Depression could be evolutionary byproduct of immune system

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Depression is common enough - afflicting one in ten adults in the United States - that it seems the possibility of depression must be "hard-wired" into our brains. This has led biologists to propose several theories to account for how depression, or behaviors linked to it, can somehow offer an evolutionary advantage.

Some previous proposals for the role of depression in evolution have focused on how it affects behavior in a social context. A pair of psychiatrists addresses this puzzle in a different way, tying together depression and resistance to infection. They propose that genetic variations that promote depression arose during evolution because they helped our ancestors fight infection.

An outline of their proposal appears online in the journal *Molecular Psychiatry*.

The co-authors are Andrew Miller, MD, William P. Timmie professor of psychiatry and behavioral sciences at Emory and director of psychiatric oncology at Winship Cancer Institute, and Charles Raison, MD, previously at Emory and now at the University of Arizona.

"Most of the genetic variations that have been linked to depression turn out to affect the function of the immune system," Miller says. "This led us to rethink why depression seems to stay embedded in the genome."

For decades, researchers have seen links between depression and inflammation, or over-activation of the immune system. People with depression tend to have higher levels of inflammation, even if they're not fighting an infection. Still, high levels of inflammatory markers are not an inevitable consequence of depression.

"The basic idea is that depression and the genes that promote it were very adaptive for helping people - especially young children - not die of infection in the ancestral environment, even if those same behaviors are not helpful in our relationships with other people," Raison says.

Infection was the major cause of death in humans' early history, so surviving infection was a key determinant in whether someone was able to pass on his or her genes. The authors propose that evolution and genetics have bound together depressive symptoms and physiological responses that were selected on the basis of reducing mortality from infection. Fever, fatigue/inactivity, social avoidance and anorexia can all be seen as adaptive behaviors in light of the need to contain infection, they write.

The theory provides a new explanation for why stress is a risk factor for depression. The link between stress and depression can be seen as the byproduct of a process that preactivates the immune system in anticipation of a wound, they write.

Similarly, a disruption of sleep patterns can be seen in both mood disorders and when the immune system is activated. This may come from our ancestors' need to stay on alert to fend off predators after injury, Miller says.

Their theory could also guide future genetic, physiological and clinical research on depression. In particular, the presence of biomarkers for inflammation may be able to predict whether someone will respond to various treatments for depression.

Miller and Raison are involved in ongoing research on whether certain medications, which are normally used to treat auto-immune diseases, can be effective with treatment-resistant depression.

More information: The evolutionary significance of depression in Pathogen Host Defense (PATHOS-D). C.L. Raison and A.H. Miller. *Mol Psychiatry.*

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