Application number/Title: 28212 - Determining the effects of objectively-measured physical activity on circuit-specific brain aging in a massive multi-modal neuroimaging community sample.

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Keywords provided by the Applicant PI to describe the research project:
cognition, dementia, fitness, obesity, physical-activity

Application Lay Summary:
Physical activity has beneficial effects on neurocognitive functions and prevention of age-related cognitive declines leading to dementia. Our long-term goal is to better understand the role of exercise on brain structural and functional health through the lifespan. Our objectives are to: (1) determine the effects of objectively-measured physical activity on trajectories of aging of multiple cognition-relevant brain circuits; and (2) parse and quantify mediation pathways between physical activity, circuit-specific brain age, and neurocognitive functioning. The expansion of the aging population, combined with decreasing mortality, has led to a diversification and growth of chronic disease morbidity, including increased prevalence of aging-related mobility and cognitive impairments and a substantial reduction in the number of nondisabled years. Our study is poised to decisively answer 2 critical unanswered questions: (1) What is the effect of physical activity on circuit-specific brain aging? and (2) Does this effect mediate the effect of physical activity on improved cognitive functioning? Our study improves upon existing studies along a number of dimensions. A recent study correlated brain volumes in 331 healthy adults with self-reported measures of physical activity. We will go beyond that study in multiple ways, including: (1) inclusion of over 15x more participants; (2) drawing from a large sample; (3) physical activity will be measured objectively (accelerometry); (4) utilization of multimodal brain imaging; (5) examination of circuit-specific aging trajectories; (6) employment of advanced deep learning methods for constructing brain age trajectories; and finally, (7) we will parse complex relationships between physical activity, brain aging, and cognitive...
functioning to gain evidence about potential causal pathways. We propose to use imaging from the subjects as extensively described (Miller KL, et al. Multimodal population brain imaging in the UK Biobank prospective epidemiological study. Nat Neurosci. 2016;19(11):1523-1536), of which over 5,400 have complete neuroimaging, accelerometer data, anthropometric and sociodemographic information, and cognitive functioning data.