Exercise training affects metabolic and locomotion deficits of *BMAL1* prenatal knockout mice

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Trainee Award Eligible

Circadian rhythms orchestrate the expression of numerous physiological processes, behaviors and more than 40% of protein coding genes. Disruption of circadian rhythms by shift work or jet lag can have detrimental effects on human health. Prenatal loss of the circadian gene *BMAL1* leads to disruption of circadian rhythms in gene expression and activity concomitant with a range of defects including premature aging, hyperglycemia, inflammation and locomotion defects. While the mechanism of how *BMAL1* interacts with the aging process is unknown, *BMAL1* has been shown to be important in the aging-related pathway, autophagy. Inducible, but not basal, autophagy is necessary for the beneficial effects of exercise. The aim of this study was to determine if endurance exercise can ameliorate defects of *BMAL1* prenatal knockout mice. We show that a relatively mild, 8-week, controlled exercise program can increase exercise tolerance, RER, and activity levels of *BMAL1* prenatal knockout mice compared to sedentary controls. Conversely, exercise appears to exacerbate hyperglycemia in this model. We conclude that, despite deficits in basal autophagy, *BMAL1* prenatal knockout mice have the capacity to respond to exercise leading to improvements in a subset of defects. Future work will investigate the mechanisms by which exercise ameliorates phenotypes arising from prenatal loss of *BMAL1*.