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Abstract

Childhood stress is a pervasive problem worldwide. Unfortunately, targeted therapies to mitigate its consequences on cognitive health are lacking. The first aim of this proposal uses preclinical behavioral models to test the hypothesis that exercise during early life, shown to benefit learning and memory across species, can rescue memory impairments after chronic early-life stress. These studies will capitalize on the inherent plasticity of the developing brain by introducing exercise soon after the chronic early-life stress has ended. Preliminary evidence from my lab demonstrates that early-life exercise can improve memory and synaptic plasticity in a lasting manner in wild-type adolescent mice. These findings suggest that the exercise experience during developmental periods may engage unique, temporally sensitive mechanisms to ultimately influence memory function. As such, the second aim in this proposal will explore whether there are long-term *epigenetic signatures* for the effects of both stress and exercise. In addition to characterizing the expression of plasticity-related genes after stress and exercise, I will evaluate histone modifications on the promoters of those genes, which may act to regulate transcriptional responsiveness after exercise and enable improved memory. The prediction is that exercise drives gene expression via the epigenome to support neuronal function and improve memory after early-life stress. Overall, these studies will reveal experience-induced modulation of gene expression after stress and exercise, ultimately informing specific therapeutic interventions and exercise prescriptions to offset the consequences of early-life stress on cognitive function.