

Alzheimer's Disease

Stanford Center for Memory Disorders

Deep within our brains, our memories live in the spaces between cells, holding the record of our lives.

New experiences create new connections and recordings; the ability to form and call up those memories relies on healthy brain cells and networks.

Just like the rest of the body, the brain changes with age. Our ability to recall memories naturally slows. Blood flow to the brain decreases; white matter and connections between brain regions begin to deteriorate. Information-carrying chemical messengers are affected.

Almost everyone over the age of 60 notices more trouble attaching a name to a face or occasionally heads into a room and wonders what they went there for.

Yet, when brain changes become overwhelming, thinking can become seriously impaired. Repeating the same question or story several times within an hour or two; needing help to find your car in the parking lot; frequently misplacing things; and getting lost while driving in a familiar environment are symptoms of concern.

The Stanford Center for Memory Disorders

The Stanford Center for Memory Disorders is dedicated to helping patients and their families in the hard fight against cognitive decline. Our physicians lead an interdisciplinary team that works together to help maintain quality of life for as long as possible.

Experts from the fields of neuropsychology, psychiatry, nursing, pharmacy, and genetic counseling collaborate closely with our behavioral neurologists to provide medical care that is both cutting edge and compassionate.

Dementia is the umbrella term for cognitive impairment that causes a loss of function in memory, verbal ability, visuospatial function or judgment that affects daily living. Because there are different causes of dementia, an accurate diagnosis by an experienced team is essential to getting the best treatment.

AT THE STANFORD CENTER FOR MEMORY DISORDERS, WE MANAGE THESE CONDITIONS:

Alzheimer's disease: A neurological disorder in which the death of brain cells causes memory loss and cognitive decline, affecting all aspects of brain function; by far the most common type of dementia

Corticobasal degeneration: A progressive cognitive and movement disorder characterized by nerve cell loss and atrophy of multiple areas of the brain; initially affects one side of the body more than the other

Creutzfeldt-Jakob disease: A rare, rapid degenerative brain disorder believed to be caused by an abnormal form of a protein called prion

Lewy body dementia: A condition causing a gradual decline in mental function, sometimes with visual hallucinations; it also causes movement problems similar to symptoms of Parkinson's disease

Frontotemporal dementia: A group of disorders that occur when the nerve cells in the frontal and temporal lobes of the brain are damaged resulting in prominent behavioral impairment or language trouble

Huntington's disease: A hereditary disorder causing degeneration in brain regions critical for movement control and behavior

Normal pressure hydrocephalus: A rare condition, presenting with cognitive impairment and trouble walking, resulting from an over-accumulation of fluid in the ventricles of the brain

Primary progressive aphasia: A progressive neurodegenerative disorder that primarily affects language function; the three subtypes include non-fluent variant, semantic variant, and logopenic variant

Progressive supranuclear palsy: A rare, complex condition that causes progressive decline in cognition, walking, and eye movements

Vascular dementia: The second most common form of dementia after Alzheimer's disease, caused by damage to brain tissue due to decreased blood flow and multiple small strokes that build up over years

At Stanford, we feel it is critical for our team to be a continuous source of support to the patient, caregivers, and family from the first visit on. Every step along the way, as the patient requires more and more care, we provide guidance for families who find themselves on this path—a difficult and often long journey.

Alzheimer's Disease

Alzheimer's disease usually begins with impairment of short-term memory followed by trouble with language and visuospatial processing, and ultimately progresses to impairing a patient's personality and ability to walk and even swallow. It is, for now, an incurable and fatal disease.

Each Alzheimer's patient travels an individual road. While each experience is different, what is common is the negative impact on physical and emotional well-being and quality of life.

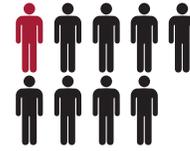
Alzheimer's disease takes away memory, abilities, communication, and judgment. Day upon day, year upon year, the losses mount.

The good news—and the bad news—is that if you've been touched by Alzheimer's disease or other memory disorders, you're not alone.

What brings on Alzheimer's?

The search continues for the exact cause for Alzheimer's. Genetics has an influence: people with a parent who has Alzheimer's are at a twofold risk of developing Alzheimer's. In rare cases, the disease is caused by gene mutations. These early-onset patients tend to get sick in their

ALZHEIMER'S STAGGERING TOLL



1 in 9
people over
the age of 65



1 in 3
people over
the age of 85



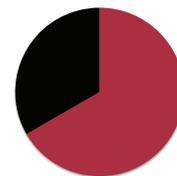
**More than
5 million**
Americans

6th

Sixth
leading cause
of death



20%
of Medicare
spending



2/3
of Americans
with Alzheimer's
are women

40s—as opposed to more common, “sporadic” or late-onset Alzheimer’s disease, which affects people in their 60s, 70s, or 80s. The main genetic risk factor for late-onset disease is a gene called APOE4.

Beyond advancing age and genetics, risk factors for the disease also include multiple strokes, family history, head trauma, and low education.

Currently, we know that at least two proteins—beta amyloid and tau—build up in the brains of Alzheimer’s disease patients. This accumulation, along with inflammation, damages and destroys the neuronal connections, or synapses. Beta-amyloid protein forms circular structures called plaques that may be toxic to the connections between brain cells. Within the brain cells, tau protein changes into abnormal folds and clusters, forming tangles that also become toxic.

As the connections are lost, the ability to learn and remember deteriorates.

Preventing Alzheimer’s

Strong data suggests that lifestyle factors—especially regular aerobic exercise—can help reduce the risk of Alzheimer’s. We recommend exercise five days per week, following a Mediterranean diet, maintaining a healthy weight and blood pressure, controlling diabetes, and minimizing exposure to head trauma. Continued cognitive engagement like socializing and hobbies is strongly encouraged. We work closely with our patients’ primary care physicians to ensure optimal levels of B12, vitamin D, thyroid hormone, and other substances.

We have recently learned that deep sleep is needed for the brain to clear amyloid protein. Long-term sleep disturbances and the interference with amyloid clearing may very well raise the risk of Alzheimer’s.

Proponents of coconut oil, coconut water, omega-3 fatty acids, DHA, and turmeric suggest these substances can increase cognition, but the studies so far have been small and inconclusive and we do not currently recommend any supplements.

How is Alzheimer’s diagnosed?

We diagnose “probable Alzheimer’s disease” based on taking a thorough history, doing an extensive neurologic examination including cognitive testing, and running blood tests and brain imaging studies to rule out other possibilities (like low thyroid, low B12, or previous strokes).

An imaging test called a PET scan of the brain looks for the presence of beta-amyloid. A lumbar puncture can detect abnormal levels of beta-amyloid and tau in the spinal fluid. As time goes on, the Alzheimer’s brain tends to shrink, and these structural changes can be seen on an MRI.

Treatment Options

Unfortunately, there are no currently available FDA-approved medications proven to delay onset or slow progression of the underlying brain degeneration and loss of synaptic connections that occur in Alzheimer’s disease. This lack of definitive treatment has been a source of unending frustration for patients

and their families, physicians and researchers, and has resulted in untold suffering and loss of life. With an aging population, future projections present an overwhelming crisis ahead.

Two groups of medications can temporarily improve the chemical neurotransmitter environment at synapses, producing a modest improvement in cognitive function, but these medications have side effects and are only minimally effective.

By the time a diagnosis of Alzheimer's disease is made, it may have been decades from the time the amyloid protein begins building up to when behavioral symptoms appear. Today, the consensus is that treatment should begin sooner; clinical trials and pharmaceutical companies are now targeting people with earlier symptoms.

Promising Research at Stanford

Stanford has some of the top neurologists and neuroscientists in the world focused on developing solutions to the Alzheimer's crisis; their research spans the full spectrum from the lab bench to the clinic and back to the lab again. The same doctors who care for patients at the Stanford Center for Memory Disorders also contribute to innovative research on Alzheimer's disease and other neurodegenerative disorders.

Our physician scientists, along with their basic science colleagues, are investigating the underlying mechanisms of how the brain works and what happens in Alzheimer's disease. They are creating groundbreaking neuroimaging technologies to find better ways to detect Alzheimer's earlier by actually seeing it in action. And they are translating their insights into new therapies.

In a major achievement, Stanford was recently selected as an Alzheimer's Disease Research Center, one of the few such centers funded by the National Institutes of Health. The NIH designation comes with a \$7.3 million award over five years to advance our interdisciplinary research on Alzheimer's disease and related disorders.

The center, directed by **Victor Henderson, MD**, professor of health research and policy and of neurology, draws on Stanford's strengths in imaging, genetics, neuroimmunity, synapse biology, biostatistics and bioinformatics, clinical assessment and research, epidemiology, and caregiver outreach.



“We plan to study patients at early stages of illness, as well as healthy older adults, and follow them over time. We hope to foster new research collaborations that advance knowledge about Alzheimer's, Parkinson's, and similar disorders in order to treat them more effectively and help prevent them from occurring.”

Victor Henderson, MD

Professor of Health Research and Policy and of Neurology

Director, Stanford Alzheimer's Disease Research Center

We have enhanced opportunities for cutting-edge clinical trials and educational opportunities for community members, patient caregivers, students, and health-care professionals. Many dozens of faculty experts are involved in putting their findings to work to help patients here and beyond.

The Advantage of Bench to Clinic Translation

Visionary scientists can view problems from an angle others don't consider. In a new way of heading off Alzheimer's, a team led by **Frank Longo, MD, PhD**, the George E. and Lucy Becker Professor and Chair of Neurology, has developed a drug—the first of its kind—that has recently started phase 2 trials in Europe that could provide real hope to families. Dr. Longo is one of the rare neurologists who has executed the full spectrum of discovering novel mechanisms causing brain degeneration and creating a viable treatment that has progressed past mice and into human trials. This unusual experience provides a key resource for Stanford translational programs and further innovation.

The drug, called C31, has the potential to bolster brain cells' innate strength to protect and defend against neurological invaders at various stages of Alzheimer's harmful process. C31 promotes signaling within brain cells and is targeted to regenerate and restore connections between brain cells, even reversing the damage done. The innovative treatment targets degenerative mechanisms linked to both amyloid and tau, and if successful, would completely change the landscape of neurodegenerative disorders.

Advanced Imaging and Genetics

Michael Greicius, MD, MPH, associate professor of neurology, has pioneered the use of network-based imaging methods to examine Alzheimer's patients. As the director of the Alzheimer's Disease Research Center Imaging Core, he is combining functional MRI and PET scans to track the activity of synapses and to see the accumulation of those abnormal proteins that interfere with memory function.

He is also discovering genes that appear to protect the brain from accumulations of toxic amyloid and tau. To do so, he has identified and recruited a large cohort of healthy people well into their 80s and 90s who, despite having the high risk APOE4 gene, remain cognitively normal. His discovery of genes conferring protection against APOE4 risk point to potentially powerful degeneration prevention strategies. Dr. Greicius' work is also at the forefront of determining why women are more prone to develop Alzheimer's than men are, and his research is discovering intriguing possibilities regarding the role of estrogen and menopause.

Uncovering the Role of Neuro-Inflammation

It is becoming clear that inflammation plays a central role in the development of neurodegenerative diseases. And Stanford scientists are finding intriguing connections between the immune system, inflammation, and the brain.

Immune cells in the brain called microglia are tasked with policing the brain, clearing up debris, calming inflammation, and nurturing neurons. If microglia don't clean up the toxins in the brain efficiently, debris left lying around can trigger inflammation and cause consequent injury to neurons.

Researchers here have discovered that in Alzheimer's disease, the brain's trash-disposal system is defective. **Katrin Andreasson, MD**, professor of neurology, is helping to lead the way in identifying specific inflammatory pathways and understanding how these processes injure brain cells and disrupt circuits when microglia stop doing their job. In a major advancement, she has developed a non-invasive technique that provides a detailed view of blood flow in the brain using carbon nanotubes and laser light.

In other research that has captured worldwide attention, **Tony Wyss-Coray, PhD**, professor of neurology, has shown that infusions of blood from young mice improve the cognitive abilities of old mice and Alzheimer's mice. To determine which specific recharging factors in the blood might be at play, he and his team have discovered that the most crucial element is a protein in plasma called colony-stimulating factor 2. If the same results hold true for humans, it could be that CSF2, already FDA approved for bone marrow transplants, could be one of the answers we've been waiting for.

Next-generation molecular brain scans will accelerate progress in developing prevention and treatment strategies. **Michelle James, PhD**, and **Elizabeth Mormino, PhD**, assistant professors of neurology and radiology are creating novel technologies for detecting brain inflammation and other early degenerative processes.

Stanford's Robust Clinical Trial Program

Clinical trials are research studies that evaluate a new medical approach, device, drug, or other treatment. As a Stanford Health Care patient, you may have access to the latest, advanced clinical trials that could impact your health or that could advance medical science.

For example, inspired by the mouse studies described above, **Sharon Sha, MD**, clinical assistant professor of neurology, is running a clinical trial in which blood plasma obtained from the Stanford Blood Center from young, healthy volunteers, is being administered to Alzheimer's patients to determine if that plasma can improve cognition.

Many other current clinical trials are collecting data such as medical, family, and medication history; following participants to better understand the mechanisms of memory that change as we age; administering various treatments; and studying new promising ways to image the brain.



“We work closely with our patients to better understand the causes of the disease and, critically, to develop novel treatments to prevent, slow, or cure Alzheimer's disease. To do so, we need the support of patients and their families lending their time, energy, optimism, and effort in fighting this battle with us.”

Michael Greicius, MD, MPH

*Medical Director, Stanford Center for
Memory Disorders*

*Imaging Core Director, Stanford
Alzheimer's Disease Research Center*

Join Us

At Stanford Medicine, we are getting closer every day to building a complete picture of Alzheimer's disease and other forms of dementia. There is good reason for hope that new strategies and effective treatments will completely change the course of these diseases and save the memories, minds, and lives of our loved ones.

Endowed Professorship | \$4 million

Endowed professorships help Stanford attract and retain top faculty. They are the highest honor the university can bestow upon its most distinguished faculty who have made extraordinary contributions to research and teaching.

Endowed Faculty Scholar | \$2 million

Endowed faculty scholar awards encourage, support, and honor outstanding young faculty members while their careers are being established. These awards last for three or four years—a period long enough to complete a segment of work but short enough to make the award available to other qualified candidates.

Endowed Postdoctoral Fellowship | \$1.2 million

Fellows play a vital role in the actual execution of research. Fellowships are crucial to our ability to offer the support needed to attract the most talented graduate and postgraduate students.

Expendable Postdoctoral Fellowship | \$100,000 or more

Supports a fellow on an annual basis. Fellowships nurture the research of young investigators and allow the center to recruit the next generation of investigators to the field of neurodegenerative disorders.

Expendable Research Funding | Any amount

The annual budget for a given faculty member's research program typically ranges from several hundred thousand to \$1 million per year. Gifts of all sizes contribute to moving research forward.

Contact Us

To find out more about how you can make a gift to advance Stanford's research in Alzheimer's disease and related disorders, including naming/ endowing the Stanford Center for Memory Disorders, please contact:

Anne Chun Longo

Medical Center Development
650.387.0161 | anne.longo@stanford.edu
medicalgiving.stanford.edu

