

Research Statement

Application for the Institute of Successful Longevity

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My research focuses on understanding the neural correlates of cognitive decline in normal and pathological aging. I use cutting-edge, state-of-the-art neuroimaging tools to pursue this focus. The ultimate goal of my research is to inform effective intervention strategies that can mitigate cognitive decline in older age. My research is built around three key components. First, I acknowledge profound inter-individual differences in brain and cognition across the adult lifespan, particularly among older adults. Second, I examine large-scale longitudinal multimodal imaging data. This gives us access to multiple compartments of the aging brain. Third, I target modifiable brain factors, such as dopamine and noradrenaline. These factors could serve as targets for pharmacological and non-pharmacological interventions.

Over the past decade, this program of research has been supported by a sustained portfolio of competitive funding. This includes a European Research Council Consolidator Grant (\$2,370,000), multiple grants from the Swedish Research Council, the Knut and Alice Wallenberg Foundation, and the Bank of Sweden. Total direct research support exceeds \$7,000,000. This funding has enabled DyNAMiC, a prospective longitudinal study of dopamine and brain connectomes across the adult lifespan. DyNAMiC has generated more than 30 peer-reviewed publications in journals such as PNAS, Neuron, Cell Reports, The Journal of Neuroscience, and eLife. Collectively, this work has established that reduced dopaminergic integrity and disrupted functional network organization are central mechanisms underlying age-related episodic memory decline. In particular, we have identified hippocampal-cortical dysconnectivity together with local hippocampal hyperconnectivity as key markers of this decline.

Building on these findings, I am now moving from characterization toward intervention. I have recently initiated a new line of research at FSU that combines transcranial magnetic stimulation (TMS) with fMRI. This work directly targets the hippocampal-cortical network implicated in memory decline. The goal is to restore functional connectivity and improve episodic memory performance in healthy older adults aged 60 to 80. This within-subject, sham-controlled study includes 33 participants. It applies a canonical repetitive TMS protocol to increase hippocampal-cortical connectivity and reduce local hyperconnectivity. In doing so, it directly tests whether a modifiable brain network can be causally manipulated to reverse markers of cognitive aging. This work extends my longitudinal imaging program into the domain of mechanistic, causal intervention. It represents the translational step needed to move from understanding cognitive aging toward mitigating it.

The Institute for Successful Longevity is uniquely positioned to support this next phase of my research program. Recruitment for the TMS-fMRI study will draw on the ISL participant registry of community-dwelling older adults. Continued access to this resource will be essential, not only for this project but for future studies examining individual differences in responsiveness to neuromodulatory intervention. In turn, I aim to contribute to ISL's mission. I will bring an integrated, multimodal approach that combines neuroimaging and neuromodulation. This approach bridges molecular methods using PET, functional methods using fMRI, and causal methods using TMS. It complements existing ISL strengths in behavioral and clinical aging research.

Looking ahead, my goals as an ISL-affiliated researcher are threefold. First, I aim to establish at FSU a longitudinal, multimodal aging cohort similar to DyNAMiC. This cohort would integrate dopamine PET, structural and functional MRI, and TMS-based intervention. Second, I aim to identify individual-difference markers, including genetic, vascular, and lifestyle factors, that predict who will benefit most from neuromodulatory intervention. This will inform more precise approaches to preserving cognitive function in later life. Third, I aim to mentor the next generation of aging researchers. This goal is consistent with my record of supervising postdoctoral fellows, Ph.D. students, and master's students across multiple institutions. I look forward to contributing this research program, and its translational potential for successful cognitive aging, to the Institute for Successful Longevity.