Alzheimer's: carriers of risk gene show brain changes in their 20s – here's why we shouldn't worry

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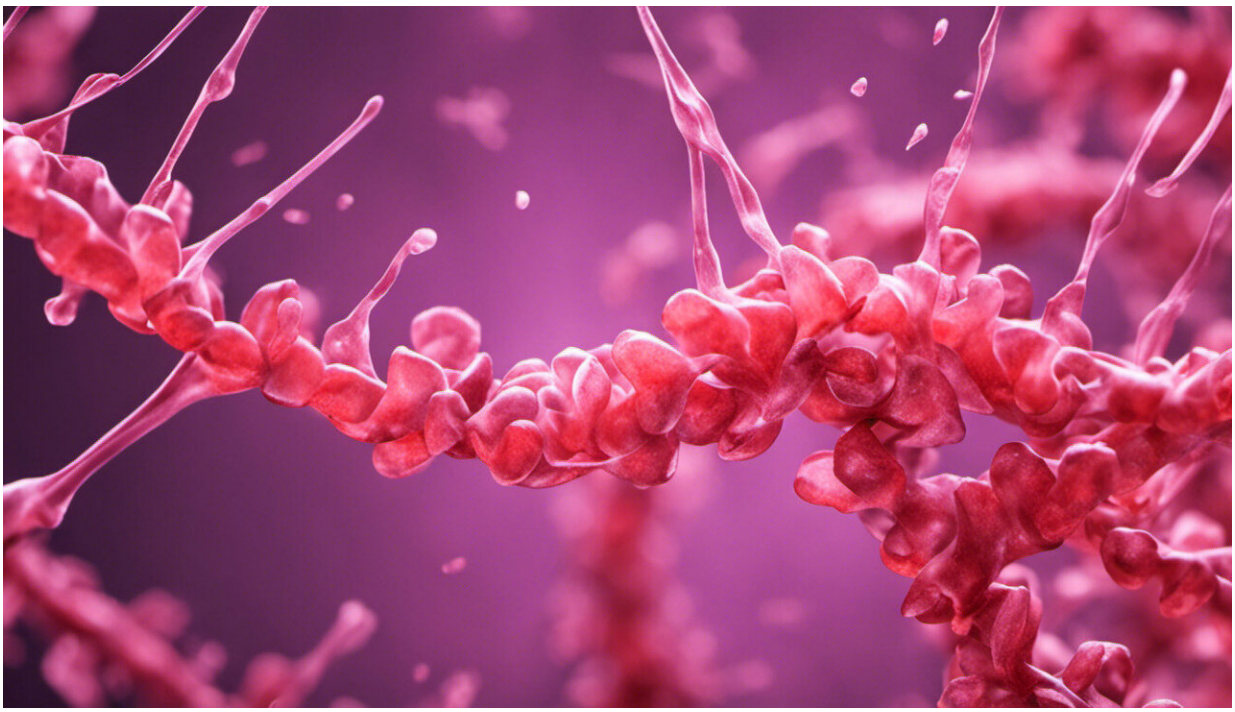

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Dramatic developments in genetics research and the availability of commercial genetics tests have put us in a very modern predicament—we can now find out (quickly, easily and cheaply) whether we personally hold genetic risk factors that put us at a

substantially increased risk of Alzheimer's disease. In addition, we have recently shown that brain changes can be identified in people holding these genetic risk variants as early as 20 years old.

Should we be testing ourselves? Should we worry? No. Here's why:

Genetic research has revealed that some individuals carry variants of specific genes that confer an increased risk of developing Alzheimer's disease in later life. For example, carriers of the ε4 variant of the APOE gene are approximately three to eight times more likely to be diagnosed with Alzheimer's disease after age 60 than individuals without this variant. The more variants, the greater the risk—with a maximum of one inherited from each parent.

In our recent research, we looked at these genetic factors in young people (around 20 years old, on average). We split them into "higher-risk" and "lower-risk" groups depending on whether they did or did not carry the APOE-ε4 gene variant, respectively.

Using advanced brain imaging techniques, we were able to show that it is possible to detect subtle differences in particular brain networks for the "higher-risk" young adults, several decades before any clinical symptoms of Alzheimer's emerge.

While brain structure and function were significantly different between the risk groups on average, it is very important to point out that not all "higher-risk" individuals go on to develop Alzheimer's disease. (Note that we say "higher" not "high" risk.)

The brains of many of these individuals were comparable to those at lower risk. This means carrying a higher-risk gene variant does not necessarily lead to early brain changes, or an Alzheimer's diagnosis later in life.

Should I get tested?

Public interest in genetics and gene testing is booming. Recent times have also seen highly publicised incidences of people responding to their own genetic risk with drastic interventions. For instance, Angelina Jolie, who has a faulty copy of the BRCA1 gene, associated with breast cancer—and had elective surgery to remove both breasts and some of her reproductive organs.

"Direct to consumer" genetic testing kits sold by companies now provide people with convenient and affordable access to their personal genetic information, including their genetic risk for specific diseases, including Alzheimer's.

But the relatively low cost of these tests reflects the fact that they typically only cover a fraction of the genome. The results, therefore, neglect the contribution of the rest of the consumer's genetic code. This will include other genes with protective, as well as negative, effects.

Of other concern, these tests have been shown to frequently generate false positive results: indeed, one study found approximately 40% of variants in a variety of genes reported in raw commercial genetic test data were false positives. This could lead to unnecessary distress, treatment and lifestyle adjustments. These tests also come with privacy and social concerns.

On the upside, the popularity of commercial genetic testing partly reflects consumers' positive desire to be proactive about their health. Consumers concerned about commercial genetic test findings should, however, request confirmatory tests from their clinician. These consumers should also understand that the disease risk reports they have purchased at best provide a partial answer to the question they are trying to address, because disease risk is about much more than genetics alone.

I am at 'higher' risk of Alzheimer's—what now?

The next step for our research is to find out what leads some people at "higher-risk" to go on to develop these early brain changes, but not others. Do these people exercise or sleep less, maintain a poorer diet, or have poorer social relationships? Many possible answers involve lifestyle factors that could potentially be altered to "buffer" individuals against their genetic risk.

The only way to properly understand which lifestyle factors may have such a protective effect, is to study large numbers of people with varying degrees of genetic risk over several decades.

We are part of an international team of scientists undertaking one such study, led by Professors Kim Graham and Andrew Lawrence at Cardiff University. The project involves collecting advanced brain imaging and cognitive test data from a large group of approximately 240 young adults. These individuals are part of a cohort that has been studied since birth, so we can access a wealth of retrospective health and lifestyle data.

Smaller, isolated studies looking at lifestyle factors might currently be missing the big picture. Brain differences have been found in these high risk groups between people who do and don't exercise regularly. This could suggest exercise has a protective effect on the brain, and may in turn mitigate Alzheimer's risk. It could also be that exercisers engage in other "protective" behaviours like eating a healthier diet. It is only with large-scale cohort studies that we can begin to disentangle the genetic and lifestyle contributions to cognitive performance, the brain and Alzheimer's risk.

Finally, if you are considering making lifestyle changes to offset your "genetic risk" for Alzheimer's, taking regular exercise and maintaining a healthy lifestyle is seldom bad advice. Other drastic lifestyle changes,

however, are likely unjustified.

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