Carriers of Alzheimer's genetic marker have greater difficulty harnessing past knowledge

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Dr. Claude Alain, a senior author on the paper and senior scientist at Baycrest's Rotman Research Institute. Credit: Provided by Baycrest.

Adults carrying a gene associated with a higher risk of Alzheimer's disease had a harder time accessing recently acquired knowledge, even though they didn't show any symptoms of memory problems, according to findings published in a joint Baycrest-University of Oxford study.

Researchers found that older adults carrying a specific strain of the gene, apolipoprotein E4, otherwise known as APOE4, weren't able to tap into information they had just learned to assist them on a listening test.

These findings suggest greater difficulty for these individuals to access knowledge from their memory to guide their attention in ways that would have improved their performance, according to the study published in the journal *Scientific Reports*. This work could lead to the development of new ways to detect individuals at risk.

The research team worked with 60 research participants (aged 40 to 61) from the Oxford Biobank who had varying combinations of APOE genes—which includes one group of individuals with a combination of APOE3/APOE4 genes, one group of individuals with a set of APOE4 genes and one group of individuals with a set of APOE3 genes. All research participants had normal hearing, scored within the normal range of cognitive assessments and completed a questionnaire about their memory.

Each research participant listened to 92 audio clips and they were told to pay attention to where the clip was coming from, whether it was presented in the left, right or both ears. After the clip was played, they were asked which side they heard the sound from and if they responded incorrectly, the sound was replayed. Participants had a one-hour break before hearing the 92 audio clips again, but this time they were asked whether there was an additional sound at the end of the clip and to press a button when they heard it. Each clip was placed twice. During the first play-through, the clip's location was replayed and during the second play-

through, the additional tone was added.

The study found that no matter the APOE genotype, all older adults were able to learn the information and remember the location of the audio clip, but individuals with the APOE4 gene had greater difficulty in identifying the additional sound at the end of the clip.

"For some reason, people with the APOE4 gene were not able to take advantage of information they learned earlier, such as the expected location of the clip, to boost their performance," says Dr. Claude Alain, a senior author on the paper and senior scientist at Baycrest's Rotman Research Institute. "This study shows we have a test that is sensitive to capture problems or challenges faced by individuals with this gene, before their deficits are observed on a standard neuropsychological assessment."

This was an exciting study looking at healthy, middle-aged people who carry a gene that increases their risk of developing Alzheimer's disease by 15-fold, says Dr. Chris Butler, a senior author on the paper and an associate professor in clinical neurosciences at the University of Oxford.

"The research could lead to more sensitive methods of detecting Alzheimer's disease in its very earliest stages, the time at which treatments are most likely to be effective," says Dr. Butler. "I was delighted to carry out this work with researchers from Baycrest."

As next steps, researchers continue to explore how the brain's ability to process what is heard changes with neurodegenerative conditions, such as mild cognitive impairment.

More information: Jacqueline Zimmermann et al, Impaired memory-guided attention in asymptomatic APOE4 carriers, *Scientific Reports* (2019). DOI: 10.1038/s41598-019-44471-1

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