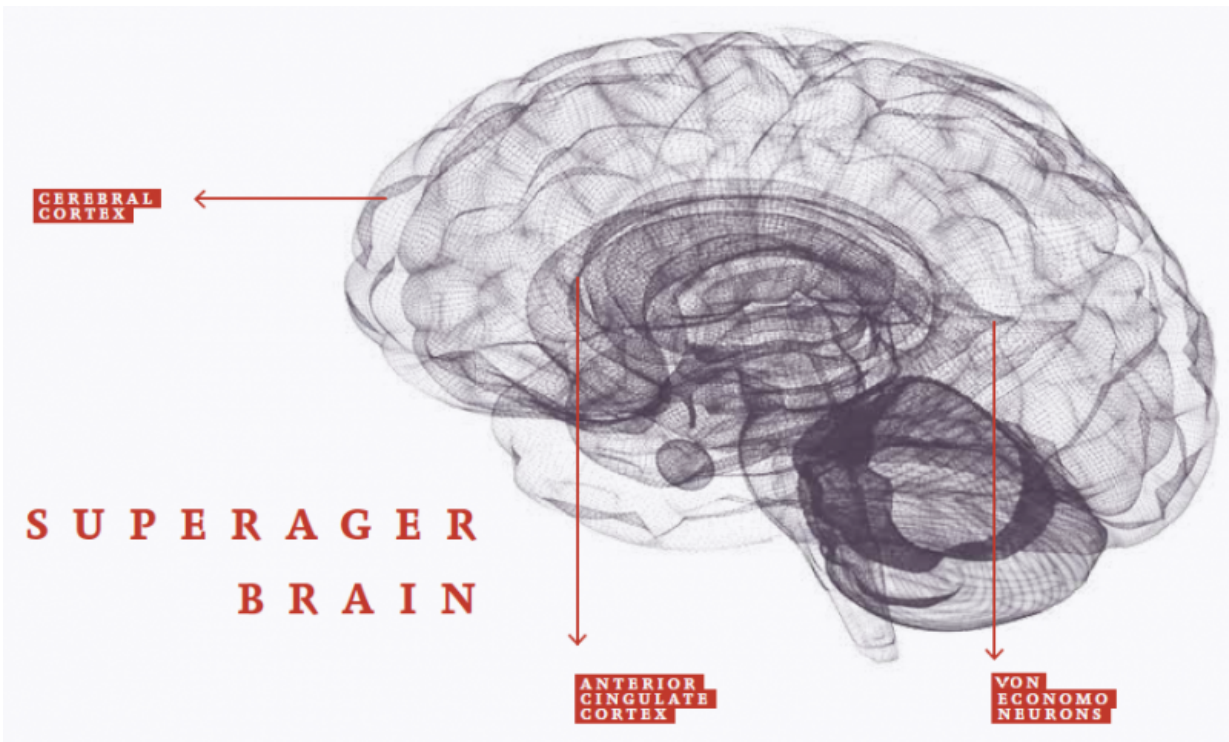


Why are some people immune to age-related cognitive decline?

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Credit: Northwestern University

Emily Rogalski, '07 PhD, is part of a team of scientists taking a glass half-full approach to studying cognitive aging. Instead of focusing on factors that can lead to dementia and neurodegenerative disease as people grow older, they concentrate on the factors that can protect memory. They do this by investigating seniors in their 80s, 90s and

beyond who have remarkable memory power, a tiny subset of the population they call SuperAgers.

"Most of the news about aging is not so great," says Rogalski, a research associate professor in Northwestern's Cognitive Neurology and Alzheimer's Disease Center (CNADC). "Your eyesight goes bad, your hair falls out, your memory gets worse. But not everybody ages that way. It's important to understand why some people are doing so much better than expected."

Definitions of successful aging vary widely, but "SuperAger" has a very specific meaning: a person age 80 or older with memory performance equal to or even better than healthy people in their 50s and 60s. To qualify, an individual must pass a rigorous set of memory tests, ones so tough that less than 10 percent of people who believe they could be a SuperAger actually qualify. Northwestern is the only institution in the world conducting this specific type of aging research.

"We wanted to focus on people who have this extraordinary memory ability and then find out what else they have in common by studying them in a really comprehensive way," Rogalski says. "We look at psychosocial factors, education, family history, physical health and the [brain](#)."

CNADC investigators could end up with hundreds of variables to weigh against aging, but they're taking the challenge one step at a time. First they showed that SuperAgers actually exist—that anecdotal reports of unusually sharp grandmothers and great-uncles hold up under scientific scrutiny.

Clues in the Brain

In 2012, Rogalski's team [published](#) research suggesting that a common

side effect of aging called cerebral atrophy—a loss of brain cells that causes [brain tissue](#) to shrink—may not apply to SuperAgers. Indeed, in the study the brains of 12 SuperAgers looked less like those of their normally aging peers and more like the brains of people 30 years their junior.

MRI scans revealed that the SuperAgers had no significant atrophy in their cerebral cortex, the important outer layer of the brain responsible for memory, attention, language and thinking. Their [cerebral cortex](#) was thicker than the normal agers, about the same size as members of the middle-aged control group. Unexpectedly, the anterior cingulate cortex, a region further inside the brain that's involved in social behavior, was thicker in SuperAgers than in both elderly and middle-aged controls.

The scientists are not gathering all of this information just to find out what's interesting about being a SuperAger. Rather, they're hoping to use it to turn conditions like Alzheimer's disease upside-down.

"We know that what goes wrong in the brain in Alzheimer's is very complex, and even though we have the brightest minds working on it all over the world, at this point we don't have an effective disease-modifying treatment," Rogalski explains. "The factors we identify could eventually become targets to go after in the laboratory to treat neurodegenerative diseases. Our MRI findings led us down a path that we never could have guessed or anticipated."

In follow-up research [published](#) in 2015, CNADC investigators studied samples of the brain under a microscope (study participants are asked to donate their brains after death to support this kind of work). The research showed that SuperAgers had fewer tangles in the [anterior cingulate cortex](#), a compelling finding considering that these twisted fibers of protein are a primary marker of Alzheimer's disease. And compared to age-matched controls and individuals with mild cognitive

impairment, SuperAgers had three to five times more von Economo neurons, a particular type of nerve cell linked to higher-order social intelligence (they're typically found only in great apes and humans).

"It is possible that SuperAgers have higher numbers of these neurons at birth and maintain this higher number throughout life," says Changiz Geula, PhD, research professor in the CNADC. "The second possibility is that von Economo neurons undergo a normal age-related loss to which SuperAgers are immune."

In ongoing research, Geula's lab is studying these special cells across the lifespan to learn how they change over time and in Alzheimer's disease.

Geula, Rogalski and Marsel Mesulam, MD, director of the CNADC, are all principal investigators of the SuperAging project, which is funded by the National Institute on Aging. Day to day, Geula handles examinations of the brain tissue samples, while Rogalski coordinates study participant enrollment and all that goes with it, from cognitive assessments to brain scans. With his "unprecedented multidisciplinary expertise," Mesulam "is the glue that holds it all together," Rogalski says.

"We work collaboratively to decide what are the most important questions we want to ask next and how can we answer them in our living participants and with the microscope," she says.

Hints Beyond the Brain

Right now there are about 60 people enrolled in the SuperAgers study. In addition to memory tests, each participant completes an IQ test, a psychosocial questionnaire and personality inventories. Some have also undergone long interviews about their lives as part of a project done in collaboration with Regina Logan, PhD, and Dan McAdams, PhD, faculty at Northwestern's Foley Center for the Study of Lives.

"You can learn a lot about people's lives and personalities through the way they tell stories about themselves," Rogalski says. "And this may be tied to your brain health. A negative outlook on life could raise your stress hormones. Too much cortisol is not good for your hippocampus, and your hippocampus is important for memory."

SuperAgers also donate blood for genetic testing—the results of which are still forthcoming—and undergo physical exams.

Rogalski stresses that the study participants represent all walks of life. The only obvious common denominator is, in fact, their memory power.

"These people don't report being superior in school. Their educations range from high school to advanced degrees," she says. "And their physical health varies, too. There are people who need canes, walkers and wheelchairs and others doing yoga and weight lifting."

Edith Smith, a former Chicago Public Schools teacher who retired in 1976, got involved in the SuperAging study about three years ago. "I've always had a good memory," says the outgoing 102-year-old. "For instance, if I learned someone's telephone number, after many, many years I still knew it."

Her secret to great memory?

"I have no idea," she says with a laugh. "It's just part of being me."

SuperAger Bill Gurolnick, however, has a theory. "I've been a very active person," says the 85-year-old, who finished a 30-mile bike ride moments before his interview for this story. "When I was in my 60s I got hooked on high-impact aerobics. My theory is the oxygenation of the brain can't hurt."

Since joining the study about a year ago, Gurolnick, a former executive at an automotive chemical company, has enjoyed learning about how the brain works.

"My father had Alzheimer's very early in his life," he says. "They tell me that my [memory](#)'s pretty good, that a decline of cognitive skills is happening slower for me than for the general population. Why is that true for some and not for others? That's what the research is all about."

The research team will follow Smith, Gurolnick and the rest of the study's participants as long as they can, with the goal of learning about what happens to SuperAgers over time. The investigators have already shown that these individuals maintain their superior cognitive performance over the course of 18 months—but will it last longer? And what else can be gleaned from SuperAgers?

"Hopefully what we're starting is really a new line of investigation that can lead us to poignant insights that our labs and others can take in important directions," Rogalski says.

More information: The SuperAging study is still enrolling participants, who must be 80 years or older and able to visit Chicago every two years for testing. Interested individuals may contact the research coordinator at 312-503-2716 or agingresearch@northwestern.edu.

Provided by Northwestern University

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