Oxidative Metabolism During the Time-course of Disuse Atrophy in Male and Female Mice

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Muscle loss is an important predictor of morbidity and mortality across a variety of diseases. Males and females appear to differ on clinical outcomes in relation to disuse-induced muscle loss, however reasons for these different responses have not been investigated. **PURPOSE:** To investigate measures of muscle oxidative metabolism during the time-course of disuse-induced atrophy in male and female mice. **METHODS:** Disuse atrophy was induced using hindlimb unloading in 50 male and 50 female mice for 0 (CON), 1, 2, 3, or 7 days (n~10/group). Muscle sections of the tibialis anterior were stained for succinate dehydrogenase (SDH, a measure of oxidative metabolism) and cross sectional area (CSA). CSA by SDH staining was used to investigate the effect of disuse on different muscle fiber phenotypes. mRNA content of \( Ppara \) was measured in the gastrocnemius, soleus, and extensor digitorum longus (EDL) muscles. Data were analyzed within each sex by one way ANOVA and trend analysis with \( p<0.05 \) indicating statistical significance. **RESULTS:** CSA of SDH positive fibers progressively decreased in both male and female mice. CON animals (male and female) had SDH positive fiber CSA of ~400 \( \mu m^2 \) and 7 day unloaded animals had CSAs of ~300 \( \mu m^2 \). Both male and female mice had an SDH negative CSA of ~650 \( \mu m^2 \), with no significant differences in fiber CSA noted across groups. In the gastrocnemius muscle, \( Ppara \) content was ~50-60\% lower at 1 day of unloading in males and females and remained depressed in all experimental groups. In soleus muscles of females, \( Ppara \) was ~60\% lower at days 1, 2, and 3 compared to CON, but then recovered back to CON levels. Whereas in males, \( Ppara \) was ~60\% lower with 1 day of unloading and remained depressed in 1, 2, 3, and 7 day groups. In females, there were no differences in \( Ppara \) content in EDL across all groups. In males, there was ~50-75\% lower \( Ppara \) in EDL content that reached statistical significance at 2 days unloading and remained depressed throughout intervention groups. **CONCLUSION:** Disuse results in muscle loss in both male and females and appears to result in similar alterations to oxidative metabolism across multiple tissues. Future studies should investigate if improving oxidative metabolism is protective against disuse atrophy in males and females.
Adherence to Telemedicine Exercise Program in Patients with Cystic Fibrosis Awaiting Lung Transplant

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Background: It is strongly recommended that cystic fibrosis (CF) patients adhere to a regular exercise routine while awaiting lung transplant. However, there are barriers to adherence for CF patients enrolled in traditional pulmonary rehabilitation (PR) programs including: greater risk of infection, proximity to rehabilitation facilities, time limitations and its design for an elderly population. Approximately 50% of CF patients enrolled in traditional PR complete all 24 sessions. A telemedicine approach to PR may be more feasible for CF patients, improving adherence and exercise capacity. Purpose: To compare exercise adherence in CF patients enrolled in a telemedicine PR program to a traditional PR program. Methods: Participants in the telemedicine PR program (n=7) were recruited by pulmonologist referral through the Columbia Cardiopulmonary Center and asked to complete a 24 exercise session program. Participants were able to determine their own workout schedule as long as they completed the program within 12 weeks. As part of the telemedicine PR program, participants accessed a cellular fitness application to select various biking, running, strength, yoga and stretching sessions. Participants were contacted by email each week to complete an exercise log. Adherence was monitored via exercise logs and the fitness application. Participants in the traditional PR program (n=8) were identified through the Columbia University Medical Center registry. Their adherence data was assessed retrospectively and compared to the telemedicine PR program. Both programs had 6-minute walk distance (6MWD) data. Results: Workout sessions completed in 12 weeks were not significantly different in the telemedicine (mean=19, SD=14) vs. traditional groups (mean=9, SD=4, p=0.107). Total number of workouts completed were also not significantly different (telemedicine: mean=37, SD=34 vs. traditional: mean=27, SD=11, p=.462). Finally, the change in 6MWD pre/post intervention was also not significantly different (telemedicine: mean=-57 meters, SD=133 vs. traditional: mean=-154 meters, SD=141, p=.450). Conclusion: Telemedicine and traditional PR program have similar exercise adherence and 6MWD results. Both are viable options as part of a pulmonary rehabilitation program for patients awaiting lung transplant.
Potential Racial Disparity in Peripheral Vascular Function Regardless of Menstrual Cycle Phase

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African American women (AAW) have the highest rates of cardiovascular disease (CVD) across the lifespan compared to women of other races. Vascular dysfunction is a non-traditional risk factor for CVD and is understudied in AAW. Previous studies have reported fluctuations in vascular function across the menstrual cycle (MC) with the changing levels of estrogen, but this relation has never been explored in the context of race. **PURPOSE:** To compare nitric oxide-mediated peripheral vascular function across 3 phases of the MC between AAW and CW using passive leg movement (PLM). **METHODS:** PLM was performed on premenopausal, healthy, female participants not using hormonal contraceptives; 7 AAW (24 ±2 years, BMI: 21.2 ±1.4 kg/m², BP: 112 ±3/74 ±3 mmHg) and 12 CW (23 ±1 years, BMI: 23.4 ±0.9 kg/m², BP: 113 ±2/70 ±2 mmHg). Phases of the MC were identified as early follicular (EF) (1-5 days post onset of menstruation; low estrogen), ovulation (OV) (within 1-3 days of luteinizing hormone surge determined by an ovulation test; high estrogen), and mid-luteal (ML) (8-10 days post ovulation; moderate estrogen). Blood velocity and diameter of the femoral artery were measured using Doppler ultrasound. A 2x3 repeated measures ANOVA was used to identify differences in vascular function between AAW and CW across 3 phases of the MC. **RESULTS:** The overall change in leg blood flow from baseline to peak (mL) was significantly lower among AAW compared to CW across the MC phases. EF (AAW: 195 ±49, CW: 356 ±64), OV (AAW: 156 ±47, CW: 451 ±102) and ML (AAW: 224 ±65, CW: 369 ±41) (p=0.02). The hyperemic response to PLM, calculated as area under the curve (mL), was significantly reduced in AAW compared to CW across the MC phases. EF (AAW: 45 ±21, CW: 131 ±40), OV (AAW: 49 ±28, CW: 144 ±40) and ML (AAW: 67 ±22, CW: 130 ±26) (p=0.03). **CONCLUSION:** AAW are experiencing an attenuated peripheral vascular response to PLM compared to CW across the menstrual phases. These preliminary data suggest an overall race-derived disparity in peripheral vascular function regardless of MC phase in young premenopausal women.

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Acute Changes in Sweat NaCl and Bone Mineral Density Following 45-Minutes of Treadmill Running

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Previous studies demonstrate a positive relationship between blood sodium concentration ([Na⁺]) and bone mineral density (BMD) in ultramarathon runners. PURPOSE: The purpose of this study was to assess relationships between sweat sodium chloride concentration ([NaCl]) versus total body BMD after 45-minutes of running. We hypothesized that higher sweat [NaCl] levels would positively correlate with decreases in total body BMD. METHODS: Seven healthy male runners participated in this randomized control crossover trial, ingesting a placebo capsule or sodium tablet. Baseline blood, sweat, and urine were collected pre-run after a 4-hour fast. A dual energy x-ray absorptiometry (DXA) scan was then performed. After 60 minutes of rest, runners completed a 45-minute self-selected speed treadmill run, with exercise-induced sweat collected using a macroduct disk affixed to the forearm (during-run). Immediately following the treadmill run, baseline testing measures were repeated (post-run). Main outcomes included pre-to post-run changes in sweat [NaCl] and BMD. RESULTS: Seven males (29±11years; 84±15kg; 1.8±0.1m; 25.6±3.5kg/m²) completed the placebo arm of the trial. Non-significant (p>0.05) differences were noted between pre-run sweat [NaCl] (56.7±14.3mmol/L), during-run sweat [NaCl] (53.4±19.1mmol/L), and post-run sweat [NaCl] (55.9±12.4mmol/L). DXA scans revealed non-significant post-run minus pre-run differences (∆) in total body BMD (0.0±0.0g/cm²), total body fat mass (-24.1±295.1g), total body lean mass (-785.2±235.2g), and total body mass (-810.5±397.8g). Non-significant increases were noted in blood [Na⁺] ∆ (1.6±1.2mmol/L) and plasma volume ∆ (0.9±2%) along with a non-significant decrease in urine [Na⁺] ∆ (-12.7±7.2mmol/L). Significant relationships were noted between BMD ∆ versus during-run sweat [NaCl] (r=0.96; p=0.001) and sweat [NaCl] ∆ (r=-0.78; p=0.04). A significant inverse relationship existed between post-run sweat [NaCl] versus post-run blood [Na⁺] (r=-0.76; p=0.04). CONCLUSION: Higher running-induced sweat [NaCl] was positively associated with increases in BMD after 45-minutes of running. These results were opposite of our hypothesis but confirm that total BMD and sweat [NaCl] change dynamically during treadmill running and appear homeostatically related.
Comparing Physiological Differences Between Sexes Drinking to Thirst Versus Drinking to a Generic Schedule

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PURPOSE: Thermoregulation and hydration have been linked for decades, resulting in athletes to rely on following hydration guidelines instead of their thirst mechanism. The purpose of this study was to examine sex differences in the physiological effects of drinking to thirst (Thirst) versus a generic schedule (Scheduled) during 2 hours of running. METHODS: In a randomized crossover study, eleven male (age=39.4±13.3yr, ht=176.4±7.7cm, wt=77.1±10.2kg, body fat=16.6±7.4%, VO2max=60.4±7.7ml/kg/min) and eleven female (age=36±9.3yr, ht=152.8±32.3cm, wt=60.2±9.9kg, body fat=21.0±8.4%, VO2max=52±8.5ml/kg/min) runners completed two experimental trials and a baseline assessment. Participants ran at 60% VO2max in a climate-controlled chamber (21˚C and 40% RH). Heart rate and core temperature were monitored continuously. In Thirst, participants drank when they felt a desire to drink and stopped when satisfied. The Scheduled trial, based on the 2000 NATA fluid replacement guidelines, required water consumption as follows: 600mL 2 hours pre-trial, 300mL 20min pre-trial, and 300mL every 10min during running. Blood samples were taken pre-trial, mid-trial, post-trial, and 20min post-trial, and analyzed for sodium. Nude body weight, sweat rate and urine volume were also obtained. Data was analyzed by two-way and one-way ANOVA and then correlated T-tests with a Bonferroni correction, and P<0.05. RESULTS: Blood sodium showed a significant difference between female scheduled and male scheduled (P<0.04). For body weight change female thirst was different from female scheduled (P<.01) and male thirst was different from male scheduled (P<.01). Performance time in female thirst was different from female scheduled and male thirst was different from male scheduled, all P<.05. Significant differences were also seen between the sexes and trials for sweat rate, urine volume, and fluid intake. There were no significant differences in core temperature between the trials. CONCLUSION: Both sex groups experienced weight gain and dilution of blood sodium in response to drinking according to the 2000 NATA guidelines. However, all participant’s physiological measures remained within normal limits when following their thirst mechanism, demonstrating that drinking to thirst is the safest hydration strategy as mentioned by the 2017 NATA fluid replacement guidelines.
Hydration position stands outline suggested volume considerations but remain somewhat ambiguous regarding frequency parameters. **PURPOSE:** To determine the effects of micro-dosing or bolus-dosing plain water (MW, BW, respectively) or a carbohydrate-electrolyte solution (MCE, BCE, respectively) on fluid retention and carbohydrate oxidation during exercise in the heat. **METHODS:** In a repeated measures cross-over design, males (n=8, 80.3 ±11.8 kg, VO₂ peak 53±5.0 ml kg⁻¹ min⁻¹) completed four 2-hour trials (treadmill, 1.3 m·s⁻¹ at a 5% grade) in a heat chamber (33°C and 30% RH) with a 15 kg pack. Fluids were delivered to equal 100% of a pre-determined hourly fluid loss familiarization trial. Micro-dosed fluids were provided at 22 doses·h⁻¹ (49±13 ml·dose⁻¹), while bolus-dosed fluids were provided at 1 dose·h⁻¹ (1075±274 ml·dose⁻¹). CE trials delivered 67±17 g CHO·hr⁻¹ and 939±239 mg Na⁺·hr⁻¹. Nude body weight, urine volume, and urine specific gravity (USG) were recorded during and 1-hour post exercise. Steady state expired air samples were collected to evaluate rates of carbohydrate oxidation. A two-way ANOVA with repeated measures was used to determine differences. Statistical significance was established at p<0.05. **RESULTS:** Total body weight loss was similar across all four trials (-0.60±0.25, -0.53±.17, -0.67±0.34, and -0.50±0.27 kg, for the BCE, MCE, BW, and MW trials, respectively, p>0.05). Cumulative urine output was similar across all four trials (725±478, 779±494, 818± 507, 718± 446 ml, for the BCE, MCE, BW, and MW trials, respectively, p>0.05). USG was additionally similar across all trials at 0, 60, 120, and 180 minutes (n=7, 1.008±0.006, 1.008±0.007, 1.007±0.007, 1.008±0.006, p>0.05). Carbohydrate oxidation was significantly higher in the CE trials when compared to the W trials (1.5±0.3 and 0.8±0.2, g min⁻¹, p< 0.05) but was not different between dosing styles of the same composition (1.6±0.3 and 1.5±0.3 g min⁻¹ for BCE and MCE; 0.8 ±0.2 and 0.8±0.3 g min⁻¹ for BW and MW, p>0.05). **CONCLUSION:** These data demonstrate minimal differences in overall fluid retention and substrate oxidation during exercise in the heat across varied fluid composition and delivery intervals. Supported by the United States Forest Service (USFS), National Technology and Development Program
Southeast Chapter

**Prediabetes Phenotype Does Not Exacerbate Microvascular Insulin Sensitivity in Metabolic Syndrome**

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Metabolic syndrome (MetS) and elevated glucose each promote microvascular dysfunction. Whether in combination these two conditions create increased dysfunction is not clear. Here, we tested whether glucose status worsens microvascular insulin sensitivity in MetS. Thirty-two sedentary, obese adults (54.2±1.2yrs; 35.9±1.3kg/m<sup>2</sup>; VO<sub>2</sub>max: 19.9±1.3ml/kg/min) with MetS (≥3 ATP III criteria) were classified as normal glucose tolerant (NGT, n=8; 6F), impaired fasting glucose (IFG; n=10; 7F) or IFG+IGT (n=14; 11F) according to ADA criteria using a 75g OGTT. Capillary perfusion (microvascular blood volume, MBV), filling rate (microvascular flow velocity, MFV) and blood flow (MBF=MBV*MFV) were assessed as the change before and after a 2hr euglycemic-hyperinsulinemic clamp (90mg/dl, 40mU/m<sup>2</sup>/min) using contrast enhanced ultrasound. Glucose infusion rate (GIR) was used to determine metabolic insulin sensitivity while carbohydrate oxidation (CHOox) was measured before and after the clamp to understand nutrient utilization. T-tests, repeated measure ANOVAs and correlations were used when appropriate. Significance was accepted as P≤0.05. There were no differences in age, BMI, VO<sub>2</sub>max or GIR (NGT: 2.26±0.48 vs. IFG: 2.66±0.46 vs. IFG+IGT: 1.91±0.37mg/kg/min, P=0.44) among groups. Insulin did not stimulate capillary perfusion (NGT: 0.16±0.19 vs. IFG: -0.02±0.14 vs. IFG+IGT: 0.08±0.12AI, P=0.40), filling rate (NGT: 0.006±0.005 vs. IFG: 0.003±0.004 vs. IFG+IGT: 0.004±0.004sec<sup>-1</sup>, P=0.11) or blood flow (NGT: 0.02±0.02 vs. IFG: 0.01±0.01 vs. IFG+IGT: 0.01±0.01AI/sec, P=0.21). CHOox was likewise unresponsive to insulin (P=0.34). Although age, BMI, fasting and 2hr glucose concentrations did not relate to insulin effects on microvascular function, fasting triglycerides was related to insulin-stimulated MBF (r=-0.39, P=0.03). Prediabetes phenotype does not worsen microvascular insulin sensitivity in adults with MetS. Future work is warranted to examine the effects of different therapies (lifestyle, medication) on microvascular function.

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Southwest Chapter

The Effects of 4 Weeks of Time Restrictive Feeding on Exercise Performance, Metabolism, and Recovery in Competitive Male Runners

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Purpose: The aim of this study was to investigate the effects of a time restricted feeding (TRF) 16/8 dietary pattern on exercise performance, metabolism, and recovery in male endurance runners. Methods: This ongoing investigation utilized a randomized crossover intervention of an 8-hour feeding window (TRF) versus a normative 12-hour feeding window (ND), with the remaining time spent fasting. Total caloric intake, macronutrients, and exercise training remained constant between the 2 interventions. At the beginning and end of each 4-week intervention subjects completed validated questionnaires to determine mood state and sport related recovery, body composition testing via DXA, a graded substrate utilization treadmill running test to analyze exercise metabolism, and a 10km treadmill time trial to assess performance. Preliminary Results: Data on 12 subjects showed that after 4 weeks of adhering to TRF, there was a greater decrease in blood lactate (+0.25±1.08 ND vs. -0.57±0.86 mmol/L TRF, p=0.02), a greater increase in rating of perceived exertion (-0.42±1.08 ND vs. +80.58±1.08 TRF, p=0.02), and a trending greater decrease in respiratory exchange ratio (-0.01±0.05 ND vs. -0.02±0.03 TRF, p=0.09) all at 90% VO2max. Adherence to 4 weeks of TRF also resulted in greater decreases in body mass (+0.31±1.27 ND vs. -1.14±2.01 kg TRF, p=0.04) but no significant alterations to lean mass (+0.42±1.24 ND vs. -0.26±1.44 kg TRF, p=0.11) or fat mass (+0.28±0.97 ND vs. -0.86±1.48 kg TRF, p=0.17), compared to a 12-hour feeding window. Following a TRF diet resulted in non-significant changes in 10km running times (-7.08±182.27 ND vs. -23.30±249.17 seconds TRF, p=0.43). Conclusion: Thus far, with limited power, results showed that adherence to a TRF diet for 4 weeks may lead to metabolic adaptations causing less mobilization of lactate, a greater reliance on fat utilization during exercise, and increased perceived difficulty maintaining high intensity running, but no significant changes in performance.
The prevalence of hypertension in Non-Hispanic Black (BL) men surpasses all other racial groups. Our laboratory has previously demonstrated exaggerated vasoconstrictor and blood pressure (BP) responses to spontaneous bursts of muscle sympathetic nerve activity (MSNA; sympathetic vascular transduction) in young, healthy BL men compared to their Non-Hispanic White (WH) counterparts. Because a family history of hypertension (FHH) further compounds cardiovascular risk, we wanted to begin to explore the potential impact of a positive (+) FHH on sympathetic vascular transduction. Whether a +FHH influences sympathetic vascular transduction in WH and/or BL men remains unknown. **PURPOSE:** To begin to explore if +FHH influences sympathetic vascular transduction within and between racial groups. **METHODS:** 22 men, nine with a +FHH (4 BL men) and 13 without a FHH (–FHH; 6 BL men) were recruited. Beat-to-beat BP (Finometer), femoral artery blood flow (Doppler ultrasound), and MSNA were measured during a 20-minute quiet rest. The mean BP and leg vascular conductance (LVC; blood flow/mean BP) responses to spontaneous bursts of MSNA were quantified via a signal averaging technique. **RESULTS:** Resting heart rate, BP, and MSNA were not significantly different between groups (all p>0.05). As previously demonstrated by our laboratory, the BL men exhibited an augmented sympathetic vascular transduction compared to the WH men (e.g., peak BP response, WH men: Δ4.1±0.3, BL men: Δ5.6±0.7 mmHg, p=0.04). When accounting for FHH within the groups, the peak BP (WH +FHH: Δ4.4±0.6 vs. WH –FHH: Δ3.8±0.4 mmHg, p=0.4) and nadir LVC responses (WH +FHH: Δ-0.5±0.07 vs. WH –FHH: Δ-0.5±0.09 ml·min⁻¹·mmHg⁻¹, p=0.7) were not significantly different between WH men +FHH and WH men –FHH. Likewise, the BL men +FHH exhibited similar peak BP (BL +FHH: Δ6.2±0.7 vs. BL –FHH: Δ5.3±1.1 mmHg, p=0.5) and nadir LVC (BL +FHH: Δ-1.1±0.44 vs. BL –FHH: Δ 0.6±0.10 ml·min⁻¹·mmHg⁻¹, p=0.2) responses to bursts of MSNA compared to the BL men –FHH. **CONCLUSION:** These preliminary findings do not support a role for +FHH in augmented sympathetic vascular transduction, therefore suggesting that racial differences in sympathetic vascular transduction are independent of FHH.