

THE BOSTON GLOBE TUESDAY, MARCH 29, 2005

Mind mystery

Alzheimer's disease appears to have multiple causes, and scientists are slowly unraveling them

By Alice Dembner
GLOBE STAFF

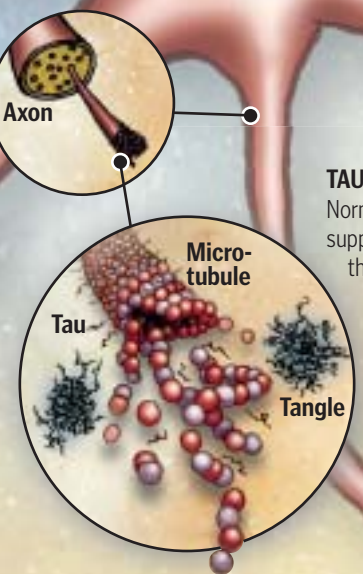
A century after Alois Alzheimer identified the debilitating dementia that carries his name, scientists are still trying to determine what causes the disease in old age. Their quest takes on increasing urgency, with predictions that unless a cure is found, the number of Americans with the disease will rise from about 4.5 million now to 13 million in 2050.

Many scientists believe that Alzheimer's results from a complex interplay of environmental factors, lifestyle choices, and genes and proteins gone haywire. But the changes in the brain that characterize the disease develop over decades and also occur in some healthy seniors, making it difficult to sort out the culprits from the bystanders.

Yet, tantalizing tidbits have surfaced in the last few weeks, including discovery of a new genetic mutation that appears to increase the risk of getting Alzheimer's and new evidence that insulin deficiencies may contribute to deterioration of the brain.

"The pieces are coming together. We've got the outline of the puzzle in place, and we're beginning to see the form," said Stephen Snyder, who oversees research on the causes of Alzheimer's for the National Institute on Aging. "It's probably five or six genes and a dozen proteins that get out of kilter," said Snyder,

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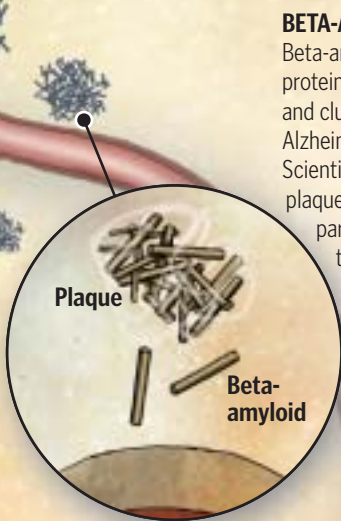
TAU TANGLES

Normally, the tau protein supports tubes inside neurons that allow movement of nerve impulses. In Alzheimer's, the tau forms tangles and the tubes collapse.

The triggers of Alzheimer's



Alzheimer's disrupts brain cells (neurons) and causes them to die. For years, scientists have targeted large clumps of two defective proteins, tau and beta-amyloid, as the likely villains. But evidence is growing for genetic causes and for other factors, such as insulin abnormalities, inflammation, stroke and other cardiovascular risks, and environmental toxins.

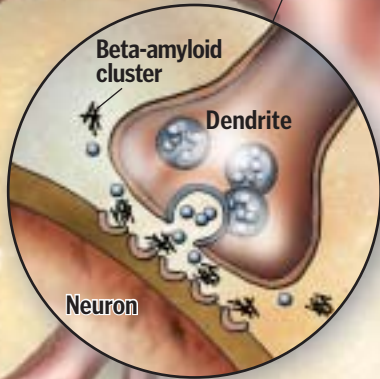


BETA-AMYLOID PLAQUES

Beta-amyloid, a common protein, becomes deformed and clumps into plaques in Alzheimer's patients. Scientists argue over whether plaques kill neurons or are part of the body's attempt to fight off Alzheimer's.

BETA-AMYLOID CLUSTERS

Sometimes beta-amyloid clumps into small clusters rather than large plaques. These clusters may enter the synaptic gap and block the chemicals that neurons use to send brain signals.



SOURCES: Alzheimer's Disease Education & Referral Center; Nature magazine
GLOBE STAFF GRAPHIC/CHRIS KIRKMAN

Engage in healthy behavior

Some everyday actions may help reduce the risk of Alzheimer's



Stay mentally active

Learn a new skill, read, do crossword puzzles. One study found that older people who engage in mentally stimulating activities were 47 percent less likely to get the disease.



Be social

Visit with friends, join a club, stay in touch with family. One study found those who were socially isolated had a 60 percent greater risk of Alzheimer's.



Stay physically active

Exercise or walk at least 30 minutes a day. One study found that sedentary men were twice as likely to develop Alzheimer's as those who walked two miles per day.



Avoid brain trauma

Wear a helmet when riding a bicycle. Use seat belts. The risk of Alzheimer's increases significantly for those who have suffered severe brain injuries.



Eat right, control your weight, avoid diabetes

Choose low-fat, low-cholesterol foods. Eat lots of fruits and vegetables, which contain anti-oxidants. One study linked diabetes with a 65 percent greater risk of developing Alzheimer's. Another found that women who were significantly overweight at age 70 dramatically increased their risk of getting dementia.



Control your blood pressure, avoid heart disease

Don't smoke. Use diet, exercise or antihypertension drugs to keep blood pressure under control. One study found that those who suffered a stroke were 60 percent more likely to get Alzheimer's, a risk that appears to be connected to underlying vascular disease.

For more information: Contact the Alzheimer's Association, www.alz.org, or 800-548-2111

DR. DARSHAK SANGHAVI Pediatric Perspective

Bleary parents crave colic cure

It's every parents' dread, and the trigger of many instances of abuse and even death at the hands of stressed care givers — a baby who won't stop crying. Yet colic, despite intensive research, continues to baffle doctors today just as it did a century ago, when the Russian writer and physician Anton Chekhov wrote in his 1906 story, "Sleepy-Eye," about a nanny who murders a colicky baby.

In the absence of any genuinely useful treatments, parents and pediatricians resort to a variety of unproven ones. In many ways, this hints at a larger issue in medicine: How do families and doctors cope with untreatable conditions? Interestingly, the lack of any one effective therapy leads us to create an entire folklore.

On average, normal newborns cry between one and three hours a day. This behavior is universal. Among the Kalahari !Kung, a hunter-gatherer tribe

PEDIATRIC PERSPECTIVE, Page E2



Discoveries

Arabidopsis plant (left) cures itself of genetic disorders. **E3**

Meeting the Minds

Sleep expert says he's been misunderstood. **E2**

Calendar

Researchers find T. Rex bones with marrow inside. **E4**

Music stirred her damaged brain

By Dr. S. Allen Counter

Judging normal brain function in a neurologically impaired person is never an easy task. The case of Terri Schiavo illustrates this challenge in a dramatic way.

A Boston-area patient I first saw when she was 32 also proved the point. The woman had been born without the portions of her brain associated with thought and awareness — a condition called hydranencephaly that's usually fatal prenatally or in infancy. But she had somehow survived, mainly through good custodial care, including being fed pureed foods by a caretaker all of her life. Her eyes were open wide, and she could move her head from side to side, and make groaning sounds, similar to Terri Schiavo. A quadriplegic, the woman was bed-ridden or strapped to a wheelchair for several hours each day. She weighed 77 pounds and was 4½ feet tall. She could swallow and breathe on her own.

The neurological evaluation revealed that the woman failed to blink in response to objects rapidly approaching her eye, indicating blindness; she had abnormal reflexes, and no clear sensitivity to touch. A bright light shone on one

side of her slightly enlarged head revealed a bright red fluid-filled cranium. A subsequent MRI revealed the absence of cerebral hemispheres, with only small remnants of cerebral tissue, and a small brain stem.

The conclusion by the attending doctors was that this woman was unresponsive to sensory stimuli, devoid of any intellectual function, and in a persistent vegetative state.

To confirm these conclusions, she was referred to me for an objective, noninvasive evaluation of her brain's electrical activity and her response to sensory stimulation, including sound, sight and touch. In summary, I found that, although her eyes were open and moving from side to side with her head, there was no brain response to visual input. Similarly, mild electrical stimulation in the fingers and toes traveled up the spinal cord to the brain stem, but no farther in the absence of the cerebral hemispheres.

I was astounded, however, that when I turned on a child's music box in the room, I observed that this hydranencephalic patient turned toward the musical device and began to smile and make sounds, as if she were enjoying

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