Abstract Title: Early Surgical Menopause is Associated with a Spectrum of Cognitive Decline

Press Release Title: Early Surgical Menopause Linked to Declines in Memory and Thinking Skills

Objective: To determine the impact of reproductive variables on the spectrum of cognitive decline.

Author(s): Riley Bove, MD, Elizabeth Secor, Lori Chibnik, PhD, Lisa Barnes, MD, Julie Schneider, MD, MS, David Bennett, MD and Philip De Jager, MD, PhD

Background: The decrease in estrogen associated with menopause has been implicated in cognitive decline. However, studies have been conflicting and the utility of hormone replacement therapy (HRT) remains unclear.

Design/Methods: Female subjects from two longitudinal studies of cognitive decline: Religious Orders Study (ROS), and Memory and Aging Project (MAP) with data on reproductive histories at baseline were included. Three types of cognition-related outcomes were assessed: (1) longitudinal measure of 5 cognitive domains and global cognition using a linear mixed effects model, (2) neuropathologic measures from brain samples obtained at death using a linear regression model and (3) clinical diagnosis of Alzheimer's Disease (AD) according to NINCDS-ARDA criteria modeled using Cox proportional hazards regression. We examined the association between age at menarche and menopause, number of cycling years, and ever use and duration of HRT. All models were adjusted for age, education, smoking and study and stratified by surgical vs. natural menopause.

Results: A total of 1837 women were included. For women with surgically induced menopause (33% of cohort), early age at menopause was associated with faster decline in semantic memory (p=0.002), episodic memory and global cognition (ps<0.001). A significant association was also seen with age at menopause and neuropathologic measures, primarily neuritic plaques (p=0.01) and global pathology score (p=0.04). No significant association was seen with incident AD (p=0.093). The number of cycling years showed similar associations. Duration of HRT was associated with slower decline in global cognition (p=0.037). These associations were not seen in women who had natural menopause.

Conclusions: Early age at surgical menopause was associated with longitudinal cognitive decline and neuropathologic outcomes in women with surgical menopause, but not natural. Ongoing evaluation of the neuroprotective effects of HRT after early surgical menopause is warranted.

Study Supported by: Research supported by NIH 5T32AI074549 (RB).