

Alzheimer's research with primates could address treatments that show promise in mice but don't help humans

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Rhesus macaques experience an aging process similar to people's. Credit: Unsplash/CC0 Public Domain

As of 2022, an estimated [6.5 million Americans](#) have Alzheimer's disease, an illness that robs people of their memories, independence and personality, causing suffering to both patients and their families. That number may double by 2060. The U.S. has made [considerable investments](#) in Alzheimer's research, having allocated [US\\$3.5 billion in federal funding](#) this year.

Why, then, are researchers no closer to a cure today than they were 30 years ago?

Back in 1995, researchers created the [first transgenic mouse model](#) of Alzheimer's disease, which involved genetically modifying mice to carry a gene associated with early-onset Alzheimer's. Myriad studies have since focused on mouse models that accumulate [abnormal proteins](#) in their brains, a hallmark of the disease. Although these studies made great strides in understanding specific mechanisms involved in the disease, they have [failed to translate](#) into effective treatments.

As [research scientists working](#) with [nonhuman primates](#), we believe that part of the problem is that mice don't reflect the full spectrum of Alzheimer's disease. A more complementary animal model, however, could help researchers better translate the results from animal studies to humans.

Why animal models?

A critical aspect of understanding what goes awry in Alzheimer's disease is the relationship between [brain](#) and behavior. Researchers rely heavily on animal models to do these types of studies because [ethical and practical issues](#) make them impossible to conduct in people.

In recent years, researchers have developed [alternative methods](#) to study Alzheimer's, such as computer models and cell cultures. Although these

options show promise for advancing Alzheimer's research, they don't supersede the need for animal models because of important limitations.

One is their inability to replicate the complexity of the human brain. The human brain has an estimated [86 billion neurons](#) that perform highly complex computations. While computer models can simulate the workings of specific neural circuits, they are unable to fully capture these complex interactions and work best when used [in concert with animal models](#).

Similarly, cell cultures and brain organoids—miniature brains derived from human stem cells—are [unable to adequately mimic](#) the aging process and all the ways the components of the human body interact with one another.

As a result of these limitations, researchers turn to animal models that better reflect human biology and disease processes.

The problem with mice

According to the National Association for Biomedical Research, approximately [95% of lab research conducted in animals in the U.S.](#) is done in mice and rats. Alzheimer's is no exception: For more than 25 years, research on Alzheimer's has [focused on using transgenic mice](#) to better understand the biological changes associated with the disease.

Because mice do not naturally get Alzheimer's, they are genetically engineered to develop [abnormal proteins](#) known as [amyloid plaques](#) and neurofibrillary tau tangles to mimic Alzheimer's in their brains. These protein accumulations impair brain function and are associated with memory impairment. While studies on [treatments that remove these proteins](#) have been able to improve cognition in mice, similar interventions have failed in people.

This highlights the challenge of [translating animal research](#) in the lab to people in the clinic. Mouse studies often mirror only a single aspect of the disease that may not be directly relevant to people. For example, most transgenic mouse models focus on amyloid protein buildup while [neglecting other crucial aspects](#) of the disease, such as overall neurodegeneration. Such limitations have led some scientists to [question the value of using mouse models for Alzheimer's research](#).

It is important to recognize, however, that [scientific knowledge](#) often advances in [incremental steps](#) through the collective results of many studies using different methods and models. Rodent studies provide the necessary foundation for animal models that better mimic the full scope of Alzheimer's—such as nonhuman primates.

Nonhuman primates offer a closer model

The specific features of a species—including brain structure, cognitive ability, [life span](#) and the extent to which they show the hallmarks of Alzheimer's—determine how suitable it is for specific research questions. Based on these factors, we believe that nonhuman primates are particularly well suited for Alzheimer's research.

[Primates](#) are a diverse group of mammals that includes humans, apes, monkeys and prosimians. Nonhuman primates are particularly valuable for understanding [human aging](#) and [Alzheimer's disease](#) because their genetic makeup, brain, behavior, physiology and aging process closely resemble those of people. Aging monkeys experience cognitive, physical and sensory decline as well as a variety of illnesses, such as cancer and cardiovascular disease, much like aging people. Perhaps most critical for Alzheimer's research, nonhuman primates live much longer than rodents and can [naturally develop some of the hallmarks associated with Alzheimer's](#) as they get older.

Using nonhuman primates in research [faces some challenges](#). Compared to mice, nonhuman primates are more expensive to house and feed, and face a growing shortage in research facilities. Nonhuman primates are also prime targets for activists seeking to stop the use of animals in research. Yet, in light of ongoing failures with rodent models, nonhuman primates could significantly help scientists better understand and treat Alzheimer's.

Scientists study Alzheimer's in nonhuman primates in a number of ways.

In one approach, researchers examine species with short life spans, such as [gray mouse lemurs](#) or [common marmosets](#), to measure how brain and behavior naturally change with age and identify potential predictors of disease. Other researchers may instead accelerate the disease process by [inducing plaque](#) or [tangle formation](#) in the brains of longer-lived species, like rhesus macaques. These approaches yield studies that are particularly promising for testing treatments in a short time frame.

A third approach takes advantage of recent advances in genomics to study marmosets [born with genetic mutations](#) involved in Alzheimer's. This method provides the opportunity to test preventive treatments during early life, well before any sign of the disease appears.

Lastly, [comparing Alzheimer-like patterns across primate species](#) may help reveal critical risk factors for developing the disease, which could be reduced to promote healthy aging.

We believe that research in nonhuman [primates](#), when conducted with the highest [ethical standards](#), provides the best chance to understand how and why Alzheimer's disease progresses, and to design treatments that are safe and effective in people.

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