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Institute: National Institute of Neurological Disorders and Stroke (NINDS)

Grant title: Central Control and Neuroinflammatory Mechanisms of Locomotion in Older Adults with HIV

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Summary: Mobility impairments including gait disorders and falls are debilitating and common, yet poorly understood in older persons with HIV (OPWH). The fronto-striatal circuitry is critical for brain control of locomotion and has been shown to be disrupted in HIV. Inflammation persists in HIV despite effective antiretroviral therapy and is a key driver of cognitive impairment among persons with HIV (PWH); the frontal cortex, which supports motivation and learning, is particularly vulnerable to the adverse effects of ongoing inflammation in the context of treated HIV, placing OPWH at risk for resulting mobility disorders. The role of brain circuits and neuroinflammation in gait and falls in OPWH has not been investigated to date, including whether walking performance under attention-demanding conditions could be durably improved with training, and thus amenable to remediation. We propose to use a validated dual-task walking paradigm (predictive of falls in older persons), a burst measurement (i.e., repeated trials) design, and functional-near-infrared spectroscopy (fNIRS) to determine the effect of HIV on brain activation levels and trajectories of walking in 120 OPWH (age \geq 50ys) and 120 controls without HIV. We will use multiple MRI methods to determine disruptions in the fronto-striatal circuitry and select markers of neuroinflammation to identify mechanisms of brain control of walking and risk of falls in OPWH. Brain activation patterns and learning trajectories of walking and improvements in their efficiency due to practice may be novel biomarkers to identify OPWH at risk of developing mobility impairments and falls as they survive into older age. Findings from this study will direct physical, cognitive, and pharmacological treatments to improve functional brain control of walking, which in turn will lead to interventions to reduce fall risk in OPWH.