ANNALS OF RESEARCH IN SPORT AND PHYSICAL ACTIVITY

Early life exercise promotes favorable changes in gut microbial ecology, persistent stress robustness, and metabolic health

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Publicado por: Imprensa da Universidade de Coimbra

URL persistente: URI:<http://hdl.handle.net/10316.2/44079>

DOI: DOI:https://doi.org/10.14195/2182-7087_ex2018_16

Accessed : 26-Apr-2023 10:14:45

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EARLY LIFE EXERCISE PROMOTES FAVORABLE CHANGES IN GUT MICROBIAL ECOLOGY, PERSISTENT STRESS ROBUSTNESS, AND METABOLIC HEALTH”

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KEY WORDS: Gut-Microbial-Brain Axis, Stress Robustness, Fecal Metabolites, Prebiotic diets, Early life exercise

Regular physical activity positively impacts mental and physical health. The benefits of physical activity are often revealed in the face of challenge, including mental/physical stressors. Evidence suggests that physical activity status is an important determinant of stress robustness. Organisms that are stress robust can endure more intense and prolonged stressors before suffering negative health consequences; and they recover more quickly from those challenges. To better understand the mechanisms of stress robustness using a preclinical model, we varied physical activity status by housing juvenile or adult rats (inbred and outbred strains) with access to either a mobile or locked running wheel in their home cages. After 3-6 weeks, rats housed with mobile running wheels display physical changes indicative of improved fitness, including increased endurance when tested on the treadmill, reduced abdominal adiposity when fed a high fat diet, increased lean body mass, changes in muscle citrate synthase etc. Most importantly for our work, however, is that physically active compared to sedentary rats have reduced adipose inflammation, no antibody suppression, no anxiety-like or depressive-like behaviors, and faster diurnal rhythm and sleep disturbance recovery, after exposure to an acute intense stressor (100, 1.5mA, 5-s tailshocks). Using this paradigm, we exploited the differences in stress robustness to reveal unique adaptations in stress responsive neurocircuitry that were necessary and sufficient for specific outcomes, including adaptations in serotonergic dorsal raphe neuronal responses responsible for anxiety-like and depressive like behaviors, and central sympathetic drive associated with immunomodulation. Our current work extends our assessment of adaptations produced by exercise to include commensal intestinal microbes (gut microbiota).

• 77

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The gut microbiota contributes to many aspects of host physiology. Changes in the gut microbiota early in development, for example, can impact host metabolism, immune function, and behavior that persist across the lifespan. In addition, the developing microbial ecosystem is more sensitive to change. We will present new evidence that physical activity 1) changes the gut microbial structure favoring a lean-promoting composition; 2) increases the abundance of beneficial microbial species; 3) increases butyrate-producing bacteria and butyrate, a short chain fatty acid implicated in metabolism and epigenetic processes. These effects are greater when running is initiated in adolescence compared to adulthood. Thus, early life presents a window of opportunity for producing adaptive changes in microbial composition that may contribute to some of the enduring positive impacts of exercise on mental and physical health.