Multi-Modal Mapping of the Aging Brain in Health and in Disease

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Older adults undergo complex neural changes as part of the typical aging process, which are greatly exacerbated by age-related neurological illnesses such as cerebrovascular disease and dementia. These neural changes contribute to the well-documented cognitive and functional decline in older adults; an increasing epidemic on society given the rapidly expansion of this population as well as the prevalence of detrimental age-associated illnesses across the globe.

The past decade has seen the burgeoning of neuroimaging research, providing unprecedented power to elucidate mechanisms healthy aging and age-associated disease across a range of domains, including brain morphometry, neural tissue microstructure, cerebral hemodynamics and dynamic neural processes. We propose to bring together four leading scientists in the areas of structural, functional, vascular and cognitive aging, applying the most current and innovative brain mapping techniques to the study of brain aging and disease. Given the goal of the OHBM to provide education on groundbreaking research across imaging modalities, we have focused on domains that we believe to be the most prominent and active in aging research. This symposium features imaging applications in aging, but also involves investigators developing cutting-edge neuroimaging techniques. We expect that this format will therefore a) provide a timely overview of brain mapping in aging to individuals new to the field; b) introduce novel techniques to veteran aging researchers; and c) underscore the need for multi-modal integration in attaining a more complete, unbiased view of aging and age-associated neurological diseases.

Learning Objectives: Having completed this workshop, participants will be able to:
1. Acquire basic understanding of neuroimaging markers of aging/dementia and associated cognitive evidence;
2. Develop high-level understanding of commonly used neuroimaging techniques and image processing procedures for studying aging and dementia; and
3. Establish an understanding of current and future challenges in neuroimaging of aging and dementia.

Anatomical Mapping: Structural Network Analysis in the Aging Brain

Alan C. Evans, McConnel Brain Imaging Centre/Montreal Neurological Institute, Montreal, QC, Canada

This talk will discuss the methodology of cortical anatomical network modelling and its application in normal aging and neurodegenerative disease. Cortical anatomy exhibits correlated variability between different regions across subjects, giving rise to the concept of cortical correlation networks that are amenable to graph theoretical analysis. These networks exhibit small-world properties and modularity that may reflect underlying functional connectivity. The network properties change with age, learning and disease in a manner that provides an insight into the brain reorganization taking place over time, both during normal aging and in neurogenerative disease such as Alzheimer's Disease and Multiple Sclerosis.

Micro-Structural Mapping: Diffusional Kurtosis Imaging (DKI) for the Assessment of Brain Tissue Microstructure in Aging

Joseph A. Helpern, South Carolina Medical Center/New York University, New York, NY, USA

Diffusion-weighted imaging (DWI) provides a powerful tool for probing tissue microstructure. Well-established diffusion metrics, such as mean diffusivity (MD) and fractional anisotropy (FA), have proven useful in assessing aging as well as a number of diseases. In conventional DWI, the diffusion displacement probability distribution is assumed to be Gaussian in form with its width (i.e. standard deviation) proportional to the diffusion coefficient. The complex structure of biological tissues, however, can cause the diffusion displacement probability distribution to deviate substantially from a Gaussian form. Since deviation from Gaussian behavior is governed by the microstructural complexity of the tissue and since tissue microstructure and function are closely coupled, knowledge of the non-Gaussian behavior of water diffusion could provide insight into tissue function and/or
Diffusional Kurtosis Imaging (DKI) is a clinically favorable technique that can quantitatively measure the non-Gaussianity of the diffusion process. The diffusional kurtosis is potentially a more specific indicator of tissue microstructure than either the MD or FA and preliminary data from normal brain aging will be discussed.

**Neurovascular Factors in fMRI of Aging: Problems and Solutions**
Thomas T. Liu, **UCSF Center for Functional MRI, La Jolla, CA, USA**

The vast majority of functional magnetic resonance imaging (fMRI) studies treat the blood-oxygenation level-dependent (BOLD) fMRI signal as a reliable, albeit indirect, measure of neural activity. While this straightforward view is typically sufficient for studies of young healthy populations, its validity is severely challenged in studies of aging. The BOLD signal is a complex function of changes in cerebral blood flow and metabolism, and as a result can be significantly modulated by changes in the vascular state. For example, changes in baseline cerebral blood flow have been shown to alter both the dynamics and amplitude of the BOLD signal. If aging-related changes in the vascular state are not considered, a relative increase in the BOLD signal due to a reduction in blood flow may be misinterpreted as an increase in neural activity. The situation is further complicated by the widespread use of vasoactive medications in the aging population. To address these challenging confounds, I will discuss how the addition of quantitative MRI measures of blood flow and metabolism may be used to improve the interpretation of fMRI studies of cognitive aging.

**Multi-Modal Mapping in Pathology: Neuroimaging Predictors of Cognitive Decline and Resilience in the Baltimore Longitudinal Study of Aging**
Susan Resnick, **Laboratory of Personality and Cognition/National Institute on Aging, Biomedical Research Center, Baltimore, MD, USA**

We are examining changes in brain structure and function as predictors of cognitive decline and impairment as well as cognitive resilience through serial neuroimaging assessments of participants in the Baltimore Longitudinal Study of Aging (BLSA). Since 1994, magnetic resonance imaging (MRI), positron emission tomography (PET) measures of regional cerebral blood flow (CBF), and neuropsychological testing have been performed annually for participants, aged 55 and older. Since 2005, PET measures of amyloid deposition using 11-C-Pittsburgh Compound B also have been obtained. Our findings indicate substantial changes in brain volumes and tissue composition in normal aging, with accelerated changes in specific brain regions in individuals who develop cognitive impairment. Consistent with autopsy data from BLSA and other studies, more than 30% of cognitively normal individuals have detectable amyloid deposition in the brain on in vivo imaging. Individuals with higher levels of beta-amyloid are older, have different patterns of longitudinal change in cerebral blood flow, show greater longitudinal decline in memory and other cognitive functions, and show greater longitudinal increase in amyloid deposition. We are continuing to follow these individuals and are examining modifiers of both structural and functional brain changes and their associations with cognitive function. Early prediction of cognitive impairment and factors that promote cognitive resilience in the face of pathology will be essential as new therapies are on the horizon.