

Estrogen influences voluntary wheel running behavior in female rats

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Regular exercise is recognized for its mental and physical health benefits in contrast to the complex risks associated with a sedentary lifestyle. Although the physiological mechanisms underlying the positive effects of exercise are well-established, the factors influencing exercise behavior and the motivation to maintain regular physical activity remain largely unknown. Using a rodent model of voluntary wheel running (VWR), we investigated the role of estrogen in exercise behavior and its regulation. We found that female rats ran more than their male counterparts, and they displayed a unique rhythm in daily activity which directly mirrored the fluctuating estrogen levels throughout the estrous cycle. This rhythm was evident in the daily running distance, speed and running duration under normal physiological conditions. Ovariectomy (OVX) significantly reduced overall VWR activity and eliminated the rhythm. Subcutaneous injections of estradiol benzoate (EB) at 1.5 µg in an OVX background reliably revived overall VWR activity to similar levels before OVX. This estrogen replacement preserved individual differences, such that high vs. low runners before OVX remain high and low runners after treatment, indicating a causal link between estrogen and VWR activity. However, this EB-induced behavioral response took more than 24 hours to manifest, suggesting a temporal arrangement and activation of estrogen/estrogen receptor-mediated genomic signaling cascades with VWR responses. Investigating the molecular events prior to the behavioral manifestation provides a unique opportunity for identifying estrogen-dependent molecular mechanisms that drive running behavior. Understanding these mechanisms is critical for improved strategies to promote physical activity in humans.

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