Imaging neuronal and capillary dysfunction deep in the rodent brain in vivo using 1700 nm Optical Coherence Microscopy and tracer-based kinetics

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Country

USA

Title of project or programme

Imaging neuronal and capillary dysfunction deep in the rodent brain in vivo using 1700 nm Optical Coherence Microscopy and tracer-based kinetics

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NIH (NIA)

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01/09/2015

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1

The project/programme is most relevant to:

Alzheimer's disease & other dementias

Keywords

Tracer, Blood capillaries, capillary, Microscopy, Optics

Research Abstract
? DESCRIPTION (provided by applicant): Subcortical pathology is a common feature in aging, Alzheimer’s disease and vascular dementia but has been extremely difficult to study with micron resolution in vivo. Optical methods such as two-photon microscopy image the superficial cortex at the micron-scale, but the resolution of these conventional microscopic methods degrades rapidly beyond 600 microns imaging depth. Standard whole-brain magnetic resonance imaging (MRI) methods do not yet provide cellular-level resolution and are often expensive to implement. Thus, there is a pressing need for methods to directly assess deep cortical and subcortical perfusion and cellular injury at the microscopic level, thus bridging the gap between existing superficial optical microscopy and macroscopic imaging. This proposal will develop and apply novel optical imaging technologies and accompanying methods to directly investigate subcortical (hippocampal and white matter) cellular and vascular changes in genetic mouse models of disease, without the need for transgenic expression of fluorescent proteins. We propose to develop and validate methods to quantify transit time distribution at the single capillary level; combine these with methods to measure neuronal cell viability, myelination, plaque distribution, atrophy; and finally, to longitudinally image the time course of deep cortical and hippocampal injury in a mouse model of Alzheimer’s disease up to a depth of 2 mm. These techniques will have a widespread impact in preclinical experimental research in therapeutics and biomarker discovery, and will advance the study of white matter injury and subcortical dementia. The initial development, validation, and demonstration proposed here will catalyze the widespread adoption of these novel techniques to study subcortical pathophysiology non-invasively in the mouse brain.

Lay Summary
PUBLIC HEALTH RELEVANCE: This proposal will develop, validate, and demonstrate advanced optical microscopy methods for longitudinal imaging of subcortical structures in the mouse brain. These methods will enable micron-scale imaging of the progression of cellular and vascular pathology in experimental models of vascular dementia, white matter stroke, aging, and Alzheimer’s disease.

Further information available at:

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Investments > €500k

Member States:
United States of America

Diseases:
Alzheimer's disease & other dementias

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