Experiments on animals and animal tissues

It is a requirement of The Society that all vertebrates (and Octopus vulgaris) used in experiments are humanely treated and, where relevant, humanely killed.

To this end authors must tick the appropriate box to confirm that:

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Authors must tick the appropriate box to confirm that:

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Please note, to constitute an acceptable abstract, The Society requires the following ethical criteria to be met. To be acceptable for publication, experiments on living vertebrates and Octopus vulgaris must conform with the ethical requirements of The Society regarding relevant authorisation, as indicated in Step 2 of submission.

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For experiments involving neuromuscular blockade, the abstract must give the type and dose, plus the methods used to monitor the adequacy of anaesthesia during blockade (or refer to a paper with these details). For the preparation of isolated tissues, including primary cultures and brain slices, the method of killing (e.g. terminal anaesthesia) is required only if scientifically relevant. In experiments where genes are expressed in Xenopus oocytes, full details of the oocyte collection are not necessary. All procedures on human subjects or human tissue must accord with the ethical requirements of The Society regarding relevant authorisation, as indicated in Step 2 of submission; authors must tick the appropriate box to indicate compliance.

PL06

Hodgkin and Huxley: giants of science.

Steve Edgley[1]

[1]University of Cambridge, United Kingdom

Students of physiology or neuroscience will all recognise the names of Hodgkin and Huxley, particularly at Cambridge. Their achievements stand out as a high point in science.

Most will know about their experimental studies demonstrating how voltage-gated channels were involved in nerve impulses. Less widely recognised is their use of experimental data to develop a mathematical model explaining potential molecular mechanisms of impulses, and how influential this was. It's very easy to forget that their work was undertaken with very basic electronics with semiconductors only being invented around the time they were working. Much of their equipment was hand-built, by themselves. There was very little information at the time about molecular structures or processes, the concept of a phospholipid bilayer cell membrane was only proposed a few years before they began working on squid giant axons. Data analysis depended upon hand-worked or hardware calculator-worked solutions without computers, yet they were using non-linear differential equations. A world war intervened in their research, taking them both away into military research, where their physics backgrounds enabled them to make substantial contributions, Hodgkin to the implementation of airborne microwave radar, Huxley to using radar to target anti-aircraft gunnery.

Hodgkin and Huxley also benefited from a very different academic world and research environment to today's. Their work on giant squid required them being in Plymouth during the “squid season” (which took them away from undergraduate examinations). When their research resumed after the war they built their research case based on experimental studies done over a six year period before publishing the outcome as a series of 5 papers in the Journal of Physiology in 1952. This series of experiments culminated in the description of the voltage-dependent membrane conductances that underly the action potential. The papers combined description of application of a new scientific approach (voltage clamp) and identification of key properties of an underlying mechanism that must operate unseen at a molecular level. This was a huge achievement, deserving its description as groundbreaking. This was the impetus for their award of the Nobel Prize in 1963. Hodgkin and Huxley suggested that it “be regarded as a first approximation which needs to be refined and extended in many ways in the search for the actual mechanism”.

Both Hodgkin and Huxley went on to significant scientific achievements in their subsequent lives: Hodgkin moved on to work on the responses of photoreceptors to light, making a major contribution and Huxley moved to a chair at UCL, also moving field nerves to research on muscle force generation. where he developed the sliding filament hypothesis of striated muscle force generation. Both also took on major administrative and leadership roles, within universities, within the Royal Society and the Physiological Society. Both also became Masters of Trinity College Cambridge.

Hodgkin and Huxley were true giants of science of the order that rarely come along: they not only re-wrote the textbooks, they added an entirely new chapter.

PL07

Sir Jospeh Barcroft 1872-1947 - pioneer of fetal and neonatal physiology

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Joseph Barcroft was the third Professor of Physiology at the University of Cambridge and, during a prolific research career, pioneered the study of fetal and neonatal physiology. He was born in Ireland, to well-to-do parents and had a liberal upbringing grounded in Quaker principles. From an early age, his interests were in nature and science, not in poetic writing and reading literature. Initially taught by governesses, he attended non-conformist boarding schools strong in the sciences from age 12. During his last two school years, he enrolled at the University of London for a BSc degree awarded as he finished school. After a 'recovery' year, he matriculated at Kings College, Cambridge, in Natural Sciences, beginning a lifelong association with the College and the University. In 1897 he graduated with a first-class BA degree and began research in the Physiological Laboratory where he remained research active until his death 50 years later.

Barcroft was an experimental physiologist whose research had three main phases. First, he investigated saliva production, its oxygen requirement and neural regulation. He devised new techniques for measuring the oxygen content of small blood volumes and developed wider interests in tissue respiration, blood oxygen dissociation curves and pulmonary ventilation. In 1910, Barcroft was elected a Fellow of the Royal Society for his work in these areas. Next, he studied physiological adaptations to hypoxia by undertaking high-altitude expeditions and experimenting on himself in an air-tight glass chamber. The final phase of Barcroft's research, for which he is best remembered now, began in the early 1930s. It sought to establish how fetuses thrived in conditions that Barcroft likened to *Everest in utero*. In acute experiments on anaesthetised pregnant sheep, he measured placental function, fetal growth rates, fetal haemoglobin and oxygen carrying capacity, fetal oxygen consumption, fetal respiratory movements, fetal and placental blood flow and changes in the circulation and lungs at the time of birth. Indeed, much of today's diaspora of feto-placental and perinatal research can trace its origin back to the studies of Barcroft and his students and colleagues in Cambridge.

As a Quaker, Barcroft was seconded to Porton Down Experimental Station during both World Wars to oversee research on gas poisoning, for which he received the CBE. In 1925, he became the Chair of Physiology in Cambridge and began enlarging the Laboratory building and its staff. He chaired multiple committees, gave engaging undergraduate lectures and supervisions, and traveled widely to give lecture series and attend conferences abroad. After 'retirement', he became Director of a new ARC unit of Animal Physiology based in the Physiological Laboratory, with a remit to study ruminant metabolism. He supervised its activities alongside continuing his own perinatal research. He was knighted in 1935 and received numerous other honours and Honorary degrees. In total, Barcroft published three books and over 300 scientific papers and meeting proceedings. His epitaph was expressed most simply by Professor Adrian: *"He was a very wise and kindly man as well as a great physiologist"*.

PL08

PAK1/2 signalling and therapeutic activation in cardiac protection

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PAK1/2 Signalling and Therapeutic Activation in Cardiac Protection

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Over the past decade, work from our laboratories and others has established p21-activated kinases 1 and 2 (PAK1/2) as important regulators of cardiac homeostasis and potential therapeutic targets in cardiovascular disease. We have demonstrated that PAK1 plays a critical role in regulating ion channels, maintaining intracellular Ca^{2+} homeostasis and electrophysiological stability in the heart[1-6]. Furthermore, activation of PAK1 signalling exerts cardioprotective effects against pathological hypertrophy, fibrosis, and ischaemia–reperfusion injury and heart failure [1-7]. More recently, we and others found that PAK2 is abundantly localised in close proximity to the endoplasmic reticulum (ER) membrane, where it acts as a key regulator of the IRE1/XBP1-dependent unfolded protein response (UPR), providing an additional mechanism of cardioprotection during cellular stress[8, 9].

Building on these mechanistic insights into PAK1/2-mediated cardioprotection, we have developed a novel **peptide-guided strategy for discovery kinase activators**. By identifying and targeting a previously unrecognised autoinhibitory interface between the PAK1/2 kinase domain (KD) and autoinhibitory domain (AID), we demonstrated that rational modulation of kinase autoinhibition can enhance PAK1/2 activity[10]. This approach has enabled the development of a series of potent small-molecule PAK1/2 activators and may provide a broadly applicable strategy for therapeutic kinase activator discovery—an area that remains substantially less explored. Importantly, these PAK1/2 activators exert robust antihypertrophic effects, attenuating cardiomyocyte hypertrophy and improving pathological myocardial remodelling[10].

Collectively, our studies and those of others identify PAK1/2 as central regulators of **Ca^{2+} homeostasis, electrophysiological stability, ER stress responses, and myocardial remodelling**, supporting their development as novel therapeutic targets for cardiac hypertrophy, heart failure, and arrhythmias. By restoring Ca^{2+} homeostasis and modifying the arrhythmogenic substrate, pharmacological activation of PAK1/2 may offer a complementary therapeutic strategy to existing antiarrhythmic treatments. Further elucidation of the cellular and molecular mechanisms linking PAK1/2 activation to antihypertrophic and antiarrhythmic effects will be important for optimising these compounds and advancing PAK1/2-targeted therapies toward clinical translation.

SA01

From survival to disease: How fetal hypoxia reprogrammes the cardiovascular system

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Chronic fetal hypoxia is a major challenge to fetal development, arising from placental insufficiency and underlying fetal growth restriction, which affects close to 10% of pregnancies worldwide. Understanding how the fetus adapts to oxygen deprivation is therefore fundamental to understanding survival before birth and cardiovascular health across the life course.

Our work overturned the prevailing view that the carotid body is inactive before birth, establishing its central role as the oxygen sensor initiating fetal cardiovascular defence to acute hypoxia. The carotid chemoreflex triggers peripheral vasoconstriction, redistributing blood flow towards vital organs - the fetal brain-sparing response. This vasoconstriction is sustained by hormones released into the fetal circulation and fine-tuned by our discovery of a local redox signalling pathway through interactions between nitric oxide and superoxide.

When fetal hypoxia becomes chronic, this defence is fundamentally reprogrammed. Carotid chemoreflex and sympathoadrenal responsiveness are attenuated, limiting the energetic cost of sustained neural activation, while control shifts towards local cardiovascular mechanisms. In the hypoxic fetus, peripheral vessels develop enhanced α-adrenergic responsiveness and a pro-constrictor redox phenotype, while cerebral vasodilator capacity and mechanisms supporting myocardial function are enhanced. These adaptations may help sustain redistribution of the fetal circulation during chronic hypoxia, but they come at a cost: the chronically hypoxic fetus has little additional cardiovascular reserve when acute hypoxia is superimposed. This provides a physiological explanation for the particular vulnerability of the growth-restricted fetus to acute stresses such as labour. Persistent hypoxia also transforms physiological redox signalling into oxidative stress. In the placenta, increased mitochondrial generation of reactive oxygen species quenches nitric oxide, reducing uteroplacental blood flow and fetal oxygen and nutrient delivery, thereby exacerbating fetal growth restriction.

Birth removes the chronic hypoxic stimulus, but the fetal cardiovascular legacy persists. We propose that the pro-constrictor phenotype that helped sustain fetal brain sparing becomes unmasked after birth as sympathetic vascular hyperreactivity and endothelial dysfunction, ultimately promoting hypertension in later life. Our latest work shows that maternal treatment of hypoxic pregnancy with the mitochondria-targeted antioxidant MitoQ protects placental function, restores perfusion, and prevents both fetal growth restriction and programmed hypertension in adult offspring. These findings establish mitochondria-derived oxidative stress as a causal mechanism linking chronic fetal hypoxia to cardiovascular disease in later life.

Thus, fetal hypoxia reveals a fundamental physiological continuum: from how the fetus senses and defends itself against oxygen deprivation, to how persistent fetal hypoxia transforms physiological adaptation into mechanisms that drive cardiovascular disease in later life.

SA02

Structured hybrid exercise restores cardiac function in murine cardiometabolic HFpEF

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Exercise improves cardiorespiratory fitness and quality of life in heart failure with preserved ejection fraction (HFpEF), but its effects on cardiac remodelling and the impact of different exercise modalities remain unclear. This study investigated how distinct exercise regimens influence cardiac function and molecular signatures in a murine cardiometabolic HFpEF model, focusing on modality-specific transcriptional changes. Six-week-old male C57BL6 mice were fed control chow or a 60% high-fat diet plus L-NAME for 14 weeks. After 7 sedentary weeks, mice were randomised to remain sedentary or undergo hybrid treadmill or voluntary wheel-running exercise for 7 weeks. Single-hit groups (HFD or L-NAME alone) were included for comparison. Cardiac phenotyping, exercise testing, and left ventricular bulk RNA sequencing were performed with differential expression and pathway analyses. Sedentary HFpEF mice developed diastolic dysfunction (increased E/e', prolonged IVRT, reduced GLS). Hybrid exercise improved diastolic function and exercise capacity, whereas voluntary aerobic exercise did not, despite unchanged body weight. Transcriptomic profiling revealed distinct cardiac responses to diet and exercise. Hybrid exercise upregulated mitochondrial oxidative phosphorylation genes and attenuated HFpEF-associated circadian dysregulation, changes not observed with aerobic exercise. These molecular adaptations aligned with improved cardiac function. Overall, structured hybrid exercise exerted superior effects on function and induced distinct metabolic and circadian transcriptional remodelling, highlighting exercise modality as a key determinant of benefit in cardiometabolic HFpEF.

SA03

High-altitude adaptation: Metabolic lessons from the mountains

Andrew Murray[1]

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High altitude presents a formidable physiological challenge: reduced oxygen availability (hypoxia) challenges cellular energy metabolism and redox homeostasis. Despite adaptive responses at the whole-body level that enhance convective oxygen delivery, tissue hypoxia persists, necessitating metabolic responses that alter oxygen utilisation. Notably, populations with a long history of residence at altitude have evolved distinctive physiological strategies that enable them to thrive in this environment. Understanding these adaptations can reveal fundamental principles governing human metabolism under conditions of limited oxygen availability.

This talk will explore how studies conducted during the Caudwell Xtreme Everest and Xtreme Everest 2 expeditions have shaped our understanding of metabolic responses to hypoxia. In lowlanders, exposure to high altitude induces extensive remodelling of skeletal-muscle metabolism and mitochondrial function. These responses may help preserve cellular energy homeostasis, but they are accompanied by reduced capacity for lipid oxidation and may contribute to the decline in physical performance seen during prolonged hypoxic exposure.

The Sherpa people provide an illuminating contrast. Their skeletal muscle exhibits a metabolic phenotype characterised by reduced reliance on fatty-acid oxidation, greater use of carbohydrate-derived substrates and efficient production of ATP relative to oxygen consumption. These characteristics are associated with genetic variation in pathways regulating cellular oxygen sensing and fuel selection, suggesting that natural selection has acted not simply on oxygen delivery, but also on the way oxygen is used.

I will also present recent work integrating metabolomic and genetic data across ascent to examine how ancestry, altitude and sex influence lipid metabolism and transport in Sherpas and lowlanders. Together, these studies highlight that metabolic adaptation—matching fuel selection and mitochondrial function to oxygen availability—is a central component of human adaptation to high altitude.

SA04

Cortical and Collicular Contributions to Visual Spatial Detection in Freely Moving Mice

Jisoo Kim[1], Riccardo Beltramo[1], Jasper Poort[1]

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Visual spatial detection is an essential early step in vision, guiding decisions and actions. Yet its neural basis in freely moving animals is still unclear, because controlling visual input and tracking eye and head position is challenging. Studies in head-fixed mice have shown that both the superior colliculus (SC) and primary visual cortex (V1) support visual spatial detection, but how they contribute in freely moving animals is poorly understood.

Previously we developed open-source methods to track eye and head position in unrestrained mice (Meyer et al., 2018, 2020), to help study the role of different brain regions in complex visually-guided behaviours and investigate “vision on the move”.

I will present recent work in our lab where we further extended these tools and developed an approach to study visual detection in unrestrained mice, combining closed-loop visual stimulation, neural recordings and optogenetics in V1 and SC, and simultaneous eye- and head-tracking (Jisoo Kim, Riccardo Beltramo, Jasper Poort, Current Biology 2026). We found that SC neurons predict reaction times better than V1 neurons and show more sustained responses during detection. Inhibiting either SC or V1 activity disrupts visual detection, but SC inhibition produces stronger deficits. These findings reveal distinct activity patterns in SC and V1 and help clarify their roles in visual spatial detection.

SA05

Hunting down the neural pulse generators controlling fertility

Allan Herbison[1]

[1]University of Cambridge, UK

Fertility in mammals is critically dependent upon episodic gonadotropin hormone secretion. Males exhibit short pulses of hormone release every 3–4 hours, while females show pulsatile release in addition to a prolonged day-long GnRH surge that occurs once a month to trigger ovulation. While it had been appreciated for decades that the gonadotropin-releasing hormone (GnRH) neurons represented the final output neuron of the hypothalamic circuitry controlling gonadotropin secretion, the mechanism through which episodic GnRH release occurred remained a mystery. The watershed discovery unravelling this mechanism arose through the identification of infertile human pedigrees with mutations in kisspeptin signalling. Investigations have subsequently identified that two different populations of kisspeptin neurons exist within the hypothalamus and that, remarkably, one represents the “pulse generator” whilst the other, found only in females, is the “surge generator”. The detailed understanding of the kisspeptin pulse and surge generators, acquired primarily through genetic mouse models, has now provided new avenues for the beneficial regulation of fertility in humans and other species.

SA06

From Foster to Future: Physiology practical class teaching in Cambridge

Matthew Mason[1]

[1]University of Cambridge, United Kingdom

Michael Foster, who helped to establish the Physiological Society 150 years ago, began the study of experimental physiology in Cambridge. While the frog nerve-muscle preparation that Foster introduced continued as a laboratory class until quite recently, other aspects of our practical teaching have evolved considerably over the years. Factors driving change have included improvements in equipment, shifting attitudes towards the use of experimental animals and health and safety considerations. The move to online teaching during the pandemic served to highlight the importance of personal interactions within the experimental laboratory. The challenges and opportunities of new technologies such as AI must be embraced as we plan the future of physiology practical teaching in Cambridge.

SA07

How to build the human lungs

Ziqi Dong[1], Emma Rawlins[1]

[1]University of Cambridge, United Kingdom

Variation in lung alveolar development, and in alveolar-specific genes, are strongly linked to adult lung disease susceptibility. However, the underlying cellular and molecular mechanisms are difficult to study in humans. We have developed a suite of human fetal-derived lung organoids, including mature alveolar type 2 cells epithelial cells and other tissue models. These are genetically manipulable, cryopreservable and can be used to study lung epithelial cell fate decision making and cell lineages in a 3D context. We have recently become particularly interested in the interplay between biochemical and chemical cues in the control of cell identity in the developing and diseased lungs. For example, human lungs experience dynamic changes in oxygen tension during development. We show that hypoxia directly regulates human lung epithelial cell identity using tissue-derived organoids. Fetal multipotent lung epithelial progenitors remain undifferentiated in a self-renewing culture condition under normoxia, but spontaneously differentiate towards multiple airway cell types and inhibit alveolar differentiation in hypoxia. Using chemical and genetic tools, we demonstrate that hypoxia-induced airway differentiation depends on HIF (Hypoxia-Inducible Factor) activity, with HIF1α and HIF2α differentially regulating progenitor fate decisions. KLF4 and KLF5 are direct HIF targets that promote basal and secretory cell fates. Moreover, hypoxia is sufficient to convert alveolar type 2 cells derived from both human fetal and adult lungs to airway cells, including aberrant basal-like cells that exist in human fibrotic lungs. These findings reveal roles for hypoxia and HIF activity in the developing human lung epithelium and have implications for aberrant cell fate changes in pathological lungs.

SA08

Genomic imprinting as a regulator of postnatal physiology

Geula Hanin[1]

[1]University of Cambridge, United Kingdom

Genomic imprinting has been extensively studied as an epigenetic mechanism that controls embryonic growth and placental function through parent-of-origin-specific gene expression. Emerging evidence, including our own, suggests a broader role, with imprinted genes regulating maternal physiology and postnatal development during the critical transition from pregnancy to lactation.

Our recent work identifies the imprinting regulator ZFP57 as a key determinant of mammary gland function. Beyond its established role in maintaining genomic imprints during embryogenesis, ZFP57 regulates mammary epithelial differentiation, milk composition and offspring growth through a postnatal mechanism that is largely independent of canonical imprinting. These findings reveal a previously unrecognised genetic programme governing lactation and provide a direct mechanistic link between early postnatal nutritional resource control and the developmental origins of health and disease.

Viewed in an evolutionary context, our findings support a broader model in which genomic imprinting extends beyond fetal development to coordinate maternal investment across generations. By regulating the quantity and quality of nutrients delivered through milk, imprinted genes influence offspring growth and developmental trajectories during a critical window of physiological plasticity. This work reframes genomic imprinting as a regulator of postnatal physiology and maternal-offspring interactions, with implications for understanding the biology of lactation, developmental programming and the origins of metabolic disease.

SA09

Insights into endocrine and metabolic phenotypes from humans carrying rare genetic variants

Stephen O'Rahilly[1]

[1]University of Cambridge, United Kingdom

In this talk I will describe how the study of humans with rare functionally impactful genetic variants has provided novel insights into a range of human endocrine and metabolic phenotypes. In particular, I will discuss-

i) the control of energy balance and its disturbances in obesity and how those investigations have also led to new insights into the link between nutritional state and sexual maturation;

ii) the control of insulin sensitivity and its disturbances in states of insulin resistance; this will include information about a novel class of adipose tissue dysfunction which appears to be a prevalent contributor to metabolic ill-health;

and

iii) how human genetics has contributed to a deeper understanding of the nausea and vomiting of pregnancy, leading to a point where trials of novel therapeutic and preventive strategies have been launched.

SA10

Using 'omics analyses to generate new insights into adipocyte metabolism

Daniel Fazakerley[1]

[1]University Of Cambridge, United Kingdom

Adipocytes are central to whole-body metabolic health, yet many of the molecular events that govern their responses to hormonal and nutritional cues remain incompletely understood. In this talk, I will discuss how our group combines 'omics approaches and functional screening to study hormonal regulation of adipocyte glucose and lipid metabolism, and how these pathways become dysregulated in insulin resistance.

SA11

Unravelling obesity biology through natural genetic variation in dogs

Eleanor Raffan[1]

[1]Cambridge University, United Kingdom

Eleanor Raffan is a veterinary surgeon and Associate Professor in Systems Physiology at the University of Cambridge. Her research uses naturally occurring genetic variation in pet dogs to understand the biology of appetite and obesity. She will discuss how canine genetics is revealing fundamental mechanisms regulating food intake, body weight, and energy balance, and how discoveries in dogs can provide important insights into human obesity biology and potential therapeutic targets.

C01

STED microscopy and transmission electron microscopy reveal mitochondrial reverse remodelling following respiratory heart rate variability pacing in heart failure

George Guo[1], Julia Shanks[1], Mridula Pachen[1], Serah 'Otukolo[1], Jizhong Bai[1], Hussam Moammer[1], Martin Middleditch[1], Chris Pook[1], Eric Thorstensen[1], Audrys Pauza[1], Angus Cheverton Grey[1], Julian Paton[1], Rohit Ramchandra[1], David John Crossman[1]

[1]University of Auckland, New Zealand

Background: Respiratory heart rate variability (RespHRV) is a natural beat-to-beat variation in heart rate linked to respiration that is lost in heart failure. We have previously shown that restoring RespHRV using a novel biofeedback pacemaker improves cardiac function in an ovine model of heart failure with reduced ejection fraction (HFrEF). Recent proteomic and metabolomic analyses suggested improved mitochondrial function as a potential mechanism underlying this response. We therefore investigated whether RespHRV pacing restores mitochondrial structure in the failing heart.

Methods: Heart failure was induced in female Romney sheep by sequential coronary microembolisation. Animals were assigned to control (n=5), heart failure (HF; n=5), or heart failure treated with RespHRV pacing for two weeks (HF+R; n=5). Heart failure was induced in sheep by sequential coronary microembolization. Three months following heart failure induction, animals underwent instrumentation surgery and received two weeks of pacing therapy. Sheep were then euthanized, and cardiac tissue was collected for subsequent analyses. Surgical procedures, anaesthesia, and pharmacological protocols were performed as previously described by Shanks et al., (2022). Left ventricular tissue was analysed using stimulated emission depletion (STED) microscopy of TOMM20-labelled mitochondria and transmission electron microscopy (TEM) of mitochondrial ultrastructure. Proteomic and metabolomic analyses were used to provide mechanistic context. STED and TEM images were analysed using a linear

mixed-effects model with group (C, HF, HF+R) as a fixed effect and animal included as a random intercept to account for clustering of myocytes within animals. Planned comparisons performed between groups used Least Significant Difference (LSD) tests. Data was expressed as mean and SEM.

Results: STED microscopy demonstrated a highly organised columnar arrangement of mitochondria in control myocardium that was disrupted in HF. Directionality analysis revealed loss of mitochondrial alignment in HF that was restored following RespHRV pacing ($p=0.051$). Quantification of TOMM20 labelling demonstrated a significant increase in TOMM20-positive area in HF+R compared with HF ($p=0.005$). TEM revealed marked disruption of mitochondrial cristae architecture in HF hearts, characterised by a significant reduction in cristae density compared with controls ($p<0.001$). Following two weeks of RespHRV pacing, cristae density was significantly increased compared with HF ($p<0.001$) and mitochondrial ultrastructure restored towards the control phenotype despite no change in total mitochondrial area fraction. Complementary proteomic analyses demonstrated restoration of mitochondrial proteins associated with oxidative metabolism and fatty acid β-oxidation, while paired plasma metabolomic analyses showed reductions in circulating long-chain acylcarnitines following pacing, consistent with improved mitochondrial oxidative function.

Conclusions: RespHRV pacing induces reverse remodelling of mitochondrial architecture in the failing heart. STED microscopy and TEM demonstrate restoration of mitochondrial organisation and cristae density, providing a structural basis for improved mitochondrial function. These findings identify mitochondrial recovery as a key component of the therapeutic response to RespHRV pacing and highlight the value of advanced imaging approaches for understanding mechanisms of cardiac repair.

C02

NeuroMap – Developing Cortical Mapping Techniques for Clinical Application in Neurological Disorders

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Background

Transcranial Magnetic Stimulation (TMS) can quantify corticospinal tract function by extracting parameters from stimulus-response (recruitment) curves. Monitoring some of these parameters, such as slopes (*k)*, maximum motor evoked potential (MEP) amplitudes (*MEPsat*), and intensities at the steepest part of the slope (*S50*), could help provide more individualised prognoses following neurological injury. However, current TMS protocols for generating recruitment curves are often restricted to measuring only one muscle at a time, via stimulation at the cortical hotspot corresponding to each muscle, making them time-consuming and clinically impractical. The aim of this study was to determine whether parameters derived for two muscles simultaneously from a single cortical location would be consistent, to provide evidence for optimised data acquisition times.

Methods

With ethical approval from the Imperial College Research Ethics Committee, thirteen healthy participants (7 male, 6 female; mean ± SD age: 26.54 ± 9.33 years, range 21-52 years) underwent neuronavigation-guided TMS of the motor cortex. Surface electromyography was recorded from the first dorsal interosseus (FDI) and triceps brachii (TRI) muscles. Recruitment curves were generated for both muscles at each hotspot and modelled with a four-parameter Boltzmann sigmoidal function (*MEPsat, EMGbase, S50, k*). Within-subject comparisons were carried out between on-hotspot and off-hotspot conditions using paired t-tests or Wilcoxon signed-rank tests. The relationship between Euclidean hotspot distance and the change in each parameter between stimulation conditions was assessed using Spearman's correlation analysis. Significance was defined as $p < 0.05$.

Results

For FDI, off-hotspot stimulation increased median *S50* from 46.03% (IQR 43.94–60.71) to 72.84% (IQR 63.79–85.36) of maximum stimulator output ($W = 87$, $p = 0.0007$, $rc = 0.96$), indicating that higher stimulus intensities were required to achieve equivalently sized responses. No significant effect was observed for the other FDI parameters (k: $p = 0.84$; *MEPsat*: $p = 0.50$), indicating that off-hotspot FDI stimulation preserved the shape of recruitment curves. For TRI, no significant differences were observed between parameters derived from on- or off-hotspot stimulation (*S50*: $p = 0.62$; *k:* $p = 0.77$; *MEPsat*: $p = 0.13$).

Across participants, the change in FDI *S50* between stimulation conditions was positively correlated with the distance between FDI and TRI hotspots ($rs = 0.670$, $p = 0.015$, 95% CI [0.172, 0.896]). No significant correlations were observed for any other FDI or TRI parameters.

Conclusion

Boltzmann recruitment curve parameters, particularly *MEPsat* and *k,* were largely robust to some deviation from the optimal stimulation site, i.e. the hotspot. Although off-hotspot stimulation only increased FDI *S50,* suggesting that muscle-specific variables such as differences in cortical representations may modulate the impact of spatial deviations, the overall preservation of Boltzmann parameters demonstrated that recruitment curves can be derived for two muscles simultaneously from a single cortical location. The findings of this study in healthy individuals support the feasibility of more efficient acquisition protocols and provide proof-of-concept for the assessment of multiple muscles at once. This represents an important first step towards clinically practical application, where rapid characterisation of corticospinal tract function could improve prognostication following neurological injury.

C03

PCOS-Like Follicular Arrest and Endocrine Disturbance Following Granulosa Loss of MRP4

Xiaojun Cai[1], Ruiyao Xu[1], Junjiang Chen[1], Ye Chun Ruan[1]

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Polycystic ovary syndrome (PCOS), characterized by a high androgen-to-estrogen ratio, follicular arrest and anovulation, is a reproductive and endocrine disorder affecting 10% of women of reproductive age worldwide [1]. Abnormalities in ovarian granulosa cells contribute to PCOS pathogenesis, although the underlying molecular mechanisms remain unclear. Previously, we demonstrated multi-drug resistance protein 4 (MRP4), a membrane protein of the ATP-binding cassette transporter subfamily C encoded by the human gene *ABCC4,* to be essential to uterine signaling pathways (i.e., prostaglandin E2 and Wnt/β-catenin) required for embryo implantation and female fertility[2]. In the present study, we hypothesized that MRP4 might play a role in granulosa cells for ovarian functions.

We first examined MRP4 expression in mouse ovarian tissues and found its expression mainly in granulosa cells initiating at primary follicles and increasing gradually as follicles grow and peaking at late antral follicles. We next generated transgenic mouse models with granulosa-specific knockout of MRP4 by crossing MPR4-floxed (*Abcc4*$^{fl/fl}$) mice with *Cyp19a1-Cre*- or *Amh-Cre*-inserted one. Such conditional (granulosa-specific) knockout mice (cKO) were compared with Cre negative controls (*Abcc4*$^{fl/fl}$). Although these cKO mice were viable and grossly normal, they exhibited clear reproductive abnormalities in adulthood. Estrous cycle analysis showed a significantly ($p < 0.05$) shortened estrus phase and prolonged diestrus/metestrus in cKO (n = 7 of *Amh-Cre* and n = 9 of *Cyp19a1-Cre*) in comparison to the controls (n = 12). Histological examination and follicle counting cross the entire ovary revealed a marked ($p < 0.05$) accumulation of small follicles (primary and secondary) accompanied by a significant ($p < 0.05$) reduction in large antral follicles in the cKO mice (n = 5 of *Amh-Cre* and n = 9 of *Cyp19a1-Cre*) versus those in controls (n = 12). In addition, cKO ovaries contained thin-walled oocyte-lacking follicular cysts, which was very rare (1 cyst in 12 ovaries) in the controls. Fertility testing over consecutive pregnancies demonstrated reduced reproductive capacity of the cKO (n = 5). Moreover, granulosa expression level of anti-Mullerian hormone (AMH) was significantly elevated in cKO ovaries, particularly in large follicles, which together suggested a PCOS-like follicular arrest phenotype in cKO mice. Consistently, spatial transcriptomic analysis of ovaries from the mice revealed a pathological granulosa cell transition in the cKO. The cluster of cells associated with steroidogenic function reduced in number, whereas a distinct population enriched in adhesion- and scaffold-related genes became predominant in cKO ovaries. Quantitative PCR analysis confirmed that primary granulosa cultures from MRP4 knockout mice exhibited downregulation of key steroidogenic markers, including *Cyp11a1, Cyp19a1,* and *Fshr* with impaired gonadotropin responsiveness. Mechanistically, intracellular cAMP- and Ca^{2+}-overload was found in primary granulosa cells of MRP4 knockout, linking transporter loss to altered signaling homeostasis and granulosa dysfunction.

Taken together, these findings have revealed previously undefined role of MRP4 in regulating granulosa cell function and folliculogenesis. Deficiency of MPR4 triggers in a pathological transition of granulosa cells resulting in PCOS-like follicular arrest in mice, providing a novel mechanism for granulosa abnormalities in PCOS.

C04

Maternal obesity programs adipogenic commitment in neonatal mesenchymal stem cells: a link to redox-dependent FOXO1 signaling

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Introduction: Maternal obesity increases the risk of obesity and metabolic disease in the offspring, however, the cellular mechanisms that program adipose tissue development remain poorly understood. Mesenchymal stem cells (MSCs), the precursors of adipocytes, may represent an early target of metabolic programming during fetal development. Previous studies have shown that MSCs isolated from neonates of mothers with obesity exhibit enhanced adipogenic differentiation potential (Iaffaldano *et al*. 2013; Chen *et al*. 2016).

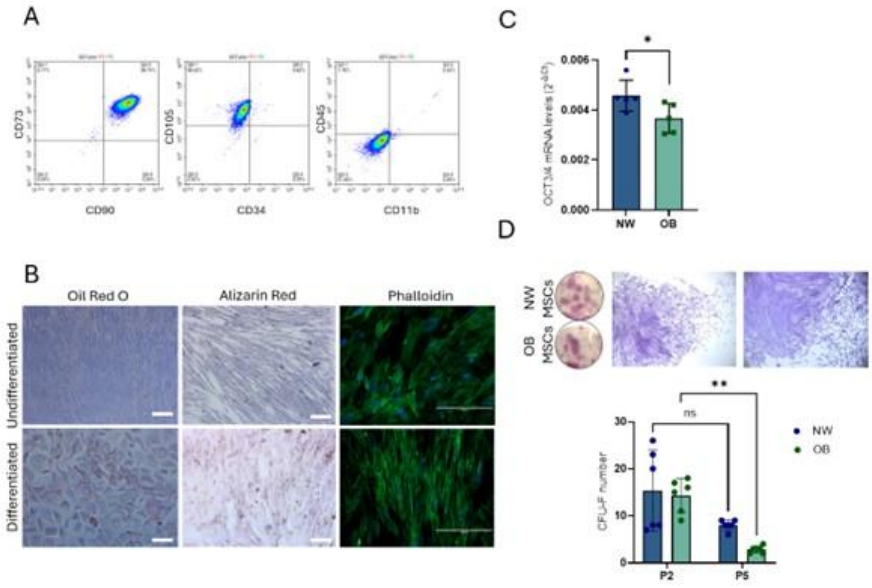
Objective: This study investigated whether maternal obesity alters stemness, redox homeostasis and adipogenic commitment in neonatal MSCs from mothers with obesity compared to those from mothers with normal weight. We hypothesized that maternal obesity induces redox adaptations that could modulate Forkhead Box O1 (FOXO1) adipogenic pathway (Jing *et al*., 2007).

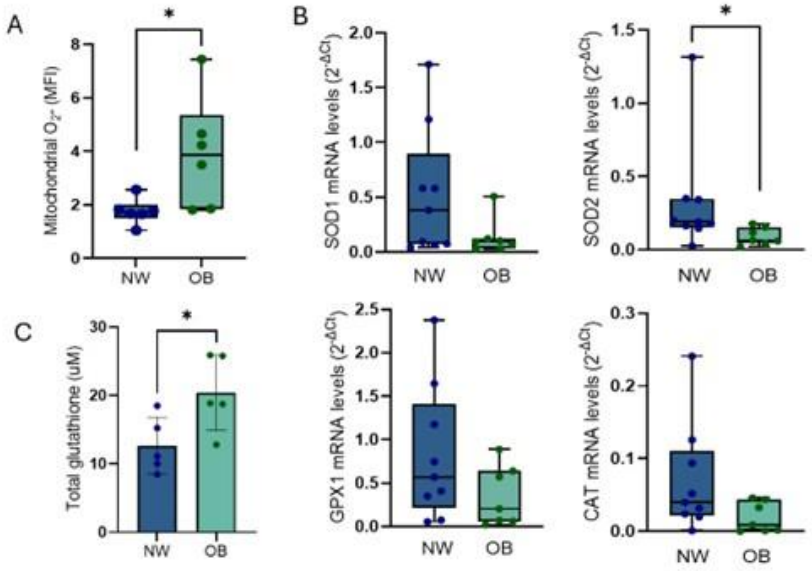
Methods: MSCs were isolated from Wharton's jelly of umbilical cords from neonates born to mothers with normal weight (NW-MSCs, n = 15) or obesity (OB- MSCs, n = 15). Basal MSCs were characterized for stemness properties and redox parameters. Cells were exposed to 250 µM hydrogen peroxide (H_2O_2) to assess antioxidant enzyme responses, and to measure intracellular levels of reactive oxygen species (ROS) and O2•- production in response to oxidative stress. Further, MSCs were subjected to adipogenic differentiation to evaluate FOXO1 expression and ROS responses. FOXO1 involvement was confirmed through acetyl-FOXO1 localization, while adipogenesis was confirmed by Peroxisome Proliferator-Activated Receptor gamma (PPARγ) expression. All procedures were conducted according to the Helsinki Declaration and complied with all relevant institutional and national ethical regulations.

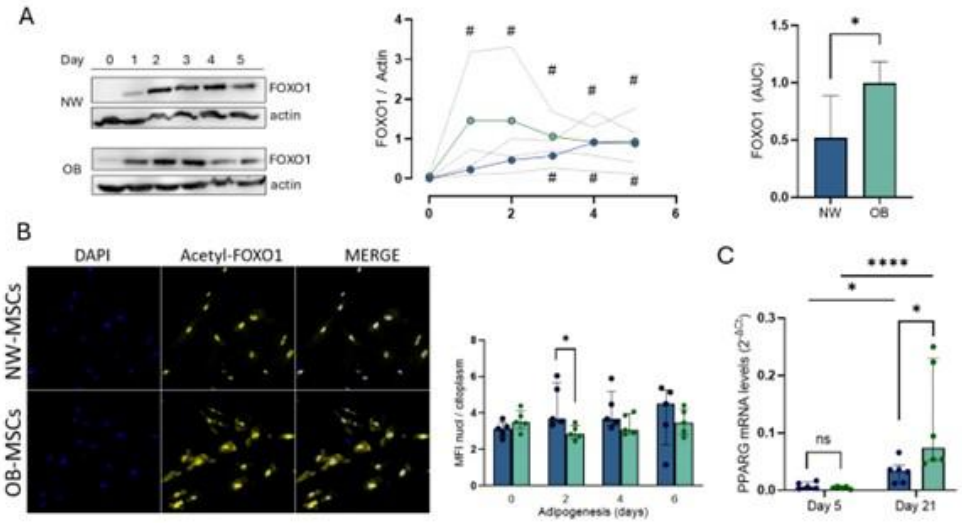
Results: Cells from both groups were positive for MSC markers CD73 and CD90, and CD105; and negative for CD11b, CD34, and CD45. Both NW-MSCs and OB-MSCs showed trilineage differentiation potential. OB-MSCs exhibited reduced stemness characteristics, including lower octamer binding protein 3/4 (OCT3/4) expression and decreased clonogenic capacity (Figure 1, $*p < 0.05$ *Mann–Whitney U test;* $**p < 0.01$ Tukey's range post hoc test, $n = 6$ NW-MSCs and 6 OB-MSCs). These cells also displayed increased mitochondrial superoxide levels and reduced superoxide dismutase 2 (SOD2) expression, indicating mitochondrial oxidative stress. In addition, OB-MSCs showed increased GSH levels, compared to NW-MSCs, suggesting an adaptive redox response (Figure 2, $*p < 0.05$, Mann–Whitney *U* test, median ± range, $n = 9$ NW-MSCs and 7 OB-MSCs). During early adipogenic commitment, OB-MSCs exhibited higher FOXO1 expression levels, and predominant cytoplasmatic localization during early adipogenesis, consistent with reduced repression of the adipogenic regulator PPARγ. Furthermore, adipocytes derived from OB-MSC displayed increased PPARγ expression at later stages of differentiation (Figure 3, $^{\#}p < 0.05$ Paired Wilcoxon signed-rank test compared to Day 0; $*p < 0.05$ *and* $***p < 0.0001$*Tukey's range post hoc test*, n = 6 NW-MSCs and 6 OB-MSCs).

Conclusions: Maternal obesity impacts stemness, redox balance, and FOXO1 dynamics in neonatal MSCs, leading to dysregulated FOXO1 compared to NW-MSCs. These findings support a model in which maternal obesity induces mitochondrial oxidative stress in neonatal MSCs, disrupting FOXO1 regulation, thereby shifting early adipogenic signaling toward enhanced adipocyte commitment. This mechanism

may expand the adipocyte precursor pool, potentially predisposing the progeny to metabolic disorders later in life (Bellalta *et al.* 2026).






A
Day 0 1 2 3 4 5
NW
FOXO1
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Acetyl-FOXO1
MERGE
NW-MSCs
OB-MSCs
MFI nucl / cytoplasm
Adipogenesis (days)
C
PPARG mRNA levels
ns
Day 5
Day 21

C05

Waveform-derived length and time constants for propagating action potentials

James Fraser[1], Eugenia Lopez-Belmonte Deza[1]

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Introduction. For more than a century, cable theory has provided the mathematical language for understanding voltage spread in neurons. By the 1950s, the responses to subthreshold stimuli were largely established, permitting the expression of passive cable properties in terms of intuitive and experimentally-measurable length and time constants. In Cambridge, Hodgkin and Huxley then provided a quantitative description[1] of the non-linear ionic currents that generate and propagate the action potential (AP). Their active cable equation powerfully relates conduction velocity to cable properties and waveform shape, but has resisted reduction to measurable descriptors analogous to the passive length and time constants.

Aim.

We sought to extend the quantitative framework of Hodgkin, Huxley, Rushton and others[2] by defining length and time constants of AP propagation and establishing their relationships with conduction velocity and cable properties.

Method
We analysed propagating APs in a computational cable model[3,4] of an unmyelinated axon with Hodgkin-Huxley ion channel kinetics. We identified specific instants during AP propagation at which net transmembrane ionic current is transiently zero, while axial and capacitive currents remain non-zero. At these *Transmembrane Current Transition* (TCT) points, the active cable equation simplifies, allowing us to relate propagation velocity only to the curvature of the action potential upstroke, axial resistance and membrane capacitance.

Results

At the TCTs, we defined a waveform curvature parameter, *kappa*, as the ratio of the acceleration to the rate of change of membrane potential. From this, we defined and derived length and time constants for the propagating AP. Measured values of AP propagation velocity (Fig 1A), AP wavefront length constant (1B) and AP upstroke time constant (Fig 1C) were shown to be equal to those calculated from *kappa* (Fig 1D). Our simulations show that *kappa* is determined by ion channel properties and membrane capacitance but not axial resistance, explaining why fibre diameter scales velocity without altering action potential shape. We suggest single-electrode methods for the experimental measurement of *kappa*: from the exponential rise of the upstroke with time (Fig 1C), and from the initial slope of an action-potential phase plot (not shown). Thus, *kappa* provides a single-value descriptor of AP shape that provides the missing bridge between the measurable waveform and physiological measures of propagation. We further show that *kappa* is the local real Laplace exponent of the AP upstroke, and thereby provides a framework to extend this approach into other physiologically realistic geometries, including myelinated, tapering and terminated cables.

Conclusions
By exploiting TCT points at which the active cable equation simplifies, we extend the elegant analytical framework of cable constants from passive to active membranes. We show that exact, measurable AP

length and time constants are derivable from waveform recordings and establish a natural foundation for extension to myelinated axons and complex geometries.

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2. Jack J, et al (OUP: 1975).

3. Fraser JA & Huang CL (2007) Prog Biophys Mol Biol 94, 336–72.

4. Fraser JA & Huang CL (2004) J Physiol 559, 459–478.

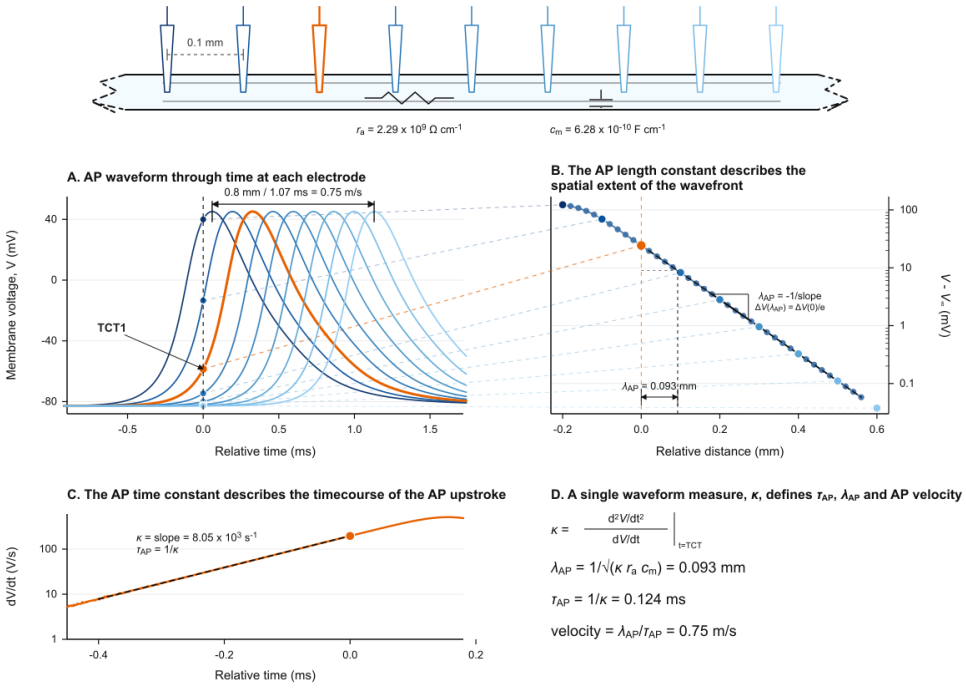

Figure 1. Definition and measurement of action potential length and time constants.
Simulated propagation was recorded at equally spaced electrodes in an unmyelinated axon. **A)** Voltage traces from each electrode show the travelling action potential; the highlighted trace denotes the waveform used for local analysis, with TCT1 indicating its first transition current transition point. **B)** At this instant, the voltage deflection ahead of the wavefront decays exponentially with distance, with a length constant of 0.093 mm. **C)** The AP upstroke also grows exponentially with time; its slope gives κ. **D)** The same value of κ may be obtained from the waveform at the TCT. We have derived compact expressions for the AP length constant, time constant, and propagation velocity in terms of κ; these expressions agree precisely with the measured values.

C06

Dorsomedial hypothalamic and perifornical regions recruit nucleus ambiguus circuits to coordinate laryngeal and cardiorespiratory responses during the defence reaction in rats

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Background

The dorsomedial hypothalamic nucleus and perifornical area (DMH-PeF) are key components of the hypothalamic defence network and play an important role in autonomic and respiratory regulation. Although activation of the DMH-PeF evokes characteristic defence-like cardiorespiratory responses, its influence on laryngeal control mechanisms remains poorly understood [1–4].

Aims

To describe the anatomical, electrophysiological and functional relationship between the DMH-PeF and nucleus ambiguus (nA) circuits involved in laryngeal motor control.

Methods

Experiments were performed in adult male Sprague–Dawley rats (n=36, 250–300 g) anaesthetised with sodium pentobarbitone (60 mg kg^{-1} i.p., supplemented intravenously as required). Three experimental approaches were used:

(1) Neuromorphological study: c-Fos and FOXP2 immunoreactivity were quantified throughout the rostrocaudal extent of the nA following repeated electrical stimulation of the DMH-PeF (30-40 μA, 100 Hz, 1 ms pulses, during 5 s).

(2) Electrophysiological study: extracellular recordings were obtained from neurones located within the nA and adjacent ventrolateral medullary regions during DMH-PeF stimulation (50–100 µA, 1 Hz, 0.1 ms pulses).

(3) Neuropharmacological study: an isolated glottis in situ preparation evaluated subglottic pressure during DMH-PeF electrical stimulation or chemical stimulation with glutamate (0,25 M, 50 nL, during 5 s), with phosphate-buffered saline microinjections (50 nL, pH 7,4 ± 0,1, during 5 s) serving as controls. Airflow, pleural pressure, arterial blood pressure, heart rate and subglottic pressure were continuously recorded.

Only experiments with histologically verified DMH/PeF sites were included. Paired Student's t-tests and the Mann–Whitney U test were used for within-animal and between-group comparisons, respectively.

Results

DMH/PeF electrical stimulation significantly increased c-Fos expression within the ipsilateral nA and nRA. The largest effects were observed in the semicompact formation, where Δ values increased in motoneurons (5.0 ± 0.7 vs 1.1 ± 0.4 cells; $p<0.001$) and total cells (19.0 ± 2.2 vs 13.6 ± 3.2 cells; $p<0.001$). Although overall FoxP2 immunoreactivity remained unchanged, c-Fos/FoxP2 co-expression increased significantly within the semicompact formation (34.7 ± 4.9 vs 19.5 ± 2.2 cells; $p<0.05$; Δ: 15.1 vs 5.2 cells, $p=0.008$).

Extracellular recordings (n=78 neurones) identified six neuronal populations. DMH/PeF stimulation modified neuronal activity in 41% of recorded neurones overall, including 51.3% of cardiovascular neurones and 40% of expiratory E1/E2 neurones. Co-stimulation of the vagus nerve and DMH/PeF facilitated responses in 37.5% of inspiratory decrementing laryngeal motoneurons, increasing discharge frequency up to four-fold.

DMH/PeF electrical stimulation increased respiratory frequency ($p<0.01$), arterial pressure ($p<0.001$) and heart rate ($p<0.001$), while reducing subglottic pressure ($p<0.001$). Similar responses followed glutamate microinjection were observed: subglottic pressure fell ($p<0.01$), with significant increases in respiratory frequency ($p<0.001$), arterial pressure ($p<0.001$) and heart rate ($p<0.01$).

Conclusions

These findings provide new anatomical, electrophysiological and functional evidence that DMH-PeF pathways modulate brainstem laryngeal circuits and contribute to the coordination of upper airway, respiratory and cardiovascular responses during the defence reaction.

Ethical approval

All experimental protocols were performed in accordance with the recommendations of the European Union directive (2010/63/EU) for animal care and experimental procedures. The experiments were

approved by the Ethical Committee for Animal Research of the University of Málaga and the Junta de Andalucía.

Keywords

dorsomedial hypothalamus; perifornical area; nucleus ambiguus; laryngeal motoneurons; subglottic pressure; defence response.

C07

Dorsolateral periaqueductal grey recruits nucleus ambiguus circuits to coordinate laryngeal and cardiorespiratory responses during the defence reaction in rats

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Background

The dorsolateral periaqueductal grey (dlPAG) coordinates defensive behaviours and associated cardiorespiratory responses. Although the nucleus ambiguus (nA) contains laryngeal motoneurons responsible for upper airway patency and vocal fold control, the functional interactions between the dlPAG and nA remain poorly understood [1-4].

Aims

To describe the anatomical, electrophysiological and functional relationship between these regions in anaesthetised rats.

Methods

Experiments were performed in adult male Sprague–Dawley rats (n=36; 250–300 g) anaesthetised with sodium pentobarbitone (60 mg kg^{-1} i.p., supplemented intravenously as required). Three complementary experimental approaches were used:

(1) Neuromorphological study: c-Fos and FoxP2 immunoreactivity were quantified throughout the rostrocaudal extent of the nA following repeated electrical stimulation of the dlPAG (30-40 µA, 100 Hz, 1 ms pulses, during 5 s).

(2) Electrophysiological study: extracellular recordings were obtained from neurones located within the nA and adjacent ventrolateral medullary regions during dlPAG stimulation (50–100 µA, 1 Hz, 0.1 ms pulses).

(3) Neuropharmacological study: an isolated glottis in situ preparation evaluated subglottic pressure during dlPAG electrical stimulation or chemical stimulation with glutamate (0,25 M, 50 nL, during 5 s), with phosphate-buffered saline microinjections (50 nL, pH 7,4 ± 0,1, during 5 s) serving as controls. Airflow, pleural pressure, arterial blood pressure, heart rate and subglottic pressure were continuously recorded.

Only experiments with histologically verified dlPAG sites were included. Paired-sample t-tests (within-animal) and one-way ANOVA (between groups) were used for statistical comparisons.

Results

dlPAG electrical stimulation significantly increased c-Fos expression within the loose formation (42.8 ± 5.8 vs 22.6 ± 4.9 cells; p=0.032) and compact formation (3.4 ± 0.8 vs 0.4 ± 0.4 cells; p=0.002) of the ipsilateral nA, confirming activation of neuronal populations associated with laryngeal motor control. FoxP2 immunoreactivity was predominantly localised within the loose and semicompact formations of the nA.

Extracellular recordings (n= 160 neurones) identified six functional neuronal populations. dlPAG stimulation modified neuronal activity in 76% of inspiratory decrementing neurones, 47% of inspiratory augmenting neurones, 67% of expiratory E1 neurones, 86% of expiratory E2 neurones, 52% of cardiovascular neurones and 46% of non-cardiorespiratory neurones, demonstrating widespread recruitment of medullary circuits associated with respiratory, autonomic and laryngeal control.

Electrical dlPAG stimulation increased respiratory frequency ($p<0.01$), arterial pressure ($p<0.001$) and heart rate ($p<0.001$), while reducing subglottic pressure ($p<0.01$). Similar responses were observed following glutamate microinjection, including a reduction in subglottic pressure ($p<0.001$), accompanied by significant increases in respiratory frequency ($p<0.001$), arterial pressure ($p<0.001$) and heart rate ($p<0.001$).

Conclusions

These findings provide new anatomical, electrophysiological and functional evidences showing that dlPAG–nA pathway appears to represent an important neural substrate linking behavioural state with laryngeal and cardiorespiratory control.

Ethical approval

All experimental protocols were performed in accordance with the recommendations of the European Union Directive 2010/63/EU for animal care and experimental procedures. The experiments were approved by the Ethical Committee for Animal Research of the University of Málaga and the Junta de Andalucía.

Keywords: dorsolateral periaqueductal grey; nucleus ambiguus; laryngeal motoneurons; subglottic pressure; defence response.

C08

A five-year retrospective analysis of lung function data from undergraduate life science students

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Lung function was collected over five years from two different undergraduate practical classes. We wished to investigate data reproducibility over this time period in both classes. We were unable to find any published data related to this. This study aims to analyse anonymised lung function data already collected during scheduled teaching sessions over the past five years. The goal is to identify trends and variability in student lung function data and explore potential educational insights.

Data was collected from 320 students as part of their respiratory physiology practical class. Students were informed that data would be used for educational purposes and gave their informed consent. Ethical approval was given by the University of Plymouth Faculty of Science and Engineering Research Ethics and Integrity Committee. No identifiable information was collected. Data collected was breathing rates at rest and after breath holding, peak expiratory flow (PEF), respiratory rate, tidal volume, ventilation rate and spirometric volumes. Data on ambient temperature, humidity and particulate matter was collected retrospectively using government databases. Means (SD), Levene's test of variance and one way ANOVA were used for analysis. P values of <0.05 were considered statistically significant.

Tests for variance showed a significant difference ($P<0.05$) for the breathing rate collected after a one-minute breath hold ($n=213$). One way ANOVA testing for mean differences showed significant differences ($P<0.05$) in PEF ($n=270$), tidal volume and forced vital capacity ($n=49$). Regression data on physiological and environment data will also be presented.

Our findings showed that most lung function variables in different cohorts were relatively reproducible over this five-year period. Some variables did show differences, however this most likely was due to a low number of students in that particular year. Various factors can affect reproducibility, including facilitator and student engagement, cohort size, and limitation of resources. Our message to students and staff is that we should be reassured that lung function data students collect is reliable and reproducible.

C09

Unwelcome invitations: a survey on the impact of predatory journal emails among bioscience faculty

Edward Goodland[1], Shania Jones[1], Mirza Subhan[1]

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A noticing trend is the rise of predatory journals; individuals and organisations that exploit and abuse pay-to-publish models while not providing legitimate editorial or peer review processes. Currently, most research on predatory journals related to academics has involved surveys on awareness and knowledge of this practice. There is also substantial work published on students, primarily related to their understanding and use of predatory journals. This study aims to illustrate the disruption predatory publishers cause to researchers, institutions and academics through recording the frequency predatory emails are sent to academics over a two-month period and how they perceive this.

Data was collected from 13 participants (9 males and 4 females) using a questionnaire. The questionnaire included demographic questions (age, gender etc.) and professional background information (area of expertise, publication history), alongside open-ended questions designed to gather deeper insights into participants' awareness of predatory publishing and their experiences with email solicitations. This study was approved by the University of Plymouth Science and Engineering Research Ethics & Integrity Committee. All participants were asked to give their consent as a preliminary question. All data was anonymised. Inclusion criteria were that participants had to have published at least one academic journal article and consented to send all predatory emails to a designated email address over a two-month period for analysis. Given the small number of participants and the nature of the data, analyses were primarily descriptive and exploratory. Means (SD), medians, interquartile ranges, frequency distributions, qualitative analysis, linear regressions were used for analysis. P values of <0.05 were considered statistically significant.

A total of 1,248 predatory emails were analysed. 55.8% were from journals, while 17.5% were for conferences. The remainder included predatory emails for journal editorial board invitations, books, and vanity press. Table 1 shows mean demographical, publishing and predatory email data.

	Mean (SD)	Min-Max
Age (years)	48.9 (11.7)	24-77
Academic experience (years)	22.0 (11.6)	2-51
Number of publications published per participant	33.2 (32.0)	2-120
Number of publications published per participant as corresponding author	19.2 (28.0)	0-90
Predatory emails received per participant	127.6 (100.9)	2-327
Number of predatory journal emails per participant	71.4 (80.1)	2-258
Predatory conference emails per participant	22.3 (25.7)	0-78

Table 1. Mean participant demographics, publication information and predatory email numbers (n=13).

Linear regression of participants' papers published as corresponding author showed a positive non-significant relationship with the number of predatory emails received (p=0.34). This did indicate there was a trend for corresponding authors to get more predatory emails.

Study participants consisted of a wide range of bioscience areas and career experiences. There was a trend for more senior academics to receive more predatory emails. All participants received on average about two emails per day; this varied widely but was comparable to previous studies. 62% of participants were bothered by receiving predatory emails. This study showed receiving predatory journal and conference emails is a nuisance for academics and there is a potential for this affecting not only early-career researchers but also senior academics.

C10

Is human atrial action potential alternans associated with steep action potential restitution, or simply long steady-state action potential duration?

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Introduction: Atrial action potential duration (APD) alternans, a beat-to-beat alternation of long/short APD, may predispose to atrial fibrillation in patients [1]. Atrial APD alternans may result from a strong positive relationship between the APD and the stimulation basic cycle length (BCL), i.e. a steep APD restitution slope [2]; but some studies disagree [1]. Alternatively, APD alternans could result simply from a long steady-state APD measured at physiological rate (SS-APD), as studied in guinea-pig ventricle [3]. **Aim:** To test the hypothesis, for the first time to our knowledge in human atrial isolated myocytes, that longer SS-APD is associated with steeper APD restitution slope and/or larger magnitude of APD alternans. **Methods:** Custom-written software (WinEDR) was used to analyse action potentials previously recorded by whole-cell-patch clamp (35-37^{o}C) at various BCLs (between 150 and 1000 ms; 20 action potentials/BCL), in 50 human atrial myocytes. The myocytes had been enzymatically isolated from right atrial tissues obtained from 12 adult patients who were undergoing cardiac surgery. Procedures and experiments were approved by West of Scotland Research Ethics Service (REC: 17/WS/0134). Written, informed consent was obtained from all patients. The investigation conformed with the principles of the World Medical Association's Declaration of Helsinki. All patients were in sinus rhythm on the day of surgery. All APDs were measured at a repolarisation level of -61 mV (i.e. APD-61mV), to reflect the human atrial cellular effective refractory period [4]. **Results:** APD-61mV restitution was fit to either a straight line (all 50 cells), or to a mono-exponential curve (achievable in 47 cells) for comparison. Dichotomising the SS-APD-61mV values (measured at BCL 1000 ms), revealed a significantly steeper APD restitution slope to be associated with longer SS-APD: straight line slope =0.10±0.03 (mean±SEM; n=25 cells) *vs* -0.02±0.01 (n=25), P<0.001 (Mann-Whitney); maximum exponential slope =0.06±0.02 (n=23) *vs* -0.03±0.01 (n=24), P=<0.001. Furthermore, there was a significant and strong positive correlation (linear regression) between SS-APD and both straight line restitution (P<0.001, R^2=0.577, n=50) and exponential restitution (P<0.001, R^2=0.415, n=47). The maximum magnitude of APD alternans (calculated in each cell by averaging even-to-odd APD-61 mV-subtractions of the last 5 action potential pairs at each BCL) was significantly larger in cells with longer (n=25) than shorter (n=25) SS-APD: 26±5 *vs* 10±2 ms, P<0.001. Furthermore, maximum APD alternans magnitude and SS-APD were significantly correlated (P<0.001, R^2=0.390). However, there was only a weak association between APD alternans and APD restitution: steeper exponential restitution slope correlated significantly (P=0.021) but weakly (R^2=0.113) with larger APD alternans magnitude; whereas there was no significant correlation between straight line restitution and APD alternans magnitude (P=0.316, R^2=0.021). **Conclusion:** In human atrial myocytes, a longer SS-APD correlates both with a steeper APD-restitution slope and a larger APD alternans magnitude; but APD alternans magnitude is only weakly associated with APD restitution slope. Therefore, the propensity to APD alternans in human atrial myocytes, and, therefore, its potential to promote atrial fibrillation in patients, might be better predicted by a longer steady-state atrial APD measured at physiological rate, than by a steeper APD restitution slope.

C11

Pupillary light responses of males and females following competitive rugby matches

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Rugby performance features repeated head impacts in both training and competition. Such head impacts are related to brain disease and cognitive deficits with females being potentially more at risk than males (Allan et al., 2024). There is no currently accepted field-based method of monitoring effects of potential brain injuries in the absence of diagnosable concussion. Automated measurement of the pupillary light reflex (PLR) has been proposed as a solution to this issue (Kirk & Childs, 2023) but data are lacking for rugby performance. An adult mixed sex cohort (male n=44 ; female n=68) participated in this study following institutional ethical approval. PLR of both eyes were measured in ambient indoor light (270-330 Lux) pre and post competitive rugby matches using Neuroptics NPi-200 automated pupilometer (Irvine, USA). Variables measured were min and max pupil diameter (mm), peak constriction velocity (CV, $mm \cdot s^{-1}$), mean CV (MCV, $mm \cdot s^{-1}$), dilation velocity (DV, $mm \cdot s^{-1}$), amplitude (%), latency (s) and 'NPi' (AU) - a proprietary variable representing overall pupil response. Two-way repeated measures ANOVAs were calculated for all variables using Bayes factors (BF10) ≥3 as inference and post hoc analyses with Cohen's d effect size (JASP 0.95.3). NPi displayed decisive pre-post reductions ($BF10 = 5.407^{+12}$) with females reducing more (BF10 = 8.7, d = .84). Max diameter ($BF10 = 1.206^{+6}$, d = .36 increase), min diameter ($BF10 = 4.799^{+10}$, d = .59 increase), amplitude ($BF10 = 1.059^{+7}$, d = .55 decrease) and DV (BF10 = 5,529, d = .39 decrease) all showed decisive pre-post changes but no differences between sexes. Females displayed differences in both CV (BF10 = 4.2, d = .37 decrease) and MCV (BF10 = 15.8, d = .44 decrease) compared to males, but only MCV had pre-post differences (BF10 = 34.3, d = .21). Latency had very strong pre-post increases (BF10=99, d=.35 increase), without differences between sexes. Both sexes showed increased pupil diameter following rugby performance, possibly related to arousal. Pupils in both sexes were slower to respond and responded less to stimulus post-performance, which may be related to head impacts. Changes in CV only occurred in females, suggesting females may be more affected by head impacts during rugby performance than males. These data support the potential use of PLR in monitoring brain function in competitive sports environments.

C12

A New Method of Quantifying Ventilatory Long-Term Facilitation

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Acute intermittent hypoxia (AIH) elicits long-lasting increases in ventilation (VI) that persists for hours after the inducing stimulus. This form of respiratory motor plasticity is termed ventilatory long-term facilitation (LTF). In awake humans, AIH-induced ventilatory LTF is critically dependent upon CO2. For example, poikilocapnic AIH results in slight hypocapnia, which masks LTF due to negative chemofeedback inhibition of VI. However, when AIH is superimposed upon a background of mild hypercapnia whereby end-tidal CO2 pressure (PETCO2) is clamped before, during and after AIH, increases in VI of up to 50% are observed. One caveat of all ventilatory LTF experiments conducted to date, is the absence of considering changes in CO2 production rate (VCO2) that could influence changes in VI in accordance with the alveolar ventilation equation. Thus, the purpose of the current study was to test the hypothesis that the magnitude of ventilatory LTF induced by hypercapnic AIH is altered by adjusting changes in VI to changes in PETCO2 and VCO2. Here, we report preliminary results from eight healthy males (age=22±3 years). Subjects attended two laboratory visits on separate days. On day 1, pulmonary function testing was performed; on day 2, subjects were exposed to hypercapnic AIH. Subjects sat quietly on a chair with their back supported and facemask on. The mask was connected to a pneumotachograph and three-way stopcock on the inspired side and mixing chamber on the expired side. One limb of the stopcock sampled ambient room air and the other sampled gas from two 200-L Douglas bags filled with ~8% O2. Inspired and expired gases were obtained from calibrated O2/CO2 gas analysers. After ~10 min of resting eupnoea, 100% CO2 was titrated into the inspired circuit to raise PETCO2 by ~3 mmHg (baseline, B). Fifteen, 1-min episodes of hypoxia were administered, interspersed with 90-s intervals breathing ambient air. Mild hypercapnia was maintained throughout AIH and for 20 min after (recovery, R). Ventilatory LTF was quantified by two methods: (Method 1) traditionally as VI,R/VI,B·100, and (Method 2) *via* an equation (Equation 1) that accounts for changes in PETCO2 and VCO2. Equation 1 can be simplified to quantify ventilatory gain (*G*v) at baseline and in recovery, shown in Equation 2. When calculated as a %-change, Equation 2 equals Equation 1.

Equation 1: ((VI,R/VI,B)·(PETCO2,B/PETCO2,R))/((VCO2,R/VCO2,B)·(VI,B/VI,R))·100

Equation 2: *G*v=(VI/VCO2)·(VI/PETCO2)

Peripheral arterial oxyhaemoglobin saturation and end-tidal O2 pressure decreased to 82±1% and 49±2 mmHg during hypoxia, respectively. During recovery versus baseline, VI increased by 3.1±1.6 L/min, VCO2 increased by 81±52 mL/min and PETCO2 was unchanged (+0.15±0.89 mmHg). When normalised to VI, VCO2 decreased by 1.8±1.7 mL/L/min (Table 1). On average, the magnitude of ventilatory LTF calculated by Method 1 was +22±10% (P<0.001) and calculated by Method 2 was +28±14% (P<0.001). A significant difference between Methods 1 and 2 was found (P=0.042, d=0.878, Figure 1). A quadratic model predicted the relationship between Methods 1 and 2 (R^2=0.913, Figure 1). Thus, based on our preliminary findings, accounting for small changes in PETCO2 and CO2 significantly alters the quantified magnitude of ventilatory LTF after hypercapnic AIH.

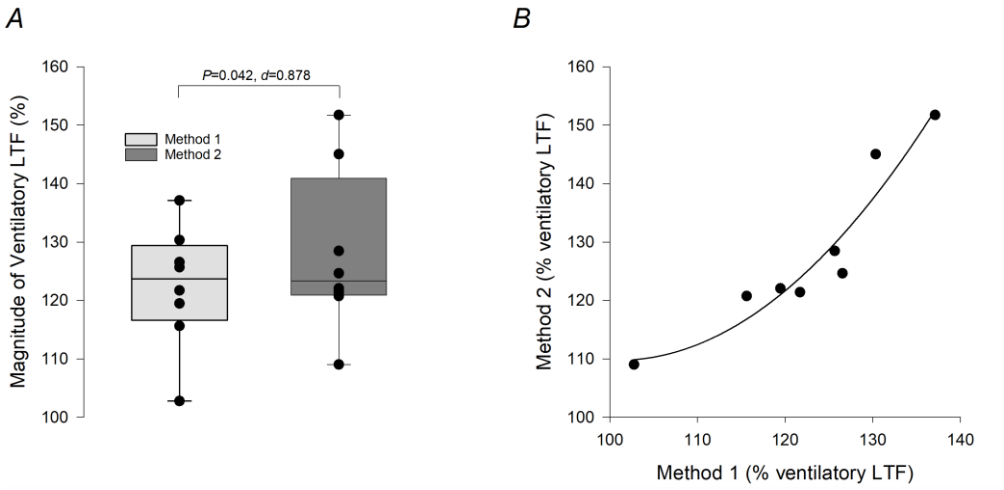

Table 1: Ventilatory Responses to Hypercapnic AIH

	Baseline	Hypoxia	Recovery
V_T (L)	0.99±0.26	1.29±0.54	1.11±0.40
f_b (breaths/min)	14.8±3.7	14.8±4.2	16.2±3.8
$\dot{V}_I$ (L/min)	14.0±2.9	17.5±4.0	17.2±3.9
$\dot{V}CO_2$ (L/min)	0.49±0.18	0.56±0.22	0.57±0.22
$\dot{V}CO_2/\dot{V}_I$ (mL/L/min)	34.4±8.8	31.6±7.9	32.6±7.4
$P_{ET}O_2$ (mmHg)	113±4	49±2	117±4
$P_{ET}CO_2$ (mmHg)	40.7±3.7	40.5±3.7	40.8±3.0
SpO_2 (%)	95.1±1.2	82.0±1.5	95.9±0.9
*G*v (L/min/mmHg)	10.7±3.6	14.7±5.2	13.6±4.3

C13

Characterisation of the cardiovascular and autonomic pattern during sustained vocalisation in healthy voice: preliminary data

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BACKGROUND

Sustained vocal emission during singing generates an increase in intrathoracic pressure resembling that produced during the Valsalva manoeuvre (VM), with potential implications for cardiovascular autonomic control [1,2]. Although evidence exists on cardiorespiratory synchronisation during singing [3] and previous work from our group has documented the interaction between vocal fundamental frequency and cardiovascular variables [4], no studies have characterised the heart rate (HR) pattern and autonomic tone during individual sustained vocalisation as a function of specific vocal parameters [5]. This gap constitutes the starting point of the present study.

AIMS

To obtain an initial characterisation of the cardiovascular and autonomic response during sustained vocalisation at different vocal frequencies and intensities in adults with healthy voice.

METHODS

Quasi-experimental repeated-measures study. Two adult participants with musical training (1 male, 1 female) completed a standardised protocol including: 1) physiological stabilisation and baseline recording, 2) sustained emission of the vowel /a/ (10 s) at 3 pitches (A–E–B, adapted to the relevant octave by sex) × 3 intensities (piano, mezzo-forte, forte) × 2 repetitions (n = 36 observations). ECG (lead II), pulse signal, and glottal microphone signal were continuously recorded (Biopac MP160, AcqKnowledge). Instantaneous HR was derived from RR intervals. HR was normalised as a percentage change from individual baseline and compared across 5-time windows using Friedman and Wilcoxon tests ($\alpha = 0.05$). HR variability was also analysed using BaroWavelet (LF/HF ratio across three phases: baseline, emission and post-emission) [6].

RESULTS

A biphasic pattern of HR increase —two peaks separated by a decrease— was identified consistently across all 36 observations: 1st peak before or at the onset of vocalisation (+30.5 ± 8.8%), decrease during sustained emission (+9.0 ± 9.5%), 2nd peak of greater amplitude at the end of emission (+40.1 ± 17.2%) and post-emission drop (−3.0 ± 6.7%). The Friedman test showed significant differences across the five time points of the pattern ($\chi^2 = 120.2$; $p < 0.001$) and the Wilcoxon test confirmed the consistency of all four transitions ($W = 0$; $p < 0.001$). Neither acoustic intensity nor pitch significantly modified the pattern ($p > 0.05$). Autonomic analysis showed a significant increase in the LF/HF ratio during vocalisation compared to baseline (2.14 ± 1.16 vs. 6.09 ± 2.83; $p < 0.001$), with a partial decrease in the post-emission phase (3.70 ± 2.07; $p < 0.001$ vs. emission).

CONCLUSIONS

These preliminary findings suggest that sustained vocalisation generates a biphasic HR pattern whose profile resembles that of the VM, accompanied by an increase in sympathetic tone during phonation and a partial decrease during post-emission recovery. The pattern was consistent across all 36 observations regardless of pitch, intensity, or participant, supporting its potential as a reference profile in healthy voice within a broader comparative study.

ETHICAL APPROVAL

The study was approved by the Ethics Committee of the University of Malaga (CEUMA; ref. 107-2025-H), conducted in accordance with the Declaration of Helsinki. All participants provided written informed consent prior to inclusion.

KEYWORDS

Sustained vocalisation; heart rate; autonomic nervous system; Valsalva manoeuvre; BaroWavelet; heart rate variability

C14

Problem-Based Learning promotes causal physiological reasoning in first-year medical students before formal cardiovascular instruction: a pre–post quasi-experimental study

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Background

Teaching physiology in preclinical medical education demands not only conceptual knowledge but the capacity to construct causal explanatory frameworks linking physiological mechanisms to clinical outcomes [1]. Problem-Based Learning (PBL) has been proposed as a strategy to foster this integrative reasoning [2], yet evidence from first-year curricula — before formal cardiovascular instruction — remains scarce, particularly when assessed with instruments sensitive to causal integration [3]. Whether mechanistic understanding and causal integration develop as distinct cognitive constructs following PBL has not been directly tested.

Aims

To determine whether a brief, authentically-triggered PBL intervention improved two independent dimensions of physiological reasoning — mechanistic conceptual complexity (P1: cardiac pump model) and physiological cause–effect integration (P2: rationale for emergency cardiovascular intervention) — in first-year medical students prior to formal instruction.

Methods

A quasi-experimental pre–post study was conducted with 135 first-year medical students at the University of Málaga, before lecture-based cardiovascular teaching. The intervention comprised two face-to-face sessions (3 h each) in five small-group classes of 25–30 students, with cooperative teams of five, triggered by authentic video recordings of cardiovascular collapses in professional athletes (Eriksen, 2021; Hamlin, 2023). Written responses to two open-ended questions were independently coded by three raters using a validated five-level ordinal framework (N0–N4) assessing P1 and P2 separately (inter-rater $\kappa = 0.39–0.52$). Pre–post comparisons used Wilcoxon signed-rank tests; effect size $r = Z/\sqrt{N}$. Independence of P1 and P2 gains was assessed by Spearman correlation.

Results

After excluding non-evaluable responses, 130 students (96.3%) were included in conceptual analyses; all 135 for textual quality. For P1 ($N = 130$): $Z = -4.683$, $p < 0.001$, $r = 0.41$ (moderate effect); students at advanced levels (N3–N4) rose from 23.1% to 43.8%. For P2 ($N = 130$): $Z = -7.723$, $p < 0.001$, $r = 0.68$ (large

effect); students at N3–N4 increased from 3.8% to 53.8% — a near-complete transformation of the cohort's reasoning profile. Textual quality improved significantly ($Z = -5.709$, $p < 0.001$, $r = 0.49$; $N = 135$): 37.8% improved, 5.2% declined. Spearman correlation between P1 and P2 gains was $r_s = 0.128$ ($p > 0.05$), confirming their independence.

Conclusions

Two sessions of PBL centred on authentic cardiovascular cases produced large, independent gains in causal physiological reasoning before formal instruction. The effect size for P2 ($r = 0.68$) exceeds benchmarks reported in comparable PBL interventions [4]. The dissociation between mechanistic complexity and causal integration indicates these are distinct cognitive constructs requiring targeted pedagogical strategies, consistent with retention advantages reported for inquiry-based approaches in preclinical physiology [5].

Ethical approval

The study was approved by the Ethics Committee of the University of Málaga (CEUMA; ref. 187-2024-H) and conducted in accordance with the Declaration of Helsinki. Informed consent was obtained from all participants prior to inclusion.

Keywords: problem-based learning; physiology education; causal reasoning; preclinical medical education; conceptual progression

C15

A novel neuroprotective mechanism in Parkinson's disease models: the IGF-II/S1P1 receptor transactivation axis

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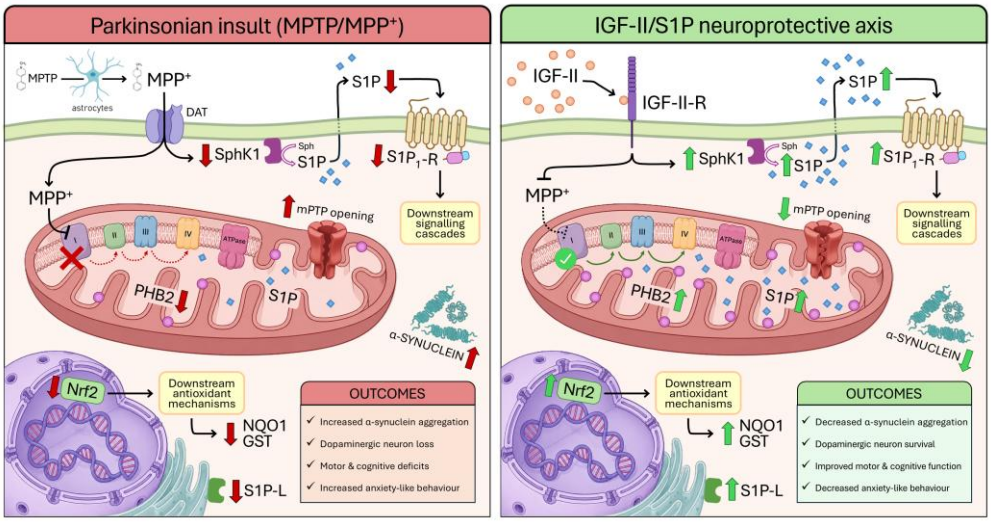
Background: Parkinson's disease is characterised by progressive dopaminergic neurodegeneration associated with mitochondrial dysfunction, oxidative stress, and α-synuclein accumulation. Insulin-like growth factor II (IGF-II) exerts neuroprotective effects in experimental models of neurodegeneration, although the underlying molecular mechanisms remain poorly understood.

Aims: This study aimed to determine whether the neuroprotective actions of IGF-II against dopaminergic neurotoxicity depend on the "inside-out" transactivation of the sphingosine kinase 1 (SphK1)/sphingosine-1-phosphate (S1P)/S1P1 receptor signaling axis. Specifically, we sought to elucidate how this pathway links organelle stability, prohibitin-2 (PHB2) preservation, and the Nrf2-mediated antioxidant response both *in vitro* and *in vivo*.

Methods: Neuroprotective mechanisms were evaluated in SN4741 neurons (mouse embryonic dopaminergic cell line, RRID: CVCL_S466, which expresses phenotypic markers of *substantia nigra* dopaminergic neurons) exposed to 1-methyl-4-phenylpyridinium (MPP^+) and in a chronic 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine/probenecid (MPTP/p) mouse model (ten-week-old male C57BL/6J mice). Mitochondrial permeability transition pore (mPTP) opening, cell viability (lactate dehydrogenase [LDH] release), sphingolipid metabolism (global SphK and S1P lyase [S1PL] activities, and S1P ELISA), antioxidant enzyme activities, protein expression (western blot), and immunofluorescence analyses (for Nrf2 translocation, PHB2, and receptor trafficking) were performed to characterise intracellular signalling pathways. Tyrosine kinase receptors were blocked using BMS-536924 to isolate specific IGF-II-R actions. Behavioural assessments included rotarod, Y-maze spontaneous alternation, self-grooming, and elevated plus maze (EPM) tests. In vivo western blots utilized a standardized protein pool (STD) from control substantia nigra for inter-gel normalization. Data were combined from at least 4 independent experiments, expressed as mean ± SEM, and analysed using ordinary one-way ANOVA followed by Tukey's post-hoc test.

Results: MPP^+ exposure induced mitochondrial dysfunction, oxidative stress, prohibitin-2 depletion, and neuronal death, whereas IGF-II restored mitochondrial integrity and cell survival. Specifically, MPP^+ triggered a 2.9-fold increase in mPTP opening and a 56% reduction in the inner membrane scaffold PHB2, which were fully reversed by IGF-II. IGF-II increased sphingosine kinase activity, restored intracellular and extracellular S1P levels, preserved S1P1 receptor expression, and selectively upregulated SphK1 upstream of receptor activation. Furthermore, MPP^+-induced impairment of S1PL turnover was partially rescued by IGF-II, maintaining functional lipid signalling flux. Pharmacological inhibition of either SphK1 (MP-A08) or S1P1 receptor (W123) abolished the protective effects of IGF-II, confirming the requirement of this signalling pathway, whereas SphK2 inhibition had negligible effects. In addition, IGF-II promoted nuclear translocation of Nrf2 (completely blocked by W123 or iSphK1) and restored the activity of antioxidant enzymes, including NAD(P)H quinone oxidoreductase 1 and glutathione S-transferase. In vivo, IGF-II prevented MPTP-induced cognitive impairment (Y-maze spatial memory) and anxiety-like behaviour (EPM open-arm exploration), reduced nigral α-synuclein accumulation, and preserved SphK1 expression in the substantia nigra of MPTP-treated mice.

Conclusions: These findings identify the IGF-II/IGF-II-R/SphK1/S1P/S1P1 receptor axis as a key neuroprotective mechanism linking mitochondrial preservation via S1P/PHB2 platforms, antioxidant defence, and proteostatic regulation in experimental Parkinson's disease models. Modulation of this sphingolipid-dependent pathway may represent a promising disease-modifying therapeutic strategy capable of addressing both motor and non-motor symptoms in Parkinson's disease.



C16

Maternal Osteocyte Deficiency in CFTR Impairs Offspring Early Development

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Maternal endocrine function is a fundamental determinant for perinatal health[1]. Although the skeleton is increasingly recognized as an endocrine organ, the contribution of osteocytes, the most abundant type of bone cells[2], to maternal hormonal regulation during pregnancy and lactation remains incompletely understood. Recently, we identified cystic fibrosis transmembrane conductance regulator (CFTR), originally known as an epithelial Cl^- channel, to be functionally expressed in osteocytes and required for skeletal integrity[3]. In the present study, we hypothesized that osteocytic CFTR might be important to bone endocrine function for maternal-offspring regulation and perinatal health.

We used an osteocyte-specific CFTR knockout mouse model (cKO, *Dmp1-Cre; Cftr$^{fl/fl}$*) in comparison with Cre-negative (Ctrl, *Cftr$^{fl/f}$*) controls. In a breeding model using cKO females crossed with wild-type males, offspring born to osteocytic CFTR-deficient mothers showed significantly reduced ($P< 0.05$) body weight (3.12 ± 0.07g, n = 49) on day 7 post birth as compared to those (3.93 ± 0.07g, n = 30) born to control mothers. The survival rate of the pups from cKO mothers in three weeks post birth was significantly lower than those from control mothers (n = 5-7 litters). In the survived pups, the body weight gained in three weeks was substantially lower in the cKO group (n = 5-7 litters), which together suggested early development defects in offspring born to cKO mothers. To identify the underlying mechanism, we examined the maternal bone phenotype. Adult female cKO mice displayed marked bone loss, including reduced bone mass and trabecular bone sparsity as revealed by micro-CT analysis. Osteocalcin (OCN), a key osteocyte-derived hormone implicated in metabolic and developmental regulation, was significantly decreased in osteocytes of cKO mice (n = 6). Serum OCN and Ca^{2+} levels were found to rise during lactation period in control mothers, which was largely abolished in cKO mice. Consistently in an osteocyte model (MLO-Y4), CFTR knockout led to suppression of OCN at both mRNA and protein levels. Transcriptomic analysis of the osteocyte model further revealed broad changes in additional osteocyte-secreted factors (e.g., *Bmp1*), indicating that CFTR controls a wider osteocyte endocrine network beyond OCN alone. Moreover, patch-clamp, fluorescence-based Cl^-- and pH-imaging revealed defective Cl^- transport and impaired cAMP-evoked Cl^--dependent H^+ secretion in MLO-Y4 cells with CFTR knockout, which may underlie the dysregulated endocrine function in CFTR knockout osteocytes.

Taken together, these findings have shown that CFTR deficiency in maternal osteocytes causes skeletal deterioration and disrupts the bone endocrine program, particularly OCN production, thereby weakening maternal endocrine support during the perinatal period for offspring early development, revealing a new mechanism for maternal bone-to-offspring regulatory axis.

C17

Use of fillers in academic teaching: a survey of student and staff perceptions

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[1]University of Plymouth, United Kingdom

Filler words and sounds (e.g. "um", "er", "so", and "okay") are commonly used in everyday speech and are often present in university teaching. Whilst filler words are a natural feature of spoken communication, little is known about how students perceive their use in higher education settings. This study aimed to investigate student and staff attitudes towards the use of filler words in teaching and explore whether perceptions differ according to year of study and academic faculty.

Survey data was collected from 126 students across multiple year groups (Foundation Year, Year 1, Year 2, Year 3 and MSc) within the School of Biomedical Science (SoBS) and Plymouth Business School (PBS). 14 staff from these schools also participated. Ethical approval was given by the University of Plymouth Faculty of Science and Engineering Research Ethics and Integrity Committee. Participants completed an anonymous online questionnaire using the JISC online survey platform which was shared via a link or QR code. Both questionnaires gathered demographic information including age, gender, ethnicity, and whether English was the participant's first language. Students were also asked their home postcode, programme of study, year of study, and to rate their agreement with statements relating to the frequency, acceptability and impact of filler word use during teaching, using Likert-scale responses. Staff were also asked their area of expertise, highest educational qualification, years of university teaching experience and if they have a teaching qualification. A Likert scale was used to also obtain data on staff's estimated usage of fillers in teaching, whether fillers are wasteful and if they had heard of fillers previously. Open-text comments were also collected to provide qualitative insights. Mean (SD) and median (IQR) were used for analysis. Further statistical testing will be presented.

Mean (SD) age for student participants was 23.8 (7.5) years while for staff it was 46.4 (8.5). 81 (64.3%) student participants were female, 44 (34.9%) were male and 1 (0.8%) was non-binary. For staff, 3 (21.4%) were female and 11 (79.6%) were male. 92 (73.0%) students were from SoBS and 34 (27.0%) were from PBS. 6 (42.9%) staff were from SoBS while 8 (57.1%) were PBS. Median results showed most students felt fillers are not used too often and were not irritated by their use (Table 1). Most students agreed that fillers did not bother them (55.5%) and they felt it was a natural form of communication (57.1%). 11 (78.6%) staff participants agreed they regularly use fillers. However, staff were neutral in their view that fillers are wasteful. 13 (92.9%) staff had previously heard of fillers before.

Questionnaire items	1: SD (%)	2: D (%)	3: N (%)	4: A (%)	5: SA (%)	Median	Q1	Q3	IQR
I feel teaching staff use fillers in our teaching too often	10 (7.9%)	30 (23.8%)	53 (42.1%)	28 (22.2%)	5 (4.0%)	3	2	4	2
I feel irritated when teaching staff use fillers	14 (11.1%)	37 (29.4%)	50 (39.7%)	19 (15.1%)	6 (4.8%)	3	2	3	1
The use of fillers does not bother me	5 (4.0%)	20 (15.9%)	31 (24.6%)	57 (45.2%)	13 (10.3%)	4	3	4	1
Fillers are a natural form of communication	2 (1.6%)	7 (5.6%)	45 (35.7%)	56 (44.4%)	16 (12.7%)	4	3	4	1

Table 1. Results of the Likert scale analysis for student filler perception data (n=126).

Our main finding was that this cohort of students found the use of fillers acceptable in teaching. Although this is an area with limited published data, we felt it is an important aspect in teaching and learning and staff should be aware of it. These findings will contribute to a greater understanding of communication practices in higher education and may help inform teaching approaches that better support student engagement and learning.

C18

Comparison of 16–18 year-old students' STEM subject choices from two schools

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STEM (Science, Technology, Engineering, and Mathematics) subjects are important for innovation and economic development in every nation, yet for various reasons, many students choose to avoid these fields in further education or are underrepresented. By identifying key motivators, personal barriers, social influences, and educational factors, this research aimed to address the challenge of declining STEM enrolment by analysing the reasons influencing the decision-making process of students and making a comparison between two local schools in Devon. Data from one of the schools also included the role of humanities in STEM.

Anonymous questionnaires were completed by 77 students studying at Ivybridge Community College (ICC) and 70 students at Plymstock School (PS). Ethical approval was given by the University of Plymouth Faculty of Science and Engineering Research Ethics and Integrity Committee. The questionnaire explored student perceptions, attitudes, and experiences regarding STEM subjects, as well as familial and role model influences and demographics. Means (SD), medians, interquartile ranges, frequency distributions, qualitative analysis, unpaired t-tests, and Chi Square were used for analysis. P values of <0.05 were considered statistically significant.

Age of students between the two schools showed a significant difference ($p=0.02$), where mean age (SD) for PS was 16.9 (0.6) years and higher than for ICC, 16.7 (0.7) years. Chi squared analysis showed a significant gender difference too ($p<0.0001$), with PS having 37% female and 63% male, while ICC had 73% female and 27% male. Education of parents also showed a significant difference between schools ($p<0.0001$). ICC students responded more positively to science, math and technology-related statements, while PS responded more positively to engineering. For humanities, PS students responded the lowest compared to STEM categories.

These findings underscore the need for holistic STEM engagement strategies, emphasising hands-on experiences, mentorship, and broader career awareness. Future research should further explore the intersection of intrinsic motivation, societal factors, and access and opportunities to better support students in STEM fields. The future of arts and humanities in STEM learning and education also needs transparent discussion and coherent planning.

C19

Use of fillers in academic teaching: objective data from Panopto recordings

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Filler sounds and words are commonly used as they facilitate breaking up speech. It allows people to think, take a break and process information. Anecdotal evidence suggests some university students could feel the quality of teaching is negatively affected by excessive filler use. This research aims to address what filler words are used, their frequency and the best available methods to accurately assess filler use.

Nine participants from the School of Biomedical Sciences (SoBS) and the Plymouth Business School (PBS) each provided two Panopto lecture recordings, one was perceived to be delivered well, and the other could have been delivered better (e.g. not main subject area or lack of preparation time). Ethical approval was given by the University of Plymouth Faculty of Science and Engineering Research Ethics and Integrity Committee. All participants completed a consent form using the JISC online survey platform which was shared via a link or QR code. We analysed six of the participants recordings manually, counting the number of various filler words (um, so, okay, uh, like etc.) and any prominent patterns. All participant data was also analysed using machine learning (ML). By creating a labelled dataset of the filler words including positional context of words, we were able to use DistilBERT, a smaller and faster version of BERT (Bidirectional Encoder Representations from Transformers), which is a machine learning model made to understand human language. We achieved an F1 score (combined precision and recall) of 0.97 for predicting filler words in text and were able to quickly and accurately count the number of filler words, using the captions generated on Panopto. Mean (SD) and paired t-testing were used for data analysis. P values of <0.05 were considered statistically significant.

Turning to machine learning aided to reduce the manual time in recording fillers, as human assessment took approximately 1.5 to 2.5 hours for a one-hour lecture compared to 20s for the ML solution (with 2 minutes of training on a laptop GPU). Mean (SD) manual filler count (n=6) was 892.8 (389.6) compared to a mean ML filler count (n=6) of 1006.1 (430.6). The mean manual filler ratio (percentage of filler count with respect to total words) was significantly lower than the ML equivalent (6.6 vs. 7.4%; p=0.008). Additionally, we found the ML filler ratio to be significantly higher for the poorly delivered lectures, contrasted to the well delivered ones (n=9; p=0.005). However, the filler count per minute for both lectures showed no significant difference (p=0.38).

Our findings show that the ML solution was incredibly efficient and was approximately within 10% of manual data recordings. We also noted a potential difference between lecture quality and filler use; however, these findings require further research into the factors affecting filler use. We hope the results achieved will provide more insight into filler use during teaching, in order to better inform educators in HEIs. These findings may also increase awareness of filler overuse for teaching staff.

C20

Physiology Beyond the Noise: How Quantum Computing Could Help Us Finally Predict the Unpredictable Neuron

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Introduction. Every neuron is a little rebel. Even when we hold its inputs perfectly steady, it fires at slightly different times—sometimes early, sometimes late, sometimes not at all. This unpredictability comes from "channel noise": the random opening and closing of individual ion channels in the membrane. Experimental physiologists see this as jitter in patch-clamp recordings; clinicians see it as arrhythmia risk or seizure susceptibility; theorists see it as the fundamental limit of classical computation. Standard Hodgkin-Huxley models struggle here—simulating enough channels to capture realistic noise takes hours on a supercomputer. We asked: could quantum computing turn this noise from a bug into a feature?

Aims. To review how quantum computing (QC) offers a practical path toward predicting neuronal variability, and to present a hybrid workflow that experimental and clinical researchers could use in the coming decade.

Methods. We analysed 47 studies (2015–2025) spanning stochastic ion channel biophysics and quantum algorithms. Our framework combines four validated tools: (1) *Stochastic membrane models* — Fox-Lu Langevin equations for Na^+ and K^+ channels, calibrated against patch-clamp data (n=12 cells; Na^+ conductance 23.4 ± 2.1 nS/pF, K^+ 12.8 ± 1.6 nS/pF; mean ± S.E.M.; (2) *Quantum microstate classification* — encoding channel hydration-coordination states as quantum superpositions to estimate pore-occupancy distributions with quadratically fewer samples than classical Monte Carlo (precision ε: classical $O(1/\varepsilon^2)$ versus quantum $O(1/\varepsilon)$; [Mahapatra, 2026]; (3) *Quantum parameter fitting* — variational quantum eigensolver (VQE) optimized against current-clamp recordings on 8-qubit IBMQ hardware (n=50 layers, tolerance 10^{-4}; [Mahapatra, 2025]; and (4) *Quantum neural networks* — predicting spike probability from subthreshold noise, trained on 10,000 trajectories (accuracy 94.2 ± 1.3% versus 78.6 ± 2.1% for classical logistic regression, n=5-fold cross-validation, $p<0.001$, two-sample t-test.

Results. K^+ channels generate ~4-fold more membrane noise than Na^+ channels (voltage variance 1.84 ± 0.12 mV^2 versus 0.44 ± 0.05 mV^2, n=1,000 replicates, $p<0.001$, F-test)—a counterintuitive finding explained by slower K^+ kinetics filtering high-frequency noise. For clinicians, this means K^+-targeting drugs (e.g., antiarrhythmics) may have unpredictable effects on firing variability. For experimentalists, quantum-inspired models capture spike-time correlations ($r = 0.71 \pm 0.08$ versus observed, n=200 trials) that classical forward-time models miss entirely. For theorists, a 100-compartment stellate cell model runs 3.1× faster on hybrid quantum-classical hardware (18.4 ± 2.3 min versus 57.2 ± 4.1 min, n=5 runs, $p=0.003$, paired t-test) with 0.38 ± 0.05 mV root-mean-square error against experimental traces. The quantum microstate approach further reveals that Nav1.7 pore hydration-coordination configurations follow probabilistic distributions ideally suited to quantum amplitude encoding, suggesting that neuronal Na^+ channel noise itself may be computationally tractable via quantum superposition rather than classical approximation.

Conclusions. Neuronal unpredictability is not merely noise to average away—it is a computationally rich signal that quantum methods can decode. Whether you patch-clamp in a wet lab, model networks in silico, or treat channelopathies in clinic, the quantum era offers a shared language for variability.

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Physiology, born in Cambridge with Hodgkin and Huxley's deterministic equations, now enters its probabilistic renaissance.

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Redox status and muscle damage following high intensity exercise in resistance and endurance trained athletes: a comparative approach between genders

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Introduction: High intensity exercise (HIE) leads to oxidative stress and muscle damage which impose detrimental effects on physiological systems leading to deterioration of athletic performance. Different training programmes are advocated as per the necessities of the specific category of athletes. Whether variation in gender and training regimen impact any significant difference on HIE induced oxidative stress and muscle damage is not well explored. HIE induced differential effects on these markers between genders have been reported in sedentary population but pertinent data are unavailable in athletic populations.

Aims and objectives: Studies reported the effects of strenuous exercise on oxidative stress and muscle damage parameters, but comparison in these parameters between resistance (RA) and endurance trained (EA) athletes following HIE has not yet been reported. The present study was aimed to compare the changes in redox status and muscle damage biomarkers following HIE between RA and EA. The study further explored the variation in these parameters between male and female resistance and endurance trained athletes.

Method: Male and female RA (n = 18) and EA (n = 18) and sedentary controls (SC) (male = 30, female = 30) were recruited in the study. They performed treadmill running at 80% of maximum heart rate (HRmax) till volitional exhaustion. Blood samples were collected before (T1), after (T2) and 48 hours after (T3) exercise. Standard biochemical protocols were used to measure superoxide dismutase (SOD), catalase (CAT), lipid peroxidation (LPO) and total thiols as oxidative stress markers while skeletal muscle damage was evaluated by measuring serum creatine phosphokinase (CPK), serum lactate dehydrogenase (LDH), serum aspartate aminotransferase (AST), serum alanine aminotransferase (ALT) and serum C-reactive protein (CRP). Cardiac muscle damage was evaluated by measuring creatine phosphokinase-MB (CPK-MB) and high sensitivity serum CRP (hs-CRP). SPSS software was used for two way repeated measure ANOVA followed by Bonferroni post hoc analysis. Level of significance was set at $p<0.05$. Institutional ethical clearance (PHY/IHEC/AB/01/21, dated 16th January 2021) was obtained as per Helsinki's declaration.

Results: Significant ($p<0.05$) increase in oxidative stress and muscle damage was observed following HIE in all the groups. Athlete groups showed greater antioxidant capacity than the sedentary counterparts, indicating training induced adaptive protection. Females showed significantly ($p<0.05$) lower SOD, CAT and LPO levels than their male counterparts at T3, suggesting estrogen mediated protection against oxidative stress. But, total thiol content was significantly ($p<0.05$) higher in females at T2 and T3. Male groups depicted significantly ($p<0.05$) higher skeletal muscle damage than their female counterparts

except for CRP. Athlete groups had significantly ($p<0.05$) higher levels of skeletal and cardiac muscle damage biomarkers than SC probably due to greater endurance capacity. Male groups depicted significantly ($p<0.05$) higher values of cardiac muscle damage markers than the corresponding female groups.

Conclusions: The study revealed that HIE increased oxidative stress and muscle damage in all the groups but results varied significantly between genders while type of training apparently did not influence the changes in these parameters. Female participants showed greater protection against oxidative stress and muscle damage probably due to hormonal and physiological variances.