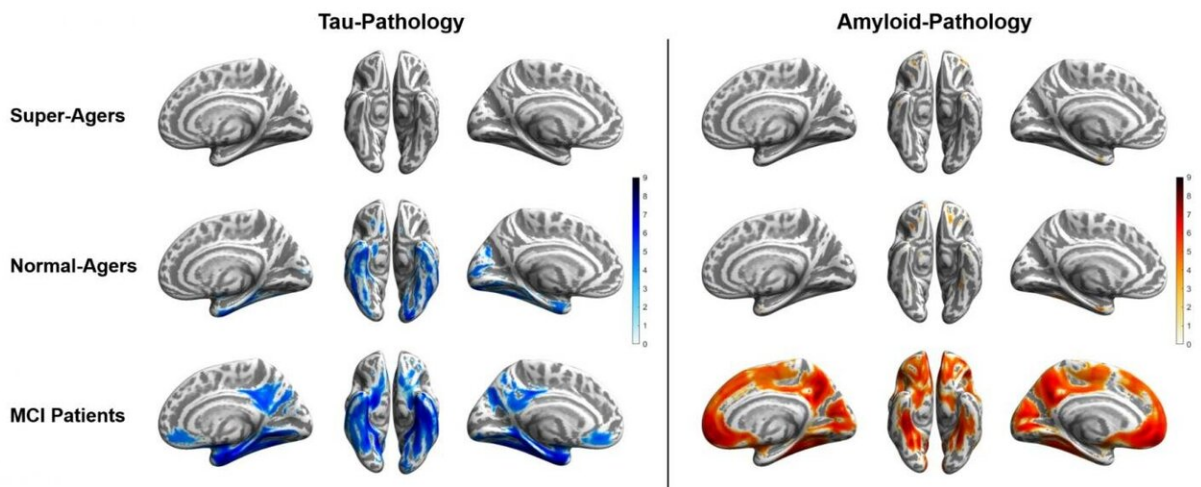


# Super-agers show resistance to tau and amyloid accumulation

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Tau (blue) and amyloid (orange) distribution patterns for super-agers, normal-agers and MCI patients, when compared to a group of younger, healthy, cognitively normal, amyloid-negative individuals. Brain projections are depicted at an uncorrected significance level of  $p$

Super-agers, or individuals whose cognitive skills are above the norm even at an advanced age, have been found to have increased resistance to tau and amyloid proteins, according to research presented at the Society of Nuclear Medicine and Molecular Imaging (SNMMI) 2020 Annual Meeting. An analysis of positron emission tomography (PET) scans has shown that compared to normal-agers and those with mild cognitive impairment, super-agers have a lower burden of tau and amyloid pathology associated with neurodegeneration, which probably allows them to maintain their cognitive performance. An image showing the comparison of tau and amyloid distribution patterns in these different cognitive

aging trajectories has been selected as SNMMI's 2020 Image of the Year.

"Our cognition reflects who we are as individuals. As we age, most of us lose some of that ability," said SNMMI's Scientific Program Committee chair, Umar Mahmood, MD, Ph.D. "The Image of the Year provides us with insight into how we can use these PET imaging biomarkers to understand behaviors and therapies that may allow more of us age better and retain more of our cognitive abilities as we get older."

Each year, SNMMI chooses an image that best exemplifies the most promising advances in the field of nuclear medicine and molecular imaging. The state-of-the-art technologies captured in these images demonstrate the capacity to improve patient care by detecting disease, aiding diagnosis, improving clinical confidence and providing a means of selecting appropriate treatments. This year, the SNMMI Henry N. Wagner, Jr., MD, Image of the Year was chosen from more than two thousand abstracts submitted to the meeting and voted on by reviewers and the society leadership.

"The phenomenon of super-aging suggests that cognitively high-functioning individuals have extraordinary mechanisms that resist brain aging processes and neurodegeneration," said Dr. Merle Hoenig, Research Center Juelich & University Hospital Cologne, Germany. Some insights have been collected on [amyloid pathology](#) in super-agers, but there is no in vivo evidence on tau [pathology](#) due to the former lack of available imaging techniques. "We know that tau pathology is more closely associated with cognitive decline than amyloid pathology," Hoenig continued, "thus, the resistance, in particular against tau pathology, likely allows these individuals to perform cognitively above average even at advanced age."

Data from the Alzheimer's Disease Neuroimaging Initiative was utilized to create three age- and education-matched groups of 25 super-agers, 25 normal-agers and 25 patients with [mild cognitive impairment](#), all above 80 years old. In addition, 18 younger, cognitively normal, amyloid-negative controls were included in the comparison as a reference group. 18F-AV-1451 and 18F-AV-45 PET images obtained for all individuals and researchers compared the tau and amyloid burden between the four groups. A logistic regression was performed to identify genetic and pathophysiological factors best predicting aging processes.

No significant differences between super-agers and the younger control group were observed in terms of in vivo tau and amyloid burden. The normal-ager group exhibited tau burden in inferior temporal and precuneal areas and no significant differences in amyloid burden, when compared to the younger control group. Patients with mild cognitive impairment showed both high amyloid and high tau pathology burden. Differences in amyloid burden dissociated the normal-agers from those with mild cognitive impairment, whereas lower tau burden and lower polygenic risk predicted super-agers from mild cognitive impairment patients.

"While super-agers may be able to resist aging-associated proteinopathies, in particular tau pathology, normal-agers may not and are thus exposed to inevitable cognitive decline due to the accumulation of neurotoxic tau tangles and the advancing aging process," noted Hoenig. "Moving further to the other extreme of aging, namely mild cognitive impairment, the synergistic effects of both [amyloid](#) and tau may accelerate the pathological aging process."

These results motivate further research to determine responsible resistance factors, which may also inspire the development of novel treatment concepts. "Given the multitude of factors involved in the aging process, it will certainly be challenging to develop therapeutics to tackle the factors involved. However, if we understand which individuals are resistant to dementia, this will help us identify potential pathways that promote successful aging—protecting against not only Alzheimer's disease but also other aging-associated diseases, such as vascular disease and other forms of dementia," said Hoenig.

Provided by Society of Nuclear Medicine and Molecular Imaging

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