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Alzheimer disease

Which test is best?

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In their article, "Imaging markers for Alzheimer disease: Which vs how," Dr. Frisoni and his colleagues looked carefully at the ways in which doctors evaluate Alzheimer disease (AD) and another problem with cognition called mild cognitive impairment (MCI).[1] Their question was simple: What test is most helpful when evaluating a person with cognitive problems? Their second question was: If there is more than one way to perform a test, which way is best?

HOW WAS THE STUDY DONE? Although a simple question, finding the answer is very complex. In order to do this, a team of doctors from around the world (Italy, France, the Netherlands, Sweden, the United Kingdom, Australia, Canada, and the United States) carefully assessed medical articles that were published on this subject between 1989 and 2012. They reviewed any article that discussed AD or MCI, and focused on articles in which diagnostic testing was assessed.

As they reviewed these articles, they realized that comparing one to the other was going to be a challenge. Not all of the tests were assessed the same way. To make the evaluations more "even," they used an analysis called the *likelihood ratio* (*LR*) to compare the results.

WHAT WERE THE RESULTS? They found that the kind of test and how the test was performed both affect how well the test works. This was true both for AD as well as MCI. However, there were some differences.

In general, tests that were used for diagnosis were more consistent than those that were used for prognosis. In other words, if the person had AD, the tests were helpful in making the diagnosis (i.e., diagnostic). If a person had MCI, the tests did not always predict that the person would develop AD (not as good at prognosis). There are a number of factors that could account for this difference. One of them is that the cognitive symptoms in MCI are much milder.

Of these tests, amyloid imaging seemed to be better than most other tests. Amyloid is a protein that builds up in the brains of people with AD. The amyloid protein can be measured. When performed, this test can be very helpful in making the diagnosis of AD.

Interestingly, MRI was one of the tests that was least "helpful." In people with AD, the *mesial temporal lobe*, a deep part of the temporal lobe, is often smaller than in healthy unaffected people. This can be measured with MRI. However, when Dr. Frisoni evaluated MRI, he found that the MRI change in the mesial temporal region was not very specific for AD. Part of the reason for this is that unaffected people can sometimes have the same finding on their MRI. In other words, this finding has been seen in people with AD as well as in people with no cognitive impairment.

In addition, Dr. Frisoni discovered that some of the tests varied a great deal. In some studies, the test looked like it was "good." In other studies, the test did not fare as well. The one test that stood out the most in this regard was the positron emission tomogram (PET = 18F-FDG PET). PET scans are read by radiologists. One factor that may have contributed to the variability is the difference in how each radiologist read the study.

WHAT DOES THIS STUDY TELL US? Dr. Frisoni and his colleagues were careful to point out that their study does not tell doctors which studies to perform in MCI or AD. Furthermore, their study does not tell doctors which tests work "best." Instead, he points out a very important fact about medical testing. The results often depend on how the test is performed and interpreted. What his study suggests is that there should be specific "rules" about how to perform tests. If everyone agrees to these rules, and performs that test in the same way, the test itself may become more specific and therefore more "helpful." In other words, the tests need to be standardized. In addition, more research in this area is needed.

REFERENCE

1. Frisoni GB, Bocchetta M, Chételat G, et al. Imaging markers for Alzheimer disease: which vs how. Neurology 2013;81: 487–500.

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About Alzheimer disease

WHAT IS ALZHEIMER DISEASE? Alzheimer disease (AD) is a neurologic disease that affects the brain. A gradual loss of memory is one of the main symptoms that a person experiences. However, memory problems are not the only issues that people with AD experience. They may also have problems with language and changes in behavior, mood, or personality. The loss of neurologic function usually occurs very gradually over a period of 5 to 20 years. At some point, if the disease becomes severe, a person with AD will need help with daily tasks such as eating, grooming, and proper hygiene. In other words, AD affects patients and the people around them.

About 4 million Americans have AD. It is estimated that more than 360,000 new cases occur each year. This number will probably increase as the population ages because aging itself is a major risk factor for the development of AD. AD is the fourth leading cause of death for adults. It kills more than 100,000 Americans each year.

To make the diagnosis of AD, a person needs to meet specific diagnostic criteria (see below). Generally, the diagnosis of AD is made when a person meets these criteria, and when the disease affects his or her ability to perform usual daily activities. However, before a person is impaired by the illness, he or she may experience very mild symptoms such as mild memory loss (without any other symptoms). The "in-between" stage is called mild cognitive impairment (MCI).

WHAT IS MILD COGNITIVE IMPAIRMENT? The Mayo Clinic defines mild cognitive impairment as "an intermediate stage between the expected cognitive decline of normal aging and the more serious decline of dementia [AD is one kind of dementia]. It can involve problems with memory, language, thinking and judgment that are greater than normal age-related changes." Having MCI increases the risk of developing a dementia like AD. However, having MCI does not automatically mean that a person will develop AD (or another kind of dementia). In fact, there are people who develop MCI that never go on to having a more serious illness.

WHY IS MILD COGNITIVE IMPAIRMENT IMPORTANT? Identifying mild cognitive problems allows a doctor to start treatment early. This may help to slow the progress of the disease. In the future, as newer treatments are available, doctors may be able to halt the illness (or hopefully reverse the damage). Medical testing often is needed to make the most accurate diagnosis. Many different medical tests are available. Which tests are the "best" still remains a question. In addition, how to perform these tests in the "best" possible way is something that needs better understanding. This was one of the reasons that Dr. Frisoni and his colleagues performed this study.

WHAT ARE THE SYMPTOMS OF ALZHEIMER DISEASE? Loss of recent memories (also called short-term memory) is usually the earliest warning. For instance, the person will repeat stories in the same conversation. They may forget the details of the previous day; for instance, they may not recall what they had for lunch. Other features include:

- Misplacing belongings
- Difficulty doing familiar tasks
- Increasing confusion and disorientation to time and place
- Trouble finding the right words, not following conversations
- Changes in mood or behavior
- Changes in personality
- Poor or impaired judgment
- Loss of initiative (no "get-up-and-go")

Because AD is so gradual, in its early stages, many people fail to recognize that something is wrong. They may assume that such behavior is a normal part of getting older. We often say to one another, "Oh, I am just having a senior moment" when we lose our train of thought. At some point, the person's family may suspect something is wrong. Although forgetting things is common, if it continues to worsen, it may be a sign of a more serious problem. The key to treatment is early diagnosis. It is critical to see a doctor when you recognize or suspect AD symptoms.

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HOW IS ALZHEIMER DISEASE DIAGNOSED? When AD is suspected, it is important to have a complete medical and neurologic workup. The purpose of this evaluation is to uncover other causes of dementia that must be treated in very specific ways. This may include:

- A complete health history and physical examination
- Screening for depression
- Neurologic and mental status testing
- Blood and urine tests
- Computerized tomography scan (CAT) or magnetic resonance imaging (MRI)
- Positron emission testing (PET)
- Single photon emission computed tomography (SPECT)

WHAT CAUSES ALZHEIMER DISEASE? The cause of AD is not fully known. It is not contagious. Although genetic forms have been identified, the most common form of AD does not run in families. Aging and inherited or genetic factors seem to play an important role.

WHAT ARE THE TREATMENTS? Although there is currently no cure for AD, there are treatments that may help.

- Treat memory symptoms. The cognitive symptoms of AD should be treated as early as possible to slow the progression of the disease. Drugs called cholinesterase inhibitors may be considered in patients with mild to moderate disease. Vitamin E may also slow the progression, but should only be used if prescribed by the doctor.
- Treat behavioral problems. Suspiciousness, aggression, or resistance to care may be treated first by understanding what triggers these behaviors. Caregivers may learn how to change things in the environment to improve cooperation. Some examples include providing low lighting and music to improve eating behaviors, taking regular walks, scheduling toileting, and following consistent routines. Certain medications may also help, including drugs to treat depression.
- Caregivers need caring too. Caregiver training programs to learn more about the disease and how to manage it help delay the time to nursing home placement. Support systems (adult day care, computer support networks, telephone support programs, and other respite programs) may also help.

PREVENTION Although there is no known way to prevent AD, researchers believe there are several things that will help keep your brain healthy:

- Avoid harmful substances—excessive drinking and drug abuse are thought to damage brain cells.
- Challenge yourself—read frequently, do crossword puzzles. Keep mentally active. Learn new skills. This strengthens the brain connections and promotes new ones.
- Exercise regularly—even low- to moderate-level activity such as walking or gardening 3 to 5 times per week can make you feel better.
- Stay socially active—family, friends, church, and a sense of community may all contribute to better brain health.

CAREGIVER HEALTH Families and friends can help by recognizing that AD affects not only the patient, but also the primary caregiver. To take the best care of the patient with AD, the primary caregiver must take care of himself or herself. Primary caregivers should be encouraged to learn more about the disease, avoid isolation, and seek support from family, friends, and professionals. Do not be afraid to ask your doctor questions!

FOR MORE INFORMATION

AAN Patients and Caregivers site
http://patients.aan.com/go/home

Alzheimer's Disease Education and Referral Center (ADEAR)
http://www.nia.nih.gov/alzheimers

National Institute of Mental Health (NIMH)
http://www.nimh.nih.gov

Alzheimer's Association
http://www.alz.org

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