ENDURANCE EXERCISE TRAINING MODES TO IMPROVE PHYSICAL FUNCTION IN OLDER MICE: HIIT VS. VWR

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With age, we experience a progressive loss of physical function. Exercise is a promising therapy to preserve muscle health and functional aptitude. Animal models are needed to examine the underlying molecular mechanisms at the intersection of aging, exercise, and functional decline. In this study, we compare the efficacy of two types of individualized endurance exercise training in older C57BL/6 mice (26-months old at completion): HIIT (high intensity interval training on a treadmill, n=10) and VWR (voluntary wheel running, n=8). We hypothesized that while both exercises would improve function, HIIT would promote more extensive adaptation. For four months the VWR mice ran 4 days/week and the HIIT group ran 3x/week. We determined function pre/post-training by utilizing our composite scoring system, the Comprehensive Functional Assessment Battery (CFAB). CFAB consists of the following: treadmill running (endurance), rotarod (overall motor function), wheel running (volitional exercise rate/activity), grip strength (fore-limb strength), and inverted cling (overall strength/endurance). EchoMRI determined body composition. After training, we found significant CFAB improvement (repeated measures t-test, $p<0.05$) in both exercise groups, specifically including: rotarod (+37%, HIIT and VWR); treadmill (+61% VWR; +58% HIIT), grip strength (+20% VWR), body mass (-17% VWR, -10% HIIT), and fat percentage (-44% VWR, -20% HIIT). Contrary to our hypothesis, HIIT did not improve function more than VWR, though we suspect increasing training intensity would improve response. Thus, future studies will need to address defining HIIT dose response and optimal training volume for older mice. We conclude that our models will be useful for future mechanistic investigations.

IMPACT OF RADIOTHERAPY ON DAILY FUNCTION AMONG OLDER ADULTS LIVING WITH ADVANCED CANCER

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Radiation therapy (RT) improves quality of life and symptomatic burden for patients with advanced malignancies. However, RT can also confer toxicity and little is known about the contribution of geriatric conditions to RT-related outcomes in older adults. This study aims to examine changes in daily function among RT patients at 1 and 6 months following RT. We reviewed charts of 137 patients who underwent RT with intent to improve daily functioning. ADL and IADL scores ranging from 0-6 and 0-8, respectively were collected at baseline, 1-, and 6-months post-RT. Latent class analysis of baseline ADL and IADL was conducted to categorize patients into two classes (high and low deficit). Latent transition analysis was used to examine transitions at each time point. One-hundred seventy courses of RT were identified; 99 were fully evaluable. Median age was 66 years. For ADL and IADL, at baseline 28.9% and 28.3% were classified as high deficit and 71.1%, 71.3% as low deficit respectively; 2% and 7% of low deficit patients had the potential to move to high deficit group at 1 month; and 20% and 13% had the potential to have the same movement from 1 to 6 months. All patients classified as high deficit for both measures at 1 month remained so at 6 months. ADL and IADL functioning may be useful in describing changes in daily function after and identifying groups of patients who may benefit from additional supportive geriatric and/or palliative care interventions.

INFLUENCE OF AGING, MACRONUTRIENT COMPOSITION AND TIME-RESTRICTED FEEDING ON THE RAT GUT MICROBIOME

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Declining health and cognition are hallmarks of advanced age that reduce both the quality and length of the lifespan. While caloric restriction has been highlighted as a strategy for increasing healthspan, time-restricted feeding and changes in dietary macronutrient composition may be more feasible alternatives with similar health outcomes. Furthermore, age-related changes in gut microbiome composition may reciprocally interact with several physiological systems – providing a good target for future therapeutic interventions. To begin to investigate the potential utility of a ketogenic (high fat, low carbohydrate) diet and/or time-restricted feeding, fully mature young (5 mo) and older (22 mo) adult male Fischer Brown Norway Hybrid rats were placed on a time-restricted feeding regimen of a ketogenic or micronutrient and calorically matched control diet for 7 months. A third group of rats was permitted to eat standard chow ad libitum. Fecal samples collected at the conclusion of the study were submitted for 16S microbiome analysis, which revealed significant differences across age and diet groups, as well as across feeding paradigms. Beta diversity analysis demonstrated distinct microbiome composition across the three diet groups regardless of age. Furthermore, diet group significantly impacted abundance in expression of several microbiota at the phylum level, including Verrucomicrobia, Cyanobacteria, Actinobacteria and Patescibacteria, though age did not. Verrucomicrobia was significantly increased ($p=0.02$) and Actinobacteria and Patescibacteria ($p<0.01$) were significantly decreased in animals fed in a time-restricted fashion. These results indicate the value of both altered macronutrient composition and altered feeding methodology for therapeutic interventions targeting the gut microbiome.