Single-Cell Imaging of Functional Connectivity as a Window into Cognitive Aging

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Principal Investigators

BURKE, SARA N

Institution

UNIVERSITY OF FLORIDA

Contact information of lead PI
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Research Abstract

Title: Single-Cell Imaging of Functional Connectivity as a Window into Cognitive Aging Sara N. Burke, Ph.D. (P.I.; 20% effort) Assistant Professor, Department of Neuroscience, University of Florida College of Medicine P.O. Box 100244 1149 Newell Drive Gainesville, FL 32611 Phone:

352-294-4979 Email: burkes@ufl.edu Andrew P. Maurer, Ph.D. (co-I.; 15% effort) Assistant Professor, Department of Neuroscience, University of Florida College of Medicine P.O. Box 100244 1149 Newell Drive Gainesville, FL 32611 Email: drewmaurer@ufl.edu Benjamin J. Clark, Ph.D. (co-I.; 15% effort) Assistant Professor, Department of Psychology 1 University of New Mexico MSC03 02 1675 Albuquerque, NM 87131-0001 Phone: 505-277-4121 Fax: 505-277-1394 Email: bnjclark@unm.edu Budget requested: $275,000.00/2 years Abstract: The number of Americans over the age of 65 is projected to reach 55 million within the next decade. With the average annual Medicare cost for the long-term care of an individual exceeding $61k, preserving one's ability to live independently is imperative for conserving public and private resources as well as maintaining personal dignity. Although a large proportion of elderly experience memory decline that interferes with their quality of life and ability to maintain independence, therapeutic interventions for treating cognitive deficits associated with aging and dementia are limited. Thus, identifying new strategies for mitigating age-related memory loss is critical. Understanding the neurobiology of memory impairments poses a significant challenge, as these processes are distributed throughout the brain and little is known about the orchestrated communication of neural networks in disparate brain areas. Moreover, current tools for evaluating large-scale circuit dysfunction do not have the spatial resolution to identify the specific neuronal populations that are most vulnerable to aging and pathology. The long-term goal of the proposed research is to determine the age-related alterations in interactions between brain regions that underlie cognitive impairments, and how aging and neurodegenerative disease acerbates these effects. The primary objective of the current proposal is to expand the application of a novel method for quantifying functional connectivity among brain regions with single-cell resolution in the context of age-associated behavioral deficits. The central hypothesis that age-related deficits within the perirhinal cortex of the medial temporal lobe lead to a reduced ability of the aged brain to link sensory information with spatial representations will be tested by pursuing the following specific aims: 1) Link reduced neural coordination in hippocampal-projecting perirhinal cortical neurons to behavioral impairments, and 2) Are feedforward and feedback perirhinal cortical projection neurons equally vulnerable to age-related dysfunction. Our rationale is that by enhancing methods for probing circuit function across disparate brain areas, with single-cell resolution, we will be better positioned to identify functional connectivity impairments in aging and Alzheimer's disease. The proposed research is innovative, because state-of-the-art neuroanatomical measures will be combined with gene expression analysis in behaviorally characterized young and aged rats to probe how local dysfunction manifests as network impairments. This novel single-cell imaging approach has not been possible until recently and has never been applied to animal models of aging and dementia. The significance of successful completion of these experiments will be a powerful tool for quantifying functional connectivity that can be applied to a wide spectrum of research fields. Additionally, these data will provide unprecedented insight into the association between cross-regional communication and cognition that will enable future interventional studies aimed at restoring memory network interactions in the context of aging and neurodegeneration.

Further information available at:

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