

# SuperAging at Northwestern: 25 Years of Progress

Up until the 1980's, cognitive aging was universally associated with decline. The concepts prior to that time included such terms as senility, senescence, involution, and regression. Most studies of cognitive aging were based on what happens to someone "on average" over the lifespan. Virtually all studies reported that comparisons between 20, 30, 40, 50, 60, 70, and 80+ year olds showed a downward trend in average test scores with increasing age. At that time, too, interest in

studying the human brain and its relationship to age-related cognitive decline was growing.

In 1987, Marsel Mesulam, MD, one of the founders of the Northwestern University SuperAging Program (NUSAP), commented on a published study that argued that age-related cognitive decline may be explained by a great loss of neurons and the gradual appearance of Alzheimer's proteins in older brains. He expressed puzzlement at this conclusion because how could that explain why wisdom, perhaps the pinnacle of cognitive development, was greatest in old age? He championed a call for research focusing on the positive aspects of cognitive aging, pointing out that there were many examples in history of octogenarians who were cognitively "sharp" and productive, such as Pablo Casals, Anna Freud, and others.

In 1991, Sandra Weintraub, PhD, another co-founder of the NUSAP, conducted a study in over 1,000 physicians ages 28-92, showing that, though average test scores decreased with age, the degree of individual variation

around the average score actually increased with age. Thus, some 65-year-olds were performing well above the average for their age and similarly to 28-year-old Harvard medical residents.

These observations led to a collaboration with Deborah Mash, PhD, founder of the Miami Brain Endowment Bank, to learn if the brains of individuals who retained their cognitive abilities into late old age could give us answers to this unusual cognitive aging trajectory. Emily Rogalski, PhD, a graduate student at Northwestern, joined the effort in 2003.

Over the next few years, we established a longitudinal study involving individuals who also were enrolled in our Alzheimer's disease center clinical core study. We recruited individuals age 80 and over who had scores at least normal for age on tests of attention, reasoning, word finding, and problem-solving. That group was then divided into two: Normal Agers (individuals whose memory test scores were normal for their age) and SuperAgers (individuals whose memory test scores

were better than normal for age and similar to scores of individuals 20-30 years younger.)

In the quarter century that has passed, we have published innovative studies on the biological features associated with SuperAging and on some of the biopsychosocial characteristics of this group. In 2021, Dr. Rogalski was awarded a grant to include four new sites in the US and Canada to expand the visibility of SuperAging. She started a new position at the University of Chicago in September 2023 and is running that multi-site grant (the SuperAging Research Initiative) from there. There are now also multiple research programs nationally and internationally that focus on SuperAging, which has been a true boon for the field.

At the Mesulam Center, we will continue to challenge outdated notions about cognitive aging and investigate the social and biological factors that promote SuperAging and normal cognitive aging by following our cohort longitudinally.

**1987**

Mesulam wrote a short commentary on why age does not have to be associated with cognitive decline.

"Perhaps a concerted belief that good aging is a biological option will refocus research away from involuntal features and more towards the mechanisms involved in the establishment and maintenance of the elusive quality called wisdom."

*(Mesulam, Neurobiology of Aging, 1987)*

**1997**

Mesulam collaborates with Dr. Deborah Mash's Miami Brain Endowment Bank. Examines the post-mortem brain of an 81 year old woman with superior cognition prior to death. He found only a single tangle in a section of the hippocampus and entorhinal cortex, sparking the idea of researching the phenomenon of resistance to age-related accumulation of Alzheimer's disease neuropathologic change.

**2001**

The study protocol focusing specifically on SuperAging is submitted to the Northwestern University Institutional Review Board.

**2005**

The Northwestern University SuperAging Program (NUSAP) was initiated in the Clinical Core of the Northwestern Alzheimer's Disease Research Center, enabling local brain donation for research.

**2012**

The first paper specifically focused on participants from NUSAP details unique brain signatures of SuperAgers compared to same-age and middle-aged controls.

*(Harrison, et al., 2004)*

**2021**

The NIA recognizes the importance of studying SuperAging and awards multi-site grants to Northwestern University and Boston University.

**2024**

**The study of SuperAgers, led by Mesulam Center researchers, Mesulam, Geula, Gefen, Weintraub, and Mather continues at Northwestern, with exciting directions for the future.**

**1994**

Weintraub and colleagues publish a paper on cognitive function in aging physicians that showed decline in average scores with increasing age but increasing variability around the mean. A group of physicians over 65 performed on par with young medical residents.

"Memory and attentional capacity deterioration does not affect all individuals, and little diminution of ability may be seen even in subjects over age 75."

*(Weintraub, et al., 1994)*

**1999**

Mesulam Center researchers start using the term "SuperAger" to describe persons over 80 with exceptional episodic memory.

**2004**

In collaboration with Dr. Mash, researchers showed that Alzheimer tau pathology in the nucleus basalis, a region important for memory, is correlated with cognitive test scores in older individuals with and without cognitive impairment.

*(Mesulam, et al., 2004)*

**2006**

NUSAP gets an initial pilot grant from the Davee Foundation to study "SuperAgers" as defined above.

**2013**

National Institute of Aging (NIA) funds a grant to support longitudinal SuperAging research at Northwestern, with Rogalski, Mesulam, and Geula as co-principal investigators

**2023**

Rogalski moves to University of Chicago and extends SuperAging research regionally with a multi-site grant from the NIA.