PROJECT SUMMARY (See instructions):

The long term objective of this research is to develop and test a novel technique for assessing neurodegenerative disease through optical imaging. Recently, a number of studies have suggested that many neurodegenerative diseases have a primary retinal pathology associated with them. Optical imaging and sensing is highly sensitive to the retinal microenvironment and may be used to detect retinal dysfunction, potentially associated with neurodegenerative conditions like Alzheimer's disease (AD). The ganglion cell layer (GCL) and the inner plexiform layer (IPL) are known to be altered by neurodegenerative diseases and because the retinal nerve fiber layer (RNFL) is a white matter tract of the brain, this structure is of interest. The imaging technologies of multiphoton microscopy and OCT offer the ability to study these key structures to correlate retinal changes to neurodegeneration, with OCT being a currently clinically viable option for early detection and monitoring of retinal changes associated with AD. We have developed a specialized OCT, scattered angle resolved OCT (SAR-OCT) expected to be particularly sensitive to the primary scatterers of the retina (synapses and mitochondria) involved in neuroretinal dysfunction. We propose to investigate the (time-dependent) relationship between Alzheimer's Disease (AD) pathology in the hippocampus and in the inner retinal layers (RNFL, GCL, IPL) using advanced optical imaging by multiphoton microscopy and SAR-OCT. Our Specific aims are: Aim 1) In a transgenic mouse model for AD, use biochemical and morphological techniques to characterize the temporal relationship between the appearance of early biochemical markers of AD (beta amyloid oligomers, calcium-dependent synaptic morphological alterations/instability, and mitochondrial dysfunction) in the hippocampus and those that can be detected and quantified in the retina, Aim 2) In the retinal flat mounts, use advanced multiphoton microscopy and OCT techniques to: 1) demonstrate that optical properties of the inner retinal layers change as a function of AD progression and 2) establish that these changes can be related to RGC and IPL structure at various timepoints after onset of AD, and Aim 3) Demonstrate the feasibility of using our novel SAR-OCT imaging technique engineered to provide a high resolution depth resolved map of the inner retinal layers and delineation of the optical scattering angle for noninvasive detection of neuroretinal dysfunction associated with neurodegenerative diseases. SAR-OCT is expected to identify optical indexes of dysfunction, which may be indicative of synaptic and mitochondrial abnormalities. The goal of the proposed research is to validate retinal imaging for the early detection and monitoring of AD with the potential to guide early therapeutic intervention of AD.

RELEVANCE (See instructions):

This research will develop a novel and sensitive approach for detecting brain neuropathology due to Alzheimer's disease through imaging of the retinal layers of the eye. The project will advance neurotechnology and advance our knowledge of how the retina and the brain are connected both of which are relevant to the UT BRAIN initiative. Furthermore, key collaborations between leading investigators in the areas of neuroscience (neurodegenerative diseases), ophthalmology, bioengineering, and optical technology development and application have been formed to advance neuroscience and neurotechnology research. Our team comprises, from UTMB: Dr. Massoud Motamedi, Professor of Ophthalmology and Director Center for Biomedical Engineering, Dr. Giulio Taglialatela, Professor of Neuroscience and Director of the Mitchel Center for Neurodegenerative Diseases, and Dr. Gracie Vargas, Associate Professor, Neuroscience and Cell Biology and Director Advanced BioOptics Imaging Lab (in nonlinear optics), partnering with UT-Austin investigators: Dr. Henry G Rylander, Professor of Biomedical Engineering and a practicing Opthalmologist, and Dr. Thomas Milner, Professor of Biomedical Engineering.