CARDIORESPIRATORY FITNESS THROUGH THE EARLY LIFECOURSE AND ATTEMPTS TO MODULATE ITS INITIAL DECLINE

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ABSTRACT

Peak aerobic capacity (VO_{2peak}) is a strong predictor of morbidity and mortality. Lifetime-apex VO_{2peak} is the highest value for VO_{2peak} during the life course and declines beginning the 3rd decade of human life. I examined the ability of chronic voluntary wheel running, or 5-weeks of AICAR administration, to delay the chronological age for the initial decline of lifetime-apex VO_{2peak} begins and potential underlying molecular mechanisms. Experiment one consisted of female rats with (RUN) and without (NO RUN) running wheels that underwent frequent VO_{2peak} tests. Lifetime apex-VO_{2peak} occurred at 19 weeks of age in both groups, decreasing thereafter. On average, VO_{2peak} measured across experiment one was ~25% higher in RUN. Experiment two used the AMPK-agonist AICAR to test if the chronological age for lifetime-apex VO_{2peak} decline could be shifted. Two groups of female rats, AICAR (0.5 mg/kg daily) and vehicle (VEH, saline) were used for 5-weeks and all animals were sacrificed at 22-weeks of age. Compared to VEH group, AICAR rats showed significantly higher body weights, muscle weights, heart weights and lower % body fat. AICAR delayed the initial decline by one-week, from 19- to 20-weeks of age. RNA-sequencing analysis of the lateral head of the tricep muscle from experiment one animals revealed mRNA differences in RUN vs. NO RUN. Two phases of life were examined, pre-apex VO_{2peak} (17- to 19-weeks of age) and post-apex (19- to 27-weeks of age). These data indicate that rat wheel running increases VO_{2peak} 25% and is not sufficient to delay the chronological age of lifetime-apex VO_{2peak} decline, whereas AICAR

delayed it one week. Transcriptomic analysis of experiment one offers target molecules that play a role in: 1) the causation of the decline occurring at 19-weeks of age, and 2) potential genes and mechanisms contributing to the initiation of decline in lifetime-apex VO_{2peak}.