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Predicting Alzheimer's—Decades in Advance

A study of college-age students may lead to early interventions.

By Michele Solis for MSN Health & Fitness

Our brains safeguard the past, storing memories as formative as the first day of school or as useless as the words to a John Denver song. Our brains guide us in the present as we weave our way through the day, making countless decisions: Right or left? Window or aisle? For here or to go?

But can our brains also hold signs of the future?

Maybe. According to a study published in April in the *Proceedings of the National Academy of Sciences*, the brains of people who are at a higher risk for developing Alzheimer's disease act differently from those without that risk. What's unsettling is that this difference can be detected *decades* before Alzheimer's typically develops.

Scientists already knew about unusual brain activation in older people whose DNA contains a version of a gene that increases their chances of Alzheimer's. But this new study, which looked at healthy college-aged students, shows that this gene version may alter the brain even earlier, long before any tell-tale memory loss or cognitive decline.

Though not a diagnosis of Alzheimer's, this brain activity may help doctors better estimate a person's chances of getting the disease, and eventually help them decide how to intervene before memories dwindle.

Different routes to memory?

The scientists studied young adults, some of whom had a version of a gene called APOE4. About 25 percent of people have APOE4 in their DNA, which at least triples their chance of developing Alzheimer's relative to those who don't have it. Using a brain scanner, Clare Mackay, Ph.D., a neuroscientist at the University of Oxford, and her team looked at the hippocampus, a seat of long-term memory in the brain and one of the first targets of Alzheimer's.

The study participants viewed different pictures—some new and some previously seen. As expected, the hippocampus was more activated by the new pictures than by the familiar ones, as though it was busily securing the new stuff into memory. However, that increase in activity was a substantial 30 percent greater in the group of people with APOE4 than in the group without it.

And yet, that heightened activity did not translate into different memory: Afterwards, both groups picked out the pictures seen in the scanner for the first time with the same degree of accuracy.

Activity in and of itself is not a bad thing; indeed, it is what makes our brains tick. But the extra activity in people with APOE4 suggests a brain in overdrive. In previous studies of older people, scientists have argued that heightened activity reflects extra mental effort. Somehow disadvantaged by APOE4, people have to think extra hard to get to the same answer.

But Mackay doesn't think this is the case in her study, because her subjects were so young, and because they had unusual activity even at rest. When we ruminate, daydream, or think of nothing at all, a constellation of brain regions hums with activity. This "default mode network" flickered on and off in people with APOE4 in a more synchronized way than expected. If compared to a crowd clapping, unlike an audience at the opera that claps randomly, the resting activity of people with APOE4 was whooping it up at the ballpark, bringing their hands together in unison.

Rather than having a brain that has to try harder, Mackay suggests something subtler is afoot in people with APOE4. "We think there is something different about how their brain is put together," she says. Constructed differently, an APOE4 brain may take a different route to get to the same answer.

Brain as crystal ball

Though it is unclear exactly how APOE4 tilts a brain toward developing Alzheimer's, it may interfere with how brain cells build connections with each other—a key process for forming memories. APOE4 could lead to different wiring diagrams in the brain, and the different activity patterns that Mackay found.

But this activity doesn't indicate anything more sinister than having APOE4 already does. Though APOE4 raises chances for Alzheimer's, it doesn't condemn a person to it. Nearly half the people with APOE4 do not get the disease.

What's not clear is whether the brain activity adds to the risk: Would the APOE4 carriers with the most activity in the hippocampus be the ones who go on to develop Alzheimer's decades later?

"That's the million-dollar question," says Mackay, and to answer it, she wants to track brain activity as people age. Although it's not feasible to do this over the course of a lifetime, Mackay says she might get a quicker answer by starting with people who are already showing mild signs of cognitive decline.

In the meantime, scientists are working to understand—and circumvent—the harmful effects of APOE4. So even if the brain does turn out to be a kind of crystal ball that can predict a future of Alzheimer's disease, science may soon figure out how to reverse this fate.

For more information on Alzheimer's, read the genetics fact sheet from the National Institutes of Health.

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After spending 15 years in the lab doing her own neuroscience research, Michele Solis is now putting her Ph.D. to work as a science writer. Her work covers a variety of topics including autism, linguistics, and animal communication. She contributes regularly to the Autism Speaks, Simons Foundation, and Crosscut Web sites.

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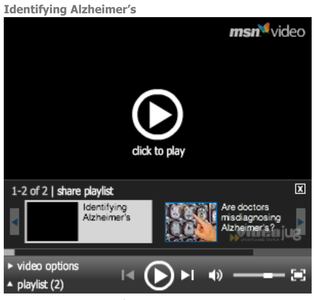

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