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PL01

Sports Nutrition: is it even a science? And how does it help us all?

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In 2012, on the eve of the Opening Ceremony at the London Olympic Games, the British Medical Journal and the Panorama television documentary program released an attack on sports science, with much of the critique focusing on sports nutrition themes and products. A feature article in the BMJ, entitled "Forty years of sports performance research and little insight gained" listed a range of flaws in the conduct and interpretation of the underpinning research related to sports drinks, but applied to sports science research more largely in other pieces. Specific criticism included small sample sizes, poor surrogate measures of performance, poor standardization of moderating factors and the bias of industry funding. The overarching message: was poor quality science with a lack of generalisability. Having spent forty years undertaking sports performance research, I feel able to respond with the insight that was missing in this critique. Undoubtedly (and perhaps even more frequently, due the explosion of open access journals), poor quality publications contribute to a lack of respect and understanding of sports nutrition, just as they do in other areas of science. However, navigating the path from molecules to medals is challenging, requiring an array of research skill sets and knowledge. This presentation will outline the unique issues of the investigation and implementation of sports nutrition science, identifying key themes such as extreme energy and fuel demands, optimisation of training adaptations, performance supplements, special models of working with elite athletes, and the neglect of key populations including female athletes. How sports nutrition research can address the specific demands of world records and gold medals, while scaling to recreational athletes and community benefits will be explored.

SA01

Personalised metabolic and behavioural responses to dietary interventions for cardiovascular health promotion.

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Diet is a key modulator of health and disease prevention, with cardiovascular diseases (CVD) a major target. High intakes of saturated fatty acids are linked to increased premature CVD events, the reduction of which has formed the backbone of dietary guidelines to prevent CVD over the past 60 years. However, variable metabolic and health outcomes to SFA reduction, together with outstanding questions regarding replacement macronutrients and food sources of SFA (dairy, meat, plants) have raised controversies over this recommendation. Increased understanding of variation in the physiological response to SFA reduction has potential to impact on the efficacy of this recommendation at a population level. While there is evidence to suggest that personalisation of guidance based on diet, phenotype or genotype is beneficial to health, when tailored advice is offered, individual motivation can become a major challenge. The potential benefits of personalised dietary advise, with a focus on total SFA, foods containing these fats and replacement macronutrients on lipid CVD risk markers and dietary behaviour change will be discussed and possible mechanisms explored.

SA02

Exploring individual differences in response to nutritional interventions: A practical example from a replicate crossover study on dietary nitrate

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Introduction and aims: Numerous studies have demonstrated that dietary nitrate supplementation increases nitric oxide (NO) bioavailability and reduces blood pressure (BP). Individual differences in the response to nitrate ingestion have been suggested, with some researchers hypothesising the existence of nitrate '*responders*' and '*non-responders*'. However, the detection of interindividual differences in response to nutritional interventions is challenging and necessitates the use of specific methodological and statistical approaches. This presentation aims to provide a practical example of one approach for exploring interindividual differences in response to nutritional interventions, drawing upon a recently completed replicate crossover study on dietary nitrate.

Methods: Fifteen healthy males took part in a randomised double-blind placebo-controlled replicate crossover trial (Trial registration: https://clinicaltrials.gov/study/NCT05514821). They visited the laboratory on four occasions. On two visits, participants consumed 140 ml nitrate-rich beetroot juice (~14.0 mmol nitrate) and, on the other two visits, they consumed 140 ml nitrate-depleted beetroot juice as a placebo (~0.03 mmol nitrate). Plasma nitrate and nitrite were measured 2.5 hours post-supplementation. BP was measured pre- and 2.5 hours post-supplementation. We quantified individual response stability using placebo-adjusted between-replicate correlations and explored treatment response variability using within-participant linear mixed models and a novel meta-analytic approach.

Results: Nitrate-rich beetroot juice supplementation elevated plasma nitrate and nitrite concentrations and reduced systolic (mean:-7mmHg, 95%CI: -3 to -11mmHg) and diastolic (mean:-6mmHg, 95%CI: -2 to -9mmHg) BP *versus* placebo. The mixed model and meta-analytic approaches provided evidence of interindividual differences in response to nitrate supplementation. For example, for systolic BP the participant-by-condition interaction response variability from the mixed model was ±7mmHg (95%CI: 3 to 9mmHg), which was consistent with the treatment effect heterogeneity t=± 7mmHg (95%CI: 5 to 12mmHg) derived from the meta-analytic approach. The between-replicate correlations were moderate-to-large for plasma nitrate, nitrite and systolic BP (r=0.55 to 0.91), indicating good response stability for these variables.

Conclusions: These data suggest that the effects of dietary nitrate supplementation on NO biomarkers and systolic BP vary significantly from participant to participant. This provides proof-of-concept as a basis for further investigations of the magnitude, durability and pervasiveness of these interindividual response differences across diverse populations. This methodological approach could be applied to investigate interindividual differences in response to other nutritional or lifestyle interventions.

SA03

Inter-individual variability in appetite and metabolic responses to exercise and eating

Alice Thackray[1]

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Background: Moderate-to-vigorous intensity exercise acutely suppresses appetite and the orexigenic hormone acylated ghrelin, increases satiety hormones (e.g., peptide YY), and reduces postprandial triacylglycerol and insulin concentrations. Meal consumption also induces appetite suppression alongside corresponding fluctuations in appetite-related hormones. Most investigations focus on mean group-level responses, yet individuals can vary considerably in their appetite and metabolic responses to exercise and eating. Robust quantification of individual differences requires methodological and statistical approaches that distinguish true inter-individual variability from natural within-subject variability. In a series of controlled laboratory experiments, we aimed to determine: (1) whether individual appetite and metabolic responses to exercise and eating are consistent; (2) whether true inter-individual variability exists; and (3) what factors might contribute to such variability.

Methods: Using replicate crossover designs, appetite outcomes (acylated ghrelin, total PYY, hunger, fullness) were assessed in an exercise (study 1: n=15 men) and a meal (study 2: n=18 men) study, while postprandial metabolic outcomes (triacylglycerol, glucose, insulin) were examined in an exercise study (study 3: n=20 men). Each study comprised two crossover cycles of paired intervention (study 1 and 3: exercise; study 2: meal) and control (study 1 and 3: rest; study 2: no meal) conditions. Between-cycle correlation coefficients quantified the consistency of individual differences between the replicates of control-adjusted intervention responses. Within-participant linear mixed-models and between-participant, random-effects meta-analyses of the replicate-averaged condition effect estimated treatment response heterogeneity. In study 2, the moderating influence of the fat mass and obesity-associated (FTO) gene was also examined.

Results: In study 1 and 2, exercise and eating suppressed mean hunger and acylated ghrelin concentrations and increased mean fullness and peptide YY concentrations versus control (main effect condition $P \leq 0.001$). Moderate-to-large positive correlations were observed between the two replicates of control-adjusted exercise responses (r range = 0.55 to 0.82, $P \leq 0.035$) and meal responses (r range = 0.41 to 0.86, $P \leq 0.091$). Participant-by-condition interactions (study 1: $P \leq 0.077$; study 2: $P \leq 0.056$), and treatment effect heterogeneity estimates from the meta-analyses (e.g., tau statistic [95% CI] for acylated ghrelin: study 1 28.1 [17.1, 48.8] pg/mL; study 2 16.6 [0, 34.1] pg/mL) indicated meaningful inter-individual variability in appetite responses. In study 2, FTO genotype-by-condition interactions showed no evidence of moderation on the magnitude of post-meal responses (all $P \geq 0.192$).

In study 3, exercise reduced mean postprandial triacylglycerol and insulin concentrations versus control (main effect condition $P \leq 0.022$), but between-condition differences were trivial for glucose ($P = 0.126$). Between-cycle correlations were small-to-moderate and not statistically significant (r range = -0.42 to

0.11, P ≥ 0.066), participant-by-condition interactions were trivial (all P ≥ 0.137), and treatment effect heterogeneity estimates were negligible (e.g., tau statistic [95% CI] for triacylglycerol: 0 [0, 0] mmol/L h).

Conclusion: Meaningful inter-individual variability was detected in appetite responses to exercise and eating, but not in postprandial metabolic responses to exercise. Further research is required to identify moderators responsible for the individual variability in appetite responses to exercise and eating, and to determine the clinical implications for weight control.

SA04

Modulation of whole body and skeletal muscle galactose metabolism by nutrition and exercise

Gareth Wallis[1]

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The monosaccharides glucose and fructose have been extensively investigated for their well-recognised roles in metabolism and human health. In contrast, galactose, the third major dietary monosaccharide, has received less attention in human volunteer research outside of its role in the pathophysiology of galactosaemias.

The acute ingestion of free galactose elicits a minimal or modest insulin response but a marked increase in blood galactose concentrations, which, depending on dose, largely returns to baseline within 2 hours. Galactose is mostly consumed within the human diet as lactose is present in milk and a well-established observation is that the co-ingestion of galactose with glucose (in free form or as lactose) partially or almost completely blunts the increase in blood galactose concentrations. We have confirmed this also occurs during exercise although the enhanced galactose clearance does not appear to increase it use as an exogenous fuel source (Odell et al, 2022).

Evidence suggests that the co-ingestion of glucose enhances splanchnic galactose extraction, with the liver, and its substantial expression of Leloir pathway enzymes, considered the major site of galactose metabolism. The prevailing view is that these effects are related to increases in blood glucose concentrations, and not the concomitant increase in blood insulin that occurs with galactose-glucose co-ingestion. However, data will be presented to suggest a role for insulin mediated plasma galactose clearance, although it is acknowledged that modulation of gastrointestinal transit by presence of other nutrients cannot be discounted.

Recent observations of postexercise muscle glycogen synthesis with aggressive galactose ingestion and evidence for skeletal-muscle expression of Leloir pathway enzymes suggested further research into the potential for extra-splanchnic galactose metabolism was warranted (Podlogar et al, 2023). Results from a collaborative project will be presented to provide evidence for galactose uptake in human skeletal muscle as determined using dynamic 2-(18)F-fluoro-2-deoxy-d-galactose ((18)F-FDGal) PET/CT approaches. Data will also be presented showing that less aggressive but still high galactose feeding modulated expression of genes related to galactose metabolism in skeletal muscle but did not stimulate short-term post-exercise muscle glycogen synthesis.

Collectively, recent investigations suggest the potential for galactose metabolism in skeletal muscle and its modulation by nutrients, insulin and/or exercise does exist, although its physiological significance requires further investigation.

SA05

Using Type 1 Diabetes as a Model to Reveal the Metabolic Potential of Milk Sugars During Exercise

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Background and Aim

Exercise improves glycemic control and cardiovascular risk profiles in individuals with type 1 diabetes (T1D), yet plasma glucose fluctuations and fear of hypoglycemia remain major barriers to physical activity. Carbohydrate ingestion prior to exercise is recommended to reduce hypoglycemia risk, but conventional carbohydrate strategies often induce pre-exercise hyperglycemia followed by rapid glucose declines during exercise. Low-glycemic index carbohydrates may represent a more physiologically stable alternative. Lactose and galactose are milk-derived low-glycemic index carbohydrates with distinct metabolic characteristics that may provide such a stable alternative. The aim of this work was to examine lactose and galactose as pre-exercise carbohydrate strategies in individuals with T1D and to use T1D as a clinical model to explore their metabolic potential during exercise.

Methods

Adults with T1D completed standardized endurance exercise sessions following ingestion of dextrose, lactose, galactose, or placebo in a randomized, double-blind, crossover design. Glycemic responses were assessed using frequent blood sampling, while substrate utilization was evaluated by indirect calorimetry.

Results

Compared with dextrose, lactose and galactose provided more stable glycemic responses during exercise, characterized by reduced hyperglycemic excursions and increased time in range. Both milk sugars also reduced time below range compared with placebo.

Conclusions

Milk sugars act as metabolically distinct pre-exercise carbohydrates in T1D, offering more stable glucose support during exercise. These findings highlight lactose and galactose as promising exercise fuels and position T1D as a valuable human model for revealing physiologically meaningful differences between carbohydrate types during exercise.

SA06

Dietary milk sugar intake and metabolic health: Friend or foe?

Javier Gonzalez[1]

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Despite being consumed by the majority (>80%) of the global population, relatively little is known about the metabolic effects of milk sugars compared with other carbohydrates. Galactose is the defining monosaccharide of the milk sugar, lactose and is thought to be primarily metabolised by the LeLoir pathway, producing glucose metabolites. However, recent evidence has challenged this understanding, on the basis that galactose ingestion results in several metabolic effects that are more similar to fructose ingestion than to glucose ingestion. In this talk, I will present previous and ongoing research in this area where we are employing several stable isotopic tracer methods to understand the how lactose and galactose affect metabolism across a range of doses. Recent data suggest that there may be several similarities between galactose and fructose metabolism, whilst also retaining some important differences.

SA07

Metabolic physiology at the onset of a ketogenic diet

Aaron Hengist[1]

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Ketogenic diets are a popular alternative to traditional dietary guidelines for individuals looking to improve body composition and metabolic health. Very low dietary carbohydrate intake (<50 g/day) increases fat oxidation and ketogenesis, even during isoenergetic conditions, compared with higher-carbohydrate diets. Rapid hormonal adaptions to the ketogenic diet involve reductions in insulin and leptin within the first 24-h that reflect integrated homeostasis and dynamic shifts in substrate oxidation. Hepatic ketogenesis and the associated increases in mitochondrial fat oxidation are oxygen-costly processes, which may explain why sleeping energy expenditure increases at the onset of a ketogenic diet. The effects on sleeping energy expenditure measured using indirect calorimetry dissipate after a few weeks of diet, whereas physical activity energy expenditure is not meaningfully altered, suggesting that energy expenditure is at least maintained in the long-term. Strategies to increase ketogenic flux at the onset of a ketogenic diet may divert stored hepatic triglyceride towards oxidation, with potential implications for metabolic dysfunction-associated steatotic liver disease (MASLD), but more work needs to be done to understand the metabolic mechanisms.

SA08

Cardiometabolic effects of ketogenic diet and intermittent fasting

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Ketogenic diets and intermittent fasting have gained attention for their potential to improve cardiometabolic health, yet their direct effects on human cardiac metabolism, myocardial perfusion, and insulin sensitivity remain incompletely defined. This presentation will highlight findings from studies employing positron emission tomography (PET) to quantify myocardial substrate utilization and perfusion, alongside hyperinsulinemic euglycemic clamp experiments that assess organ-specific insulin sensitivity. Together, these approaches reveal how dietary modulation of systemic fuel availability reshapes cardiac energy metabolism and insulin action across tissues. The emerging data provide mechanistic insight into the cardiometabolic consequences of ketogenic and fasting-based interventions and underscore the need for further research to determine their long-term clinical relevance.b

SA09

Exploring the relationships between dietary habits, physical function and quality of life in adults living with muscular dystrophy

Nathan Hodson[1]

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Muscular dystrophy (MD) encompasses inherited myopathies characterised by progressive skeletal and cardiac muscle degeneration, chronic inflammation and metabolic dysfunction. Whilst much of the research spanning the previous three decades has focussed on identifying and developing cures and pharmacological therapies for these conditions, very few have translated from pre-clinical models and even successful therapies are rarely approved for NHS use due to cost constraints. Therefore, it is important that easy-to-implement, cost-effective non-pharmacological interventions are developed which can improve, or offset deteriorations in, skeletal muscle strength and function in these conditions and thereby improve quality of life further into disease progression. One factor which is easily modifiable is diet, with previous dietary interventions showing benefits to skeletal muscle size, strength and function in non-dystrophic clinical conditions. Importantly, given the progressive nature of muscular dystrophy, diet modulation may be of even greater importance given the potential inability of those with dystrophy to complete regular exercise/activity later in disease progression. However, currently very little is known about the habitual dietary practices of adults living with muscular dystrophy and whether such habits are associated with skeletal muscle size, strength and function as well as subjective measures such as quality of life, ability to complete activities of daily living and fatigue. This talk will focus on recent data from our group with explores these relationships across a relatively large cohort of adults living with various dystrophinopathies before discussing planned future dietary interventions based off these findings.

SA10

Nutritional recommendations for patients with myopathy: Focus on Pompe and myotonic MD

Mark Tarnopolsky[1]

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The myopathies represent a diverse group of genetic and acquired disorders that negatively affect skeletal muscle structure and funciton. In general, these disorders lead to a reduction in strength and/or endurance. I will focus the current talk on two common forms of muscular dystrophies (myotonic MD type 1 (DM1)), fascio-scapulohumeral MD (FSHD)) and two metabolic disorders (Pompe disease, mitochondrial myopathy). Although the primary cause of each disorder is unique, weakness and/or exercise intolerance typically leads to a general reduction in energy expenditure that further constrains nutrient recommendations due to a lower energy intake required to maintain optimal body composition. Our recent data suggests that most myopathy patients have obesity with low lean mass (OLMM). We have also reported sub-optimal intake of most micronutrients in patients with several types of muscular dystrophy and also found low blood levels of vitamin D, vitamin B12, folate and vitamin E. We and others have found low levels of muscle creatine and phosphocreatine in several myopathies and multiple studies have shown that creatine monohydrate supplementation can increase muscle strength and mass by ~ 7 % in MD. Higher oxidative stress is seen in most myopathies and targeted anti-oxidant cocktails have shown benefits in mitochondrial myopathies, Pompe disease and FSHD. A higher protein intake (> 1.2 g/kg/d) is also recommended for myopathy patients, especially Pompe disease. We are currently evaluating whether supplementation with milk protein, creatine monohydrate, vitamin D, calcium and a multi-ingredient supplement will enhance the gains made from multi-modal exercise training in patients with DM1 and Pompe.

SA11

Metabolic Dysfunction in Spinal Cord Injury: Understanding the Mechanisms of Glucose Control

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Individuals with spinal cord injury (SCI) experience a markedly elevated risk of cardiometabolic disease, including obesity, dysglycaemia, insulin resistance, dyslipidaemia, and hypertension. These abnormalities emerge early following injury and contribute substantially to reduced life expectancy. The physiological drivers of cardiometabolic dysfunction in SCI are multifactorial, arising from paralysis-induced reductions in skeletal muscle mass, impaired autonomic regulation, altered body composition, and substantial barriers to engaging in sufficient physical activity.

The nutritional needs of individuals with SCI remain poorly characterised, and dietary recommendations developed for the general population are unlikely to be appropriate. Injury-related physiological changes mean that standard nutritional guidelines may systematically overestimate or underestimate true requirements, potentially exacerbating metabolic dysregulation. Such nutritional mismatches may contribute to the early development of obesity, dysglycaemia, and insulin resistance following SCI, highlighting the need for condition-specific dietary and metabolic strategies.

Although physical activity is commonly advocated as a cornerstone of cardiometabolic disease prevention, its effectiveness in SCI is inherently constrained. Current guidelines predominantly recommend upper-body exercise; however, absolute exercise capacity and energy expenditure are limited compared with lower-limb exercise, restricting the achievable cardiometabolic stimulus. While exercise interventions can improve certain aspects of cardiorespiratory fitness and metabolic health in chronic SCI, evidence for consistent improvements in glycaemic control remains equivocal. Acute studies demonstrate minimal effects of pre-meal exercise on postprandial glucose, and although high-intensity interval training can induce metabolic adaptations, responses are variable and feasibility remains challenging.

Neuromuscular electrical stimulation (NMES) represents a promising adjunct or alternative strategy by activating large lower-limb muscle groups independent of voluntary motor control, with evidence indicating improvements in postprandial glucose regulation. This talk will present preliminary findings from our ongoing work quantifying the acute effects of NMES on glucose control using dual stable isotope tracer methodology during an oral glucose tolerance test, alongside assessments of real-world feasibility and acceptability.

Ultimately, beyond its clinical relevance, SCI provides a unique human model of extreme deconditioning, muscle atrophy, and disrupted central and peripheral regulation, offering a powerful opportunity to

interrogate the physiological mechanisms governing metabolic control in vivo and inform targeted nutritional and metabolic interventions.

SA12

Obesogenic lifestyle and the regulation of cerebral blood flow

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In the UK, nearly 26% of adults are obese, 22% are physically inactive, and 69% do not meet the recommended “5-a-day” fruit and vegetable intake. Additionally, recent analyses of dietary data from the UK Biobank revealed high consumption of energy-dense and nutrient-poor foods and beverages. These unhealthy lifestyle behaviours have been steadily increasing in recent years. This trend is concerning, as physical inactivity, a high-calorie diet, and the resulting positive energy balance and weight gain are important independent risk factors for cardiometabolic diseases. More recently, these same behaviours have also been strongly associated with an increased risk of dementia and other cerebrovascular diseases, which are respectively the first and fourth leading causes of death in the UK. The pathways linking an obesogenic lifestyle to dementia and cerebrovascular disease remain poorly understood. Emerging evidence suggests that the underlying mechanisms may involve systemic and cerebral vascular dysfunction, leading to reduced and dysregulated cerebral blood flow (CBF).

To further elucidate the links between obesogenic lifestyles and the regulation of CBF, we asked healthy young individuals to follow one week of controlled obesogenic behaviour characterised by increased caloric intake and reduced daily step counts. Assessment of CBF regulation consisted of a comprehensive battery including measurements of middle cerebral and posterior cerebral artery blood velocity at rest, as well as in response to manipulations of blood pressure (i.e., dynamic cerebral autoregulation) and cognitive stress.

Our data indicate that one week of obesogenic behaviour induces significant detrimental effects on CBF regulation, including reduced CBF velocity and blunted cerebrovascular responses to cognitive challenge. Importantly, one week of resumption of usual, non-obesogenic behaviour only partially reversed the impairments induced by the obesogenic intervention.

These findings establish important mechanistic links between obesogenic lifestyle and cerebrovascular dysfunction, and provide novel evidence that even brief periods of obesogenic behaviour (such as those typically occurring during long holidays) can adversely affect brain vascular health. Furthermore, the incomplete recovery following return to habitual behaviour suggests that passive resumption alone may be insufficient to fully restore cerebrovascular function, highlighting the need for targeted strategies to mitigate obesogenic-induced vascular dysfunction or actively promote recovery following periods of extended overfeeding and/or inactivity.

SA13

(Poly)phenols and mental health:role of the gut-brain axis

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[1]King's College London , UK

Mental health disturbances and stress-related symptoms are increasingly prevalent across the life course, with young adulthood and midlife in women, particularly during the menopause transition, representing periods of increased vulnerability. In young adults, particularly university students, the transition to adulthood involves academic, social, and financial pressures, coinciding with the period when many common mental disorders first emerge, typically before age 25. In women, menopause is linked to mood disturbances, anxiety and depressive symptoms, driven by hormonal fluctuations, sleep disruption, vasomotor symptoms and psychosocial stressors. Dietary (poly)phenols, bioactive compounds abundant in plant-based foods, are emerging modulators of mental well-being, with growing evidence for gut–brain axis related mechanisms involving gut microbiota, microbial metabolites and neuroendocrine pathways. In a scoping review we have recently conducted, human studies consistently reported benefits of dietary (poly)phenols for depressive symptoms and mood, while effects on stress and anxiety were less consistent. The review also highlighted key limitations in the current literature, including heterogeneity in study designs, populations, interventions and outcome measures, variable dosages and durations of supplementation, and inconsistent assessment of both (poly)phenol intake and mental health outcomes, which together limit comparability and interpretation of findings.This lecture will present evidence from recently conducted observational and intervention studies examining relationships between (poly)phenol intake, circulating metabolites, stress physiology, cognition, gut microbiota and mental health in university students and postmenopausal women.

In a cross-sectional study of over 300 university students, higher intakes of anthocyanins, flavanones, flavonols and tyrosols were associated with lower stress, anxiety, depression and mood disturbances, while higher consumption of flavan-3-ols was associated with reduced cortisol levels, with multiple urinary metabolites supporting biological plausibility. In a double-blind randomised controlled trial, 12 weeks of (poly)phenol-rich cranberry supplementation did not alter self-reported mood or distress but reduced diurnal cortisol and improved short-term and phonological memory, alongside modulation of gut–brain axis metabolites, suggesting that physiological and cognitive benefits may occur independently of perceived mental health changes.

Preliminary data from a double-blind crossover trial in postmenopausal women examined whether (poly)phenols alone or combined with probiotics could alleviate menopause-related symptoms via gut microbiota pathways. Both interventions supported well-being but through distinct mechanisms: the combined intervention enhanced cognition, including learning, memory and concentration, with increased (poly)phenol bioavailability and propionate-producing taxa, whereas the (poly)phenol-only intervention was linked to greater vitality, sexual activity and motivation, with higher abundance of butyrate-producing bacteria.

These findings highlight dietary (poly)phenols as modulators of stress regulation, cognition and mental health across life stages, with emerging evidence supporting a role for gut–brain axis pathways.

SA14

Shielding the Brain: Dietary Flavonoids Modulate the Cerebral Vasculature

Catarina Rendeiro[1], Alexander Friend[1], Jasmine Yeh[1], Claire M Williams[2], Samuel Lucas[1], Rosalind Baynham [1]

[1]University of Birmingham, United Kingdom, [2]University of Reading, United Kingdom

Introduction: Flavonoids are small molecules that can be found ubiquitously in plants (e.g. cocoa, berries, grapes, apples) and can protect humans against vascular disease, as evidenced by improvements in peripheral endothelial function, likely through nitric oxide (NO) signalling. Emerging evidence also suggests that diets rich in these compounds may be beneficial for cognitive health, but the underlying mechanisms are not well established.

Aims: To investigate the effects of dietary flavonoids on executive function in young healthy adults and their underlying mechanisms of action within the vasculature.

Methods: In a series of acute (1-2 h, within subject) and chronic (8 weeks, between-subject) randomized, counterbalanced, double-blind, placebo-controlled studies, healthy young adults consumed either a high or low flavonoid intervention in the context of different cerebral physiological challenges, such as hypercapnia (5% CO2), incremental exercise (low, moderate, high intensity) and cognitive tasks. Pre-frontal cortical oxygenation (TOI) and total haemoglobin (THI, index of blood flow), was measured using Near Infrared Spectroscopy (NIRS) before and after the flavonoid interventions. Executive function performance was also assessed by Stroop/Double Stroop, Modified Attention Network Task (MANT) and Task Switching Test (TST).

Results: Our studies suggest that flavonoids are effective at improving executive function acutely (Double Stroop: p=0.045, *N=18*) and chronically (TST: p=0.019, *N=50*) in a resting state, but can also enhance cognition post-exercise (MANT: p=0.026, *N=58*), with benefits being apparent particularly when cognitive demand is high. This may be driven by more efficient cerebral oxygenation (*sparing of oxygen*) after flavonoid consumption, as some of our data suggests flavonoid intake leads to faster (by approx. 1 min; $p < 0.001$, N=18) and greater cortical oxygenation (p=0.030) in response to an hypercapnic challenge, as well as higher oxygenation during low-intensity exercise (p=0.042), without further changes in total cortical blood flow (THI). In agreement with this, during post-exercise cognitive performance, acute flavonoid intake also resulted in higher TOI in high-fit individuals (p=0.015, *N=58*). In contrast, low-fit individuals experienced a reduction in TOI (p=0.024, *N=58*), despite similar cognitive benefits, likely suggesting improved capacity to utilise available oxygen *(i.e., greater oxygen extraction)*.

Conclusions: Together our data suggests that flavonoid-rich foods might be an effective dietary strategy to improve cognitive function acutely and chronically in young healthy adults. These benefits may be particularly important in the context of tasks with high cognitive demand. Interestingly, intake of flavonoids modulates cortical oxygenation, but specific mechanisms may be dependent on the levels of cardiorespiratory fitness of the individual. These findings have important implications for future research to explore the relationship between flavonoid-rich food choices in situations in which brain physiology is challenged, such as cognitive performance and/or exercise.

SA15

Driving in reverse: ethnic distinctions in the pathophysiology of type 2 diabetes

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People of African and Caribbean heritage experience a disproportionate burden of type 2 diabetes, with higher prevalence, younger age of onset, and poorer clinical outcomes compared with white European populations. Notably, this excess risk occurs despite lower levels of visceral and intra-organ fat, a phenomenon often referred to as the *African Paradox*. These observations suggest fundamental ethnic distinctions in the physiological mechanisms underlying type 2 diabetes that are not adequately captured by prevailing disease models.

This plenary talk will focus on insights from the Diabetes UK–funded South London Diabetes & Ethnicity Phenotyping study, a pioneering programme of experimental medicine designed to elucidate the physiological drivers of diabetes risk in people of African ancestry. The talk will outline how advanced metabolic phenotyping approaches—including stable isotope techniques and magnetic resonance imaging—have been used to interrogate fat metabolism, insulin resistance, β-cell function, and intra-organ lipid deposition.

The central focus will be on evidence demonstrating that type 2 diabetes in people of African ancestry is characterised by distinct pathophysiological features, particularly reduced hepatic insulin clearance, as a primary defect, leading to hyperinsulinaemia, alongside relative sparing of visceral and intra-organ fat. These findings challenge the long-standing paradigm that insulin resistance is the primary initiating defect in type 2 diabetes and highlight the need to reconsider current physiological models.

The talk will conclude by exploring the broader implications of these findings for metabolic physiology and clinical practice, including their relevance to current intervention strategies such as dietary remission approaches. By highlighting the importance of ethnic diversity in physiological research, this work underscores the need for mechanism-based, tailored strategies to improve equity in diabetes prevention and treatment.

C01

Acute dietary nitrate supplementation attenuates caffeine-induced increase in arterial stiffness in healthy adults

Abbie Mclellan[1], Jarred Acton[2], Nur Ahmad[3], Emma O'Donnell[4], Samantha Rowland[4], Lewis James[4], Anthony Shepherd[5], Maria Perissiou[5], Tom Clifford[4], Stephen Bailey[4]

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Purpose: Inorganic nitrate (NO_3^-) supplementation has been reported to improve, whilst caffeine consumption has been reported to increase strain on, various aspects of cardiovascular function. Since it has been suggested that the efficacy of NO_3^- supplementation to improve cardiovascular function may be enhanced with increased cardiovascular strain, the purpose of this study was to test the hypotheses that dietary NO_3^- ingestion would blunt the acute perturbations to cardiovascular function following caffeine ingestion, and that such effects would be greater than the improvement in cardiovascular function with NO_3^- ingestion compared to placebo in the absence of caffeine-induced cardiovascular strain.

Methods: Twenty-four (17 males, 7 females; mean ± SD: age 24 ± 3 yr, BMI 24 ± 3 kg/m^2, systolic BP 109 ± 10 mmHg) healthy participants completed four experimental conditions in a double-blind, randomized, crossover design. The experimental conditions were NO_3^--rich (400 mg NO_3^-) and NO_3^--depleted (92 mg NO_3^-) beetroot powder consumed acutely, with (BR-CAF and CAF) and without (BR and PL) 6 mg/kg caffeine. Post-supplement assessments were conducted 2.5 h post NO_3^--rich and NO_3^--depleted beetroot ingestion and 1 h post caffeine and placebo capsules. Brachial and central blood pressure (BP) and arterial stiffness variables were measured pre- and post-supplementation with macrovascular endothelial function assessed via flow mediated dilation (FMD) post-supplementation. Venous blood was also sampled post-supplementation for the assessment of plasma concentrations of nitrite ([NO_2^-]) and cyclic guanosine monophosphate ([cGMP]). Data were assessed using linear mixed models, with Holm Bonferroni post-hoc analyses and statistical significance accepted as $P < 0.05$.

Results: Augmentation pressure and index were higher after CAF (3 ± 2 mmHg and 10 ± 9%) than PL (1 ± 3 mmHg and 4 ± 11%) and BR (0 ± 3 mmHg and 1 ± 11%; $P < 0.001$-0.007), with no difference between BR-CAF (1 ± 3 mmHg and 3 ± 10%) and PL or BR ($P = 0.505$-0.689). Compared to PL, brachial BP, central BP and macrovascular endothelial function were not altered with BR or CAF ($P = 0.067$-0.359). Plasma [nitrite] was higher in BR and BR-CAF than PL and CAF ($P < 0.001$), with no differences between BR and BR-CAF ($P = 1.000$). There were no between-group differences in plasma [cGMP] ($P = 0.370$).

Conclusion: Caffeine ingestion adversely impacted augmentation pressure and index compared to PL, with this effect attenuated after NO_3^- and caffeine co-ingestion such that augmentation pressure and index were not different between PL and BR-CAF. Acute NO_3^- ingestion did not independently improve arterial stiffness variables compared to PL. Neither acute caffeine nor NO_3^- ingestion altered central or brachial BP or FMD compared to PL. These findings suggest that NO_3^- supplementation can attenuate arterial stiffness elicited by caffeine consumption, but that NO_3^- supplementation did not improve cardiovascular function variables independently and when caffeine did not invoke strain on a given cardiovascular function variable. These data improve our understanding of the cardiovascular health benefits of dietary NO_3^- supplementation and support the notion that the efficacy of NO_3^- supplementation to improve cardiovascular health appears to be linked to baseline cardiovascular strain.

C02

Three tracers tell the tale: ketones lower postprandial glycaemia by delaying exogenous glucose appearance across consecutive meals in people with type 2 diabetes.

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Background

We previously demonstrated that ingesting a ketone monoester (KME) supplement before a single meal delays the rate of exogenous glucose appearance, leading to lower postprandial glycaemia in individuals with type 2 diabetes. This occurred despite a concomitant rise in endogenous glucose appearance later in the postprandial period, suggesting that the effect may not persist during subsequent meals in the day, and underlining that the origin of endogenous glucose remains unknown. We aimed to test the hypothesis that pre-meal KME ingestion consistently delays rate of exogenous glucose appearance and decreases postprandial glycaemia across consecutive meals. We also sought to investigate the contribution of glycogenolysis and gluconeogenesis to endogenous glucose appearance.

Methods

Twelve participants with type 2 diabetes (age 61±2 years, 4 females/8 males, BMI 30.9±0.5 kg/m^2, HbA1c 63±3 mmol/mol [7.9±0.3%]) completed two consecutive 4-hour mixed-meal tolerance tests (MMTT1 and MMTT2) on two separate visits. Participants consumed either 0.5 g/kg body mass KME or a non-caloric, taste-matched placebo 30 minutes prior to each MMTT in a randomised, double-blind, crossover design. Primed continuous [^{2}H2]-glucose infusions were used to trace rates of total glucose appearance (Ra-T) and disappearance (Rd-T), combined with orally ingested [^{13}C6]-glucose to derive exogenous (Ra-Exo) and endogenous (Ra-Endo) glucose appearance. Orally ingested ^{2}H2O enabled determination of the contribution of gluconeogenesis and glycogenolysis to Ra-Endo. Blood samples were collected regularly to quantify circulating glucose and ketone (beta-hydroxybutyrate; bOHB) concentrations and isotope enrichments. Differences between condition and time were analysed by 2-way ANOVAs (statistical significance P<0.05).

Results

Plasma bOHB concentration was 13±1-fold higher with KME versus placebo, and remained elevated at all timepoints throughout each MMTT (interaction P<0.001). Blood glucose concentration increased during each MMTT, but peak concentration was 12±2% and 16±2% lower during MMTT1 and MMTT2, respectively, with KME versus placebo (P<0.001). This suppression remained for up to 2 h in MMTT1 and 2.5 h in MMTT2 (interaction P<0.001). Rd-T increased during each MMTT but was unaffected by KME (time P<0.001). Ra-T increased during each MMTT, but was 27±9% and 32±8% lower with KME at 0.5 h following MMTT1 and MMTT2, respectively, persisting for 1 h after each MMTT (interaction P<0.001). Ra-Exo increased during each MMTT but was 31±6% and 37±8% lower with KME at 0.5 h following MMTT1 and

MMTT2, respectively, persisting for 1 h after each MMTT (interaction $P<0.001$). Ra-Endo decreased during each MMTT (time $P<0.001$) but was unaffected by KME during each MMTT (interaction $P>0.05$) though tended to be greater across the entire 8-hour visit with KME (condition $P=0.05$). Glycogenolysis and gluconeogenesis decreased during each MMTT (time effects $P<0.001$). Although KME did not affect this change (interactions $P>0.05$), gluconeogenesis was 12±4% greater across the trial with KM (condition $P<0.05$).

Conclusion

We show for the first time that ingesting a ketone monoester supplement before consecutive meals consistently delays exogenous glucose appearance and lowers postprandial blood glucose concentration, without a substantial change in endogenous glucose production or disposal. Exogenous ketones show promise as an effective nutritional tool to manage blood glucose homeostasis in people living with type 2 diabetes.

C03

Omega-3 Fatty Acid Intake Is Associated with Improved Markers of Insulin Sensitivity in Apparently Healthy Adults

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Background: Obesity is characterized by chronic low-grade inflammation, which contributes to metabolic dysfunction and insulin resistance. Polyunsaturated fatty acids (PUFAs) play a central role in inflammatory regulation: omega-6 PUFAs serve as precursors for pro-inflammatory eicosanoids, whereas omega-3 (n-3) PUFAs [eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA)] give rise to specialized pro-resolving mediators (SPMs) that actively promote resolution of inflammation. Thus, n-3 PUFAs may exert metabolic benefits through upregulation of SPM molecules, which can decrease inflammation and its detrimental effects. **Purpose:** To examine the relationship between dietary n-3 fatty acid intake and markers of metabolic health in apparently healthy adults. **Methods:** Sixty-one adults completed anthropometric and body composition assessment (DXA), a 75-g 2h oral glucose tolerance test, and fasting blood sampling. Dietary intake from the previous month was assessed using the DHQIII food frequency questionnaire. Participants were stratified into low (n=37, < 1.5 g/day) or adequate (n=24, ≥ 1.5 g/day) n-3 intake groups based on DHQIII results. Independent t-tests were used for statistical analysis and data are presented as mean ± standard deviation. **Results:** Average daily intake for low n-3 was 0.96 ± 0.31 g/day and 2.12 ± 0.51 g/day for adequate n-3 ($p<0.01$). There was no difference between groups in BMI, %body fat, or fasting and 2h blood glucose concentrations. However, individuals with adequate n-3 intake exhibited significantly lower fasting insulin concentrations (5.1 ± 2.4, $p=0.01$) and reduced insulin resistance (HOMA-IR: 1.2 ± 0.6, $p=0.02$) compared with those reporting low n-3 intake (fasting insulin: 7.0 ± 3.7 mU/L, HOMA-IR: 1.6±0.9). There was no difference in diet quality between the two groups. The total HEI score was 64.7 ± 8.2 in the adequate n-3 group and 63.7 ± 11.5 in the low n-3 in group ($p=0.70$). **Conclusion:** Higher dietary n-3 fatty acid intake is associated with improved markers of insulin sensitivity in apparently healthy adults. These findings support the concept that metabolic dysfunction may reflect (or start with) impaired inflammatory resolution, due to a low dietary intake of n-3 fatty acids. Further work examining the specific role and expression of SPMs in individuals with obesity and their impact on metabolic health is warranted.

C04

The phase-shifting effect on plasma metabolites of a 5-hour delay in meal timing

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Introduction. Metabolic responses to meals vary depending on time of day[1]. However, evidence surrounding the phase shifting effects of meal timing in humans remains limited. We have previously shown that delaying regular meals substantially delays plasma glucose rhythms even when light-dark and sleep-wake schedules are kept constant [2 3]. This analysis aimed to examine further phase-shifting effects of meal-timing by comparing the circadian dynamics of intermediates of metabolism in plasma, using our well-established targeted metabolomics approach[4].

Methods. After a 10-day at-home protocol, designed to maximise synchrony of participants' circadian rhythms, ten healthy men were enrolled into a 13-day crossover study in our clinical research facility[2]. The sleep and wake times during the laboratory protocol were the same as during the at-home protocol (Figure 1). A 3-day early meal schedule (3-meals; 0.5, 5.5 and 10.5-h after wake) and a 6-day late meal schedule, (same meals, delayed by 5-h) were each followed by a 37-h constant routine, which allows measurement of endogenous rhythmicity. During constant routine conditions (dim light, hourly snacks, semi-recumbent posture), 2-hourly blood sampling was performed over a 30-hour period. Plasma from these blood samples was then analysed via targeted UPLC-MS/MS metabolomics[4], with 127 metabolites detected. Linear mixed effects cosine models[5] identified metabolites that displayed circadian rhythms, paired t-tests assessed the impact of the delayed meal schedule on metabolite acrophase.

Results. Circadian rhythms were observed in 31/127 metabolites ($p < 0.05$). Amino acids mostly peaked at the time aligned with the previous dark period, whereas lipid-class metabolites peaked at the time aligned with the previous light period (Figure 2). Notably, there were no rhythmic biogenic amines. Of the 31 rhythmic metabolites, 17 exhibited a significant phase shift ($p < 0.05$). Of these, 3 lipid-class metabolites exhibited an average phase advance of 3.5h. Of the 14 metabolites exhibiting significant phase delays, amino acids (arginine, asparagine, glycine, isoleucine, ornithine and serine) delayed by 4h, whereas the lipid related metabolites ($n = 8$) were delayed 2.7h. This showed that 11 % of the detected metabolites (14/127) exhibited phase shifts that were intermediate to delayed meal-timing and the unchanged light-dark cycle.

Conclusion. In conclusion, delaying meal timing whilst keeping the light/dark and sleep/wake constant, resulted in smaller metabolite phase shifts than was observed in plasma glucose rhythms. This phase shifting showed a differential effect dependent on metabolite class.

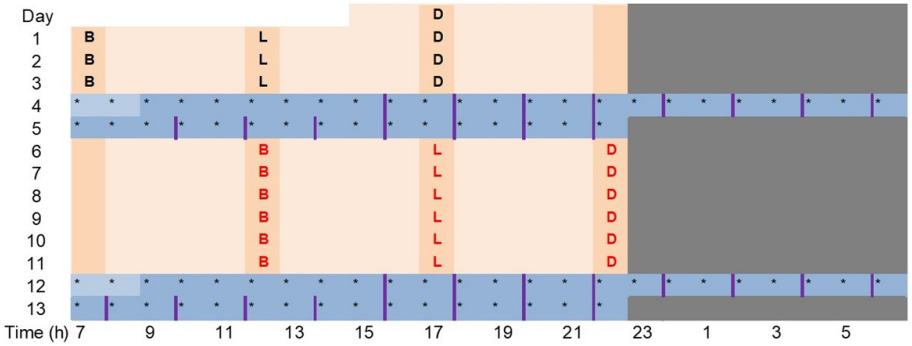

Figure 1. Laboratory protocol, representative of self-selected bedtime of 23:00; participants slept in individual bedrooms in darkness (0 lux; grey bars). During waking hours on days 0-3 and 6-11, participants were mobile in a communal area in bright room light (500 lux in direction of gaze; light orange bars). Days 1-3, isocaloric meals (B, L, D) were given 0.5, 5.5, and 10.5 hr after wake and days 6-11 isocaloric meals (B, L, D) were given 5.5, 10.5, and 15.5 hr after wake (dark orange). Days 4 and 12, participants were mobile in their rooms (<8 lux; light blue bars) before the 37-hr constant routines (individual rooms <8 lux; blue bars, hourly isoenergetic snacks; asterisks). Blood was drawn immediately before each snack and samples for metabolomics were measured every 2-h (purple bars).

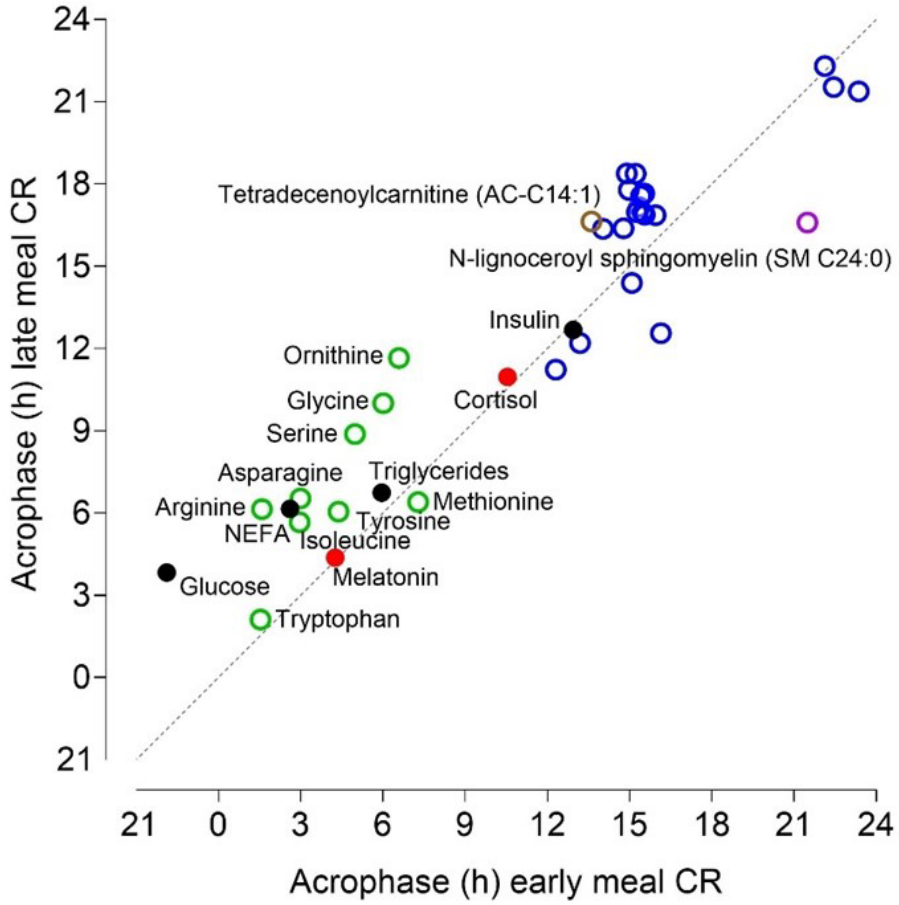

Figure 2. Phase shifts of metabolites with circadian rhythms. Acrophase during the constant routine following the early meal schedule (x axis) and the late meal schedule (y axis). Time is indicated as clock time in hours (21:00 to 00:00). Green: amino acids, blue: phospholipids, purple; sphingomyelin, red: melatonin and cortisol (for reference) and black: glucose, insulin, triglycerides and NEFA (for reference). Metabolites further away from the dashed diagonal line indicate increased phase-shifting effect of meal timing.

C05

Mitigating Muscle Wasting During Rheumatoid Arthritis Flares: A Randomised Controlled Trial

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Introduction: Rheumatoid arthritis (RA) is characterised by episodic flares of disease activity with increased levels of inflammation and functional limitations. Treatments involve corticosteroids which compound the catabolic environment of an RA flare. Essential amino acids (EAAs) can initiate anabolic effects and could be a useful intervention for maintaining muscle health in RA patients experiencing a flare.

Aims: The aims of this investigation were, i) to investigate muscle health changes following an RA flare, and ii), to assess the efficacy of EAA supplementation in mitigating muscle health deterioration in this cohort.

Methods: This randomised controlled trial (NCT06400316), conducted in collaboration with Leeds Teaching Hospital Trust, recruited 16 patients who were randomised to standard care (n=8) or a 4-week intervention (n=8) consuming 2 EAA supplements per day. A thorough assessment of muscle health (mass, quality, strength and function) was conducted at baseline, 2- and 4-weeks. Other data collected included disease activity scores, patient-reported outcome measures, physical activity, and dietary recall. Blood samples were collected and analysed for plasma amino acid concentrations and vitamin D3. Generalised Estimating Equations (GEE) determined between-group differences in all outcome measures. Spearman's rank correlation tests were used to identify associations between variables, and linear regression was used to determine predictive validity of outcome measures against each other. All experimental procedures were conducted in accordance with the Declaration of Helsinki.

Results: Short Physical Performance Battery (SPPB) (p = 0.017) and 6-minute walk test (p = 0.014) performance were both significantly improved in the intervention group above that of the control group. Muscle mass was maintained in both groups with no significant differences between groups. Regression analysis revealed that muscle quality indices (pennation angle) and rectus femoris cross-sectional area significantly predicted improvements in muscle function (SPPB; p = 0.022, p = 0.02, respectively).

Conclusion: EAA supplementation significantly improved muscle function in RA patients experiencing a flare compared to standard care. Implementation of EAA supplementation alongside standard care should be considered in RA patients to mitigate the deterioration in muscle health during a disease flare.

C06

Post-prandial glycaemia and substrate oxidation in response to sequential meals amongst women and men with various skeletal dysplasias and other extreme morphologies.

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Obesity is prevalent amongst individuals with achondroplasia (the most common form of disproportionate short stature), yet few studies exist on the metabolic health profile of these individuals, and none have examined post-prandial responses. Therefore, this study characterised the post-prandial responses of systemic metabolites and metabolic substrate oxidation rates of 40 individuals with various forms of extreme morphology (ACHON, individuals with achondroplasia, n = 22; OTHER SD, individuals with a diagnosed form of skeletal dysplasia other than achondroplasia, n = 4; SMALL, individuals with no diagnosed form of restricted growth but matched for fat-free mass (<47.5 kg), n = 4; and LARGE, individuals with high fat-free mass (>57.25 kg for females and 75.35 kg for males, as comparators), n = 10). Participants visited the laboratory for an oral glucose tolerance test (OGTT; 75 g glucose, including 150 mg of [U-^{13}C] glucose), followed 3 hours later by a mixed-meal tolerance test (MMTT; 100 g carbohydrate, 50 g fat and 30 g protein). Arterialised blood samples were collected throughout the post-prandial periods, with expired breath samples analysed to calculate substrate oxidation via indirect calorimetry and exogenous carbohydrate oxidation via EA-IRMS (elemental analyser - isotope ratio mass spectrometry; Sercon Hydra 20-20 IRMS). Across the 180-minute OGTT, the ACHON group oxidised the highest absolute quantity of the ingested carbohydrate (mean 24.0 g; 95 % CI 22.0, 26.0 g), relative to the OTHER SD, SMALL and LARGE groups. Individuals in the ACHON group also oxidised more carbohydrate across the MMTT (52.0 ± 31.1 g·180 min^{-1}; mean ± standard deviation); over 4-fold greater than that measured in the SMALL group (11.9 ± 10.6 g·180 min^{-1}, $p < 0.001$), and almost 3-times greater than that measured in the OTHER SD group (17.8 ± 11.2 g·180 min^{-1}, $p < 0.001$), but a similar quantity to the LARGE group (50.0 ± 30.6 g·180 min^{-1}, $p = 0.867$). Plasma glucose incremental area under the curve (iAUC) for the OGTT was higher in the ACHON group (545 ± 166 mmol·L^{-1}·180 min), compared to individuals with SMALL (428 ± 219 mmol·L^{-1}·180 min) and LARGE body size (368 ± 253 mmol·L^{-1}·180 min). At 120 minutes into the OGTT, plasma glucose concentrations were on average highest in the ACHON group (8.4 ± 1.5 mmol·L^{-1}), compared to the OTHER SD (7.6 ± 1.4 mmol·L^{-1}), SMALL (6.0 ± 1.7 mmol·L^{-1}) and LARGE groups (7.5 ± 3.5 mmol·L^{-1}). In summary, individuals with achondroplasia appear to prioritise exogenous carbohydrate oxidation when ingesting a glucose bolus and mixed-macronutrient meal, compared to those with other forms of skeletal dysplasia and varied/extreme body sizes and proportions. In contrast to previous reports of normoglycaemia within achondroplasia, the current cohort of individuals with achondroplasia displayed dysregulated glycaemic control on average, with 16 individuals in the prediabetic/diabetic range.

C07

Protein Intake Positively Associates with Body Composition and Quality of Life Independent of Mobility Status in Adults with Muscular Dystrophy

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Introduction

Muscular Dystrophy (MD) encompasses a group of inherited myogenic disorders characterised by progressive muscle wasting of variable severity and distribution affecting skeletal and cardiac muscle. Despite progress in gene therapies in pre-clinical models, curative treatments remain unavailable. However, advancements in clinical care have increased longevity in adults with MD, though loss of ambulation still occurs in 20-100% (1-3). We have recently observed that adults with MD consume less dietary protein than non-dystrophic individuals and, in MD, protein intake was positively associated with lean mass, grip strength and quality of life. In similar chronic conditions, mobility is a known barrier to nutritional adequacy(4), however the impact of mobility on habitual diet in MD remains unexamined. Therefore, the present study evaluated the impact of mobility on nutritional status in MD adults and probed for associations between nutrition, skeletal muscle parameters and quality of life (QoL) while considering mobility as a cofounding factor.

Methods

Secondary analysis from two adult MD cohorts (FSHD, LGMD, BMD, DM1), stratified by mobility: ambulatory (AB, n=37; 56±2 yrs; 27.4±4.5 kg/m^2) and non-ambulatory (NAB, n=22; 54±2 yrs; 27.8±5.5 kg/m^2) was conducted.Participants completed two three-day food diaries separated by eight weeks; a series of validated questionnaires assessing perceived functional ability and QoL; and a battery of physical assessments, including body composition, forearm muscle thickness, and various upper body strength measurements. Group differences were analysed using t-tests or Mann–Whitney U tests, correlations with Pearson's r or Spearman's ρ, and dietary intake distribution with linear mixed models with Bonferroni- corrected pairwise *t*-tests performed *post hoc*. Significance was set at $p<0.05$, corrected for multiple comparisons where appropriate.

Results

No differences were found between groups for BMI, lean mass percentage and self-reported physical activity ($p>0.05$). NAB reported lower absolute (g) (-16%, $p=0.003$) but not relative (g/kg) (-13%, $p=0.088$) protein intake, with no difference in total energy intake. NAB also reported lower protein intakes as a percentage of RDI (-24%, $p=0.002$) and derived less energy from protein (17% vs 19%, $p= 0.005$). Mobility had no significant effect on energy distribution across mealtimes; both groups consumed more energy at dinner than at lunch (+30%) or breakfast (+62%) (both $p<0.001$). A similar pattern was observed for relative protein intake, with dinner 0.07 g/kg higher than breakfast and 0.05 g/kg higher than lunch (both $p<0.001$). NAB exhibited 49–54% lower strength (all $p<0.05$) but similar forearm muscle thickness.

Adjusted for mobility, relative protein intake (g/kg) correlated positively with lean mass (r=0.34, *p*=0.029), lower limb function (r= 0.386, *p* = 0.006), and QoL (r=0.353, *p*=0.013).

Conclusion

Non-ambulatory adults with MD exhibit lower absolute protein intakes than those who remain mobile, despite comparable energy intakes. This finding is particularly relevant, as dietary interventions such as increased protein consumption may exert a greater relative benefit in populations with reduced mobility by attenuating inactivity-induced declines in muscle mass and strength. As positive associations between protein intake, body composition, and QoL were observed irrespective of mobility status, nutritional interventions promoting adequate protein intake should be prioritised for all individuals with MD.

C08

Cerebral Autoregulation Remains Unchanged Despite Increased Arterial Pressure Variability During 2-hour Oral Glucose Tolerance Test (OGTT) in Healthy Young Adults

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Introduction: Individuals with metabolic syndrome or type 2 diabetes are at increased risk of stroke and vascular dementia (1). Currently, little is known about the early drivers of cerebrovascular dysfunction in the context of metabolic disease pathophysiology; however, episodic hyperglycaemia, even in otherwise healthy individuals, may transiently challenge cerebrovascular regulation. Indeed, recent evidence indicates that acute hyperglycaemia may disrupt overall cardiovascular control and impair regulation of arterial blood pressure (ABP) in healthy young adults (2-4). Herein, we hypothesize that acute hyperglycaemia will not only impair regulation of ABP, but also the regulation of cerebral blood flow (CBF) via impairments in the dynamic cerebral blood flow autoregulation (dCA). Confirmation of this hypothesis could shed light on the early mechanisms through which glycaemic disturbances contribute to cerebrovascular dysfunction in metabolic disease.

Objectives: To assess the effects of acute hyperglycaemia on the regulation of ABP and CBF, and on dCA, in healthy young adults.

Methods: Ten healthy young adults (age 28 ± 7 years; BMI 22 ± 4 kg/m^2; fasting glucose 4.54 ± 0.41 mmol/L) underwent assessments of blood glucose levels (capillary sampling), CBF, and ABP regulation at baseline and at 30-minute intervals during a 2-hour OGTT (75g). At each time point, hemodynamic parameters were evaluated both at rest and during forced oscillations of ABP induced by a 0.10 Hz paced breathing manoeuvre. CBF was assessed via middle cerebral artery blood velocity (MCAv) using transcranial Doppler (WAKie, Atys Medical), while ABP was continuously recorded using finger photoplethysmography (NIBP, ADInstruments). CBF and ABP regulation were characterized by their respective mean levels and spectral variability (quantified as power spectral density [PSD]) at rest and during forced ABP oscillations in the frequency domain using Fast Fourier analysis. Additionally, dCA was assessed using transfer function analysis between ABP and MCAv. Cerebrovascular responses across the OGTT were analysed using two-way ANOVA. Pearson's correlation assessed associations between glucose and dCA iAUC.

Results: Blood glucose levels increased within the normal range during 2-hour OGTT (iAUC: 227±75 mmol/L·min). Increases in glucose levels during OGTT were accompanied by elevations in mean ABP (baseline = 98±4 vs 120min = 108±6 mmHg, P = 0.002) and ABP variability (baseline = 3.59±0.78 vs 7.20±2.19 mmHg^2, 120min, P =0.039), confirming that acute hyperglycemia impairs systemic ABP regulation. Despite these changes, there were no detrimental alterations in CBF mean levels, variability or dCA, suggesting that in healthy young adults, cerebral autoregulatory mechanisms maintain stable CBF under hyperglycaemic conditions. However, post-hoc exploratory analyses indicated a trend toward impaired CBF regulation in individuals exhibiting the largest hyperglycaemic responses (r = 0.814, P = 0.004) (Fig.1), suggesting that cerebrovascular control during OGTT-induced acute hyperglycaemia may be altered in individuals with impaired glucose metabolism.

Conclusion**:** OGTT-induced acute hyperglycaemia may compromise ABP regulation, but cerebral autoregulatory mechanisms appear sufficient to maintain stable CBF in this cohort of healthy young adults. The observed trend between the magnitude of hyperglycaemia and CBF regulation indicates that cerebrovascular responses may be compromised in individuals with impaired glucose metabolism, a hypothesis that warrants further investigations.

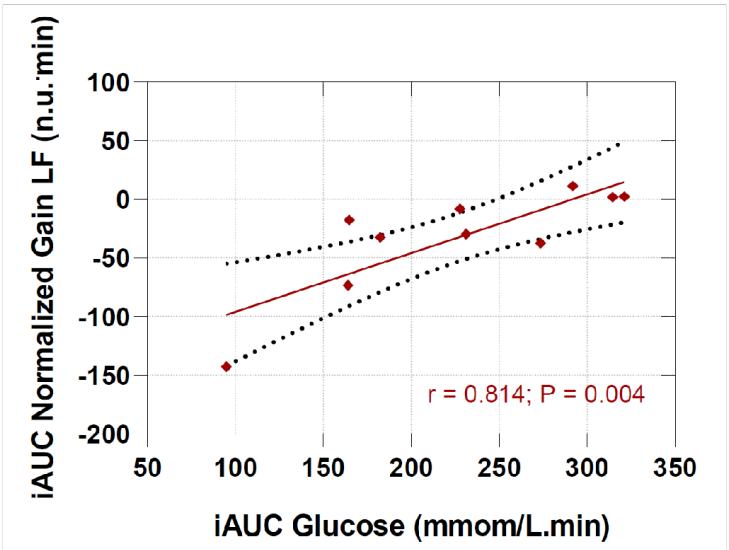

Figure 1. Association between glucose and dCA incremental area under the curve (iAUC). Pearson's correlation, r = 0.0814; P = 0.004; (N = 10)

C09

Dietary Selenium Modulates Oxidative and Inflammatory Responses to High-Sucrose Feeding in Drosophila melanogaster

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Dietary Selenium Modulates Oxidative and Inflammatory Responses to High-Sucrose Feeding in *Drosophila melanogaster*

Introduction
High dietary sugar intake induces metabolic stress characterised by oxidative imbalance and low-grade inflammation, contributing to diet-related disease risk. Selenium is a redox-active micronutrient, yet its physiological effects under high-sucrose conditions, alone or combined with metformin, remain unclear.

Aim
To evaluate the effects of dietary selenium supplementation on oxidative stress and inflammatory markers in high-sucrose-fed *Drosophila melanogaster*.

Methods
Adult female *Drosophila melanogaster* (Harwich strain) were allocated to five groups (n = 150 flies/group; 5 replicates of 30 flies). Flies were fed normal diet (ND) or high-sucrose diet (HSD) for 7 days, followed by 5 days of ND, metformin, sodium selenite, or metformin plus selenite; controls remained on ND. Superoxide dismutase (SOD), catalase (CAT), malondialdehyde (MDA), TNF-α and IL-6 were quantified. Data were analysed using one-way ANOVA with Tukey's post-hoc test; $p < 0.05$ was considered significant. Results were expressed as mean ± standard deviation.

Results
In comparison with ND, HSD significantly ($p < 0.05$) reduced CAT activity (27.49±0.55 U/mg protein Vs 24.18±0.59 U/mg protein) and increased MDA (0.65±0.02 µM Vs 0.92±0.01 µM), TNF-α (8.75±0.15 pg/ml Vs 13.49±0.56 pg/ml) and IL-6 (11.68±0.44 pg/ml Vs 17.37±0.45 pg/ml). Selenium supplementation attenuated CAT suppression (28.22±0.72 U/mg protein) and reduced MDA (0.88±0.03 µM), TNF-α (12.22±0.27 pg/ml), and IL-6 (13.69±0.36 pg/ml). Metformin alone further reduced CAT activity (17.61±0.27 U/mg protein), while combined metformin–selenium treatment showed non-additive effects ($p>0.05$) on CAT (27.74±0.46 U/mg protein) and MDA (1.18±0.12 µM). SOD activity was not significantly altered between ND and HSD controls.

Conclusion
Dietary selenium modulates oxidative and inflammatory responses to high-sucrose feeding, but its interaction with metformin is not uniformly synergistic. These findings highlight the complexity of dietary–pharmacological interactions in metabolic stress.

Keywords: High-sucrose diet; Selenium; Oxidative stress; Inflammation; *Drosophila melanogaster*; Metabolic stress

C11

Effect of chronic melatonin supplementation on exercise-induced oxidative stress parameters and muscle damage indices in sedentary young men: a randomized controlled trial

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Introduction: Melatonin's potential goes beyond its chronobiotic role and owing to its non-toxic nature and high safety profile has also garnered much attention as a safe supplement to be used in humans. **Aims and Objectives:** The present study aimed to investigate time-dependent alterations in the sedentary population's ability to fight oxidative stress brought on by long-term exogenous melatonin intake. **Method:** A single-blinded randomized controlled trial was carried out involving 28 healthy, sedentary young men aged between 21 and 26 years. Participants were randomly assigned to either the melatonin group (n=14) (MG) consisting of 14 individuals or the placebo group (n=14) (PG) also comprising 14 individuals. The MG received a daily oral dose of 3 mg of melatonin for four weeks, administered nocturnally 30 to 60 minutes prior to bedtime, while the PG received a placebo comprising of starch in gelatinous capsule. Measurements were taken weekly in the morning, with a six-day interval between consecutive sessions. Participants engaged in a treadmill running exercise according to a predetermined trial protocol, and blood samples were collected both before and after the exercise. Ethical clearance for the work was obtained from the Institutional Human Ethical Committee of the Department of Physiology, University of Calcutta. All the participants who took part in the study gave their written informed consent expressing their willingness. The study has been performed in accordance with the principles as suggested in the Declaration of Helsinki by the World Medical Association. **Results:** The serum levels of glutathione (GSH) and malondialdehyde (MDA), along with the antioxidant enzymes superoxide dismutase (SOD) and catalase (CAT), were assessed. Additionally, markers of muscle damage were evaluated by measuring serum lactate dehydrogenase (LDH) and serum creatine kinase B (CK-B). A mixed model repeated measures analysis of variance (ANOVA) was conducted for independent samples to analyze the repeated measures of two factors: time and exercise, with a significance level established at $p<0.05$. The findings of the current study indicated a notable treatment effect regarding the concentrations of CAT and LDH in the melatonin group (MG) when compared to the placebo. The antioxidant defense system, as indicated by GSH and enzymes such as SOD and CAT, showed an increase in the MG, while their levels decreased following exercise. This suggests that melatonin has a beneficial role in mitigating exercise-induced oxidative stress. Additionally, a reduction in lipid peroxidation was observed, evidenced by lower levels of MDA in the MG, with the most significant effect occurring in Week 4. However, the results also indicate that melatonin did not significantly influence another muscle damage marker, CK-B isoform, in reducing exercise-induced oxidative stress among sedentary young men. **Conclusion:** Our current research supports the antioxidant capabilities of chronic nocturnal melatonin supplementation in reducing exercise-induced oxidative stress and muscle damage in sedentary young men.

C12

De-stressing the brain: Can eating grape polyphenols during periods of mental stress protect brain and vascular health in young adults?

Rosalind Baynham[1], Richard Horniblow[1], Jet Veldhuijzen van Zanten[1], Catarina Rendeiro[1]

[1]University of Birmingham, United Kingdom

Background: Psychological stress is well known to have consequences for human health, specifically; by increasing the risk for cardiovascular diseases, as well as contributing to decline in brain function and cerebrovascular health. Food choices during periods of stress can modify the consequences of stress for vascular health. For example, high-fat foods, which are typically preferred during stressful periods, result in worsening of vascular function both in the brain and in the peripheral vasculature. On the other hand, polyphenol interventions can prevent the harmful effects of stress on the vascular system and have been extensively shown to improve peripheral and cerebrovascular function in the absence of stress. This highlights the potential of polyphenol-rich grapes, as an alternative healthier snack, that can be protective for cardiovascular and cerebrovascular health during stressful times. Specifically, this study aims to investigate the effect of grape intake on cerebrovascular and peripheral vascular function, and cognition, in the context of an episode of psychological stress.

Methods: In a randomised, placebo-controlled, crossover, counterbalanced, double-blinded, acute study, 40 young adults (aged 18 – 40 years, gender balanced) ingested a grape drink (60 g freeze dried, equiv. to 300 g fresh containing approx. 262.2 mg of polyphenols) or a placebo (polyphenol-free, matched for all other macro and micronutrients) 1 hour before an 8-minute mental stress task (Paced-Auditory-Serial-Addition-Task, PASAT). Cognitive ability was assessed pre-and post-intervention, during which pre-frontal cortical oxygenation (measured using near-infrared spectroscopy, NIRS) was assessed. Pre-frontal cortical oxygenation was also assessed during a post-intervention baseline and during stress. Endothelial function (measured by flow-mediated dilatation, FMD) was assessed pre-intervention and 60- and 90-minutes following stress. This study is registered in clinical trials.gov (NCT number: NCT06923722, Protocol ID: ERN_17-1755H).

Results: At present, n = 36 participants (19 female, *mean* age: 25 ± 4 years, *mean* BMI: 22.7 ± 2.9 kg/m^2) are enrolled in the study (n = 28 participants completed all visits). Data analysis is ongoing, but all data is planned to be analysed, and interventions unblinded, by April 2026. Data will be analysed using 2-way repeated measures ANOVAs, with time (baseline, stress, post-stress) and intervention (high or low-polyphenol grape) as main within factors.

Conclusion/significance: Stress is widespread in society and is a known risk factor for cardiovascular diseases, also affecting brain health. Outcomes from this work are expected to help inform the public about healthy food choices that are protective during periods of heightened stress.

C13

Connecting diet and disease: Using Mendelian randomisation to bridge the gap

Benedita Deslandes[1], Meda R Sandu[1], Matthew A Lee[2], Lucy J Goudswaard[1], Laura J Corbin[1], Rhona A Beynon[1], Lucy McGeagh[3], George Davey Smith[1], Julian PT Higgins[1], Naveed Sattar [4], Michael EJ Lean[5], Roy Taylor[6], J Athene Lane[1], Richard M Martin[1], Françoise Koumanov[7], Javier T Gonzalez[7], Rebecca C Richmond[1], Emma E Vincent [1]

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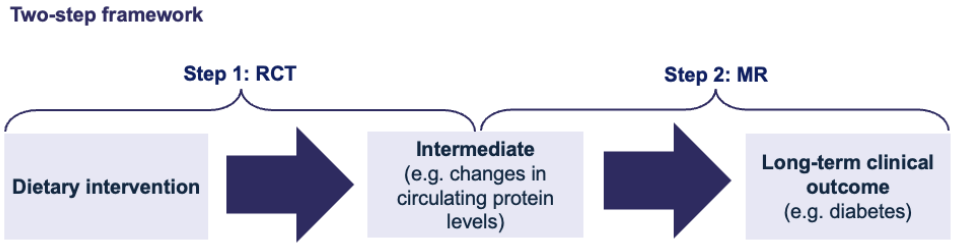
Establishing causal relationships in nutrition research is challenging because dietary exposures are typically complex, intercorrelated, and difficult to measure over long timeframes. Although randomised controlled trials (RCTs) are the gold standard for causal inference, long-term dietary intervention studies that investigate disease endpoints are often impractical due to cost, duration, and ethical constraints. Shorter dietary RCTs, however, can still provide valuable insight by identifying intermediate biomarkers, that may lie on the pathway from a dietary intervention to a long-term health outcome.

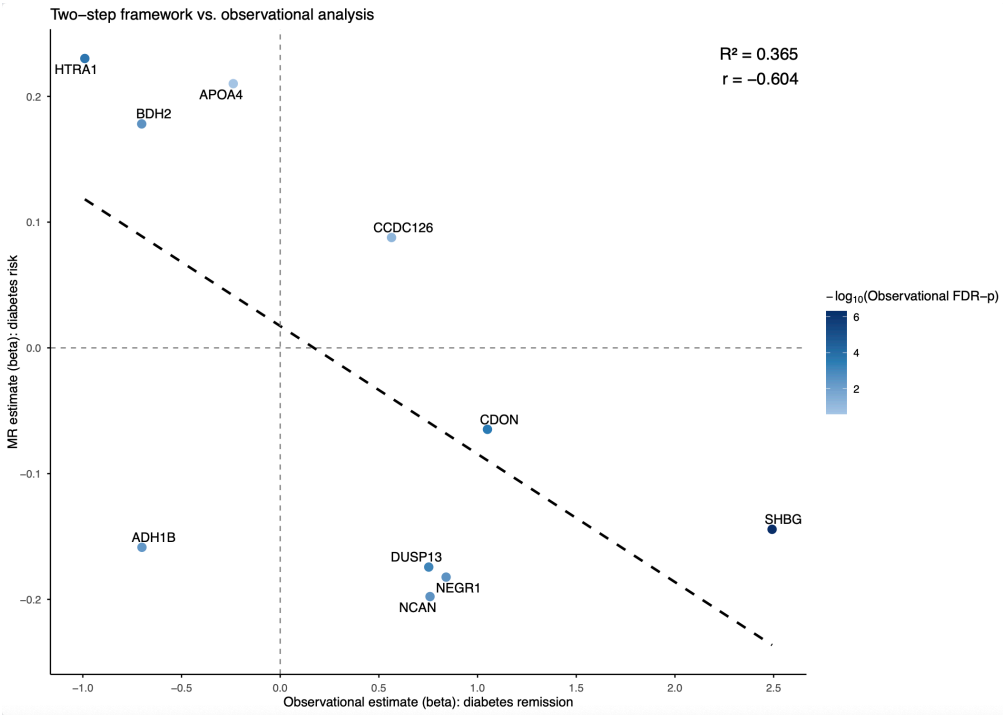
Mendelian randomisation (MR), a popular epidemiological tool to assess causality between exposures and outcomes, uses genetic variants as proxies for modifiable exposures, thus reducing issues of confounding and reverse causation. However, complex dietary patterns are extremely difficult proxy with a genetic variant. To address this, we introduce a “two-step” framework that integrates evidence from dietary RCTs and intermediate biomarkers, with MR to infer potential long-term effects of dietary interventions. In step 1, we use RCT data to identify intermediates that change in response to the intervention. In step 2, we apply MR to test whether these intermediates have a causal effect on a long-term clinical outcome (Figure 1).

We demonstrate the robustness of the framework using data from the DiRECT trial (Lean et al., 2018), which evaluated the effect of a structured diet programme on type 2 diabetes (T2D) remission. First, blinded to remission outcomes, we identified 216 circulating proteins that changed following the dietary intervention (step 1). We then applied MR to estimate the causal relevance of each protein for T2D risk, identifying 10 proteins with evidence of a causal effect (step 2).

After unblinding, we compared these MR-derived estimates with the observed associations between protein levels and T2D remission in DiRECT. Seven of the ten MR-identified proteins showed strong alignment with the trial’s observational findings, with directions of effect that were consistent and a high degree of correlation ($r \approx -0.60$, $R^2 = 0.37$, Figure 2). Proteins predicted by MR to increase T2D risk were also found to be lower in individuals who achieved remission, and vice versa. This mirroring of effects supports the robustness of the framework and demonstrates that intermediate molecular responses to diet can reliably indicate longer-term clinical outcomes.

Overall, this two-step framework extends the utility of both dietary RCTs and MR in nutrition research. By linking short-term biological changes to long-term disease outcomes, it offers a novel method in causal inference in settings where long-term dietary RCTs are not feasible.





C14

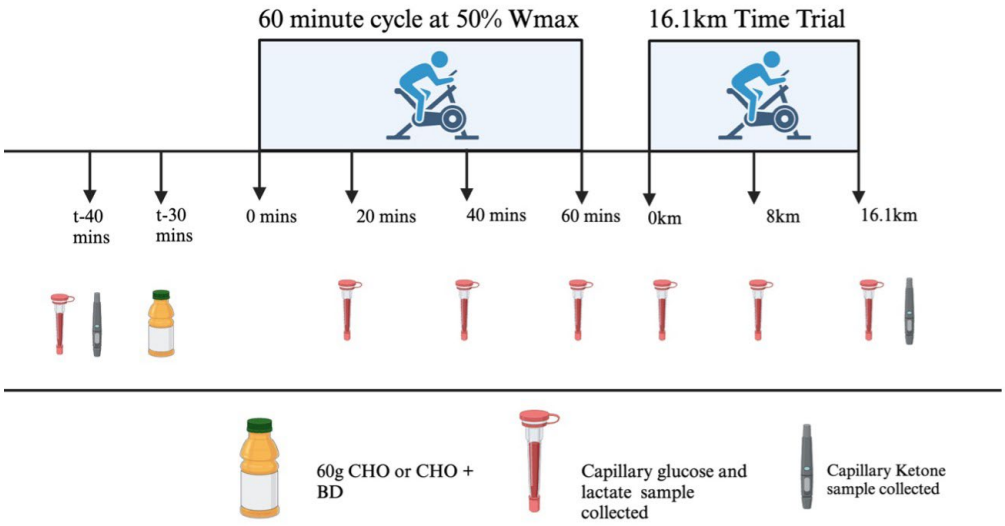
The Effect of Exogenous Ketone Supplementation on Endurance Performance in Chronically Ketogenic Individuals.

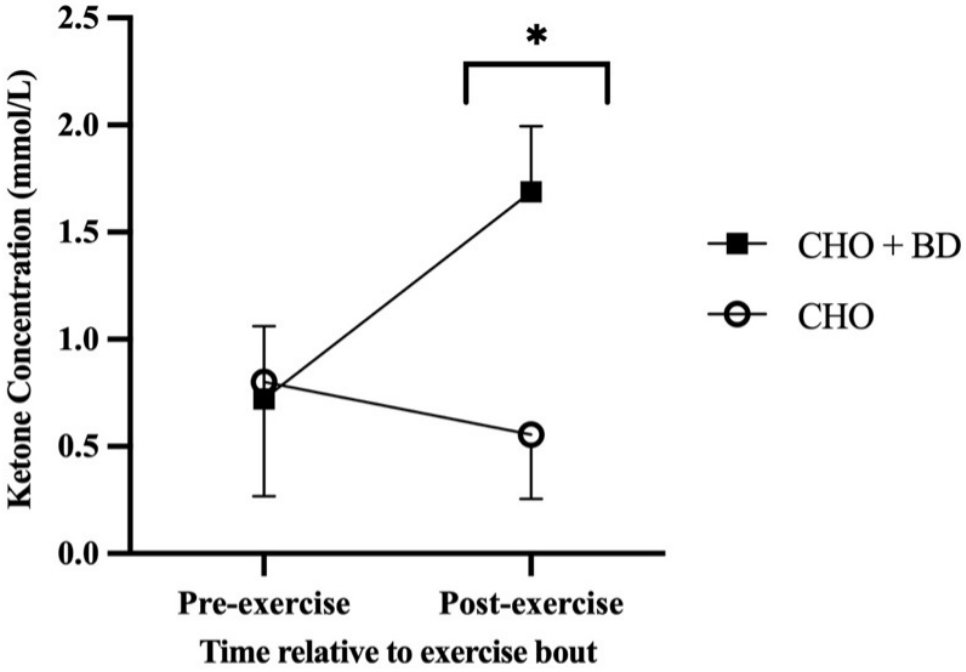
Matthew Carpenter[1], James Brouner[2], Owen Spendiff[2]

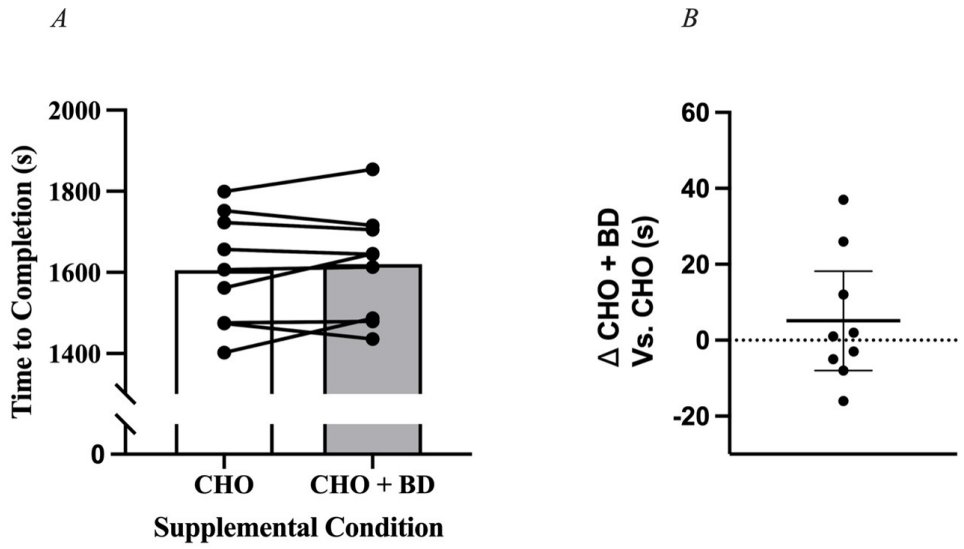
[1]University Of Northampton, United Kingdom, [2]Kingston University, United Kingdom

Abstract

Introduction: Exogenous ketone supplementation (1,3 butanediol) has gained popularity as a potential ergogenic aid due to its theorised role in altering exercise efficiency and muscle metabolism to spare glycogen. Most findings on the effect of pre-exercise exogenous ketone ingestion are equivocal, likely due to the role of exogenous ketones in suppressing glycolytic flux and the low rates of ketone oxidation observed following supplementation. However, there is minimal research investigating the impact of exogenous ketones in ketogenic individuals. Increasing ketogenic enzymes through prolonged ketogenic feeding may enhance the effects of exogenous ketone ingestion and allow for performance enhancement in this cohort. Therefore, the aim of this study was to investigate the impact of increasing circulating ketone bodies through exogenous ketone supplementation on endurance performance in athletes chronically adapted to a ketogenic diet. **Methods:** Nine recreationally active males (age 42 ± 9 years; stature 176 ± 5 cm; mass 74.4 ± 6.1 kg) chronically adapted (minimum 12 months) to a ketogenic diet (defined as daily carbohydrate consumption was <50g/day, or <10% of total calories) volunteered to take part in the study. Participants visited the lab four times, the first visit determined their V̇O2max, and the second visit accustomed them to test procedures. In a counterbalanced design, visits 3 and 4 involved the consumption of a 60g carbohydrate beverage (CHO), or a beverage comprising 60g carbohydrate and 0.5g/kg 1,3-butanediol (CHO + BD). Participants then completed a 60-minute continuous exercise bout, followed by a 16.1km time trial. This study was approved by Kingston University ethics and all procedures and conduct complied with the Declaration of Helsinki. **Results:** βHB significantly increased in CHO + BD group compared to CHO ($P<0.01$). During continuous exercise, there was no effect of supplementation on lactate concentration, substrate oxidation, exercise economy, RPE or heart rate ($P>0.05$). However, glucose was significantly lower at minute 60 of continuous exercise in CHO + BD compared to CHO ($P=0.01$). There was no effect of supplemental condition on lactate concentration, substrate oxidation, exercise economy, RPE, heart rate or time to completion during the time trial ($P>0.05$). **Conclusion:** This study demonstrated that 1,3-butanediol (1,3BD) supplementation did not enhance 16.1km time trial performance in chronically ketogenic individuals despite a significant increase in blood ketone levels following the CHO + BD condition. Additionally, there was minimal impact on exercise metabolism following CHO + BD ingestion in spite of increased circulating ketones. This is the first study to the authors knowledge, to assess the impact of exogenous ketone ingestion on performance in chronically ketogenic individuals, with no synergistic effect observed between chronic carbohydrate restriction and exogenous ketone ingestion when consumed pre-exercise. The results demonstrate equivocal effects of 1,3BD ingestion on endurance performance in chronically ketogenic individuals. Despite metabolic changes, such as increased βHB concentrations following ketone ingestion, there were no significant changes in substrate oxidation during continuous exercise. Future research should explore the synergy between chronic ketosis and exogenous ketone ingestion to determine whether long-term dietary adaptation influences the impact of exogenous ketones on exercise performance.


60 minute cycle at 50% Wmax
16.1km Time Trial
t-40 mins
t-30 mins
0 mins
20 mins
40 mins
60 mins
0km
8km
16.1km
60g CHO or CHO + BD
Capillary glucose and lactate sample collected
Capillary Ketone sample collected


Ketone Concentration (mmol/L)
2.5
2.0
1.5
1.0
0.5
0.0
*
Pre-exercise
Post-exercise
Time relative to exercise bout
CHO + BD
CHO


A
B
2000
1800
1600
1400
0
Time to Completion (s)
CHO
CHO + BD
Supplemental Condition
60
40
20
0
-20
Δ CHO + BD
Vs. CHO (s)

C15

Effect of a novel macroalgae protein hydrolysate on postprandial glucose control in healthy adults.

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Introduction

The global rise in impaired glucose tolerance, insulin resistance, and type 2 diabetes underscores the urgent need for effective nutritional strategies to improve postprandial glycaemic control (1). *Palmaria palmata* (dulse), a red seaweed rich in bioactive peptides, offers a novel marine-derived alternative and sustainable protein with potential glycaemic benefits. Such hydrolysates have been demonstrated to increase incretin secretion and β-cell function *in vitro*, and attenuate postprandial glycaemia in mice, thus warranting further investigation in humans (2).

Aim

To investigate the effect of a dulse protein hydrolysate on postprandial blood glucose, insulin and incretin concentrations, and β-cell function in healthy adults.

Methodologies

Six healthy adults (age 44±7 y; height 170±3 cm; body mass 72.4±4.9 kg; body fat 24.0±3.1%) participated in a randomised, double blind, crossover feeding study. Written informed consent was obtained from all participants, the study was approved by the local Ethics Committee (2022_12_14_EHS) and registered at ClinicalTrials.gov (NCT05850429).

Following a >10 h overnight fast, participants consumed a beverage containing 0.6 g·kg body mass $(BM)^{-1}$ maltodextrin, with either 0.150 g·kg BM^{-1} (High), 0.075 g·kg BM^{-1} (Low) or no (CON) dulse protein hydrolysate, in randomised order. Blood samples were taken prior to and 15, 30, 45, 60, 90, and 120 minutes post ingestion. Glucose, insulin, C-peptide, glucagon, GIP and GLP-1 concentrations were measured in plasma and expressed as incremental Area Under the Curve (iAUC) and across time. β-cell function parameters derived from mathematical modelling of glucose and C-peptide data were assessed, including insulin secretion rate, glucose sensitivity (insulin response to glucose) and rate sensitivity (early insulin response). Differences in iAUC and time-course data were tested for using one-way and two-way repeated measures ANOVAs, respectively, with post-hoc Dunnett's to compare differences between protein and control conditions. Effect sizes were calculated using Hedge's g. The alpha level was set at $p<0.05$. Data are Mean±SD.

Results

The 2-hour Glucose iAUC was significantly different between conditions (High: 265±135; Low: 228±108; CON: 380±203) ($P<0.05$), with post-hoc testing indicating a significant difference between Low and CON

conditions only (P<0.05), with a large effect size (g=-0.9, 95% CI (-1.8, -0.1)). Concentrations of all analytes increased significantly after consumption of each beverage (main effect of time: P<0.05), with no between beverage differences observed (P>0.05). Time course of insulin secretion rate (ISR) was affected by condition (*P*<0.01). High augmented ISR by 81±125 and 86±114 pmol·min^{-1}·m^{-2} at 15 and 20 min, respectively, versus CON (*P*<0.01). Conversely, Low decreased ISR by 62±62, 62±62 and 64±59 pmol·min^{-1}·m^{-2} at 75, 80 and 85 min, respectively (*P*<0.05).

Conclusions

This study demonstrated the potential of a novel dulse protein hydrolysate to reduce postprandial blood glucose concentrations in a cohort of healthy individuals, though we did not observe a dose-response. These data are consistent with the literature on co-ingestion of other protein sources, which have been previously observed to attenuate postprandial glycemia (3). While this study is limited by a small sample size, large effect sizes were observed for potential enhancements in glucose and ISR in protein conditions. These findings suggest *palmaria palmata* as a potential alternative and sustainable bioactive protein for regulation of glucose control.

C16

Whole-body and skeletal muscle metabolic responses to galactose feeding at rest and after exercise

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[1]School of Sport, Exercise and Rehabilitation Sciences, University of Birmingham, United Kingdom, [2]Department of Public Health and Sport Sciences, University of Exeter, United Kingdom, [3]Department of Clinical Medicine, Steno Diabetes Center Aarhus, Denmark, [4]Department of Nuclear Medicine and PET Centre, Aarhus University Hospital, Denmark, [5]School of Sport, Exercise and Nutrition, Massey University, New Zealand

Introduction:

Galactose is primarily metabolised in the liver by Leloir Pathway enzymes. The presence of these enzymes in human skeletal muscle suggests it could be a site for galactose metabolism. Recently, galactose feeding after exercise was shown to appreciably replenish glycogen stores (Podlogar et al., 2023). However, understanding of the metabolic response to galactose feeding in the context of exercise and skeletal muscle metabolism remains limited.

Aim:

To explore whole-body and skeletal muscle metabolic responses to galactose feeding at rest and after exercise.

Methods:

Ethical approval was obtained from an NHS Research Ethics Committee (24/EM/0067). Participants (N=8) were healthy, active adults (2 females/6 males, age 25±6 years, height 177.6±10.0 cm, body mass 69.2±11.9 kg, $\dot{V}O2peak$ 53.2±8.6 $mL \cdot kg^{-1} \cdot min^{-1}$). In a randomised crossover design, participants completed two experimental trials (overnight-fasted, 24-hour standardised diet and physical activity) starting with 60 minutes of rest or interval cycling exercise (4x 90-sec at 110% Wmax interspersed with 11 min at 30-50% Wmax) and then continued resting while consuming 2.25 $g \cdot kg^{-1}$ of galactose throughout a 3-hour period. Blood samples were collected before (-60 min) and immediately after (0 min) rest/exercise, and following galactose ingestion at 30, 60, 90, 120, 150, 180 min to determine plasma galactose, glucose, lactate and insulin concentrations. Skeletal muscle biopsy samples were obtained from the vastus lateralis at timepoints -60, 60, and 180 min to determine glycogen concentrations and gene expression of *PPARGC1A*, Leloir Pathway enzymes (*GALM, GALK1, GALT, GALE*) and other galactose disposal pathways (*UGP2, PGM1, AKR1B1*).

Statistical analyses were conducted using linear mixed models in SAS accounting for baseline and repeated-measures random effects (Kenward & Roger, 2010). All data were log-transformed to manage heteroscedasticity. Estimates were back-transformed to percent effects and 95% confidence intervals.

Results:

Plasma galactose concentrations increased over time after galactose ingestion equally with rest and exercise conditions (both P<0.001, Figure 1). Glucose concentrations decreased over time with rest (P=0.017, Figure 1) and exercise (P=0.030). Lactate concentrations increased over time with both conditions (both P<0.001, Figure 1). Post-hoc analyses showed higher lactate with exercise at 0 min and 30 min compared to rest (both P<0.001). Insulin levels did not change from 0 to 180 min with either condition (P>0.050, Figure 1), but post-hoc analyses showed decreased insulin concentrations with exercise at 0 min (P=0.037), 30 min (P<0.001), and 150 min (P=0.006) compared to rest.

Baseline glycogen concentrations were 363 [308, 429] mmol·kg^{-1} dry weight. Glycogen levels decreased at 60 min (-50% [-69, -19]%, P=0.012) and 180 min (-44% [-51, -35]%, P<0.001) with exercise compared to rest. Gene expression of enzymes *GALM*, *GALT*, *GALE, UGP2 PGM1* decreased at 60 min with rest, whilst *GALM*, *GALE, AKR1B1* expression decreased at 180 min with exercise (Figure 2).

Conclusions:

Galactose feeding increased circulating galactose and lactate levels across time, produced a peak in insulin levels 30 min after feeding started, and temporarily (60 min) decreased skeletal muscle gene expression of some enzymes. These responses were modulated by prior exercise with decreased muscle glycogen levels, smaller insulin peak, and delayed (180 min) decrease in gene expression for some enzymes.

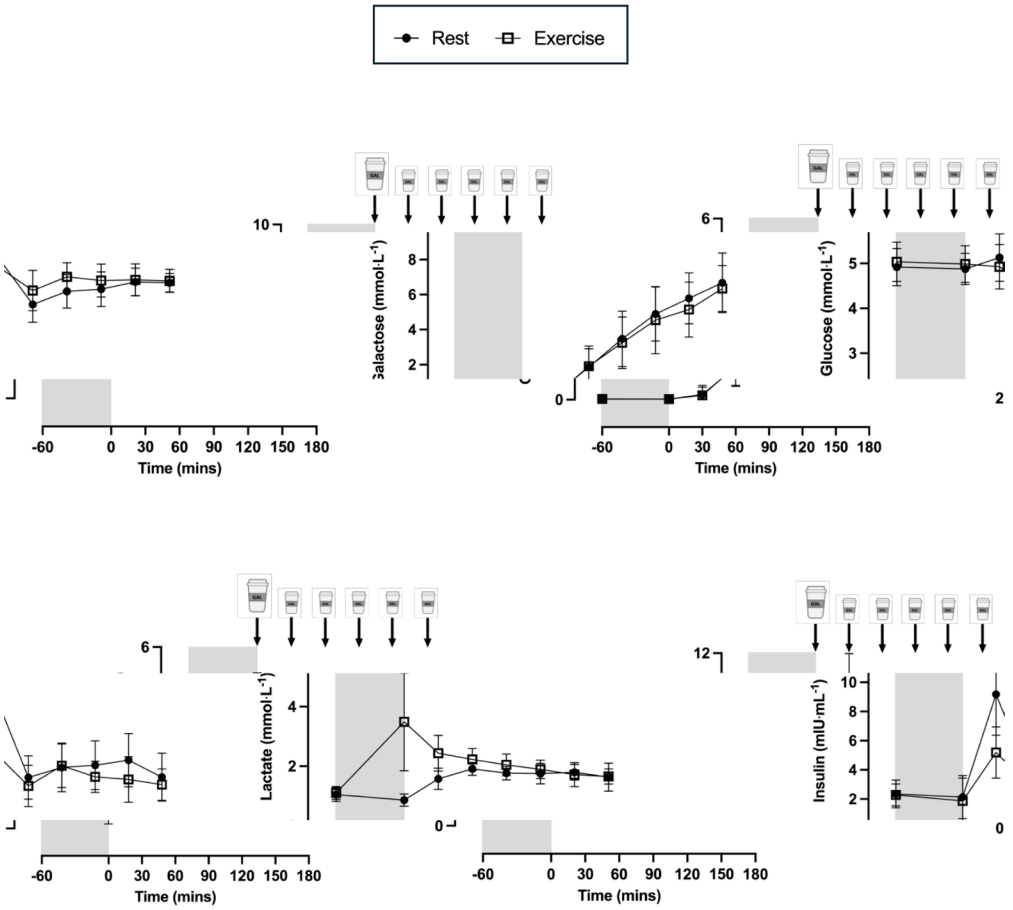


Figure 1. Plasma concentrations of galactose, glucose, insulin, and lactate across the study trials (raw data). Grey shaded area signifies the rest or exercise period.

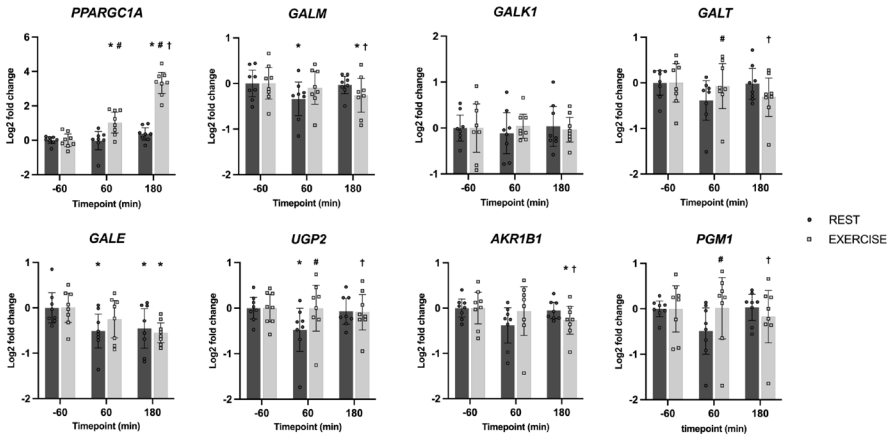


Figure 2. Gene expression (fold change relative to baseline, $2^{-\Delta\Delta Ct}$) of Peroxisome proliferator-activated receptor gamma coactivator 1-alpha (*PPARGC1A*), Galactose mutarotase (*GALM*), Galactokinase (*GALK1*), Galactose-1-phosphate uridyltransferase (*GALT*), UDP-galactose 4-epimerase (*GALE*), UTP-glucose-1-phosphate uridylyltransferase (*UGP2*), Aldo-keto reductase family 1 member B1 (*AKR1B1*), Phosphoglucomutase-1 (*PGM1*). * signifies a statistically significant difference compared to -60 min (baseline). # signifies a statistically significant difference between conditions (exercise vs rest). † signifies a statistically significant difference between conditions on the change from 60 to 180 min. Dark grey bars (mean ± confident intervals) and circles (individual data points) represent REST condition and light grey bars and squares represent EXERCISE condition.

C17

Can plant-flavanols protect human vascular function from mental stress in a black male population?

Rebecca Cupac[1], Rosalind Baynham[1], Veldhuijzen van Zanten Jet[1], Rendeiro Catarina[1]

[1]University of Birmingham, United Kingdom

Background: Mental stress has been shown to induce acute endothelial dysfunction. Black ethnicities experience a disproportionately higher burden of cardiovascular disease, with stress-related vascular responses proposed as a contributing factor. Although flavonoid-rich foods, particularly cocoa flavanols, can mitigate stress-induced decline in endothelial function, evidence in high-risk populations remains limited. This study investigates the influence of cocoa flavanols on vascular responses to mental stress in healthy, black male volunteers.

Methods: A randomised, placebo-controlled, double-blind, counterbalanced within-subject acute study was used to evaluate the effects of cocoa flavanols on stress-induced vascular responses. Healthy black participants (n=9) completed two sessions and consumed either a high-flavanol cocoa (150 mg (-)-epicatechin) or a low-flavanol cocoa (< 4 mg (-)-epicatechin), prior to undergoing mental stress (8-minute paced auditory serial addition task: PASAT). Vasodilatory responses (forearm blood flow, FBF), systolic and diastolic blood pressure (BP), heart rate (HR), heart rate variability (HRV), and pre-ejection period (PEP), were assessed pre-flavanol consumption (Baseline), post-flavanol consumption at rest (Rest) and during mental stress (Stress). Endothelial function (as measured by brachial artery flow-mediated dilatation, FMD) was assessed at Baseline and 30-and-90 minutes post-mental stress (i.e., 2-3-hours post-flavanol intake).

Results: Preliminary results (n = 9) show that stress induced significant increases in systolic and diastolic BP, HR, HRV, and PEP in comparison to baseline (Baseline/Rest, p's<.05). FBF also significantly increased during stress compared to Baseline (p= .004, +2.19 ± 0.46). There was no significant decline in FMD following mental stress, yet FMD was significantly higher 30 minutes post-stress following high-flavanol cocoa compared to low-flavanol cocoa (p=.014, +2.74 ± 0.87) and compared to Baseline (p=.024, +2.10 ± 0.60). No differences in PASAT performance were observed between dietary interventions (p= .0678). Data from a full sample of 14 participants is expected to be analysed by April 2026.

Conclusion: The mental stress task evoked the expected cardiovascular and vasodilatory responses across both dietary interventions. Whilst cocoa flavanols did not affect physiological responses during stress, they did improve endothelial function following mental stress in young, black participants.

Keywords: mental stress, cardiovascular diseases, endothelial function, cocoa flavanols, ethnicity

C18

Oral Consumption of Calabash Chalk Alters Uterine Hormone Receptor Expression During Pregnancy in Wistar Rats

Daniel Edeha [1], Freddy Agoreyo [1], Magdalene Omigie[1]

[1]University of Benin , Nigeria

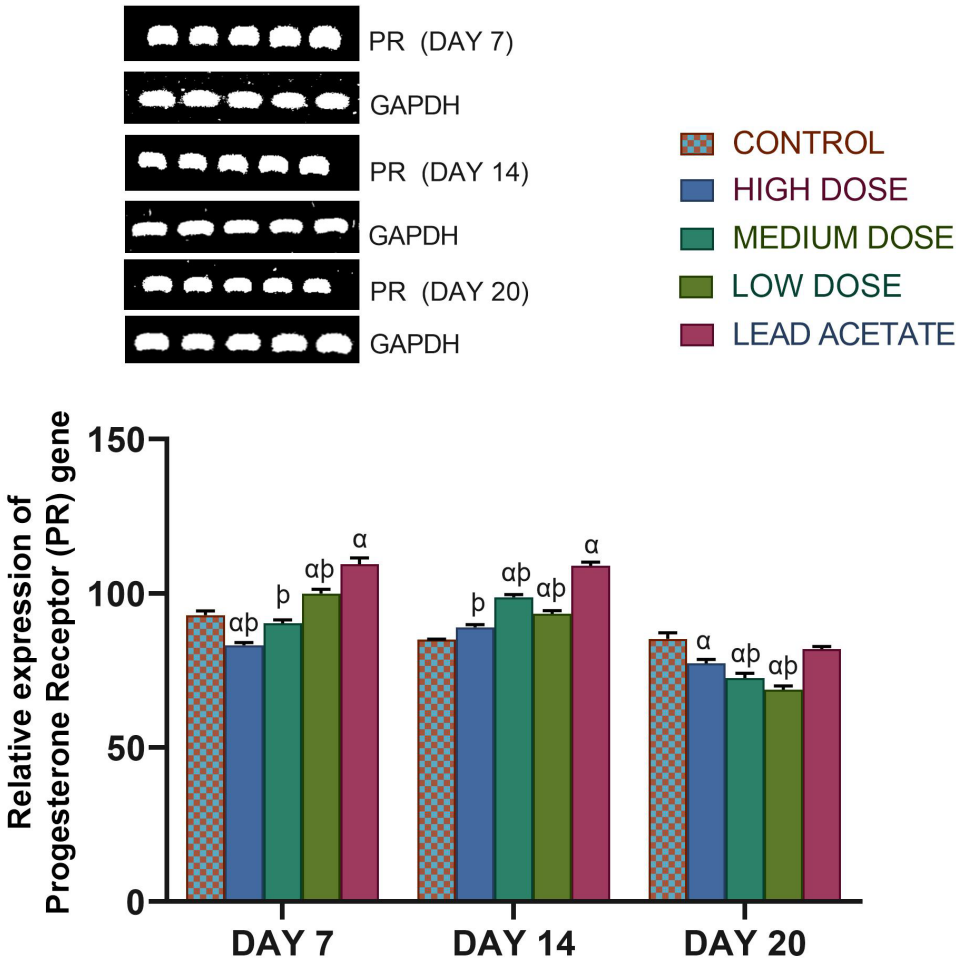
Introduction: The consumption of earth materials such clay as is a common practice in various parts of the world. It is particularly prevalent among pregnant women and children, largely due to medicinal, nutritional, and cultural beliefs. Despite the widespread use of edible clay particularly by pregnant women, its effects on key reproductive hormone receptor modulation have not been explored. Hence this study was aimed to fill this gap. This study investigated the expression of estrogen (ER), progesterone (PR) and oxytocin (OXR) receptor genes in uterine tissue following oral ingestion of edible clay (calabash chalk) during pregnancy.

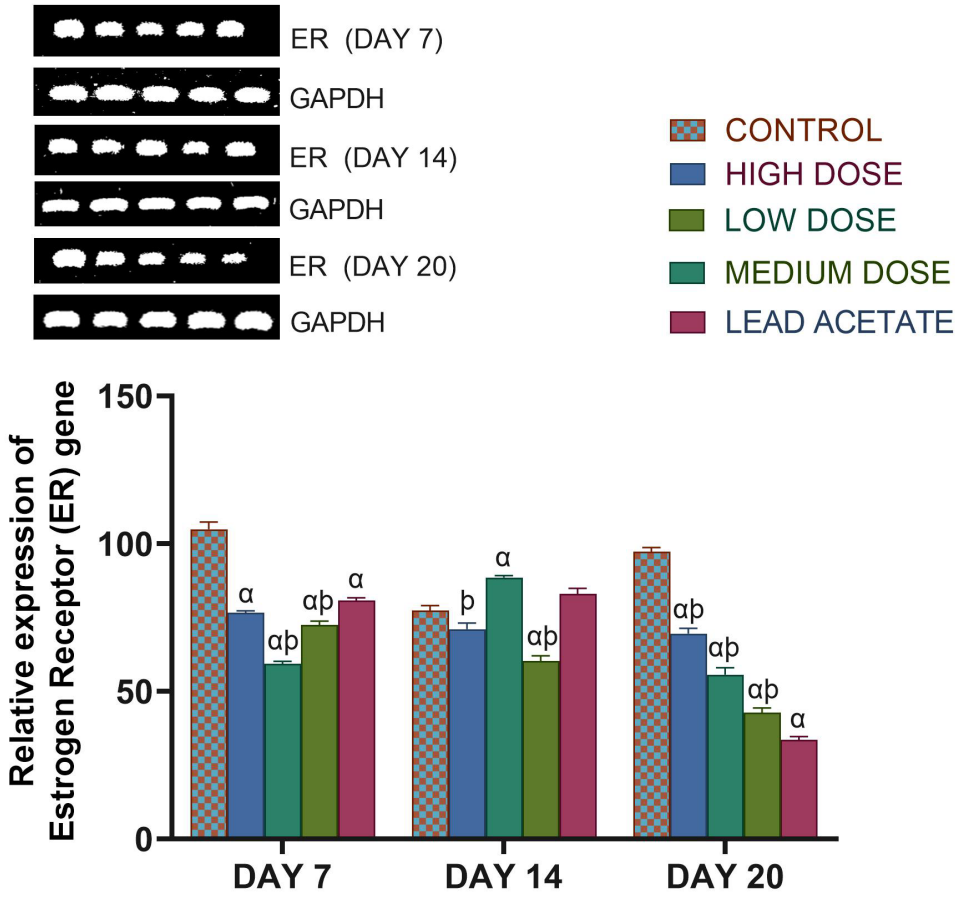
Method: Edible clay samples were sourced from New Benin market, Edo State, Nigeria. The sample blocks were pulverized into a fine powder with a mortar and pestle. A 40g sample of the powder was dissolved in 400ml of distilled water and the mixture was stirred continuously to produce a well-dispensed suspension. Ninety-six (96) pregnant Wistar rats, separated into four groups and three subgroups (n = 8), representing gestational day (GD) 7, 14, and 20, were orally administered 2000 mg/kg (high dose), 1000 mg/kg (medium dose), and 500 mg/kg (low dose) of edible clay and distilled water (control). Uterine tissues were harvested on GD 7, 14 and 20, and gene expression of ER, PR and OXR were analyzed using real-time quantitative polymerase chain reaction (RT-PCR). The mean and standard error of mean were determined using Graphpad prism version 8.2.2. The two-way ANOVA followed by Tukey's post hoc analysis were used to determine the difference in means among the groups. The difference in means was considered significant at $P<0.05$. Ethical approval for this study was be obtained from the Research and Ethics committee, College of Medical Sciences, University of Benin, Benin City. Results: At GD 7, ER expression was significantly down-regulated in all clay-treated and lead acetate groups ($p < 0.05$). PR expression was significantly reduced in the high-dose group, increased in the low-dose and lead groups, and unchanged in the medium-dose group. OXR expression was significantly decreased in the high-dose group, increased in the medium-dose and lead groups, and unchanged in the low-dose group ($p < 0.05$). At GD 14, PR and OXR were significantly up-regulated in the medium-dose group, while ER was up-regulated in medium dose, down-regulated in low dose, and unchanged in others. By GD 20, ER, PR, and OXR were significantly down-regulated across all edible clay-treated groups, with ER and OXR also reduced in the lead group.

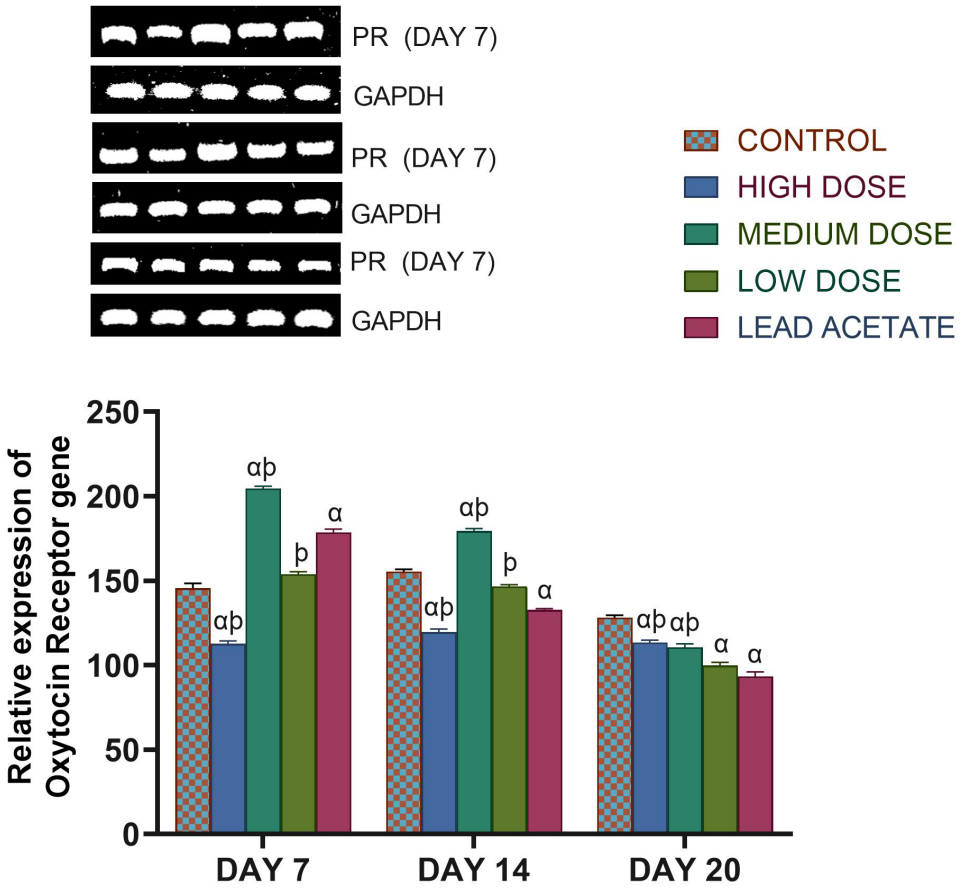
Conclusion: The study demonstrates that oral ingestion of edible clay (Calabash chalk) during pregnancy modulates the expression of estrogen and progesterone receptor genes in a dose and gestational dependent manner, suggesting potential disruption of uterine hormonal responsiveness critical for implantation, fetal development, and labor initiation.

Keywords: Calabash chalk, pregnant uterus, estrogen receptor, progesterone receptor, oxytocin receptor

Abbreviations: Estrogen receptor (ER), Progesterone receptor (PR) and oxytocin receptor (OXR), Gestation Day (GD).


PR (DAY 7)
GAPDH
PR (DAY 14)
GAPDH
PR (DAY 20)
GAPDH
CONTROL
HIGH DOSE
MEDIUM DOSE
LOW DOSE
LEAD ACETATE
Relative expression of Progesterone Receptor (PR) gene
150
100
50
0
αþ
þ
αþ
α
αþ
þ
αþ
α
α
αþ
αþ
DAY 7
DAY 14
DAY 20


ER (DAY 7)
GAPDH
ER (DAY 14)
GAPDH
ER (DAY 20)
GAPDH
CONTROL
HIGH DOSE
LOW DOSE
MEDIUM DOSE
LEAD ACETATE
Relative expression of Estrogen Receptor (ER) gene
150
100
50
0
α
αþ
αþ
α
þ
α
αþ
αþ
αþ
α
DAY 7
DAY 14
DAY 20


PR (DAY 7)
GAPDH
PR (DAY 7)
GAPDH
PR (DAY 7)
GAPDH
CONTROL
HIGH DOSE
MEDIUM DOSE
LOW DOSE
LEAD ACETATE
Relative expression of Oxytocin Receptor gene
250
200
150
100
50
0
αþ
αþ
þ
α
αþ
αþ
þ
α
αþ
αþ
α
α
DAY 7
DAY 14
DAY 20

C19

Assessing the effects of chronic beetroot extract supplementation in an age-varied population: An assessment of skeletal muscle enhancement following 12-months of supplementation

Hope Rose Edwards[1], Andrea Berry[2], Jamie Morton[2], Jamie Moseley[3], Thomas Marshall[3], Sherif El-Khamisy[2], Chinonso Igwesi-Chidobe[3], Matthew Farrow [4], Huw Simon Jones[2]

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There has been much research performed surrounding dietary nitrate supplementation in young, healthy, and athletic populations, especially in the form of acute beetroot juice consumption(1). However, chronic supplementation in an age-varied population has remained a largely neglected field. This study supplemented healthy participants (aged 24-86 years) with two beetroot extract pills per day (~600 mg of beetroot extract, ~2.8-3.0 mg nitrate) for 12-months (n=42). At baseline, three, six, nine, and twelve-months the participants took part in a suite of tests to assess muscle mass, size, and strength outcomes. Bioimpedance analysis was used to assess skeletal muscle mass (SMM) and an ultrasound measurement of the lateral head of the gastrocnemius was used to report muscle thickness (MT). Handgrip strength (HGS) and a knee extension (KE)/flexion (KF) protocol (concentric–concentric at 60°/s) were used to assess isometric and isokinetic strength, respectively. Following the chronic supplementation period no changes in SMM ($p=0.103$) or MT ($p=0.0684$) were observed at any time-point. However, all mean muscle strength outcomes improved by 3-months compared to baseline (HGS 1.09 ± SD 2.19 Kg ($p=0.028$), KE 15.12 ± SD 23.65 Kg ($p=0.003$), KF 5.82 ± SD 10.54 Kg ($p=0.008$)). Furthermore, the improvements in HGS and KF demonstrated continued improvement as the supplementation period progressed (12 months: HGS 2.03 ± SD 2.80 Kg ($p=0.002$), KF 12.71± SD 14.98 Kg ($p<0.0001$).

A subgroup analysis was also undertaken to observe if the efficacy of supplementation was affected by age. The participants were split into two subgroups, 'Young' (aged 24-59 years, n=31) and 'Older' (aged 60+ years, n=11). The 'Older' sub-group demonstrated no statistically significant improvement in isometric or isokinetic strength at any point during the supplementation period, whereas the 'Young' sub-group demonstrated significant improvements in all strength outcomes (HGS $p=0.017$, KE $p=0.019$, KF $p<0.0001$), perhaps suggesting that beetroot supplementation is more effective at improving muscle strength in a younger population.

Overall, these findings suggest that strength increases post-supplementation cannot be attributed to an increase in muscle mass or volume, but improved muscle quality and physiological efficiency, as in agreement with the recent literature(2). Interestingly, the beetroot extract used in this study has relatively little nitrate content (~2.8-3.0 mg) compared to previous beetroot juice supplementation studies(3, 4), suggesting that nitrate may not be the key driver of the effects observed in this study. To corroborate these findings a larger, powered study would be required, ideally with the inclusion of a placebo or no intervention group.

Ethical approval for this study was obtained from the London-Brighton and Sussex Research Ethics Committee (REC Ref: 22/PR/1028).

C20

Comparative Effects of Butter, Coconut Oil, and Olive Oil-Based Ketogenic Diets on Liver and Kidney Function in Wistar Rats

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Abstract
A ketogenic diet (KD) is characterized by high fat, very low carbohydrate, and moderate protein intake, leading to a state of ketosis. Although commonly employed for weight management and therapeutic purposes, its potential impacts on hepatic and renal function remain a subject of debate. This study evaluated the effects of different dietary fat sources in a high fat KD coconut oil, olive oil, and butter on liver enzymes, renal markers, and body weight in albino Wistar rats.

Forty rats were acclimatized for two weeks under standard laboratory conditions with appropriate ventilation, a 12-hour light dark cycle, and constant temperature, following the National Research Council's Guide for the Care and Use of Laboratory Animals (NRC, 2011). The animals were then randomly assigned to four groups (n = 10). Group A (control) received standard rat chow, while Groups B, C, and D were fed a 65% high fat KD formulated with butter, coconut oil, or olive oil, respectively, for eight weeks. Body weights were recorded weekly. At the end of the experiment, 24-hour urine samples were collected in metabolic cages. Blood was obtained via cardiac puncture under chloroform anesthesia, and serum was separated by centrifugation. Liver function was assessed by determining aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase (ALP), and total protein, albumin, and globulin levels. Renal function was evaluated through serum and urinary urea, creatinine, and urinary albumin. Data were analyzed by ANOVA, with significance accepted at $P < 0.05$.

KD feeding significantly reduced body weight compared with control ($P \leq 0.05$). Hepatic enzyme activities increased markedly, particularly in coconut oil fed rats. AST levels were 160.1 ± 9.5 U/L (control), 143.4 ± 8.2 U/L (butter), 196.1 ± 3.9 U/L (olive oil), and 260.1 ± 17.8 U/L (coconut oil). ALT increased from 36.0 ± 3.9 U/L (control) to 91.2 ± 18.7 U/L (coconut oil). ALP increased from 9.90 ± 0.74 U/L (control) to 24.9 ± 2.5 U/L (butter). Total protein and albumin levels decreased significantly ($P = 0.0032$), while globulin remained unchanged.

Renal markers showed no deterioration. Serum urea decreased from 64.20 ± 3.41 g/dl (control) to 39.40 ± 4.70 g/dl (butter), 29.90 ± 1.46 g/dl (coconut oil), and 40.20 ± 2.62 g/dl (olive oil). Serum creatinine fell from 1.42 ± 0.04 mg/dl to 1.05 ± 0.09 mg/dl (butter), 0.85 ± 0.07 mg/dl (coconut oil), and 1.03 ± 0.07 mg/dl (olive oil). Urinary albumin declined from 0.22 ± 0.03 g/dl to 0.19 ± 0.02 g/dl (butter), 0.15 ± 0.02 g/dl (coconut oil), and 0.13 ± 0.01 g/dl (olive oil). Urinary creatinine was 3.84 ± 1.02 mg/dl (control), 3.84 ± 0.90 mg/dl (butter), 1.75 ± 0.46 mg/dl (coconut oil), and 4.31 ± 0.70 mg/dl (olive oil). Albumin:creatinine ratio decreased from 120.6 ± 32.0 to 94.6 ± 23.0 (butter), 174.7 ± 61.8 (coconut oil), and 41.3 ± 8.3 (olive oil).

In conclusion, high fat ketogenic diets induced hepatocellular stress, particularly with coconut oil, but did not compromise renal function. Olive oil based KD exhibited the most favorable hepatic and renal profiles.

Bottom of Form

C21

Short-term treatment with low-dose aspirin improved metabolic status and attenuated atherothrombotic risk factors in female rats exposed to combined oral contraceptives

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Short-term treatment with low-dose aspirin improved metabolic status and attenuated atherothrombotic risk factors in female rats exposed to combined oral contraceptives

Abstract

Background: Atherothrombosis is a chronic and progressive disease responsible for a significant number of deaths globally, and it has become essential to understand how this consequence contributes to enhanced cardiovascular disease in women on combined oral contraceptives (COC).

Objectives: To assess the impact of COC administration on metabolic status and the risk of atherothrombotic disorder in female rats, beyond evaluating the therapeutic effects of short-term treatment with low-dose aspirin (LDA).

Methods: Thirty (n=30) five-week-old female Sprague Dawley rats were given low-dose COC (LCOC) or a high-dose COC (HCOC) for six weeks before treatment with LDA for another four weeks. These rats were compared to those that were only given LCOC or HCOC without treatment with LDA. Whereas rats that received distilled water (as a vehicle) and LDA only served as controls. Body weights and metabolic status were measured weekly. Whereas parameters related to glucose regulation, lipid profiles, inflammatory cytokines, hematological indices, coagulation, and endothelial dysfunction were recorded at the terminal end of the experiment.

Results: Rats exposed to HCOC presented with abnormal metabolic status and lipid profiles, as seen with impaired glucose tolerance ($p < 0.001$), which was accompanied by significantly higher levels of insulin, triglycerides, and very low-density lipoprotein when compared to the controls ($p < 0.05$). The HCOC treatment was also consistent with enhanced platelet count ($p = 0.02$), and elevated markers of inflammation and endothelial dysfunction, including interleukin 6 ($p < 0.05$); tumour necrosis factor-alpha ($p < 0.05$); monocyte chemoattractant protein-1 ($p < 0.001$), as well as tissue factor ($p < 0.001$), D-dimer ($p < 0.001$), Von Willebrand factor ($p < 0.05$), and low nitric oxide ($p < 0.001$). Notably, systolic blood pressure and mean arterial pressure were also significantly higher ($p = 0.02$) in these animals, suggesting an increased cardiovascular disease risk in response to HCOC. Surprisingly, short-term LDA attenuates cardiovascular risk by improving metabolic status, reducing inflammation levels, and mitigating endothelial dysfunction in rats exposed to HCOC.

Conclusion: A high dose of COC is associated with an increased risk of cardiovascular disease (CVD) in female rats, whereas short-term LDA attenuates the various factors associated with CVD risk by improving metabolic status, reducing inflammatory responses, and enhancing endothelial function.

However, additional studies are essential to unravel the plausible mechanistic interaction between LDA and COC.

Keywords: combined oral contraceptive; cardiovascular disease; low-dose aspirin; inflammation; coagulation; endothelial dysfunction.

C22

Negative energy balance interacts with meal timing to shift human central clock timing and peripheral metabolic rhythms

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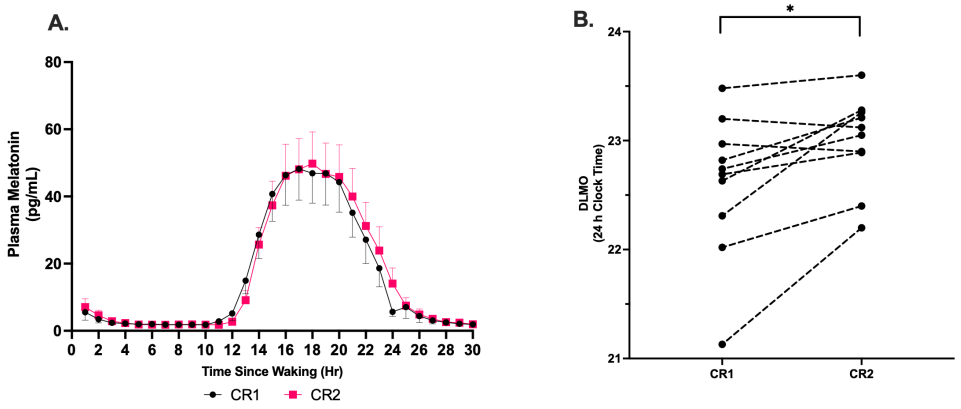
[1]University of Surrey, United Kingdom

Introduction: The circadian timing system, metabolism and nutrition are closely interlinked [(1)]. Previous research from our group has shown that, in conditions of energy balance, a 5-hour delay in meal timing causes a delay in plasma glucose phase, while melatonin, a marker of the central clock, remains aligned to the light-dark cycle [(2,3)]. We hypothesised that during negative energy balance, central clock markers would exhibit a phase shift following a 5-hour delay in meal timing.

Methods: Healthy male participants were recruited to allow comparison with previous work [(2)]. For 10 days leading up to the laboratory session, participants maintained a consistent sleep-wake cycle and meal timing. Participants then entered the laboratory for a 13-day/night residential protocol, during which their environment and behaviours, including dietary intake, were strictly controlled. The first two days in the laboratory were spent in energy balance, with 3 meals provided 0.5, 5.5, and 10.5 hours after waking, respectively. Participants then underwent a "constant routine" [CR1], a 37-hour protocol which enables measurement of endogenous circadian rhythms, followed by six consecutive days with a 30% energy deficit and meal timing delayed by 5 hours. Participants then underwent a second "constant routine" [CR2] to measure circadian rhythms, which were compared to CR1.

Results: Ten participants (age = 30 ± 4.4 years; BMI = 25.4 ± 1.0 kg/m^2; mean ± SD) were included in the final analysis. Mean energy intake during the energy balance control days was 2,371kcal/d [± 186], and mean energy intake during the energy deficit days was 1,693kcal/d [± 144]. Mean weight loss during the energy deficit was –1.3% [± 0.8%]. There was a significant phase delay in dim-light melatonin onset [DLMO] from CR1 to CR2 [CR1 = 22:36 h ± 00:39 h; CR2 = 23:00 h ± 00:24 h; difference = 24mins; 95% CI, 6–41min; p = 0.013; paired t-test]. The plasma cortisol acrophase was also significantly delayed between CR1 [23:58 h ± 00:15 h] and CR2 [24:35 h ± 00:17 h] by 36 minutes [95% CI, 20–52 mins; p = 0.0001; 2-sample summary t-test]. There was a significant delay in plasma glucose acrophase between CR1 [13:52 h ± 01:21 h] and CR2 [20:39 h ± 00:54 h] by 06:46 h [95% CI, 05:40 h to 07:52 h; p < 0.0001; 2-sample summary t-test]. Finally, there was a significant delay in the acrophase of HDL-C from CR1 to CR2 [CR1 = 10:57 h ± 00:53 h; CR2 = 12:11 h ± 00:30 h; difference = 01:14 h; 95% CI, 00:32 h to 01:56 h; p = 0.001; 2-sample summary t-test]. There was no significant phase shift in triglycerides, total or LDL-cholesterol.

Conclusions: The phase delay in plasma glucose rhythms is consistent with previous work demonstrating meal timing as a dominant time-cue for the circadian control of glucose. However, our findings demonstrate for the first time a delay in markers of human central clock phase. This reveals an increased potential of chrono-nutrition interventions to regulate the human circadian system.


A.
Plasma Melatonin (pg/mL)
80
60
40
20
0
0 2 4 6 8 10 12 14 16 18 20 22 24 26 28 30
Time Since Waking (Hr)
CR1
CR2
B.
*
DLMO (24 h Clock Time)
24
23
22
21
CR1
CR2

C23

The Effect of Caffeine on Neuromuscular Function and Fatigue Resistance in Healthy Younger and Older Adults

Elsa Greed[1], Rapheal Hamel[2], Eduardo Martinez-Valdes[1], Catarina Rendeiro[1], Gareth A Wallis[1], Ned Jenkinson[1]

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Background: Loss of muscle strength and fatigue resistance with ageing contribute to frailty, loss of independence, and reduced quality of life. These changes reflect not only muscular decline but also deteriorating communication between the brain and muscles, mediated by the corticospinal tract (CST). Supporting CST function may therefore help maintain mobility and prevent age-related functional decline. Caffeine, one of the most widely consumed dietary compounds globally, is well established to enhance alertness and performance. Acting primarily through adenosine receptor antagonism, caffeine influences both central and peripheral aspects of neuromuscular control. However, its potential to mitigate age-related declines in corticospinal and muscular function remains poorly understood.

Methods: In a randomised, placebo-controlled, crossover, counterbalanced, double-blinded acute study, 20 younger (23.6 ± 2.87y) and 20 older (70.9 ± 5.30y) healthy adults ingested caffeine (3 $mg \cdot kg^{-1}$) or placebo (maltodextrin). Transcranial magnetic stimulation (TMS) and electromyography (EMG) were used to quantify corticospinal excitability (CSE) via stimulus–response (SR) curves at 3 time points: baseline, post-ingestion (60-minutes), and post-fatigue (120-minutes). Functional measures included elbow flexion and handgrip maximal voluntary contractions (MVCs) and time to fatigue (TTF). Experimental conditions remain blinded as 312 and 794 until analysis is complete.

Results: Condition 312 elicited greater CSE than condition 794 in older adults at post-ingestion and post-fatigue, particularly at mid-range stimulation intensities (State 3; p=0.011; 0.41 ± 0.21 vs 0.31 ± 0.21 mV). This effect was not observed in younger adults (p=0.137; 0.42 ± 0.21 vs 0.39 ± 0.16 mV). Overall, older adults demonstrated lower CSE than younger adults (p= 0.041; 0.46 ± 0.14 vs 0.52 ± 0.14 mV). TTF was significantly longer in condition 312 compared with 794 (p= 0.028; 327 ± 145 vs 287 ± 145 s), with older adults exhibiting greater fatigue resistance than younger adults (386 ± 147 vs 227 ± 91 s), though no age x condition interaction was present (p=0.875). Handgrip MVC revealed a significant age x condition x time interaction (p=0.009), with older adults showing greater post-ingestion strength improvements in condition 312 compared with 794 (186 ± 80 vs 163 ± 72 N).

Discussion and implications: These findings indicate that one experimental condition enhanced both central (CSE) and peripheral (strength and fatigue resistance) aspects of neuromuscular performance, with the most pronounced effects in older adults. The selective increase in CSE in older adults indicates a potential capacity to counteract age-related reductions in central neural drive, possibly by reducing adenosine-related inhibition within motor pathways. Notably, these neurophysiological changes translated to functional improvements relevant to mobility and independence, highlighting the potential of dietary compounds to support healthy ageing and reduce disease risk.

Future direction: Ongoing work will examine spinal excitability and voluntary activation to further localise caffeine's neuromuscular effects and clarify its role in preserving movement capacity with ageing. By integrating neurophysiological and functional outcomes, this research aims to uncover how everyday dietary factors can be used to both support and study the neural mechanisms underpinning movement and contribute to the prevention of age-related mobility decline.

C24

Preferential Therapeutic Potential of Ficus carica Against Monosodium Glutamate and Metanil Yellow-Evoked Hepato-Renal Injury: In Vivo and In Silico Approaches

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Food preservatives can compromise food safety, and exposure to monosodium glutamate (MSG) and the azo dye metanil yellow (MY) has been linked with hepato-renal injury involving oxidative stress and apoptosis. We tested whether methanolic Ficus carica (fig) leaf extract (FC) protects liver and kidney against MSG- or MY-induced toxicity and explored supportive mechanisms using molecular docking.

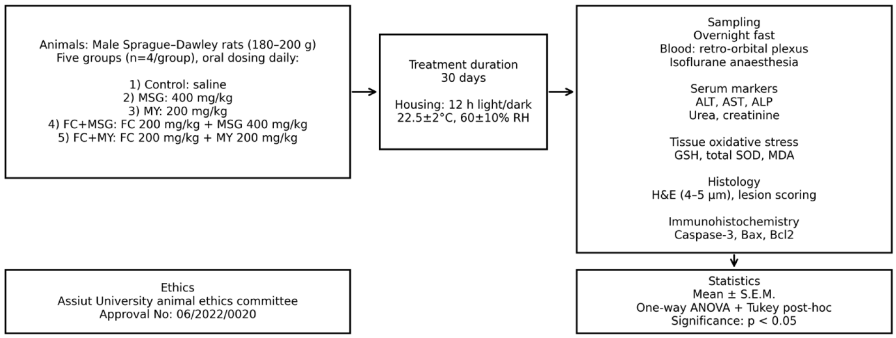
Methods: Male Sprague–Dawley rats (180–200 g) were acclimatized for 2 weeks and allocated to five groups (n=4/group): control (saline), MSG (400 mg/kg/day, oral), MY (200 mg/kg/day, oral), FC+MSG (FC 200 mg/kg/day plus MSG 400 mg/kg/day, oral), and FC+MY (FC 200 mg/kg/day plus MY 200 mg/kg/day, oral) for 30 days. After overnight fasting, blood was collected from the retro-orbital plexus under isoflurane anaesthesia and serum was separated. Serum ALT, AST, alkaline phosphatase, urea and creatinine were measured. Liver and kidney tissues were homogenized and assayed for total superoxide dismutase (SOD) activity, reduced glutathione (GSH) and malondialdehyde (MDA). Histopathology on 4–5 µm hematoxylin and eosin sections was semi-quantitatively scored as none, + (3–6 sections), ++ (7–19) or +++ (20–30). Immunohistochemistry assessed caspase-3, Bax and Bcl2 expression. Data were expressed as mean±S.E.M. and analysed by one-way ANOVA with Tukey post-hoc testing ($p<0.05$). All procedures were approved by the Assiut University animal ethics committee (Approval No: 06/2022/0020).

Results: FC showed phytochemical richness and antioxidant potency (total flavonoids 12.03 mg quercetin equivalents/g extract; total phenolics 26.83 mg gallic acid equivalents/g extract) with strong antioxidant activity (DPPH IC50 50.66±0.68 µg/mL; ABTS 487.28 µM Trolox equivalents/mg; ferric reducing antioxidant power 189.95 µM Trolox equivalents/mg; oxygen radical absorbance capacity 1386.71±258.5 µM Trolox equivalents/mg; iron (II) chelation 28.89±2.26 µM EDTA equivalents/mg). MSG and MY significantly increased serum liver enzymes (ALT, AST and alkaline phosphatase) and renal indices (urea and creatinine) versus controls ($p<0.05$). Both toxicants increased hepatic and renal MDA and decreased GSH and SOD, whereas FC co-administration reduced MDA and restored GSH and SOD toward control values. Histopathology showed in MSG and/or MY groups hepatic vascular congestion, vacuolar degeneration, inflammatory infiltration, Kupffer cell proliferation and occasional thrombosis/necrosis, and kidney vascular congestion, edema, glomerular swelling, tubular vacuolar degeneration, fibrosis and inflammatory infiltration; these lesions were largely absent or reduced to mild in FC co-treated groups. Immunohistochemistry revealed increased nuclear caspase-3 and cytoplasmic Bax with decreased Bcl2 in MSG/MY tissues, raising the Bax/Bcl2 ratio; FC reduced caspase-3 and Bax and enhanced Bcl2 in liver and kidney. Docking indicated interactions of MSG and MY with cellular antioxidant targets including glutathione synthetase and SOD isoforms (for example, MSG −5.33 kcal/mol and MY −8.26 kcal/mol with glutathione synthetase). FC bioactive compounds showed high affinity for Bax (−9.39 to −9.03 kcal/mol) and caspase-3 (−9.84 to −9.36 kcal/mol), consistent with anti-apoptotic potential.

Conclusion: Methanolic fig leaf extract mitigated monosodium glutamate- and metanil yellow-evoked hepato-renal injury in rats by reinforcing antioxidant defences and suppressing apoptosis, supported by

biochemical, histological, immunohistochemical and in silico evidence. These data highlight FC as a promising natural protective supplement and justify further dose–response, safety and translational studies in additive-rich diet settings and risk assessment.

Figure 3. Study design and outcome measures
Methanolic Ficus carica leaf extract vs. monosodium glutamate or metanil yellow in rats



Upload as a supporting figure. This diagram is self-contained and colour-blind accessible (no colour-only encoding).

C25

Protein Intake Is Associated with Body Composition and Quality of Life in Adults with Becker Muscular Dystrophy

Isobel Haslam[1], Meg Leaver[2], Paul Orme[3], Paul Morgan[4], Kelly Bowden-Davies[4], Christopher Morse[4], Nathan Hodson[1]

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Introduction. Becker Muscular Dystrophy (BMD) is a rare X-linked genetic condition characterised by reduced dystrophin expression, causing progressive skeletal muscle and functional decline, and ultimately poor quality of life (QoL). With no current pharmacological cure, practical easy-to-implement strategies are needed to improve QoL in BMD. Elevated dietary protein intake is known to be beneficial in muscle-wasting conditions such as sarcopenia [1] and cachexia [2], and can improve lean body mass [3] and reduce pain [4] in certain conditions. However, little is known about habitual dietary practices and their relationship with muscle size, strength, physical function and QoL specifically in BMD.

Aim. To characterise habitual dietary practices in adults with BMD and examine associations with muscle size, strength, physical function and self-reported QoL.

Methods. Adult males with BMD (n = 20; 46 ± 12 years) and age-matched controls (n = 12; 47 ± 13 years) completed two weighed food diaries ~6 weeks apart. In addition, participants completed a battery of physical testing including assessments of body composition and muscle size, strength and function as well as validated questionnaires on perceived physical function, pain/fatigue, QoL, and nutritional knowledge. Between-group differences were assessed using independent t-tests or Mann-Whitney U tests and correlations with Pearson's R or Spearman's Rho depending on normality (p value threshold < 0.05). Ethical approval was obtained from institutional level research ethics committee and all procedures conformed to Declaration of Helsinki.

Results. Adults with BMD reported 29% lower daily energy intake compared with controls (1602 vs. 2229kcal, p<0.001), with 25-30% lower carbohydrate and fat ingestions (p<0.01). Protein intake (relative to bodyweight) was 21% lower in BMD (0.86±0.28 vs. 1.08±0.24g/kg/day, p=0.028) with only 10% of individuals meeting The European Society for Clinical Nutrition and Metabolism (ESPEN) recommendations for protein intake in those with disease-related protein catabolism (1.2g/kg/day). Despite reduced energy intake, adults with BMD exhibited greater body fat percentage (31.1±4.7 vs. 22.9±6.9%, p=0.002) and 40% of the cohort were classified obese (BMI >30kg/m^2). BMD also exhibited lower *tibialis anterior* muscle thickness, strength and physical function, reported reduced QoL, lower limb function and activities of daily living, and higher pain and fatigue compared to controls (all p<0.05).

In the BMD cohort specifically, relative protein intake was positively correlated to lean mass percentage (r=0.619; p=0.018) and QoL (r=0.596; p=0.006) and negatively associated with BMI (r=-0.571, p=0.009). Lean mass (%) was negatively associated with self-reported fatigue (r=-0.591, p=0.026) whilst BMI correlated positively with pain (r=0.689, p<0.001).

Conclusion. Here, we show that adults with BMD report lower energy consumption, compared to non-dystrophic individuals, yet display unfavourable body composition. Moreover, relative protein intake was substantially lower than guidelines for similar clinical conditions, suggesting habitual dietary practices

are not sufficient to offset muscle deterioration in this condition. Importantly, we observed protein intake to be moderately-to-strongly correlated with lean mass and QoL in BMD indicating interventions which elevate protein consumption could positively affect these outcomes. Together, this highlights the need for further research to inform potential future dietary guidance for those living with BMD.

C26

Weight loss during omnivorous or plant-based energy restriction lifestyle interventions: preliminary findings.

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Background:
Weight loss and subsequent maintenance improves cardio-metabolic health in individuals with obesity. Very-low-calorie diets (VLCD), typically high in animal protein, are effective for weight loss, but difficult to maintain [1, 2]. There is increasing interest in alternative dietary protein sources, but it is unclear if they offer comparable efficacy regarding weight loss [3]. Mycoprotein is a fungal-derived non-animal protein source, rich in fibre that has been reported to promote satiety and improve cardiometabolic risk factors relative to animal proteins [4, 5]. This suggests utility of mycoprotein as a promising alternative dietary protein source for diets designed for weight management.

Aim:

This study evaluates whether a mycoprotein-rich VLCD (MYC) induces and maintains clinically meaningful weight loss in adults with obesity compared with a conventional omnivorous VLCD (OMN).

Methods:
Adults with obesity (BMI≥30 $kg \cdot m^{-2}$) were stratified by age, sex, and BMI before randomisation to OMN (n=5) or MYC (n=5) diets, or a non-intervention control (n=2) group (CON). Phase 1 of the intervention comprised a six-week VLCD phase, with energy intake prescribed at 800 $kcal.day^{-1}$ and protein derived from the specified source providing 85 $g \cdot day^{-1}$, corresponding to 42.8 ± 1.1 %En·day. Phase 2 involved a six-week controlled weight-maintenance phase, with 70% estimated energy requirements prescribed, and the remaining 30% self-selected. Body mass and composition, resting energy expenditure and cardiometabolic health markers were assessed weekly. Data were analysed using repeated-measures ANOVA with group and time as factors, with statistical significance set at P<0.05.

Results:

During Phase 1, body mass remained unchanged in CON (from 111.0±5.4 to 112.2±5.3 kg) but decreased (P<0.001) to a similar degree in OMN (−10.0±1.1 kg; −10.0±1.3%) and MYC (−9.9±1.2 kg; −9.7±0.6%), respectively. During Phase 2, body mass remained stable in CON (from 112.2±5.3 to 112.6±5.1 kg) but continued to decrease (P<0.001) in OMN (−4.1±1.1 kg; −4.8±1.4%) and MYC (−4.6±1.4 kg; −5.0±1.5%), respectively, with no differences between intervention groups. In Phase 1, body fat mass remained unchanged in CON (53.9±2.8 to 55.1±3.1 kg) but decreased significantly (P<0.001) in both intervention groups, decreasing in OMN (−7.6±1.0 kg; −16.9±1.9%) and MYC (−7.6±1.0 kg; −15.6±2.0%), with no differences between intervention groups. During Phase 2, body fat mass remained unchanged in CON (55.1±3.1 to 56.3±1.3 kg) but decreased (P<0.001) in both OMN (-3.5±0.9 kg; -8.1±2.2%) and MYC (-5.7±0.9 kg; -13.8±2.3%) intervention groups to a similar extent. During Phase 1, skeletal muscle mass remained unchanged in CON (from 27.3±1.3 to 26.9±1.5 kg) but decreased (P=0.005) in both intervention groups to a similar extent; in OMN by −0.88±0.3 kg (−3.8±1.30%) and in MYC by −1.42±0.30 kg

(−5.8±1.2%). Skeletal muscle mass did not change during phase 2 in any of the groups. *Further participants and outcomes will be completed and presented by the time of the meeting.*

Conclusion:
Thus far, both OMN and MYC high protein VLCDs have been equivalently effective at inducing large reductions in body mass and body fat. The findings so far indicate the utility of mycoprotein as an alternative dietary strategy to achieve short- and medium- term weight management which may suit weight loss goals of individuals with different dietary preferences.

C27

The effects of insect vs. whey protein supplementation on postprandial aminoacidemia after resistance exercise.

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Background: Skeletal muscle mass is regulated primarily by muscle protein synthesis, which is optimised via synergistic effects of resistance exercise and dietary protein ingestion. Specifically, increased plasma amino acid availability stimulates muscle protein synthesis. Previous research suggests that whey protein, due to its superior amino acid composition and rapid digestibility, stimulates muscle protein synthesis most effectively. However, certain insect protein sources, such as crickets, possess comparable amino acid profiles to whey, whilst offering greater sustainability. Nevertheless, the efficacy of insect protein ingestion alongside resistance training, to provide necessary amino acids for skeletal muscle development, remains relatively unexplored.

Aim: The purpose of this study was to compare postprandial plasma amino acid availability following insect (cricket) and whey protein ingestion after resistance exercise.

Methods: Using a randomised, crossover design, recreationally active males and females (n = 12; age 25 ± 7 years) ingested 0.4 g·kg body mass^{-1} of unflavoured whey protein concentrate (WPC) or cricket protein (CP), on separate days, after a bout of full-body resistance exercise. Due to cricket protein's higher energy density, an additional experimental trial consisting of a quantity of cricket protein that was isocaloric to the whey protein supplement (CPC) was included for each participant. Venous blood samples were obtained immediately prior to supplement ingestion and 20 40, 60, 90, 120, and 180 minutes after. Plasma concentrations of total amino acids (TAA), essential amino acids (EAA), branched chain amino acids (BCAA), and leucine (LEU) were derived from each sample. Ethical approval was granted from the Faculty of Medicine and Life Sciences Research Ethics Committee at the University of Chester, prior to commencing data collection. All data were collected in accordance with the Declaration of Helsinki.

Results: Two-way repeated measures ANOVAs (time [7] x supplement [3]) with *post hoc* Sidak comparison tests revealed that peak TAA concentrations were greater after WP ingestion than CP (4059 ± 845 vs. 3047 ± 828 μmol·L^{-1}, p = 0.021). Peak EAA were higher for WP (1931 ± 409 μmol·L^{-1}) than CP (1097 ± 192 μmol·L^{-1}, p < 0.001) and CPC (1258 ± 275 μmol·L^{-1}, p < 0.001). Peak BCAA were greater after WP (1078 ± 198 μmol·L^{-1}) ingestion compared to CP (559 ± 143 μmol·L^{-1}, p < 0.001) and CPC (593 ± 145 μmol·L^{-1}, p < 0.001). Peak LEU concentrations were higher with WP (391 ± 78 μmol·L^{-1}) compared to CP (164 ± 44 μmol·L^{-1}, p < 0.001) and CPC (178 ± 43 μmol·L^{-1}, p < 0.001). TAA, EAA, BCAA, and LEU overall availability during 180 minutes, expressed as area under the curve, were greater after WP ingestion (591 ± 111, 263 ± 48, 142 ± 20, and 49 ± 8 mmol·180 min·L^{-1}, respectively) compared to CP (523 ± 110, 189 ± 37, 91 ± 17, and 27 ± 5 mmol·180 min·L^{-1}, respectively) and CPC (591 ± 111, 263 ± 48, 142 ± 20, and 49 ± 8 mmol·180 min·L^{-1}, respectively) (p < 0.001 for all).

Conclusions: Ingesting whey protein, post-exercise, elicits greater plasma amino acid bioavailability than an isonitrogenous or isocaloric quantity of cricket protein.

C28

Evening macronutrient intake, sleep quality and next-morning glycaemic control.

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Poor sleep and late eating are independently associated with adverse metabolic outcomes, yet research has yet to establish whether the macronutrient composition of an evening meal influences sleep and/or next-day metabolism. Therefore, this randomised crossover, open-label study objectively characterised sleep duration and quality after pre-bed ingestion of carbohydrate or protein in 26 young healthy women (n=13) and men (n=13) who were free from sleep disorders. Evening glycaemic responses and next-morning glucose tolerance were also measured to explore associations between pre-sleep nutrient intake, sleep parameters and metabolic responses to each meal. Participants completed three home-based conditions, each separated by a washout interval ≥1-week. During each condition, participants consumed one of three evening 'snacks' at 2100 h: (1) WATER (300 mL); (2) CARBOHYDRATE (75 g maltodextrin + 300 mL water); (3) PROTEIN (75g unflavoured whey isolate + 300 mL water). The carbohydrate and protein conditions were matched for total energy content (~300 Kcal). Capillary samples were taken at baseline, 15 min, 30 min and 60 min during the 1-hour postprandial period. Participants were in-bed trying to sleep from 2230-0715 h, with sleep parameters recorded using respiratory polygraphy (SOMNOmedics GmbH, SOMO HD Eco). The next-morning participants completed a 75 g oral glucose tolerance test (OGTT), and capillary glucose concentrations were measured at 0, 15, 30, and 60 min. There were no significant differences across conditions in [median and inter-quartile range] total sleep time (WATER, 489 [474-496] min; CARBOHYDRATE, 479 [466-495] min, and PROTEIN, 482 [451-491] min), sleep efficiency (WATER, 89.9 [87.6-91.8] %; CARBOHYDRATE, 88.4 [85.3-91.1] %; and PROTEIN, 88.1 [84.3-90.9] %), or sleep onset latency (WATER, 3 [1-10] min, CARBOHYDRATE, 6 [1-17] min; and PROTEIN 5 [1-11] min). Pairwise comparisons indicated fewer total wakeups/arousals in the WATER condition (58 [50–65]) compared with the PROTEIN condition (70 [54–94]; P= 0.035). Capillary glucose total AUC for next-morning OGTT differed between conditions (one-way repeated measures ANOVA, p = 0.040), specifically with lower tAUC following the PROTEIN condition (357.5 ± 46.5 mmol·L^{-1}·120 min) compared with CARBOHYDRATE (387.2 ± 52.1 mmol·L^{-1}·120 min; p = 0.005). In summary, acute evening ingestion of carbohydrate or protein following a standardised evening meal did not significantly affect objective measures of sleep in healthy adults without sleep disorders. However, the evening protein condition did result in lower glycaemic responses the following morning.

C29

Paternal White Rice Consumption Programs Transgenerational Insulin Resistance Phenotypes in Drosophila melanogaster

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Introduction:
High-glycaemic index diets, particularly those containing white rice, are strongly associated with insulin resistance and type 2 diabetes. While maternal dietary effects are well described, the contribution of paternal diet to offspring metabolic health remains underexplored. Understanding paternal dietary programming has implications for disease prevention across generations.

Aim:
This study investigated whether paternal consumption of white rice induces intergenerational and transgenerational metabolic dysfunction in offspring, compared with brown rice and control diets.

Methods:
Male *Drosophila melanogaster* were raised on control, 50% white rice, or 50% brown rice diets and maintained for 7 days (n = 30 per group, three biological replicates). Males were mated with virgin females on a standard diet to generate F1 and F2 offspring. Offspring were maintained on either a standard or high-sugar diet. Metabolic outcomes assessed included body weight, locomotor performance, haemolymph glucose, trehalose, glycogen, triglycerides, and mRNA expression of insulin-like peptide 2 (ILP2) and acetyl-CoA carboxylase (ACC). Data were analysed using one-way and two-way ANOVA with Bonferroni post-hoc tests ($p < 0.05$).

Results:
Paternal consumption of white rice induced insulin-like phenotypes, including hyperglycaemia, hypertriglyceridemia, elevated trehalose, and reduced locomotor performance in fathers. Female F1 and F2 offspring exhibited significantly increased glucose, trehalose, and triglyceride levels despite no direct dietary exposure ($p < 0.05$). Male offspring showed elevated triglycerides with milder glycaemic effects. ILP2 expression was upregulated predominantly in female offspring, while ACC expression was increased in both sexes. These effects were exacerbated by a high-sugar dietary challenge. Offspring of brown rice showed metabolic profiles comparable to those of controls.

Conclusion:
Paternal white rice consumption programs sex-specific insulin resistance–like phenotypes across generations, with female offspring being more vulnerable. These findings highlight paternal diet as a modifiable factor in metabolic disease prevention and support dietary quality, not just caloric intake, as a transgenerational health determinant.

Ethical Compliance:
All experimental procedures were conducted in accordance with institutional guidelines for invertebrate research and approved by the relevant departmental research ethics committee.

Keywords: White rice, paternal dietary programming, transgenerational inheritance, insulin resistance, metabolic health

C30

Multiorgan observations following consumption of ketogenic diet in prolonged experimental diabetes mellitus

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Introduction: Oxidative stress and inflammation have been identified as key mediators in either the progression, or amelioration of diabetes mellitus. Dietary interventions, especially ketogenic diet, has been reported to exert ameliorative effects in diabetes mellitus. However, its likely benefit in prolonged diabetes mellitus is unclear.

Objective: This study was designed to evaluated the likely beneficial effects of ketogenic diet on systemic and selected organ oxidative stress and inflammation in experimentally induced diabetic Wistar rats.

Methods: Wistar rats (N=40) were equally divided into Control and Diabetic (streptozotocin 55mg/kg in 2% citrate buffer) animals. Control (I-II) and diabetic animals (III-IV) where divided into 2 groups (n=10) and exposed to either standard chow (SC) or ketogenic diet (KD), for 14 days, respectively. Animals were exposed to the different diets, 7 days after induction of diabetes mellitus. Thereafter, blood samples were obtained and evaluated for blood glucose, lipid profile, liver and renal function tests, and serum oxidative stress and inflammations indices. Cardiac, renal, knee joint and hepatic samples were also obtained and evaluated for histology, and oxidative stress and inflammation indices.

Results: Blood glucose, systemic, cardiac, renal and knee joint oxidative stress and inflammation were elevated while hepatic and renal functions were impaired in the SC exposed diabetic group compared to controls. Exposure of diabetic animals to KD resulted in reduced blood glucose and alleviated systemic inflammation in varying degrees. Impaired renal and hepatic functions were however not reversed. Similarly, tissue specific oxidative stress and inflammation though somewhat ameliorated, were however still persistent.

Conclusion: This study suggests that consumption of ketogenic diet alone in preexisting or prolonged diabetes mellitus may ameliorate fasting blood glucose and reduce systemic inflammation but does not reverse completely, tissue-specific aberrations caused by diabetic mellitus.

C31

Handgrip strength and subjective physical function are lower in South Asians than White Europeans with Type 2 Diabetes in the United Kingdom, independent of fat-free mass

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Background: Frailty and physical disability are emerging as a third major category of complications in diabetes (Wong et al., 2013). Sarcopenia, which is the loss of muscle mass, strength, and physical function, is accelerated in T2D and central to frailty and physical disability development (Marcotte-Chénard et al., 2023). South Asian populations typically have lower fat-free mass and greater fat mass than White Europeans (Hull et al., 2011), yet less is understood regarding differences in strength and physical function. Growing evidence across the general population has shown lower cardiorespiratory fitness (Ghouri et al., 2013), hand grip strength (Ntuk et al., 2017), sit-to-stand performance (McBride et al., 2022) and greater risk of functional limitation (Heald et al., 2025; Williams et al., 2020). However, it is not clear whether such differences persist in those with T2D, or if they are independent of ethnic differences in body composition. This study examined differences in objective and subjective markers of physical function between White Europeans and South Asians, controlling for age, sex and fat-free mass.

Methods: Data were analysed from the ongoing 'Chronotype of Patients with Type 2 Diabetes and Effect on Glycaemic Control' (CODEC) clinical trial. Body mass, body composition and physical function were assessed in adults of South Asian (n=139) and White European (n=947) heritage, with T2D. Fat-free mass percentage was estimated using bioelectrical impedance analysis. Lower body function was evaluated using the Short Physical Performance Battery (SPPB) and Sit-to-Stand 60 (STS-60). The SPPB (scored 0-12) comprises three components: balance, 4-m gait speed and time to complete 5 sit-to-stand repetitions, while the STS-60 reflects the number of sit-stand transitions completed in 60 s. Upper body strength was assessed via maximum hand grip using a dynamometer. Subjective physical function was measured using The Duke Activity Status Index (DASI) (scored 0-58.2) based on self-reported functional capacity in daily activities. Ethnic differences in physical function measures were examined using generalized linear models, adjusted for age, sex and fat-free mass. Other population characteristics were compared between ethnicities using independent-samples *t* or Mann-Whitney U tests, depending on data normality, or Chi-Squared test for categorical data.

Results: Population characteristics and comparisons between ethnicities are presented in Table 1. Handgrip strength and DASI score were 4.7 (3.1, 6.2) kg and 7.3 (0.2, 14.4) au greater in White Europeans than South Asians, respectively. Neither SPPB total score, gait speed, sit-to-stand speed, or STS-60 were different between ethnicities.

Conclusions: Upper body strength and subjective physical function were significantly lower in South Asians than White Europeans with T2D, even after adjusting for fat-free mass. Importantly, the observed difference in DASI score surpassed the minimally clinically important difference (Arena et al., 2007), suggesting that these disparities may have meaningful implications for daily activities and quality of life. Combined with modest, but clinically relevant differences in handgrip strength, an established predictor of mortality and disability (Stressman et al., 2022; Rantanen et al., 1999) these findings underscore the

importance of addressing both physical and perceived functional limitations in South Asian populations through tailored interventions.

Table 1. Participant characteristics and physical function comparisons between White Europeans and South Asians.

	White European (n=947)	South Asian (n=139)	*p* value
Participant characteristics			
Age (yrs)	65 ± 8	61 ± 9	<0.001
Sex			0.043
Male (%)	67.7	59.0	
Female (%)	32.3	41.0	
HbA1c (%)	7.1 ± 1.2	7.2 ± 1.1	0.33
Height (cm)	170.9 ± 9.6	163.6 ± 10.0	<0.001
Body mass (kg)	91.3 ± 17.6	78.8 ± 15.9	<0.001
BMI (kg/m^2)	31.2 ± 5.13	29.3 ± 4.8	<0.001
Relative fat free mass (%)	66.3 ± 8.7	67.0 ± 8.8	0.39
Physical function			
SPPB total score (au; 0-12)	10 (10, 10)	10 (10, 11)	0.56
4-m gait speed (s)	4.0 (3.9, 4.1)	4.2 (4.0, 4.5)	0.14
Sit-to-stand speed (s)	13.9 (13.9, 14.3)	13.3 (12.3, 14.2)	0.23
STS-60 (repetitions)	22 (22, 23)	23 (22, 23)	0.46
Handgrip strength (kg)	31.3 (30.7, 31.9)	26.6 (25.2, 28.0)	<0.001
DASI score (au; 0-58.2)	46.7 (44.1, 49.4)	39.4 (33.8, 46.1)	0.045

Participant characteristics are mean ± SD or percentage within the respective ethnic group; physical function variables are adjusted mean (95% confidence intervals); HbA1c = glycated haemoglobin; BMI = body mass index; SPPB = Short Physical Performance Battery; STS-60 = Sit-to-Stand 60; DASI = Duke Activity Status Index.

C32

Associations between (poly)phenols intake and mental health among university students: the FoodMood cross-sectional study

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Background: There are increasing rates of university students with mental health issues, including stress, anxiety, depression, and mood disorders. Dietary (poly)phenols, bioactive compounds found in plant-based foods are emerging as potential modulators of mental well-being, possibly through a mechanism involving gut microbiota interactions. **Objectives:** To examine the associations between (poly)phenol intake, circulating (poly)phenol metabolites and mental health in university students. **Methods:** A cross-sectional study was conducted from September 2022 to June 2024 at King's College London including 307 healthy university students aged 17-30 years. Participants completed validated 24-hour dietary recalls for 3 days using online Intake24 and the KCL (poly)phenol food frequency questionnaire (KP-FFQ). (Poly)phenol intake was quantified using an in-house database based on Phenol-Explorer and USDA databases. Mood, stress, anxiety and depression outcomes were assessed using the Profile of Mood States 2nd Edition–Adult (POMS 2-A), Perceived Stress Scale (PSS), and Hospital Anxiety and Depression Scale (HADS), respectively. A total of 114 (poly)phenol metabolites were quantified in 24 h urine samples by Liquid Chromatography-Mass Spectrometry using a validated method. Generalized Linear Model analysis was conducted to examine the association between (poly)phenol intake and mental health. **Results:** A higher consumption of anthocyanins associated with lower anxiety and stress ($p < 0.01$); higher intake of flavanones with lower depression and mood ($p < 0.05$); higher flavonols intake with lower anxiety, depression and stress ($p < 0.05$); higher tyrosols and lower all four outcomes ($p < 0.001$) after full adjustment for potential confounding factors. Additionally, higher flavan-3-ol consumption was associated with lower cortisol levels ($p < 0.05$), and urinary (poly)phenol metabolites were significantly associated with mental health outcomes ($p < 0.05$). **Conclusion:** The findings suggest that consumption of anthocyanins, flavanones, flavonols and tyrosols, are associated with a lower prevalence of mental health symptoms among university students, including lower cortisol levels. Further studies are needed to confirm these associations.

C33

Acute improvement in glycaemic control results from late time-restricted eating in individuals with type 2 diabetes

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Introduction: Type 2 diabetes mellitus (T2DM) is a major cause of morbidity and mortality across the world. The importance of glycaemic control in T2DM is well-established and remains a key treatment target, as poor glycaemic control is associated with diabetes-related complications(1). Alongside HbA1c, best practice guidelines(2) highlight the clinical significance of short-term measures of glycaemic variability to assess glycemia in those with T2DM. Long-term adherence to dietary and behavioural strategies to manage glycaemia is often poor, so novel approaches are warranted. It is well-known that circadian rhythms play a key role in human metabolism(3). For example, glucose tolerance is typically optimal in the morning compared to later in the day. Time-restricted eating (TRE) – where energy intake is typically limited to <12 hours per day – may be a simple and effective dietary approach to the management of T2DM as it considers the importance of meal timing(4). Research thus far suggests the metabolic benefits associated with TRE are driven by the position of the eating window and studies have shown that early-TRE may promote superior metabolic benefits in healthy individuals(5). However, studies in those with T2DM are sparse.

Aims/hypothesis: To compare early versus late-TRE in adults with T2DM. We hypothesised that a daily 16-hour fast would lower mean 24-hour glucose concentration and improve other markers of glycaemic control, in individuals with T2DM. We hypothesised that these changes would be greater following early-TRE than late-TRE.

Methods: This study received a favourable ethical opinion from the University of Surrey Ethics Committee. Written informed consent was obtained prior to screening participants for eligibility for this 9-day cross-over, controlled eucaloric dietary intervention study. Eligible participants (n = 8) were fitted with continuous glucose monitors and allocated to group A or group B. All participants completed a 3-day control diet (eating window [EW] 7:00h to 19:00h), then Group A followed 3 days of early-TRE (EW 7:00h to 15:00h) while Group B commenced 3 days of late-TRE (EW 12:00h to 20:00h) before crossing over. All food (3 meals per day) consumed by participants during the study period was provided by the research team.

Results: Repeated measures ANOVA with post hoc tests using Bonferroni corrections were used to analyse measures of glycaemic control. Data are presented as mean ± SEM unless otherwise specified, with p<0.05 considered significant. Indices of glycaemic variability (CV and SD) were significantly lower in the late-TRE group compared to the control and early-TRE groups (CV, p<0.001 and p<0.001 respectively; SD, p = 0.007 and p = 0.003, respectively). A reduction in the 3-hour postprandial responses in the late-TRE group for meal 2 and meal 3 was observed, compared to the early-TRE group (p = 0.036 and p = 0.026, respectively). Late-TRE, but not early-TRE, increased time in glucose target range (3.9-10.0

mmol/L) – 78.4 ± 4.2 % in the late-TRE group compared to 68.9 ±4.4 % in the control group (p = 0.026) – Figure 1.

Conclusions/interpretation: Our data suggest that short-term late-TRE provides superior benefits to acute markers of glycaemic control compared with early-TRE in T2DM.

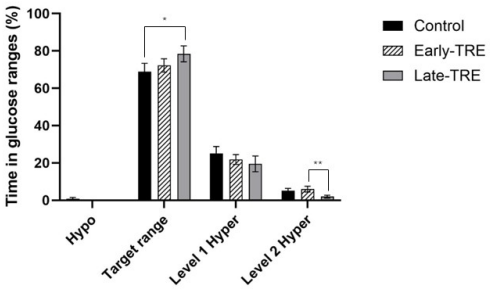

Figure 1. Early versus late time-restricted eating in T2DM: time in glucose ranges. Time in glucose ranges were measured using CGM for data collected on day 2 and 3 of each 3-day diet: Control diet (with meals at 7:00h, 13:00h and 19:00h); Early-TRE (8-hour TRE with meals at 7:00h, 11:00h and 15:00h) and late-TRE (8-hour TRE, with meals at 12:00h, 16:00h and 20:00h). Time spent in glucose target range was significantly higher in the late-TRE group compared to the control group (*p = 0.026) and time spent in level 2 hyperglycaemia was significantly lower in the late-TRE group compared with the early-TRE group (** p = 0.021). Hypo, hypoglycaemia defined as glucose levels <3.9mmol/L; target range defines as 3.9 – 10.0 mmol/L; level 1 hyper, level 1 hyperglycaemica defined as >10.0 –13.9 mmol/L; level 2 hyper defined as >13.9 mmol/L. CGM, *continuous glucose monitor*; TRE, *time-restricted eating*; T2DM, *type 2 diabetes mellitus*.

C34

A ketone monoester drink reduces postprandial glycaemia, but not forearm glucose handling, in young healthy individuals following a mixed meal.

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Introduction: Ketone monoester (KME) ingestion has been shown to attenuate postprandial glycaemia in young healthy individuals and those with Type 2 diabetes. This appears to be mediated by a reduced exogenous rate of glucose appearance, without affecting whole-body glucose disposal. However, the effect of KME ingestion on glucose handling within muscle, and its relation to ketone and non-esterified fatty acid (NEFA) handling, is less well characterised. This study investigated the effect of KME ingestion, prior to a mixed meal (MTT), on postprandial concentrations of β-Hydroxybutyrate (β-OHB), glucose, NEFA, and insulin, utilising a forearm arterialised-venous deep-venous (AV) balance model to characterise skeletal muscle substrate handling.

Methods: Seven young healthy individuals (*m=5*, *f=2*; age 27±5 y; BMI 24.3±1.8 $kg \cdot m^{-2}$) completed two trials, in a randomised, double-blind, placebo-controlled, crossover design. Participants consumed KME [(R)-3-hydroxybutyl (R)-3-hydroxybutyrate; 0.5 $g \cdot kg^{-1}$ body weight] or a noncaloric taste-matched placebo (CON), 30 min before consuming an MTT (1.1, 0.3 and 0.2 $g \cdot kg^{-1}$ body weight carbohydrate, protein, and fat, respectively) at t=0 min. Circulating arterialised-venous and deep-venous β-OHB, glucose, NEFA, and insulin concentrations were subsequently measured over 3 hours, with fractional extraction calculated for glucose and β-OHB (the AV difference relative to arterialised-venous concentration).

Results: Circulating β-OHB concentration remained at baseline during CON (0.2±0.0 mM), whereas it increased to a peak of 3.5±0.4 mM at t=30 in KME, averaging 2.2±1.1 mM throughout the postprandial period (P<0.0001). In turn, fractional β-OHB extraction was elevated in KME, but not CON (P=0.0060), peaking at t=0 before returning to baseline at t=60. Arterialised-venous blood glucose concentration increased from 4.4±0.3 mM in the postabsorptive state to a peak of 7.0±0.5 mM at t=15 in CON, whereas this rise was attenuated in KME, increasing from 4.1±0.3 mM to 5.9±0.5 mM (P=0.007), equating to a 44±29% suppression in postprandial glucose iAUC. Fractional glucose extraction increased following the MTT (P<0.0001), peaking at t=45, but was not different between conditions (P=0.4514). NEFA concentrations were suppressed more rapidly and to a greater extent in KME compared with CON (P=0.0063), which corresponded to a 49±20% suppression in NEFA iAUC. Circulating lactate concentrations increased in both conditions, but to a greater extent in KME (P=0.0244), averaging 0.75 mM in CON and 0.92 mM in KME. Serum insulin concentrations increased similarly in both trials, peaking at 87±16 mU and 81±19 mU at t=15 min in CON and KME, respectively.

Conclusion: The ingestion of KME before a mixed meal robustly increased circulating β-OHB concentrations, which was associated with a marked attenuation of postprandial glucose and NEFA concentrations in young healthy individuals, occurring independently of insulin. KME did not alter relative glucose extraction across the vascular bed of the forearm musculature, although it did increase relative β-OHB extraction, suggesting that β-OHB uptake in muscle does not significantly affect muscle glucose metabolism. This evidence implies KME attenuates postprandial glucose concentrations via mechanisms independent of skeletal muscle glucose uptake.

C35

Gut microbiome diversity and uric acid in serum and urine

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Introduction: An increasing body of evidence has shown the importance of the gut microbiota in modulating serum uric acid (SUA) levels. In this study, we aimed to determine the association between gut microbiome diversity, diet, SUA, and fractional excretion of uric acid (FEUA) in the kidney.

Methods: A cross-sectional study was conducted in 53 adults with normal or elevated SUA and estimated glomerular filtration rate (eGFR) range from 37 to 124 ml/min per 1.73 m^2. Fecal microbiome composition was analyzed using 16S ribosomal RNA sequencing; and alpha diversity was expressed as reverse Simpson, Shannon, and Richness indices. Dietary data were collected, and dietary patterns were identified using principal component analysis. Unadjusted linear regression and models adjusted for sex, waist-hip ratio (WHR), and eGFR were used to study the association between gut microbial diversity, dietary pattern scores, and SUA/FEUA.

Results: Shannon index was negatively associated with SUA after multiple adjustment (β -36.4, 95% CI [-66.2 to -6.7], $P = 0.017$; adjusted $R^2 = 0.62$, $P < 0.001$). Sex (standardized β = 0.52) and WHR (standardized β = 0.35) had the highest effect on SUA, followed by Shannon diversity index (standardized β = -0.22). We found that Shannon index (standardized β = 0.49, $P < 0.001$) was positively associated with FEUA after adjustment for sex and "sweet" dietary pattern. This model explained 40% of the variability in FEUA ($P < 0.001$). None of the dietary patterns were associated with SUA or FEUA.

Conclusion: A higher gut microbial diversity was associated with lower SUA and more efficient elimination of uric acid by the kidneys. There is a need for studies assessing efficacy and safety of interventions on the gut microbiome as a treatment of hyperuricemia.

C36

Branched-chain amino acid omission from an amino acid-carbohydrate drink does not alter insulin sensitivity assessed by forearm glucose uptake

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Elevated circulating levels of branched-chain amino acids (BCAAs) in humans are associated with insulin resistance, and muscle BCAA accumulation accompanies the development of insulin resistance during muscle disuse. Conversely, long-term restriction of BCAAs improves insulin sensitivity in obese, insulin resistant rats, and diets characterised by low BCAA content (e.g. vegan diets) are associated with greater insulin sensitivity. Although BCAAs acutely augment insulin secretion, the effect of acute BCAA restriction on insulin sensitivity in humans remains unclear. *This study investigated the effect of omitting BCAAs from an amino acid-carbohydrate drink on forearm glucose uptake in healthy young individuals*.

Twenty healthy participants were randomly allocated to either a control group (CON: 4/5 M/F; 26±2 yrs; 23.6±1.0 kg·m^{-2}) or BCAA-omitted group (BCAA-: 5/6 M/F; 24±1 yrs; 23.2±0.4 kg·m^{-2}). Both groups visited the laboratory on one occasion, during which they consumed a test drink with 0.4 g·kg body mass^{-1} total amino acids, 1.1 g·kg body mass^{-1} of dextrose, and 2 g cocoa powder. CON contained all amino acids in the ratio found in milk protein (~20% BCAA); the isonitrogenous BCAA- drink contained all amino acids except BCAAs. Repeated arterialised-venous forearm balance measurements were performed in the fasted state and every 20 min for four hours following drink ingestion to determine glucose, insulin concentrations and forearm glucose uptake (calculated as the arterialised–venous glucose difference × brachial artery blood-flow). Data (mean±SEM) were analysed using repeated-measures ANOVA with group and time as factors. Glucose, insulin, and forearm glucose uptake iAUC and time-to-peak values were *compared using independent sample t-tests*. All subjects gave their informed consent for inclusion prior to participation. The study was conducted in accordance with the Declaration of Helsinki, and the protocol was approved by national ethics committee (Protocol Number: NL82984.028.23).

Arterialised glucose increased from fasted (3.87±0.10 mmol·L^{-1}) to peak values (6.81±0.21 mmol·L^{-1}; P<0.001) at 47±5 min post drink ingestion, with no differences between groups (all P>0.05). There was a significant time effect for serum insulin, which increased from fasted (8±1 mU·L^{-1}) to peak values (125±11 mU·L^{-1}; time effect P<0.05). Despite observed higher arterialised insulin concentrations in CON, no significant group (P=0.238) or interaction (P=0.359) effects were observed. In line, insulin iAUC and time to peak were not different between groups (all P>0.05). Forearm glucose uptake increased by ~5.5-fold from fasted (0.6±0.1 µmol·100 g forearm-mass^{-1}·min^{-1}) to peak (6.1±0.8 µmol·100 g forearm-mass^{-1}·min^{-1} (P<0.001), at 85±12 min, similarly between groups (P>0.05). Analogously, there was no difference in forearm glucose uptake iAUC over the 4-hour postprandial period between groups (P>0.05).

In conclusion, BCAA omission from an amino acid-carbohydrate drink does not alter acute postprandial arterialised glucose or insulin concentrations, despite observed higher insulin responses in the group

that consumed BCAAs. This resulted in similar postprandial forearm glucose uptake between groups. Based on the observed lower insulin response after the BCAA-omitted drink, we speculate that repeated or prolonged exposure, testing under insulin-clamp conditions, and/or application in insulin-resistant populations, may provide insights into BCAA metabolism that are not evident acutely in our population of healthy young individuals.

C37

AMELIORATIVE POTENTIALS OF COMBINED METFORMIN AND KETOGENIC DIET IN EXPERIMENTAL DIABETIC CARDIOMYOPATHY

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Introduction: Diabetic cardiomyopathy (DCM) is an asymptomatic condition responsible for almost 80% of diabetic deaths via interconnected pathways. There is currently no specific effective pharmacological or lifestyle modification regimen prescribed to mitigate its development, although many monotherapies have been suggested. Treatment with metformin (MET) and consumption of ketogenic diets (KD) have individually demonstrated anti-hyperglycaemic effects however, whether they can synergistically exert ameliorative effects against DCM remains largely unknown.

Objective: This study was designed to evaluate the ameliorative potentials of co-exposure to metformin and ketogenic diet on experimental DCM using male Wistar rats.

Methods: Experimental DCM was induced using 10% fructose drinking water and streptozotocin (40 mg/kg *i.p.*). Forty-nine male Wistar rats (100-150g) were divided into seven groups (n=7). Groups I-IV had experimental DCM and were exposed to Normal Diet (ND), ND+MET (300mg/kg/day, *p.o.*), KD, and MET+KD, while Groups V-VII were non-diabetic and exposed to KD, ND+MET, and ND, respectively, for 4 weeks. Thereafter, blood samples were obtained and analysed for glucose regulatory indices (glucose, HbA1c, insulin), lipid profile and BNP. Cardiac samples were also evaluated for metabolic indices (AMPK, GLUT-4), oxidative stress (Nrf2, MDA, MPO), and cell apoptosis (Bax, Bcl-2, and Caspase-3). Insulin resistance was estimated mathematically, while cardiac histology was evaluated using standard H&E. Data obtained evaluated using ANOVA and descriptive statistics at $p<0.05$.

Results: DCM was characterised by significantly reduced body weight, left ventricular hypertrophy hyperglycaemia, hyperinsulinaemia, and dyslipidaemia compared to control. Body weight increased, while impaired glucose regulatory indices and dyslipidaemia was improved ($p<0.05$) in the DCM animals exposed to MET+KD compared to DCM exposed to normal diet. Impaired cardiac cell metabolism and oxidative stress observed in the experimental DCM only group was somewhat reversed following exposure to MET+KD. Compared to DCM exposed to normal diet, cardiomyopathy and apoptosis markers in the DCM exposed to MET+KD were also significantly reduced and was accompanied by improved left ventricular histoarchitecture. The DCM animals exposed to either ND+MET or KD alone individually showed similar, though not so potent responses, as that obtained in the DCM animals exposed to MET+KD.

Discussion and Conclusion: This study suggests that consumption of ketogenic diet and treatment with metformin may exert a synergistic effect in mitigating diabetic cardiomyopathic symptoms as against using either treatment regimen individually.

Keywords: Diabetic cardiomyopathy, metformin, ketogenic diet, hyperglycemia, cardiac inflammation, cardiac apoptosis

C38

Impact of preterm birth on metabolic maturation and growth

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Each year, around 1 in 10 infants are born prematurely and require extra care and nutrition to support proper growth [1]. Complications due to preterm birth are among the leading causes of mortality in children under 5 globally; these problems can include restricted growth and impaired metabolic processes [1]. Understanding the impact of preterm birth on the metabolic development of infants is essential to inform optimum nutritional support as they age. Through the use of metabolomic analysis, we aim to gain insight into changes occurring in preterm infants as they age.

In this study, urine samples were collected from 54 preterm infants with birth gestational ages ranging from 23 to 31 weeks. These infants were sampled from birth and up to week 18 of life. Nuclear magnetic resonance (NMR) spectroscopy was used to measure the metabolic profiles of these samples. Projection to latent structures (PLS) models were used to identify metabolites associated with gestational age and growth, defined as change in weight-for-age z-score between birth and discharge. Metabolites of interest were subsequently investigated *in vitro* by treating C2C12 myotubes. Morphological analysing and gas chromatography-mass spectrometry (GC-MS) was used to assess the effects of metabolite treatment on muscle growth and metabolism.

Metabolites linked to a greater gestational age were involved in energy metabolism, namely the TCA cycle (citrate and succinate), muscle growth (valine) and choline metabolism (betaine and DMG). Higher excretion of glucose was associated with lower gestational age, which decreased over the first months of life ($Q^2Y = 0.236$, $p = 0.001$). Citrate excretion was also associated with better growth and was increased when infants were provided with greater amounts of certain nutrients, including choline, fat and carnitine ($Q^2Y = 0.22$, $p = 0.001$). In addition to this, betaine treatment *in vitro* increased myotube diameter (control mean = 14.7 ± 1.98 SD , betaine treatment mean = 15.8 ± 2.27 SD) and altered the metabolome.

The findings highlight urinary biomarkers that can predict growth outcomes in preterm infants and guide nutritional support. Specifically, citrate was associated with greater growth and could be increased with nutritional intake in preterm infants. Glucose may be another biomarker to investigate further as it is commonly measured in the clinic and could be viably monitored to assess biochemical maturation in these infants. Betaine was associated with greater gestational age and an increase in myotube diameter, so may be helpful for muscle growth. These results indicate metabolic processes that may be dysregulated in preterm infants contributing to poor growth and highlight pathways of interest for further research.

C39

Impact of a ketogenic diet on body composition and strength in recreationally active adults

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Ketogenic diets are increasingly adopted by physically active individuals, yet their physiological effects on body composition and strength outside elite sport remain unclear. KD, defined by carbohydrate intake below 50 g·day^{-1} with increased fat intake, induces nutritional ketosis and is frequently adopted to improve body composition; however, comparative effects versus HC on resistance-training outcomes remain incompletely characterised. Thirteen participants (33 ± 9 years; 8 males, 5 females) were assigned to KD or HC and completed 14 supervised resistance-training sessions incorporating drop-set protocols targeting the squat (SQ), deadlift (DL), and bench press (BP). One-repetition maximum (1RM) performance and skinfold-derived body composition were assessed pre- and post-intervention. Capillary β-hydroxybutyrate (β-HB) and blood glucose were measured to verify metabolic response. Within-group analyses indicated significant reductions in body mass (BM) and body fat percent (BF%) in KD (BM: $p = 0.007$; BF%: $p = 0.002$), alongside significant increases in BP, DL, and SQ (all $p \leq 0.019$). In HC, AbBF and SQ changed significantly ($p = 0.019$ and $p = 0.025$, respectively), whereas BM, BF%, BP, and DL did not reach statistical significance ($p \geq 0.051$). Repeated-measures ANOVA identified significant main effects of time for all outcomes ($p \leq 0.017$), with no evidence of time × diet interactions, indicating comparable longitudinal adaptations between diets. Post-intervention between-group comparisons showed higher DL and BP values in KD ($p = 0.022$ and $p = 0.036$), but these cross-sectional differences were not supported by diet-specific interaction effects. Capillary β-HB increased to approximately 1.1 mmol·L^{-1} by Week 2 and stabilised near 0.8 mmol·L^{-1} in KD, consistent with nutritional ketosis and accompanied by reductions in blood glucose. In summary, six weeks of resistance training elicited meaningful improvements in body composition and maximal strength under both KD and HC conditions. While KD showed clearer within-group reductions in BM and BF%, repeated-measures analyses provided no evidence of diet-specific superiority in training-induced adaptations over time. These findings support a context-specific role for KD in resistance training, particularly during early training phases or fat-loss interventions. KD may therefore represent a viable nutritional strategy for improving body composition without compromising strength in non-elite physically active populations.

Anthropometrics

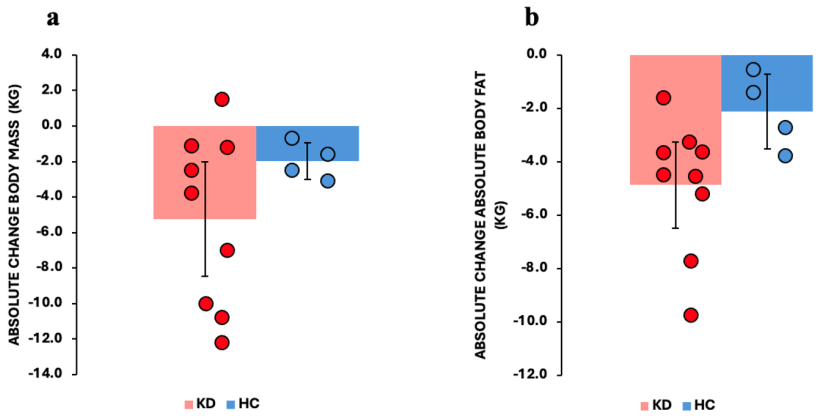

Figure 1. Changes in body mass and absolute body fat following a 6-week resistance training intervention under ketogenic (KD) and habitual high-carbohydrate (HC) dietary conditions. Bars represent group mean changes from baseline to post-intervention, with error bars indicating ± SEM. Individual data points are overlaid to illustrate within-group variability. Negative values indicate reductions from baseline. A significant main effect of time was observed for both outcomes ($p < 0.05$), with no significant time × diet interaction, indicating comparable longitudinal changes between dietary conditions.

Performance

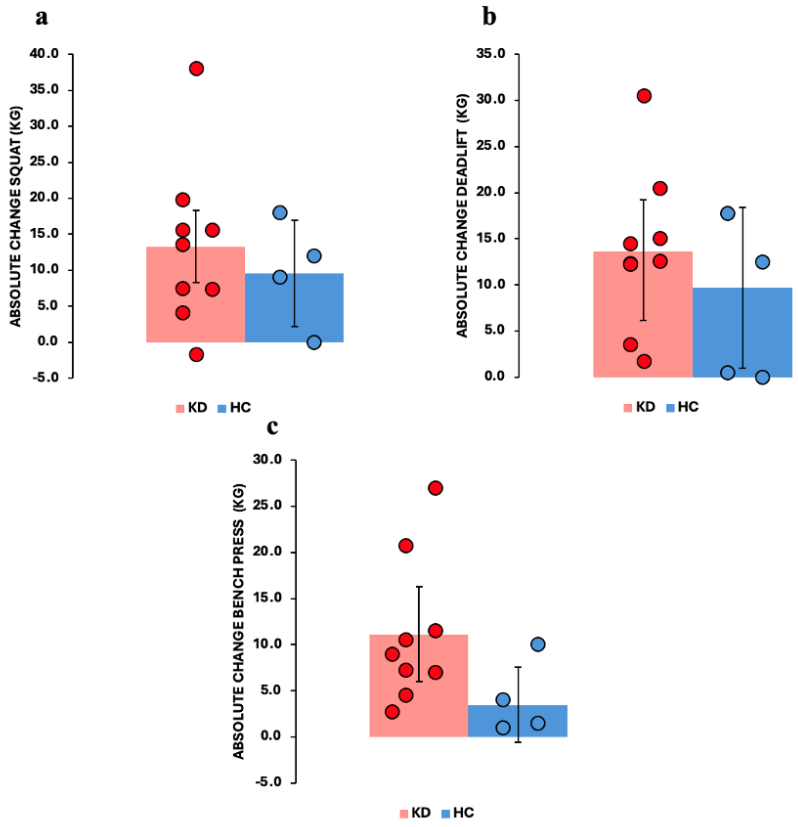

Figure 2: Within-group changes in body mass, body fat percentage, and abdominal body fat following a 6-week resistance training intervention under ketogenic (KD) and habitual high-carbohydrate (HC) dietary conditions. Bars represent group mean changes from baseline to post-intervention, with error bars indicating ± SEM. Individual participant data points are overlaid to illustrate inter-individual variability. Positive values indicate reductions from baseline. Repeated-measures analyses revealed significant main effects of time for all body composition outcomes ($p < 0.05$), with no significant time × diet interactions, indicating comparable longitudinal adaptations between dietary conditions despite numerically greater reductions in the KD group.

C40

Measuring and Modulating Brain Creatine Through Supplementation: Current Evidence and Technical Challenges

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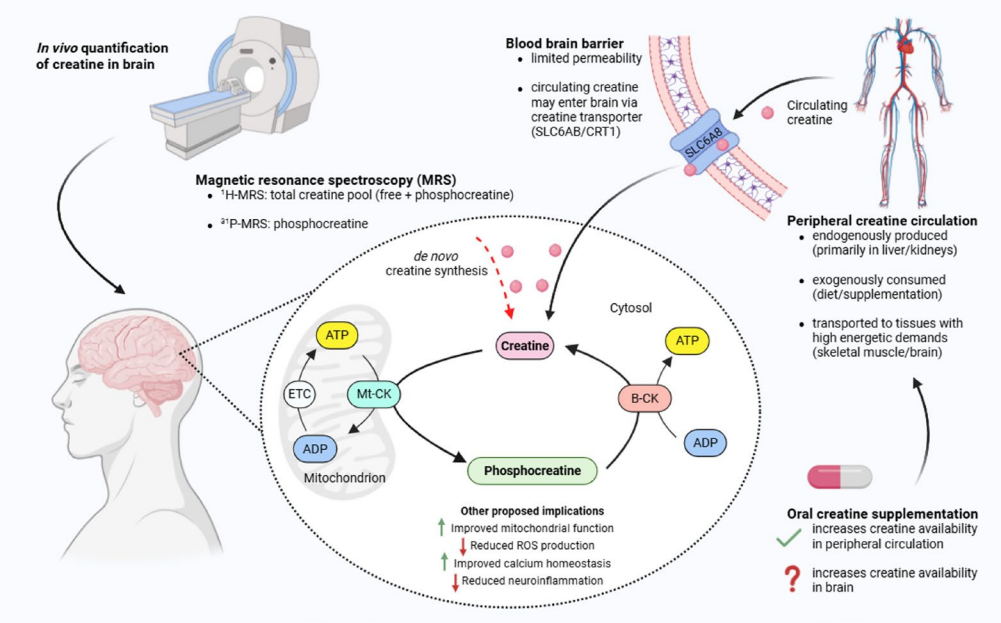
Increasing brain creatine availability through dietary supplementation has attracted significant interest as a potential strategy to support brain health and cognitive function. Magnetic resonance spectroscopy (MRS) enables non-invasive quantification of brain creatine and phosphorylcreatine *in vivo*, thereby providing a valuable opportunity to examine how creatine supplementation may influence brain energy metabolism via the creatine kinase system. Progress in the field has been constrained, thus far, however, by substantial methodological variability and challenges in achieving accurate and reproducible brain creatine measures. Technical and analytical factors, such as voxel relocalisation accuracy, spectral quality, and processing pipeline, combined with poorly understood levels of biological variability, can significantly affect the reliability and validity of brain creatine estimates. These challenges complicate the interpretation of existing supplementation studies, and, ultimately, lead there to be critical knowledge gaps in our understanding of how, and to what extent, brain creatine can be modulated through dietary supplementation in humans.

A small body of evidence suggests that creatine supplementation, typically between 5 to 20 $g \cdot day^{-1}$ for up to 8 weeks, may increase brain creatine levels by between 3 and 10%, with the largest effects shown in people facing elevated metabolic demands, such as those with neurological disease. The magnitude and regional specificity of the responses to supplementation vary substantially, however, and their functional significance on broader metrics of brain health and cognitive function remain unclear. Another important consideration is that large error margins have been reported for brain creatine quantification, yet most existing supplementation studies do not report reproducibility estimates, making it impossible to confidently distinguish true physiological effects from measurement error.

This presentation will a) outline the rationale for why modulating brain creatine through supplementation may be of relevance to human health, b) discuss key technical considerations when applying, or interpreting MRS-derived brain creatine measurements, including recent repeatability data from our group, and c) summarise current evidence for the efficacy of creatine supplementation to increase brain creatine concentrations.


In vivo quantification of creatine in brain
Blood brain barrier
• limited permeability
• circulating creatine may enter brain via creatine transporter (SLC6AB/CRT1)
SLC6AB
Circulating creatine
Magnetic resonance spectroscopy (MRS)
• ^{1}H-MRS: total creatine pool (free + phosphocreatine)
• ^{31}P-MRS: phosphocreatine
de novo creatine synthesis
Cytosol
Creatine
ATP
ATP
ETC
Mt-CK
B-CK
ADP
ADP
Mitochondrion
Phosphocreatine
Other proposed implications
Improved mitochondrial function
Reduced ROS production
Improved calcium homeostasis
Reduced neuroinflammation
Peripheral creatine circulation
• endogenously produced (primarily in liver/kidneys)
• exogenously consumed (diet/supplementation)
• transported to tissues with high energetic demands (skeletal muscle/brain)
Oral creatine supplementation
increases creatine availability in peripheral circulation
increases creatine availability in brain

C41

Does inulin-propionate ester modulate fat-free mass accumulation via insulin-like growth factor-1?

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Background

Short-chain fatty acids (SCFAs) are products of microbial fermentation that have important roles in host metabolism and energy balance. The iPREVENT randomised-controlled trial investigated whether daily supplementation with 10 g inulin-propionate ester (IPE) for 12 months could prevent weight gain in adults aged 20-40 years at high risk of future weight accumulation. Although weight gain trajectories did not differ between IPE and the inulin control study arms, an increase in fat-free mass (FFM) was observed in the IPE group. Evidence from animal studies indicates that SCFAs, can elevate circulating insulin-like growth factor-1 (IGF-1), a hormone that promotes FFM accretion, particularly within musculoskeletal tissue. This secondary analysis therefore aimed to determine whether the increase in FFM with IPE supplementation was allied with changes in serum IGF-1 concentrations.

Methods

Stored fasting serum samples collected at baseline and 12 months from a subset of iPREVENT participants (N=78) were analysed for IGF-1 using an Enzyme-linked immunosorbent assay (ELISA). Mean %CV of assay was 7.4%. Between group differences in change in IGF-1 (ΔIGF-1) concentrations at 12 months were assessed using analysis of covariance (ANCOVA), adjusting for age, sex, BMI, and IPE/inulin compliance. Associations between ΔIGF-1 and change in FFM (ΔFFM) and the effect of study arms were evaluated using regression analysis.

Results

Baseline IGF-1 concentrations were comparable between groups, (IPE (median [IQR]): 144.2 (67.81) ng/mL and inulin: 135.4 (57.22) ng/mL; p = 0.758). ANCOVA indicated that ΔIGF-1 was not significantly influenced by study arm, age, sex, BMI, or IPE/inulin compliance. Regression analyses demonstrated that ΔIGF-1 did not predict ΔFFM (B = -0.015, p = 0.093), and there was no significant interaction between ΔIGF-1 and study arm (B = -0.001, p = 0.932).

Conclusions

Although evidence from animal studies indicates that microbial metabolites such as propionate may enhance circulating IGF-1 and thereby promote increases in FFM, this secondary analysis did not identify any significant increase in IGF-1 concentration between the IPE and inulin groups. Furthermore, changes

in IGF-1 were not significantly associated with previously reported increases in FFM. These findings suggest that the IPE-related alterations in body composition are not mediated by IGF-1. Further research is warranted to identify alternative mechanisms driving the observed increases in FFM in response to IPE supplementation.

C42

Effect of ketogenic diet and ketone supplementation on fasting and postprandial glucose concentrations independent from energy balance: An interim analysis of the KETO-GENETIC study

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Introduction: Excess weight can increase the risk of several non-communicable diseases, impairing both metabolic function and quality of life. Lifestyle interventions offer a promising avenue to reverse some of the negative effects of excess weight gain. Previous studies have shown that a low-carbohydrate (ketogenic) diet can lower fasting glucose concentrations, however findings are often confounded by weight loss, therefore the isolated effects of ketosis on fasting glucose remains unclear. Additionally, the nutritional composition of ketogenic diets (high-saturated fat/red meat, and low-fibre) has been linked to several negative health outcomes, such as increased LDL-cholesterol concentrations. As an alternative to dietary manipulation, ketone supplements can increase circulating ketone concentrations without needing to adhere to a potentially harmful diet.

Aims/ Objectives: The aim of this interim analysis is to *a)* assess the ability to maintain energy balance and thus maintain weight as part of a short-term randomised controlled trial, with either a ketogenic diet or ketone supplementation and *b)* assess fasting and postprandial glucose responses to the interventions.

Methods: Currently, 25 individuals with overweight and/or obesity (age 44±11 years; 19 females) have been randomised to either control (n = 9, habitual diet), ketone supplementation (*n*=9, thrice daily alongside habitual diet) or ketogenic diet (*n*=7) condition (all prescribed at energy balance) for 28 days. The diet group caloric intake was determined as resting metabolic rate (RMR, determined by indirect calorimetry) plus physical activity energy expenditure (determined from Fitbit inspire 3) and diet induced thermogenesis. Body mass, body composition (via dual energy x-ray absorptiometry) and fasting glucose concentrations were assessed before and after the intervention. Postprandial plasma glucose concentrations (determined via iAUC) were also assessed over 3 hours following ingestion of a mixed-macronutrient meal (20% of resting metabolic rate). Additionally, participants wore continuous glucose monitors (CGMs) throughout a screening week and the intervention period. Change from baseline to follow-up were compared between groups with a one-way ANOVA.

Results: There was no evidence of a difference in body mass or fat-free mass between groups from baseline to follow up (Figure 1, Panels a-c). Fat mass was significantly different between groups (p=0.0196), whereby the diet group decreased, and supplement group increased (Δpost-pre = -0.69±0.89 *vs* 0.52±0.72 kg, p=0.0167). Plasma glucose concentrations (fasting and postprandial iAUC) were significantly different between groups (p=0.02 and p=0.002, respectively). Fasting glucose also decreased to a greater extent in the diet group compared to control (Δpost-pre = -0.44±0.51 *vs* 0.12±0.17 mmol/L, p=0.03), whereas glucose iAUC increased in the diet group compared to both the: supplement

(Δpost-pre = 180±112 *vs* 27±69 mmol/L*180 min, *p*=0.01) and control (Δpost-pre = -66±99 mmol/L*180 min, *p*=0.002). There was no evidence of a difference between groups in average glucose concentrations during the intervention, as determined by CGMs (*p*=0.4908).

Conclusion: Early results suggest neutral energy balance can be maintained while individuals with excess weight follow a short-term ketogenic diet. Fasting glucose appears to decrease while following the ketogenic diet. Increases in the iAUC during a mixed meal may suggest reduced glucose tolerance, independent from energy balance.

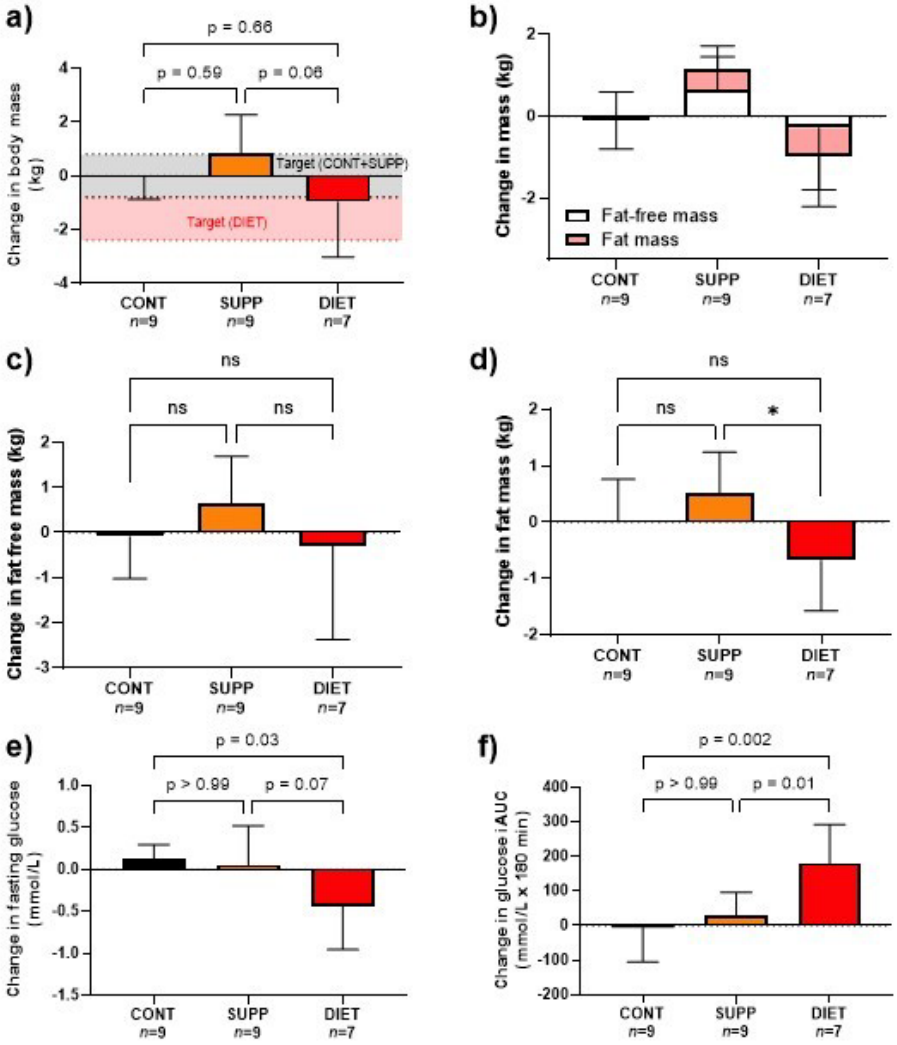

Figure 1: Change values for body mass (**Panel A**), fat and fat free mass (**Panel B**), fat mass (**Panel C**), fat free mass (**Panel D**), plasma fasting glucose (**Panel E**) and glucose iAUC (**Panel F**) for control group (CONT, black), supplement group (SUPP, orange) and diet groups (red). Bars display group means and standard deviations. Pairwise comparisons are displayed within figures.

C43

The Adiponectin–Leptin Ratio as a Marker of Insulin Resistance: A Cross-Ethnic Comparison

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Introduction:
Adipose tissue dysfunction contributes to insulin resistance in type 2 diabetes (T2D). Adipokines such as adiponectin, leptin, and their ratio are potential markers of this dysfunction, but their relevance may vary by ethnicity. This study aimed to investigate ethnic variation in how these adipokines relate to insulin resistance in people with T2D.

Methods:
Adults with T2D and no history or symptoms of cardiac disease were prospectively recruited at a single centre (NCT03132129) and underwent comprehensive phenotyping that included demographics, standard biochemistry, quantification of plasma adipokines (adiponectin and leptin), and insulin resistance was estimated using the homeostatic model assessment (HOMA-IR). In this study, White Europeans (WE) were compared to non-WE. Skewed variables were log-transformed. The association between the adipokines and their ratio (A/L) with HOMA-IR were examined using Pearson correlation. To determine if there was an independent relationship between HOMA-IR and each adipokine or their ratio, general linear regression modelling was applied, adjusting for age, sex and BMI, including an interaction term between ethnicity and the A/L ratio. Ethnicity-stratified models evaluated whether the A/L ratio and HOMA-IR associations differed between groups.

Results:

A total of 196 participants (109 WE and 87 non-WE) were included. All continuous variables are presented as mean ± SD unless stated otherwise. WE participants were slightly older (63.8 ± 6.8 vs. 61.9 ± 6.2 years), had higher BMI (31.6 ± 6.0 vs. 27.8 ± 4.4 kg/m^2), with a similar proportion of men in both groups (61% vs. 59%). There were no statistically significant differences between WE and non-WE groups in adiponectin levels (reported as median [IQR]), 7.67 (6.05–10.17) vs. 7.14 (5.81–9.48) ng/mL, leptin levels 24.10 (13.27–43.31) vs. 22.39 (13.00–37.01) ng/mL, or the A/L ratio 0.288 (0.160–0.662) vs. 0.342 (0.168–0.652). The A/L ratio correlated with HOMA-IR in WE ($r = -0.39$, $p < .001$) but not in non-WE individuals ($r = -0.03$, $p = 0.77$). In multivariable linear regression, a significant interaction was seen between ethnicity and A/L ratio for HOMA-IR (B= -0.8, p= 0.003). Stratified analyses showed that in WE participants, A/L ratio was an independent predictor of HOMA-IR ($B = -1.01$, $p < .001$), with the model explaining 17% of the variance. In contrast, in non-WE participants, neither the A/L ratio ($B = -0.02$, $p = 0.77$) nor the overall model was significant.

Conclusion:

Our data indicate that the A/L ratio is a significant independent predictor of insulin resistance in WE, but not in non-WE individuals with T2D. The lack of a significant association between A/L ratio and HOMA-IR in non-WE individuals could suggest that there are other contributing factors (e.g., genetics) to insulin resistance pathways.

C44

No evidence that regular protein-enriched breakfasts alter energy balance compared to either typical carbohydrate-rich breakfasts or extended morning fasting: A randomised controlled trial in healthy adults.

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Background: The majority of adults in the UK consume breakfast daily , yet this meal is typically lower in protein and higher in carbohydrates than other eating occasions. While carbohydrate-rich breakfasts can result in higher physical activity thermogenesis and glycaemia than morning fasting, less is known about whether enriching the morning meal with protein may enhance energy expenditure, moderate glycaemia, and improve appetite control.

Aims/Objectives: The aim of this study was to establish the short/mid-term (i.e., days; weeks) free-living behavioural and metabolic responses when fortifying breakfasts with protein, relative both to isocaloric carbohydrate-rich breakfasts and to complete omission of morning meals.

Methods: Thirty-four healthy adults (11 M/23 F; 35 ± 6 years; 23.6 ± 2.9 $kg \cdot m^{-2}$) were randomised to one of three 28-day interventions: (1) a daily carbohydrate-rich breakfast (providing 7.3 $mg \cdot kJ\ RMR^{-1}$ of carbohydrate per breakfast meal) before 1200 h (n = 11), (2) a daily whey protein-enriched breakfast (~6 mg·kJ-1 of carbohydrate per breakfast meal with an additional 15 g of whey protein to match the carbohydrate-rich breakfast for energy content) before 1200 h (n = 10), or (3) daily extended morning fasting until 1200 h (n = 13). Participants attended the laboratory on three occasions: preliminary screening, baseline postprandial and anthropometric assessment, and follow-up assessment. Participants also completed 7 days free-living monitoring of physical activity and energy intake prior to, and during weeks 1 and 4 of the intervention.

Results Four weeks of daily carbohydrate-rich (1264 ± 341 $kcal \cdot d^{-1}$), protein-enriched (1061 ± 470 $kcal \cdot d^{-1}$) or extended morning fasting (1261 ± 470 $kcal \cdot d^{-1}$) did not result in significant differences in physical activity thermogenesis (Group p = 0.51), self-reported energy intake (Condition x Time p = 0.18), body mass (Group × Time p = 0.68), or postprandial metabolic responses (Condition x Time x Timepoint p > 0.05). No changes in resting metabolic rate, dietary-induced thermogenesis, substrate oxidation, or appetite were observed.

Summary: The current study provides no evidence that daily consumption of either a protein-enriched, or carbohydrate-rich breakfast did not result in differences in energy balance, or metabolic control compared to extended morning fasting.

C45

Mitochondrial bioenergetics in overweight and obese individuals following a ketogenic diet or ketone supplementation, an interim exploratory analysis of the KETO-GENETIC study.

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Introduction: It is well established that adipose tissue has a strong influence on whole-body insulin sensitivity, glucose and lipid metabolism. Previous studies examining mitochondrial function in muscle in obese individuals have shown lower expression of transcript levels of genes related to oxidative phosphorylation and lower transcription factors (e.g., PGC-1α) suggesting decreased mitochondrial biogenesis. Although research interest related to adipose tissue bioenergetics in overweight and obese individuals has been increasing in recent years, only one study, to our knowledge, has examined how human adipose tissue correlates to a ketogenic diet. However, this study had only 5 participants in each condition, and diet was self-reported. Therefore, to our knowledge, this will be the first study to explore adipose mitochondrial bioenergetics in humans, and how it responds to a 4-week intervention following a ketogenic diet or ingesting a ketone ester.

Aims/ Objectives: The aim of this exploratory analysis is to a) understand how a ketogenic diet or ketone supplementation influences mitochondrial respiratory capacity in the adipose tissue, and b) if there are correlations between baseline values of mitochondrial respiration in the adipose tissue and other baseline measurements.

Methods: Currently, 33 individuals (age 45±12 years; 24 females, BMI 30.0±3.6) have been randomised to 4 weeks of either a control (n = 12, habitual diet), ketone supplementation (n = 11, thrice daily alongside habitual diet) or ketogenic diet (n = 10) condition (all prescribed at energy balance), with 23 having completed their respective interventions. Baseline measurements (e.g., body mass, body composition via dual energy x-ray absorptiometry, PAEE) and mitochondrial respiration in the adipose tissue were assessed before and after the intervention. Mitochondrial bioenergetics were established by measuring through high-resolution respirometry (Oxygraph-2k, Oroboros Instruments, Innsbruck, Austria) by following a substrate-uncoupler-inhibitor titration (SUIT) protocol SUIT-008 DL (DIG-1PM-2D-2c-3G-4S-5U-6Rot-7Ama). The protocol consisted of adding specific substrates related to each mitochondrial complex (e.g., succinate for Complex II) to investigate its contribution to the electron transport chain (ETC). Change from baseline to follow-up were compared between groups with a one-way ANOVA.

Results: There were no significant differences between groups in relation to LEAK ($p > 0.05$, Fig-1A), Complex I ($p > 0.05$, Fig-1B) and ETC ($p > 0.05$, Fig-1D). However, there was a significant difference in

Complex I+II linked respiration between the control group and ketone supplementation group ($p < 0.05$, Fig-1C). Significant negative correlation was found between the total release of energy by the electron transport chain in the adipose tissue and waist circumference ($R = -0.48$, $p = 0.005$, Fig-2E) and waist to hip ratio ($R = -0.49$, $p = 0.004$, Fig-2F). No other significant correlations were found among baseline measurements.

Conclusion: Ingestion of ketone supplementation significantly increases the activity of mitochondria's complexes I and II in the adipose tissue in relation to a standard diet. Possibly via direct contribution of the ketone ester oxidation to NADH and acetoacetyl-CoA for the mitochondrial respiration. Additionally, correlation results indicate that higher waist circumference and waist-to-hip ratio are associated with lower baseline oxidative phosphorylation capacity.

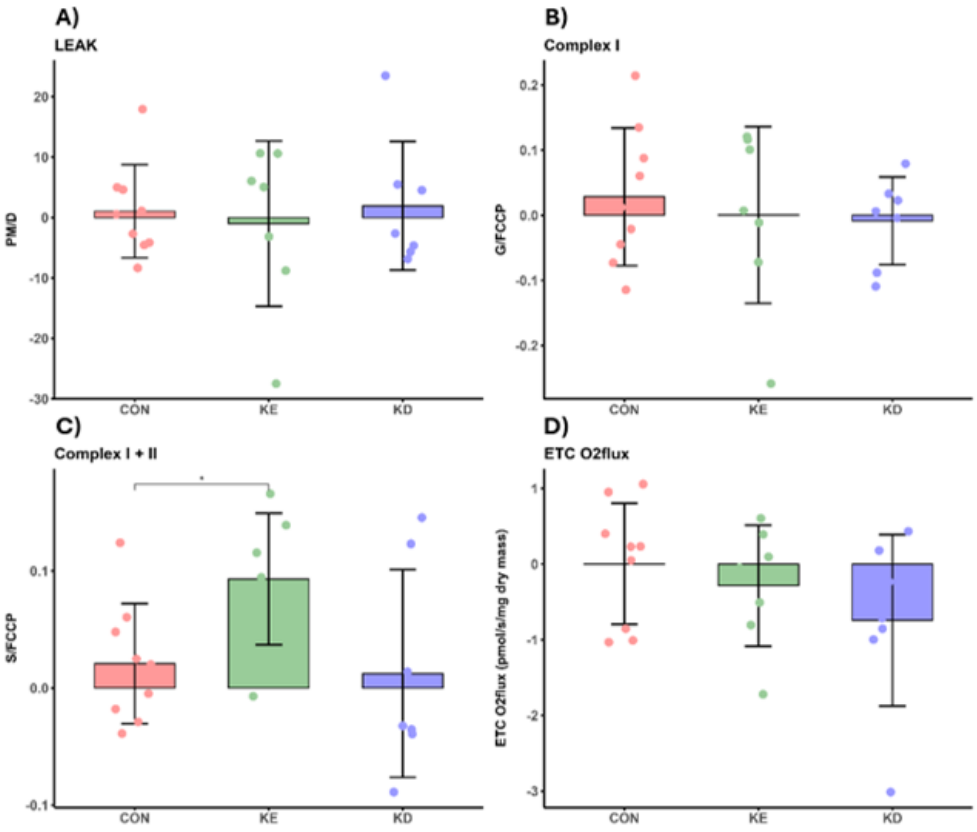

Figure 1. Pre to post comparison between groups following 4 weeks of a control diet (CON), ketone supplementation (KE) or ketogenic diet (KD) for LEAK, Complex I, Complex I + II, and Electron Transport Chain (ETC). Bars represent group means, and standard errors. Only significant pairwise comparisons are displayed within figures. PM: pyruvate plus malate; D: adenosine diphosphate; G: glutamate; FCCP: carbonyl cyanide p-(trifluoromethoxy)phenylhydrazone; S: succinate. * $p < 0.05$.

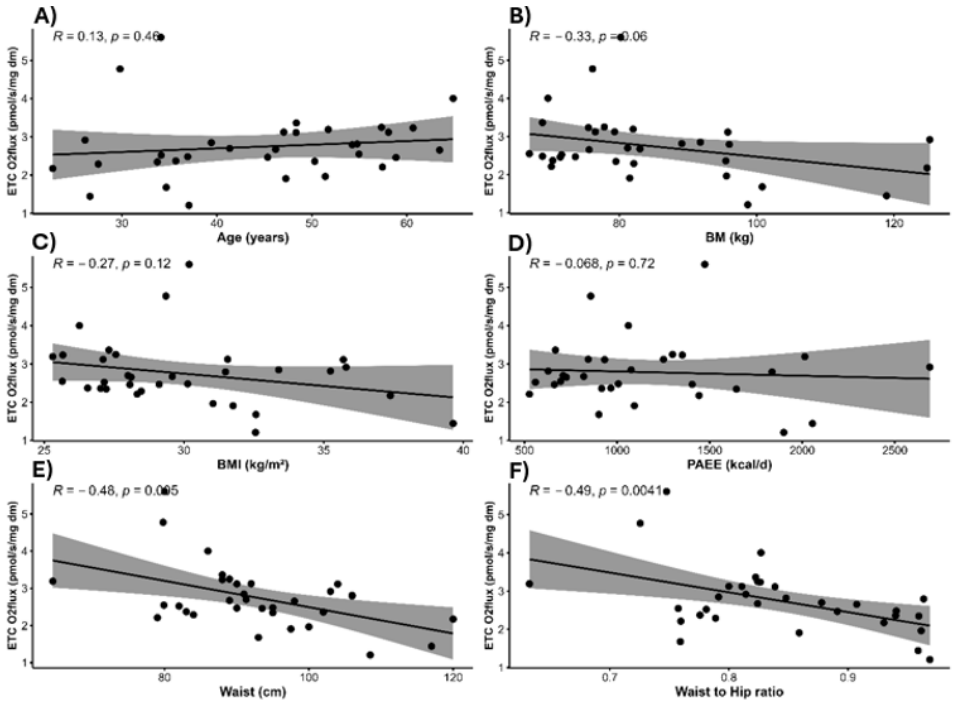

Figure 2. Correlations between maximal respiratory capacity produced by the electron transport chain and different baseline measurements. ETC: electron transport chain; PAEE: physical activity energy expenditure; BM: body mass; Waist: waist circumference; dm: dry mass.

C46

The effect of blueberry supplementation on intra-articular inflammation and post-operative recovery in patients undergoing total knee replacement for osteoarthritis

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Background: Osteoarthritis (OA) is a painful, chronic condition affecting 40% of those >70 years [1]. Inflammation is an aetiological factor in OA [2]. Blueberries are rich in polyphenols, which are anti-inflammatory [3]. Previously, blueberry supplementation reduced arthritic pain [4]. This study assessed the effect of blueberry supplementation on a) the inflammatory pathophysiology of OA and b) pain and joint function in patients undergoing total knee replacement (TKR). **Methods:** All procedures accorded with ethical standards and the principles of the World Medical Association's Declaration of Helsinki. Sixty-one patients scheduled for total knee replacement (TKR) were randomised to receive blueberry powder (c.480 mg anthocyanins/day) (n=32, 69 ± 8 years; BMI 32.1 ± 5.5 kg/m^2) or placebo powder (n=29, 69 ± 7 years; BMI 31.7 ± 5.1 kg/m^2) for 6 weeks pre- and post-TKR. Serial assessments of pain and joint function were performed using the validated WOMAC questionnaire at baseline, week 3, pre-TKR, 1-week post-TKR, 3 weeks post-TKR and 6 weeks post-TKR. During TKR, synovial fluid, synovium, infrapatellar fat pad (IFP), articular cartilage, and subchondral bone were collected. Gene expression analysis was conducted using Taqman OpenArray targeting 56 genes related to OA pathophysiology. Differential gene expression analysis was performed using limma in R (v 4.3.2) on −ΔCT-transformed qPCR data (blueberry vs. placebo). Synovial fluid samples were profiled using multiplex Luminex assays. Group comparisons were performed using t-tests. Linear mixed-effects models were fit for WOMAC outcomes. Tandem-mass-tagged proteomic analysis was performed on a subset of synovium samples (N=30). Data were analysed using Reactome differential pathway analysis (blueberry vs placebo) via the CAMERA algorithm. Exploratory analysis looked at associations between ssGSEA enrichment scores and post-operative (6–12-week) ΔWOMAC using linear regression. **Results:** From week 3 onwards, blueberry participants improved by 1.28 WOMAC function points per week, while placebo participants improved more slowly, by 0.69 points less per week (p = 0.041). Blueberry supplementation upregulated adiponectin mRNA in synovium (Log2FC +1.38; p=0.040), IFN-γ in IFP (Log2FC +1.37; p=0.008) and COL13A1 in cartilage (Log2FC 1.58; p=0.039) versus placebo. CX3CL1 mRNA (Log2FC −0.72; p=0.032) and Apolipoprotein E (Log2FC −0.67; p=0.036) were downregulated in bone. Blueberry supplementation reduced insulin concentrations in synovial fluid (mean placebo: 293.2 pg/mL; mean blueberry: 164.5 pg/mL; p = 0.048). Blueberry supplementation significantly altered synovium protein expression in 54 pathways (FDR < 0.05). Pathways related to complement activation (e.g., Initial triggering of complement, Classical antibody-mediated complement activation) and B cell/immune regulation (e.g., CD22-mediated BCR regulation, Antigen activates BCR) were downregulated ($\log_2$FC −0.20 to −0.58, FDR 0.0002–0.036). Pathways including GLUT4 translocation, Membrane trafficking, Cristae formation and Mitochondrial calcium transport were upregulated ($\log_2$FC 0.09–0.23, FDR 0.002–0.047). Several synovium pathways previously modulated by blueberry supplementation were nominally associated with post-operative WOMAC improvements. B cell/immune regulation pathways and complement-related pathways showed positive associations (estimates 5.7–9.2, p 0.009–0.024). These results are exploratory and should be interpreted cautiously due to potential circularity. **Conclusions**: Blueberry supplementation may ameliorate OA pathology by modulating key molecular pathways involved in joint tissue inflammation and repair.

C48

Whey protein isolate co-ingestion reduces the plasma galactose response to galactose feeding

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Coingestion of glucose with galactose attenuates elevations in circulating galactose concentrations typically observed following ingestion of galactose alone, and is largely attributed to elevated concentrations of glucose rather than insulin (Williams et al., 1983). This study investigated the metabolic response to galactose and whey protein coingestion and examined whether whey protein induced elevations in insulin are sufficient to lower circulating galactose concentrations.

In a randomised crossover design, twelve metabolically healthy participants (8 males, 4 females; age: 26 ± 6 years; height: 174.2 ± 8.4 cm; body mass: 68.8 ± 10.3 kg; body mass index: 22.5 ± 1.8 kg·m^{-2}) undertook three experimental trials. Participants consumed 300 mL water containing either 25 g galactose (GAL), 25g galactose and 25 g glucose (GAL+GLU), or 25g galactose and 25 g whey protein isolate (GAL+WHEY). On each occasion, participants arrived in an overnight fasted (~10-h) state having adhered to 24-h diet and physical activity replication. Arterialised blood samples were obtained in a fasted state, and at 15, 30, 45, 60, 90 and 120 min during the postprandial period to determine the plasma metabolite and hormone response to the test beverages. Time independent variables were analysed by one-way repeated measures ANOVA, with Bonferroni post-hoc corrections applied for multiple comparisons. Data are mean ± SD.

Peak galactose concentrations were highest in GAL (0.424± 0.445 mmol·L^{-1}) and were reduced in GAL+GLU (0.029 ± 0.027 mmol·L^{-1}; P=0.0002) and GAL+WHEY (0.057 ± 0.083 mmol·L^{-1}; P=0.0003), with no difference in peak concentrations between GAL+GLU and GAL+WHEY. Plasma galactose incremental area under the curve (iAUC) followed the same pattern, with GAL+GLU (1 ± 2 mmol·L^{-1}·120min; P=0.0014) and GAL+WHEY (1 ± 2 mmol·L^{-1}·120min; P=0.0008) significantly lower than that of GAL (14 ± 15 mmol·L^{-1}·120min). Postprandial insulin response (iAUC) did not differ significantly between GAL+GLU (2399 ± 1936 pmol·L^{-1}·120min) and GAL+WHEY (2191 ± 1544 pmol·L^{-1}·120min; P>0.9999) but were significantly higher than GAL (424 ± 286 pmol·L^{-1}·120min; both P<0.0001). Plasma glucose total area under the curve (tAUC) was higher in GAL+GLU (657 ± 40 mmol·L^{-1}·120min) than GAL (605 ± 39 mmol·L^{-1}·120min; P=0.0048). Glucose tAUC was reduced further in GAL+WHEY (581 ± 44) compared to GAL+GLU (P=0.0002) and GAL (P=0.0123). The postprandial plasma glucagon response (tAUC) following GAL+WHEY (1663 ± 714 pmol·L^{-1}·120min) was above that of GAL (630 ± 369 pmol·L^{-1}·120min; P<0.001) and GAL+GLU (443 ± 161 pmol·L^{-1}·120min; P<0.001), with GAL and GAL+GLU differing (P=0.0089). Plasma lactate (iAUC) did not differ between GAL+WHEY (48 ± 17 mmol·L^{-1}·120min) and GAL (69 ± 33 mmol·L^{-1}·120min; P=0.0576) but was significantly lower than GAL+GLU (93 ± 30 mmol·L^{-1}·120min; P<0.0001). GAL+GLU and GAL did not differ (P=0.0942).

Coingestion of whey protein isolate with galactose attenuates the typical rise in plasma galactose concentrations observed when galactose is ingested alone. The absence of a clear increase in plasma

glucose concentrations with whey protein coingestion suggests a rise in glucose is not essential for galactose clearance, rather the data suggest a role of insulin mediated plasma galactose clearance.

C49

Total energy and protein intake in mild-moderate COPD patients compared to healthy non-smoking individuals

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Background:
Muscle wasting and weight loss are systemic manifestations of chronic obstructive pulmonary disease (COPD), particularly in those with severe airflow obstruction. Sedentarism, appetite changes, oxidative stress, inflammation, and tissue hypoxia contribute to sarcopenia in COPD [1]. Low fat-free mass index (FFMI) and BMI are associated with poor outcomes, including increased mortality [2]. Despite elevated energy requirements, malnutrition is prevalent in up to 30% of COPD patients, particularly in inpatients and advanced disease. However, little is known about the nutritional status of younger, mild-to-moderate COPD patients in outpatient settings [3].

Objective:
To assess energy and protein intake, body composition, and functional capacity in mild-to-moderate COPD patients compared with healthy non-smoking individuals (HNS).

Methods:
COPD participants (mean age 58.1 years) had FEV1/FVC <0.7 and FEV1 ≥50% predicted (mean 74.8%). All were current or former smokers with ≥10 pack years; 50% used inhaled corticosteroids. HNS (mean age 54.8 years) were age- and sex-matched non-smokers with normal lung function. Functional capacity was assessed using Short Physical Performance Battery (SPPB: standing balance, 4-meter gait speed (4MGS), and five-repetition sit-to-stand motion (5STS)), 6 Minute Walk Test (6MWT), Timed Up and Go (TUG) and Handgrip Strength (HGS).

Energy and protein intakes were measured using the EPIC-Norfolk Food Frequency Questionnaire and a 7-day food diary, analysed with FETA [4] and Nutritics software [5]. Participants not meeting ≥75% of estimated requirements were classified as nutritionally inadequate. Body composition was assessed using bioelectrical impedance analysis; low FFMI was defined as <15 kg/m^2 (females) and <17 kg/m^2 (males). Proportion of participants not meeting protein and energy requirements were calculated using PENG guidelines [6]. Comparisons between groups were assessed using independent t-tests, Mann-Whitney U tests, or Chi-squared tests, as appropriate. See Tables 1 and 2

Results:
Body composition did not differ significantly between COPD and HNS (%FFM: 66.8 vs. 69.3; FFMI: 18.9 vs. 19.1 kg/m^2). A higher, though non-significant, proportion of COPD patients had low FFMI (9.5% vs. 0%, p=0.22). Most participants were overweight (BMI >25 kg/m^2), and ~75% showed high central adiposity.

Mean daily energy intake was similar between groups (COPD 1857 kcal vs. HNS 1917 kcal, p=0.64). Protein intake was lower in COPD (75.7 g vs. 83.2 g, p=0.14). Significantly more COPD patients did not meet protein requirements (75% vs. 14%, p<0.01), and 35% consumed <75% of estimated needs. In COPD, both energy and protein intake correlated moderately with SPPB performance (r=0.57, p=0.02; r=0.50, p=0.049), but not with other functional measures.

Conclusions:
Younger, mild-to-moderate COPD patients often present as overweight with excess central fat yet demonstrate inadequate protein intake. Despite preserved body composition, low dietary protein may predispose this group to future sarcopenia. Since overweight status can mask muscle loss, nutritional risk may be overlooked in clinical care. Early multidisciplinary intervention, including dietary assessment and targeted nutritional support, may help prevent sarcopenia progression in this population.

Table 1: Characteristics of participant with mild COPD vs healthy non-smokers

Characteristics	**COPD (n=21)**	**HNS (n=15)**	**p-value**
Sex (M/F)	10/11	8/7	0.74
Age	58.1 (6.0)	54.8 (6.3)	0.13
FEV_1 (L)	2.2 (0.5)	3.2 (0.8)	<0.0001
FEV_1 % predicted	74.8 (14.0)	104.0 (12.2)	<0.0001
FEV_1/FVC ratio	57.1 (7.3)	77.1 (5.4)	<0.0001
Body composition			
BMI (Kg/m^2)	27.3 (5.2)	27.9 (3.6)	0.68
Underweight (<18.5)	1(4.8)	0 (0)	0.39
Normal weight (18.5-24.9)	3 (14.3)	2 (13.3)	0.87
Overweight (25-29.9)	14 (66.7)	11 (73.3)	0.67
Obese (≥30)	3 (14.3)	2 (13.3)	0.94
WC (cm)	95.1 (15.7)	93.6 (10.7)	0.76
Normal	4 (19.0)	3 (26.7)	0.94
High (>94 (M) or 80 (F))	15 (71.4)	12 (73.3)	0.56
WHtR	0.57 (0.08)	0.55 (0.06)	0.54

Table 2: Nutritional intake of participant with mild COPD vs healthy non-smokers

Nutritional intake	**COPD (n=21)**	**HNS (n=15)**	**p-value**
Energy requirement (kcal)	2475.0 (606.9)	2178.8 (399.0)	0.05
Protein requirement (g)	95.3 (24.0)	63.2 (8.5)	<0.001
Average measure			
Energy intake (kcal)	1916 (530.1)	1917.43 (225.47)	0.94
Protein intake (g)	76.39 (15.6)	83.18 (13.73)	0.07
Energy requirements not met			
% of requirement met (energy)	79.69 [34.55-158.00]	85.62 [66.15-141.10]	0.49
% of requirement met (protein)	79.48 [45.87-118.0]	128.4 [88.54-200.3]	0.0001
Patients not meeting energy requirement	16 (80.0)	10 (71.4))	0.56
Patients not meeting protein requirement	15 (75.0)	2 (14.3)	0.0005
Proportion of individuals not meeting 75% energy requirement	9 (45.0)	4 (28.6)	0.33
Proportion of individuals not meeting 75% protein requirement	7 (35.0)	0 (0.0)	0.01

C50

Impact of chronic cocoa flavanol supplementation on cognitive function in healthy young adults: a randomised controlled trial

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Introduction: Age-related cognitive decline is a leading cause of disability in the UK, with incidences projected to triple by 2060. With no effective disease-modifying therapies currently available, modifiable lifestyle factors—which account for up to 35% of dementia risk—offer a promising approach to slow cognitive ageing. Diets rich in flavonoids have been linked to better cognitive outcomes, and acute high-flavanol cocoa supplementation has been shown to transiently improve cognitive function in young adults. However, it remains unclear whether these benefits can be sustained, or further enhanced, through daily, chronic supplementation. This study therefore aims to investigate the effects of both acute and chronic high-flavanol cocoa supplementation on cognitive performance in healthy young adults, providing crucial insights into dietary strategies for maintaining brain health.

Methods: In this double-blind, placebo-controlled, parallel, randomised trial, 50 healthy young adults (18 – 40 years; gender-balanced) were supplemented daily for 8 weeks with either high-flavanol cocoa (15.5 g; 792.33 mg total flavanols, 137.65 mg monomeric flavanols, e.g., (-)-epicatechin) or low-flavanol cocoa (15.5 g; 30.12 mg total flavanols, 18.13 mg monomeric flavanols). Cognitive function was assessed using the Stroop Task, Modified Attention Network Task (MANT), and Task Switching Task (TST) at four timepoints: (i) day 1, before supplementation (0 h; baseline); (ii) day 1, 2 h after supplementation (acute effect); (iii) ~ day 56, before supplementation (chronic effect); and (iv) ~ day 56, 2 h after supplementation (acute-within-chronic effect). All procedures were conducted in accordance with relevant ethical guidelines and regulatory standards. This study is registered with the ISRCTN clinical trials registry (ISRCTN29176549).

Results: All participants (N = 50; mean age: 23.36 ± 4.74 years, mean BMI: 25.59 ± 15.33 kg/m^2) have completed the intervention. Data analysis is currently ongoing, with results expected the be fully analysed by time of presentation. Data will be analysed using a linear mixed model with intervention (high- or low-flavanol cocoa), time (at the acute, chronic, and acute-within-chronic timepoints), and their interaction as fixed effects, baseline values as a covariate, and participants included as a random effect.

Conclusion: As the population ages, preserving brain health has become a major public health priority. Outcomes of this study will establish if benefits in cognition in young adults are apparent beyond acute effects, with the focus of future work extending to older adults. The findings will help inform evidence-based dietary strategies for mitigating age-related cognitive decline and support public health recommendations for healthy ageing.

Keywords: cocoa flavanols, flavonoids, cognition function, executive function

C51

Nocturnal grazing and meal-feeding enhance fat storage in female mice by a ghrelin-dependent mechanism

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The physiological impact of the contemporary shift from regular meal consumption to grazing/snacking behaviour[1,2], remains poorly understood. We have reported previously that feeding male rodents three meals/night enhances growth hormone (GH) rhythmicity and skeletal growth by activating the GH secretagogue receptor (GHSR)[3], whereas grazing elevates fat mass. Similar endocrine responses occur in men receiving patterned nasogastric enteral feed[3]. Here we examine the impact of these feeding patterns and the role of GHSR in female mice.

5 week-old female wild-type (WT) and loxTB-GHSR (GHSR-null) littermate mice, were fed either *ad libitum* (AL), grazing (1/24th daily AL consumption every 30 mins in the dark phase), or in meals (3x1hr periods of AL feeding at the start, middle and end of the dark phase) for 3 weeks (n=9-12 per group) (Animal procedures were performed in accordance with the Animals (Scientific Procedures) Act, 1986 (UK), the Cardiff University Animal Welfare Ethical Review Body (AWERB) and reported as *per* the ARRIVE guidelines). Mice were anaesthetized with Dolethal (200mg/kg; i.p.) nose-anus length measured and decapitated. Femora and tibiae were dissected and the length measured with a hand-held micrometer, tibial epiphyseal plate width (EPW) being determined by light microscopy. A range of tissues were dissected and weighed. All data reported are mean ± SEM, with statistical comparisons performed by 1-way ANOVA with Bonferroni's multiple comparison *post hoc* test.

Cumulative food intake (cF/I), overall weight gain and indices of longitudinal growth were unaffected by either feeding pattern in WT females. However, meal-fed GHSR-null mice showed a 12% reduction in cF/I (P=0.0002 *vs* AL-fed GHSR-null mice), a 60% reduction in weight gain (P=0.0099 *vs* AL-fed GHSR-null mice) and a 2.5% reduction in femoral length (P=0.0192). Tibial EPW, an accurate marker of growth rate, was reduced by 18% in both grazing and meal-fed WT females (P=0.0158; P=0.0029 *vs* AL-fed WT female), this effect being less pronounced in GHSR-null females. Liver, kidney, pituitary and ovarian weights were unaffected by these feeding patterns in either WT or GHSR-null mice, adrenal weight being reduced by 19% in meal-fed GHSR-null females (P=0.0309 *vs* AL-fed GHSR-null mice). Although inguinal and omental white adipose tissue (WAT) weights were unaffected by grazing or meal-feeding in WT mice, grazing elevated proportionate retroperitoneal WAT weight in WT females by 32% (P=0.0219 *vs* AL-fed WT mice), mean proportionate interscapular brown AT weight in grazing WT females being 121% of that in AL-fed mice (P=0.0724). These effects were abolished in GHSR-null mice.

Unlike in males, meal-feeding failed to accelerate skeletal growth in female mice, but activation of the ghrelin-GHSR axis is essential for maintaining food intake and body weight in meal-fed females. In contrast, grazing-enhanced lipid storage in WT female mice is more widespread in males and dependent upon GHSR activation in both sexes. Thus, while feeding patterns appear to modulate the ghrelin system

similarly in males and females, the enhancement of GH pulsatility is male-specific. Thus, the contemporary shift from regular meal consumption to grazing/snacking behaviour may be detrimental to growth and metabolic outcomes, particularly in males.

C52

The impact of different acute interventions on β-cell function in people without diabetes after bariatric surgery

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Background:

Bariatric surgery creates anatomical changes that substantially alter nutrient delivery to the gut, leading to major physiological effects on glucose regulation. Although glucose homeostasis often improves after surgery, including remission of type 2 diabetes, the altered nutrient flow can also disrupt the normal feedback relationship between plasma glucose and insulin secretion. This impaired β-cell regulation can cause an exaggerated early postprandial glucose rise followed by excessive insulin release, predisposing some individuals to postprandial hyperinsulinaemic hypoglycaemia. Several strategies have been proposed to mitigate these effects, including pharmacotherapy and dietary modifications. Given their distinct mechanisms, the aim of this secondary analysis was to compare the effectiveness of three acute interventions on improving postprandial glucose homeostasis and β-cell function in people who have previously undergone bariatric surgery, to better understand their relative contributions.

Methods:

Data were pooled from three similarly designed acute, randomised, cross-over trials (*n*=38, BMI=37.9±10.2 kg/m^2, age=54.9±9.9 years, sex=31F). Each trial was approved by an HRA research ethics committee (REC ref: 20/YH/0123, 20/YH/0339, 20/YH/0177). Each trial included two visits (treatment and control). Treatments included 300mg canagliflozin (CANA) or 28g brazil nuts (NUTS) consumed 30 minutes before a mixed-meal, or 2g salt (SALT) consumed with a mixed-meal. Controls were 100ml water 30 minutes before the mixed-meal for CANA and NUTS, and the same meal without added salt for SALT. Blood samples were collected over 3 hours to assess plasma glucose, insulin, C-peptide, and total glucagon-like peptide-1 (GLP-1). C-peptide deconvolution was performed to evaluate β-cell function parameters (insulin secretion rate, potentiation ratio and insulin clearance). Generalised estimated equations were performed with β-cell function parameters as dependent variables, and treatment (intervention or control) and trial (CANA, NUTS, SALT) as predictor variables. The model assessed the main effect of treatment and trial and their interaction (treatmentXtrial). If a significant interaction term was observed, data were then stratified by trial.

Results:

A reduction in early glucose response (-5.9% in AUC0-30 mins, *P*=0.004), insulin secretion rate (*P*=0.002), insulin potentiation ratio (*P*=0.001) and a 10.4% increase in basal insulin clearance (*P*=0.047) were observed in response to acute intervention (treatment main effect). CANA was the most effective intervention for improving mean postprandial glucose and insulin, mean insulin clearance and early (AUC0-30 mins), and overall (AUC0-180 mins), insulin and glucose response, treatmentXtrial *P*<0.05. NUTS increased basal insulin secretion rate by 10.9±4.3% and decreased insulin potentiation ratio by 44.4±10.2%, and impacted these parameters to a greater extent than SALT and CANA (*P*<0.05). SALT did not out-perform CANA or NUTS on any parameter.

Conclusions:

Among the interventions investigated, 300mg of canagliflozin was the most effective for improving postprandial β-cell function and glucose homeostasis. In contrast, consuming a portion of brazil nuts prior to a mixed-meal increased basal insulin secretion rate and was more effective in lowering the insulin potentiation ratio throughout the entire postprandial period, consistent with the effect of canagliflozin acting predominantly in the early postprandial phase. These findings could suggest potential complementary effects, and future research could explore how pharmacological and dietary strategies might be combined to optimise postprandial glucose regulation in individuals following bariatric surgery.

C53

The skeletal and reproductive impact of the 5:2 diet in mice: consequences of the infradian stimulation of the ghrelin axis

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The broad physiological impact of the 5:2 diet, a popular weight-loss strategy, is poorly understood. We have shown that this diet fails to induce adult hippocampal neurogenesis or neurogenesis-dependent behaviour in mice[1] and induces weight loss in males, while elevating lipid storage in both sexes[2]. Here we examine the impact of this dietary strategy on skeletal morphology and biomechanical performance and indices of reproductive axis activity.

Adolescent (7 week-old) male and female wild-type (WT) and loxTB-GHSR (growth hormone secretagogue receptor (GHSR)-null) littermate mice, were fed standard rodent chow in either *ad libitum* (AL) or 5:2 (5 days AL:2 non-consecutive 24hr fasting periods) pattern for 3 or 6 weeks (n=6-9 per group) (Animal procedures performed in accordance with the Animals (Scientific Procedures) Act, 1986 (UK), the Cardiff University Animal Welfare Ethical Review Body (AWERB) and reported as *per* the ARRIVE guidelines). Femoral length was quantified with a hand-held micrometer, with biomechanical strength and proximal trabecular architecture assessed by 3-point bending and micro-CT[3,4]. Testes, seminal vesicles and ovaries were weighed *post mortem*, with spermatozoa and follicular development quantified in histological sections. Circulating LH, FSH, testosterone and oestrogen (E2) were quantified by ELISA in terminal plasma samples. All data reported are mean ± SEM, with statistical comparisons performed by Students unpaired t-test or 2-way ANOVA with Sidak's multiple comparison *post hoc* test.

Three weeks of the 5:2 diet had no effect on femoral length, mid-diaphysial diameter or cross-sectional area. In contrast, lateral and medial wall thicknesses were elevated and reduced by 13% respectively in 5:2-fed males (P=0.044; P=0.002), with anterior and posterior wall thicknesses unchanged. Despite the significant influence of sex (P=0.0036), neither overall biomechanical strength, tissue strength (ultimate tensile stress) nor the geometric contribution to strength (2nd moment of area) were significantly changed by the 5:2 diet. However, the 5:2 diet induced a 12% elevation in trabecular bone density (BV/TV; P=0.009), accompanied by a 10% reduction in lattice fragmentation (Tb.Pf; P=0.0495). Trabecular surface (BS/BV), number (Tb.N), thickness (Tb.Th), separation (Tb.Sp), and cross-sectional shape (Structure-modal index (SMI)) were unaffected.

Three weeks of the 5:2 diet reduced seminal vesicle weight by 16% (P=0.016), without affecting testicular weight or spermatozoa counts. Although mean circulating LH was halved (P=0.095) and mean circulating FSH was 92% of that in AL-fed male mice (P=0.077), circulating testosterone was unaffected. However, by 6 weeks, circulating testosterone was reduced by 88% (P=0.023). This was reversed in GHSR-null males. In females, 3 weeks of the 5:2 diet had no significant effect on ovarian weight or the number or morphology of primary follicles, graafian follicles or corpora lutea. Mean circulating oestrogen were 75% of that in AL-fed females (P=0.075), with circulating LH halved (P=0.262) and FSH unaffected. After 6 weeks, the 5:2 diet had no impact on circulating oestrogen in either WT or GHSR-null mice.

Thus, infradian stimulation of the ghrelin axis by the 5:2 diet induces a collapse in circulating testosterone in male mice. When combined with previous evidence of enhanced lipid storage, this weight loss strategy elicits some undesirable physiological consequences.

C54

The effect of a 4-week ketogenic diet and ketone ester supplementation on substrate utilisation and metabolic flexibility – An interim analysis of the KETO-GENETIC diet.

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Introduction: The respiratory exchange ratio (RER) reflects the balance between carbohydrate and lipid oxidation, with values from 0.7 to 1.0 indicating predominant fat or carbohydrate oxidation, respectively. The food quotient (FQ), derived from dietary intake, estimates the expected RER under energy balance, and the alignment between fasting RER and FQ serves as an indicator of metabolic flexibility. A greater mismatch between FQ and RER is commonly observed in individuals with excess weight. Although ketogenic diets, a common weight loss strategy, lower RER by promoting fat oxidation, their impact on substrate oxidation relative to the diet's reduced FQ has not been well characterised in overweight or obese adults. Ketone ester supplementation increases circulating ketone bodies without carbohydrate restriction or altering FQ, but its effects on fasting substrate utilisation and metabolic flexibility also remain unclear.

Aims and objectives: This interim analysis examined 1) fasting substrate oxidation and 2) metabolic flexibility, measured as FQ - RER, after a 4-week controlled weight-maintaining ketogenic diet (WMKD), ketone ester supplementation (SUPP), or habitual control diet (CON) in overweight and obese adults.

Methods: In this ongoing three-arm, four-week intervention, 32 adults (44.9 ± 11.7 years; BMI 30 ± 3.6; 21 females) were randomised to WMKD (n = 11), SUPP (n = 11), or CON (n = 10). Fasted, rested RER was measured via indirect calorimetry (Servoflex miniMP52000, Servomex Group Ltd.) at baseline and week four. Baseline FQ was calculated from three days of dietary records collected during a one-week monitoring period. During the intervention, FQ was assumed stable for SUPP and CON. WMKD participants received all foods with an estimated daily FQ of 0.75, assumed constant despite variation in additional foods required to meet individual energy needs. Dietary data were analysed using Nutritics (Version 6.15).

Statistical analysis: All 32 participants were included (26 completed the intervention; 6 provided baseline only). Follow-up RER and FQ - RER were analysed using baseline-adjusted ANCOVA with Tukey's Honestly Significant Difference test for pairwise comparisons. Significance was set at $p < 0.05$. Analyses were conducted in RStudio (version 4.4.0).

Results: After four weeks, WMKD showed a significantly lower fasting RER than CON (estimate = −0.08 ± 0.03, p = 0.01). SUPP did not differ from CON (estimate = −0.02 ± 0.02, p = 0.49), and no significant difference was found between WMKD and SUPP (estimate = −0.05 ± 0.03, p = 0.10). Baseline-adjusted estimated marginal means (EMMs) for FQ − RER at follow-up were 0.002 (95% CI: −0.04 to 0.04) in CON, −0.02 (−0.067 to 0.03) in WMKD, and 0.02 (−0.02 to 0.07) in SUPP. No significant group differences were detected (F = 1.70, p = 0.199). Tukey-adjusted contrasts for CON vs WMKD, CON vs SUPP, and WMKD vs SUPP were not significant (p = 0.80, p = 0.80, p = 0.43, respectively).

Conclusion:
Four weeks of a weight-maintaining ketogenic diet, but not ketone ester supplementation, reduced

fasting substrate utilisation. No differences in baseline-adjusted FQ - RER were observed between groups. Incorporating postprandial RER measurements in future work may help identify more dynamic changes in metabolic flexibility.

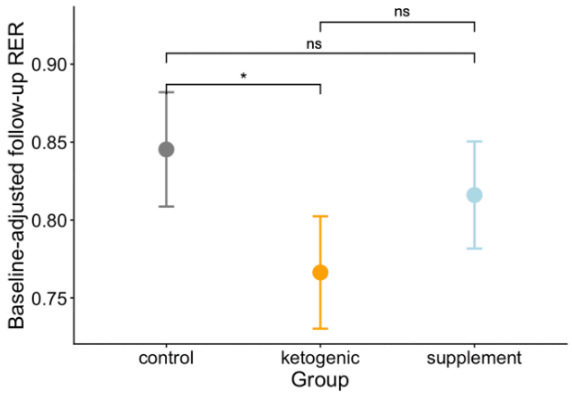

Figure 1. Baseline-adjusted fasting RER by group. Baseline-adjusted estimated marginal means (±95% CI) for fasting respiratory exchange ratio (RER) after four weeks in the control (CON), ketogenic diet (WMKD), and ketone ester supplementation (SUPP) groups. WMKD showed a significantly lower fasting RER than CON (*P < 0.05), while SUPP did not differ significantly from either group (ns).

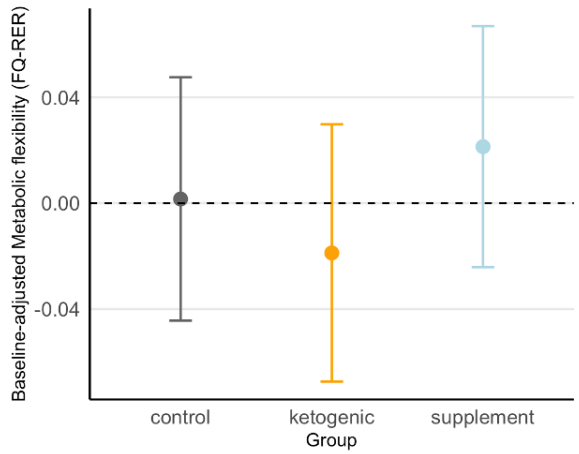

Figure 2. Baseline-adjusted fasting metabolic flexibility (FQ-RER) by group. Baseline-adjusted estimated marginal means (±95% CI) for metabolic flexibility (FQ-RER) after four weeks in the control (CON), ketogenic diet (WMKD), and ketone ester supplementation (SUPP) groups. No significant differences were detected between groups (all pairwise comparisons ns). The dashed line represents a difference of 0, indicating alignment between fasting RER and dietary FQ.

C55

Operating in the heat - The impact of carbohydrate ingestion on physical work capacity and thermoregulatory responses.

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Introduction: Carbohydrate (CHO) availability is a key determinant of physical work capacity (PWC), particularly during prolonged activity in hot environments where thermal strain, cardiovascular load, and fatigue are elevated. As such, identifying nutritional strategies that support both metabolic stability and heat tolerance has growing relevance for occupational, military, and sporting settings, against the backdrop of increased global warming.

The glycaemic index (GI) of carbohydrate (CHO) sources reflects the rate at which glucose enters circulation, thereby shaping substrate utilisation and fatigue resistance, with downstream implications for metabolic heat production, thermoregulatory strain and ultimately ohysical work capacity. Indeed, rapidly absorbed, high-GI carbohydrates can provoke sharp fluctuations in blood glucose and insulin, which may impair metabolic stability and gastrointestinal comfort. In contrast, low-GI carbohydrates provide a slower, more sustained glucose release that may better preserve endogenous glycogen stores and support prolonged work under thermal stress.

While low-GI CHO ingestion has been shown to enhance endurance performance in temperate environments, evidence under heat stress remains limited. Recent work suggests that heat exposure reduces the oxidation of rapidly absorbed carbohydrates due to impaired exogenous glucose utilisation under thermal strain, increasing reliance on muscle glycogen and highlighting the potential advantage of slower-release CHO sources. However, the interaction between CHO glycaemic index, heat strain, and physiological tolerance during prolonged submaximal work remains poorly understood.

Aim: To examine the impact of high- versus low-GI CHO ingestion on physical work capacity and heat tolerance during prolonged activity in the heat. Furthermore, this study aims to characterise the underlying physiological mechanisms during carbohydrate (CHO) ingestion in the heat, including metabolic, thermoregulatory, cardiovascular, and gastrointestinal responses.

Method: This study employs a repeated-measures, double-blind, randomised crossover design. Healthy adults (n = 27-30) will complete four experimental conditions under simulated heat stress: (1) rest with high-GI CHO, (2) rest with low-GI CHO, (3) exercise with high-GI CHO, and (4) exercise with low-GI CHO. Each condition will follow a 12-hour fast after which, participants will ingest 1 $g \cdot kg^{-1}$ body mass of either a fast-release or slow-release CHO drink.

Resting trials will involve three hours of supine rest, while exercise trials consist of three hours of treadmill walking while carrying a 7 kg rucksack to simulate occupational or military load carriage. Exercise intensity will be clamped at 130 $beats \cdot min^{-1}$ (governed by adaptive treadmill speed/inclined), reflecting World Health Organisation (WHO) safe upper limits for prolonged manual work.

Environmental heat stress will be induced using a water-perfused suit to replicate temperatures typically experienced during heat-wave conditions. Core and skin temperatures will be continuously monitored to assess mechanistic heat strain and ensure participant safety. Continuous glucose monitoring, capillary and venous blood sampling, indirect calorimetry, and cardiovascular measures will assess glucose regulation, substrate utilisation, energy expenditure and gut permeability.

Applications: This study will provide novel insight into how CHO glycaemic index modulates physiological tolerance and work capacity under heat stress, with implications for nutritional strategies aimed at sustaining human performance, productivity and function in increasingly hot environments. This study is undergoing ethical approval before participant recruitment.