

How Exercise May Keep Alzheimer's at Bay

By GRETCHEN REYNOLDS

Alzheimer's disease, with its inexorable loss of memory and self, understandably alarms most of us. This is especially so since, at the moment, there are no cures for the condition and few promising drug treatments. But a cautiously encouraging new study from The Archives of Neurology suggests that for some people, a daily walk or jog could alter the risk of developing Alzheimer's or change the course of the disease if it begins.



For the experiment, researchers at Washington University in St. Louis recruited 201 adults, ages 45 to 88, who were part of a continuing study at the university's Knight Alzheimer's Disease Research Center. Some of the participants had a family history of Alzheimer's, but none, as the study began, showed clinical symptoms of the disease. They performed well on tests of

memory and thinking. "They were, as far as we could determine, cognitively normal," says Denise Head, an associate professor of psychology at Washington University who led the study.

The volunteers had not had their brains scanned, however, so the Washington University scientists began their experiment by using positron emission tomography, an advanced scanning technique, to look inside the volunteers' brains for signs of amyloid plaques, the deposits that are a hallmark of Alzheimer's. People with a lot of plaque tend to have more memory loss, though the relation is complex.

Next they genetically typed their volunteers for APOE, a gene involved in cholesterol metabolism. Everyone carries the APOE gene, but scientists have determined that those who have a particular variation of the gene known as e4 are at 15 times the risk of developing Alzheimer's compared with those who do not carry the variant. The report also noted that carriers tend to show symptoms of dementia at a younger age, beginning in their late 60s, on average, instead of in their early 80s for people without the variant.

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Fifty-six of the volunteers, of various ages and both sexes, turned out to be positive for APOE-e4. (A family history of Alzheimer's may suggest that someone is a carrier for the e4 variant, Dr. Head says, but it also may not; there are probably many other, still-unknown genetic causes of the disease, she says.)

Finally, the scientists asked the volunteers to fill out detailed questionnaires about their exercise habits during the past 10 years. Recently, many studies have looked at whether being active can lessen someone's risk for Alzheimer's, but the results have been inconsistent, with some studies, in both animals and people, suggesting that regular exercise has a protective effect and others finding little discernible benefit.

One reason for the inconsistency, Dr. Head suspected, might be that many earlier studies did not differentiate between people with the e4 variant and those without, and each group, at least potentially, could respond differently to exercise.

And that certainly proved to be the case in this study. For the group as a whole, exercise provided marginal benefits. The volunteers who reported walking or jogging often — meeting (or, in rare instances, exceeding) the American Heart Association's exercise recommendation of 30 minutes of moderate or vigorous activity five times a week — had fewer amyloid plaques than the volunteers who reported almost never exercising. But the preventive value of the exercise was small, barely reaching the level of statistical significance.

That situation changed, however, when the scientists examined the results for people with the e4 gene variant. Most of those who carried the APOE-e4 gene displayed much larger accumulations of amyloid plaques than those without it.

Unless they exercised. The carriers of the gene who reported walking or jogging for at least 30 minutes five times a week had plaque accumulation similar to that of volunteers who were e4-negative. In essence, the APOE-e4 gene carriers mitigated their inherited risk for developing Alzheimer's by working out. Or, as the study authors wrote, a “physically active lifestyle may allow e4 carriers to experience brain amyloid levels equivalent to e4-negative individuals.”

“The good news is that we found that activity levels, which are potentially modifiable, could have an impact” on plaque accumulation — and presumably on the course of Alzheimer's — in people with a genetic predisposition to the condition, Dr. Head says.

But the findings came with a downside, too. An overwhelming majority of the people in the study were sedentary, and for them, an inactive lifestyle seemed to be accelerating the accumulation of amyloid plaques. Those with the e4 variant who rarely or never

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exercised had the most plaques, putting them at heightened risk for the memory loss of Alzheimer's in the years to come.

At the moment, it's not known whether beginning to exercise after plaques have started to build up might alter that outcome, Dr. Head says. But, she continues, experiments in mice bred to develop memory loss "have shown that elderly animals that began a running program benefited." They experienced less dementia than mice that didn't run.

Still, countless questions remain about the interactions of exercise, genetics and Alzheimer's, including why the protective benefits of exercise in this study seemed substantial only for those with the gene variant. "It is looking as if there is some still-unexplained biochemical interplay between being e4-positive and inactive," Dr. Head says, "which heightens risk" for the disease.

"But that doesn't mean that everyone shouldn't exercise," she continues, regardless of whether they suspect they have a genetic risk for dementia. "There are so many benefits to exercise," she says, "and one may be that it helps the brain" to defend itself against the slow leaking away of memory.