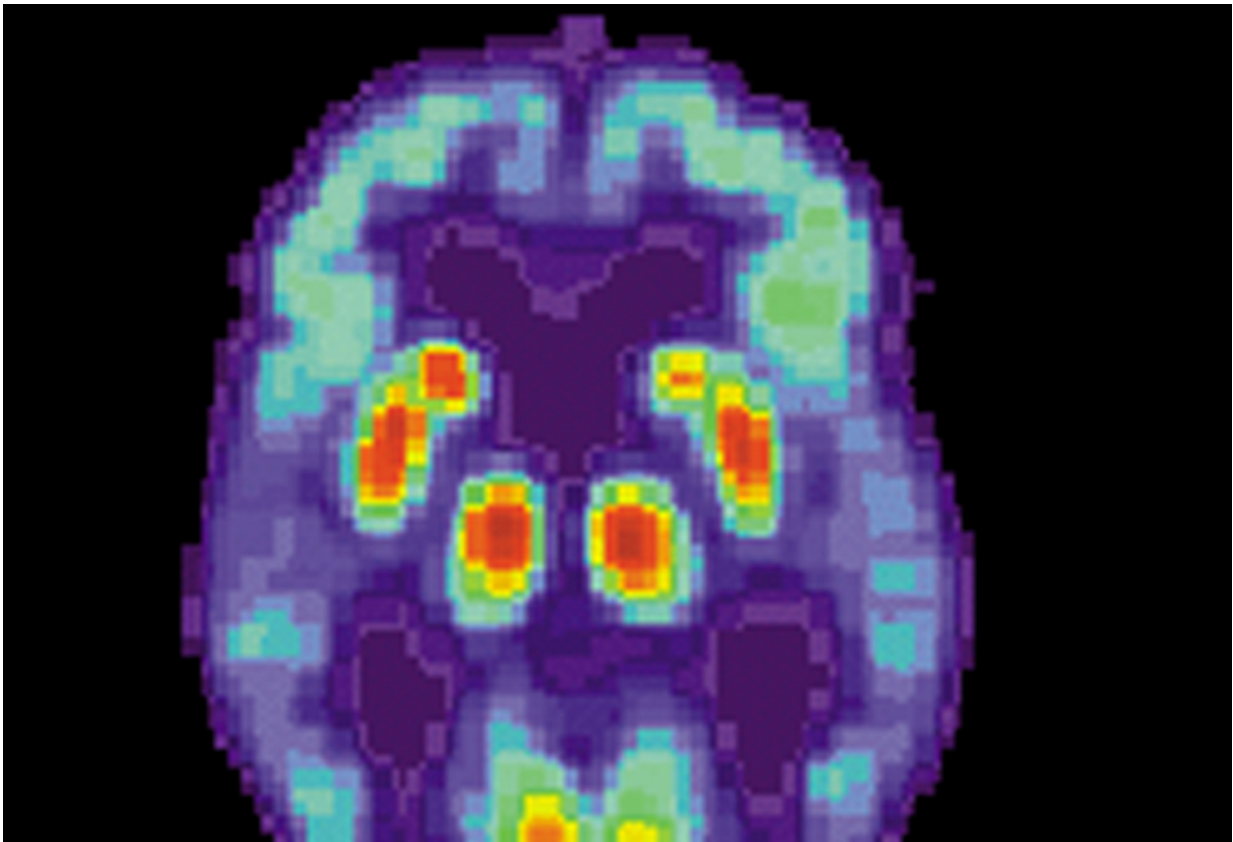


So my brain amyloid level is 'elevated'—What does that mean?

October 23 2017



PET scan of a human brain with Alzheimer's disease. Credit: public domain

Testing drugs to prevent or delay the onset of Alzheimer's dementia and using them in the clinic will mean identifying and informing adults who have a higher risk of Alzheimer's but are still cognitively normal. A new

study from the Perelman School of Medicine at the University of Pennsylvania has shed light on how seniors cope with such information.

The study examined cognitively normal adults 65 years and older who had been accepted into a large Alzheimer's prevention trial based on brain scans showing an "elevated" level of beta amyloid protein plaques. Beta Amyloid plaques are one of the biomarkers of Alzheimer's-disease. The Penn Medicine researchers found that for many of these seniors, being told that their amyloid levels were "elevated" on brain scans led to frustration and a desire for more detailed information.

"Clinicians who give these results to people should be prepared to explain how and why measurements of amyloid are termed 'elevated' and what that means in terms of Alzheimer's [dementia](#) risk," said Jason Karlawish, MD, a professor of Medicine, Medical Ethics and Health Policy, and Neurology, and co-director of the Penn Memory Center.

The study, published on October 23, 2017 in *JAMA Neurology*, comes as Alzheimer's researchers and the pharmaceutical industry have begun to think more in terms of preventing dementia than in trying to treat after it has been diagnosed. To date, every candidate drug tested in large-scale clinical trials in patients with Alzheimer's dementia has failed to show a significant effect in slowing the usual 5-10 year course of this fatal illness.

Developing a preventive therapy is challenging for a number of reasons, not least because it entails the ethically challenging task of testing potentially risky drugs on people who are cognitively normal. Research over the past two decades has found, however, that certain types of brain scan as well as blood and spinal fluid tests can sort people into categories of higher or lower risk of developing Alzheimer's dementia.

For example, positron emission tomography (PET) using a radiotracer

that sticks specifically to Alzheimer's-associated amyloid plaques can measure the extent of [amyloid plaques](#) in the brain. Having no plaques means having essentially no near-term risk of Alzheimer's dementia. Most elderly people will have some amyloid plaque burden, and although that doesn't make Alzheimer's dementia a certainty in a normal lifespan, plaque loads beyond a certain threshold have been linked to a higher risk of this illness.

The most prominent Alzheimer's prevention trial now underway, the NIH-sponsored A4 trial, has enrolled seniors based on the PET finding elevated amyloid. Karlawish and colleagues sought to determine how these seemingly healthy seniors handled the information that they had elevated brain amyloid.

The researchers interviewed 50 seniors (ages 65-85) who had enrolled into the A4 trial. They found that about half had expected their amyloid PET scan result, based on a family history of Alzheimer's or a recent experience with memory problems. Most understood the basic facts provided by the A4 trial clinicians, namely that their brain amyloid levels were elevated, indicating a higher but not certain risk of developing Alzheimer's dementia. A smaller percentage appeared to believe mistakenly that they either had no increased risk of dementia or had 100 percent risk—even "early Alzheimer's."

A large minority of the subjects (20 of the 50) were dissatisfied with the ambiguity of the message that their brain amyloid level was "elevated." One 71-year old woman commented, accurately enough: "I don't know how elevated the risk is. It could be like right over the edge, and other people are right under the edge." Similarly a 75-year old man complained that he found the uncertainty frustrating: "my background is in a technical area, and I'm used to having facts and data."

"What this is telling us is that, in the future, Alzheimer's biomarkers will

have to get more predictive, or we'll simply have to educate people to cope with the uncertainty," Karlawish said.

He emphasized that for now, disclosing amyloid PET result to cognitively normal adults is something that occurs only in experimental contexts such as the A4 trial. Amyloid PET scans are available for people who already have cognitive problems, to help distinguish Alzheimer's from other forms of dementia.

Alzheimer's researchers hope, however, that trials such as the A4 trial, which is testing an anti-amyloid drug, will lead eventually to preventive therapies to cognitively normal adults, particularly those considered to have high Alzheimer's risk based on PET [amyloid](#) levels and other biomarkers.

"In the future, learning this kind of information will be a normal part of going to the doctor, like finding out you have a high cholesterol level," Karlawish said. "The challenge is to anticipate what it will be like for seniors to learn this, and to develop effective strategies to help them cope with problems that may result, such as being stigmatized socially or losing their usual sense of well-being."

Provided by Perelman School of Medicine at the University of Pennsylvania

Citation: So my brain amyloid level is 'elevated'—What does that mean? (2017, October 23) retrieved 28 April 2024 from

<https://medicalxpress.com/news/2017-10-brain-amyloid-elevatedwhat.html>

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