Defining the Renal or Extra-Renal origin of Hypomagnesemia: diagnostic cutoff values based on urinary magnesium

Aude RITTER[1, 2, 3], Arthur MICHON COLIN[1, 2, 3], Anne BLANCHARD[1, 2, 3, 7, 8, 9], Marguerite HUREAUX[1, 2, 3, 4, 5, 8], Stéphanie BARON[1, 2, 3, 4, 8], Maude LANEY[1, 2, 3, 4, 5], Elise BOUDERLIQUE[1, 2, 3, 7, 8, 9], Marie COURBEBAISSE[1, 2, 3, 6, 8], Pascal HOUILLIER[1, 2, 3, 7, 8, 9], Caroline PROT-BERTOYE[1, 2, 3, 7, 8, 9]

[1] *Service de Physiologie-Explorations Fonctionnelles, Hôpital Européen Georges-Pompidou, Assistance Publique - Hôpitaux de Paris, Paris, France*

,

[2] *Centre de Référence constitutif des Maladies Rénales Héréditaires de l'Enfant et de l'Adulte (MARHEA), Filière de santé des maladies rares ORKID, Paris, France*

,

[3] *Centre de Référence constitutif des Maladies Rares du métabolisme du calcium et du phosphate CaP, Filière de santé des maladies rares de l'os, du calcium et du cartilage (OSCAR), Paris, France*

,

[4] *Université Paris Cité, Inserm, PARCC, Paris, France; Centre de Recherche Cardio-vasculaire de Paris, UMR970, Paris, France*

,

[5] *Service de Médecine Génomique, Hôpital Européen Georges Pompidou, Fédération de Génétique e de Médecine Génomique Assistance Publique-Hôpitaux de Paris Centre Université Paris Cité, Paris, France;*

,

[6] *Institut Necker Enfants Malades, INSERM U1151, Paris, France*

,

[7] *CNRS ERL 8228 - Laboratoire de Physiologie Rénale et Tubulopathies, F-75006 Paris, France.*

,

[8] *Faculté de Médecine, Université Paris Cité Paris, France*

,

[9] *Centre de Recherche des Cordeliers, INSERM, Sorbonne Université, Université Paris Cité, F-7500(Paris, France.*

Introduction :

Hypomagnesemia is a common electrolyte disorder with heterogeneous etiologies. Distinguishing renal from extrarenal magnesium loss is crucial for diagnosis and management but remains challenging in routine practice. We aimed to compare the diagnostic performance of urinary magnesium-based indexes and to establish clinically relevant cutoff values.

Methods :

We conducted a retrospective, single-center study including 88 adults with hypomagnesemia (≤0.63 mmol/L) who underwent a reference magnesium loading test to classify renal versus extrarenal origin. Nine urinary magnesium indexes were evaluated, including fractional excretion of magnesium (FEMg), magnesium-to-urinary creatinine ratio, urinary magnesium concentration, urinary magnesium excretion rate factored by glomerular filtration rate (UMgV̇/GFR), and 24-hour urinary magnesium excretion. Diagnostic performance was assessed

using ROC curves. Cutoff values were defined targeting ~90% specificity. External validation was performed in an independent cohort of 80 patients with genetically confirmed renal hypomagnesemia.

Results :

Fasting FEMg was an effective discriminator of renal magnesium loss (AUC 0.818; 95% CI 0.73 to 0.906). Fasting FEMg ≤1.2% predicted extrarenal hypomagnesemia with a specificity of 89% (sensitivity of 44%), whereas FEMg ≥3.5% predicted renal loss with a specificity of 91% (sensitivity of 51%). Fasting urinary magnesium concentration, fasting UMg$\dot{V}$/GFR, and FEMg calculated from 24-hour urine sample also performed adequately (AUC >0.75). Twenty-four-hour urinary magnesium excretion was not efficient to determine the origin of hypomagnesemia (AUC 0.681).

Conclusion :

Fasting fractional excretion of magnesium is an effective index for diagnosis between extrarenal and renal hypomagnesemia; 24-hour urinary magnesium excretion should no longer be used for this purpose.

Topic/s: Physiologie rénale

PLA2G4A mutations induce kidney damage resembling analgesic nephropathy through impaired prostaglandin signaling

Paul Coulot[1], Fabienne Charbit-Henrion[2], Olivier Corcos[2], Gérard Lambeau[3], Jean-Michel Correas[2], Emmanuel Letavernier[1, 4]

[1] *INSERM UMR S 1155*

,

[2] *Assistance Publique des Hôpitaux de Paris (AP-HP)*

,

[3] *CNRS*

,

[4] *Sorbonne Université*

Introduction

A 31-year-old patient presented with inflammatory bowel disease beginning in infancy, as well a stage 3 chronic kidney disease. Measured glomerular filtration rate (GFR) was 49.4 mL/min/1.7 m². Computed tomography revealed massive bilateral renal papillary calcifications associated with kidney stones, and Dynamic Contrast-Enhanced Ultrasound (DCE-CEUS) showed impaired papillary perfusion. Several stones were composed of calcium oxalate monohydrate (type Ia) an exhibited Randall's plaque (papillary calcifications). His older brother also presented with similar intestinal and kidney features.

Methods and Results

Whole-exome sequencing identified a homozygous pathogenic variant in the PLA2G4A gene in both brothers, establishing the diagnosis of cryptogenic multifocal ulcerating stenosing enteriti (CMUSE). PLA2G4A mutations impair A2 phospholipase activity, preventing the conversion of membrane glycerophospholipids into arachidonic acid. This deficiency results in reduced prostaglandin synthesis. Of note, analgesic nephropathy, caused by chronic use of acetaminophen, aspirin, and/or non-steroidal anti-inflammatory drugs, is characterized by massive papillary calcification, sharing similarities with lesions observed in both patients. Treatment with the prostaglandin E1 analogue misoprostol was initiated. GFR rapidly increased to 67.1 mL/min/1.73 m² (+36%) and remained stable 1 year later. DCE-CEUS showed decreased vascular resistance in the papilla and a reduction in papillary calcification. The same treatment was then proposed for his brother.

Conclusion

This case highlights the key role of prostaglandins in GFR regulation and papillary homeostasis and may help explain the analgesic nephropathy phenotype. Because the renal papilla is a majo source of prostaglandins in the kidney, their deficiency can lead to chronic medullary hypoperfusion, necrosis, and calcification.

Topic/s: Physiologie rénale

Improving eGFR Estimation Across Adolescence and Young Adulthood: interest of the EKFC Equation

Laurence Derain-Dubourg[1, 2, 3], Sandrine Lemoine[1, 2, 4], Laurence Chardon[5], Pierre Letourneau[1], Justine Bacchetta[6, 7], Aurélie De Mul[1, 2, 5]

[1] *Service de Néphrologie, Dialyse, Hypertension et Exploration Fonctionnelle Rénale, Centre de Référence des Maladies Rénales Rares MAREGE, filière maladies rares ORKID, Hôpital E. Herriot, Hospices Civils de Lyon, Lyon*

,

[2] *Faculté de Médecine Lyon Est, Université de Lyon*

,

[3] *CNRS UMR 5305, University of Lyon 1, Lyon*

,

[4] *INSERM CARMEN 1060 IRIS Team, Lyon*

,

[5] *Service de Biochimie et Biologie Moléculaire, Laboratoire de Biologie Médicale Multi-Sites (LBMMS), Hospices Civils de Lyon, Bron*

,

[6] *Centre de Référence Des Maladies Rénales Rares, Centre de Référence Des Maladies Rares du Calcium Et du Phosphore, Filières Maladies Rares ORKiD, OSCAR Et ERK-Net, Hôpital Femme Mère Enfant, bron*

,

[7] *INSERM UMR 1033 LYOS, Lyon*

Introduction

Estimating glomerular filtration rate (GFR) is essential for chronic kidney disease (CKD) diagnosis and management. The transition from pediatric (CKiD-U25) to adult (CKD-EPI 2009) equations during adolescence may induce implausible variations in estimated GFR (eGFR). The EKFC equation was developed to provide a continuous, age-adapted estimation across the lifespan. This study compares the performance of these equations in adolescents and young adults.

Materials and Methods

We included 1,278 patients aged 12–40 years with measured GFR (mGFR) assessed by iohexol clearance. EKFC performance was compared with CKiD-U25 and CKD-EPI equations. Results are expressed as median (IQR) or percentages.

Results

Median age was 21.9 years, and median mGFR was 82.4 mL/min/1.73 m². CKD stages were: 36.5% stage 1, 44.2% stage 2, 17.2% stage 3, and 2.1% stages 4–5.

In patients aged 12-15 and 15–18 years, CKiD-U25 and EKFC showed similar performance (P30 > 83%). In the 18–25 group, both remained comparable (P30 ~75%), whereas CKD-EPI performed poorly (P30 48.5%). In adults aged 25–40 years, EKFC outperformed CKD-EPI (P30 76.9% vs. 69.4%, p=0.006).

Conclusions

CKiD-U25 and EKFC perform similarly between 12 and 25 years, while CKD-EPI is unsuitable in younger populations and inaccurate in young adults. From 25 to 40 years, EKFC slightly outperforms CKD-EPI. EKFC may therefore be preferred during the transition to adulthood to avoid abrupt eGFR changes and improve early CKD detection.

Topic/s: Physiologie rénale

ASSESSMENT OF THE NEPHROTOXIC EFFECTS OF *Carlina gummifera* L. INCENSE: A BIOCHEMICAL AND HISTOPATHOLOGICAL APPROACH

Dorsaf Hallegue[1], Rania Ben Salah[1], Houda Bellamine[2], Mohsen Sakly[1], Khemais Ben Rhouma[1]

[1] *University of Carthage, Faculty of Sciences of Bizerte, Integrated Physiology Laboratory LR17ES02 Zarzouna 7021, Bizerte, Tunisia.*

,

[2] *Regional Hospital Menzel Bourguiba, Department of Anatomy and Cytological Pathology, Bizerte, Tunisia.*

Introduction: Incense derived from *Carlina gummifera* L. is traditionally burned for religious and ritual purposes. This study aims to evaluate the toxicological and oxidative effects induced by incense from the rhizome of *Carlina gummifera* L. on renal function in Wistar rats.

Material and Methods: *Carlina gummifera* L. rhizomes were collected, dried, and finely ground. Adult Wistar rats were divided into three treated groups and exposed daily, for 60 minutes over 15 consecutive days, to incense smoke from the rhizome at doses of 2 g (2C), 4 g (4C), and 6 g (6C), while a control group was subjected to the same conditions in the absence of smoke.

Results: Inhalation of incense generated from the combustion of the rhizome induced renal atrophy across the three doses, accompanied by a significant increase in renal biomarkers (creatinine and urea; $p<0.01$) compared with control animals breathing ambient air. Assessment of oxidative status and evaluation of the antioxidant system revealed that the incense exhibits pro-oxidant activity, as evidenced by an elevation in malondialdehyde levels at all tested doses compared with controls. Our results also indicate that the incense causes an imbalance in the antioxidant system, leading to a state of oxidative stress. Microscopic analysis revealed an alteration of tissue architecture as well as structural damage to the organs compared with control animals.

Conclusion: The deterioration of renal biomarkers and the antioxidant system, together with histological abnormalities, suggests that nephropathy induced by incense from *Carlina* occurs through an oxidative mechanism mediated by the adrenal gland.

Topic/s: Exposome

Efficient removal of oxalate from tea by pre-infusion

Cécile CLEMENT[1], Jordan Desenclos[1], Valentine FORTE[1], Carole MARTORI[1], Michel DAUDON[1, 2], Emmanuel LETAVERNIER[1, 2, 3]

[1] *Service des Explorations Fonctionnelles Multidisciplinaires – Hôpital Tenon, APHP – Paris –France*
,
[2] *Inserm UMR S 1155 – Hôpital Tenon – Paris –France*
,
[3] *Sorbonne Université, UFR de médecine – Paris – France*

Most kidney stones are made of calcium oxalate. Dietary oxalate comes from plants, including tea. Many kidney stone formers stop drinking tea, which is not always replaced by other beverages, resulting in reduced diuresis and a paradoxically increased risk of lithogenesis. The oxalate in tea diffuses rapidly during infusion. We hypothesized that pre-infusion of tea could significantly reduce its oxalate content.

Tea bags were infused for 30 seconds, 1 minute, 2 minutes or 3 minutes in 200 mL water, with or without a pre-infusion of 10, 30 or 60 seconds (16 conditions, n=4/condition). Oxalate concentration was measured by ion chromatography. A blind organoleptic analysis was carried out by 4 operators, with satisfaction scores and an analysis of 9 tea characteristics.

Without pre-infusion, oxalate concentration rose from 0.36±0.05 mmol/l after 30 seconds to 0.63±0.09 mmol/l at 3 minutes ($p<0.05$), with a plateau after 2 minutes. A 10-second pre-infusion reduced oxalate concentration by 10 to 33% depending on infusion time ($p<0.05$). A 30 seconds pre-infusion reduced it by 38 to 51% ($p<0.05$) and a 1 minute pre-infusion by 59 to 65% ($p<0.05$). Prolonged infusion enhanced certain tea characteristics (taste, astringency, etc.), but pre-infusion had no significant impact on satisfaction scores for taste, smell or visual appearance.

Pre-infusion of tea significantly reduces oxalate intake (by up to 2/3 depending on conditions), while moderately affecting the organoleptic qualities of the tea. This simple method could be recommended to kidney stone formers.

Topic/s:Métabolisme et Nutrition

BODY COMPOSITION OF ATHLETE'S: A COMPARATIVE STUDY BETWEEN FOOTBALL AND BASKETBALL PLAYERS

Abdou Khadir SOW[1, 2], Chérif Ousseynou Laye THIOM[1], Mame Diarra Bousso NDIAYE[1], Mor DIAW[1 2], Mame Saloum COLY[3], Salimata Diagne HOUNDO[1], Maimouna TOURE[1, 2], Aissatou SECK[1], Awa BA[2, 4], Abdoulaye BA[1, 2]

[1] *Laboratoire de Physiologie et d'Explorations Fonctionnelles, FMPO/UCAD, Sénégal*

,

[2] *Laboratoire de Recherche International Environnement, Santé & Sociétés, CNRS-UCAD, Dakar, Sénégal*

,

[3] *Laboratoire de Physiologie, UFR des Sciences de la Santé, Thiès, Sénégal*

,

[4] *UFR de Santé et Développement durable, Université Alioune Diop de Bambey*

Introduction: Body composition measurement is of great interest for the physical preparation of athletes due to its predominant role in athletic performance. Changes in body compartments related to practice can vary depending on the sport. This is how we compared the body composition of football players to that of basketball players.

Methods: This was a cross-sectional study aimed at comparatively analyzing the body composition measured by electronic bio impedance analyzer of football players with that of Senegalese basketball players. Parameters such as fat, lean and muscle mass were classified according to reference values. Body composition parameters are also related to the squared height to obtain the fat mass index (FMI), lean mass index (LMI) and skeletal muscle mass index (SMI).

Results: A total of 44 athletes (31 football players) participated in the study. They were all male and comparable in terms of age and BMI. However, fat mass and its index were significantly higher in football players. Unlike lean and muscle mass, LMI and SMI were more important in basketball players. Comparison of the frequency between the classes of body fat showed a significant difference with high body fat in 58.1% of football palyers vs 0%. High muscle mass was significantly more frequently found in basketball players with 92.3% vs 38.7%.

Conclusion: Basketball players seemed to have composition parameters better suited to high-level sports practice than the football players we explored.

Topic/s: Sport, Exercice

FIELD EVALUATION OF THE SICKLE CONFIRM™ POINT-OF-CARE TEST FOR HEMOGLOBIN S AND ZYGOSITY IN SUB-SAHARAN AFRICA

Mor DIAW[1, 2], Awa DIOP[3], Abdou Khadir SOW[1, 2], Louis A. Diaga DIOUF[4], Aissatou SECK DIOP[1], Salimata H DIAGNE FAYE[1], Maimouna TOURE[1], Abdoulaye BA[1, 2]

[1] *Laboratoire de Physiologie Humaine, Faculté de Médecine, de Pharmacie et d'Odontologie, Université Cheikh Anta Diop, Dakar, Sénégal.*

,

[2] *2 IRL3189 – CNRS Environnement, Santé, Sociétés, Dakar, Sénégal.*

,

[3] *Saint Louis University, St. Louis, MO, USA.*

,

[4] *Laboratoire de Biophysique Pharmaceutique, Université Cheikh Anta DIOP, Dakar, Senegal*

Introduction: Sickle cell disease (SCD) remains underdiagnosed in sub-Saharan Africa due to limited

access to reliable, affordable, and field-adapted diagnostic tools. This study aimed to independently assess the diagnostic performance of the Sickle Confirm™ test under routine clinical conditions in Senegal.

Material and Methods : A total of 100 participants were enrolled at the National Blood Transfusion Center (CNTS) in

Dakar. Genotypes were confirmed via hemoglobin electrophoresis and compared to results from the Sickle Confirm™ test. The cohort included individuals with HbSS (56%), HbAS (21%), and HbAA (23%) genotypes. Diagnostic metrics, sensitivity, specificity, and Cohen's kappa, were calculated with 95% confidence intervals (CIs).

Results : Sickle Confirm™ demonstrated perfect concordance with the reference method across all

genotypes. The test identified all 56 HbSS, 21 HbAS, and 23 HbAA cases without any false positives or false negatives. Sensitivity and specificity were 100% (95% CI: HbSS – 93–100%; HbAS – 84–100%; HbAA – 85–100%), and Cohen's kappa was 1.00, indicating perfect agreement. The test maintained excellent performance in a real-world setting characterized by high temperatures (30–35 °C), relative humidity levels ranging from 55% to 80%, despite limited laboratory infrastructure.

Discussion/Conclusion: Sickle Confirm™ is an accurate, cost-effective (~$1/test), and field-adapted complement to

existing sickle cell diagnostic tools. While it demonstrates excellent diagnostic accuracy, its

current format requires a tabletop centrifuge and prior hematocrit measurement, which may

limit use in some low-resource settings. Further evaluation of the qualitative version is needed

to enhance practicality and broaden its applicability across healthcare settings in Africa.
Topic/s: Physiologie respiratoire

Enhanced Fibrogenic Pathways Define Scleromyositis Within the Spectrum of EULAR/ACR Myositis Subsets

Margherita Giannini[1, 2], Giulia Quiring[2], Benjamin Ellezam[3], Yves Troyanov[4], Léa Debrut[2], Gilles Laverny[5], Bernard Geny[2, 6], Marie Hudson[7], Océane Landon-Cardinal[8], Alain Meyer[1, 2]

[1] *Service de Physiologie et explorations fonctionnelles, University Hospital of Strasbourg, Strasbourg, France ; Centre de Référence des Maladies Autoimmunes Rares, University Hospital of Strasbourg, Strasbourg, France*

,

[2] *Unité de Recherche 3072 (UR3072), Centre de Recherche en Biomédecine, University of Strasbourg, Strasbourg, France*

,

[3] *Division of Pathology, Centre Hospitalier Universitaire (CHU) Sainte-Justine, Department of Pathology and Cell Biology, Université de Montréal, Montréal, QC, Canada*

,

[4] *Division of Rheumatology, Hôpital du Sacré-Coeur, Department of Medicine, Université de Montréal, Montréal, QC, Canada*

,

[5] *Université de Strasbourg, CNRS, Inserm, IGBMC UMR 7104-UMR-S 1258, Illkirch, France*

,

[6] *Service de Physiologie et explorations fonctionnelles, University Hospital of Strasbourg, Strasbourg, France*

,

[7] *Division of Rheumatology, Jewish General Hospital, Department of Medicine, McGill University, Montréal, QC, Canada*

,

[8] *Division of Rheumatology, Centre Hospitalier de l'Université de Montréal (CHUM), Autoimmunity Research Laboratory, CHUM Research Center, Montréal, QC, Canada Department of Medicine, Université de Montréal, Montréal, QC, Canada*

Introduction: The current EULAR/ACR classification criteria recognize four subsets of inflammatory myopathies (IM): dermatomyositis (DM), immune-mediated necrotizing myopathy (IMNM), inclusion body myositis (IBM), and antisynthetase syndrome (ASyS). We and others have identified scleromyositis (SM) as a fifth subset that differs from the above by the presence of scleroderma features (fulfilling or not the 2013 ACR/EULAR criteria for systemic sclerosis (SSc)), SSc-specific or overlap autoantibodies (most frequently anti-PM/Scl, -U1-RNP, and -Ku), and a distinctive muscular capillaropathy [Ellezam B. Neuropathol Appl Neurobiol. 2022 Dec;48(7):e12840]. These patients are often misclassified as seronegative IMNM or ASyS using current EULAR/ACR IM criteria. We tested the hypothesis that this subset also differs from other IM subsets by a distinct muscle transcriptomic signature.

Material and methods: In a bicentric cohort (Strasbourg–Montreal), 54 untreated patients with IM at the time of diagnosis were included (SM=23, DM=10, IMNM=8, ASyS=9, IBM=4), along with 7 non-neuromuscular controls. Clinico-sero-pathological data were collected at diagnosis and at last follow-up. Transcriptomic sequencing was performed using total RNA extracted from diagnostic muscle biopsies, and pathway enrichment analysis was conducted on differentially expressed genes ($|logFC|>0.5$; adjusted $p<0.05$) using WebGestalt 2024.

Results: Subjects in each subset were comparable regarding age at diagnosis, sex ratio, muscle biopsy site, and sample origin ($p>0.05$). Compared to other IM subsets, SM patients exhibited higher frequencies of sclerodactyly (62%, $p<0.0001$), Raynaud's phenomenon (61%, $p=0.002$), limited cutaneous sclerosis (57%, $p=0.0006$), telangiectasias (52%, $p=0.003$), interstitial lung disease (47.6%, $p=0.03$), puffy fingers (38%, $p=0.02$), and arthritis (38%, $p=0.07$). The SM cohort encompassed a broad serological spectrum of the disease, including 4 anti-PM/Scl+, 5 anti-U1-RNP+, 4 anti-Ku+, 2 anti-RNA Pol III+, 1 anti-NVL+, 1 anti-Scl70+, 1 anti-RuvBL1/2+, and 5 seronegative patients. A total of 239 genes were specifically dysregulated in SM muscle compared with the four other IM subsets and controls (168 upregulated, 71 downregulated). These genes were enriched in pathways related to collagen formation and extracellular matrix remodelling.

Discussion/Conclusion: Consistent with their distinctive clinical, serological, and histopathological features, SM patients differ from other IM subsets by enhanced activation of fibrogenic molecular pathways in muscle tissue. These findings further support the hypothesis that SM represents a distinct IM subset that should be recognized in future IM classification criteria, and that myositis constitutes a target organ involvement in SSc. Muscle fibrosis activation may represent both a diagnostic biomarker and a potential therapeutic target for SM

Topic/s: Muscle

Claudin 10 plays a critical role in ion transport in the thick ascending limb of Henle’s loop

Yann Boudard[1, 2], Gaëlle Brideau[1, 2], Pravina Muthan[1, 2], Camille Griveau[1, 2], Lydie Cheval[1, 2], Loïc Lievre[1, 2], Pascal Houillier[1, 2, 3, 4, 5], Caroline Prot-Bertoye[1, 2, 3, 4, 5]

[1] *1. Centre de Recherche des Cordeliers, INSERM, Sorbonne Université, Université de Paris, F-7500 Paris, France.*

,

[2] *2. CNRS ERL 8228 - Laboratoire de Physiologie Rénale et Tubulopathies, F-75006 Paris, France.*

,

[3] *3. Assistance Publique-Hôpitaux de Paris, Hôpital Européen Georges Pompidou, Département de Physiologie, F-75015 Paris, France.*

,

[4] *4. Centre de Référence des Maladies Rénales Héréditaires de l'Enfant et de l'Adulte (MARHEA), F-75015 Paris, France.*

,

[5] *5. Centre de Référence des Maladies Rares du Calcium et du Phosphate, F-75015 Paris, France.*

Background :

Claudins (Cldn) determine the permeability and selectivity of the paracellular pathway. Cldn10b is expressed in the thick ascending limb (TAL) of Henle’s loop, where the paracellular pathway is more permeable to sodium than to chloride (PNa>PCl), allowing for the generation of a lumen positive transepithelial voltage (Vte), which drives passive cation reabsorption. Cldn10b variants cause HELIX syndrome, including a renal loss of sodium chloride and hypermagnesemia. Parathyroid hormone (PTH) increases cation reabsorption in the cortical TAL (CTAL), but whether Cldn10b is involved in its effects is unknown. We aim to delineate the role of Cldn10b in basal and PTH-stimulated transepithelial ion transport in the CTAL.

Methods

Murine Cldn10+/+ and Cldn10-/- CTALs were microperfused in vitro to measure Vte, paracellular ion permeabilities and PNa/PCl. All measurements were made under control conditions and/or after peritubular addition of PTH (10-10 M).

Results

In CTAL, Cldn10b decreases PCl and increases Vte. PNa/PCl fluctuates along Cldn10+/+ CTAL in parallel with Cldn10 expression. PTH increases PNa/PCl via an effect on Cldn10b, mediated by cAMP- and cytosolic calcium-dependent signaling, and changes in intracellular protein trafficking. Cldn10b increases the energetic yield of transepithelial ion transport, both under baseline and PTH-stimulated conditions.

Conclusions

In CTAL, Cldn10b determines the paracellular chloride permeability and Vte oscillations. Both directly and indirectly, Cldn10b plays a critical role in basal and PTH-stimulated paracellular

reabsorption of sodium and divalent cations.
Topic/s: Physiologie rénale

Growth Differentiation Factor 15 in Gitelman Syndrome : a potassium regulator ?

Emmanuel Wirth[1, 2], Gilles Crambert[1], Lydie Cheval[1]

[1] *Centre de Recherche des Cordeliers*

,

[2] *Pediatrics, Grenoble Universitary Hospital*

Introduction:

Hypokalemia represents a major clinical challenge in patients with Gitelman syndrome (GS), a genetic tubulopathy caused by biallelic Sodium-Chloride Cotransporter (NCC) inactivation. The severity of hypokalemia and the response to potassium supplementation vary widely among GS patients, yet the underlying factors of this variability remain unclear. Growth differentiation factor 15 (GDF15), a stress-responsive factor, has been shown to enhance renal potassium reabsorption in potassium-depleted mice, by stimulating the proliferation of type A intercalated cells (AICs) in the outer medullary collecting duct (OMCD). This study aims to investigate the role of GDF15 regarding potassium homeostasis in GS.

Material and Methods:

Urinary GDF15 level was measured in GS patients and healthy controls (living kidney donors). Urinary GDF15 to creatinine ratio (uGCR) was compared between groups, and correlations between uGCR and routine biological parameters were assessed among GS patients. Additionally, wild-type and GDF15 knockout mice will be subjected to a 15-day hydrochlorothiazide treatment to induce a Gitelman phenotype. To evaluate the effect of GDF15 in Gitelman-like mice, potassium homeostasis markers will be compared between the two groups, notably plasma potassium level and the proportion of AICs in OMCD. Prior to this comparative analysis, dose and route of the hydrochlorothiazide treatment are currently being optimized in wild-type mice, based on potassium depletion markers.

Results:

GS patients exhibited a 3.1-fold higher uGCR than controls ($p < 0.001$), though no correlation was observed between uGCR and the other parameters in GS patients (univariate and adjusted models). Animal experiments are currently ongoing.

Conclusion:

Elevated urinary GDF15 in GS patients may reflect chronic potassium depletion and potentially represents a compensatory mechanism to mitigate hypokalemia.

Topic/s: Physiologie rénale

Assessment of kidney function in football referees in Burkina Faso.

Wendsèndaté Yves SEMPORE[1], Amidou SAWADOGO[2], Mêdedonê Arielle Cynthia PALENFO[1], Valentin OUEDRAOGO[3], Arnaud Florent Tiendrebéogo TIENDREBEOGO[4], Teddy KOMBASSERE[1], Nafi OUEDRAOGO[1]

[1] *Physiology Laboratory, Institut Supérieur des Sciences de la Santé, Université Nazi BONI, Bobo-Dioulasso, Burkina Faso*

,

[2] *Nephrology Department,Centre Hospitalier Universitaire Sourô Sanou, Bobo-Dioulasso, Burkina Faso*

,

[3] *Faculty of Health Sciences, Université Lédéa Bernard Ouédraogo, Ouahigouya, Burkina Faso*

,

[4] *Faculty of Health Sciences, Université Joseph Ki-Zerbo, Ouagadougou, Burkina Faso*

Introduction: Good kidney function is essential for homeostasis. Repeated intense physical activity in athletes leads to hemodynamic and metabolic changes that can impair kidney function. Our main objective was to assess kidney function in football referees in Burkina Faso.

Materials and methods: We conducted a multicenter, cross-sectional study using prospective data collection among football referees in Burkina Faso. Glomerular filtration rate (GFR) was estimated based on fasting morning serum creatinine levels and calculated using the Cockcroft and Gault, the Modification of Diet in Renal Disease (MDRD) and the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) formulas. Urine test strips were used to screen for proteinuria, haematuria and leukocyturia. Data were recorded, processed and analyzed using EPI Data 3.1, Stata SE 13 and Microsoft Excel 2016 at a significance level of 5%.

Results: A total of 213 referees, including 20 women (9.39%), were included. The mean age was 30.58 ± 5.02 years. The mean body mass index (BMI) was 22.81 ± 3.23 kg/m², and 34 (14.55%) had a BMI above the normal range. The mean serum creatinine level was 111.51 ± 72.90 µmol/ for men and 93.84 ± 21.76 µmol/L for women. The mean glomerular filtration rate (GFR) estimated using the Cockcroft and Gault, MDRD and the CKD-EPI formulas was 105.4 ± 27.90 ml/min/1.73 m², 110.5 ± 29.68 mL/min/1.73 m² and 114.2 ± 27.25 mL/min/1.73 m² respectively. Using the CKD-EPI formula, 32 (15%) had a reduced GFR of between 60–89 mL/min. We noted proteinuria in 12 (5.63%), leukocyturia in 14 (6.57%) and haematuria in 2 (0.94%). Overall, a kidney abnormality was observed in 55 referees (25.82%). In bivariate analysis, age over 30 years (p=0.038) and federal grade (p=0.016) were significantly associated with the presence of a kidney abnormality.

Conclusion: Kidney function among football referees in Burkina Faso is generally satisfactory, despite the presence of abnormalities among the oldest and most experienced referees. This finding suggests that medical monitoring of these referees should be strengthened in order to detect any potential kidney disease at an early stage. It paves the way for a study into the impact of dehydration and heat stress on kidney function in athletes in our context.

Topic/s: Physiologie rénale

Characterization of calcineurin and its endogenous inhibitors in glomerulonephritis.

Anne-Lison VON NAGEL, Lilia Abbad, Christos Chatziantoniou

INSERM UMR-S 1155, Common and Rare Kidney Diseases, Hôpitla Tenon, Sorbonne Université, Paris, France

Background. Glomerulonephritis remains a common cause of end-stage kidney disease worldwide. Despite mechanistic advances, current treatments remain non-specific and partially effective. When undergoing renal kidney failure, patients may need a transplantation with immunosuppressive treatments. These are in general pharmacological calcineurin inhibitors (CNI), a serine/threonine phosphatase with inflammatory effects. Upregulated activation of calcineurin is involved in the development of glomerular diseases and CNI can be used against these glomerulopathies. Indeed, studies have shown that calcineurin binds to cytoskeletal proteins of podocytes leading to disruption of glomerular filtration barrier and the development of proteinuria. However, long-term use of these pharmacological inhibitors present serious side effects such as vascular cytotoxicity, the mechanisms of which remain unclear. Moreover, the existence of endogenous calcineurin inhibitors, Cabin1, Carabin and RCAN1, suggest physiological regulatory mechanisms that may represent a safer and more targeted therapeutic alternative. Calcineurin endogenous inhibitors have been wildly studied in the immune system and some have been investigated in the kidney, particularly in podocytes, but beyond this, few studies exist. The expression of calcineurin itself remains insufficiently characterized, especially in human tissues.

Here we aim to characterize the expression and localization of calcineurin and its endogenous inhibitors in experimental glomerulonephritis and seek the physiological relevance in human biopsies of different kinds of glomerulonephritis.

Materiel and methods. To explore the expression of calcineurin and its endogenous regulator in mouse kidney, we used a nephrotoxic serum (NTS)-induced glomerulonephritis preclinical model. To study the expression and localization of the catalytic subunit of calcineurin in humans we used the RNAscope method on renal biopsies from patients presenting different types of glomerulonephritis (lupus, IgA nephropathy, ANCA vasculitis).

Results. Cabin1 mRNA expression decreases as the disease progresses in total kidneys of NTS mice whereas RCAN1 and Carabin expression increases. In immunohistochemistry, Cabin1 is expressed in glomerular nuclei and immune cells, RCAN1 is expressed in tubules and Carabin is ubiquitous and appears to be localized in glomerular nuclei.

Calcineurin mRNA expression is downregulated with disease progression in kidneys of NTS mice. However, immunohistochemistry and mRNA of isolated glomeruli show that its glomerula expression increases. Calcineurin activity increase in NTS mice kidneys compared to the controlled.

Conclusion. Taken together, our data provide new insights into the expression and localization of endogenous calcineurin inhibitors and show that calcineurin activity increases in total kidney

with an upregulation of its glomerular expression under pathological conditions.
Topic/s: Physiologie rénale

Incidence and Characteristics of Antisynthetase Syndrome: A Quadruple-Source Capture-Recapture Survey Using the American College of Rheumatology/European League Against Rheumatism Classification Criteri

Margherita Giannini[1, 2], Léa Debrut[2, 3], Benoît Nespola[4], Béatrice Lannes[5], Delphine Klein[6], Michel Velten[6], Jean Sibilia[7], Bernard Geny[2, 8], Alain Meyer[1, 2]

[1] *Service de Physiologie et explorations fonctionnelles, University Hospital of Strasbourg, Strasbourg, France ; Centre de Référence des Maladies Autoimmunes Rares, University Hospital of Strasbourg, Strasbourg, France*

,

[2] *Unité de Recherche 3072 (UR3072), Centre de Recherche en Biomédecine, University of Strasbourg*

,

[3] *Faculty of Sport Sciences, European Centre for Education, Research and Innovation in Exercise Physiology (CEERIPE), University of Strasbourg, Strasbourg, France*

,

[4] *Laboratoire d'Immunologie, Plateau technique de Biologie, Strasbourg University Hospital, Strasbourg, France*

,

[5] *Département d'Anatomopathologie, Strasbourg University Hospitals, Strasbourg, France*

,

[6] *INSERM UMR-S1113, Registre des cancers du Bas-Rhin, Fédération de Médecine Translationnelle, University of Strasbourg, Strasbourg, France*

,

[7] *Centre de Référence des Maladies Autoimmunes Rares, University Hospital of Strasbourg, Strasbourg, France ; Rheumatology Department, Strasbourg University Hospitals, Strasbourg, France*

,

[8] *Service de Physiologie et explorations fonctionnelles, University Hospital of Strasbourg, Strasbourg, France*

Introduction: The ACR/EULAR criteria for antisynthetase syndrome (ASyS) have been recently developed (Zanframundo. Arthritis Rheumatol. 2024; 76 (suppl 9)).

The ASyS incidence using these criteria has never been studied in a population-based cohort.

Alsace (a region in Eastern France) hosts specialized centers for autoimmune, neuromuscular, and interstitial lung diseases (ILD). Universal health coverage and full reimbursement for ASyS make it an ideal setting for epidemiologic research.

This study aimed to determine the ASyS incidence in Eastern France using the ACR/EULAR ASyS criteria and to compare their performance with the 2017 EULAR/ACR inflammatory myopathies (IM) criteria.

Material and methods: The study covered 2006–2012, during which the IM incidence according to the 2017 EULAR/ACR criteria had been established (Debrut. Arthritis Rheumatol. 2023 Oct;75(10):1850-1855). Potential ASyS cases were identified from general practitioners and community specialists, public and private hospital records, laboratory databases, pathology

archives. For all potential cases, data were extracted using a standardized form after manual review of medical records. Incident cases (diagnosed between January 1, 2006, and January 1, 2013, among Alsace residents), meeting at least “possible ASyS” ACR/EULAR criteria were included. Incomplete case ascertainment across the four sources was adjusted using a capture–recapture analysis.

Results: Among 1742 potential ASyS cases identified, after excluding patients who did not meet IM or ASyS criteria (n=1030), those living outside Alsace (n=284), and those with incident IM before the study period (n=308), 28 patients were diagnosed with ASyS between 2006 and 201 (definite=21, probable=2, possible=5).

The estimated number of cases missed by any source was 3.2 after capture-recapture analysis. Estimated incidence was 2.11 cases/million inhabitants/year (95% CI 1.37–2.85).

Most patients were female (75.9%) with a median age of 57.5 years (IQR 41.8–69.5). Twenty patients tested positive for anti-Jo-1, 6 for anti-PL12, 2 for anti-PL7.

At last follow-up, only 8/26 patients (30.8%) showed the complete clinical triad. ILD and arthriti were isolated triad features in 5/25 (20%) and 5/27 (18.5%) patients, respectively. Myositis was always associated with arthritis in 2/14 (14.3%) or ILD in 4/15 (26.7%) patients.

Only 14 of the ASyS patients (50%) also met the 2017 EULAR/ACR IM criteria (definite: n=9; probable: n=5. Polymyositis: n=11, dermatomyositis: n=3).

Conclusion: This population-based study provides a reliable estimate of ASyS incidence and highlights the high frequency of ILD and arthritis. Half of the cases were missed by the 2017 EULAR/ACR IM criteria, emphasizing the improvement enabled by the ACR/EULAR ASyS criteria.

Topic/s: Muscle

Hand radiographs lesions in antisynthetase syndrome arthritis versus rheumatoid arthritis: a monocentric case control cross-sectional study

Margherita Giannini[1], Cerise Guillochon-Petitcuenot[2], Thibault Willaume[3], Guillaume Bierry[3], Julien Blaess[4], Giulia Quiring[5], Simone Perniola[6], Julien Campagne[7], Bernard Geny[4, 5], Alain Meyer[1, 2]

[1] *Service de Physiologie et explorations fonctionnelles; Centre de Référence des Maladies Autoimmunes Rares, University Hospital of Strasbourg; UR3072, Centre de Recherche en Biomédecine, University of Strasbourg, France*

,

[2] *Service de Rhumatologie, Centre de Référence des Maladies Autoimmunes Rares, University Hospital of Strasbourg, France*

,

[3] *Service de Radiologie, University Hospital of Strasbourg, France*

,

[4] *Service de Physiologie et explorations fonctionnelles, University Hospital of Strasbourg, France*

,

[5] *UR3072 Centre de Recherche en Biomédecine, University of Strasbourg, France*

,

[6] *Rheumatology Unit, University Hospital of Bari, Italy*

,

[7] *Internal Medecine, UNEOS Metz, France*

Introduction. Arthritis occurs in up to 90% of patients with antisynthetase syndrome (ASyS). It i a hallmark of this disease and is associated with poor quality of life.

Peculiar hand radiographs patterns have been described in rheumatoid (RA) and psoriasis arthritis. Whether ASyS arthritis is also characterised by typical hands radiographs lesions has been poorly studied.

The aim of this study was to assess the hand radiographs findings of ASyS arthritis versus RA.

Methods. A systematic literature review (SLR) was performed to retrieve candidate lesions on hand radiographs.

All ASyS patients with arthritis and available hand radiographs were included. Consecutive RA patients of the same centre, matched for age, sex and disease duration, were included as controls.

ASyS was defined by Connors' criteria and anti-CCP and rheumatoid factors negativity. RA was diagnosed according to 2010 ACR/EULAR criteria and ASyS antibodies negativity. Arthritis was defined by clinical and/or sonographic synovitis of small joints (with or without large joints involvement).

The last available hand radiographs were read by two rheumatologists and one radiologist blinded for the diagnosis. Candidate lesions identified in the SLR (bone erosions, joint narrowing, joint subluxations and capsular calcifications) were quantified on both hands fingers and carpal joints as previously described (Sharp JT. Arthritis Rheum. 1985 Dec;28(12):1326-35)

Results. Forty ASyS patients (30 females, 75%) and fifty-four RA patients (34 females, 62.3%), age of 55 (±14.1) and 60.4 (±14.1) years respectively (p=0.1), were included. Disease duration at the hand radiographs time was 5.1 (±6.6) and 7.2 (±6.5) years respectively (p=0.1).

Hand radiographs lesions were found in 21 ASyS patients (47%) including bone erosions (n=4), joint narrowing (n=16), joint subluxations (n=13) and capsular calcifications (n=13).

In ASyS, the capsular calcification score was 7-fold higher than in RA [4 ± 8 vs 0.6 ± 1.4, p=0.003]. The DIP joint of the second and the third fingers were the most frequently involved. Subluxation score was not significantly different [0.9 ± 2.1 vs 1.8 ± 4.3, p=0.2]. In ASyS, subluxations mainly involved the distal joints and the thumb. In contrast, the joint narrowing score was about 7 times lower [3.6 ± 7.4 vs 24.5 ± 28.9, p=0.0001] while bone erosion score was more than 20-fold lower [0.4 ± 1.8 vs 9.2 ± 17.3, p=0.001] in ASyS.

Conclusion. Capsular calcinosis and joint subluxations of distal joints and thumb are hallmarks of ASyS arthritis supporting it as a peculiar rheumatic disease, part of the syndrome.
Topic/s: Muscle

QUALITY AUDIT OF SPIROMETRY TESTS PERFORMED IN OUAGADOUGOU BURKINA FASO

Arnaud Jean Florent TIENDREBEOGO[1, 2], K. Augustin SAWADOGO[1], Soumaïla MAIGA[1, 2], Valentin OUEDRAOGO[3], W. Yves SEMPORE[4], Nafi OUEDRAOGO[4], Edmond BONSA[1], Ghislain BOUGMA[2], Martial OUEDRAOGO[1, 2]

[1] *U.F.R.S.D.S. - Université Joseph KI-ZERBO*

,

[2] *Service de Pneumologie - CHU Yalgado OUEDRAOGO*

,

[3] *ESSAN - Université Lédéa Bernard OUEDRAOGO*

,

[4] *INSSA - Université Nazi BONI*

Introduction - Spirometry, which measures lung volumes and airflow rates, is the basic functional test of the respiratory system. Assessing the quality of these tests, a systematic prerequisite to interpretation, is essential to ensure the reliability of the results and optimize patient care. The objective was to study the quality of spirometry tests performed in Ouagadougou. Material and Methods - This was a descriptive and analytical cross-sectional study involving retrospective data collection over an eight-year period from January 2017 to December 2025, covering all spirometry tests performed in three respiratory function testing centres in Ouagadougou. Results - A total of 1,664 spirometry tests were included in our study. The study population was predominantly male (52.3%), with a mean age of 43.9 ± 14 years and a mean BMI of 26.1 ± 6 kg/m². The duration of forced expiratory flow and the absence of artefacts on the flow-volume curve were the most difficult quality criteria to achieve, in 38.6% and 65.1% of cases, respectively. The overall acceptability rate of spirometry tests was 65.4% (1,088/1,664 tests). Of 345 tests (20.1%) with at least two acceptable curves, 153 were reproducible (44.4%). In total, 16.8% of spirometry tests (281/1664) were judged to be of satisfactory quality (grades A, B, and C) according to the ATS/ERS-2019 standards. Advanced age (OR = 1.01 per year; p = 0.008) and male sex (OR = 0.79; p = 0.025) were significantly associated with the risk of poor-quality spirometry. Discussion/Conclusion - Our results are well below the 80% of good quality tests expected according to international standards for spirometry quality, and reinforce the importance of mastering and practicing the different stages of performing spirometry, a crucial condition for ensuring reliable results.Keywords - Audit - Quality - Spirometry - Ouagadougou - ATS/ERS
Topic/s: Physiologie respiratoire

PREVALENCE OF SMOKING AMONG HIGH SCHOOL STUDENTS IN OUAGADOUGOU IN 2026.

Arnaud Jean Florent TIENDREBEOGO[1, 2], Issa OUEDRAOGO[1], Ghislain BOUGMA[2], Valentin OUEDRAOGO[3], W. Yves SEMPORE[4], Soumaïla MAIGA[1, 2], Edmond BONSA[1], Martial OUEDRAOGO[1, 2], Nafi OUEDRAOGO[4]

[1] *U.F.R.S.D.S. - Université Joseph KI-ZERBO*

,

[2] *Service de Pneumologie - CHU Yalgado OUEDRAOGO*

,

[3] *ESSAN - Université Lédéa Bernard OUEDRAOGO*

,

[4] *INSSA - Université Nazi BONI*

Introduction - Although smoking is declining among adults according to WHO data, it is regaining popularity among adolescents due to the advent of new tobacco products. Our objective was to assess smoking rates among high school students in Ouagadougou.

Material and Methods - This was a cross-sectional descriptive and analytical study with prospective data collection, using a self-administered questionnaire supplemented by measurement of exhaled carbon monoxide using a carbon monoxide tester (Smokerlyzer®). The study took place from January 5 to 18, 2026, in a private high school in Ouagadougou.

Results - A total of 260 students were included in our study, with 65.38% being girls, and a mean age of 17.48 ± 1.64 years. Nearly half of the students (46%, n=120) had smoked at least once previously, and active smoking was reported by 82 students (31.5%) according to the questionnaire and 24 students (9.2%) according to CO measurement ($p<0.001$). Smoking initiation was early, between 13 and 15 years of age, for the majority of smokers (45%, or 54 students), with curiosity being the main reason (40.8%) ; and hookah being the most commonly used form of tobacco (36.6%). Factors associated with smoking according to both methods were sex, presence of smoking friends, and presence of a co-addiction (alcoholic beverages, energy drinks, psychoactive substances) ($p<0.05$).

Discussion/Conclusion - Smoking in all its forms remains a widespread practice in schools in Ouagadougou. However, the trend is toward the use of new tobacco products and early initiation of smoking, with curiosity being the primary motivation among students.

Keywords - smoking ; student ; carbon monoxide ; co-addiction ; Ouagadougou.
Topic/s: Physiologie respiratoire

POSITIONAL OBSTRUCTIVE SLEEP APNEA DIAGNOSED BY RESPIRATORY POLYGRAPHY : PREDICTIVE FACTORS AND PHENOTYPIC STABILITY COMPARED TO POLYSOMNOGRAPHY

Chakib AHMED ALI[1, 2], Naira Mkrtchyan[1, 2], Virginie FERRY[1, 2], Marie-Pia D Ortho[1, 2, 3], Justine FRIJA[1, 2, 3]

[1] *Assistance Publique Hôpitaux de Paris, Paris, France*

,

[2] *Université Paris Cité*

,

[3] *Inserm Neurodiderot*

Introduction

Positional obstructive sleep apnea (POSA), defined by a supine AHI at least twice the non-supine AHI, represents a clinically relevant phenotype that may influence therapeutic decisions. Respiratory polygraphy (RP) is widely used as a first-line diagnostic tool, but its ability to reliably identify POSA compared to polysomnography (PSG) remains uncertain. This study aimed to identify predictive factors of POSA diagnosed by RP and to assess the phenotypic stability between RP and PSG.

Methods

This retrospective study included patients investigated for obstructive sleep apnea at Bichat Hospital (Paris, France) between 2020 and 2024. Two analyses were conducted. First, POSA patients (n=316) were compared to non-positional OSA patients (n=261) on clinical, symptomatic and polygraphic variables. Univariate logistic regression was performed to identify predictors of POSA. Second, among POSA patients who subsequently underwent PSG (n=75), a intra-patient paired analysis assessed phenotypic stability between the two recordings. Continuous variables were expressed as median [IQR] and compared using Mann-Whitney or Wilcoxon signed-rank tests. Categorical variables were compared using Chi-square or Fisher's exact tests. Statistical significance was set at $p<0.05$.

Results

In the comparative analysis (n=577), lower BMI (OR=0.95, 95%CI [0.93–0.98], p<0.001), male sex (OR=1.40, 95%CI [1.00–1.94], p=0.048), lower total AHI (OR=0.96, 95%CI [0.95–0.97], p<0.001), higher mean oxygen saturation (OR=1.14, 95%CI [1.06–1.23], p<0.001) and lower oxygen desaturation index (OR=0.97, 95%CI [0.95–0.98], p<0.001) were significantly associated with POSA. In the paired analysis (n=75), PSG recorded significantly higher AHI values compared to RP (total AHI: 23.1 [13.9] vs 10.2 [8.2], p<0.001; supine AHI: 31.8 [27.6] vs 19.0 [18.0], p<0.001). Oxygen desaturation index was also significantly higher on PSG (14.6 [13.7] v 10.3 [8.0], p<0.001), while mean oxygen saturation remained stable. Phenotypic concordance between RP and PSG was observed in only 58.7% of patients (44/75, 95%CI [47.4%–69.1%]).

Conclusions

POSA diagnosed by RP is associated with specific polygraphic and demographic characteristics, particularly the distribution of respiratory events across sleep positions. However, phenotypic stability between RP and PSG is limited, with only 58.7% of patients retaining a positional phenotype on PSG. These findings suggest that RP may not be a reliable tool for POSA phenotyping, with potential implications for therapeutic decision-making.

Topic/s: Physiologie respiratoire

CORTICOSTERONE PROMOTES SWEET PREFERENCE AND METABOLIC ALTERATIONS LEADING TO OBESITY IN PSAMMOMYS OBESUS

Hassiba BENBAIBECHE[1], Abdenour BOUNIHI[2], Hamza SAIDI[2], Naim Akhtar Khan[3]

[1] *Laboratoire de Valorisation et Bio-ingénierie des Ressources Naturelles, Faculté des Sciences, Université Alger 1, Benyoucef Benkhedda. Algérie*

,

[2] *Université des sciences et de la technologie Houari Boumediene, Faculté des sciences biologiques, Laboratoire de biologie et physiologie des organismes, Équipe de bioénergétique et métabolisme intermédiaire, Alger, Algérie*

,

[3] *Physiologie de la Nutrition & Toxicologie, UMR U1231 INSERM « CTM », Université Bourgogne Europe, 21000, Dijon, France*

Introduction. A shift to a laboratory-based high-energy diet triggers obesity in *Psammomys obesus (P. obesus)*. However, another factor, such as stress due to captivity, may also play a significant role in metabolic alterations. We conducted this study to explore the potential link between stress, sweet taste preference, and metabolic alterations leading to obesity. **Material and Methods.** To induce a stressful condition, we administered corticosterone (25 mg/kg) intraperitoneally, 20 min before a two bottles sucrose preference test (4% w/v). RT-qPCR was used to measure mRNA expression of the TAS1R2/TAS1R3 heterodimeric receptor in fungiform taste buds, and glucose-6-phosphatase (G-6-P), phosphoenolpyruvate carboxykinase 1 (PEPCK1 and stearoyl-CoA desaturase-1 (SCD-1) in the liver. Western blot analysis was used to measure the protein expression of TAS1R2/TAS1R3 in the fungiform taste buds. **Results.** Corticosterone (CORT) administration increased the preference for sweet solutions in a two-bottle choice test. Furthermore, it significantly upregulated the mRNA expression of the sweet taste receptor subunit TAS1R3 and the protein expression of both TAS1R2 and TAS1R3. CORT also upregulate the mRNA expression of gluconeogenic enzymes, including G-6-P and PEPCK1, as well as the key lipogenic enzyme stearoyl-CoA desaturase-1 (SCD-1). However, CORT decreased the levels of gut peptide YY (PYY) and insulin in the blood. **Conclusion.** This study demonstrates that CORT, known to be released during the captivity period, might play a key role in the development of obesity by affecting sweet taste perception, reducing PYY secretion, and enhancing lipid/glucidic metabolic enzyme pathways in *P obesus*.

Keywords: Corticosterone; G-6-P; Obesity; PEPCK1; PYY; Sucrose; TAS1R2; TAS1R3

Conflict of interest

The authors declare no conflict of interest.
Topic/s:Métabolisme et Nutrition

Steroid imaging in normal adrenocortical tissue using chemical derivatization and MALDI-FTICR

Fidéline Bonnet-Serrano[1, 2], Louis Thomeret[1], Florian Violon[1, 3], Karine Perlemoine[1], Maryline Favier[4], Paul Renquet[5], Jérôme Bertherat[1, 6], Guillaume Assié[1, 6], Edith Nicol[5], David Touboul[5]

[1] *Team « Genomics and Signaling of Endocrine Tumors », Institut Cochin, INSERM U1016-CNRS UMR8104-Université Paris-Cité, Paris*

,

[2] *Hormonology department, Hôpital Cochin, AP-HP, Paris*

,

[3] *Pathology department, Hôpital Cochin, AP-HP, Paris*

,

[4] *HistiM platform, Institut Cochin*

,

[5] *Laboratoire de Chimie Moléculaire, Institut Polytechnique, Paris*

,

[6] *Endocrinology department, Hôpital Cochin, AP-HP, Paris*

Introduction

Steroidogenesis in the adrenal cortex proceeds through a tightly regulated enzymatic cascade that converts cholesterol into mineralocorticoids in the zona glomerulosa, glucocorticoids in the zona fasciculata, and androgens in the zona reticularis. In adrenocortical tumors, this finely tuned process is frequently dysregulated, yielding atypical steroid profiles via alternative pathways and, in many cases, clinically significant hormone excess. Despite the central role of these metabolites, the spatial distribution of steroids and their precursors linked to their biosynthesis pathways remains poorly resolved. Our goal was thus to use MALDI-FTICR to describe the spatial distribution of steroids inside adrenal tissue.

Methods

Two normal adrenal and one pheochromocytoma fresh-frozen samples were included. 15-µm sections of each sample were performed using a cryostat at −30°C and mounted onto conductive indium-tin-oxide–coated MALDI target glass slides. 10 µm-consecutive sections were also performed for Hematoxylin-Eosin coloration. Due to very low ionization efficiency, in-situ derivatization with Girard reagent (including Girard P, Girard T and deuterated Girard reagents to differentiate some signals subject to interferences) was performed on the different sections after spraying the solution using the iMLayer from Shimadzu. HCCA was employed as the matrix, and acquisitions were performed in the positive ion mode on a MALDI-FTICR instrumen (Bruker SolariX XR 9.4 T).

Results

For the first time, the spatial distribution of precursors (pregnenolone, progesterone, 17-hydroxypregnenolone, 17-hydroxyprogesterone), gluco-/mineralo-corticoids (isomers corticosterone/11-desoxycortisol, cortisol) and androgens (androstenedione, isomers DHEA/testosterone, 11-hydroxyandrostenedione) was determined on human tissue sections at a

spatial resolution of 30 µm. Spatial distribution of steroids mapped to the anatomical structure of adrenal glands. This approach also allowed the annotation of additional lipids (phosphatidylcholines, triglycerides, sphingomyelins…) specific to each adrenal layer. As a negative control, pheochromocytoma tissue yielded no detectable steroid ions, whereas the adjacent normal adrenal cortex on the same section displayed the expected steroid signals.

Discussion

Validated in normal human adrenal tissue, this approach establishes a robust spatial atlas of adrenal steroid biochemistry and is readily transferrable to adrenocortical tumor specimens to characterize pathway rerouting and steroidogenesis disorganization.
Topic/s: Physiologie rénale

PROTEOMICS ANALYSIS HIGHLIGHTS THE REGULATION OF LIPOLYSIS AND ANTIOXIDANT DEFENSE IN ADIPOSE TISSUE OF BROWN BEARS (*Ursus arctos*) DURING HIBERNATION

Reiko Nakao[1, 2], Anna Ziemianin[1, 3], Charlotte Brun[1, 3], Isabelle Chery[4], Alina Evans[5], Jonas Kindberg[6, 7], Guillemette Gauquelin-Koch[8], Etienne Lefai[9], Stéphane Blanc[4], Fabrice Bertile[1, 3]

[1] *Université de Strasbourg, CNRS, IPHC UMR 7178, Laboratoire de Spectrométrie de Masse BioOrganique*

,

[2] *Institute of Biomedical Sciences, Tokushima University Graduate School*

,

[3] *Infrastructure Nationale de Protéomique ProFI*

,

[4] *Université de Strasbourg, CNRS, IPHC UMR 7178, Département Ecologie Physiologie et Ethologie*

,

[5] *Department of Forestry and Wildlife Management, University of Inland Norway*

,

[6] *Norwegian Institute for Nature Research*

,

[7] *Department of Wildlife, Fish, and Environmental Studies, Swedish University of Agricultural Sciences*

,

[8] *Centre National d'Etudes Spatiales*

,

[9] *Université Clermont-Auvergne, INRAE, UNH UMR1019*

Introduction

Despite prolonged reliance on lipid-based metabolism, it remains unclear how hibernating animals regulate lipolytic activity to adjust fat reserve mobilization throughout the hibernation context of reduced energy needs and apparent avoidance of lipotoxicity. We hypothesized that hibernation induces coordinated seasonal remodelling of white adipose tissue (WAT) metabolism in bears, characterized by alterations in lipid metabolism and antioxidant systems, and that these changes contribute to the maintenance of oxidative stress homeostasis. To elucidate the mechanisms by which bears avoid WAT lipotoxicity under these conditions, we performed a proteomic analysis of bear WAT alongside oxidative stress- and ferroptosis-related measurements.

Material and Methods

Sub-adult (2- to 4-year-old) brown bears (*Ursus arctos*) from Dalarna and Gävleborg counties (Sweden) were captured. Each bear has been captured only twice, first in February during hibernation and then in June of the same year during the summer-active period. Biopsies of subcutaneous WAT were collected from bear thigh. Blood samples were collected from the jugular vein to prepare plasma. These samples were immediately frozen on dry ice until storage at -80°C. These procedures were approved by the Swedish Ethical Committee on Animal

Experiment, the Swedish Environmental Protection Agency, and the Swedish Board of Agriculture.

Results

Our analysis revealed an upregulation of monoacylglycerol lipase (MGLL) and fatty acid binding protein 4 (FABP4) in hibernating bear WAT. Meanwhile, guanine nucleotide-binding protein G(i) subunit alpha-3 (GNAI3) was also upregulated, which suppresses adenylyl cyclase activity and inhibits lipolysis, suggesting that lipid mobilization and anti-lipolytic mechanisms are concurrently activated during hibernation. Despite reduced metabolic rate, proteins involved in beta-oxidation, the Krebs cycle, and electron transport chain showed comparable expression between seasons, and adipocyte size was greater during hibernation. These findings suggest the presence of mechanisms that regulate protein function in WAT independently of changes in protein abundance. In addition, antioxidant enzyme expression was maintained, with upregulation of superoxide dismutase 1 (SOD1), and no significant differences in oxidative stress markers. Although iron levels in WAT were markedly reduced during hibernation, ferritin heavy chain 1 (FTH1) and ceruloplasmin (CP), which mediate intracellular iron sequestration and export, were upregulated. Together, these data suggest that bear WAT prevents oxidative damage under conditions of sustained fatty acid mobilization/utilization and reduced physical activity by maintaining antioxidant capacity and an enhancing iron detoxification during hibernation.

Discussion/Conclusion

These mechanisms may represent unique adaptations that enable long-term survival through the efficient utilization of body fat reserves without lipotoxicity during hibernation.
Topic/s: Ecophysiologie

Regulation and disruption of circadian clocks in the female reproductive system

Léa SAMANNI, Elisa NIED, Eva ESTEVE, Valérie SIMONNEAUX

Institut des Neurosciences Cellulaires et Intégratives (INCI), Strasbourg

Objective : This study aims to investigate the impact of a rotating light schedule (mimicking shift work) on both the central circadian clock as well as on peripheral clocks within the hypothalamic-pituitary-ovarian (HPO) axis in female mice.

Material and Methods : Adult female PER2::LUCIFERASE mice (C57BL/6J background) were used. In these model, the promoter of the clock gene Per2 regulates the rhythmic expression of the gene coding for the luciferase, an enzyme which, by oxidizing luciferin, produces bioluminescence proportional to Per2 activity. The animals were divided into two experimental groups. The control group (CTL, n = 18) was maintained under a stable 12-hour light/12-hour dark cycle (12L/12D). The rotating shift group (RS, n = 18) was exposed to a shifting light schedule consisting of repeated cycles of a 10-hour advance of the light for 4 consecutive days, followed by a 10-hour delay for 3 days. Mice were subjected to their respective lighting conditions for 4 weeks. At the end of this period, the reproductive cycle stage of each mouse was assessed by vaginal smear prior to sacrifice. Several structures of the HPO axis were then collected including the suprachiasmatic nucleus (SCN), the anteroventral periventricular nucleus (AVPV), the anterior pituitary, one whole ovary, and a fragment of uterus. Explants were cultured in a medium containing luciferin and placed in a Lumicycle (Actimetrics). Bioluminescence was recorded over a period of 7 days. The resulting data were then extracted and analyzed using Lumicycle Analysis software.

Results : We demonstrated a significant lengthening of the SCN period in the RS group. Rotating shift also induced greater inter-individual dispersion of SCN acrophases. In the CTL group, a shift in ovarian acrophase was observed depending on the stage of the cycle (diœstrus metœstrus versus prœstrus-œstrus), whereas this variation disappeared under RS conditions. These results suggest that rotating shift alters the physiological circadian modulation of the ovary across the different stages of the cycle.

Discussion : In female mammals, reproductive function relies on precise temporal coordination among the components of the HPO axis. The preovulatory LH surge, which is essential for ovulation, is tightly regulated by circadian rhythms. Disruption of these rhythms may therefore impair the synchronization required for proper ovulation, potentially affecting fertility. The rotating shift model used here reproduces some of the circadian disturbances observed in individuals exposed to repeated schedule shifts, particularly shift workers, in whom fertility disorders have already been reported.

Topic/s: Rythmes Biologiques

Direct effects of light on food intake, energy metabolism and locomotor activity: brain mechanisms in diurnal and nocturnal models

Pablo SAIDI-PLOUSSARD, Etienne CHALLET

INCI

Ambient light is a major regulator of physiology, with effects that depend on the time of day at which it is perceived. Light at night, from screen use or shift work, is associated with increased risk of obesity and type 2 diabetes. The master circadian clock in the suprachiasmatic nuclei (SCN) is entrained by light via the retinohypothalamic tract and projects to hypothalamic structures controlling arousal, feeding, and energy metabolism. The histaminergic and orexinergic systems are central drivers of wakefulness, yet their role in direct light effects on metabolism remains poorly understood. Since light promotes wakefulness in diurnal species but sleep in nocturnal ones, comparing chronotypes is an effective approach to disentangle circadian from direct (masking) effects of light.

The nocturnal C57BL/6J mouse and the diurnal Sudanian grass rat Arvicanthis ansorgei were exposed to alternating 1-hour light / 1-hour dark cycles (LD 1:1) over 24 hours. Indirect calorimetry provided continuous recording of food intake, locomotor activity, respiratory exchange ratio (RER), and energy expenditure. Continuous glucose telemetry will allow 24-hour glycemic monitoring without handling stress. Plasma levels of leptin, ghrelin, glucose, and insulin will be measured to assess metabolic responses to light and dark. To map brain regions activated by light, c-Fos immunofluorescence combined with whole-brain atlas registration (ABBA) will be performed in animals exposed to light or darkness. To characterize the neurochemical pathways, orexin and histamine knockout mice, as well as mice and Arvicanthis treated with histamine and orexin receptor agonists or antagonists, will be monitored by indirect calorimetry.

A masking index was calculated to quantify acute photic responses during the subjective day and night. In nocturnal C57BL/6J mice, light significantly suppressed locomotor activity and RER only during the night, with a trend toward reduced food intake, indicating that light inhibits active behaviors during the nocturnal phase. In Arvicanthis ansorgei, light significantly increased locomotor activity only during the day, showing that light stimulates activity during the active phase of this diurnal species. Energy expenditure was unaffected by light exposure in both species, suggesting that direct light effects act primarily on behavior rather than on basal energy metabolism.

These results demonstrate opposing masking responses between chronotypes and support the hypothesis that direct light effects on feeding are differently regulated in diurnal versus nocturnal mammals. Characterizing the neurochemical pathways mediating the light-induced regulation of feeding should provide preclinical validation of phototherapy as a strategy for treating eating disorders, diabetes, and obesity.

Topic/s: Rythmes Biologiques

Hibernation cycles depend on cerebral thyroid hormones

Aurélia Cès, Valérie Simonneaux

Institut de Neurosciences Cellulaires et Intégratives, CNRS

Introduction

Hibernation in mammals is a remarkable physiological adaptation during which individuals drastically reduce their body temperature and energy expenditure to survive harsh winter conditions. During the hibernation period, most species alternate between multi-day phases of "hypothermic" (torpor) and "normothermic" (arousal) states.

These cycles appear after a period of exposure to short photoperiods, which inhibit reproduction, as well as cold temperatures.

Our previous work has highlighted the central role of melatonin and TSH/T3 signaling in regulating seasonal reproduction and energy metabolism. The aim of this study is to determine whether these hormones are also involved in the seasonal endocrine programming of hibernation.

Methods

Male Syrian hamsters were first transferred to a short photoperiod for four weeks, then equipped with an intraperitoneal telemetric sensor (Anipill, BodyCap) to monitor body temperature, as well as a surgical system allowing intracerebral administration of solutions. Two systems were used: on the one hand, an osmotic minipump connected to an intracerebroventricular cannula for constant administration of TSH (5 mU/day) or vehicle (CSF) and on the other hand, a rechargeable programmable minipump (iPrecio) allowing the solution to be switched from CSF to TSH once the animals had exhibited 3 or 4 torpor episodes. Two weeks after surgery, the hamsters were transferred to a cold room (8°C) for up to 8 weeks. Some hamsters were gonadectomized to test whether the putative stimulatory effect of TSH on testosterone production could influence hibernation processes.

Results

We found that constant perfusion of TSH for 4 weeks prevented the hamsters from entering hibernation, unlike animals receiving the vehicle. Using the rechargeable minipumps, we observed that TSH could also block the arousal-torpor cycles once hibernation had already begun. In both experiments, TSH reactivated the reproductive system (increase in testicular size). Prior castration of some hamsters induced a similar profile of TSH-induced torpor inhibition.

Conclusion

Overall, these data demonstrate that the reduction in central TSH/T3 signaling induced by a short photoperiod is necessary for the onset of hypometabolic torpor, acting directly on hypothalamic mechanisms, and that this is independent of sex hormones.

Topic/s: Rythmes Biologiques

Towards mitochondrial transplantation: optimizing cryopreservation of mitochondria isolated from skeletal muscle

Elodie Payet[1, 2], Anne-Laure Charles[1], Anne Lejay[1, 3], Michel Kindo[1, 3]

[1] *Biomedicine Research Center of Strasbourg (CRBS), UR3072 « Mitochondrie, Stress oxydant et plasticité musculaire », Université de Strasbourg, France*

,

[2] *G-Life Quantum, Épagny-Metz-Tessy, France*

,

[3] *Department of CardioVascular Surgery, Transplantation and Cardiac Assistance, University Hospita of Strasbourg, France*

Background. Ischaemic heart disease remains the leading cause of death worldwide. Despite timely revascularization, ischaemia–reperfusion (IR) injury may account for up to 50% of final infarct size, largely through severe mitochondrial dysfunction that compromises cardiomyocyte survival and cardiac recovery. To date, no pharmacological strategy has demonstrated reproducible clinical efficacy against IR injury. Mitochondrial transplantation, defined as the direct injection of exogenous viable mitochondria into ischaemic myocardium, has yielded encouraging results in preclinical models and early-phase human pilot studies. However, this approach currently relies on freshly isolated organelles, a constraint incompatible with the time sensitive management of acute coronary syndromes. Cryopreservation may offer a pragmatic solution by enabling the constitution of ready-to-use mitochondrial biobanks.

Objective. To identify the cryopreservation conditions that best preserve structural integrity and respiratory function of mitochondria isolated from murine skeletal muscle.

Methods. Mitochondria were isolated from gastrocnemius muscles of C57BL/6 mice (n = 18; age 8–12 weeks; both sexes; 33 muscles). Three cryoprotectant formulations were evaluated: (i) trehalose alone, (ii) trehalose + 5% DMSO, and (iii) trehalose + 10% DMSO, each combined with two freezing protocols: snap-freezing in liquid nitrogen versus controlled-rate freezing (−1 °C/min) in an isopropanol-based cryocontainer. Mitochondrial coupling efficiency (respiratory control ratio, RCR) and outer membrane integrity (mitochondrial fragility index, IFM, reflecting cytochrome c release) were assessed by high-resolution respirometry (Oroboros Oxygraph-2k) at day 0 (fresh, J0), day 1 (J1), and day 14 (J14) post-cryopreservation.

Results. Cryopreservation induced a 45% decrease in RCR ($p < 0.0001$), with no further decline between J1 and J14, irrespective of the freezing method employed. The IFM increased 11-fold with trehalose alone and 7-fold with trehalose + 10% DMSO. In contrast, trehalose + 5% DMSO combined with controlled-rate freezing limited the IFM increase to only 5-fold—a value not significantly different from fresh mitochondria (J0). No further deterioration was observed between J1 and J14, confirming short-term cryostability.

Conclusion. Trehalose combined with 5% DMSO and controlled-rate freezing in an isopropano cryocontainer best preserves outer mitochondrial membrane integrity among the conditions tested. The stability of cryopreserved mitochondria over 14 days constitutes a meaningful translational advance towards the development of an off-the-shelf organelle source for

mitochondrial transplantation. Complementary functional assessments, including mitochondrial membrane potential (ΔΨm), ATP synthesis capacity, and susceptibility to mitochondrial permeability transition pore (mPTP) opening, are underway to validate the therapeutic applicability of cryopreserved mitochondria for cardiac repair.

Topic/s: Physiologie cardio-vasculaire

Beyond mean differences: overlap and variability of spirometric variables between men and women

Gabriel Joulain[1], Elouan Voisin[1], Raphael Dery[1], Manon Guibot[1], Pascale Kuntz[1, 2], Patricia Lemarchand[1], Dorian Hassoun[1]

[1] Nantes Université, CHU Nantes, CNRS, INSERM, l'institut du thorax, F-44000 Nantes, France

[2] Nantes Université, Laboratoire des Sciences du Numérique de Nantes, CNRS, F-44000 Nantes, France

Introduction

Respiratory function is commonly described as depending on height, age, ethnicity and sex. Regarding sex, differences between men and women are mainly considered through mean values, thereby downplaying inter-individual variability within each group and underestimating distributional overlap. To date, few raw data are available to precisely assess sex-related differences in the distributions of respiratory function variables. This study aimed to describe sex-related differences in the forced spirometric variables and to specifically identify the influence of age and height on these differences.

Material and Methods

We selected healthy UK Biobank participants with no history of respiratory disease, who had never smoked and had good-quality spirometry. Sex-related differences in forced vital capacity (FVC), forced expiratory volume in 1 second (FEV_1) and FEV_1/FVC ratio were quantified relative to women. The degree of overlap between distributions was assessed using Cohen's d, which accounts for both effect size and distributional overlap. To evaluate the influence of age and height on observed sex-related differences, participants were also stratified by age, using 5-yea intervals, and by height, using 1-cm intervals, and analysed using the same approach.

Results

A total of 134,403 individuals were analysed, including 85,716 women and 48,687 men, with a mean age of 56 ± 8 years. In the overall cohort, the relative sex-related difference in mean FVC was 41.3% (men: 4.55 ± 0.81 L; women: 3.22 ± 0.59 L). Despite this large mean difference, the distributions showed substantial overlap, estimated at 35%, with a Cohen's d of 1.87, reflecting marked variability within each group. This relative difference remained stable across comparable FVC deciles, while it increased with age, from 36.3% at 40 years to 45.0% at 70 years, and to a lesser extent with height, from 14.0% at 1.55 m to 17.7% at 1.85 m. After stratification for both age and height, the relative difference in FVC was reduced but persisted at 18%. Similar patterns were observed for FEV_1, whereas the FEV_1/FVC ratio did not differ between men and women, either overall (0.89%) or after stratification (1.04%).

Conclusion

Sex-related differences mainly concerned FVC, with substantial overlap between distributions. After accounting for height and age, a sizeable residual sex-related difference in FVC persisted.

As with ethnicity, these findings highlight the need for integrative approaches enabling the joint analysis of biological, environmental and social dimensions that may contribute to better understand the observed differences between men and women.
Topic/s: Physiologie respiratoire

DISCRIMINATORY PERFORMANCE OF ANTHROPOMETRIC PARAMETERS IN PREDICTING DYSLIPIDEMIA AMONG PATIENTS WITH TYPE 2 DIABETES

Abdenour BOUNIHI[1, 2, 3], Hassiba BENBAIBECHE[1, 4], Hamza SAIDI[1], Ratiba HANNACHI[5], Elhadj Ahmed KOCEIR[1]

[1] *Université des sciences et de la technologie Houari Boumediene, Faculté des sciences biologiques, Laboratoire de biologie et physiologie des organismes, Équipe de bioénergétique et métabolisme intermédiaire, Alger, Algérie*

,

[2] *École supérieure des sciences de l'aliment et des industries agroalimentaires (ESSAIA), Laboratoir ALIMENTS, Equipe PVNTA, Alger, Algeria*

,

[3] *Université de la formation continue-Centre Nord Alger/ Bouzareah*

,

[4] *Département des sciences de la nature et de la vie, Faculté des sciences, Université d'Alger 1, Alger, Algérie*

,

[5] *Service de diabétologie, CHU Mustapha Bacha, Alger, Algérie*

Introduction: This study aimed to identify anthropometric markers (AMs) associated with dyslipidemia in patients with type 2 diabetes (T2D). Patients and Methods: A total of 1348 patients with T2D, of both sexes, underwent a lifestyle interview and a clinical examination including anthropometric measurements. The most recent biological data were retrieved from patients' medical records. Dyslipidemia was defined according to the National Cholesterol Education Program Adult Treatment Panel III criteria. The discriminatory performance of AMs was assessed using receiver operating characteristic (ROC) curve analysis and the area under the curve (AUC). Optimal cut-off values were determined using the Youden index. Results: The study population consisted of 894 women and 454 men, yielding a sex ratio of 1.96. Dyslipidemia was identified in 72.4% of cases. The visceral adiposity index (VAI) demonstrated the highest discriminatory performance, with an AUC of 0.785 (95% CI: 0.761–0.809; P = 0.000), followed by the triglyceride-glucose index [AUC = 0.741 (95% CI: 0.713–0.768); P = 0.000] and the lipid accumulation product index [AUC = 0.713 (95% CI: 0.685–0.741); P = 0.000]. The specificity and sensitivity of the VAI for predicting dyslipidemia were 86% and 59%, respectively. Conclusion: The VAI appears to be the most relevant AM for predicting dyslipidemia in patients with T2D.

Topic/s: Physiologie cardio-vasculaire

Effect of Dry Immersion vs Bedrest on Energy Metabolism - the VIVALDI III Study

INES AKOUTEI[1], Baptiste Chambrey[1], Philippe St-Martin[1, 2, 3], Alexandre Zahariev[1], Pascale Vasseur[11], Marie-Pierre Bareille[4], Angélique Van Ombergen[8], Claire Laurens[9], Marc-Antoine Custaud[10], Audrey Bergouignan[12]

[1] *Université de Strasbourg, CNRS, IPHC UMR 7178, 23 rue du Loess, CEDEX 2, 67037, Strasbourg, France*

,

[2] *Université de Sherbrooke, Faculty of Physical Activity Sciences, Sherbrooke, QC J1K 2R1, Canada*

,

[3] *Research Centre on Aging, Sherbrooke Geriatric Institute, Université de Sherbrooke, Sherbrooke, QC J1H 4C4, Canada*

,

[4] *Institut de Médecine et Physiologie Spatiales (MEDES), 2 Av. de l'Aérodrome de Montaudran, 41400, Toulouse, France*

,

[5] *Biochemistry Department, Hospices Civils de Lyon, Pierre-Bénite, France*

,

[6] *Centre de Recherche en Nutrition Humaine Rhône-Alpes, INSERM, INRAE, Université Claude Bernard Lyon 1, Hospices Civils de Lyon, Pierre Bénite, France*

,

[7] *Institut de Médecine et Physiologie Spatiales (MEDES), 2 Av. de l'Aérodrome de Montaudran, 41400, Toulouse, France*

,

[8] *European Space Agence (ESA), Noordwijk, The Netherlands*

,

[9] *Institute of Metabolic and Cardiovascular Diseases, INSERM, Paul Sabatier University, UMR1297, Toulouse, France*

,

[10] *Univ Angers, CRC, CHU Angers, Inserm, CNRS, MITOVASC, Equipe CARME, SFR ICAT, F-49000, Angers, France.*

,

[11] *Université de Picardie Jules Verne, Amiens, France*

,

[12] *Anschutz Health and Wellness Center, Division of Endocrinology, University of Colorado, Anschutz Medical Campus, 12348 E. Montview Blvd, Aurora, CO, USA*

INTRODUCTION

Maintenance of energy balance (i.e., the difference between total energy expenditure (TEE) and energy intake (EI)) is critical in spaceflight, as even modest energy imbalances can exacerbate spaceflight-induced alterations across multiple physiological systems, including musculoskeletal, cardiovascular, immune, and metabolic functions. Characterizing changes in energy metabolism induced by ground-based space analogues is essential to understanding microgravity-related adaptations. The two commonly most used models are -6° head-down tilt bedrest (HDBR) and dry immersion (DI), which reproduce key effects of spaceflight, including hypokinesia,

hypodynamia, and body fluid redistribution. However, their sustained effects have never been directly compared, which was the objective of the ESA-sponsored VIVALDI III study. A widely accepted but untested assumption is that DI induces more pronounced physiological deconditioning than HDBR; however, whether this translates into a greater reduction in energy expenditure remains unknown. We hypothesized that the more restrictive conditions of DI would result in a greater reduction in TEE than HDBR, reflecting accelerated metabolic deconditioning.

METHOD

Twenty healthy and physically active men (age: 31.5±5.3 years; BMI: 23.8±1.8 kg/m^2; VO2max: 44.9±7.6 mL/min/kg) were randomly assigned to either HDBR and DI for 10 days, preceded by 5-day baseline data collection and followed by a 5-day recovery phase. Habitual diet (3-day dietary log) and physical activity levels (10 days of 3D-accelerometry) were assessed prior to the study. TEE and its components (resting metabolic rate, diet-induced thermogenesis, and physical activity-related energy expenditure) were measured by using doubly labeled water method and indirect calorimetry before and during the interventions. EI was continuously monitored by weighing all provided food and subtracting leftovers, and body weight and composition were measured frequently using DXA.

RESULTS

Data are still under analysis.

DISCUSSION

The expected results will refine estimates of energy requirements in HDBR and DI, clarify whether DI induces more rapid metabolic deconditioning, and contribute to improved nutritional control during ground- based space analogue studies.

Topic/s:Métabolisme et Nutrition

Plasma proteomics highlights metabolic responses and pathways of protein and muscle sparing during fasting - preliminary data

Baptiste Chambrey[1], Audrey Bergouignan[1, 2], Franziska Grundler[3, 4], Anthony Damiot[1], Isabelle Chery[1], Alexandre Zahariev[1], Guillemette Gauquelin-Koch[5], Stéphane Blanc[1], Fabrice Bertile[1], Françoise de Wilhelmi de Toledo[3]

[1] *Institut Pluridisciplinaire Hubert Curien, Université de Strasbourg, CNRS, Strasbourg, France*

,

[2] *Division of Endocrinology, Metabolism and Diabetes, Anschutz Health & Wellness Center, University of Colorado, Anschutz Medical Campus, Aurora, CO, USA*

,

[3] *Buchinger Wilhelmi Clinic, Überlingen, Germany*

,

[4] *Charité-Universitätsmedizin Berlin, corporate member of Freie Universität Berlin, Humboldt-Universität zu Berlin, and Berlin Institut of Health, Berlin, Germany*

,

[5] *Centre National d'Études Spatiales, Paris, France*

Introduction: Fasting has gained increasing attention as a potential therapeutic approach for metabolic disorders and as an adjunct strategy in cancer care. However, limited data are available on the physiological impact of prolonged fasting. In a prospective trial, we previously observed that 10 days of fasting combined with a physical activity program was safe and preserved muscle function in healthy men. To obtain an integrated, dynamic view of the physiopathological state of food-restricted organisms, we characterized the plasma proteome in fed, food-restricted, and refed conditions.

Material and Methods: Eleven men (41 ± 11 years; BMI: 25.9 ± 2.6 kg/m²) completed a supervised 10-day fasting, consisting in daily energy intake restricted to 200-250 kcal, combined with up to 3 h/day of low-intensity physical activity, according to the validated Buchinger Wilhelmi protocol. Plasma samples were collected at baseline, after 3 and 10 days of fasting, and after 2 days of refeeding to assess fasting-induced systemic molecular changes by untargeted proteomic analysis using a sample preparation procedure favoring the enrichment of low-abundance proteins onto paramagnetic beads combined with so called DIA-based mass spectrometry.

Results: Among 1,405 proteins identified after initial filtering, 517 were significantly altered after 10 days of fasting. Pathway analysis of circulating proteins known to be secreted revealed major alterations in protein metabolism, muscle function, growth, endoplasmic reticulum function, immune response, lipid metabolism, oxidative stress, and insulin signaling. Specifically, proteins associated with anabolic inhibition and metabolic adaptation were markedly modulated. Fasting induced major and persistent changes in the plasma proteome, notably increased Transforming growth factor beta 1 and Sex hormone-binding globulin (+45.6% and +64.9%, respectively; $p<0.05$), which remained elevated after refeeding, suggesting sustained metabolic and tissue remodeling adaptations. Proteins involved in proteolysis and coagulation regulation (ANT3 : +76.5%, $p<0.0001$, PAI1 : +76%, $p<0.001$) and innate immune signaling (CD14 : (+49.4%, $p<0.05$) were also increased, while Macrophage migration inhibitory factor (−63.4%,

p<0.05) and ANXA1 (−70.7%, p<0.0001) decreased, indicating altered inflammatory and stress responses. In parallel, fasting markedly reshaped lipid metabolism, with decreased Fibrinogen alpha chain (−80.4%, p<0.05) and APOA4 (−50.4%, p<0.0001) and increased APOB (+37.3%, p<0.05), highlighting a shift toward lipid mobilization and prolonged metabolic adaptation beyond the fasting period.

Conclusions : Prolonged fasting triggers a systemic shift toward anabolic suppression, controlled proteostasis, and lipid-based metabolism, accompanied by tissue remodeling processes and the regulation of few signaling pathways that may support protein sparing and maintenance of muscle function.

Topic/s: Métabolisme et Nutrition

Comparison of Iohexol and 99mTc-DTPA for glomerular filtration rate measurement

Timothée Fearon, Alexandre Lahens, Séverine Brabant, François Rouzet, Nahid Tabibzadeh, Dominique Prié, Martin Flamant, Emmanuelle Vidal-Petiot

Assistance Publique - Hôpitaux de Paris

Background

Plasma clearance of Iohexol is the most widely used method for glomerular filtration rate (GFR) measurement. However, only few, mostly small studies have evaluated its performance against gold standard GFR, with heterogenous results, and even less have tested the potential reliability of urinary clearance of the tracer. We compared the performances of plasma and urinary clearances of Iohexol and Technetium-99m-diethyletriaminepentaacetic acid (^{99m}Tc-DTPA).

Methods

In a single-center prospective study, ^{99m}Tc-DTPA and Iohexol were simultaneously injected to 228 patients, and their urinary and plasma clearances were measured during six 30-min periods after a 90-min equilibrium time. Plasma clearance was calculated from 6 samples (105 to 255 minutes after injection), using the slope-intercept method with the Brøchner-Mortensen correction.

Results

Analysis were conducted in 218 patients with regular voiding, urinary clearance of 99mTc-DTPA being considered as the reference GFR. Mean age was 50 ± 14 years, 60% were men. Urinary clearances of ^{99m}Tc-DTPA and Iohexol were 73.0 ± 24.6 and 68.6 ± 24.0 mL/min/1.73m², respectively, with a mean bias of -4.3 ± 4.5 mL/min/1.73m² [-6,2 ± 5,5%], an accuracy within 10% (P10) of 84% [95% CI 79-88], a P30 of 100%, a coefficient of determination (R^2) of 0.970 and a mean intrinsic precision of 4.1% ± 5.4. An equation correcting for this slight but highly reproducible underestimation of urinary clearance of Iohexol (y=1.0074x+3.8049) allowed to reach an excellent overall accuracy (P10=94%). Plasma clearances of ^{99m}Tc-DTPA and Iohexol were 76.7 ± 24.8 and 72.8 ± 23.3 mL/min/1.73m², respectively, with a mean bias of -3.9 ± 5.9 mL/min/1.73m² [-4.5% ± 7.2], a P10 of 83% [95% CI 78 - 87], a P30 of 99% [95% CI 99 - 100], a R^2 of 0.944 and a mean intrinsic precision of 5.7% ± 6.5. In most outliers for plasma clearance of iohexol, apparent distribution volume of iohexol was aberrant, suggesting erroneous injection of the tracer.

Conclusion

Plasma clearance of Iohexol is a reliable alternative to plasma clearance of 99mTc-DTPA, although aberrant values likely due to injection issues can only be identified when urinary clearance and apparent distribution volume are simultaneously analysed. Urinary clearance of Iohexol displays a slight negative bias compared to urinary clearance of 99mTc-DTPA , but excellent intrinsic precision. We advocate for the simultaneous use of plasma and urinary

clearance of Iohexol for robust GFR measurement, and put forward a correcting equation for Iohexol urinary clearance, yielding optimal accuracy.
Topic/s: Physiologie rénale

Water turnover in astronauts onboard the International Space Station – Preliminary results from the ENERGY study

Pierre Bourdier[1, 2], Alexandre Zahariev[1], Isabelle Chery[2], Alain Maillet[3, 4], Cécile Thevenot[3, 4], Laurie Van Den Berghe[5], Guillemette Gauquelin-Koch[6], Chantal Simon[5, 7], Stéphane Blanc[2], Audrey Bergouignan[2, 8]

[1] *Université de Haute-Alsace, IRIMAS UR7499, Mulhouse, France*

,

[2] *Université de Strasbourg, CNRS, IPHC UMR 7178, Strasbourg, France*

,

[3] *MEDES, Institut de Médecine et Physiologie Spatiales, Toulouse, France*

,

[4] *CADMOS-CNES, 18 Av. Edouard Belin, 31401 Toulouse, France*

,

[5] *Human Nutrition Research Centre of Rhône-Alpes, Hospices Civils de Lyon, Lyon, France*

,

[6] *Centre National d'Etudes Spatiales, Paris France*

,

[7] *CarMeN Laboratory, Centre de Recherche en Nutrition Humaine Rhône-Alpes, INSERM, INRAE, U1060, Univ Lyon, Université Claude Bernard Lyon 1, Pierre-Bénite, France*

,

[8] *Division of Endocrinology, Metabolism and Diabetes, Anschutz Health & Wellness Center, Universit of Colorado, Anschutz Medical Campus, Aurora, CO, USA*

The next phase of space exploration will involve longer-duration missions conducted in isolated and resource-constrained environments. Under these conditions, food and water supplies are limited and must be planned with precision. While even a small overestimation may substantiall increase onboard storage requirements and mission costs, underestimating crew needs could negatively affect astronaut health and mission success.

The ENERGY study (2011-2017) was designed to estimate the energy requirements of eleven astronauts onboard the International Space Station (ISS) during a 6-month mission. To do so, free-living total energy expenditure was measured over a 10-day period using the gold-standard doubly labeled water (DLW) method before and after 3 months onboard the ISS. The measurement of deuterium elimination rates (through water in urine or sweat) also allows the determination of the average daily water turnover. A 10-day food record, including photos of meals, snacks, and drinks, was used to assess macronutrient intake on the ground and in-flight. By combining data from the estimated daily macronutrient intake with ISS environmental temperature, pressure, and humidity, we can further estimate the different components of wate influx, including metabolic water, inspiratory water (moisture content of inhaled air) transcutaneous water intake (water absorbed by the skin) and preformed water, (which is the water consumed orally from beverages and water in the food), using validated equations.

All samples have been analyzed, and calculations are being completed.

This will be the first study to investigate water turnover in astronauts during long-term spaceflight, providing valuable insights to refine nutritional strategies and ensure the success o upcoming missions to the Moon and Mars.
Topic/s:Métabolisme et Nutrition

Impact of Self-paced concurrent Training practiced in fasted state on Cardiometabolic Health, anthropometric measurements and Functional capacity in adults with Type 2 Diabetes.

Sirine C. Miladi[1], Sonda Jallouli[2], Dalenda Ibn Elwefi[3], Warda Lahouel[2], Mohamed Ali Hbaieb[4], Kawther Ben Hamed[3], Mouna Turki[5], Tarak Driss[1], Omar Hammouda[1]

[1] *Interdisciplinary Laboratory in Neurosciences, Physiology, and Psychology: Physical Activity, Health, and Learning (LINP2), UFR STAPS, Paris Nanterre University, Nanterre, France.*

,

[2] *Research Laboratory: Education, Motor Skills, Sports, and Health, EM2S, LR19JS01, University of Sfax, Sfax, Tunisia.*

,

[3] *Research Laboratory Molecular Bases of Human Pathology LR19ES13, Faculty of Medicine, University of Sfax, Sfax, Tunisia.*

,

[4] *Laboratory Mobilité, Vieillissement, Exercice (MOVE) (UR20296), Faculty of Sport Sciences, University of Poitiers.*

,

[5] *Biochemistry Laboratory, Hedi Chaker University Hospital, University of Sfax, Sfax, Tunisia.*

Introduction: type 2 Diabetes (T2D) complications are well known causes of morbidity and mortality, which can be prevented through a healthy diet and regular physical activity.

Objective: To evaluate the combined effects of Ramadan fasting (RF) and self-paced concurrent training (SCT) on cardiometabolic health, dietary behavior, body composition, and physical performance in persons with type 2 diabetes (PwT2D).

Methods: Twenty-nine PwT2D were randomly assigned to either a RF group (n=16; 49.38±6.59 years; HbA1C: 7.69±1.70%) or a combined RF and SCT (RF+SCT) group who performed a fasted walking at moderate-intensity (75% of heart rate reserve) combined with four resistance exercises (3-4 sets×10-12 repetitions per exercise) (n=13; 54.53±7.65 years; HbA1C: 7.83±1.43%) . Participants were evaluated before and after the 1-month intervention.

Results: The RF+SCT group showed a reduction in fasting glucose and alanine aminotransferas levels, as well as body mass, fat mass, body mass index, waist and hip circumferences, body fat percentage, body water compared with the RF group ($p<0.001$, $g=1.43$; $p=0.005$, $g=1.16$; $p=0.01$, $g=0.97$; $p=0.005$, $g=1.07$; $p=0.002$, $g=1.27$; $p=0.008$, $g=1.05$; $p=0.002$, $g=1.02$; $p=0.005$, $g=1.11$; $p=0.01$, $g=0.91$, respectively). The predicted peak oxygen uptake increased i the RF+SCT comparatively with the RF group ($p<0.001$, $g=1.17$) and lower- and upper-limb muscle strength significantly increased in the RF+SCT group compared with the RF group ($p<0.001$ and $p=0.007$, respectively).

Conclusion: The RF+SCT combination can be recommended as an effective therapeutic strategy for attenuating hyperglycemia and hepatic damage, as well as for improving cardiorespiratory fitness and anthropometric profile in PwT2D patients.

Topic/s: Sport, Exercice

Effects of a Five-Day Repeated Napping Micro-cycle on basketball-specific Physical performance and Cardiac Autonomic Responses in High-Level Adolescent Basketball Players During a Congested Training Schedule

Mehdi J SOUABNI[1], Maher SOUABNI[1, 2], Omar HAMMOUDA[1, 3], Mathieu NEDELEC[4], Achraf AMMAR[1, 3, 5], Tarak DRISS[1]

[1] *Interdisciplinary Laboratory in Neurosciences, Physiology and Psychology: Physical Activity, Healtl and Learning (LINP2), UFR STAPS (Faculty of Sport Sciences), Paris Nanterre University, Nanterre, France.*

,

[2] *LBEPS, Univ Evry, IRBA, Université Paris-Saclay, Evry, France*

,

[3] *Research Laboratory, Molecular Bases of Human Pathology, LR19ES13, Faculty of Medicine, University of Sfax, Sfax, Tunisia*

,

[4] *Laboratory of Sport, Expertise and Performance (EA 7370), French National Institute of Sport (INSEP), Paris, France*

,

[5] *Department of Training and Movement Science, Institute of Sport Science, Johannes Gutenberg-University Mainz, 55122 Mainz, Germany*

Introduction: Intensive training camps and congested training micro-cycles may exacerbate sleep disturbances, which could adversely affect health and athletic performance. Although daytime napping is increasingly used as a recovery strategy for athletes, little is known about the effects of repeated napping. Therefore, the present study investigated the effects of a five-day micro-cycle of 60-min daytime nap opportunities on nocturnal sleep parameters, basketball-specific performance, and perceptual and autonomic responses in high-level adolescent athletes.

Methods: Twelve high-level male adolescent basketball players (15.75 ± 0.62 years) completed a randomized crossover protocol involving two experimental conditions: five consecutive days with a 60-min daytime nap opportunity (NAP) and five consecutive control days without napping (CON). Sleep parameters were continuously monitored using wrist actigraphy. Subjective recovery status (Hooper questionnaire) and resting autonomic responses (heart rate variability, HRV) were assessed before and after each condition across the five-day intervention. Basketball-specific performances including offensive and defensive agility, upper body power, repeated jumps (RJ), and rating of perceived exertion (RPE) after RJ were evaluated 90-min following both conditions on days 1 and 5.

Results: Compared with CON, NAP significantly increased 24-h total sleep time ($p = 0.003$, $d = 0.40$). Repeated napping was associated with improved autonomic regulation, reflected by higher total HRV power and lower objective stress index, alongside lower subjective fatigue, muscle soreness, and RPE scores ($0.002 \leq p \leq 0.035$, $0.28 \leq d \leq 2.10$). Five consecutive days of napping improved offensive and defensive agility and repeated jump performance ($0.001 < p \leq 0.015$, $0.83 \leq d \leq 1.61$).

Conclusion: Repeated napping helped to meet sleep recommendations, improved perceptual and physiological responses, and basketball-specific abilities, supporting its use as a practical

recovery strategy in adolescent basketball players during congested training periods and training camps.
Topic/s: Rythmes Biologiques

Performance of PMSI Coding for the Identification of Idiopathic Inflammatory Myopathies: A Sensitivity Study Based on the PREMIA Cohort

Astrid REBERT-PLACIDE[1], Clémence RISSER[2], Thierry LAVIGNE[1], Alain Meyer[3]

[1] *Equipe Opérationnel d'Hygiène, Hôpitaux Universitaires de Strasbourg*

,

[2] *Département d'information Médicale, Hôpitaux Universitaires de Strasbourg*

,

[3] *Service de Physiologie et d'explorations fonctionnelles, Hôpitaux Universitaires de Strasbourg*

Introduction

Idiopathic inflammatory myopathies (IIM) are a heterogeneous group of rare diseases. ICD-10 codes are widely used for large-scale epidemiological research, but their reliability for identifying IIM, sensitivity and specificity, remains poorly characterised. Hannah et al. (2022) reported code combinations with satisfactory sensitivities without describing their specificity. The PREMIA study, the only IIM epidemiological cohort based on 2017 ACR/EULAR criteria using capture-recapture methodology, offers a unique opportunity to validate code sensitivity and describe specificity.

Material and Methods

Our approach followed three steps. First, a literature review identified ICD-10 combinations with the best sensitivity for IIM. Second, these were evaluated in the PREMIA cohort, a population-based study in Alsace identifying incident cases between 2006 and 2012 from four independent sources with 2017 ACR/EULAR confirmation. Fourteen codes were retained: IIM-specific codes (M36.0, M33.9, M33.1, M33.0, G72.4, M60.8, M33.2, M60.9), interstitial lung disease (J84.9), and unspecified myopathy codes (G71.8, G71.9, G72.8, G72.9, G73.7). Children were excluded except those coded M33.0; sensitivity and PPV were calculated with 95% CI. Third, specificity of the best combinations was determined.

Results

Individual code performance was heterogeneous: M36.0 and M33.0 yielded high PPV but low sensitivity; M33.2 and M33.9 provided better sensitivity at lower PPV. Compared with Hannah et al. (PPV 78–94%, sensitivity 22–89%), PPVs in PREMIA were systematically lower. The best combinations were: DM codes only (M33.1 or M33.9), PPV 42.5%, sensitivity 34.9%; specific codes (M36.0, M33.1, M33.9, M33.0, G72.4), PPV 42.2%, sensitivity 42.5%; two or more co-occurring codes, PPV 35.6%, sensitivity 53.0%. Any-code strategy reached the highest sensitivity at 62.9% [55.8–69.5%].

Discussion / Conclusion

This study evaluates ICD-10 code combination performance for IIM diagnosis against a robust gold standard — an incident population identified by four independent sources using 2017 ACR/EULAR criteria. Certain combinations show satisfactory performance, supporting the feasibility of IIM epidemiological research using medico-administrative databases. The optimal

algorithm could be applied to the PDH-ATIH platform to estimate IIM prevalence in France, analyse interregional variations, and study temporal trends.
Topic/s: Muscle

DEVELOPMENT OF NOVEL ADMINISTRATION ROUTE FOR SYSTEMIC DELIVERY OF ANTISENSE OLIGONUCLEOTIDES IN NEUROMUSCULAR DISORDERS.

Romane Cloix[1, 2], Simon Guiraud[1], Marine Geoffroy-Guiraud[1], Cyriaque Beley[1], Marcel Bonay[2, 3], Luis Garcia[1]

[1] *SQY Therapeutics, 78280 Guyancourt, France*

,

[2] *PHARMAColigo, UR20261, des Sciences de la Santé-Simone Veil, Université de Versailles Saint-Quentin-en-Yvelines, 78180 Montigny-le-Bretonneux, France*

,

[3] *Physiology and Functional Exploration Department Physiology and Functional Exploration Department; Ambroise Paré hospital and Bicêtre hospital, 92100 Boulogne-Billancourt, France*

Antisense oligonucleotides (ASOs) mediated exon skipping has emerged[SG1] as a promising and rapidly expanding [SG2] therapeutic approach[SG3] for genetic disorders. We have developed tricyclo-DNA ASOs for several neuromuscular diseases, notably one candidate currently evaluated by intravenous injection in a Phase 2 clinical trial for Duchenne[SG4] muscular dystrophy. Evaluation of non-invasive administration routes represents a major challenge, in particular the pulmonary and the sublingual routes. Due to strong vascularization and high permeability of the sublingual mucosa, sublingual administration offers access to the systemic circulation while avoiding first-pass hepatic metabolism. We evaluated two regimens in rat model: a daily treatment for 7 days and a prolonged treatment over one month. Plasma concentrations as well as tissue biodistributions were analyzed to characterize systemic exposure of the tcDNA ASO. Our results highlight systemic passage after sublingual administration in both tested conditions. Although the plasma and tissue concentrations observed remain lower than those obtained by intravenous route, these initial results demonstrate the feasibility of the sublingual route for ASO administration and constitute a basis for future formulations and administration regimen optimizations.

1.Guiraud, S. et al. The Pathogenesis and Therapy of Muscular Dystrophies. Annual Review of Genomics and Human Genetics 16, 281–308 (2015).

2.Relizani, K. et al. Palmitic acid conjugation enhances potency of tricyclo-DNA splice switching oligonucleotides. Nucleic Acids Res 50, 17–34 (2021).

3.Laurent, J. et al. Systemic distribution of tricyclo-DNA antisense oligonucleotide following intratracheal instillation in the mouse. NAR Mol Med 3, ugag001 (2026).

4.Brako, F. & Boateng, J. Transmucosal drug delivery: prospects, challenges, advances, and future directions. Expert Opinion on Drug Delivery 22, 525–553 (2025).

Topic/s: Endocrinologie

THE EFFECTS OF A TWO-MONTH SPIRULINA ENRICHED WITH ZINC SUPPLEMENTATION ON PATIENTS WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE: A TUNISIAN PILOT RANDOMIZED CLINICAL TRIAL

Balsam BARKOUS[1, 2], Amani SAYHI[1, 2], Sonia ROUATBI[1, 2], Imed LATIRI[1, 2]

[1] *Faculté de Médecine de Sousse - TUNISIE*

,

[2] *Hôpital Farhat Hached de Sousse - TUNISIE*

Introduction: Chronic Obstructive Pulmonary Disease (COPD) is a major global health concern due to its increasing prevalence and significant impact on morbidity and mortality. Depression and anxiety are prevalent among COPD patients, contributing to worsened health outcomes. This study aimed to explore the effects of a two-month supplementation of spirulina enriched with zinc on pulmonary function, life quality (LQ), sleep quality (SQ), and mental health (MH) aspects in patients diagnosed with COPD.

Material and Methods: A Randomized Controlled Trial was conducted with 28 COPD patients, randomly assigned to either the intervention group receiving spirulina enriched with zinc or the control groupin the department of physiology and functional explorations in the University hospital of Fahat HACHED Sousse. Pulmonary function, LQ, SQ, and MH were assessed using total body plethysmography, 6-minute walk test (6MWT) for the measure of 6-minute walk distance (6MWD), COPD Assessment Test (CAT) score, Pittsburgh Sleep Quality Index (PSQI), and Hospital Anxiety and Depression (HAD) scale at baseline and after two months.

Results: Both groups (cases and controls) were matched for anthropometric, clinical and functional data at the enrollment day. The intervention group showed significant improvements in spirometric data (FEV1, FVC, PEF, FEV1Q), 6MWD and overall LQ as indicated by a substantial decrease in CAT-score compared to the control group. However, there were no significant effects on static lung volumes, SQ, or MH. A decrease in Estimated Lung Age (ELA) (74.02±12.64 at day0 vs. 71.12±13.17 at day60, p=0.037) was noted. This suggested an anti-aging effect in the lungs following supplementation.

Discussion/Conclusion: Supplementation with spirulina enriched with zinc demonstrated a potential in improving respiratory function and enhancing LQ in COPD patients. The anti-aging effect observed in the lungs adds further interest to spirulina's therapeutic potential.
Topic/s: Physiologie respiratoire

Sarcopenia screening in intermittent claudication PAD patients.

Olivier Rouyer[1, 2, 3], Romain Durif[2, 3], Anargyros Verdilos[4], Gwenael John[3], Slim Bettaibi[3], Fabien Thaveau[3], Frederic Costes[1, 4]

[1] *INRAe, UMR 1019, UNH, CRNH Auvergne, 63 000 Clermont-Ferrand*

,

[2] *Unité d'Exploration et de Consultation de Médecine Vasculaire, CHU Clermont Ferrand, 63 000 Clermont Ferrand*

,

[3] *Service de Chirurgie Vasculaire et Endovasculaire, CHU Clermont Ferrand, 63 000 Clermont Ferrand*

,

[4] *Plateforme d'Exploration de la Mobilité, CHU Clermont Ferrand, 63 000 Clermont Ferrand*

Introduction

Peripheral arterial disease (PAD) at the stage of intermittent claudication induces ischemia-reperfusion phenomena responsible for myopathy, leading to impaired walking capacity. Withou appropriate management, progression toward chronic limb-threatening ischemia increases the risk of revascularization procedures as well as morbidity and mortality. Sarcopenia, with a prevalence of 34% across all stages of PAD, further worsens functional limitations and prognosis. Early screening during the stage of intermittent claudication may allow appropriate management and help limit disease progression.

Materials and Methods

This retrospective study included men with PAD from the EVALMOB cohort (NCT04375280) at Clermont-Ferrand University Hospital, evaluating mobility between January 2019 and June 2025.

The objective was to screen for sarcopenia according to the EWGSOP2 criteria. Sarcopenia was defined as an appendicular skeletal muscle mass lower than 20 kg.

Results

A total of 79 patients were included (median age: 67 years [32–82]), with a BMI of 28.84 ± 4.96 80% had a BMI ≥25 kg/m². The mean 6-minute walk test (6MWT) distance was 352.47 ± 119.9 m. Among the 75 completed SARC-F questionnaires, 15% (11) were positive for suspected sarcopenia. Overall, reduced handgrip strength, impaired chair stand test performance, and decreased appendicular skeletal muscle mass were observed in 8% (6), 13% (10), and 22% (17) of cases, respectively. Physical performance was impaired in 14% (11) of cases, while gait speed was reduced in 13% (10) of cases.

Regarding sarcopenia screening, the SARC-F demonstrated a sensitivity of 27%, a specificity of 80%, and a positive predictive value of 19%. When combined with handgrip strength and chair stand test assessments, these values reached 37%, 84%, and 44%, respectively. Only handgrip strength was significantly lower in the sarcopenic group ($p<0.001$).

Discussion/Conclusion

In our population, sarcopenia at the stage of intermittent claudication showed a prevalence of 22%, consistent with the literature. This prevalence highlights the importance of screening to identify a population at higher risk of complications. However, conventional screening tests use in elderly populations and recommended by the EWGSOP2 consensus do not appear to be relevant in this setting because of their low sensitivity and positive predictive value .

In this PAD population, further studies may help redefine the detection thresholds of the different screening tests, potentially supported by additional anatomical criteria, such as calf circumference, or functional parameters, such as muscle quality.

Topic/s: Métabolisme et Nutrition

DOES METFORMIN INTERFERE WITH CARDIORESPIRATORY AND SUBSTRATES OXIDATION ADAPTATIONS TO EXERCISE TRAINING?

Jabeur Methnani[1, 3], Imed Latiri[1, 2], Asma Omezzine[1, 3], Ezdine Bouhlel[1, 2]

[1] *Ministère de l'Enseignement Supérieur*

,

[2] *Hôpital Farhat Hached Sousse*

,

[3] *Hôpital Sahloul Sousse*

Introduction. Metformin and aerobic exercise are routinely co-prescribed in metabolic syndrome, yet evidence regarding their interaction on cardiorespiratory and substrate-oxidation adaptations remains inconsistent. We investigated the effects of combined metformin and aerobic training on peak oxygen uptake (V̇O2peak), maximal fat oxidation (MFO), submaximal substrate utilization, and perceived exertion in metformin-naïve adults with metabolic syndrome.

Materials and Methods. In this randomized, placebo-controlledtrial, 24 metformin-naïve adults with metabolic syndrome were allocated to receive metformin (1,000 mg/day; MET-EX) or matched placebo (PLA-EX) in combination with supervised aerobic training (5 sessions/week, 60% V̇ O2peak, 500 kcal/session) for five weeks; 22 participants (n = 11 per group) completed the protocol. V̇ O2peak, MFO, fat and carbohydrate oxidation, energy expenditure, and rating of perceived exertion (RPE; Borg 6–20) were assessed before and after the intervention.

Results. Absolute V̇O2peak gain was attenuated in MET-EX relative to PLA-EX (group × time interaction $p = 0.042$; +0.11 vs +0.26 $L \cdot min^{-1}$). Conversely, MFO increased markedly more in MET-EX (+0.13 vs +0.04 $g \cdot min^{-1}$; $p = 0.001$), with significantly higher fat oxidation, energy expenditure, and RPE at moderate-to-high submaximal intensities post-intervention. The V̇O2peak gain correlated negatively with age exclusively in MET-EX ($r = -0.87$, $p < 0.001$).

Discussion/Conclusion. Metformin seems to produce a dissociated adaptation profile during aerobic training in metabolic syndrome - enhancing lipid oxidation while attenuating cardiorespiratory adaptation and amplifying perceived effort, particularly in older patients.
Topic/s: Sport, Exercice

EFFECTS OF DANCE- AND GAME-BASED PHYSICAL EDUCATION ON COGNITIVE FUNCTIONS IN PRIMARY SCHOOL CHILDREN

Nada Ben Aziza[1, 2, 3], Karim Ben Ayed[1, 3], Imed Latiri[1, 2]

[1] *Ministère de l'Enseignement Supérieur*

,

[2] *Hôpital Farhat Hached de Sousse - Tunisie*

,

[3] *Institut Supérieur d'Education Physique du Kef - Université de Jendouba*

Introduction:

Physical education curricula in North Africa, including Tunisia, remain largely dominated by traditional activities and receive less academic and institutional attention than other school subjects [1–3]. Previous studies suggest that physical activity, informal sport, aerobic exercise, and game-based approaches may improve children's cognitive functions, including attention, inhibition, memory, executive functions, and academic performance [4–7]. Dance- and game-based physical education may therefore represent an innovative strategy to enrich school curricula and support cognitive development [8, 9]. This study aimed to evaluate the effects of a two-trimester dance- and game-based physical education intervention on cognitive functions in primary school children aged 8–10 years.

Materials and Methods

A total of 103 healthy pupils from the 3rd and 4th grades participated voluntarily in the study. Participants were allocated to three groups: a dance-based physical education group, a game-based physical education group, and a control group following the traditional curriculum. In the experimental groups, weekly physical education time was increased from 1 to 2 hours, sessions were mixed-gender, and activities were led by a licensed physical education teacher specialized in body expression and dance. Cognitive performance was assessed before and after the intervention using the Trail Making Test, the Stroop Test, and the Digit Span Test [10–12].

Results

For Trail Making Test execution time, repeated-measures ANOVA revealed a significant effect o testing time/group condition, indicating improvement from pre-test to post-test ($F(2,194) = 10.4$; $p < 0.005$). A significant group-related error effect was also observed ($F(2,194) = 3.66$; $p < 0.03$), as well as a significant school-level effect by group ($F(1,194) = 14.3$; $p < 0.002$). In the Stroop test, the number of wrong words decreased significantly, reflecting improved inhibition ($F(2,194) = 7.46$; $p < 0.007$). For Digit Span Forward, the dance group achieved the highest memory score ($p < 0.0006$), while the control group slightly outperformed the games group.

Discussion/Conclusion

A two-trimester enrichment of physical education through dance- and game-based activities wa associated with significant improvements in attention, inhibition, and immediate memory amon

primary school children. Dance-based physical education appeared to produce the strongest cognitive benefits, supporting the integration of expressive and diversified activities into school curricula.
Topic/s: Sport, Exercice

MODELING PSYCHO-SPIRITUAL FACTORS AND PERFORMANCE PERCEPTION DURING RAMADAN FASTING IN MUSLIM FOOTBALLERS IN A MUSLIM MAJORITYCONTEXT

Aymen Yacoubi[1, 2, 5], Chadlia Fitouri[1, 3], Karim Chamari[1, 4], Imed Latiri[1, 2]

[1] *Ministère de l'Enseignement Supérieur*

,

[2] *Hôpital Farhat Hached*

,

[3] *Faculty of Education and Arts, University of Sohar, Oman*

,

[4] *Naufar, Wellness and Recovery Center, Doha, Qatar*

,

[5] *Institut Supérieur d'Education Physique du Kef - Universite de Jendouba*

Introduction. We present an integrative model examining the direct and indirect relationships among self-perceptions of Ramadan (SPR), intrinsic religious motivation (IRM), extrinsic religious motivation (ERM), positive mood (P-Mood), negative mood (N-Mood), and perceived performance (PP) among 470 Tunisian Muslim-faith footballers competing while observing Ramadan fasting (RF).

Materials and Methods. Data were collected using online questionnaires and were analyzed via structural equation modeling to identify the psycho-spiritual and emotional processes associated with athletic performance in the month of Ramadan.

Results. The structural model shows that SPR is the strongest predictor of PP. The SPR exerts both a substantial direct effect (β= 0.41) and two indirect effects through heightened emotional vitality (β= 0.61) and reduced negative emotion (β= -0.49). SPR exerts a positive indirect effect on PP through P- Mood (β = 0.18. p < .001) and notably also through N- Mood (β = 0.11. p < .001).

Discussion/Conclusion. These findings indicate that the SPR enhances PP via a dual affective mechanism, wherein it concurrently boosts positive emotional states and mitigates negative ones. IRM has a direct adverse effect on PP indicating a potential attentional burden associated with intensified spiritual engagement, whereas ERM remains nonproductive. Neither IRM nor ERM showed a significant indirect effect through mood, highlighting the unique role of persona subjective appraisal of the RF experience as the key driver influencing PP through emotional pathways.

Topic/s: Sport, Exercice

EXERCISE AND PSYCHOLOGICAL OUTCOMES FOLLOWING ZINC-ENRICHED SPIRULINA SUPPLEMENTATION IN COPD: FINDINGS FROM A PILOT RANDOMIZED CONTROLLED TRIAL

Amani Sayhi[1, 2], Balsam Barkous[1, 2], Sonia Rouatbi[1, 2], Imed Latiri[1, 2]

[1] *Ministère de l'Enseignement Supérieur*

,

[2] *Hôpital Farhat Hached*

Introduction: Chronic obstructive pulmonary disease (COPD) is a progressive respiratory condition characterized by persistent airflow limitation, reduced exercise tolerance, and psychological impairment. Nutritional antioxidant supplementation has been proposed as a potential adjunctive strategy in COPD management. Zinc-enriched spirulina, owing to its antioxidant and anti-inflammatory properties, may confer beneficial physiological effects in this population. This study aimed to investigate the effects of two months of zinc-enriched spirulina supplementation on exercise capacity and mental health in patients with moderate-to-severe COPD.

Materials and Methods: A pilot randomized controlled trial was conducted in patients with COPD recruited from the Department of Physiology and Functional Explorations at Farhat Hached University Hospital, Sousse. Participants were randomly assigned to either an intervention group (IG) receiving zinc-enriched spirulina (1g/day orally for 60 days) in addition to standard care, or a control group (CG) receiving standard care alone. Exercise capacity was assessed using the 6-minute walk test, while psychological status was evaluated using the Hospital Anxiety and Depression (HAD) scale. Assessments were performed at baseline and after 60 days.

Results: Final analyses included 12 patients in the IG and 11 in the CG. Baseline anthropometric, clinical, and functional characteristics were comparable between groups. Exercise capacity improved significantly in the IG, as reflected by an increase in 6-minute walk distance from 597.3 ± 48.5 m at baseline to 644.0 ± 66.8 m at Day 60 ($p = 0.045$), whereas no significant change was observed in the CG ($p = 0.5$). Anxiety and depression scores (HAD-A and HAD-D) did not change significantly in either group over the study period.

Discussion/Conclusion: These preliminary findings suggest that two-month supplementation with zinc-enriched spirulina may improve exercise capacity in patients with moderate-to-severe COPD. Larger, double-blind, placebo-controlled trials are warranted to confirm its efficacy and safety.

Topic/s: Physiologie respiratoire

Adaptation to high-salt diet requires H,K-ATPase type 2 dependent NaCl secretion

Chloé Rafael[1], Luciana Morla[1], Justine Billiet[1], Samia Lasaad[1], Sandrine Placier[2], Nicolas Picard[3], Gilles Crambert[1]

[1] *Université Paris Cité, Sorbonne Université, Inserm, CNRS, Centre de Recherche des Cordeliers, F-75006, Paris, France*

,

[2] *Common and Rare Kidney Diseases (CoRaKID) Unit, INSERM, Sorbonne Université U1155, F-7502 Paris, France.*

,

[3] *Laboratory of Tissue Biology and Therapeutic Engineering, UMR 5305 CNRS, University Lyon 1, Lyon, F-69367, France*

Introduction: The kidney controls the extracellular volume and the blood pressure because of its ability to excrete efficiently Na^+ and Cl^- ions. These last decades in Western countries the consumption of salt has dramatically increase and the question arises as to how the kidney adapts to this chronic situation. Up to now, the mechanisms described to excrete a large load of salt consist in the inhibition of Na^+ reabsorption all along the nephron. We have identified a novel pathway that mediates the secretion of Na+ in the collecting duct (Morla, L. et al. 2016). This system involves A-type intercalated cells (AIC), NKCC1 and the H,K-ATPase type 2 (HKA2), which is known to be able to transport Na^+. Here, we investigated the role of HKA2 in NaCl renal secretion, as well as the physiological relevance of this secretory pathway in vivo, in response to salt load.

Material and Methods: C57BL6J mice wild type or knockout for the Atp12a gene (HKA2-KO) were used and placed under a control (NS) or high-Na^+ (HS) diets for 3 days. Outer medullary collecting ducts (OMCD) of WT mice under NS or HS were isolated for RNAseq and RT-PCR analysis. Type A intercalated cells were isolated by FACS (following labelling with c-kit antibodies) from WT mice under NS or HS for RT-PCR analysis. The mice were also placed in metabolic cages for measurements of physiological parameters (food and water intakes, urine excretion, plasma parameters). Blood pressure was assessed by tail-cuffed measurement.

Results: The RNA seq analysis of OMCD revealed that, as expected, genes involved in Na+ reabsorption (ENaCa, SGK) are downregulated. However, we also observed that HS diet also leads to an increased expression of the Atp12a gene that encodes for the catalytic subunit of the HKA2 both in OMCD and ICA. To understand the role of the HKA2, we placed the HKA2-KO mic under high-salt diet and observed that those mice exhibit a salt loosing phenotype with low blood pressure that is due to a stronger down-regulation of NKCC2 than in WT in the same context. Therefore, the absence of HKA2 is over-compensated by the inhibition of a reabsorptio pathway.

Conclusion: Altogether, these results demonstrate that the secretion of Na^+ in OMCD is stimulated in response to high salt intake.

Topic/s: Physiologie rénale

Haemodynamic constraints during exercise associated with pulmonary hyperinflation in severe asthma

Lucien JURET[1, 2], Jonathan TREMBLAY[3], Ruddy RICHARD[1, 2], Camille ROLLAND DEBORD[2], Frédéric COSTES[1, 2]

[1] *CHU Clermont Ferrand*

,

[2] *Clermont Auvergne University, INRAE, Human Nutrition Unit, Clermont Ferrand*

,

[3] *University of Montreal, School of Kinesiology and Physical Activity Sciences, Canada*

Introduction.

Exercise tolerance is reduced in severe asthma with significant dyspnoea. In cases of severe bronchial obstruction, dynamic hyperinflation during exercise limits haemodynamic adaptations and exercise tolerance. This has been demonstrated primarily through an indirect measure of systolic ejection, the oxygen pulse (VO_2/heart rate). In severe asthma, without underlying sever bronchial obstruction, we sought to determine whether dynamic hyperinflation during exercise interfered with maximal exercise capacity and haemodynamic adaptations.

Material and Methods.

We included 50 patients with stable severe asthma and residual exertional dyspnoea (median characteristics [95% CI]: age 59 years [46;68]; 41% men; BMI 27 kg/m² [25;32]; FEV1 78% predicted [61; 89.5]; Tiffeneau ratio 73.5% [64; 79]). During an incremental exercise test, we measured exhaled gases (VO_2 determination), ventilation with determination of inspiratory capacity every two steps (Ergocard Medisoft). Cardiac output was measured non-invasively and continuously using thoracic impedance (Qc, Physioflow, Manatec). Dynamic hyperinflation (DH) was defined as a decrease of at least 150 mL in Inspiratory Capacity during exercise compared with the resting measurement.

Results.

Twenty-one patients (42%) had DH. They did not differ from the other subjects in terms of age or BMI; baseline bronchial obstruction was more severe in the DH group. Exercise-induced bronchospasm, as measured by spirometry, was confirmed in 7 patients. Maximal aerobic capacity was lower in the HD group than in the NHD group (VO_2peak = 16.4 ± 4.7 $mL \cdot kg^{-1} \cdot min^{-1}$ vs 20.7 ± 6.5, $p < 0.001$, respectively). The Qc/VO_2 ratio was significantly reduced (3.8 vs 5.8, $p<0.001$) in the HD group. Qc adaptation to exercise occurred mainly through an increase in heart rate, with systolic ejection volume remaining stable. The arteriovenous O2 difference (calculated as VO_2/Qc) tended to be higher at each exercise stage i HD group (p=0.5).

Discussion/Conclusion.

These results demonstrate, in patients with severe asthma, the existence of haemodynamic stress during exercise linked to dynamic hyperinflation (impaired ventricular filling) restraining peak VO_2. The mechanisms underlying this adaptation, in the absence of severe bronchial obstruction, warrant further investigation.

Topic/s: Physiologie respiratoire

Autonomic cardiac regulation during sleep in adults with ADHD and sleep complaints: an exploratory polysomnographic HRV analysis

Louise Mesanguy[1, 2], Emilie Claeys[2], Hubert Bourdin[2], Malika Bouhaddi[3], Silvio Galli[1, 2]

[1] *Université Marie et Louis Pasteur, INSERM, UMR 1322 LINC, F-25000 Besançon, France*
,
[2] *CHU Besançon, Service d'exploration du sommeil et de la vigilance, Besançon, F-25030, France*
,
[3] *CHU Besançon, Service Physiologie-Explorations fonctionnelles, Besançon, F-25030, France*

Introduction: Attention-deficit/hyperactivity disorder (ADHD) in adults is frequently associated with sleep complaints, including insomnia symptoms, altered sleep quality, and increased daytime sleepiness. However, objective sleep findings remain heterogeneous across studies, and little is known about autonomic cardiac regulation during sleep in this population. In particular, stage-specific cardiac autonomic dynamics, as assessed through heart rate variability (HRV), have been scarcely investigated in adult ADHD, despite growing evidence of autonomic dysregulation in this disorder.

Material and Methods: This retrospective observational study aimed to characterize sympathovagal regulation across sleep stages in adults with ADHD undergoing clinical polysomnography (PSG) for sleep complaints, and to explore the potential effect of methylphenidate (MPH) treatment on nocturnal autonomic activity. Eight adult patients diagnosed with ADHD (four treated with MPH and four untreated) were included after applying strict exclusion criteria to remove confounding psychiatric, neurological, and major sleep disorders. Sleep architecture was scored according to American Academy of Sleep Medicine (AASM) standards. Electrocardiographic signals recorded during PSG were processed to extrac RR intervals, which were analyzed using Kubios HRV software. HRV indices reflecting parasympathetic activity (RMSSD, high-frequency power [HF], pNN50), global variability (SDNN), and baroreflex-related regulation (low-frequency power [LF]) were computed across validated stationary segments (median duration: 5,3 min, IQR: 3.0-11.0 min) obtained during wakefulness, non-rapid eye movement (N2 and N3) sleep, and rapid eye movement (REM) sleep Between-stage comparisons were performed using Kruskal-Wallis tests; between-group comparisons (MPH vs. untreated) using Mann-Whitney U tests.

Results: No statistically significant differences in vagal HRV indices were found across sleep stages at the group level, although trends approaching significance were observed for RMSSD ($p = .054$) and pNN50 ($p = .062$), likely reflecting insufficient statistical power. When comparin treatment groups, parasympathetic activity (RMSSD, HF) and global variability (SDNN) were significantly lower in MPH-treated patients during N2 and N3 sleep, with no significant differences during wakefulness or REM sleep.

Discussion/Conclusion: Although non-significant at the group level, these findings are consisten with a disruption in the expected parasympathetic upregulation during restorative sleep stages in adult ADHD, and suggest a stage-specific modulation of nocturnal autonomic activity by stimulant medication. The small sample size, the absence of a neurotypical control group, and

the retrospective design limit the generalizability of these results. Further prospective studies with larger samples and healthy control groups are needed to better understand the autonomic dysfunction in adult ADHD and its interaction with sleep physiology and psychostimulant treatment.

Topic/s: Physiologie cardio-vasculaire

Impact of an antioxidant nutrient cocktail on metabolic flexibility during 60 days of simulated microgravity

Anthony DAMIOT[1], Elisa LEROUX[1], Donal J. O'GORMAN[2, 3], Isabelle CHERY[1], Alexandre ZAHARIEV[1], Guillemette GAUQUELIN-KOCH[4], Michel PROST[5], Chantal SIMON[6, 7], Stéphane BLANC[1], Audrey BERGOUIGNAN[1]

[1] *Université de Strasbourg, CNRS, IPHC UMR 7178, 67000 Strasbourg, France*

,

[2] *National Institute for Cellular Biotechnology & School of Health and Human Performance, Dublin City University, Ireland*

,

[3] *3U Diabetes Consortium, Dublin City University, Ireland*

,

[4] *Centre National d'Études Spatiales, Paris France8Laboratoire de recherches appliquées Spiral/Kirial International, 21560 Couternon, France*

,

[5] *Laboratoire de recherches appliquées Spiral/Kirial International, 21560 Couternon, France*

,

[6] *CarMen Laboratory, INSERM 1060, INRAE 1397, University of Lyon 1, Oullins, France*

,

[7] *Centre de Recherche en Nutrition Humaine Rhône-Alpes, Hospices Civils de Lyon, Lyon, France*

Introduction:

Microgravity induces profound physiological and metabolic alterations, including muscle atrophy, insulin resistance, hypertriglyceridemia, impaired lipid oxidation, ectopic fat accumulation, and metabolic inflexibility, defined as a reduced capacity to adapt substrate oxidation to nutrient availability. Although exercise countermeasures remain the cornerstone of spaceflight prevention strategies, they only partially mitigate these impairments. In a previous pilot study, we showed that antioxidant/anti-inflammatory nutritional supplementation attenuated lipid metabolism alterations induced by physical inactivity in healthy men. We therefore investigated whether a nutrient cocktail could mitigate short- and long-term metaboli alterations induced by prolonged simulated microgravity.

Material and Methods:

Twenty healthy men were randomly assigned to either a dietary antioxidant cocktail group (polyphenols, omega-3 fatty acids, quercetin, resveratrol, vitamin E, and selenium; n=10) or a control group (n=10) during 60 days of -6° head-down bed rest (HDBR). Before bed rest and after 9 and 49 days of HDBR, body composition (DXA/MRI), systemic inflammation, oxidative stress markers, insulin sensitivity, and metabolic flexibility were assessed. Metabolic flexibility was evaluated over 15 h after a eucaloric breakfast followed by a carbohydrate overfeeding lunch using indirect calorimetry combined with repeated measurements of substrate oxidation, insulin, glucose, triglycerides, and non-esterified fatty acids. Linear mixed-effects models were used to assess time, group, and interaction effects.

Results:

HDBR rapidly altered substrate utilization, with increased fasting carbohydrate oxidation, reduced lipid oxidation, and higher fasting NPRQ, consistent with the development of metabolic inflexibility. These alterations were accompanied by hypertriglyceridemia, reduced insulin sensitivity, and a progressive increase in pro-inflammatory markers throughout bed rest. Postprandial responses further demonstrated impaired metabolic adaptation, with lower carbohydrate oxidation despite greater insulin stimulation. The antioxidant cocktail modestly attenuated fasting and postprandial triglyceride alterations and transiently improved adipose tissue insulin resistance indexes during the early phase of HDBR. However, supplementation had limited effects on whole-body insulin sensitivity and metabolic flexibility, particularly after prolonged bed rest and under high-carbohydrate overfeeding conditions.

Discussion/Conclusion:

Prolonged simulated microgravity induced metabolic alterations consistent with metabolic inflexibility and low-grade inflammation. Although antioxidant nutritional supplementation partially improved lipid metabolic regulation during early inactivity, it did not fully preserve insulin sensitivity and substrate switching capacity. These findings suggest that nutritional supplementation alone provides limited protection against long-duration inactivity-induced metabolic disturbances and should likely be combined with exercise countermeasures.
Topic/s:Métabolisme et Nutrition
