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New studies reveal that age-related nerve decline is associated with inflammation, differs by gender

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New research investigating neurological decline in a population of "super healthy" elderly subjects found that the decline in neurological function of the peripheral nervous system attributed to aging may be related to metabolic factors, such as blood sugar levels, even if these factors are within the normal range.

In a related study of peripheral nerve function, the same group found that aging affects the nerves of men more than women later in life.

The findings imply, the researchers say, that age-related declines in peripheral nerve function may not be the consequence of the aging process alone but instead the consequence of aging, gender, plus metabolic factors that may be modifiable. The peripheral nerves are the nerves in the limbs that connect to the central nervous system (brain and spinal cord).

Outcomes from the two studies were presented today by UCSF researchers during the annual American Academy of Neurology scientific meeting in Toronto.

"Reduced sensation from a decline of nerve function may contribute to overall morbidity and reduced quality of life in the elderly," said Ari Green, MD, co-lead investigator, assistant director of UCSF's Multiple Sclerosis Center and director of the Neurodiagnostics Center. "The

medical community considers this decline a consequence of aging. Our findings suggest that low levels of inflammation and impairment in glucose metabolism may accelerate the decline of nerve function."

Both studies involved a unique population of healthy elderly individuals between the ages of 65-90 called the Myelin and Aging Cohort. As part of this work, subjects underwent extensive neurological, laboratory and physical testing, and had to be free of any major chronic illnesses such as diabetes, hypertension, cognitive impairment, neuropathy and cardiovascular disease. For this project, researchers focused on the results from peripheral nerve conduction studies and laboratory findings.

"We know that the function of peripheral nerves declines with age but wondered whether other biologic processes were at play and if we could eventually predict this decline," said John W. Engstrom, MD, co-lead investigator and clinical chief of the UCSF Neurology Service. "These findings provide an opportunity to identify risk factors for the decline in peripheral nerve function."

In the first study, the team assessed conduction velocity, or the speed at which information traveled along peripheral nerves using nerve conduction studies. They found an association between age and slower nerve conduction in elderly men only.

"Everyone ages differently; there are different levels of normal," said co-investigator Chris Songster, a specialist in the UCSF Department of Neurology. "We want to understand if there are modifiable risk factors that, if addressed, could help people age well."

In the second study, the research team measured blood levels for highly sensitive C-reactive protein (hs-CRP) and hemoglobin A1c, which are standard tests for diabetes and systemic inflammation. Using the same conduction studies but evaluating the amplitude of the response to an

electrical stimulus rather than its speed, the researchers found decline even in subjects with mild elevations in hs-CRP and hemoglobin A1c. The subjects' levels were within the normal, non-diabetic range for those measures.

"Even within 'normal ranges' for measures of inflammation and glucose metabolism, we are seeing an accelerated aging process that could contribute to progressive neuropathy," said Green. "These findings suggest that age, mild inflammation and mildly impaired glucose metabolism may be bad for nerve cells. Perhaps in the future, we can investigate whether a therapeutic intervention could delay the effect of age on peripheral nerve function. This may just be the tip of the iceberg. We have a lot to learn from this study population."

Both studies are important elements of a broad UCSF effort to learn how nerves age, developed in a groundbreaking collaboration between the UCSF Memory and Aging Center (Drs. Bruce Miller and Joel Kramer), the UCSF Multiple Sclerosis Center (Drs. Stephen Hauser, Ari Green and Jorge Oksenberg) and the UCSF Nerve Injury Clinic (Drs. John Engstrom and Amy Lee). The work was developed in advance of these groups moving together to the new Neurosciences Laboratory and Clinical Research Building at Mission Bay. Laboratory measures were performed in collaboration with the UC Davis Department of Pathology (Drs. Ralph Green and Josh Miller).

The UCSF team is looking at many factors related to how aging effects the connections between nerves and plans many future research studies with this population.

"An important next step is to test whether modification of risk factors like inflammation has an impact on nerve function," Green said.