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Longitudinal Study of Brain Aging and Cognitive Change Receives $19 Million Grant

Researchers at University of California San Diego School of Medicine, with colleagues at Boston University and elsewhere, will receive almost $19 million over five years to launch the fourth phase of the Vietnam Era Twin Study of Aging (VETSA 4). Funded by the National Institute on Aging, the grant will support ongoing research, including large-scale behavioral genetics studies, of cognition, aging and the risk for mild cognitive impairment (MCI) and Alzheimer's disease (AD).

VETSA is a set of longitudinal projects with a primary focus on examining genetic and environmental influences on brain function and aging, beginning at midlife. It was originally launched in 2002. To date, more than 1,600 identical and fraternal male-male twins have participated, all with military service at some point between 1965 and 1975, though most report no combat experience.

"At this point, they are all older men living in all 50 states. They are roughly comparable in terms of lifestyle, education and health characteristics to American men of their age," said William S. Kremen, PhD, one of three principal investigators of VETSA 4 with Carol E. Franz, PhD, and Michael Lyons, PhD. Kremen and Franz are both professors of psychiatry and co-directors of the Center for Behavior Genetics of Aging at UC San Diego School of Medicine. Lyons is a professor in the Department of Psychological & Brain Sciences at Boston University.

The participants' narrow range of age is a key feature of the study. All participants were in their 50s when baseline assessments were taken, with new testing regularly conducted every few years. Participants undergo tests of cognitive and sensory functioning, relevant biomedical characteristics, psychosocial functioning, neuroendocrine status and genotyping — the last a method of determining differences in the genetic makeup of individuals. A large subset has also undergone magnetic resonance imaging.

"Clinical trials of dementia patients have been unsuccessful, and current thinking is that a major reason is that the disease has already progressed too far by that time," said Franz.

“Because it is now well known that the pathological process of AD begins as much as 20 years before onset of dementia, there has been a major focus on early identification of risk as the key to slowing or preventing disease progression. With its baseline in midlife, the VETSA is in many ways ideally suited for advancing the goal of early identification. In addition, the twin design helps determine the extent to which characteristics are due to genetic or environmental influences.”

It’s estimated that nearly 6 million Americans age 65 and older are living with AD; 80 percent are 75 or older, according to the Alzheimer’s Association. MCI is a prodromal phase of AD in which there is cognitive impairment, but dementia has not yet developed. “That makes identifying MCI early an important part of efforts toward early diagnosis and treatment,” said Kremen.

Previous VETSA research has shown that extensive cognitive testing can identify MCI in adults who are still in their 50s. Genotyping has allowed researchers to assign an AD polygenic risk score. VETSA investigators have also found that common major midlife adverse events, such as divorce or death of a family member, can accelerate aging in the brain.

A novel aspect of VETSA is that researchers have test scores of general cognitive ability dating back to participants’ military service when they were in their 20s. “It is well known that more education, greater occupational complexity and greater engagement in cognitively stimulating activities are associated with reduced risk of dementia,” said Kremen. “This presents a chicken-egg dilemma: Do these things cause the reduced risk or is it that people with higher cognitive ability tend to be higher on these factors?”

A VETSA study showed that it was primarily the latter.

In the fourth phase of VETSA, the average age of participants will be 74 years. Researchers expect a greater increase in cognitive decline and development of MCI and AD. “The potential value of this ongoing project for contributing to our understanding of risk for later life cognitive decline and dementia is only likely to increase,” said Franz.

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