

Inflammation could be a core feature of depression

May 17 2021



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People with depression have higher levels of inflammation in their bodies than those without depression, regardless of socioeconomic background, ill health or unhealthy behaviors, a study by King's College London finds.

C-reactive protein (CRP), a marker for inflammation in the body, was found in higher levels in [depressed people](#) compared to non-depressed people in the largest ever study into the genetic, environmental, lifestyle, medical pathways leading to inflammation in major depressive disorder (MDD).

The effect was reduced but remained significant when factors known to be related to increased inflammation such as smoking, body mass index (BMI) and trauma were taken into account, adding to the body of evidence that there may be a direct biological link between inflammation and depressive disorders. The study was conducted by researchers funded by the NIHR Maudsley Biomedical Research Center and NARSAD (National Alliance for Research on Schizophrenia & Depression) and it was published in the *American Journal of Psychiatry*.

Largest study of its kind

In any given week in England 3 in 100 people will have depression. The economic costs of mental illness in England have been estimated at £105.2 billion each year by the government which includes direct costs of services, lost productivity at work and reduced quality of life.

This study used the largest ever community-based sample with information on [mental health](#), inflammation, [genome-wide association study](#) (GWAS) data linking genes to certain diseases, environment, lifestyle and physical health with approximately 86 thousand participants.

Researchers analyzed blood samples, [genetic data](#) and physical and mental health questionnaires collected by UK Biobank, the large-scale biomedical database and research resource with over half a million UK participants who were recruited between in 2006-2010. Of the 86,000 participants included in the study just under a third (31%) were

classified as having major depressive disorder. This percentage is similar to estimates found by other studies on the global prevalence of depression occurring during a person's lifetime.

The study showed that depressed participants had raised C-reactive protein (CRP) levels in their blood compared to non-depressed participants, and were more likely to have low-grade inflammation, defined as CRP levels in the blood of over 3 mg per liter. Inflammation is a biological response which is predominantly directed to fight infection but also has an important role in regulating behavior. CRP is one marker for inflammation.

Further analysis showed that this increased inflammation in depression is only partially explained by clinical and sociodemographic factors including age, sex, body mass index (BMI) smoking, alcohol consumption, exposure to early life trauma, socio-economic status and self-reported health status.

Genetics x environment

The study found that the greater the genetic risk for depression, the greater the level of inflammation.

The [polygenic risk score](#) gives an estimate of how likely an individual is to have a given trait based only on genetics. The researchers calculated polygenic risk score in participants for major depression was strongly associated with levels of CRP. However, this association was no longer present when BMI and smoking were taken into account. In contrast, polygenic risk scores for three immune disorders—biliary cirrhosis, Crohn's disease and rheumatoid arthritis- are all positively associated with CRP levels even after controlling for BMI and smoking.

First author Maria Pitharouli, Research Associate at the Institute of

Psychiatry, Psychology & Neuroscience, King's College London said: "Our study provides the most conclusive evidence to date that people with depression have proteins in their blood indicating activation of the inflammatory system. Furthermore, through in-depth analysis of data from over 86,000 people we have discovered more about the mechanisms that may be behind the relationship between inflammation and depression."

Joint senior author, Professor Cathryn Lewis who leads the Social, Genetic and Developmental Psychiatry Center at the Institute of Psychiatry, Psychology & Neuroscience, King's College London said: "Our study highlights how genetics can be used as a tool for dissecting mental health disorders. Here we've shown that the genetic contribution to inflammation in depression comes mostly from eating and smoking habits. That finding is important to help us understand depression better—and one further piece in the jigsaw puzzle towards improving care for people with depression."

Joint senior author, Professor Carmine Pariante from the National Institute for Health Research Maudsley Biomedical Research Center says: "Our large-scale analysis of data removed socioeconomic background, ill health, unhealthy habits as well as genetic predisposition to immune dysfunction as the only explanations for the relationship between depression and inflammation. By this process of elimination, we show that there may be a core [biological process](#) that is behind the association between depression and increased [inflammation](#). If we can identify this process and uncover more detail about its role in the development of [depression](#), we can pave the way for trialing new treatments for this widespread mental health disorder."

The paper, "Depressed patients have elevated c-reactive protein independently of genetic, [health](#) and psychosocial factors, in the UK Biobank," was published today [Friday 14 May 2021] in the *American*

Journal of Psychiatry.

More information: Maria C. Pitharouli et al. Elevated C-Reactive Protein in Patients With Depression, Independent of Genetic, Health, and Psychosocial Factors: Results From the UK Biobank, *American Journal of Psychiatry* (2021). [DOI: 10.1176/appi.ajp.2020.20060947](https://doi.org/10.1176/appi.ajp.2020.20060947)

Provided by King's College London

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