Nutrition Obesity Research Center
UNIVERSITY OF COLORADO ANSCHUTZ MEDICAL CAMPUS

2025 Colorado NORC Retreat: Poster Abstracts

Poster #1

Better baseline sleep is associated with greater weight loss during behavioral treatment of obesity

Presenter: Matthew J. Breit
Postdoctoral Fellow
University of Colorado Anschutz Medical Campus

Overview

Better baseline sleep is associated with greater weight loss during behavioral treatment of obesity

Matthew J. Breit[1], Laura K. Kaizer[2], Asma Taheri[2], Danielle M. Ostendorf[1,3,4] Zhaoxing Pan[2], Paul S. MacLean[1,3], Daniel H. Bessesen[1,3], Edward L. Melanson[1,5], and Victoria A. Catenacci[1,3], Seth A. Creasy[1,3]

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Introduction: Poor sleep may undermine adherence to dietary and physical activity recommendations during behavioral weight loss treatment. The objective of this analysis was to determine whether baseline sleep parameters were associated with changes in energy intake (EI), total daily energy expenditure (TDEE), and body weight during a behavioral weight loss intervention involving intermittent fasting or daily caloric restriction.
Methods: 165 adults (mean±SD; age 42±9 years, BMI 34.1±4.4 kg/m^2, 74% female) without diabetes mellitus or cardiovascular disease were randomized to intermittent fasting (4:3 IMF, 80% energy restriction on 3 nonconsecutive days/wk) or daily caloric restriction (DCR, ~34% energy restriction every day) for 12 months, followed by a 6-month unsupervised, maintenance phase (i.e., 18 months total). The prescribed weekly dietary energy deficit was similar between 4:3 IMF and DCR (34%). Both intervention arms received group-based behavioral support and a recommendation to increase moderate-intensity physical activity to 300 min/wk. Data from 117 participants (n=64 4:3 IMF and n=53 DCR; age 43±9 years, BMI 33.9±4.3 kg/m^2, 74% female) with valid, objective sleep data at baseline, and follow-up weight change data were included in this secondary data analysis. Weight was measured at 0, 6, 12, and 18 months. Time in bed (TIB), bedtime, waketime, midpoint of sleep, and sleep regularity (SD of waketime) were assessed at baseline using the activPAL thigh-worn accelerometer. The activPAL was worn for 7 consecutive days and analyzed in combination with self-reported sleep/wake logs. TDEE was measured with the doubly labeled water (DLW) method at 0, 6, and 12 months. EI was quantified using the DLW intake-balance method over 6 and 12 months. Linear mixed models, adjusted for randomized group, were used to examine the change in outcomes within and between baseline sleep categories over 18 months.
Results: Individuals with >9h TIB at baseline had significantly greater weight loss at 18 months compared to individuals sleeping 7-9 hours (mean difference: -3.43 kg [95%CI-6.13,-0.72]). Individuals waking up between 06:00 - 08:00 at baseline had significantly greater weight loss at 18 months compared to individuals waking up after 08:00 (mean difference: -4.16 kg [95%CI:-7.67, -0.65]). Individuals with a midpoint of sleep between 02:00 - 04:00 at baseline had significantly greater weight loss at 12 and 18 months compared to individuals with a midpoint of sleep before 02:00 and after 04:00. Individuals with sleep regularity of <1h at baseline had significantly greater weight loss at 18 months (mean difference: -8.78 kg [95%CI: -14.21, -3.35]) compared to individuals with a sleep regularity >2h. Having better sleep at baseline was not associated with greater increases in TDEE or decreases in EI across the intervention.
Conclusions: Better sleep at baseline was associated with greater weight loss, but not improvements in objectively measured TDEE and EI. Improving sleep health prior to or during a behavioral weight loss intervention may improve long-term weight loss. Future, prospective, randomized trials are needed to confirm these findings.

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Poster #2

Pro-Fibrotic Immune Cells and Fibro-Adipogenic Progenitors Contribute to Skeletal Muscle Extracellular Matrix Remodeling and Fibrosis in Cancer Cachexia

Presenter: Thomas Cardaci
Postdoctoral Fellow
Colorado State University

Overview

Pro-Fibrotic Immune Cells and Fibro-Adipogenic Progenitors Contribute to Skeletal Muscle Extracellular Matrix Remodeling and Fibrosis in Cancer Cachexia

Thomas D. Cardaci[1]; Arianna V. Bastian[2]; Kasie Roark[2]; Brooke M. Bullard[2]; Mitchell M. NeSmith[2]; Christian A. Unger[2]; Robert L. Price[3]; Jason L. Kubinak[2]; E. Angela Murphy[2]; Brandon N. VanderVeen[4]

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[4]Department of Cancer Biology, Wake Forest University School of Medicine, Winston-Salem, NC

Objectives: To determine the contribution of pro-fibrotic immune cells and fibro-adipogenic progenitors (FAPs) to skeletal muscle extracellular matrix (ECM) remodeling and fibrosis in cancer cachexia. The hypothesis was that cachexia induces immune cell infiltration and FAP expansion that promote excessive ECM deposition and muscle dysfunction.
Methods: Male CD2F1 mice (n=35) were randomized into control, weight-stable (CT26), or cachectic (C26) groups. Tumor cells (1×10^6) were implanted subcutaneously. Body weight, muscle mass, and physical function (grip strength, rotarod) were assessed. Skeletal muscle was analyzed using scanning and transmission electron microscopy (SEM/TEM) to evaluate ECM structure, and high-dimensional flow cytometry to quantify immune cells, FAPs, and satellite cells. Gene expression of fibrogenic markers was quantified by RT-PCR.
Results: C26 mice exhibited reduced survival ($\chi^2=7.22$, $p=0.027$), body weight (-13.4%, $p=0.004$), and muscle mass (soleus -37%, $p<0.0001$) with impaired grip strength (-34%, $p<0.0001$) and rotarod performance (-58%, $p=0.0145$). Skeletal muscle showed significant ECM thickening in perimysium (+61%, $p=0.002$) and endomysium (+79%, $p=0.002$). Flow cytometry revealed elevated neutrophils (+934%, $p<0.000001$), pro-fibrotic $CD206^{+}MHCII^{-}$ macrophages (+43%, $p=0.034$), and FAPs (+73%, $p=0.022$). SEM and TEM identified clusters of infiltrating immune cells and FAP-like cells localized to fibrotic ECM regions. Cachectic muscle displayed upregulated fibrogenic genes including TGF-β (+71%, $p=0.023$), HIF1α (+2.3-fold, $p<0.0001$), Col1 (+65%, $p=0.047$), and Fn1 (+88%, $p=0.015$).
Conclusions: Cachexia induces infiltration of pro-fibrotic immune cells and expansion of FAPs, resulting in excessive ECM deposition in skeletal muscle. These changes underlie fibrosis, impaired function, and worsened outcomes, highlighting therapeutic potential in targeting immune cells and FAPs in cachexia.
Funding Sources: Supported by the National Cancer Institute of the National Institutes of Health grants F31CA278490 (TDC), F99CA294251 (TDC), U01CA272977 (EAM), K99CA276891 (BNV), and NIH award 1S10OD032271 (RLP)

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Poster #3

β-Adrenergic Receptor Regulation of Vitamin D: Implications for Oxidative Stress

Presenter: Christina Cheng
Graduate Student
Colorado State University

Overview

β-Adrenergic Receptor Regulation of Vitamin D: Implications for Oxidative Stress

Christina Cheng[1]; Taylor Ewell[1]; Gregory Dooley[2]; David Thomson[1]; Christopher Bell[1]

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[2]Department of Environmental and Radiological Health Sciences, Colorado State University, Fort Collins, Colorado

Objectives: Vitamin D is essential for proper physiological function. Deficiency is clinically determined by measuring circulating concentration; however, due to its lipophilic nature, most vitamin D is stored in adipose. Prevalence of vitamin D deficiency is high in adults with excessive adiposity (i.e., sedentary adults with body mass index (BMI)>25 kg/m^2), suggesting deficiency may be attributed to bioavailability. Acute exercise temporarily increases circulating vitamin D, presumably coinciding with fat breakdown for use as fuel (i.e., lipolysis), which is mediated by beta-adrenergic receptor (β-AR) stimulation. Our first aim is to determine if pharmaceutical β-AR stimulation increases circulating vitamin D. In sedentary adults with BMI>25 kg/m^2, oxidative stress attenuates β-AR responsiveness. Our second aim is to determine if co-administration of an antioxidant (vitamin C) augments the vitamin D response to β-AR stimulation.
Methods: On two randomly ordered occasions, sedentary adults with BMI>25 kg/m^2 received three continuous incremental intravenous doses of a non-selective β-AR agonist (isoproterenol) co-infused with either saline or vitamin C. Blood was sampled and analyzed for vitamin D concentration at baseline and after each dose.
Results: During β-AR stimulation, vitamin D concentration appeared to increase: Dplasma [25(OH)D_3] (1.29±0.56, 1.30±0.97, 1.48±1.08 ng/mL), however, this effect was abrogated with the co-infusion of vitamin C (0.00±0.60, 0.07±0.61, -0.16±0.50 ng/mL).
Conclusions: In contrast to our hypothesis, our preliminary data suggest that the presence of oxidative stress may be necessary for β-AR regulation of vitamin D.
Funding Sources: This study is not currently funded.

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Poster #4

Hepatocyte cell-intrinsic mechanisms for increased gluconeogenic capacity in the growth-restricted fetus

Presenter: Kiarra Coger
Graduate Student
University of Colorado Anschutz Medical Campus

Overview

Hepatocyte cell-intrinsic mechanisms for increased gluconeogenic capacity in the growth-restricted fetus

Kiarra J. Coger[1], Molly M. McGuckin[1], Dong Wang[1], Ken Jones[2], Paul J Rozance[1], Laura D. Brown, Stephanie R. Wesolowski[1].

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Introduction: Fetal sheep with growth restriction (FGR) have increased hepatic gluconeogenesis and insulin resistance. Isolated hepatocytes from FGR fetuses have increased gluconeogenic capacity. A better understanding of the mechanisms is needed, as children and adults born with FGR have dysregulated gluconeogenesis, a hallmark of diabetes.
Objective: Identify cell-intrinsic gene regulation supporting increased gluconeogenic capacity and insulin resistance in FGR hepatocytes.
Methods: Hepatocytes were isolated from normal (CON) and FGR (n=4 each) fetal sheep and incubated in glucose-free media to measure glucose output. Hepatocytes were also incubated in media with nutrients representing normal fetal concentrations and used for bulk RNA-sequencing to determine transcriptional differences, predicted pathways, and regulators intrinsic to the hepatocyte.
Results: Hepatocytes from FGR versus CON fetuses produced more glucose basally and in response to gluconeogenic substrates (lactate+pyruvate) and activators (dexamethasone+cAMP) (2-way ANOVA; FGR: $P<0.001$, Treatment: $P<0.001$). RNA-sequencing identified 92 up- and 45 down-regulated genes in FGR versus CON hepatocytes. We found an upregulation of hypoxia-regulated metabolic genes, including *LDHA*, *SLC2A1* (GLUT1), *PGAM1*, *HMOX1*, and *SLC16A3* (MCT4, lactate transporter). Additionally, of the top 25 KEGG pathways, seven were related to inflammation. Four predicted upstream regulators (MYC, JUN, HIF1A, TP53) are also targets previously found upregulated in FGR fetal liver tissue.
Conclusion: Increased lactate production and transport (*LDHA* and *SLC16A3* genes) may facilitate increased gluconeogenic capacity in FGR fetal hepatocytes. Activation of inflammatory pathways may promote insulin resistance. We speculate that hypoxemia in FGR fetuses may initiate these cell-intrinsic effects in FGR hepatocytes.
Funding Sources: Supported by NIH-R01-DK108910 and HD079404

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Poster #5

Cross-Sectional Correlates of Pancreatic Fat Content and Pancreatic Volume in a General Risk Population of Youth in Colorado

Presenter: Catherine Cohen, PhD, RDN
Research Associate
University of Colorado Anschutz Medical Campus

Overview

Cross-Sectional Correlates of Pancreatic Fat Content and Pancreatic Volume in a General Risk Population of Youth in Colorado

Catherine C. Cohen[1,2], Curtis Tilves[1,2], Erin K. Englund[3], Houchun Hu[4], Megan M. Kelsey[5], Dana Dabelea[1,2,5]

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[3]Department of Radiology, Colorado School of Medicine, University of Colorado Anschutz Medical Campus, Aurora, CO.
[4]Department of Radiology, Mayo Clinic, Jacksonville, FL.
[5]Department of Pediatrics, Colorado School of Medicine, University of Colorado Anschutz Medical Campus, Aurora, CO.

Objectives: To examine cross-sectional associations of child traits and adiposity measures with pancreatic fat (PF) and pancreatic volume (PV) in a general risk population of youth.
Methods: Quantitative magnetic resonance imaging (MRI) was used to assess PF and PV, hepatic fat (HF), and abdominal visceral and subcutaneous adipose tissue (VAT and SAT) areas in 215 children (8-14 y) in the Colorado Healthy Start Study. Other relevant assessments included pubertal maturation (Tanner stage) based on physical exam and dysglycemia based on 3-hour oral glucose tolerance tests. Associations of child traits and adiposity measures with PF and PV were assessed using bivariate and multivariate regression.
Results: Mean±SD was 3.3±1.9% for PF and 42.4±15.9 cm^3 for PV. In bivariate (unadjusted) analyses, PF and PV did not differ by prediabetes status, but PF was higher in youth with obesity and was directly correlated with all adiposity measures; whereas, PV was associated with age and higher pubertal stage (all $p<0.05$). In multivariable-adjusted regression models with age, sex, Tanner stage, BMI percentile category, HF, VAT, and SAT as predictors, and log-PF or PV as the outcome, abdominal SAT was most strongly associated with log-PF (β [95% CI]: 0.16 [0.01,0.31]), and pubertal stage was most strongly associated with PV (β [95% CI]: 19.9 [12.7,27.1] for Tanner 4/5 vs. 1).
Conclusions: Our findings provide insights into individual characteristics associated with variation in PF (↑abdominal adiposity) and PV (↑pubertal maturation) among healthy youth. Future studies examining prospective associations of PF and PV with youth-onset T2D risk are needed.
Funding Sources: NIDDK (K99DK136503, R01DK133235).

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Poster #6

The Effect of a Prebiotic Supplement on Glucose Levels During Combined Sleep Restriction and Circadian Misalignment

Presenter: Virginia Edwards
Graduate Student
University of Colorado Boulder

Overview

The Effect of a Prebiotic Supplement on Glucose Levels During Combined Sleep Restriction and Circadian Misalignment

Virginia K. Edwards[1] Sabrina K. Linton[1] Christopher M. Depner[1,2] Luisa P. Marot[1] Dana Withrow[1] Kenneth P. Wright Jr.[1]

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[2]Department of Health and Kinesiology, University of Utah, Salt Lake City, Utah, USA

Objectives: Insufficient sleep and circadian misalignment dysregulate glucose homeostasis. Interventions are needed when insufficient sleep and circadian misalignment cannot be avoided. Prebiotics have been shown to beneficially affect glucose metabolism in non-human preclinical models and in humans.
Methods: 5 healthy adults (aged 25.4±3.5, 2 females) completed a 39-day randomized, double-blind, placebo-controlled, cross-over study comparing a prebiotic–7.5g/day each of Galacto-oligosaccharide (GOS) [Frieslad Campina] and Polydextrose (PDX)[Dupont Nutrition & Biosciences] or placebo (maltodextrin[Grain Processing Corporation]) sachets dissolved in water with breakfast for 14 days while maintaining ~8h sleep and consistent mealtimes prior to in-laboratory study of combined sleep restriction and circadian misalignment with 3h sleep opportunities. Prebiotic and placebo conditions continued in-laboratory. Glucose levels were monitored every 15 min for ~60h using a continuous glucose monitor (FreeStyle Libre Pro [Abbott]). Participants had a washout period prior to repeating the protocol with the second condition. Mixed-model ANOVA with subject as a random factor and prebiotic vs. placebo condition and baseline (BL) vs. SRCM as fixed factors.
Results: Average postprandial glucose area under the curve was significantly lower for prebiotic versus placebo. Average postprandial glucose difference from pre-snack during BL and SRCM conditions and pre-dinner during BL were significantly lower with the prebiotic supplement. Glucose difference from pre-dinner during SRCM showed non-significant trends.
Conclusions: Preliminary findings suggest that a PDX/GOS prebiotic supplement may help reduce postprandial glucose responses during combined sleep restriction and circadian misalignment. Additional research is warranted.
Funding Sources: Office of Naval Research MURI (N00014- 15-1-2809), NIH/NCATS (UL1TR002535), NIH T32 HL149646, CU Undergraduate Research Opportunities

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Poster #7

Long-term effects of reduced docosahexaenoic acid placental transfer on offspring neurobehavioral outcomes in mice

Presenter: Marta Hita Hernanadez
Postdoctoral Fellow
University of Colorado Anschutz Medical Campus

Overview

Long-term effects of reduced docosahexaenoic acid placental transfer on offspring neurobehavioral outcomes in mice.

Marta Hita Hernandez[1], Kenneth Barentsen[1], Katie Bidne[1], Jamie Henry[2], Robert Dietz[2], Thomas Jansson[1], Theresa L. Powell[1,2]

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Objectives: Docosahexaenoic acid (DHA) is critical for fetal brain development. Inadequate supply during the perinatal period has been associated with an impaired neurological function in children. DHA is transported from the mother to the fetus via the placenta by the Major Facilitator Superfamily Domain Containing 2a (MFSD2a) transporter. We hypothesize that placenta-specific knockdown (KD) of MFSD2a in mice causes neurobehavioral changes in adult offspring.
Methods: We generated placenta-specific KD of MFSD2a using a mouse model of trophectoderm lentivirus transfection and embryo transfer. Neurobehavioral functions such as cognition, memory, motor skills and anxiety-like behaviors as well as social interaction were tested at 3 months of age in male and female mice from placental MFSD2a KD and non-coding transfection (SCR) pregnancies using Open field, Contextual Fear Conditioning, Three-Chamber Sociability and Rotarod test.
Results: Adult mice from pregnancies with placental MFSD2a KD demonstrated a significant increase of anxiety-like behavior (n=34 SCR and n=39 MFSD2a KD, p-value<0.0001) with an impaired mobility (n=41 SCR, n=46 MFSD2a KD, p-value<0.001) and cognition (n=20 SCR, n=20 MFSD2a KD, p-value<0.05) predominantly in females.
Conclusions: Our results suggest that placental DHA transfer by MFSD2a during pregnancy is critical for long-term neurodevelopment.
Funding Sources: This study has been supported by NIH HD104644.

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Poster #8

Association of Maternal Serum Per- and Polyfluoroalkyl Substances (PFAS) with Offspring Mesenchymal Stem Cell (MSC) Transcriptome and DNA Methylation

Presenter: Suzanna (Suzzi) Kafer
Graduate Student
University of Colorado Anschutz Medical Campus

Overview

Association of Maternal Serum Per- and Polyfluoroalkyl Substances (PFAS) with Offspring Mesenchymal Stem Cell (MSC) Transcriptome and DNA Methylation

Suzanna C. Kafer[1,2], Cheyret Wood[3], John L. Adgate[4], William B. Allshouse[4], Antonia, M. Calafat[5], Elizabeth J. Davidson[6], Ivana V. Yang6,[7], Katerina Kechris[3,8], Dana Dabelea[7,8], Anne P. Starling[7,8,9], and Kristen E. Boyle[1,7]
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[9]Department of Epidemiology, Gillings School of Global Public Health, University of North Carolina at Chapel Hill, Chapel Hill, NC, USA

Objectives: The goal of this study was to determine the association between maternal serum PFAS levels and transcriptome and DNA methylation of infant umbilical cord mesenchymal stem cells (MSCs).
Methods: 113 mother-infant dyads from the Healthy Start cohort were included in this study. We measured levels of four PFAS chemicals: perfluorooctanoic acid (PFOA), perfluorooctane sulfonate (PFOS), perfluorononanoic acid (PFNA), and perfluorohexane sulfonic acid (PFHxS)- in maternal serum (median = 27 weeks gestation).. We cultured MSCs from umbilical cord tissue after birth. We isolated RNA and genomic DNA from MSCs, then performed RNA sequencing and measured DNA methylation using the EPIC array. We performed analyses in to determine differentially expressed genes (DEG) using DESEq2, and pathways using Fast R Gene Set Enrichment Analysis (GSEA), adjusting for infant sex, pre-pregnancy BMI, and gestational age. We differentially methylated regions (DMR) using Methylated CpGs Set Enrichment Analysis.
Results: We found associations with MSC DEGs for prenatal concentrations of all PFAS tested: PFOS (n=8), PFOA (n=4), PFNA2 (n=3), and PFHxS (n=22). Our GSEA analysis showed prenatal PFOS concentrations were associated L1 signaling and neurofascin pathways (n=3). Prenatal PFOA concentrations were associated with 35 pathways, mainly related to cell cycle, Rho GTPase signaling, and infection, while prenatal PFHxS concentrations were associated with these same pathways in addition to DNA repair and antiviral pathways (n=70). Prenatal PFAS concentrations were associated with DMRs in related genes for PFOS (NFASC, TRIM55, WNT4, L1CAM) and with 4 DMR.
Conclusions: These results could provide important clues for understanding the impact of prenatal exposure to persistent chemical toxicants on child health.
Funding Sources: This work was supported by grants from the National Institute of Environmental Health Sciences (R01ES022934), NIH Environmental Influences on Child Health Outcomes (ECHO) Program (NIH 1UG3OD023248 to DD), R01DK117168 to KEB, the American Diabetes Association (1-18-ITCS-016 to KEB), the parent Healthy Start Study (NIH R01 DK076648 to DD), and the Colorado Clinical and Translational Sciences Institute (UL1 TR001082) for maternal visits and collection of birth measures. The CU Anschutz Genomics Shared Resource that analyzed the RNA sequencing is supported by CU Anschutz Cancer Center (P30CA046934).

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Poster #9

Impact of Insufficient Sleep on Respiratory Quotient and Substrate Utilization

Presenter: Luisa Marot
Postdoctoral Fellow
University of Colorado Boulder

Overview

Impact of Insufficient Sleep on Respiratory Quotient and Substrate Utilization

Luisa P. Marot[1], Dana Withrow[1], Christopher M. Depner[1,2], Edward L Melanson[3,4], Janine A Higgins[3], Kenneth P. Wright Jr[1,3].

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Objectives: The aim was to evaluate substrate utilization over 24h, specifically during nighttime hours, under insufficient sleep conditions.
Methods: Thirty-six healthy participants[18 women, 25.5±4.7y, body mass index (BMI)22.4±1.7kg/m^2] completed a 13-16d in-laboratory study. Participants were randomly assigned to one of three groups with different sleep opportunities simulating two work weeks (WW1 and WW2) and one weekend between them. After three baseline (BL) days of 9h sleep/night, the control group (n=8) had 10d of 9h sleep/night; the sleep restriction (SR) group (n=14) had 10d of 5h sleep/night, and the weekend recovery (WR) group (n=14) had 5d of 5h sleep/night (WW1) followed by 2d of ad libitum weekend recovery sleep, then 3d of 5h sleep/night (WW2). Participants were provided an energy-balanced diet for 3d prior and during the BL days. Food intake was ad libitum during WW1 and WW2. Whole room indirect calorimetry assessed hourly substrate utilization on days 3(BL), 5(WW1) and 11(WW2). Respiratory quotient (RQ), fat and carbohydrate utilization were assessed by oxygen consumption and CO_2 production. Within-group differences across BL, WW1, and WW2 were analyzed over 24h.
Results: WR group showed higher 24h RQ and carbohydrate utilization in WW1 and WW2 compared to BL($p<0.05$). Sleep restriction significantly($p<0.05$) increased carbohydrate utilization during the 4h before bedtime, during WW1 (SR:0.28g.min-1±0.02; WR:0.31g.min-1±0.02) and WW2 (SR:0.30g.min-1±0.02; WR:0.31g.min-1±0.02)compared to BL (SR:0.15 g.min-1±0.02; WR:0.14g.min-1±0.02).
Conclusions: Insufficient sleep combined with ad libitum food intake appears to increase nighttime carbohydrate utilization prior to bedtime. These findings enhance our understanding of how insufficient sleep alters energy metabolism in humans.
Funding Sources: NIH HL109706, DK111161, TR001082, DK048520, and Sleep Research Society Foundation grant 011-JP-16.

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Poster #10

Afternoon Exercise Attenuates Impaired Insulin Sensitivity during Insufficient Sleep.

Presenter: Grissy Simé-Mora
Graduate Student
Colorado State University

Overview

Afternoon Exercise Attenuates Impaired Insulin Sensitivity during Insufficient Sleep.

Grissy Simé Mora[2], Emily M. Marbas[1], Oliver A. Knauer[1], Edward L. Melanson[3,4], Josiane L. Broussard[1,2,3], Kenneth P. Wright Jr.[1,3]

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[3]Division of Endocrinology, Metabolism and Diabetes, University of Colorado Anschutz Medical Campus, Aurora, CO
[4]Department of Geriatrics, University of Colorado Anschutz Medical Campus, Aurora, CO

Introduction: About one-third of U.S. adults report insufficient sleep (IS), which is linked to impaired insulin sensitivity and elevated risk for type 2 diabetes. Regular physical activity improves insulin sensitivity, but whether it can improve the adverse metabolic effects of insufficient sleep is unknown. We tested the hypothesis that prior physical activity attenuates the reduction in insulin sensitivity due to IS.
Methods: Eleven active (6F, 23.5 ± 1.0y, BMI 22.1 ± 0.7 kg/m², VO_2max 48.2 ± 2.3 ml/kg/min) and eleven sedentary adults (6F, 24.9 ± 1.3y, BMI 22.3 ± 0.5 kg/m², VO_2max 41.5 ± 6.6 ml/kg/min) completed a 5-day inpatient protocol. Participants had one night of habitual sleep (9h time in bed; baseline, BL) followed by four nights of IS created by delaying bedtime 4h while maintaining habitual wake time (5h sleep opportunity). Oral glucose tolerance tests were performed on day 2 (BL) and day 5 (IS). During IS, active participants performed 60-min of treadmill running at 65% of maximal heartrate 8.5 h after waking; sedentary participants remained inactive.
Results: Sedentary participants showed reduced insulin sensitivity (Matsuda index: 14.4 ± 2.6 BL vs 9.7 ± 1.3 IS; p =0.005). Active participants showed no significant change (11.8 ± 1.6 BL vs 10.0 ± 1.2 IS; p =0.332). Glucose AUC did not differ between conditions. Insulin AUC increased with IS in sedentary participants (p =0.008) but not in active participants (p =0.09).
Conclusion: IS decreased insulin sensitivity in sedentary but not active adults, suggesting regular physical activity may mitigate some of the metabolic consequences of IS.
Funding: This work was supported in part by T32HL149646 to GSM, the Sleep Research Society Foundation Early Career Development Award, National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) K01DK110138, and Society in Science—The Branco Weiss Fellowship, administered by the ETH Zürich to JLB, and the National Institute of Heart, Lung and Blood (NHLBI) R01HL132150 to KPW

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Poster #11

Move More, Feel Better: Physical Activity as a Driver of Well-Being Among Cancer Survivors

Presenter: Hannah Parker
Post-Doctoral Fellow
Colorado State University

Overview

Move More, Feel Better: Physical Activity as a Driver of Well-Being Among Cancer Survivors

Hannah Parker[1]; Elena Lancioni[1]; Hadalyn Anderson[1]; Heather Leach[1]

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Objectives: This study examined the relationship between changes in physical function (ΔPF) and quality of life (ΔQoL) following a 12-week exercise intervention among cancer survivors and evaluated whether changes in physical activity (ΔPA) modify this relationship.
Methods: Participants completed virtual exercise sessions 2x/week and 3 PA behavior change discussion sessions. Self-reported light PA, moderate-vigorous (MVPA) and strength training (GLTEQ), QoL (FACT-G), and physical function (30-second sit-to-stand) were assessed pre- and post-intervention. Paired t-tests and Wilcoxon signed rank tests were conducted to compare pre- and post-intervention values. Linear regressions tested whether ΔPF predicted ΔtotalQoL and ΔfunctionalQoL, with Δlight PA, ΔMVPA and Δstrength as moderators.
Results: Cancer survivors (*N*=47, 58.7±10.6yrs; 83% female, stage I/II (51%) Breast (30%), Ovarian (19%) or other (%) cancer) were included in analyses. Functional and Total QoL did not significantly change (Δ-0.4 (0.3), p=0.03; Δ-0.3(0.9), p=0.2; respectively). Participants significantly increased PF (Δ3.2(0.26), p=0.00) and all PA per week (Δ35.5 (9.1), p=0.0003 light PA; Δ57.8 (16.4), p=0.0000 MVPA; Δ46.9 (4.2), p=0.00 strength). ΔPF was weakly correlated with ΔtotalQoL (r=0.03) and ΔfunctionalQoL (r=0.14). ΔMVPA significantly predicted ΔtotalQoL (0.03(0.01), p=0.01) and ΔfunctionalQoL (0.01(0.01), p=0.01); however, there was no significant moderation effect of ΔPA on the relationship between ΔPF and ΔQoL.
Conclusions: Changes in PF were only weakly associated with changes in QoL among cancer survivors. While all PA increased significantly, only MVPA directly predicted improvements in QoL. This suggests that enhancing MVPA may be more influential for QoL than changes in PF alone, highlighting the importance of promoting sustained PA in survivorship care.
Funding Sources: This project was funded by the National Cancer Institute within the National Institutes of Health (R33CA256656).

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2025 Colorado NORC Retreat: Poster Abstracts

Poster #12

Quantifying the Impact of First Foods on the Infant Gut Microbiota and Immune Health via IgA

Presenter: Jing Qian
Graduate Student
University of Colorado Boulder

Overview

Quantifying the Impact of First Foods on the Infant Gut Microbiota and Immune Health via IgA

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Objectives: Our overall objective is to quantify how early diet influences the infant immune system. We hypothesize that introducing fiber-rich, plant-based foods versus protein-rich, meat-based foods will alter IgA antibody targeting patterns of beneficial symbionts and opportunistic pathogens in early life, which is indicative of a change in the infant-microbe immune relationship.
Methods: We analyzed fecal samples from 12 healthy infants in a randomized controlled trial comparing plant-based (n=8) versus meat-based (n=4) complementary feeding from 5 months to 12 months of age. We optimized Metagenomic Immunoglobulin Sequencing (MIg-Seq) protocol for low-biomass infant samples. This involves using PE anti-IgA antibody staining, magnetic bead separation, and deep metagenomic sequencing to identify IgA-targeted microbes at the strain level.
Results: Our optimized protocol reliably profiled the IgA-coated microbiome in low-biomass fecal samples. The overall IgA-targeting profiles differed significantly between diet groups (Wilcoxon rank-sum test, p=0.008). Specifically, the plant-based diet was associated with lower IgA coating of beneficial symbionts like *Faecalibacterium prausnitzii* and *Bifidobacterium* spp. In contrast, the meat-based diet led to progressively higher IgA targeting of opportunistic pathogens, including multiple species within the *Clostridium* and *Enterococcus* genera.
Conclusions: Here we discover the first evidence that an infant's first foods create a significant and potentially long-lasting imprint on immune-microbial IgA interactions in early life. These findings provide preliminary evidence for a mechanistic link between diet and mucosal immune development, contributing to the scientific evidence base that may one day inform future nutritional guidelines for promoting infant health.
Funding Sources: This research was supported by a Colorado NORC Pilot & Feasibility Program Award to Dr. Matthew Olm (P30DK048250).

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2025 Colorado NORC Retreat: Poster Abstracts

Poster #13

Histone Deacetylase Inhibition as a Novel Mechanism to Reverse Obesogenic Epigenetic Memory

Presenter: Lorien Salyer
Postdoctoral Fellow
University of Colorado Anschutz

Overview

Histone Deacetylase Inhibition as a Novel Mechanism to Reverse Obesogenic Epigenetic Memory

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Objectives: A recent RNA-sequencing study identified epigenetic modifications, including decreased histone acetylation, that persist during periods of weight loss and weight gain. Thus, blocking the action of the erasers of acetylation, histone deacetylases (HDACs), to increase histone acetylation could be a mechanism to reverse obesogenic transcriptional repression. The objective of this study is to identify the transcriptional, metabolic, and cardiovascular consequences of HDAC inhibition in a mouse model of recurrent weight gain. We hypothesize that HDAC inhibition will increase histone acetylation to reverse obesogenic epigenetic memory and sustainably improve metabolic and cardiac function.
Methods: We fed a cohort of wild-type mice a pan-HDAC inhibitor, ITF2357, for one week. We then isolated histones from their heart and adipose tissue and used Western blot to probe for histone and protein acetylation.
Results: Mice fed ITF2357 had an increase in histone and protein acetylation in adipose and cardiac tissue. Additionally, we previously published that ITF2357-fed mice had improved cardiac function in a model of diastolic dysfunction. Together, these data suggest feeding ITF2357 is sufficient to modify both histone acetylation and cardiac function.
Conclusions: To further investigate the effect of HDAC inhibition on obesogenic epigenetic memory, mice will be fed HFD to induce obesity, followed by ITF2357 or chow, followed HFD to replicate the ‘yo-yo’ effect of weight-loss and regain. We will evaluate epigenetic, metabolic, and cardiovascular changes in these mice. Successful completion of these studies will support the use of HDAC inhibition as a novel therapeutic mechanism to reverse obesogenic epigenetic memory and improve cardiometabolic outcomes.
Funding Sources: National Institutes of Health (NIH) R01HL171711 & R01HL181226 and an American Heart Association Collaborative Sciences Award (24CSA1255857) (TAM). American Heart Association postdoctoral fellowship (25POST1373908) (LGS).

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2025 Colorado NORC Retreat: Poster Abstracts

Poster #14

GPR182 is a lipoprotein receptor for dietary fat absorption

Presenter: Zhiwei Sun
Postdoctoral Fellow
University of Colorado Anschutz

Overview

GPR182 is a lipoprotein receptor for dietary fat absorption

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Abstract: The lymphatic system plays a central role in lipid absorption by transporting triglyceride-rich particles called chylomicrons (CMs) from the small intestine to the systemic circulation. However, the molecular mechanism by which CMs get into the intestinal lymphatics is unknown. Here we demonstrated that GPR182, an atypical chemokine receptor in lymphatic endothelial cells, mediates dietary fat absorption. GPR182 knockout mice exhibit a selective increase in circulating high-density lipoproteins and are resistant to dietary-induced obesity. GPR182 ablation in mice leads to poor lipid absorption and thereby a delay in growth during development. GPR182 broadly interacts with and transports lipoproteins. Transmission electron microscopy analysis reveals that mechanistically, loss of GPR182 prevents CMs from entering the lacteal lumen of the small intestine. Consistent with this, GPR182 blockade with monoclonal antibodies protects mice from diet-induced obesity and treats existing obesity. Together, our study identifies GPR182 as a lipoprotein receptor that mediates dietary fat absorption and supports GPR182 blockade as a feasible approach to treat obesity and related disorders.

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2025 Colorado NORC Retreat: Poster Abstracts

Poster #15

Consistency of Interindividual Differences in the Amplitude of Daily Energy Expenditure and Respiratory Quotient Rhythms During Circadian Alignment and Circadian Misalignment in Healthy Adults

Presenter: Zoe Meredith
Graduate Student
University of Colorado Boulder

Overview

Consistency of Interindividual Differences in the Amplitude of Daily Energy Expenditure and Respiratory Quotient Rhythms During Circadian Alignment and Circadian Misalignment in Healthy Adults

Zoe Meredith[1], Andrew W. McHill[1,2,6], Hannah K. Ritchie[1], Tristan B. Dear[1], Victoria Catenacci[2], Karen Shea[2], Elizabeth Connick[3], Thomas M. Moehlman[1], Ellen R. Stothard[1,4], Janine Higgins[2], Edward L. Melanson[2,5], Kenneth P. Wright Jr[1, 2]

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Objectives: To determine whether trait-like interindividual differences in the daily amplitude of energy expenditure (EE) and respiratory quotient (RQ) exist and remain stable during circadian misalignment.
Methods: Two in-laboratory studies were conducted in healthy adults using whole-room indirect calorimetry with minute-by-minute EE and RQ measurement. Study 1 (n=15, age 23.3±3.4, 7 females) used a 4-day protocol with three randomized light conditions. Study 2 (n=13, age 26±5, 8 females) used a 5-day simulated shiftwork protocol (circadian misalignment on days 4–5 with sleep beginning 1 h after habitual wake time). In both, participants remained on constant bed rest with 8-h sleep opportunities and energy-balanced diets. Daily EE and RQ amplitude were quantified using non-orthogonal spectral analysis with two harmonics. Mixed-model ANOVA tested light or circadian condition effects, with participant as a random factor, with and without covariates (sex, age, fat-free mass, energy intake, thermic effect of food). Intraclass correlation coefficients assessed stability.
Results: During circadian alignment and misalignment, a significant main effect of participant was observed for EE and RQ amplitude ($p<0.01$), whereas the main effect of day was not significant ($p>0.1$). Stability of EE amplitude was “almost perfect” (ICC=0.91) during circadian alignment and “substantial” (ICC=0.70) during circadian misalignment. RQ amplitude stability was “moderate” (ICC=0.47) during circadian alignment and “substantial (ICC=0.45) during circadian misalignment.
Conclusions: These findings indicate stable, trait-like interindividual differences in EE daily amplitude that were less robust in RQ daily amplitude. Future work should examine other populations and conditions and disentangle circadian from sleep–wake factors in daily metabolic rhythms.
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