AIMING FOR CHANGE

A former Navy SEAL and firearms expert writes about why there should be changes to current gun laws and discusses the importance of gun safety.
SD4

NEW HOPE AGAINST ALZHEIMER'S

BY BRADLEY J. FIKES

San Diego researchers study how boosting brain activity, early drug therapies can ward off disease

The human brain is the most complex object on Earth, and what causes this seat of consciousness to slowly and irreversibly deteriorate from Alzheimer's disease is one of science's greatest mysteries.

We still don't know how to stop Alzheimer's or reverse the degeneration it causes, and time is of the essence as America's aging population means an explosion in the number of people with the affliction.

But we've also made unprecedented progress in learning about Alzheimer's — what it is, how to diagnose it and even how to lower the odds of contracting it. Experts increasingly stress that the lifestyle tools for building up long-lasting, protective brain power must be used decades before any mental decline appears. In other words, it's foolish to think only seniors and the elderly should worry about the disease.

There's also rising hope on the treatment front: Never before has lab research led to as many experimental therapies being tried in Alzheimer's patients, and right behind them is a growing list of other potential medications being readied for testing in people.

As the mystery is lifting, so is the sense of helplessness. Much of this demystifying work is taking place in San Diego, which has been a vibrant, internationally respected center of Alzheimer's research for decades.

Here's a look at the latest discoveries about Alzheimer's, newest strategies for battling the disease and most authoritative advice on how to preserve your brain power.

SEE **RESEARCH • SD2**

Magnified image shows how Alzheimer's disease severs important connections between neuron cells in the brain. NATIONAL INSTITUTE ON AGING

GOOD WEEK / BAD WEEK

Your news score card

GOOD WEEK

Park party!: Billy Joel returns to San Diego for the first time in 15 years with a May 14 concert at Petco Park. Big-shot ticket presales start Monday. The rest of youse can wait until Friday.

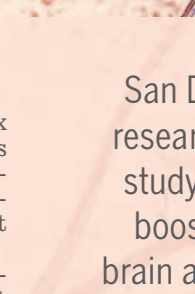
Al fresco tunes: The San Diego Symphony wins approval for a permanent waterfront concert venue on Embarcadero Marina Park South. The moon approves.

Stroke hopes: Scientists from Carlsbad's Ionis Pharmaceuticals find that an experimental drug designed to reduce damage from strokes shows promise in animal testing. Fingers crossed! Paws, too.

Apple: The number of paid Apple Music subscribers hits the 10 million mark after just six months, a total Spotify took six years to reach. There's gold in those streams.

Pachyderms: The Ringling Bros. and Barnum & Bailey circus will end its Asian elephant act in May, and the elephants will retire to Florida. We'll be needing bigger early bird specials.

BAD WEEK



Dean Spanos: What was behind NFL Door No. 1? No Carson stadium for the Chargers owner. We feel for you. Except that we totally don't.

Rock lovers: David Bowie dies at the age of 69, leaving a titanic musical legacy and a flood of shock and loss. Rebel rebel, we're kind of a mess.

CVS: Fresh & Easy's plan to sell its Point Loma lease to CVS is put on hold when neighbors object and the owner balks. Bring on the generic analgesics.

Gossip Inc.: The anonymous complaint about local Immigration and Customs Enforcement workers being recruited for sex parties turns out to be false. Some people are no fake fun at all.

Golden Globes: Viewership of this year's Golden Globe Awards broadcast was down 4 percent from last year. In the nasty spirit of host Ricky Gervais, we blame Ricky Gervais.

KARLA PETERSON • U-T

By the numbers

5.3 million

The estimated number of Americans who had Alzheimer's disease last year, including nearly 590,000 in California and more than 60,000 in San Diego County. Experts said up to half of these patients haven't been diagnosed with the affliction.

The number of new cases of Alzheimer's and other dementias is projected to double by 2050. In California, the doubling is expected to occur by 2030.

Almost two-thirds of Alzheimer's patients in the U.S. are women.

60 to 80

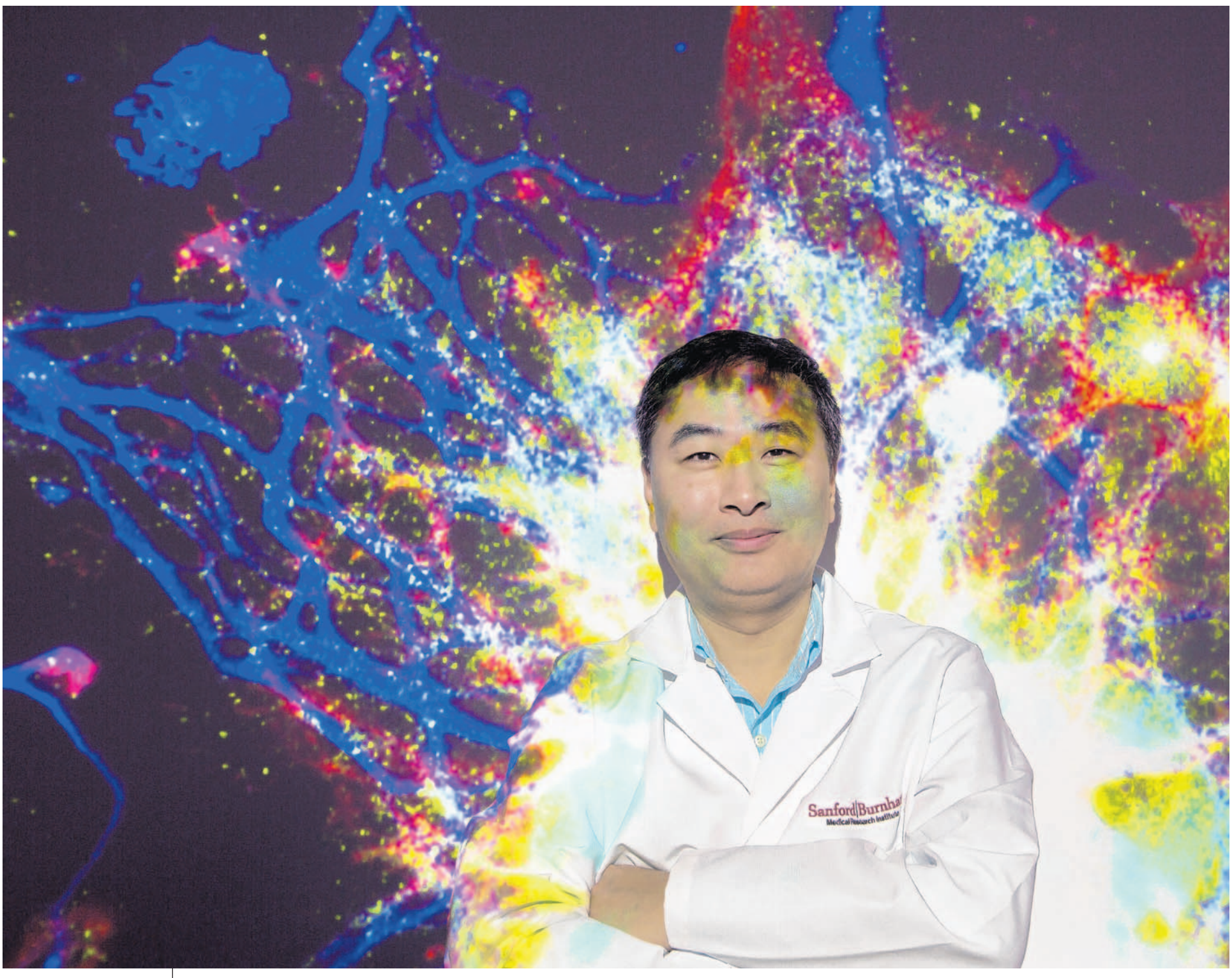
The percentage of all dementia cases nationwide attributed to Alzheimer's disease.

The disease is the third-leading cause of death in San Diego County and the sixth nationally.

$226 billion

Last year's estimated bill for Alzheimer's and other dementias. The figure included medical treatment, the expense of other support services and the lost financial productivity for family members and others who provide caregiving. By 2050, the annual cost is projected to reach $1.1 trillion.

Source: U-T research



HOWARD LIPIN U-T

A photo of a neuron is projected on Alzheimer's researcher Huaxi Xu at the Sanford Burnham Prebys Medical Discovery Institute.

RESEARCH • Scientists want to understand what causes disease

FROM **SD1**

Appetite for learning

More than ever, scientists agree that one of the most important ways to ward off Alzheimer's and other aging-related mental declines is to strengthen your ability to analyze, imagine and process new information, much as you would strengthen your muscles with workouts at the gym.

The idea is to stretch your thinking by engaging in cognitively demanding tasks such as acquiring an additional skill, learning a second language and even adjusting to a different profession. Studies have found that fundamental cognitive skills such as memory increase when people expose their brains to these complex, unexplored territories of thought.

"If you learn something new, you build up more synapses in the brain," said Dr. Mark Tuszynski, director of UC San Diego's Center for Neural Repair.

While it helps to consistently work out your brain from childhood onward, you don't have to be young to benefit. Older people improve their memory by picking up skills that require constant use of memory and reasoning, research has shown.

This ageless benefit points to the much-discussed topic of neuroplasticity — the ability of the brain to adapt by rewiring itself. When parts of the brain are damaged, as in a stroke, other parts learn to compensate. And contrary to long-held dogma, the adult brain can create new neuron cells.

Sophisticated conceptual work and even physical exercise have been found to increase that regenerative feature. Scientists are trying to devise new treatments to further stimulate this self-repair phenomenon.

All of these insights were made possible by research led by Fred "Rusty" Gage of the Salk Institute for Biological Studies in La Jolla and Peter Eriksson of Sahlgrenska University Hospital in Gothenburg, Sweden.

In 1998, they made the groundbreaking discovery that the human hippocampus, a part of the brain involved in memory, produces new neurons throughout life.

Further research not only confirmed that conclusion, it established that new brain cells are generated in other parts of the brain.

Moreover, studies have found that highly educated people generally have a lower risk of Alzheimer's disease. While correlation doesn't automatically mean causation, these converging lines of evidence increasingly suggest that vigorous mental and physical activity protects against mental degeneration.

Earlier treatments

If neural regeneration can be stimulated by increased intellectual activity, some biochemical changes must take place to produce this effect. So presumably, medications could be developed to directly stimulate brain growth and repair.

Tuszynski is an advocate of that approach, using what are called nervous system growth factors. These are chemicals promoting cell survival and function that become deficient because of Alzheimer's disease, he said.

"One of the things we're trying to do is not only replace deficient growth factors, but also provide extra amounts ... to try and prevent cell death and stimulate cell function. And in animal (testing), they're quite effective, and the effects are replicated across many different academic laboratories."

In the longer term, scientists want to understand just what causes Alzheimer's. While the disease is age-related, it's far from an inevitable part of aging. People can remain lucid well into their 90s and beyond, although some deterioration of memory and thinking generally occurs.

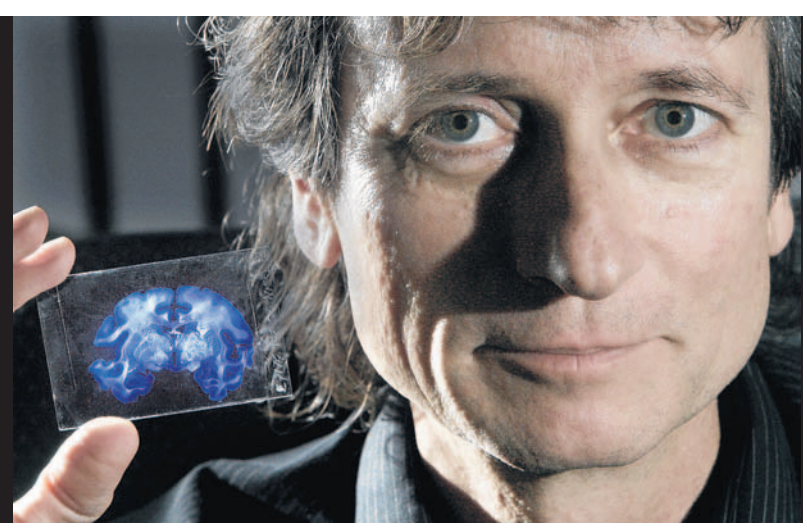
During the past two decades, scientists have concentrated on two major mechanisms linked with the onset of Alzheimer's. Both of them deal with abnormal forms of proteins that play vital roles in how the brain's neurons function.

One is a tangled form of protein called beta amyloid, which appears to accumulate in neurons and damage them. Several amyloid-removing drugs have been tested in people, with only very modest signs that they can slow down Alzheimer's.

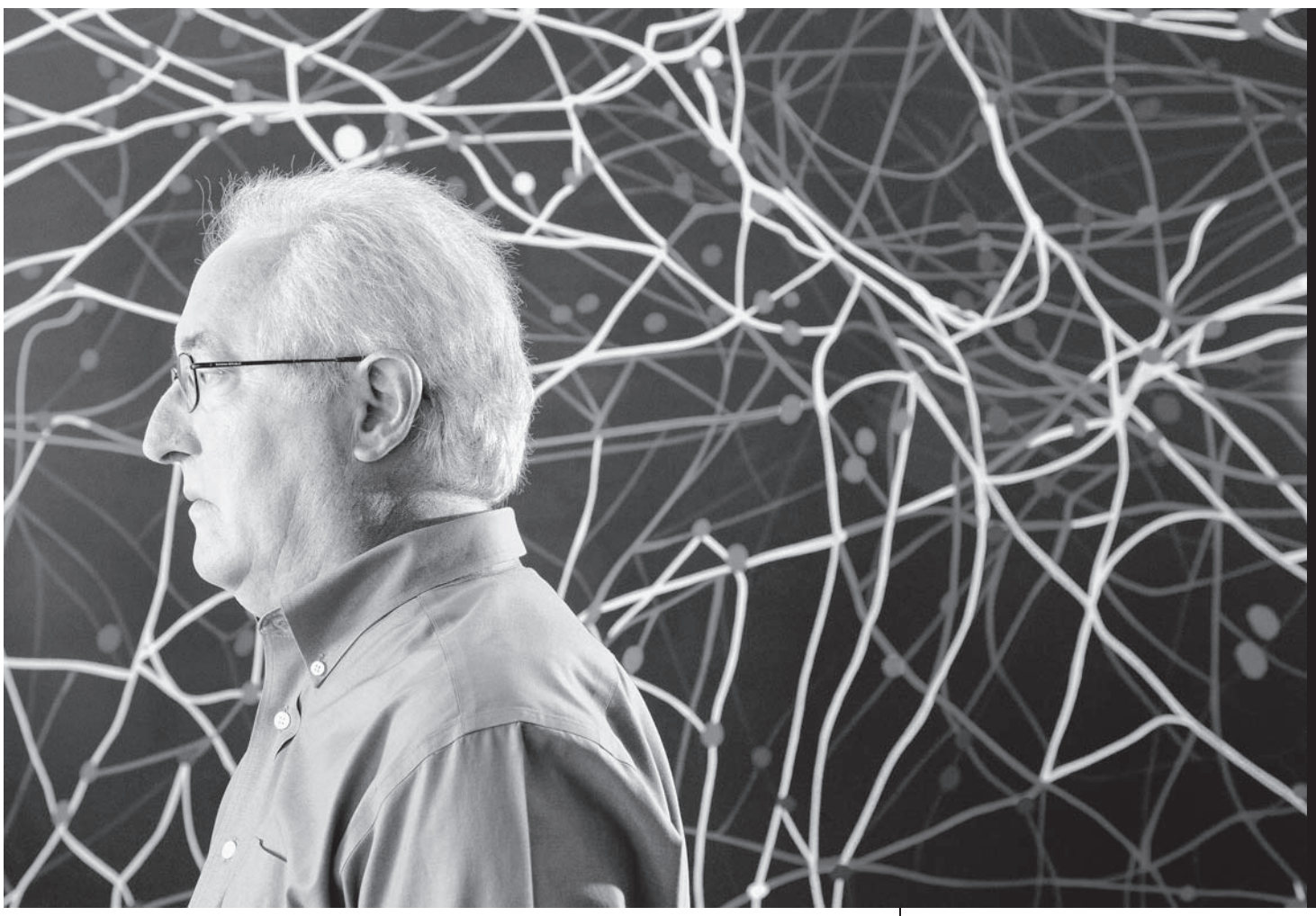
One of the medications, solanezumab, is being tested in people 65 or older who don't have any Alzheimer's symptoms — to see if it can prevent the disease from manifesting. More information is available at j.mp/soladcs.

"If you learn something new, you build up more synapses in the brain."

Dr. Mark Tuszynski, director of UC San Diego's Center for Neural Repair



EDUARDO CONTRERAS U-T

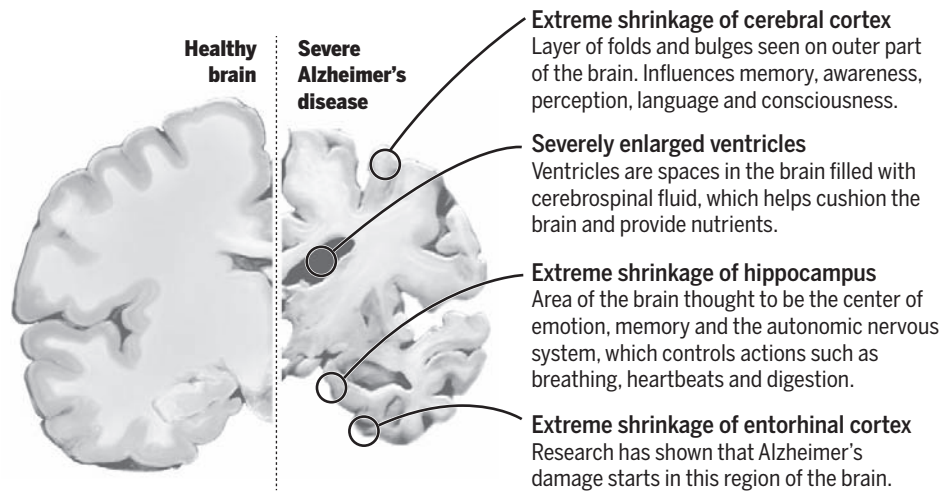


"There is hope that new approaches under way will result in new therapeutic interventions, but there is still a great deal about how brain cells fail in this disease that we don't understand"

Larry Goldstein Alzheimer's researcher and director of UC San Diego's stem cell program

EARNIE GRAFTON U-T

How Alzheimer's disease damages the brain



Source: U.S. Department of Health and Human Services; Image courtesy of the National Institute on Aging/National Institutes of Health

AARON STECKELBERG & AARON ATENCIO U-T

The theory is that Alzheimer's is the end stage of a long disease process, one that builds for many years before symptoms show up clearly.

More and more, scientists are exploring the concept that drugs and other therapies should be given earlier in life, before the mental damage becomes outwardly obvious.

The other protein, tau, is also believed to harm neurons when it becomes defective.

Abnormal tau seems to allow structures called microtubules to unravel. Microtubules help maintain the cytoskeleton, which in turn enables cells to move and keep their shape or change it.

New medications aimed at combating aberrant tau are entering clinical trials. Also, the U.S. Food and Drug Administration is considering whether to let researchers test whether certain medications previously approved for other diseases can block the destruction of defective tau.

At the earliest, it will likely take a few years to determine whether these drugs work well.

Another approach is to downplay theories of causation and look for compounds that demonstrate effectiveness in protecting the brain's functions.

One significant line of inquiry involves curcumin, which is found in a component of curry called turmeric. Research has shown that curcumin produces an anti-inflammatory effect, and brain inflammation is a major part of the Alzheimer's profile.

Working with that evidence, scientist Dave Schubert and his colleagues at the Salk Institute have developed a drug candidate that not only appears to protect against Alzheimer's in a mouse model, but also exerts a broader anti-aging effect.

Diagnosing the living

Before any disease can be treated, it must be diagnosed. And identifying Alzheimer's has long been difficult, at least in living patients.

The telltale toll of beta amyloid plaques and tau-related tangles were first discovered in an autopsy performed in 1906 by Aloysius "Alois" Alzheimer, the physician who gave his name to the disease.

Recently, the FDA approved a test to detect beta amyloid plaques in living people, and a similar test for tau is coming, said Huaxi Xu, a researcher at the Sanford Burnham Prebys Medical Discovery Institute in La Jolla.

The amyloid test uses a radioactive isotope that binds to beta amyloid, making it visible through a PET scan.

Other diagnostic tests are being developed to gain a finer read on the brain's condition, Xu said. This includes examination of the cerebrospinal fluid, which bathes the brain and provides various types of support to its cells.

Overall, it's now possible to screen people for signature evidence of Alzheimer's well before they show symptoms of the disease.

"I think that's one of the major breakthroughs," Xu said.

In September, he and his colleagues published a study indicating a possible mechanism for tau degeneration, the overabundance of a protein called appoptosin. Other tau-associated diseases include frontal temporal dementia and progressive supranuclear palsy, or PSP.

An assortment of factors, including those still to be identified, is probably responsible for the formation of Alzheimer's, Xu said. He envisions scientists coming up with more diagnostic tests and treatments to account for these other influences.

A comprehensive battery of tests and cocktails of drugs could be more effective than treating isolated dimensions of the disease.

New wave of drugs

UC San Diego's Larry Goldstein is both an Alzheimer's researcher and director of the university's stem cell program. He marries the two fields by studying the Alzheimer's process in neurons grown from artificial embryonic stem cells.

Cultured in the lab, these cells provide a "disease in a dish" model that allows scientists to examine the development of neurons with various risk factors for Alzheimer's disease. They also provide a new way for testing potential drugs.

With a particular kind of stem cell technology, researchers can take skin samples from Alzheimer's patients and turn them into brain cells. This approach gives them unprecedented insights into the pathology of the disease. (It's a violation of scientific ethics to open up a living person's brain to extract cell samples.)

Goldstein's lab is studying the brain cells of J. Craig Venter of La Jolla, the genetics and genomics pioneer, that were obtained using such stem cell technology. Venter learned years ago that he has a genetic risk factor for Alzheimer's, yet at 69 remains mentally unimpaired.

Analysis of Venter's brain cells has revealed how one of the known risk factors operates, Goldstein said. The lab has compared Venter's brain-cell sample with samples obtained from patients at the Shiley-Marcos Alzheimer's Disease Research Center in La Jolla.

"What we've also done is take his genome, and make changes in that genome, and study how they change the behavior of the cells and also screen for new drugs," Goldstein said.

Testing with such cells, from a defined genetic background, gets rid of a lot of the "noise" in data from people with divergent genetic backgrounds, he said. This helps researchers trace the complicated molecular pathways that gene variants regulate.

Ultimately, Goldstein said, "There is hope that new approaches underway will result in new therapeutic interventions, but there is still a great deal about how brain cells fail in this disease that we don't understand and must understand before we can implement therapies that significantly alter the course of the disease. I remain hopeful but sobered by the difficulty of the problem."

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Resources

Alzheimer's Association, San Diego-Imperial chapter: alz.org/sandiego or (800) 272-3900

Alzheimer's San Diego: alzsd.org or (858) 492-4400

U.S. Department of Health and Human Services: alzheimers.gov

National Institute on Aging: overview fact sheet about Alzheimer's disease at 1.usa.gov/1IoRcXo or (800) 438-4380

Alzheimer's Foundation of America: alzfdn.org or (866) 232-8484

Alzheimer's Forum: alzforum.org

San Diego Elder Care Center: sandiegoelderlaw-.com or (619) 235-4357

Elder Law & Advocacy: seniorlaw-sd.org or (858) 565-1392

Southern Caregiver Resource Center: caregivercenter.org or (858) 268-4432

Facts about Alzheimer's

Alzheimer's is a neurodegenerative illness that causes physical and mental symptoms. Physically, neurons are gradually damaged and then die. The damage is associated with tangled protein deposits called amyloid beta and another protein called tau, although other factors are likely involved. When these proteins become defective, they harm neurons.

With this destruction, the brain begins to shrink. The changes are visible through imaging technology or with an autopsy.

Alzheimer's disease starts decades before symptoms emerge, according to a growing body of evidence. This means prevention and treatment efforts may have to start well before symptoms arise in order to be effective.

Symptoms appear slowly. In the early stages, progressive loss of short-term memory begins to interfere with daily life. Routine tasks, such as driving to a familiar location, become more difficult. As the disease progresses, long-term memory fails. Patients struggle to find desired words and carry on conversations. They forget important events in their lives, and even people well-known to them become strangers. Their moods may change and fluctuate; depression, social withdrawal, suspicion and hostility sometimes emerge.

Unintentional mistreatment often makes the condition worse. Alzheimer's care centers may have their residents follow a set daily regimen, such as adhering to specific waking and sleeping hours, eating a certain range of foods and engaging in programmed activities. These could take away the patients' remaining sense of independence. Experts say sedation is needed in some cases, but only as a last resort.

The risk of Alzheimer's goes up with age, but the relationship is imperfect. The disease can strike in middle age or even earlier. Conversely, many people in their 80s or even 90s retain clear minds. Other forms of dementia appear more often with age.

Genetics can influence the risk of Alzheimer's. There is one extremely rare form of the disease that's clearly linked to genetics: People with this genetic variant are virtually certain to develop Alzheimer's. It's unclear how pertinent this form is in studying the far more common "sporadic" Alzheimer's, in which genes appear to play a lesser role.

Of the 10 leading causes of death in the United States, Alzheimer's disease is the only one that has neither a cure nor an effective treatment.

No medication or other therapy currently available can reverse or even stop the progression of Alzheimer's. Some drugs provide temporary benefits, but the neurodegeneration underlying the disease continues. Numerous attempts to develop Alzheimer's drugs to fight amyloid buildup have failed.

BRADLEY J. FIKES

Alzheimer's care centers may have their residents follow a set daily regimen, such as specific waking and sleeping hours, eating certain foods and engaging in regular activities.

NELVIN C. CEPEDA U-T