Link between depression and cardiovascular disease explained: They partly develop from same gene module

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Depression and cardiovascular disease (CVD) are serious concerns for public health. Approximately 280 million people worldwide have depression, while 620 million people have CVD.

It has been known since the 1990s that the two diseases are somehow related. For example, people with depression run a greater risk of CVD, while effective early treatment for depression cuts the risk of subsequently developing CVD by half. Conversely, people with CVD tend to have depression as well. For these reasons, the American Heart Association (AHA) advises to monitor teenagers with depression for CVD.

What wasn't yet known is what causes this apparent relatedness between the two diseases. Part of the answer probably lies in lifestyle factors common in patients with depression and which increase the risk of CVD, such as smoking, alcohol abuse, lack of exercise, and a poor diet. But it's also possible that both diseases might be related at a deeper level, through shared developmental pathways.

Now, scientists have shown that depression and CVD do indeed share part of their developmental programs, having at least one functional gene module in common. This result, published in *Frontiers in Psychiatry*, provides new markers for depression and CVD, and could ultimately help researchers to find drugs to target both diseases.

"We looked at gene expression profile in the blood of people with depression and CVD and found 256 genes in a single gene module whose expression at levels higher or lower than average puts people at greater risk of both diseases," said first author Dr. Binisha H Mishra, a postdoctoral researcher at Tampere University in Finland.

The authors define a gene module as a group of genes with similar expression patterns across different conditions and hence likely to be functionally related.

Young Finns study

Mishra and colleagues studied gene expression data in the blood of 899 women and men between 34 and 49 years old who were participants in the Young Finns study, one of largest studies of cardiovascular risk factors from childhood to adulthood to date. The Young Finns study began in 1980 with a cohort of almost 4,000 children and adolescents, then between three and 18 years old, randomly selected from five cities in Finland. The health of these participants has been followed ever since.

Finland has the highest estimated incidence of mental disorders in the EU, and is the ninth-highest ranking country in the world for the prevalence of depression. In contrast, the country has a relatively low prevalence of CVD, ranking in the bottom 20% worldwide for this class of diseases.

In 2011, the researchers running the Young Finns study tested the participants for symptoms of depression with a tried-and-tested questionnaire: Beck's depression inventory (BDI-II), whose score increases with more severe symptoms. They also tested them for the risk of developing CVD through AHA's "ideal cardiovascular health" score, on a scale from zero (highest risk) to seven (lowest risk). The team further analyzed these data for the present study.

It's all in the blood

In 2011, whole blood had also been taken from each participant, and Mishra and colleagues analyzed these samples with state-of-the-art gene expression methods.

They used advanced statistics to identify 22 distinct gene modules, of which just one was associated with both a high score for depressive symptoms and a low score for cardiovascular health.

"The top three genes from this gene module are known to be associated

with neurodegenerative diseases, bipolar disorder, and depression. Now we have shown that they are associated with poor cardiovascular health as well," said Mishra.

These genes are involved in biological processes, such as inflammation, that are involved in pathogenesis of both depression and cardiovascular disease. This helps to explain why both diseases often occur together.

Other genes in the shared module have been shown to be involved in brain diseases such as Alzheimer's, Parkinson's, and Huntington's disease.

"We can use the genes in this module as biomarkers for depression and cardiovascular disease. Ultimately, these biomarkers may facilitate the development of dual-purpose preventative strategies for both the diseases," said Mishra.

More information: Binisha Hamal Mishra et al, Identification of gene networks jointly associated with depressive symptoms and cardiovascular health metrics using whole blood transcriptome in the Young Finns Study, *Frontiers in Psychiatry* (2024). DOI: 10.3389/fpsyt.2024.1345159

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