Researchers outline the connection between inflammation and depression

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In a paper published recently in *Pharmacological Reviews*, Emory University School of Medicine researchers outlined the impact of inflammation on motivation as it relates to depression.

The researchers propose that low grade inflammation affects brain chemicals and brain circuits that regulate motivation, ultimately leading to motivational deficits and a loss of interest or willingness to engage in usually pleasurable activities including work and play. These motivational deficits are reflected as anhedonia, a core and likely the most disabling symptom of depression, as well as other psychiatric disorders.

The paper also outlines how these effects of inflammation on the brain are an adaptation to the energy demands of inflammation that require conservation of energy resources, and thus the shutting down of behavior. Low grade inflammation can be caused by lifestyle changes such as poor diet and sedentary behavior.

"A vicious cycle can occur where poor lifestyle habits lead to increased inflammation that in turn reduce the wherewithal or motivation to change those habits. Such a vicious cycle may be especially relevant during pandemic life when even greater energy resources are required to sustain healthy eating and physical activity," says Andrew H. Miller, MD, William P. Timmie Professor of Psychiatry and Behavioral Sciences, Emory University School of Medicine. Miller co-authored the paper, along with his colleagues in the Department of Psychology and the Emory Behavioral Immunology Program, where he serves as director.

Miller says novel treatment strategies to break this vicious cycle are currently under development. He and his colleagues raise the possibility of developing treatments specifically for the motivational deficits caused by inflammation, thus moving to a much more targeted approach to therapeutic development in psychiatry, as now seen in the oncology field, versus the current use of outdated and non-specific diagnostic categories of psychiatric disease such as "depression."

"We believe more therapies targeted to specific pathophysiologic pathways and symptoms will lead to better outcomes and more precision care. Non-specific therapies as represented by conventional antidepressants, which are still embraced by regulatory agencies, do not instill the confidence that a more personalized approach does. There is widespread interest in moving in this direction internationally," says Miller.

More information: Michael J. Lucido et al, Aiding and Abetting Anhedonia: Impact of Inflammation on the Brain and Pharmacological Implications, *Pharmacological Reviews* (2021). DOI: 10.1124/pharmrev.120.000043

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