# Why isn't there a gene for depression?

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Credit: AI-generated image (disclaimer)

Depression is sometimes categorised as a mental, rather than a physical illness – as though somehow mental health is different from physical health. But the brain is not a magical black box inside your head. It is an organ, just like the heart or lungs, made up of cells and supplied with blood.

These brain cells grow and develop, making contact with other brain

cells to communicate with one another. They control all of our behaviour, emotions and actions. And sometimes they go wrong, leading to illnesses like depression.

Depression does run in families, which could mean depression is genetic, an inherited condition. But families don't just share genes – they also experience a similar environment. So how can we separate genetic influences on depression from environmental factors?

Twins are a useful tool for studying the influence of genes and the environment on many diseases. They can be identical (one egg splits to form two babies) and share the exact same genetic make up, or nonidentical (two separate eggs form two babies), sharing half of the genes. By studying genetically identical twins raised together in the same family environment, we can examine whether differences in depression rates might be due to non-shared environmental factors.

Analysis in 2005 of a large number of twin studies indicated that around 40% of the risk of developing depression is genetic, and the remaining 60% associated with non-shared environmental factors. It is therefore too simplistic to say diseases like depression are either genetic or environmental. Both play their part.

Given that depression, like cancer, is not one single illness, it is perhaps not surprising that a single gene for depression has not been found. The variety of experiences also makes it difficult to find the right patient groups to study. People with depression may experience a single episode, or repeated episodes. They may develop depression in childhood, adolescence or later in life. Symptoms can vary, and include sleep disturbance, body weight changes, loss of interest in everyday activities, feelings of guilt and worthlessness, and suicidal thoughts.

The psychiatric genetics consortium group is a collaboration of hundreds

of international scientists from 38 countries who share data from almost a million depressed patients worldwide. It concluded in 2015 that most of the genetic effects found so far in the scientific literature are not very reliable or robust. But this does not mean genes are not involved. It just means we haven't really done the right studies yet – because depression is such a variable condition.

Grouping together people with different diagnoses of depression also makes it hard to identify genetic contributions. Breakthroughs in understanding cancer in the last 20 years have really come from being able to separate breast cancer from lung cancer from prostate cancer. But this is yet another challenge in depression research where symptoms and diagnoses are relied upon rather than a blood test for specific markers that can tell us that one patient has the same type of depression as another patient.

Another consortium of scientists known as CONVERGE has had some success in identifying genes involved in depression in an ongoing research project. They published findings from a carefully defined subgroup of severely depressed Chinese women patients with recurrent major depressive disorder. Over 10,000 participants had their DNA sequenced, which revealed small changes in two genes that were linked to major depressive disorder: the LHPP gene and the SIRT1 gene. Both are involved in cellular metabolism (how cells generate energy and signals) but their potential function in depression is not yet known.

Then a recent US study of more than 300,000 people of European descent reported different genes being associated with depression. In contrast to the CONVERGE group, they tried to get as many people as possible to have their DNA analysed via a commercial genomics company. This resulted in a very different population being studied including people self-reporting with depression. It remains to be tested whether these latest "genes for depression" can be verified.

## Environmental factors

Some people don't like the idea that there are "genes for depression" because they think that means getting the illness is somehow inevitable. But this view overlooks the adaptable nature of our brains and our genes. Genes are like a set of very complex instructions which tell the cells what proteins to make, and their activity can change, helping brain cells adapt to different situations. And let's not forget the other factor determining liability to develop depression: the environmental influences you are exposed to, such as stress.

So is there a gene for depression? No, there isn't. We don't have genes for diseases, we have genes that encode proteins that serve functions in cells.So does that mean if your DNA has the relevant change in your LHPP or SIRT1 genes that you are going to develop depression? No, it probably means you may have an increased risk to develop depression depending on the environment you experience.

In the same way that we think about heart disease, cancer, obesity as having multiple "susceptibility genes", the same is probably true for depression. It is likely that there are small changes in a number of genes, each contributing a little bit to dysfunction of your brain cells, which can then lead to you developing depression. We are finding out more all the time – and that is surely an uplifting thought.

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