

Solving the Alzheimer's PUZZLE

▶ What we know, what we don't know, and where the promise lies. BY Katherine Hobson

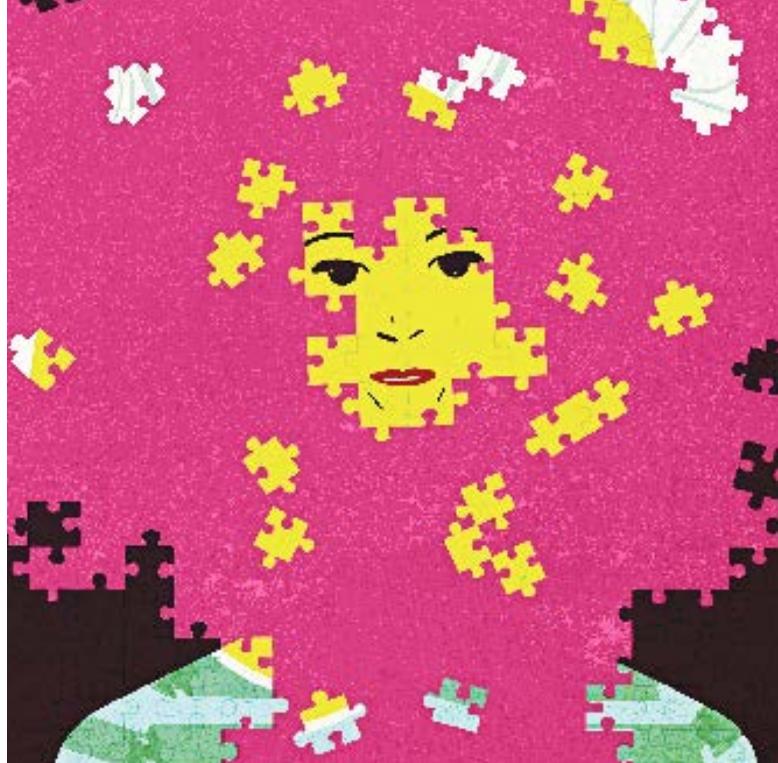


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OUR BRAINS AT RISK

An estimated
5.5 million
Americans have
Alzheimer's
disease, about
5.3 million
of them age 65
and older.

MANY PEOPLE THINK Alzheimer's equals dementia equals senility—and that all three are just another way of saying “She’s getting old.” In fact, *senility* is an outdated word for *dementia*, which is a catch-all term referring to a cognitive decline that involves life-disrupting changes to thinking, memory, reasoning, and, in many cases, personality. And Alzheimer's disease is the most common form of dementia. It can be devastating for patients and their families, but it's important to realize that dementia is not a normal part of aging. Other key facts to keep in mind:

While no one knows exactly what causes Alzheimer's, we're getting better at identifying what contributes to it.

Alzheimer's is distinguished from other kinds of dementia by the presence of two proteins in the brain: beta-amyloid, which forms clumps called plaques, and tau, which forms tangles. Experts have yet to nail down the origins of these proteins, but genetics and age-related brain changes likely play a role. Inflammation, insulin resistance, diabetes, vascular problems, and high cholesterol may also increase the risk of developing the disease, says Ronald Petersen, MD, PhD, director of the Mayo Clinic Alzheimer's Disease Research Center.

One gender is more affected...

Women account for nearly two-thirds of those who have Alzheimer's (of people age 71 and older, 16 percent of women have Alzheimer's or other dementias, compared with 11 percent of men). Researchers are finally taking steps to find out why: The Cure Alzheimer's Fund now requires investigators to use female mice as well as males in the lab. Scientists are currently exploring the role of sex chromosomes and the impact of hormones on the brain at menopause, factors that may change women's risk or resilience. There's evidence that the disease develops and progresses differently in the sexes; for example, studies suggest that women may be more vulnerable to the risk gene APOE4. The bottom line: “Women suffer disproportionately in terms of pure numbers, and we need to understand how sex biology contributes,” says Dena Dubal, MD, PhD, assistant professor of neurology at the University of California, San Francisco.

...but there's no way to tell for sure who will develop the disease.

Some people don't appear to be affected by plaques and tangles—their presence is revealed only after an autopsy, says Dubal. And not everyone with APOE4 gets Alzheimer's (the gene is found in roughly 20 to 25 percent of people; having one copy can increase the risk of getting the disease by two to three times, while two copies can increase the risk twelvefold). The best advice for all of us is to mind our brain health (see page 74).

Drugs aren't yet cures, but they can help.

Nearly all clinical trials of drugs targeting beta-amyloid or tau have failed. One hypothesis: A drug might need to be given before lasting harm is done to the brain or at least at the earliest stage of symptoms, says Rudolph Tanzi, PhD, vice-chair of neurology at Massachusetts General Hospital and part of a team researching this. He's also investigating whether drugs that control inflammation could be a better strategy for some advanced cases. And as with heart disease, HIV, and cancer, drug combinations may be the way of the future. In the meantime, says Tanzi, medication can produce small, temporary improvements in memory, lucidity, and mood.