

## DIAGNOSING DEMENTIA

■ Researchers say new blood tests to screen for Alzheimer's and other forms of dementia are showing considerable promise

By **Marilynn Marchione**  
Associated Press

LOS ANGELES — Scientists are closing in on a long-sought goal — a blood test to screen people for possible signs of Alzheimer's disease and other forms of dementia.

On Monday at the Alzheimer's Association International Conference, half a dozen research groups gave new results on various experimental tests, including one that seems 88% accurate at indicating Alzheimer's risk.

Doctors are hoping for something to use during routine exams, where most dementia symptoms are evaluated, to gauge who needs more extensive testing. Current tools such as brain scans and spinal fluid tests are too expensive or impractical for regular checkups.

"We need something quicker and dirtier. It doesn't have to be perfect" to be useful for screening, said Maria

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— **Dr. Richard Hodess**,  
director, National Institute on Aging

Carrillo, the Alzheimer's Association's chief science officer.

Dr. Richard Hodess, director of the National Institute on Aging, called the new results "very promising" and said blood tests soon will be used to choose and monitor people for federally funded studies, though it will take a little longer to establish their value in routine medical care.

"In the past year we've seen a dramatic acceleration in progress" on these tests, he said. "This has happened at a pace that is far faster than any of us would have expected."

It can't come too soon for patients like Tom Doyle, a 66-year-old former university

professor from Chicago who has had two spinal fluid tests since developing memory problems four years ago. First he was told he didn't have Alzheimer's, then that he did. He ultimately was diagnosed with different problems — Lewy body dementia with Parkinson's.

"They probably could have diagnosed me years ago accurately if they had had a blood test," said Doyle, who represents patients on the Alzheimer's Association's board.

About 50 million people worldwide have dementia, and Alzheimer's is the most common form. There is no cure; current medicines just temporarily ease symptoms. Dozens of hoped-for treatments have failed. Doctors think studies may have enrolled people after too much brain damage had occurred and included too many people with problems



Teresa Crawford / Associated Press

Dr. Jori Fleisher, a neurologist, examines Thomas Doyle, 66, at the Rush University Medical Center in Chicago. Doyle, 66, hopes blood tests may someday replace the invasive diagnostic testing he endured to be diagnosed 4.5 years ago with Lewy body dementia.

other than Alzheimer's.

A blood test — rather than subjective estimates of thinking skills — could get the right people into studies sooner.

One of the experimental blood tests measures abnormal versions of the protein that forms the plaques in the brain that are the hallmark of Alzheimer's. Last year, Japanese researchers published a study of it and Monday they gave results from validation testing on 201 people with Alzheimer's, other types of dementia, mild impairment or no symptoms.

The blood test results closely matched those from the top tests used now — three types of brain scans and a mental assessment

exam, said Dr. Akinori Nakamura of the National Center for Geriatrics and Gerontology in Obu, Japan. The test correctly identified 92% of people who had Alzheimer's and correctly ruled out 85% who did not have it, for an overall accuracy of 88%.

Shimadzu Corp. has rights to the test and is working to commercialize it, Nakamura said.

Another experimental test looks at neurofilament light, a protein that's a marker of nerve damage. Abdul Hye of King's College London gave results of a study comparing blood levels of it in 2,300 people with various neurological conditions — Alzheimer's, other dementias, Parkinson's, depression, multiple sclerosis, Lou Geh-

rig's disease — plus healthy people for comparison.

Levels were significantly higher in eight conditions, and only 2% of healthy folks were above a threshold they set for raising concern. The test doesn't reveal which disorder someone has, but it may help rule one out.

Dr. Randall Bateman of Washington University School of Medicine in St. Louis estimates a screening test could be as close as three years away.

What good will that do without a cure? An Associated Press-NORC Center for Public Affairs Research poll last year found that most Americans would want to know if they carried a gene tied to a disease even if it was incurable.

## Scientists study brains of addicts trying to quit opioids

By **Lauran Neergaard**  
Associated Press

BETHESDA, Md. — Lying inside a scanner, the patient watched as pictures appeared one by one: a bicycle, a cupcake, heroin. Outside, researchers tracked her brain's reactions to the surprise sight of the drug she'd fought to kick.

Government scientists are starting to peek into the brains of people caught in the nation's opioid epidemic to see if medicines proven to treat addiction, like methadone, do more than ease the cravings and withdrawal. Do they also heal a brain damaged by addiction? And which one works best for which patient?

They're fundamental questions considering that far too few of the 2 million opioid users who need anti-addiction medicine actually receive it.

One reason: "People say you're just changing one drug for another," said Dr. Nora Volkow, director of the National Institute on Drug Abuse, who is leading that first-of-its-kind study. "The brain responds differently to these medications than to heroin. It's not the same."

Science has made clear that three medicines — methadone, buprenorphine and extended-release naltrexone — can effectively treat what specialists prefer to call opioid use disorder. Patients who stick with methadone or buprenorphine in particular cut their chances of death in half, according to a report.

Opioid addiction changes the brain in ways that even when people quit can leave them vulnerable to relapse, changes that researchers believe lessen with long-term abstinence.

Volkow's theory: Medication-based treatment will help those damaged neural networks start getting back to normal faster than going it alone. To prove it, she'll need to compare brain scans

from study participants like the woman who quit heroin thanks to methadone with active heroin users and people who are in earlier stages of treatment.

"Can we completely recover? I do not know that," Volkow said. But with the medications, "you're creating stability" in the brain, she said. And that helps recondition it to respond to everyday pleasures again.

The challenge now is finding enough people willing, and healthy enough, to have their brains scanned for science at the same time they're struggling to quit.

Addiction is a brain disease, "not a choice, not a personality flaw, not a moral failing," said Dr. Jody Glance, an addiction specialist at the University of Pittsburgh Medical Center, who hopes the brain scans will help overcome some barriers and improve the public health response to the opioid crisis.

Not offering the medicines to someone who needs them "is like not offering insulin to someone with diabetes," she said.

**How opioids change the brain**

When you sense something pleasurable — a special song, the touch of a loved one, a food like Volkow's favorite chocolate — the brain releases a natural chemical called dopamine that essentially trains the body to remember, "I liked that, let's do it again."

That's the brain's reward system, and opioids can hijack it by triggering a surge of dopamine larger than nature ever could. Repeated opioid use overloads circuits in multiple brain regions, including those involved with learning and memory, emotion, judgment and self-control. At the same time, the brain gradually releases less dopamine in response to other things the person once found pleasurable. Eventually they seek more of

the drug not to get high, but to avoid constantly feeling low.

**Testing how addiction medicine helps**

Volkow aims to test 80 people, a mix of untreated heroin users and patients using different medication-based treatments, inside brain scanners at the National Institutes of Health's research hospital. Her team is measuring differences in the brain's ability to release dopamine as treatment progresses, and how the functioning of other neural networks changes.

For example, does a patient's brain remain fixated on "cues" related to drug use — like seeing a picture of heroin — or start reacting again to normal stimuli like the sight of a cupcake?

Another test: Ask if a patient would take an offer of \$50 now, or \$100 if they could wait a week, checking how much motivation and self-control they can muster.

"You need to be able to inhibit the urge to get something" to recover, Volkow noted. "We take for granted that people think about the future. Not when you're addicted."

Like in any disease, each medication may work better in certain people — because not everyone's brain circuitry reacts exactly the same way to opioid abuse — but that hasn't been studied.

Methadone and buprenorphine are weak opioids, the reason for the misperception that they substitute one addiction for another. They stimulate the dopamine sys-

tem more mildly than other opioids, leveling out the jolts so there's no high and less craving. People may use them for years. Naltrexone, in contrast, blocks any opioid effects.

**It's a tough sell**

Volkow's team has screened more than 400 people who expressed interest in the study, but have found only about three dozen potential

candidates who qualify, seven of whom have enrolled so far.

The main problem: Study participants must have no other health problem that might affect the brain's chemistry or functioning.

Volkow said it's worth the struggle to find such rare volunteers if before-and-after scans wind up showing truly different looking brains as people get treated.

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