $kg.m^{-2}$) underwent a 4-week supervised multiple-muscle MCT intervention. MCT was completed unilaterally, 3 x per week, consisting of 6 complex isometric muscle contractions for the knee extensors (KE) and dorsi flexors (DF) in a randomised order at 10, 25 and 40% of an individuals predetermined maximal voluntary contraction (MVC). Levels of MC, derived from complex oscillating force tracking tasks (differing to those completed as part of MCT), were represented as the level of deviation from the target line. Straight line force steadiness (FS) was additionally determined at 10, 25 and 40% MVC. Intramuscular electromyography (iEMG) was utilised to sample individual MUs from the vastus lateralis (VL) and tibialis anterior (TA) muscles during sustained contractions, prior to and post intervention. Data were analysed by paired Student's t-test, with statistical significance accepted at $p<0.05$.

Both MVC and FS showed no differences for KE and DF following 4 weeks MCT. KE complex forcing tracking improved following MCT at 10% MVC (-39.24%, *p*=0.005), 25% MVC (-28.62%, *p*=0.043) and 40% MVC (-29.13%, *p*=0.015). DF complex force tracking also significantly improved post intervention at each contraction intensity (10% MVC, -25.73%, *p*=0.002; 25% MVC, -33.35%, *p*=0.0006; 40% MVC, -30.06%, *p*=0.049). Although MU firing rate (FR) remained unchanged across both muscles, FR variability significantly reduced post intervention in VL only (*n*=5; -16.36%, *p*=0.031).

Our results suggest improved levels of MC following MCT at different contraction intensities and, importantly, across different muscle groups. Such improvements in MC may be explained by the observed reduction in FR variability. These data from young individuals suggest MCT may lead to substantial improvements or maintenance of muscle control in older adults, an area to be subsequently explored, to aid mechanistic insight into the plasticity of movement control across the lifespan.

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PC0121

N$^{\omega}$-Nitro-L-Arginine Methyl Ester (L-NAME) induces liver dysfunction in male albino Wistar rats which is attenuated by Curry Tea intake

Williams Nabofa[1], Ime Ani[1], Olutayo Omobowale[2], Ajuzie Nnenna[1], Jubilee Ajemigbitse[1], Akinola Alada[3]

[1]Babcock University, Ilishan-Remo, Nigeria [2]University of Ibadan, Ibadan, Nigeria [3]Department of Physiology, College of medicine, University of Ibadan., Ibadan, Nigeria

Background: Nitric oxide (NO) bioavailability is important for the normal metabolic function of the liver. *Murraya koenigii* has been reported to positively affect liver function. However the effect of *Murraya koenigii* as tea on N^{ω}-Nitro-L-Arginine Methyl Ester (L-NAME) induced liver dysfunction is unknown.

Aim: The present study was thus designed to investigate the effect of *Murraya koenigii* leaves as tea on L-NAME induced liver dysfunction.

Material and Methods: Curry tea was produced either entirely from the dried and powdered leaves of *Murraya koenigii* or with aril of *Thaumatococcus danielii.* The 2 different Curry tea types were administered for 21 days to adult male albino Wistar rats divided into 6 groups (n=8). Group I animals served as control and were given 0.5ml/Kg of distilled water. Groups II and V animals were administered with curry tea (CT). Group III and VI animals were administered with curry thaumatin tea (CTT). Concurrently, L-NAME (40mg/kg) was administered to groups IV-VI respectively for 21 days. Blood and liver samples were collected at the end of the study for biochemical, histological and immunohistochemical analysis.

Results: L-NAME induced liver dysfunction evidenced by liver histology, increased activities of ALT, AST, hyperlipidemia, hepatic oxidative stress and increased hepatic NfKb expression. CT and CTT intake ameliorated the L-NAME induced liver dysfunction evidenced by liver histology, increased NO hepatic bioavailability, reduced activity of ALT and AST, increased hepatic antioxidant system and decreased hepatic NfKb expression. Thaumatin added to curry as tea didn't significantly reduced the hepatoprotective, antioxidant and anti-lipidemic property of curry tea intake in rats.

Conclusion: Non-selective inhibition of NO impaired liver function in rats. Curry administration as tea interfered with the ability of L-NAME to inhibit NO synthesis and this interference was associated with improved hepatic function in rats.

PC0123

Polyethylene Glycol 35 (PEG35) protects against inflammation in experimental of acute necrotizing pancreatitis and associated lung injury.

Ana Ferrero-Andrés[1], Arnau Panisello-Roselló[1], Anna Serafin[2], Joan Roselló-Catafau[1, 3], Emma Folch-Puy[1, 3]

[1]Institute of Biomedical Research of Barcelona (IIBB - CSIC) , Barcelona, Spain [2]PCB Animal Facility-Parc Científic of Barcelona, Barcelona, Spain [3]Center of Biomedical Research Network of Hepatic and Digestive Diseases (CIBEREHD), Institute of Biomedical Research August Pi i Sunyer (IDIBAPS), Barcelona, Spain

Acute pancreatitis is an inflammatory disorder of the pancreas. Its presentation ranges from self-limiting disease to acute necrotizing pancreatitis (ANP) with multiorgan failure and a high mortality

(1). Currently, the medical treatment for this disease still remains supportive and directed to prevent the systemic complications. Polyethylene glycols (PEGs) are non-immunogenic, non-toxic, and water-soluble chemicals composed of repeating units of ethylene glycol (2). They are widely accepted by the Food and Drug Administration for use in food, cosmetic, and pharmaceuticals. In clinical, they are currently used as additives to organ preservation solutions to attenuate the damage associated with cold ischemia-reperfusion (3). The present study explores the effect of 35-kDa PEG (PEG35) administration on reducing the severity of ANP and associated lung injury.

Male Wistar rats were housed in a controlled environment following all European Union regulatory standards for animal experimentation (Directive 2010/63/EU on the protection of animals used for scientific purposes). The Ethical Committee for Animal Experimentation (CEEA, ethic approval number: 211/18, University of Barcelona, 11/04/2018) approved the animal experiments.

Rats were anesthetized with an intraperitoneal injection of pentobarbital (50 mg/kg). Then, ANP was induced by injection of 5% sodium taurocholate into the biliopancreatic duct. PEG35 was administered intravenously in a single dose (10 mg/kg) either prophylactically or therapeutically. Three hours after ANP induction, animals were euthanized, and samples were evaluated. Histopathological examination of pancreatic and lung tissue was accomplished choosing randomly microscopic fields. Secondarily, plasma lipase activity was measured to determine the severity of the pancreas damage. To evaluate the inflammatory response, gene expression of pro-inflammatory cytokines (IL-6, IL-1β, and TNF-α) and chemokine (CXCL-2) and the changes in the presence of myeloperoxidase and adhesion molecule levels (p-selectin and ICAM-1) were determined in both the pancreas and the lung. To study the cell death, lactate dehydrogenase (LDH) activity and apoptotic cleaved caspase-3 localization were determined in plasma and in both the pancreatic and lung tissue, respectively.

Lipase activity was diminished with the PEG35 pre-treatment in both pancreas and lung, while the therapeutic administration was not able to reduce the pancreas injury. However, PEG35 reduced the histopathological injuries in lung tissue when it was administered therapeutically. We also showed the levels of proinflammatory cytokines and chemokine were significantly decreased when PEG35 had been administrated after ANP induction. In addition, therapeutic administration of PEG35 lessened neutrophil recruitment and extravasation in the lung, indicating a significant protection against the systemic complications. To further study, we observed that therapeutic treatment with PEG35 significantly reduced the expression of P- selectin and ICAM-1 in the lung. Finally, on inflammation induced cell-death, the therapeutic treatment with PEG35 significantly reduced LDH activity and the cleaved caspase-3 levels in the lung.

Collectively, our data highlight the potential use of PEG35 as a treatment to ameliorate the severity of the inflammatory damage in acute pancreatitis and to modulate its progression to a lethal condition (4).

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PC0126

regular gait changes the perfusion adaptation in the foot specially in older individuals

Margarida Florindo[1, 2], Sérgio Miguel Loureiro Nuno[1, 3, 4], Luis Monteiro Rodrigues[1]

[1]Universidade Lusófona CBIOS - Research Center for Biosciences and Health Technologies, Av Campo Grande, 376, 1749-024, Lisboa, Portugal [2]Escola Superior de Saúde Cruz Vermelha Portuguesa (ESSCVP), Portuguese Red Cross Health School. Área de Ensino de Fisioterapia, Department of Physiotherapy, Lisboa, Portugal [3]Clínica S João de Deus – CTD, Lisboa, Portugal [4]Escola Superior de Tecnologia da Saúde de Lisboa – Instituto Politécnico de Lisboa, ESTeSL Polytechnic Institute of Lisbon, Av. D. João II, Lote 4.69.01, Lisboa, Portugal

Alterations of the lower limb perfusion in particularly in the foot, are regarded as relevant manifestation of ageing. However objective information on this subject is still insufficient, often complicated by the prevalent co-morbidities (e.g. overweight, diabetes) that affect this population. Our aim was to identify any perfusion changes detected before and after a period of 5 min of walking within two different age groups. This pilot involved eight healthy individuals, all reporting non-sedentary lifestyles, practicing regular exercise, grouped according to age – Group I with young adults (21.7 ± 1 y.o.) with a body mass Index (BMI) of 22.9 ± 1,6 Kg/m^2 and Group II older adults, 54.5 ± 3 y.o and BMI 23.7 ± 1.9 Kg/m^2. Both groups included two men and two women. The evaluation protocol was divided into two phases, each with 5 minutes duration - phase 1 – standing still position before starting walking (baseline) and phase 2 a standing still register after 5 min walking, with a comfortable pace, in the lab area on a pre-established circuit. Perfusion was assessed in the dorsal region of both feet by Laser Doppler flowmetry (Perimed S), photoplethysmography (Bioplux, P) and polarised spectroscopy (TiVi, Wheelsbridge, S) providing assess at different depths, according with the respective wavelengths. Phase 1 measurements have shown that perfusion in group II is always lower than in group I but not statistically significant (ns). Also interesting, measurements obtained immediately after walking, in phase 2, have shown a clear reduction of perfusion in all participants, regarding phase 1 (ns). This is probably due to the muscular activation still high. Recover to baseline values takes place slower in group II. However, no significant differences between groups could be

found for any of the measured variables. Our study involves a very reduced number of participants, all healthy and active. Nevertheless the age-related reduction in vascular function reported in literature is present and should be further investigated in different pathophysiological conditions.

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PC0128

Blubber morphology responses to changes in fatness in grey seals

Laura Oller[1], Mark Dagleish[2], Joel Rocha[1], Ailsa Hall[3], Kimberley Bennett[1]

[1]Abertay University, Dundee, United Kingdom [2]Moredun Institute, Edinburgh, United Kingdom [3]SMRU - University of St Andrews, St. Andrews, United Kingdom

With oceans warming, marine mammals might face additional physiological challenges to maintaining energy and thermal balance. Seals' insulation and energy storage depend on blubber thickness. Blubber has a thermal conductivity gradient and metabolic stratification, suggesting it might also be morphologically stratified. However, grey seals alternate fasting and feeding periods and therefore undergo natural periodic changes in blubber thickness. Seal's energetic reservoir and thermoregulation capacity thus fluctuates annually. In autumn, pregnant females come ashore to give birth, where they will face additional heat dissipation constrains with different air temperatures and humidity than at sea. Females fast during lactation, therefore diminishing fat stores. In contrast, pups triple their size during the three weeks suckling period. The fatter they get, the more likely they are to survive their first year. Females face a trade-off between fattening their pups and keeping enough blubber for their own survival upon returning to sea. Quick adaptation to thermal and energy needs is vital for seals and its balance can be affected by raising temperatures. Better understanding on how seals' blubber morphology adjusts to body composition changes is needed to predict potential responses to climate warming. Here we investigated how fat cells and vascularity change throughout blubber depth during weight fluctuations at different age classes in wild grey seals. Blubber biopsies from the dorsal flank were collected from mother and pup pairs (n=6) at early and late lactation and at pup's early weaning. Appropriate Zoletil age dependant dose (Females: 0.01mL/Kg, IM; pups: 0.002 mL/Kg, IV) and Lignol (2mL, SC) were administrated as anaesthetics by experienced licensed personnel. Samples were fixed in formalin, processed and stained with Masson's Trichrome. Blubber was divided into three depth sections: inner, middle and outer. Five microphotographs of each section were taken, and adipocyte size and vascularity were analysed with Image J. Linear mixed models were used to investigate association with body mass, tissue depth and feeding *vs* fasting within each age class. Preliminary results showed adipocyte size was positively associated with body mass in both mothers (LME: AIC=493.6; N=6; n=30, p=0.03) and pups (LME: AIC=700.9; N=6; n=46, p<0.01). However, pups' adipocytes are smaller than their mothers' (mothers = 4018 ± 898 μm^2, pups 3360 ± 1310 μm^2), despite pups' fat percentage being generally higher than mothers at this stage. Vascularity was not significantly associated with any measurements in mothers. However, in pups, vascularity increases at late suckling, particularly in the inner and middle

blubber. These results suggest angiogenesis happens alongside adipogenesis, but it is independent from adipocytes hypertrophy. Analysis distinguishing between capillaries *vs* big blood vessels is underway to investigate the perfusion capacity during extreme fattening and fasting. Based on these results, grey seals' blubber structure is not morphologically stratified across depth except at early age, when tissue is expanding for first time. Insulation capacity will be affected by the dramatic fatness fluctuations during breeding season, with no apparent morphological changes in vascularity to counteract thermoregulatory constrains. Changing environment is a concern to maintain the delicate trade-off female seals face during breeding season.

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PC0129

Exogenous reactive oxygen species cause acutely mitochondrial complex I dysfunction in skeletal muscle

Ryan Awadhpersad[1], Rob Wüst[1]

[1]Laboratory for Myology, Department of Human Movement Sciences, Faculty of Behavioral and Movement Sciences, Vrije Universiteit Amsterdam, Amsterdam, The Netherlands

The mitochondrial consequences of reactive oxygen species (ROS) are commonly implicated in many acute and chronic diseases. Generally, ROS damage can be caused by various ROS-generating enzymes such as xanthine and NADPH oxidase, reverse electron transfer flow at complex I, and various environmental factors. ROS damage leads to a reduced mitochondrial function, via 1) cytochrome c release leading to mitophagy and apoptosis, 2) membrane damage leading to mitochondrial uncoupling, 3) cardiolipin peroxidation and 4) cristae remodelling. Studying the effect of ROS on mitochondrial function is complicated by the fact that the initial alteration in mitochondrial function is unknown, and a vicious cycle of damage-mediated ROS-damage is generally assumed. What the initial alterations in mitochondrial bio-energetic function are after acute ROS exposure is surprisingly little understood. Here, we determined the acute effects of pyrogallol, a superoxide ($O_2^{\cdot-}$) and hydrogen peroxide (H_2O_2) donor on mitochondrial respiration in permeabilized skeletal muscle fibres.

Methods Mitochondrial respiration of ~5 mg soleus muscle from 8 <1 year-old female Wistar rats was measured by a substrate-uncoupler-inhibitor-titration protocol using high-resolution respirometry (Oroboros, Austria). NADH-linked respiration was measured after the addition of malate, pyruvate and 5 mM ADP. Outer-mitochondrial membrane integrity was assessed by cytochrome c. Oxidative phosphorylation (OXPHOS) capacity was measured after additional succinate, and maximal uncoupled electron transport capacity by FCCP. Mitochondrial complex I was

blocked by rotenone to assess succinate-linked respiration. Values after the addition of 0 (CON), 50 and 100 µM pyrogallol were compared by ANOVA. Since pyrogallol converts oxygen into $O_2^{\cdot-}$ and H_2O_2, we corrected for this increased background respiration.

Results Mitochondrial leak respiration was significantly lower after pyrogallol exposure (both p<0.001), with the lowest values at the highest pyrogallol concentration. NADH-stimulated respiration was lower after exposure to 100 µM (16±9 pmol O_2/s/mg; mean±SD) compared to 50 µM (49±13 pmol O_2/s/mg) compared to CON (56±9 pmol O_2/s/mg). Maximal OXPHOS only tended to be lower after 100 µM pyrogallol (p=0.07). Succinate-linked respiration was not different between groups (p=0.61), indicative of mitochondrial complex I dysfunction upon acute exposure to pyrogallol. This was confirmed by a lower normalised respiration for NADH-substrates after 50 µM pyrogallol (0.50±0.12) and 100 µM pyrogallol (0.31±0.15) versus CON (0.60±0.08, p=0.003). Normalised succinate-linked respiration was significantly higher after pyrogallol exposure (p=0.04). There was a dose-dependent effect on mitochondrial outer-mitochondrial membrane damage after pyrogallol exposure.

Conclusion The acute exposure of skeletal muscle to $O_2^{\cdot-}$ and H_2O_2 resulted in complex I dysfunction and mitochondrial outer-membrane damage, possibly due to mitochondrial supercomplex instability. Future experiments are aimed to understand whether ADP-sensitivity is altered after pyrogallol exposure and if stabilizing cardiolipin with SS-31 can alleviate these negative effects.

PC0132

Effect of Sub-maximal Exercise Stress on Cold Pressor Pain: A Gender Based Study in Engineering students of National College of Engineering, Nepal

Ehsan Ansari[1], akram ansari[2]

[1]National College of Engineering , Lalitpur Kathmandu , Nepal [2]Dhaka Community Medical College, 190/1, Baro Moghbazar, Wireless Rail gate, Dhaka-1217, , Bangladesh

Analgesic effect of exercise is long been debated and controversial topic as it may result in hyperalgesia or hypoalgesia. The aim of the study is to compare the effect of exercise on cold induced acute pain in male and female. The subjects were asked to immerse his/her dominant hand in ice cold water (20 to 40C) and pain threshold (start of feeling pain) and pain tolerance time (total time up to which pain can be tolerated) were recorded. Blood pressure, heart rate and respiratory rate were recorded during and after cold pressor pain test and exercise to study cardiovascular effects. To minimize the analgesic effects of female sex hormones, experiments on females were done in mid-luteal phase (21 to 24 days of menstrual cycle). For exercise, bicycle ergometer was used. Initial load for exercise was 25 watts, which increases with 25 watts at the interval of every 2 minutes and exercise was continued until the heart rate reached the 60 to 75 % of the maximal heart rate for that subject. There was significant increase in all pain parameters just after exercise (Pain threshold from 14.25 ±10.2 sec to 20.83±13sec after exercise, p< 0.001; pain tolerance from 39.5 ±25

sec to 54.67±31 sec, p<0.001). Exercise had much effect on pain tolerance than pain threshold (from 26.2±20 sec to 36.2±23.5 sec, p<0.01). The effect of exercise on pain perception was significant in both male and female, the analgesic effect being more enhanced in female than male. Exercise-induced hypoalgesia: potential mechanisms in animal models of neuropathic pain. Schmitt A, Wallat D, Stangier C, Martin JA, Schlesinger-Irsch U, Boecker H.et al., Eur J Pain. 2019 Nov. doi: 10.1002/ejp.1508. [Epub ahead of print] Exercise-induced hypoalgesia: A meta-analysis of exercise dosing for the treatment of chronic pain. Polaski AM, Phelps AL, Kostek MC, Szucs KA, Kolber BJ. PLoS One. 2019 Jan 9;14(1): e0210418 The analgesic effect of music on cold pressor pain responses: The influence of anxiety and attitude toward pain. Choi S, Park SG, Lee HH. PLoS One. 2018; 6: 13(8). Exercise-induced hypoalgesia: potential mechanisms in animal models of neuropathic pain. Kami K, Tajima F, Senba E. Anat Sci Int. 2017; 92(1):79-90. The Effects of Cold Pressor-Induced Pain on PASAT Performance. Tapscott BE, Etherton J. Appl Neuropsychol Adult. 2015; 22(3):227-32. The Effects of Cold Pressor-Induced Pain on PASAT Performance. Tapscott BE1, Etherton J. Appl Neuropsychol Adult. 2015;22(3):227-32.

PC0133

Experience-Dependent Cardiorespiratory Effects Resulting from Two Patterns of Acute Intermittent Hypoxia in Healthy Humans

Joanna Keough[1], Michael Tymko[1, 2, 3], Lindsey Boulet [1, 2], Glen Foster[2], Alenna Jamieson[1], Trevor Day[1]

[1]Mount Royal University, Calgary, Canada [2]University of British Columbia Okanagan , Kelowna, Canada [3]University of Alberta, Edmonton, Canada

Peripheral respiratory chemoreceptors monitor breath-by-breath changes in arterial CO_2 and O_2, mediating ventilatory changes through a peripheral chemoreflex. Intermittent bouts of hypoxia (IHx) elicit hypoxic ventilatory responses, with well-described experience-dependent effects (EDEs), mostly from work in animal models using 5-min intermittent bouts. These EDEs include post-hypoxia frequency decline (PHxFD), progressive augmentation (PA), and long-term facilitation (LTF). Comparisons of these EDEs between animal models and humans using similar IHx protocols have not been extensively performed. In addition, whether shorter bouts of IHx elicit EDEs in humans is unknown. Respiratory (frequency, inspiratory tidal volume and minute ventilation; f_R, V_{TI} and $\dot{V}_I$) and cardiovascular (heart rate and mean arterial pressure; HR and MAP) variables were measured during and following two patterns of acute isocapnic IHx in 14 healthy human participants: 5x5-min on/off and 5x90-sec on/off (normoxia vs. hypoxia [45 Torr $P_{ET}O_2$]) using steady-state dynamic end-tidal forcing. We found that (a) PHxFD and PA were not present in either pattern of IHx (P>0.14), but that (b) LTF was present in $\dot{V}_I$ following 5-min on/off IHx (P<0.001) and 90-sec on/off IHx (P<0.001) and (c) LTF was present in MAP following 5-min on/off IHx (P<0.001) but not following 90-sec on/off IHx (P=0.058). Our data suggest that (a) most EDEs characterized in animal models in response to acute IHx are absent in healthy humans and/or absent following shorter IHx bouts and (b) caution should be exercised when using reduced animal models to extrapolate understanding of human responses

to blood gas perturbations.

PC0136

Time Course and Magnitude of Ventilatory and Renal Acclimatization Following Rapid Ascent and Residence to 3800m over Nine Days

Jordan Bird[1], Glen Foster[2], Caroline Rickards[3], Jack Leacy[4], David Burns[4], Ken O'Halloran[4], Nick Jendzjowsky[5], Richard Wilson[5], Craig Steinback[6], Peter Ondrus[6], Trevor Day[1]

[1]Department of Biology, Faculty of Science and Technology, Mount Royal University, Calgary, Canada [2]Centre for Heart, Lung, and Vascular Health, School of Health and Exercise Sciences, University of British Columbia, Kelowna, Canada [3]Cerebral & Cardiovascular Physiology Laboratory, Department of Physiology & Anatomy, University of North Texas Health Science Center, Fort Worth, Texas, The United States of America [4]Department of Physiology, School of Medicine, College of Medicine and Health, University College Cork, Cork, Ireland [5]Hotchkiss Brain Institute, Cumming School of Medicine, University of Calgary, Calgary, Canada [6]Neurovascular Health Laboratory, Faculty of Kinesiology, Sport, and Recreation, University of Alberta, Edmonton, Canada

Rapid ascent to high altitude imposes an acute hypoxia and acid-base challenge. Several interrelated acclimatization processes work to counter these perturbations, in part through ventilatory and renal systems. Specifically, a hypoxic ventilatory response (HVR) improves oxygenation, but elicits acute hypocapnia and respiratory alkalosis. In response, the kidney tubules eliminate bicarbonate, eliciting a compensatory relative metabolic acidosis, protecting arterial pH(a). However, the time course and magnitude of these acclimatization processes are highly variable between-individuals and between organ systems. Using a previously developed metric of renal reactivity (RR) that indexes the relative change in arterial bicarbonate concentration ($\Delta[HCO_3^-]a$; i.e., renal response) over the relative change in arterial pressure of CO_2 ($\Delta PaCO_2$; i.e., renal stimulus), we aimed to assess whether: (a) RR magnitude increased with duration at altitude and (b) whether RR was inversely correlated with relative changes in pH (ΔpHa) with time spent at altitude. Resident lowlanders (n=16) were tested at 1045m (day 0) prior to ascent, and on days D2 and D9 upon arrival and during residence at 3800m. On days 0, 2 and 9, arterial blood draws from the radial artery were obtained to measure and/or calculate blood gas variables PaO_2, [Hb], SaO_2 and CaO_2, and acid-base variables $PaCO_2$, $[HCO_3^-]a$ and pHa. RR increased from D2 to D9 ($P=0.056$), suggesting plasticity in renal acid-base compensatory mechanisms. We observed a strong negative correlation between RR and ΔpHa from baseline on D2 and D9 ($r \leq -0.95$; $P<0.00001$). The high variability in blood gas and acid-base variables on D2 suggests three distinct phenotypes for how individuals acclimatize within the first 24 hours of altitude exposure: (a) no HVR, and thus no renal compensation, (b) HVR with no renal compensation and (c) HVR with renal compensation. Our study highlights the differential time course and magnitude of ventilatory and renal acclimatization following rapid ascent and residence at high altitude.

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PC0137

Respiratory muscle dysfunction in the *mdx* mouse model of muscular dystrophy: Role of NADPH oxidase (NOX)?

Aoife Slyne[1], Sarah Drummond[1], David Cussen [1], Ken O'Halloran[1], David Burns[1]

[1]*Department of Physiology, School of Medicine, University College Cork, Cork, Ireland*

Duchenne muscular dystrophy (DMD) is characterized by skeletal muscle weakness that extends to the respiratory musculature. In DMD, the diaphragm muscle is highly susceptible to inflammation and oxidative stress and death ultimately occurs due to cardio-respiratory failure. Oxidative stress occurs due to increased reactive oxygen species (ROS) and/or decreased antioxidant capacity. Oxidative stress has been described in the respiratory and locomotor muscles of DMD patients. NADPH oxidase (NOX) is a ROS-generating complex and a putative candidate for mediating ROS production in DMD. We hypothesized that NOX contributes to respiratory muscle weakness in dystrophin deficient *mdx* mice.

Diaphragm muscle isometric and isotonic performance were determined *ex vivo* for 2- and 6-month old wild-type (n=19) and *mdx* (n=19) mice. We used apocynin (putative NOX inhibitor), to assess the contribution of NOX to diaphragm muscle weakness in *mdx* mice. Quantitative real-time polymerase chain reaction (qRT-PCR) was used to determine the mRNA expression of NOX isoforms (NOX1, NOX2, NOX4, Duox1, Duox2) and NOX regulatory subunits ($p22^{phox}$, $p40^{phox}$, $p47^{phox}$, $p67^{phox}$, Rac) in the diaphragm muscle of both 2- and 6-month-old wild-type and *mdx* mice. Data were statistically compared using two-way ANOVA with Bonferroni *post hoc* test. $P<0.05$ was considered statistically significant.

Profound diaphragm muscle weakness was observed in 2- and 6-month-old *mdx* mice in comparison to wild-type. Apocynin had a positive inotropic effect in both wild-type and *mdx* mice at 2 months of age, increasing force-generating capacity. In the 6-month-old mice, apocynin did not improve force-generating capacity. The mRNA expression of NOX isoforms (NOX1, NOX2, NOX4, Duox1) were significantly increased in the diaphragm muscle of *mdx* mice compared to wild-type at both ages. Similarly, diaphragm mRNA expression of the NOX regulatory subunits ($p22^{phox}$, $p40^{phox}$, $p47^{phox}$, $p67^{phox}$, Rac) was significantly increased for *mdx* compared to wild-type. Diaphragm mRNA expression of the NOX regulatory subunit $p40^{phox}$ was significantly decreased for wild-type diaphragm at six- compared to two-months of age. Diaphragm mRNA expression of the NOX isoform NOX2 and NOX regulatory subunits ($p22^{phox}$, $p40^{phox}$, $p47^{phox}$, $p67^{phox}$, Rac) were significantly decreased for *mdx* mice at six- compared to two-months of age.

Functional experiments using apocynin suggest an age-dependent decline in the physiological role of NOX in the diaphragm. These studies also demonstrate that there is an age-related decline in the mRNA expression of NOX and associated isoforms in *mdx* diaphragm. NOX mRNA expression is increased in the diaphragm muscle of *mdx* mice compared to wild-type. Apocynin increased *mdx* diaphragm force. These data extend our understanding of redox remodelling in dystrophic respiratory muscle and are relevant to the search for new therapeutic targets. Physiological suppression of NOX may have application in the treatment of muscular dystrophy in early disease.

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PC0138

EVALUATION OF THE EFFECT OF NICKEL AND STRESS ON ANXIETY AND DEPRESSION IN WISTAR RATS

Progress Ajayi[1], Oritoke Aluko[1]

[1]*Department of Physiology, School, of Health and Health Technology, Federal University of Technology, Akure, Nigeria*

The study evaluated the effect of nickel (Ni) and stress on anxiety and depression in wistar rats. Forty rats, divided into control and three test groups (n = 10), were injected intraperitoneally with normal saline (0.9% NaCl) or nickel (II) chloride ($NiCl_2$) solution - 25 mg/kg dosage - and some were stressed using restraint model for 2 weeks. After the treatment period, animals were tested using forced swim test and tail suspension for depressive-like behavior and in the elevated plus maze for anxiety-like behavior. The brain of each animal was taken for biochemical examination. The results showed that Ni administration and stress significantly increased depressive-like behavior. A significant increase in anxiety-like symptoms was also exhibited by Ni treated and stressed rats. With regard to biochemical analysis, activity of catalase (CAT) and myeloperoxidase enzyme were significantly decreased. Consequently, Ni administration and stress exposure induced depression, anxiety and biochemical dysfunctions.

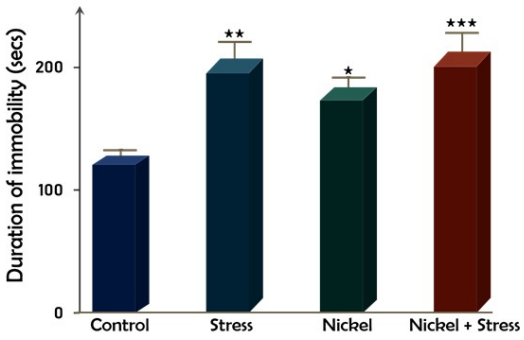

Figure 4.1: Effect of Nickel and Stress on duration of immobility in Tail suspension test. Each column represents mean ± S.E.M for animals in each group. *P < 0.05 compared with the control group. The number of (*) depict the strength of the significance level. (ANOVA followed by Tukey's post-hoc test).

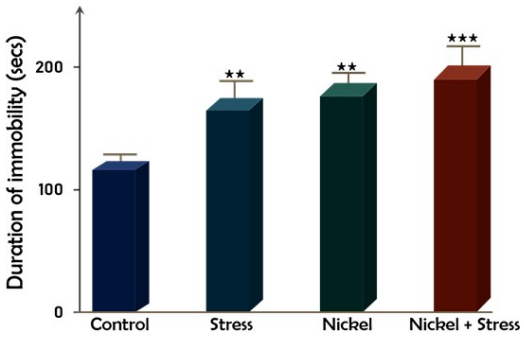

Figure 4.2: Effect of Nickel and Stress on duration of immobility in Forced Swim test. Each column represents mean ± S.E.M for animals in each group. *P < 0.05 compared with the control group. The number of (*) depict the strength of the significance level. (ANOVA followed by Tukey's post-hoc test).

Table 4.1: Effect of Nickel and Stress on parameters recorded in Tail Suspension test

Groups	Latency of First Immobility (secs)	No. of immobility episodes	Duration of mobility (secs)	Ave. duration of immobility (secs) **(secs)**
Control	19.5 ± 0.29	8.8 ± 1.32	172 ± 5.15	15.9 ± 2.81
Stress	10.5 ± 1.32	13.5 ± 1.32	93 ± 13.73*	15.8 ± 1.92
Nickel	7.8 ± 2.48*	8.2 ± 1.28	116 ± 8.46*	24.9 ± 4.14
Nickel + Stress	14.2 ± 3.99	5.8 ± 0.58	87 ± 15.54*	39.2 ± 6.91*

Values represent mean ± S.E.M for animals in each group. *p < 0.05 compared with the control group. (ANOVA followed by Tukey's post-hoc test).

Table 4.2: Effect of Nickel and Stress on parameters recorded in Forced Swim test

Groups	Active swimming time (secs)	No. of pauses	Duration of mobility (secs)	Ave. duration of immobility (secs) **(secs)**
Control	76 ± 9.37	10.8 ± 1.38	177 ± 4.97	11.9 ± 1.10
Stress	89 ± 12.46	7.8 ± 0.63	125 ± 8.34*	22.8 ± 1.11
Nickel	71 ± 6.82	6.6 ± 0.51*	109 ± 6.03*	29.8 ± 2.80*
Nickel + Stress	100 ± 27.10	6.8 ± 1.11*	99 ± 14.99*	33.2 ± 7.27*

Values represent mean ± S.E.M for animals in each group. *p < 0.05 compared with the control group. (ANOVA followed by Tukey's post-hoc test).

EVALUATION OF THE EFFECT OF NICKEL AND STRESS ON ANXIETY AND DEPRESSION IN WISTAR RATS

TABLES AND FIGURES

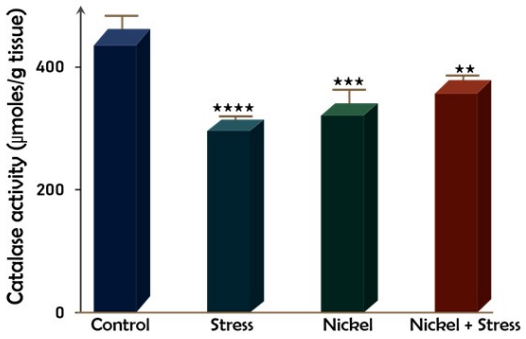

Figure 4.6: Effect of Nickel and Stress on catalase activity in the brain. Each column represents mean ± S.E.M for animals in each group. $^{*}P < 0.05$ compared with the control group. The number of (*) depict the strength of the significance level. (ANOVA followed by Tukey's post-hoc test).

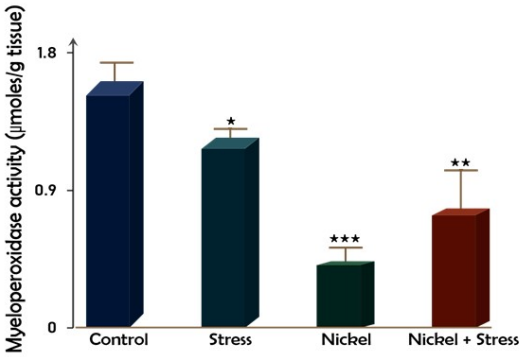

Figure 4.5: Effect of Nickel and Stress on myeloperoxidase activity in the brain. Each column represents mean ± S.E.M for animals in each group. *P < 0.05 compared with the control group. The number of (*) depict the strength of the significance level. (ANOVA followed by Tukey's post-hoc test).

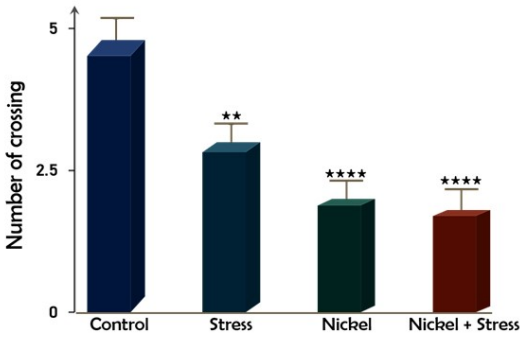

Figure 4.4: Effect of Nickel and Stress on number of crossing into open compartment in Elevated plus maze. Each column represents mean ± S.E.M for animals in each group. *P < 0.05 compared with the control group. The number of (*) depict the strength of the significance level. (ANOVA followed by Tukey's post-hoc test).

Table 4.3: Effect of Nickel and Stress on parameters recorded in Elevated plus maze test

Groups	Time in open compartment (secs)	No. of crossing	Latency of first movement (secs)	Time spent in closed compartment (secs)
Control	129 ± 13.25	4.8 ± 0.37	51 ± 15.95	171 ± 13.25
Stress	92 ± 1.08*	3.0 ± 0.32*	40 ± 8.04	208 ± 1.08*
Nickel	48 ± 2.31*	2.0 ± 0.32*	15 ± 6.64	252 ± 2.31*
Nickel + Stress	67 ± 7.69*	1.8 ± 0.37*	48 ± 26.42	233 ± 7.69*

Values represent mean ± S.E.M for animals in each group. *p < 0.05 compared with the control group. (ANOVA followed by Tukey's post-hoc test).

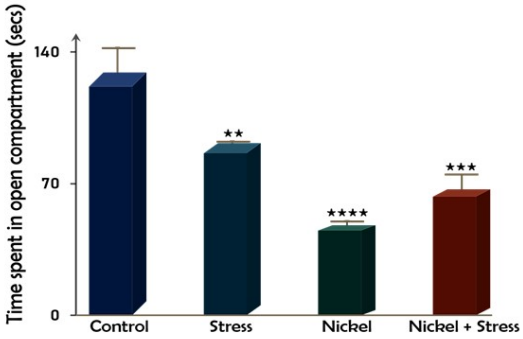

Figure 4.3: Effect of Nickel and Stress on time spent in open compartment in Elevated plus maze. Each column represents mean ± S.E.M for animals in each group. *P < 0.05 compared with the control group. The number of (*) depict the strength of the significance level. (ANOVA followed by Tukey's post-hoc test).

PC0140

TRONA, A COMMONLY USED FOOD ADDITIVE DISRUPTS REPRODUCTIVE FUNCTIONS OF MALE WISTAR RATS

Opeyemi Akindele[1], Olufadekemi Kunle-Alabi[1], Oluwakemi Ogunyelu[1], Yinusa Raji[1]

[1]*Laboratory for Reproductive Physiology and Developmental Programming, Department of Physiology, University of Ibadan, Ibadan, Nigeria*

Trona, an evaporite mineral containing sodium carbonate and erroneously referred to as "potash" is largely consumed in African countries. Trona naturally coexists in nature with other substances which are consumed along with it. Studies have indicated that intake of high sodium diet could be detrimental to reproductive capability. However, there is dearth of information on the actual effects of trona on male reproductive functions. The effects of three varieties of trona locally named *bilala*, *morinso* and *lobutu* were investigated on reproductive functions in male Wistar rats.

Three varieties of trona were obtained from Bodija Market, Ibadan, Oyo state, Nigeria. Geochemistry and mineralogy of the three samples was done at the Activation Laboratories Limited, Ancaster, Ontario, Canada. Twenty male Wistar rats (130 – 150 g) were divided into four groups (n=5) and treated for 56 days as follows: group 1 received distilled water; group 2 received 400 mg/kg of trona-*bilala*/day; group 3 received 400 mg/kg of trona-*morinso*/day; and group 4 received 400 mg/kg of trona-*lobutu*/day. The animals were weighed at the end of each week. At sacrifice, blood was collected via cardiac puncture and reproductive organs were harvested and weighed using a digital weighing scale. Serum levels of testosterone, Luteinising Hormone (LH) and Follicle Stimulating Hormone (FSH) were analyzed via ELISA. Testicular malondialdehyde level, Superoxide Dismutase (SOD), and catalase activities were assessed by spectrophotometry. Histology of testis was done. Data were summarised as mean±SEM and analyzed using ANOVA at $p \leq 0.05$.

Geochemistry showed trona content of trona-*bilala,* trona-*morinso,* trona-*lobutu* to be 83.8%, 69.2% and 59.3%, respectively. The other constituents which are amorphous, pirssonite, halite, sylvite, merlinoite, magadite, and quartz were present at different proportions. Relative weights of testes and seminal vesicles increased significantly in the trona-*lobutu* group (0.60±0.02, 0.43±0.02) compared with trona-*morinso* (0.49±0.03, 0.27±0.04) and control (0.48±0.02, 0.02±0.04) groups. In trona-*morinso* and trona-*lobutu* groups, serum FSH level (18.29±1.01, 17.94±0.40 vs 0.26±0.01, 0.28±0.02 µIU/mL; $p \leq 0.05$; [n=4 in trona-*lobutu* group]) increased compared with trona-*bilala* and control group while testosterone (2.27±0.78, 2.15±0.52 vs 11.91±2.71 ng/mL; $p \leq 0.05$) decreased relative to control group. The LH level decreased in trona-*lobutu* group relative to trona-*bilala*, trona-*morinso* and control groups (0.23±0.01 vs 12.93±0.59, 13.87±0.68, 12.81±0.96 µIU/mL; $p \leq 0.05$). Testicular MDA level (6.10±0.40, 7.62±1.02 vs 2.67±0.52, 2.50±0.32 µM; $p \leq 0.05$) increased while SOD (0.32±0.06, 0.40±0.50 vs 1.01±0.03, 0.72±0.04 U/mL; $p \leq 0.05$) decreased in trona-*morinso* and trona-*lobutu* groups compared with trona-*bilala* and control groups. Testicular histology showed different degrees of aberration in the three treated groups.

The three varieties of trona used in this study disrupted reproductive functions of male Wistar rats with trona-*morinso* and trona-*lobutu* exerting more severe detrimental effects. These two varieties of trona had lower trona content than trona-*bilala* suggesting that the substances that coexist with trona have more damaging effects on the testes and reproductive hormones than trona itself. The ingestion of trona should be discouraged among the general populace, most especially among those who erroneously use it as a therapy against reproductive dysfunction.

PC0141

Sparse presynaptic distribution of Kv3.3 K^+ channels fine-tunes synaptic noise and improves coherent neuronal activation

Timothy Olsen[1, 2], Alberto Capurro[1, 3], Masa Svent[1], Nadia Pilati[4], Charles Large[5], Nick Hartell[1], Martine Hamann[1]

[1]University of Leicester, Leicester, United Kingdom [2]University of California, San Francisco, San Francisco, The United States of America [3]University of Newcastle, Newcastle, United Kingdom [4]Autifony Therapeutics, Stevange, United Kingdom [5]Autifony Therapeutics, Stevenage, United Kingdom

Synaptic noise is fundamental to information processing and transmission in the central nervous system, as it amplifies and optimizes sub-threshold signals, thereby improving action potential initiation and reliable firing maintenance (Ermentrout et al., 2009; Faisal et al., 2008; Wiesenfeld & Moss, 1995). This is particularly important at auditory synapses where acoustic information is encoded by rapid and temporally precise firing rate. In the auditory system, an excess of synaptic noise has been shown to be detrimental to acoustic information, as it contributes to the generation and maintenance of tinnitus and hyperacusis (Kaltenbach, 2006; Wu et al., 2016). Although numerous studies have examined the role of synaptic noise on single cell excitability, little is known about the contribution of presynaptic boutons to synaptic noise within a local circuit, owing in part to the problems of combining noise modulation with monitoring synaptic release. Here we show that positive Kv3 K^+ current modulation using 30 µM AUT1 (provided by Autifony Therapeutics) in the dorsal cochlear nucleus of mice reduces the level of synaptic bombardment onto its principal fusiform cells. Using a transgenic mouse line (SyG37) expressing SyGCaMP2-mCherry, a calcium sensor that targets presynaptic terminals, we show that positive Kv3 K^+ current modulation decreases calcium fluorescence in a third of individual presynaptic boutons. Furthermore, while maintaining rapid and precise spike timing, positive Kv3 K^+ current modulation increased local cross-unit synchrony, a result arising from a reduction in spontaneous activity. In conclusion, our study identifies a unique presynaptic mechanism which contributes to noise reduction, and consequently the coherent activation of neurons in a local circuit.

Reference 1 :- Ermentrout, G.B., Galán, R.F. and Urban, N.N., 2008. Reliability, synchrony and noise. *Trends in neurosciences*, *31*(8), pp.428-434.

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Reference 3 :- Kaltenbach, J.A., 2006. Summary of evidence pointing to a role of the dorsal cochlear nucleus in the etiology of tinnitus. *Acta Oto-Laryngologica*, *126*(sup556), pp.20-26.

Reference 4 :- Wiesenfeld, K. and Moss, F., 1995. Stochastic resonance and the benefits of noise: from ice ages to crayfish and SQUIDs. *Nature*, *373*(6509), pp.33-36.

Reference 5 :- Wu, C., Martel, D.T. and Shore, S.E., 2016. Increased synchrony and bursting of dorsal cochlear nucleus fusiform cells correlate with tinnitus. *Journal of Neuroscience*, *36*(6), pp.2068-2073.

Acknowledgements :- This project was a CASE PhD studentship funded by Autifony Therapeutics and Medical Research Council

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PC0145

The physiological effects of passive heating: Does the thermoneutral zone of humans have an upper critical temperature?

Mary Henderson[1]

[1]*University of Roehampton, London, United Kingdom*

Little is known about the human upper thermoneutral zone and whether humans have an upper critical temperature. Some authors suggest that there may be (Withers, 1992; Faerevik et al., 2001; Pallubinsky et al., 2019). There are few studies having investigated resting metabolic rate (RMR) at higher temperatures and even fewer on the effects of associated physiological variables.

To investigate potential changes in respiratory gas exchange, cardiovascular variables and body temperature during rest at high temperatures, thirteen healthy individuals (μ= 32.7 ± 8.2 years; 7 females) rested in five environmental conditions, each one hour in length, of increasing environmental severity (i.e. increasing temperature and relative humidity (RH)). Participants experienced a baseline condition of 28°C and 50% RH, and 40°C and 50°C both at dry (25% RH) and wet (50% RH) conditions which were ranked from 1 (baseline) to 5 (50°C 50% RH). All participants repeated conditions 2 to 5. At 20, 40 and 60 minutes into the experiments expired air was collected and analysed using the Douglas Bag method. Core and skin temperatures, heart rate, blood pressure, movement levels and breathing rate were recorded throughout each condition. Some Douglas bag data were discarded due to the rapid saturation of drierite required to remove water from the sample passed to the gas analyser.

A repeated measures one-way ANOVA indicated evidence for differences in metabolic rate between conditions ($F(4,37) = 2.38$, $p = 0.070$; n = 8); a Tukey's HSD post-hoc test revealed a statistically significant increase in VO_2 between baseline and condition 5 (0.091 lO_2 min^{-1} ±0.030(SEM), p=0.033). Mean metabolic rate per condition ranged from 0.20 lO_2 min^{-1} ±0.020(SEM) to 0.29lO_2 min^{-1} ±0.026. Other physiological variables also indicated a response to this heat stress. Skin temperature and heart rate increased whilst diastolic blood pressure fell with rising core temperature. A one-way ANOVA followed by a Tukey's HSD post-hoc test confirmed a marked step change in these variables occurring at condition 5 (n=13, $F(8,106) = 10.73$, $p = 0.000$; μ=3.81°C, SEM=0.39, p=0.000;

μ=36.95bpm, SEM=5.44, p=0.000; μ=11.02mmHg, SEM=5.28, p=0.038; μ=1.15℃, SEM=±0.14, p=0.000, respectively).

A small number of previous studies offer tentative evidence for an increase in metabolic rate in naked humans above about 40℃ (Faerevik et al., 2001). However, many individuals do not show any increase (Pallubinsky et al., 2019) and none of these studies controlled for movement levels, which might well represent a confound. This study found evidence for increased RMR at 50℃ 50%RH compared to baseline, a condition not tested in the aforementioned research. Further analyses of the data will uncover whether movement levels explain this increase in RMR and indicate whether breathing rate varied across conditions or were affected by the breathing masks worn during expired air collection.

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Reference 2 :- Færevik, H.,et al. (2001)The thermoneutral zone when wearing aircrew protective clothing, *Journal of Thermal Biology*,26, 4–5, Pp 419-425,doi.org/10.1016/S0306-4565(01)00054-7 Accessed: 15th February 2019.

Reference 3 :- Pallubinsky, H. et al. (2019) Exploring the human thermoneutral zone – A dynamic approach,*Journal of Thermal Biology*,79, Pp. 199-208, doi.org/10.1016/j.jtherbio.2018.12.014, Accessed: 10th February 2019.

Acknowledgements :- I was awarded the VC Scholarship from the University of Roehampton to carry out my PhD.

PC0146

Amelioration of rat male gonadal function affected by alcohol and stress using oral vitamin E

Olufadekemi Kunle-Alabi[1], Opeyemi Akindele[1], Yinusa Raji[1]

[1]*Department of Physiology, College of Medicine, University of Ibadan, Ibadan, Nigeria*

Stress is a major reason for alcohol consumption in males. The adverse effects of alcohol and stress on all aspects of male reproductive functions have been widely reported in literature. These effects have been majorly linked to mechanisms resulting in the generation of oxidative stress. Oxidative stress-induced male infertility accounts for a large percentage of male infertility cases globally. Vitamin E is a potent lipid soluble antioxidant; its effects on alcohol- and stress-induced male gonadal dysfunction were investigated in this study. Male Wistar rats (150-180 g) were randomly placed in eight groups of five rats each and treated daily for three weeks as follows; Control (distilled water), Vitamin E (200 mg/Kg), Alcohol (3 mL/Kg), Alcohol+Vitamin E, Stress (2 hours of immobilisation-induced stress), Stress+Vitamin E, Alcohol+Stress and Alcohol+Stress+Vitamin E. After treatment animals were euthanized. Weights of reproductive organs, epididymal sperm profile and serum reproductive hormone levels were assessed. Vitamin E increased the sperm concentration (mean±SEM; 97.2 ± 2.3 versus 96.8 ± 6.1 x 106/mL) and serum testosterone levels (1.0 ± 0.1 versus 0.3 ± 0.1 ng/mL) reduced by alcohol+stress exposure. Gonadal tissues from the alcohol and stress

groups showed structural derangements on histological examination which were prevented or reduced by vitamin E. These results suggest a fertility-protecting role for vitamin E in males who live sedentary lifestyles and also consume alcohol.

PC0153

Motor unit recruitment strategies of the human vastus lateralis do not differ in healthy males and females

Daniel McCormick[1], Jessica Piasecki[2], John Gladman[1], Paul Greenhaff[1], Philip J Atherton[1], Mathew Piasecki[1]

[1]MRC Versus Arthritis Centre for Musculoskeletal Ageing Research & NIHR Nottingham BRC, University of Nottingham, Derby, United Kingdom [2]Musculoskeletal Physiology Research Group, Sport, Health and Performance Enhancement Research Centre, School of Science and Technology, Nottingham Trent University, Nottingham, United Kingdom

The greater decline in force steadiness (FS) observed in older males (Tracy and Enoka 2002), is indicative of a sex-specific attenuation of motor control (Castronovo et al. 2018). There is growing evidence that FS (Jakobi et al. 2018) and recruitment strategies (Nishikawa et al. 2017) in young adults are also sexually dimorphic. Increases in force production of a muscle require the recruitment of additional, progressively larger motor units (MU) and increases in MU firing frequency, and alterations of these strategies may directly influence FS. We hypothesised that any sex-differences found in FS of the knee-extensors would also be observed in recruitment strategies of the vastus lateralis (VL).

30 healthy and recreationally active young adults (Males n =15, Age 22 ± 2 yrs., BMI 25 ±4 and Females n = 15, Age 23 ± 2 yrs., BMI 24 ± 3) were recruited. Muscle cross-sectional area (CSA) was measured using ultrasound. Knee-extensor strength was assessed with isometric maximal voluntary isometric contraction (MVC), and FS was quantified as the coefficient of variation from force applied to targets held at 10%, 25% & 40% MVC for ~12s. Simultaneous intramuscular electromyography provided sampling of individual MUs from the VL. The area of the motor unit potential (MUP) was used as an indicator of MU size and the MU firing rate (FR) calculated from consecutive occurrences of the same MUP (Piasecki et al. 2019). Unpaired t-tests were used to compare MVC and CSA, and 2-way ANOVA performed on individual means of FS, MUP area and FR, with sex and contraction level as factors. Significance was accepted at $p<0.05$.

Knee-extensor MVC was higher in males (589 ± 139 N) than in females (419 ± 120 N, $p <0.01$). Likewise, VL CSA was significantly larger in males (3,061 ± 1, 054 mm^2) compared to females (1,974 ± 348 N, $p < 0.01$). There was no *sex* x *contraction level* interaction effect of FS, MUP area, or FR (all $p > 0.2$). When comparing FS, MUP area, and FR at each intensity (Figure 1), there was no main effect of sex observed in any of the measures (all $p > 0.1$). There was a main effect of contraction intensity observed in all measures (FS $p < 0.0001$; MUP $p = 0.001$; FR $p = 0.007$). In summary, FS was superior

(less deviation) at higher intensities, and MU size and FR increased with increasing contraction intensity.

These data confirm previous findings that FS improves with increasing contraction intensity, although we observed no significant difference between sexes, as previously reported (Tracy and Enoka 2002). As expected, in both sexes, the mean size of the recruited MU and MU FR increased with contraction intensity. The lack of a sex-based interaction demonstrates MU recruitment strategies of the VL do not differ between young adults. Our data highlight a lack of rationale for selecting healthy young participants based on sex for neuromuscular studies. Further work is required to elucidate the mechanisms of fluctuating sex-hormones and their influence on neuromuscular function.

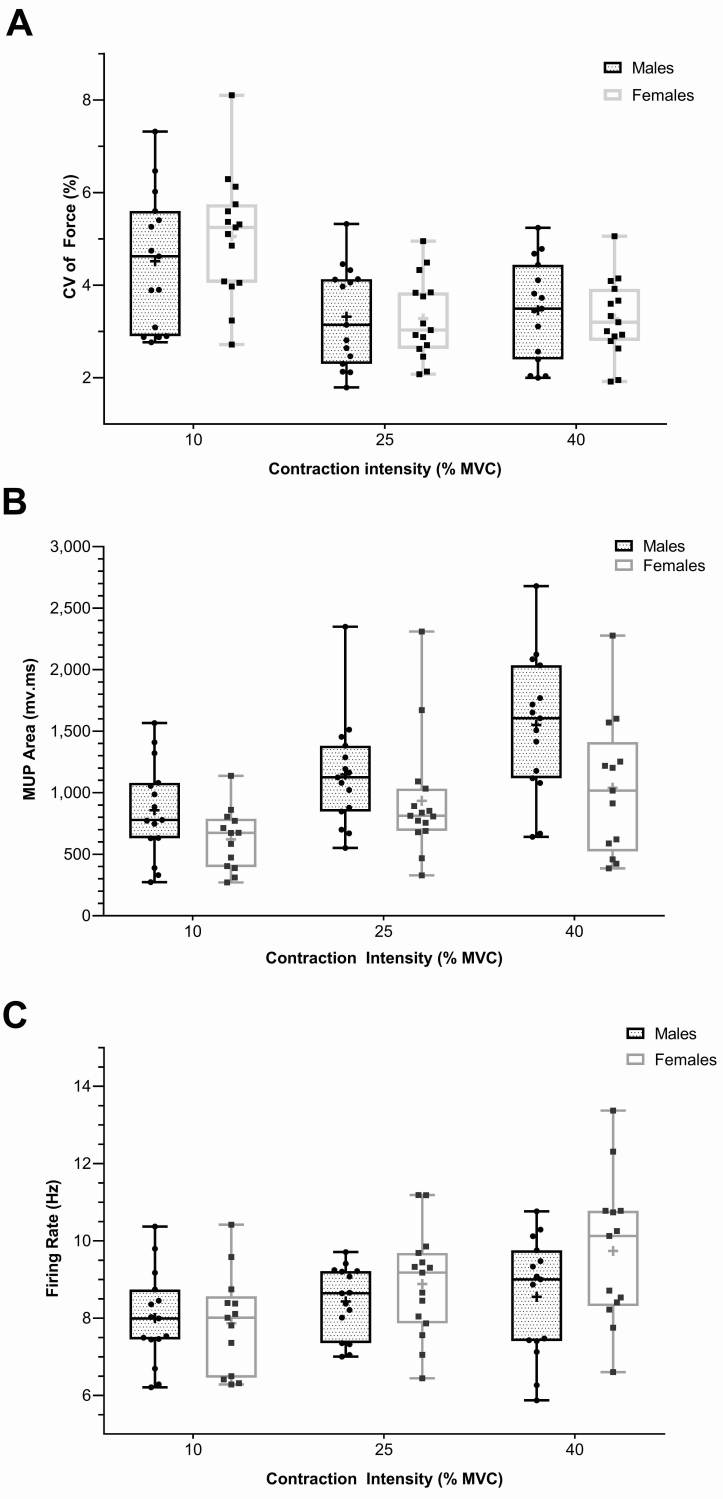

Figure 1 - A) Force Steadiness (%), B) Motor unit potential area (mV.ms), and C) Firing Rate (Hz) from contractions held at 10, 25, and 40% MVC in males and females. All parameters showed a significant effect of contraction intensity.

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Reference 2 :- Jakobi, J.M., Haynes, E.M.K., Smart, R.R., 2018. Is there sufficient evidence to explain the cause of sexually dimorphic behaviour in force steadiness? *Applied physiology, nutrition, and metabolism = Physiologie appliquee, nutrition et metabolisme*, 43(11), pp.1207–1214. 10.1139/apnm-2018-0196.

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PC0154

Lifelong exercise results in more homogeneous motor unit characteristics across deep and superficial areas of vastus lateralis.

Eleanor J Jones[1], Jessica Piasecki[2], Alex Ireland[3], Philip J Atherton[1], Bethan E Phillips[1], Jamie S McPhee[4, 5], Mathew Piasecki[1]

[1]MRC Versus Arthritis Centre for Musculoskeletal Ageing Research & NIHR Nottingham BRC, University of Nottingham, Derby, United Kingdom [2]Musculoskeletal Physiology Research Group, Sport, Health and Performance Enhancement Research Centre, School of Science and Technology, Nottingham Trent University, Nottingham, United Kingdom [3]School of Healthcare Science, Manchester Metropolitan University, Manchester, United Kingdom [4]Department of Sport and Exercise Sciences, Musculoskeletal Science and Sports Medicine Research Centre, Manchester Metropolitan University, Manchester, United Kingdom [5]Department of Physiology, University of Padova, Padova, Italy

Motor unit (MU) numbers decline in older age and contribute to reductions of muscle mass, strength and function [1]. The compensatory process of MU remodelling enables the rescue of denervated muscle fibres via axonal sprouting and reinnervation, helping to reduce fibre loss and atrophy. A number of findings suggests older master athletes are more successful at this remodelling process, displaying larger MU potentials (MUP) assessed via muscle electrophysiology [2], and fewer histochemical markers of denervation [3] when compared to less active controls. Furthermore, data from healthy young has demonstrated that MUs are not randomly located within a muscle, with those located superficially larger than those located deeper within the muscle [4]. The aims of this study were to determine the effects of ageing and exercise on the heterogeneity of MU properties across deep and superficial aspects of the vastus lateralis (VL).

Intramuscular electromyography (iEMG) was used to sample individual MUPs from the VL of 85 males consisting of 15 young controls (Y, 26±5yrs), 19 young athletes (YA, 27±4yrs), 22 old controls (O, 70±4yrs), and 29 competitive master athletes (MA, 70±5yrs, sprint and endurance). All MUPs were recorded during a sustained isometric contraction held at 25% of the participants maximum voluntary contraction. A total of 1414 MUs were isolated, with a mean of 17 ± 7 per person from which multiple MU properties were assessed. MUP amplitude was measured from the maximal positive and negative peaks and is indicative of MU size. The number of turns from the template MUPs indicates the level of firing synchronicity of individual muscle fibres within a single MU. The near fibre MUP (NF MUP) shows the contributions from fibres closest to the recording electrode as a measure of fibre density. Multilevel mixed effects linear regression models were performed on each group to account for within-subject variability and to determine effects of depth on these parameters. Significance was assumed when $p<0.05$.

Motor unit potential amplitude was larger in deep MUPs from Y, YA and O (all $p<0.05$), when compared to superficial, but did not differ across depth in MA ($p=0.182$). Near fibre (NF) MUP area was greater in deep MUPs from Y, YA and O (all $p<0.01$), but similar to MUP amplitude, it did not differ in MA across depth ($p=0.067$). MU complexity, represented by the number of turns in the MUP template, was also greater in deep MUPs compared to superficial MUPs from Y, YA and O (all $p<0.01$), with no difference across depth in the MA ($p=0.716$).

These data suggest MUs of the VL are not randomly located within the VL and exhibit a level of plasticity that is influenced by both age and activity levels. Importantly, the finding of a more homogenous distribution of MU characteristics across muscle depth adds further evidence to a greater level of age-related MU remodelling in life-long exercisers.

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PC0155

Electrophysiological characteristics of the quadriceps following involuntary fatiguing protocols

Thomas Inns[1], Daniel McCormick[1], Carolyn Greig[2], Bethan Phillips[1], Mathew Piasecki[1]

[1]MRC Versus Arthritis Centre for Musculoskeletal Ageing Research & NIHR Nottingham BRC, University of Nottingham, Derby, United Kingdom [2]University of Birmingham, Birmingham, United Kingdom

Skeletal muscle is a vital organ for many aspects of health and the age-related loss of mass and function, termed sarcopenia, contributes to not only decreased functional capacity but also increased mortality (1). Neuromuscular electrical stimulation (NMES) has been shown to attenuate sarcopenia (2), and has also proven useful in situations of critical illness to recover muscle function (3). However NMES methodologies are inconsistent and exertional effects are not always apparent (3). The m-wave, a collation of motor unit potentials recorded from an activated muscle, has been studied previously using both muscle and nerve NMES (4) but with little data available in relation to fatigue. Our aim was to investigate electrophysiological factors associated with vastus lateralis (VL) muscle fatigue induced by NMES, applied via the femoral nerve or directly to the muscle.

Sixteen young, healthy individuals (27(5) years, 8 male, BMI 23.3(3.8) kg/m^2) participated in two separate modalities of NMES; muscle stimulation (mStim), applied over the quadriceps and nerve stimulation (nStim), applied over the femoral nerve. Maximal voluntary contraction (MVC) was measured before and after each test. Stimulation intensity was determined by a single 30 Hz pulse eliciting 30% MVC, and each protocol consisted of sixty 30 Hz pulses, 1-second on/1-second off, over 2 minutes. Involuntary force was recorded throughout using a force transducer. Surface EMG was recorded throughout from the medial motor point of the VL. Repeated-measures ANOVA with Šidak's multiple comparisons were used for analysis unless otherwise stated. Significance was accepted as $p<0.05$. Where relevant data are displayed as mean (SD).

Stimulation intensity required to reach 30% MVC was greater for mStim versus nStim (132(55) mA vs 90(25) mA, $p<0.001$). Voluntary force decreased following both modalities by a similar extent (-12(9) % and -10(8) % respectively, $p<0.001$). Involuntary force (mean of first and final three stimulated contractions) also decreased following both modalities to a similar extent (-45(12) % and -27(27) % respectively, $p<0.001$). Relaxation delay was measured from the peak of the final m-wave (representing the final muscle excitation) to the onset of force decline, and was seen to progressively increase throughout mStim (4.3(1.1) mS to 8.3(2.5) mS; $p<0.001$), but did not differ throughout nStim (4.6(1.3) mS to 5.5(1.8) mS, $p=0.75$). Similarly, no other electrophysiological characteristics of the m-wave (area, amplitude, stimulus conduction time, m-wave duration) changed throughout nStim. With

mStim, m-wave duration increased progressively (0.9(1.7) mS to 1.1(2.2) mS; p<0.001).

These data demonstrate that the m-wave characteristics of area and amplitude are not affected by fatigue in the VL of healthy young people, regardless of stimulation modality or fatigue type (voluntary or involuntary). M-wave duration was not altered in response to fatigue via nStim, however it did progressively increase with mStim. This, combined with the differences observed in relaxation delay, suggests mStim acts only to stimulate and fatigue a localized area of muscle located superficially, potentially limiting its beneficial effects on muscle hypertrophy and function. As such, nStim may be preferable to mStim for the purposes of rehabilitation.

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PC0156

Neuromuscular function and motor unit recruitment of the tibialis anterior in the fasted and fed state

Siobhra Dooley[1]

[1]*School of Agriculture, Food Science and Veterinary Medicine, University College Dublin, Dublin, Ireland*

Introduction

Effective motor control is reliant upon successful communication and integration of the peripheral nervous system and skeletal muscle (1), with increases in muscle force reliant upon the recruitment of additional, progressively larger motor units (MU). The control and functioning of the tibialis

anterior (TA) muscle is essential in performing activities of daily living (ADL), such as standing balance and walking. Although ingestion of carbohydrate is known to facilitate motor output, with effects believed to largely occur centrally (2),the effects of feeding on the peripheral motor system is poorly understood. Therefore, the aim of the study was to determine the effects of a standardised low-glycaemic index meal on neuromuscular control and MU recruitment strategies of the TA.

Methods

Eight young, healthy participants (3 males, 28±7 years) completed a series of neuromuscular assessments after an overnight fast (~12hrs) and subsequently after consumption of a standardised low-GI meal, normalised to body mass. Maximal voluntary contraction (MVC) of the dorsiflexors was recorded using an isometric dynamometer. To determine motor control, force steadiness was assessed via a isometric contraction held at 25% MVC for 15 seconds, with visual feedback. The same procedure was used to determine complex force tracking with an oscillating line around 25% MVC (±4%). Postural sway was assessed on a commercially available force plate (Footscan, 200 Hz, RScan International, Belgium) during 30-second single leg balance tasks (eyes open and closed). Intramuscular electromyography (iEMG) was used to measure MU potential (MUP) area, which is indicative of MU size, during isometric contractions (3). All data was statistically compared using paired Student's t-tests with a p-value of <0.05 considered significant.

Results

Dorsiflexion MVC did not differ greatly between the post-absorptive and postprandial conditions ($p=0.48$, 202.25±104.75 vs. 189.25±94.75). Neither force steadiness ($p=0.97$, 5.98±3.06 vs. 5.97±4.29) nor complex force tracking ($p=0.24$, 45.06±13.68 vs. 41.01±11.44) in the TA were changed following feeding. There was no notable change in standing balance either with eyes open ($p=0.46$) or eyes closed ($p=0.35$). The mean MUP area in TA showed a 30% decrease ($p=0.01$) following feeding.

Conclusion

The results of this study demonstrate that in young, healthy individuals feeding of a mixed macronutrient meal has no significant effect on a number of functional neuromuscular parameters, suggesting that performance of this postural muscle is not influenced by feeding status. The TA is known for its ability to resist fatigue and its fibre type composition may partly explain its ability to resist performance decrements in the fasted state. The significant decrease in MUP area upon feeding may be explained by reduced perceived effort in the fed state reflecting positively in centrally mediated motor commands (4) and resulting in recruitment of smaller MUs.

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PC0157

Determining the effects of feeding status on motor nerve characteristics and neuromuscular performance in healthy young individuals

Sarah Miller[1]

[1]*School of Agriculture, Food Science and Veterinary Medicine, University College Dublin, Dublin, Ireland*

Introduction

Motor control (MC) is an aspect of physical function that is directly related to neuromuscular function, which can be defined as the production of purposeful and coordinated movement (1), and effective MC relies upon successful communication between the motor nerve and muscle at the neuromuscular junction (NMJ). The effect of various methods of feeding on aspects of physical performance is well established, particularly in a sporting context, however the effects of feeding status on MC and NMJ transmission stability are less apparent.

Methods

8 healthy young adults (3 male; age, 27±9 years; BMI, 23.46± 6.02 $kg \cdot m^2$) underwent a battery of neuromuscular assessments, pre and post ingestion of a standardised low glycaemic index mixed carbohydrate meal, normalised to body mass. Strength and power were assessed via isometric maximal voluntary contraction (MVC) of the knee extensors and accelerometery of a squat jump. Force steadiness measures were taken from isometric tracing of an oscillating target fluctuating around 25% (±4%) of their MVC, referred to as complex force tracking. Deviation from the target line was used as a measure of neuromuscular control. Needle electrodes and intramuscular electromyography were used to sample individual motor units (MU) from the *Vastus lateralis* (VL) during isometric contractions, and NMJ transmission stability was calculated based on the variability of consecutively occurring MU potentials emanating from the same MU (2). Fasted and fed parameters were compared using paired t-tests and significance was accepted at $p<0.05$.

Results

Isometric MVC decreased by 15% post feeding (502.25±259.75 vs. 430.79±261.22, p=0.0045), with no significant difference in the power produced from a jump squat post feed (p=0.17). Feeding significantly increased complex force tracking by 20% (39.09±25.05 vs. 29.52±9.55, p=0.035) when measured at 25% of MVC. There was no significant difference in NMJ transmission stability from fasted to fed status (p=0.135).

Conclusion

These results show an increased level of control in complex force tracking of the knee extensors in the fed state when compared to fasted, demonstrating an improvement in motor control. These effects do not appear to be mediated by improved nerve-muscle communication as assessed via NMJ transmission stability. Further research is needed at additional contraction levels, and in other muscles contributing to knee extensor function to conclude the effect of feeding on MC.

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SA01

The dependence of life histories on body size and temperature

Richard Sibly[1]

[1]*University of Reading, Reading, United Kingdom*

I was asked in this talk to set the topic in the context of my career. After a degree in Mathematics I moved into Animal Behaviour starting with a PhD and postdoc at Oxford. Then I got a two-year lectureship at Glasgow and starting working with Peter Calow on how selection acts on life histories that are subject to constraints. We put our work together in a book, 'The Physiological Ecology of Animals', in 1986. There followed some difficult years for physiology, but in 2004 I was invited to talk on Life Histories to a Gordon Research Conference devoted largely to the new metabolic theory of ecology. That was the year that 'Towards a metabolic theory of ecology', was published, and I met one of the principal protagonists, Jim Brown, at the conference, and started a fruitful collaboration.

The metabolic theory of ecology (MTE) holds that the rate at which power can be delivered to the cells of bodies scales with body size and temperature according to power laws. The scaling with body mass follows Kleiber's law, scaling as $M^{0.75}$. The scaling with temperature follows the Arrhenius

equation. The result is that smaller organisms or organisms at higher temperatures can deliver power faster, per gram of organism, than larger organisms. So an organism's metabolic rate sets the rate of resource allocation to the processes that regulate survival, growth, and reproduction. As a consequence, biological rates, such as birth rates, the rate of biomass production, developmental rates, and population growth rate, should scale allometrically to the − 1/4 power of body mass and the − 0.65 power of inverse absolute temperature. Biological times should scale to the + 1/4 power of body mass and the + 0.65 power of inverse temperature. A broad mass of data on plants, invertebrates, fish, reptiles, mammals, and birds generally supports MTE predictions, and there is at present no viable alternative framework within which to interpret these results.

MTE provides a basic mechanistic explanation for why larger organisms and those with lower body temperatures grow more slowly, reproduce later, and are less productive when they do reproduce. My version of the explanation is that production and survival rates are selected to increase but are held back by constraints arising from the laws of physics, chemistry, and biology. MTE holds that productivity is limited by metabolic rate because of logistical constraints in supplying oxygen and other resources around the bodies of individual organisms, but there are unresolved problems with the theoretical formulation of this explanation.

I will finish with a brief outline of another major outstanding life-history problem. Juvenile growth curves are generally sigmoid in shape: growth is initially nearly exponential, but it slows to near zero as the animal approaches maturity. The drop-off in growth rate is puzzling because, everything else being equal, selection favours growing as fast as possible. I will outline some existing attempts to find a solution to this puzzle.

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SA02

Heat dissipation limit theory: origin and application

Elżbieta Król[1], John R. Speakman[1, 2, 3]

[1]*Institute of Biological and Environmental Sciences, Integrative and Environmental Physiology, University of Aberdeen, Aberdeen, United Kingdom* [2]*State Key Laboratory of Molecular Developmental Biology, Institute of Genetics and Developmental Biology, Chinese Academy of Sciences, Beijing, China* [3]*CAS Center of Excellence in Animal Evolution and Genetics, Kunming, China*

Rising ambient temperatures have reinvigorated interest in thermal physiology and limits to energy expenditure in endotherms, including humans. There is growing evidence that maximal rates at which animals can acquire and expend energy may frequently be limited intrinsically by an individual's physiology rather than extrinsically by food supply. The nature of these limits is central to understanding many aspects of animal performance, including reproductive output, foraging behavior and thermoregulatory capabilities, which then shape species distribution patterns, population dynamics and ecosystem processes. It has been debated whether intrinsic constraints act "centrally" (capacity of alimentary tract to process the ingested food), "peripherally" (capacity of peripheral organs to perform work) or through a "heat dissipation limit" (HDL), that is capacity to get rid of excess body heat and avoid hyperthermia. Attempts to distinguish between these three ideas have focused on lactation in small mammals. By monitoring food intake, litter growth and milk production in laboratory mice, we demonstrated that animals with experimentally enhanced capacity to dissipate body heat (*via* exposure to low ambient temperatures or fur removal) ate more food, produced more milk and weaned heavier litters than mice lactating at high ambient temperatures (Król and Speakman 2003) or those with intact fur (Król et al. 2007). At room temperature (~21°C), the amount of lactogenic heat generated as a by-product of synthesizing ~12 mL milk per day, doubles the daily energy expenditure of lactating mice compared with virgin females, and eliminates their need for thermoregulatory heat production (Fig. 1). On average, the activity of brown adipose tissue during lactation is downregulated by ~50% when compared with females outside reproduction (Król and Speakman 2019). Both empirical evidence and theoretical considerations have led us to postulate that endotherms are limited in their performance by the capacity to dissipate body heat (Speakman and Król 2010, 2011). The HDL theory provides a comprehensive framework to study interplay between physiology, behaviour and the environment in endothermic animals, emphasizing the importance of thermal constraints on animal performance as the climate continues to warm.

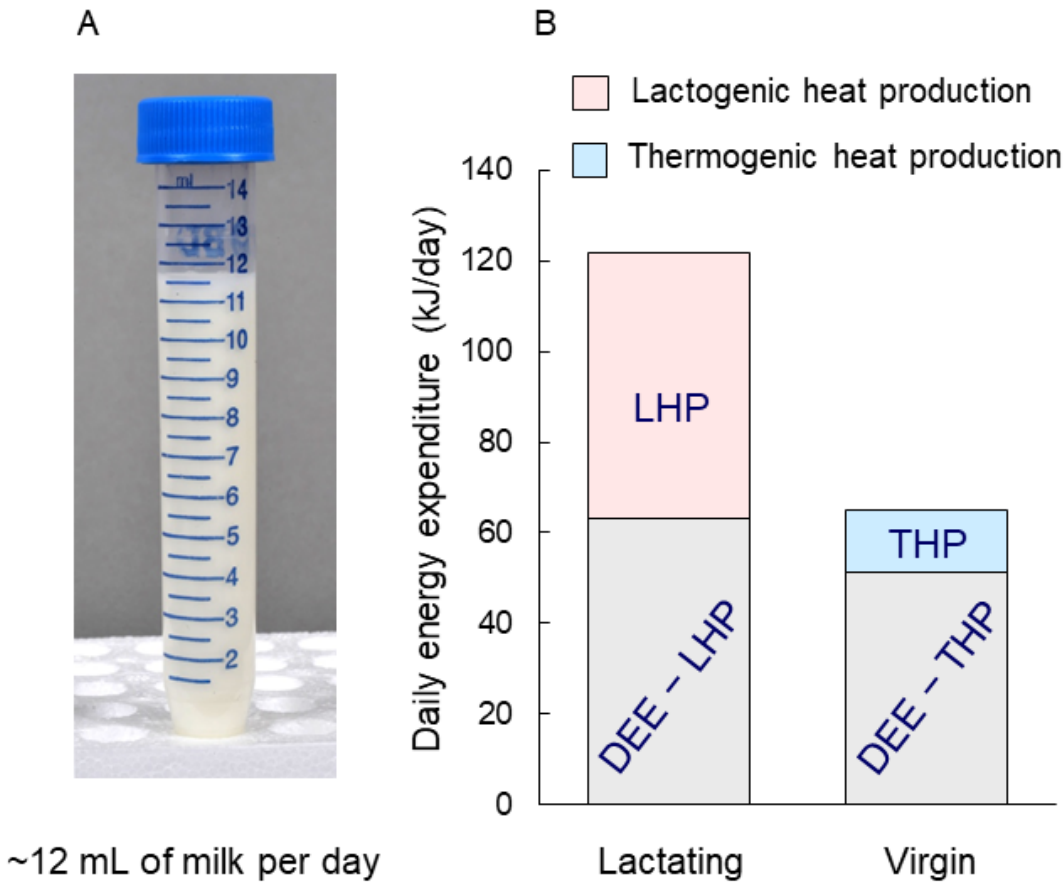

Fig. 1. Contribution of lactogenic (LHP) and thermogenic (THP) heat production to daily energy expenditure (DEE) in MF1 female mice at room temperature (~21°C). A) Mice at peak lactation produce on average ~12 mL of milk per day, with milk energy export of 144.5 kJ/day and milk production efficiency of 71.1%. B) DEE overlaid with LHP (lactating mice) and THP (virgin mice) was measured by the doubly water technique and averaged 121.8 and 65.0 kJ/day in lactating and virgin mice, respectively. For details see Król and Speakman 2019.

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SA03

Shared scaling of heating tolerance in fish individuals and populations

Nicholas Payne[1]

[1]*Trinity College Dublin, Dublin, Ireland*

Extrapolating patterns from individuals to populations informs climate vulnerability models, yet biological responses to warming are uncertain at both levels. Here we contrast data on the heating tolerances of fishes from laboratory experiments with abundance patterns of wild populations. We find that heating tolerances in terms of individual physiologies in the lab and abundance in the wild decline with increasing temperature at the same rate. At any given temperature, however, tropical individuals and populations have broader heating tolerances than temperate ones. These congruent relationships implicate a tight coupling between physiological and demographic processes underpinning macroecological patterns, and identify vulnerability in both temperate and tropical species.

SA04

Mammals and birds in a changing world

Andrew Clarke[1]

[1]*British Antarctic Survey, Cambridge, United Kingdom*

The traditional picture of an endotherm is of an organism that maintains a high constant body temperature, fuelled by a correspondingly high food intake. Recent studies using a suite of new logging devices have shown that the reality is a lot more nuanced. Birds and mammals allow their

body temperatures to vary on a daily and seasonal basis, have different set-points for pregnant females compared with males, and also allow different parts of the body to have different temperatures in response to environmental challenges. In this talk I will summarise recent work, and discuss the light it throws on the evolution of endothermy, torpor and hibernation. This shift in our view also has important consequences for understanding how endotherms may respond to continuing climate change.

SA05

Human Thermoregulation: Can We Beat The Heat?

Emily Watkins[1]

[1]*University of Roehampton, London, United Kingdom*

Humans are homeotherms and as such typically maintain a core body temperature of 37 ± 1°C. Environmental extremes in temperature challenge the homeostasis of the body, but our physiological systems have the capacity to adapt. Regular exposure to environmental temperatures greater than that normally experienced can lead to reductions in heart rate and core temperature, alongside increases in plasma volume and improvements in perception of effort. These adaptations can enable humans to be able to live, work and perform physical activity in hotter temperatures, it even enables humans to be able to run marathons in the desert. However, our ability for responding to these environments does have a limit and elevations of body temperature can be associated with heat illnesses. These illnesses lie on a continuum, the most severe being heat stroke which can prove fatal without immediate treatment. Global warming has resulted in a 0.8˚C – 0.9˚C increase in global mean temperature over the last century and projections predict further increases in temperature and heat wave frequencies. Heat waves are associated with increased heat illness hospital admissions and a rise in mortality rates. Consequently, this presentation will examine if humans have the capacity to cope with increased environmental temperatures, identify which populations and occupations may be at a greater risk, and discuss what interventions might be able to help.

SA06

The physical activity transition: Global sedentarization and increase in the prevalence of chronic diseases in humans

Audrey Bergouignan[1, 2]

[1]*CNRS IPHC UMR7178, Strasbourg, France* [2]*University of Colorado - Division of Endocrinology, Denver, Colorado, The United States of America*

Decades of research have unfortunately failed to prevent the continuous rise of chronic diseases prevalence. Understanding modern health problems cannot be achieved without an evolutionary and ecological approach. The evolutionary approach recognizes the biological constraints imposed by the fact that most of human evolution took place when our ancestors were hunter-gatherers. Indeed, 95% of human biology, and probably human behavior, was naturally selected at the time of the emergence of the modern human genome with the appearance of Homo sapiens about 200,000 years ago. Since then, our genetic heritage, although in constant evolution, has undergone few mutations and has remained relatively stable in terms of our physiology. Although genes play a role in regulating human metabolism through individual susceptibility, they alone cannot explain the recent evolution of chronic diseases, including obesity, insulin resistance, type 2 diabetes, cardiovascular and coronary heart disease, dyslipidemia, non-alcoholic fatty liver disease, cancers, etc., whose prevalence keeps increasing.

A potential reason for our inability to prevent obesity and the associated chronic diseases is that the complex interactions between the biological, behavioral, and socio-ecological factors as well as their respective role in the regulation of body weight is still not well understood. The epidemiological transition model summarizes the changes in nutrition, physical activity and culture/lifestyle that initiated the onset of obesity in Westernized countries. Studying in real-time populations from pre-industrialized countries where the epidemiological transition is ongoing is an ideal paradigm to determine the causes of the obesity epidemic. The Fulani people living in Senegal offer the exceptional opportunity to address this question. They are composed of sub-populations who are at different stages of the epidemiological transition, i.e. those living in urban environment (Dakar) and those living in rural environment (Ferlo) either in villages with access to diverse food and a borehole for water, in camps at 10-15km of a borehole, or in camps where a borehole will be built in 2020, which will dramatically accelerate the impact of the transition. Those in the Ferlo are nomadic people, known to leave for long months in transhumance, and are still in the process of settling down. This population offers a unique opportunity to understand the impact of major changes in lifestyles, diet and physical activity induced by urbanization and epidemiological transition on weight regulation.

In this presentation, we will introduce the physical activity transition and the associated impact on human cardiometabolic health. We will present our first data on the daily pattern of physical activity in the Fulanis living in contrasted environments. We will then present recent evidence from population, cross-sectional and intervention studies showing the effects of large volumes of sedentary behaviors and low levels of physical inactivity on metabolic health outcomes. Finally, we will provide with information about potential strategies to combat the adverse health effects of sedentary behaviors and physical inactivity.

Acknowledgements :- Research that will be presented in this presentation has been funded by FRM/Danone Institute, the CNRS Labex DRHIIM, the CNRS MITI, the CNRS INEE, the French Society of Nutrition, the French Space Agency (CNES), NIH/NIDDK DK10045, NIH CCTSI UL1 TR002535, T42OH009229-10 from CDC NIOSH Mountain and Plains Education and Research Center, NIH P30

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SA07

The effect of increasing environmental temperature on human thermophysiology and cardiometabolic health

Hannah Pallubinsky[1], Esther Phielix[1], Bas Dautzenberg[1], Gert Schaart[1], Niels Connell[1], Vera de Wit - Verheggen[1], Lisje Schellen[2], Bas Havekes[3], Marleen A. van Baak[4], Patrick Schrauwen[1], Wouter D. van Marken Lichtenbelt[1]

[1]Dept. of Nutrition and Movement Sciences, Maastricht University, Maastricht, The Netherlands [2]School for the Built Environment and Infrastructure, Gilde Opleidingen, Roermond, The Netherlands [3]Dept. of Internal Medicine, Division of Endocrinology, Maastricht University Medical Centre+, Maastricht, The Netherlands [4]Dept. of Human Biology, Maastricht University, Maastricht, The Netherlands

Background: The plasticity of the human physiological system and behavioural adjustments made it possible for the human species to adapt to a wide array of climatic zones. Today, we manipulate the thermal environment to our desire, rather than adapting to the natural habitat. This is true for most developed countries, where people are rarely exposed to the variation of outdoor conditions, as they spend the majority of time indoors. Due to climate change, heat waves (such as 2003, 2018, 2019) will be more common, exposing the people living in Western and Central Europe to heat more often – both outdoors *and* indoors. In this context, the question arises on how increasingly frequent, long, and intense heat waves will affect human physiology and health. Even though heat waves may lead to excess mortality, especially among vulnerable populations, a controlled 'heat training' has the potential to increase resilience and has been suggested to even improve metabolic and cardiovascular health. Although it is well-known that active, exercise-induced heat acclimation enhances human performance in the heat, data on passive (without exercise) and milder heat acclimation regimens is lacking. Therefore, we performed two passive heat acclimation (PHA) studies, assessing the effect of exposure to elevated ambient temperature on thermophysiology and cardiometabolic parameters in healthy young and middle-aged overweight individuals.

Methods: Eleven young healthy men (YH, 24.6±2.7y, BMI:22.6±2.9kg/m2) and eleven middle-aged, overweight (MO, 65.7±4.9y, BMI:30.4±3.2kg/m2) men participated in the two separate studies. Both populations were acclimated to heat (YH:7d, ~33˚C; MO:10d, ~34˚C) for 4-6h/d. Before and after PHA, core temperature (Tcore) and mean arterial pressure were measured during a temperature ramp protocol. In MO only, whole-body insulin sensitivity was assessed with a 1-step hyperinsulinemic-euglycemic clamp before and after PHA. Substrate oxidation was measured using indirect calorimetry during the clamps, and blood samples were drawn to assess markers of metabolic health.

Results: Mean Tcore decreased in both groups post-PHA (YH:Δ-0.14±0.15˚C, P=0.026; MO:Δ-0.19±0.26˚C, P=0.036), and mean arterial pressure decreased in both populations after heat acclimation, to a variable extent. In MO, PHA reduced basal (9.7±1.4 pre vs. 8.4±2.1umol/kg/min post-PHA, P=0.038) and insulin-stimulated (2.1±0.9 pre vs. 1.5±0.8umol/kg/min post-PHA, P=0.005) endogenous glucose production (EGP). Consistently, fasting plasma glucose (6.0±0.5 pre vs. 5.8±0.4mmol/L post-PHA, P=0.013) and insulin (97±55 pre vs. 84±49pmol/L post-PHA, P=0.026) concentrations decreased. Moreover, fat oxidation increased, and free-fatty acids, as well as cholesterol concentrations in plasma, decreased after PHA.

Conclusion: PHA induces distinct thermophysiological and cardiovascular adaptations in both young healthy and middle-aged overweight individuals, which indicate increased resilience to heat. In the middle-aged overweight men, PHA also improves glucose homeostasis and enhances fat metabolism. Our results show that humans of both younger and older age and different bodily constitutions readily adapt to heat. Strikingly, heat acclimation seems to have the potential to improve cardiometabolic health, but underlying mechanisms are not yet fully understood. Even though it is well-known that heat waves may entail fatalities in vulnerable populations, it is worthwhile to further explore how heat affects our metabolic health and how resilience to heat can be improved.

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SA08

Interactions between physiology, behaviour and the environment in a large carnivore

Michael Scantlebury[1]

[1]*Queen's University Belfast, Belfast, United Kingdom*

Ecological physiology aims to understand how organisms function in and respond to their natural environment, including periods that might be stressful. Examining how individuals respond to different conditions provides an indication of how species and populations survive and how they might persist under global change. Using large carnivores in a desert environment as a model system, we explore the physiological and morphological responses to inhabiting harsh conditions.

Large carnivores are interesting model organisms because they are physiologically adapted to chase, capture and subdue prey. This process is unpredictable, often resulting in failure, and also may be energetically costly especially when prey are sparsely distributed. In addition, many of the environments where these species occur are particularly sensitive to global change, and so

individuals may also have to deal with aspects such as increasing aridity and avoidance of hyperthermia. We examined energy expenditure, heat production and foraging behaviours in Kalahari cheetahs to assess whether and how environmental constraints might limit their viability.

SA09

Protein from dairy, meat, or plant sources: What's the difference for ageing muscles?

oliver witard[1]

[1]*King's College London, London, United Kingdom*

The best choice of protein source for preserving muscle mass with advancing age is a topic of considerable interest in nutrition for both health and sustainability reasons. Scientists generally agree that the primary driver of muscle loss with advanced age — at least in healthy individuals — is the reduced stimulation of muscle protein synthesis (MPS) in response to anabolic stimuli, such as protein intake and/or physical activity. This phenomenon is termed "anabolic resistance" and presents a public health challenge to "growing older with health and vitality." The focus of this presentation is on how proteins derived from dairy, meat, and plant sources differ in their capacity to stimulate MPS and therefore preserve muscle mass in older adults.

Animal sources of protein are often touted as more anabolic than plant proteins. This viewpoint is commonly attributed to a greater digestibility and superior essential amino acid and leucine profile of most animal-derived proteins compared with plant-based proteins. Consistent with this notion, studies conducted within a controlled laboratory setting have demonstrated that either beef, milk, or whey protein ingestion stimulates a greater postprandial response of MPS compared with a dose-matched soy or wheat protein source in physically active young and older adults.

However, as a note of caution, the validity of this claim that animal proteins are more anabolic than plant proteins is limited to the comparison to only two plant-based proteins, namely soy and wheat. This presentation challenges this broad viewpoint by highlighting the anabolic potential of alternative plant-based protein sources with application to maintaining the size and quality of ageing muscles.

Reference 1 :- Gorissen SHM & Witard OC Characterising the muscle anabolic potential of dairy, meat, and plant-based protein sources in older adults. Proceedings of the Nutrition Society. 29: 1-12, 2017.

Reference 2 :- Witard, OC., McGlory C, Hamilton DL., Phillips SM. Growing older with health and vitality: A nexus of physical activity, exercise and nutrition. Biogerontology. 17(3):529-46, 2016.

Reference 3 :- Witard OC, Wardle SL, Macnaughton LS, Hodgson AB and Tipton KD (2016). Protein considerations for optimizing skeletal muscle mass in healthy young and older adults. Nutrients. 8,

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