Brain differences seen in young adults at genetic risk of Alzheimer's

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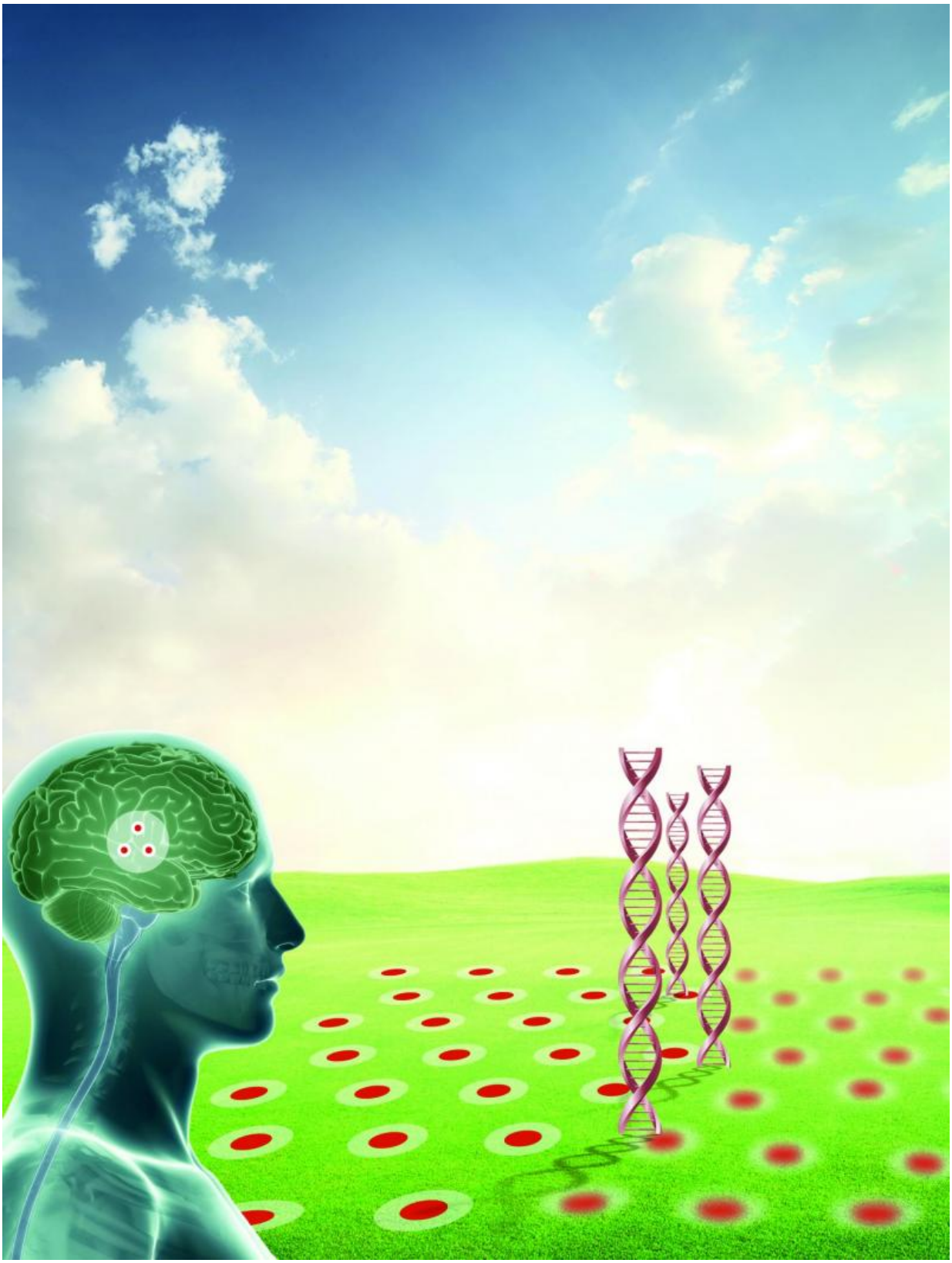

Genetic risk for Alzheimer's disease is linked to reduced grid-cell-like representations during virtual navigation. Credit: Created by bureaublauwgeel.nl, commissioned by doellerlab.com

(HealthDay)—Young adults who have an increased genetic risk for Alzheimer's disease may already show differences in how their brains handle spatial navigation, a small study suggests.

The researchers said it's too soon to know whether the brain differences are a harbinger of Alzheimer's.

"That is still unclear and needs to be investigated in further studies," said senior researcher Dr. Nikolai Axmacher, of the German Center for Neurodegenerative Diseases, in Bonn.

But the hope, he said, is that the findings will improve researchers' understanding of the earliest processes that lead to Alzheimer's—the most common form of dementia.

And if the brain differences do turn out to predict Alzheimer's disease years later, that information could be used to pinpoint high-risk people early, Axmacher added.

Other researchers said the findings were important, because everyone wants to find reliable biological signs that indicate a person has a high risk of Alzheimer's later in life.

The study, published in the Oct. 23 issue of *Science*, involved 75 young adults, half of whom carried a variant of the APOE gene that is believed to boost the risk of Alzheimer's.

It's estimated that one in six people carry the variant, known as APOE4, Axmacher said. They have a threefold greater risk of Alzheimer's than non-carriers do.

The researchers used an advanced form of MRI to study a brain area known as the entorhinal cortex, which contains so-called "grid cells." Those cells, Axmacher explained, are important in spatial navigation—one of the first skills to go awry when Alzheimer's begins.

The team tracked activity in those grid cells as study participants navigated a "virtual" task that gauged their spatial memory: They had to remember the spatial location of objects in a virtual arena, then place those objects in the correct place.

It turned out that, on average, the APOE4 carriers showed less functioning in their grid cells during the task, versus young adults who did not carry the gene variant.

Still, both groups performed similarly on the test.

That raised the question of whether APOE4 carriers tended to compensate by using other brain regions to navigate, the study authors noted.

"Indeed, we found that the less intact the grid cell system was, the more active an adjacent brain area, the hippocampus [was]," Axmacher said.

What's more, he added, the APOE4 carriers tended to show a different strategy during the test: Typically, they navigated from a vantage point along the border of the virtual arena, while non-carriers preferred to operate from the center.

Exactly what it all could mean is unclear. But, Axmacher said, other

research has hinted that excess activity in the hippocampus is part of the process that leads to Alzheimer's.

"These findings are interesting and exciting," said Dr. Luco Gilberto, a neurologist with North Shore-LIJ's Cushing Neuroscience Institute, in Manhasset, N.Y.

The results have to be confirmed in larger studies, Gilberto said. And longer-term work is needed to see whether the reduced grid cell function actually predicts Alzheimer's.

"Right now, we have no therapies that prevent Alzheimer's," Gilberto said. But if and when such treatments become available, doctors will need reliable ways to pinpoint high-risk individuals who could benefit.

Biological markers are also needed to find the best candidates for clinical trials testing experimental therapies, Gilberto said.

Dean Hartley, director of science initiatives for the Alzheimer's Association, agreed that the study results hint at a possible new biological marker.

He said the findings also offer more clues about the roots of Alzheimer's, which could help in developing new therapies.

"The field is trying to figure out, when does this disease process really begin?" Hartley said.

Researchers already know that abnormal proteins called "plaques" can be present in the brain 20 years before any symptoms of Alzheimer's arise, Hartley pointed out.

The latest findings, he said, add to evidence that the disease is a decades-

long "continuum."

More information: "Reduced grid-cell–like representations in adults at genetic risk for Alzheimer's disease," by L. Kunz et al. www.sciencemag.org/lookup/doi/ … 1126/science.aac8128