**NACC Project #2006-09**

**Hippocampal Glucose Metabolism in Aging: Relationships to Cognitive Decline**

**Principal investigator**
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**Collaborating centers**
Arizona ADC, University of California Los Angeles, Brookhaven National Labs

**Project description**
This is a 4-site collaborative FDG-PET project that will contribute to the preclinical diagnosis of AD. Recent studies suggest that the hippocampus (HIP) is a major early target for Alzheimer’s disease (AD) that is largely spared with normal (NL) aging. While this has facilitated PET and MRI prediction studies for mild cognitive impairment (MCI) to AD transitions, still little is known about the using imaging to predict the NL to MCI transition. With this unique opportunity to combine data from several of the leading PET centers in America, we will examine the regional cerebral metabolic rate for glucose (MRglc) in a project that has two principal aims. First, in a cross-sectional sample of 906 normal individuals we will characterize the MRglc of the HIP and other regions over adult lifespan. With this data set, we will examine age-related regional changes with the hypotheses that reductions of the frontal lobe MRglc occur earlier and are more pronounced over the lifespan than MRglc reductions of the HIP. There are no prior observations on the aging of the HIP MRglc, but this hypothesis is supported by our pilot work. We will also study the relationship between regional brain MRglc and age as influenced by the well established risk factor for late-onset AD, the ApoE genotype. Second, we will examine 224 NL subjects studied twice over 2 years. This longitudinal study will include 35 subjects who decline to MCI (including 12 E4+) and will enable the first examination of the interaction between genotype and HIP MRglc predictors of clinical decline. We will test the hypothesis that baseline HIP MRglc reductions are a necessary and anatomical specific predictor of cognitive decline.

Prior ApoE studies individually did not have sufficient numbers of decliners to make such an observation possible and the HIP was never examined. This project is possible because the PET data has been collected on ADNI-certified PET instruments with adequate spatial resolution to sample the HIP. Moreover, such a large-scale project is feasible because our laboratory has developed and validated procedures that are automated and sufficiently precise to sample the HIP and other brain regions. Moreover, we also are experienced with other automated voxel-based approaches, such as Statistical Parametric Mapping (SPM), and have developed improved atrophy correction protocols. All technical and machine related needs for his project are in place and there is adequate statistical power for testing the hypotheses.

**Contact information**
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