Study reveals why some depressed patients have blood inflammation

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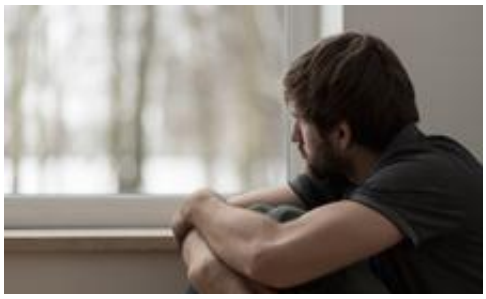

A new King's College London study reveals why some - but not all - people have depression that appears to be caused by blood inflammation.

These insights could help researchers to develop novel treatment strategies for the many depressed patients who do not get better using current antidepressants.

Recent research suggests that patients with depression have measurable changes in the blood that indicate activation of the inflammatory system - a biological response which is predominantly directed to fight infection but which also has an important role in regulating mood and behaviour.

Blood inflammation is known to worsen oxidative stress in the brain, which occurs when the body both overproduces and then struggles to remove molecules called 'free radicals.' These free radicals break down brain connections and disrupt the brain's chemical signalling, which in turn can lead to the development of depressive symptoms by reducing the brain's protective mechanisms.

This new King's research, published in *Neuropsychopharmacology*, indicates that some depressed patients are predisposed to develop depression when their inflammatory system is activated because they are more 'biologically sensitive' to inflammation. As a result, their brains are more likely to suffer.

Researchers have known for many years that approximately one third of patients who take an anti-viral immune drug called 'interferon-alpha' develop depression, because this drug activates the inflammatory system. The King's College London research team set out to study patients taking interferon-alpha as a model for inflammation-induced depression, in order to dissect the mechanisms through which an activated inflammatory system causes depressive symptoms in some but not all individuals.

They measured the activation of multiple biological systems in the blood of 58 patients before and after the inflammatory activation with interferon-alpha, and correlated changes in these systems with the onset of depressive symptoms.

The researchers found that patients who developed depressive symptoms following the inflammatory activation tended to be more biologically sensitive to interferon-alpha. Specifically, they had a more reactive inflammatory system, and also showed more changes in biological systems involved in oxidative stress and in the protection of brain cells.

Dr Nilay Hepgul, lead author of the study from the Institute of Psychiatry, Psychology & Neuroscience (IoPPN) at King's College London, said: 'Our results are important not only for understanding the high prevalence of depression amongst individuals receiving interferon-alpha treatment, but also to identify those at risk of developing depression in the context of high inflammation due to other causes, such as severe stress or medical illnesses.'

Professor Carmine Pariante, senior author of the study from the IoPPN at King's College London, said: 'Both oxidative stress and brain protective mechanisms can be considered future targets for the development of novel, effective antidepressant

strategies, especially for patients with high levels of inflammation who do not get better using current antidepressants.'

Professor Pariante added: 'Our next aim is to understand the implications of this increased inflammation in the blood and whether it has direct consequences for the brain, using neuroimaging techniques.

'We also need to understand why some patients are more biologically sensitive to increased inflammation. Do they have a specific genetic profile that makes them more susceptible, or has exposure to stress life events had an impact - or both?'

More information: Nilay Hepgul et al. Transcriptomics in Interferon-?-Treated Patients Identifies Inflammation-, Neuroplasticity- and Oxidative Stress-Related Signatures as Predictors and Correlates of Depression, *Neuropsychopharmacology* (2016). DOI: 10.1038/npp.2016.50