U.S. Department of Veterans Affairs:
The Oregon Brain Aging Study

The Oregon Brain Aging Study focuses on healthy brain aging to determine factors that may confer resistance to cognitive decline in aging. "Average healthy" oldest old were found more resistant to dementia at advanced age than those "exceptionally healthy.

Lead Agency:
U.S. Department of Veterans Affairs (VA)
 Veterans Health Administration (VHA)

Agency Mission:

"To care for him who shall have borne the battle and for his widow and his orphan."

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Partner Agency:
National Institutes of Health/National Institute of Aging (NIH/NIA)

General Description:

Oregon Brain Aging Study

The Oregon Brain Aging Study is a longitudinal study focused on factors associated with healthy brain aging. Current research questions are directed toward establishing biomarkers of brain aging protection associated with a recently identified, resistant to cognitive decline phenotype among the oldest old, and determining how these biomarkers map to rates or trajectories of functional decline prior to the emergence of dementia. Finally, the study ultimately focuses on establishing whether the resistive phenotype of cognitive decline and brain aging is associated with distinct neuropathology.

Subjects enrolled in the longitudinal aging study are followed semiannually with standardized clinical, cognitive and volumetric Magnetic Resonance Imaging (MRI) to mark the trajectories of the healthy aging cohorts who are more or less resistant to developing mild cognitive decline. The accelerated atrophy associated with incipient cognitive impairment will be tracked with annually obtained biomarkers that have been shown to be associated with relevant age-related neuropathology in elderly subjects. Subjects will be followed to autopsy. Post mortem examination will be used to correlate common age-associated pathologies (*e.g.*, neuritic plaques, neurofibrillary tangles, micro infarcts) with rates of volume loss established with Magnetic Resonance Imaging, as well as the change in peripheral biomarkers.

Standardized clinical examinations and psychometric tests are used to identify trajectories of cognitive and functional change over time. Volumetric Magnetic Resonance Imaging is used to measure the rates of atrophy characterizing subjects destined to develop cognitive impairment compared to those relatively resistant to decline. Biomarkers of plasma amyloid, antioxidant stress (F2- isoprostanes), vascular disease and brain damage (24S- hydroxycholesterol, plasma lipids, homocysteine) are measured annually and examined for their change relative to MRI established brain atrophy and cognitive decline. Post mortem brain examination will follow a standardized histopathological protocol and the coding system of the National Alzheimer's Consortium.

Findings/Progress to Date: A cohort of average healthy oldest old have been discovered to paradoxically be more resistant to developing dementia at advanced age relative to an exceptionally healthy age-matched group. This suggests a human aging phenotype associated with the phenomenon of hormesis where chronic, non-lethal stressors may precondition the brain to be more capable of resisting insults than naïvely aging brains. Those relatively resistant to cognitive decline have a two phase acceleration of age-associated brain loss (on MRI) prior to developing cognitive decline such that there is a long premonitory period of accelerating loss followed by a more rapid phase of volume loss occurring approximately 2-3 years prior to apparent cognitive decline. This newly identified trajectory provides the opportunity to map plasma biomarkers as they emerge over time to detect signals of possible mechanisms associated with the earliest stages of neurodegeneration leading to cognitive decline. To date, plasma biomarkers have been collected on 96 individual subjects and are undergoing assay analysis.

Excellence: What makes this project exceptional?

Following a group of initially healthy aging subjects over time with semiannual standardized clinical examinations and psychometric tests that are used to identify trajectories of cognitive and functional change.

Significance: How is this research relevant to older person, populations and/or an aging society?

This study will establish the different characteristics of neuropathology in two groups of healthy oldest old patients, those that do and do not develop dementia.

Effectiveness: What is the impact and/or application of this research to older persons?

This study will establish biomarkers in blood that may predict early stages of neurodegeneration leading to cognitive decline. The identification of these biomarkers, in aged individuals with and without the development of dementia, may also provide insights to the mechanism(s) that contributes to the normal and abnormal brain aging.

Innovativeness: Why is this research exciting or newsworthy?

To date, there are no reliable blood biomarkers that can predict the development of dementia. With the identification of these biomarkers, it will be possible to identify individuals in the very early stages of the development of dementia. Early diagnosis is important for physicians to identify treatable causes of dementia, to effectively manage dementia and related illnesses, and to offer support services to the patient and family.