



Press Release

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An Omega-6 Fatty Acid May Reduce the Risk for Bipolar Disorder

A study published in Biological Psychiatry focuses on the role arachidonic acid plays in bipolar disorder, paving the way for potential lifestyle or dietary interventions

Philadelphia, April 30, 2024 – A genetic propensity to higher circulating levels of lipids containing arachidonic acid, an omega-6 polyunsaturated fatty acid found in eggs, poultry, and seafood, has been found to be linked with a lower risk for bipolar disorder, according to a [new study](#) in *Biological Psychiatry*, published by Elsevier. This new evidence paves the way for potential lifestyle or dietary interventions.

Bipolar disorder is a debilitating mood disorder characterized by recurring episodes of mania and depression. Although its etiology is still unclear, previous studies have shown that bipolar disease is highly heritable. The findings of this study indicate a link between bipolar disorder and altered metabolite levels, supporting the notion that circulating metabolites play an important etiological role in bipolar disease and other psychiatric disorders.

Lead investigator David Stacey, PhD, Australian Centre for Precision Health, University of South Australia; UniSA Clinical and Health Sciences; and South Australian Health and Medical Research Institute, Adelaide, Australia, explains, "*Accumulating evidence indicates a role for metabolites in bipolar disorder and other psychiatric disorders. By identifying metabolites that play causal roles in bipolar disorder, we hoped to be able to highlight potential lifestyle or dietary interventions.*"

By applying Mendelian randomization, a powerful causal inference method, the researchers identified 33 out of 913 metabolites studied present in the blood that were associated with bipolar disorder, most of them lipids.

Researchers also found that a bipolar disorder risk gene cluster (*FADS1/2/3*), which encodes enzymes associated with lipid metabolism, mediated the association between bipolar disorder and the levels of arachidonic acid and other metabolites.

Commenting on the findings, John Krystal, MD, Editor of *Biological Psychiatry*, says, "*Arachidonic acid is typically a widely present omega-6 fatty acid in the body and brain that contributes to the health of cell membranes. This study provides a fascinating step forward in the effort to develop blood biomarkers of bipolar disorder risk, particularly in those patients with bipolar disorder and risk gene variations in the FADS1/2/3 gene cluster.*"

Dr. Stacey notes, "*Intriguingly, we observed a pattern whereby a genetic propensity to higher levels of lipids containing an arachidonic acid fatty acid side chain was associated with a lower risk of bipolar disorder, while the inverse was true of lipids containing a linoleic acid side chain. Since arachidonic acid is synthesized from linoleic acid in the liver, this suggests arachidonic acid synthesizing pathways are important for bipolar disorder.*"

Given its presence in human milk, arachidonic acid is considered essential for infant brain development and is added to infant formula in many countries. Therefore, it may exert an effect on bipolar disorder risk by affecting neurodevelopmental pathways, which would be consistent with contemporary views of bipolar disorder as a neurodevelopmental disorder. Arachidonic acid can be sourced directly from meat and seafood products or synthesized from dietary linoleic acid (e.g., nuts, seeds, and oils).



Caption: Arachidonic acid, an omega-6 polyunsaturated fatty acid found in eggs, poultry, and seafood, has been found to lower the risk of bipolar disorder, according to a new study in *Biological Psychiatry* (Credit: iStock.com/a_namenko).

Dr. Stacey concludes, *"To our knowledge, ours is the first study to highlight a potential causal role between arachidonic acid and bipolar disorder. Preclinical studies and randomized controlled trials will be necessary to determine the preventive or therapeutic value of arachidonic acid supplements, perhaps with a particular focus on people with a compromised arachidonic acid synthesizing pathway or with poor natural dietary sources. Our findings also support potential avenues for precision health interventions focused on early life nutrition to ensure that infants and children are receiving enough arachidonic acid and other polyunsaturated fatty acids to support optimal brain development, which may also reduce the risk of bipolar disorder."*

Notes for editors

The article is "A Metabolome-Wide Mendelian Randomization Study Identifies Dysregulated Arachidonic Acid Synthesis as a Potential Causal Risk Factor for Bipolar Disorder," by David Stacey, PhD, Beben Benyamin, PhD, S. Hong Lee, PhD, and Elina Hyppönen, PhD (<https://doi.org/10.1016/j.biopsych.2024.02.1005>). It appears online in *Biological Psychiatry*, published by Elsevier.

The article is openly available at [https://www.biologicalpsychiatryjournal.com/article/S0006-3223\(24\)01106-5/fulltext](https://www.biologicalpsychiatryjournal.com/article/S0006-3223(24)01106-5/fulltext).

Copies of this paper are also available to credentialed journalists upon request; please contact Rhiannon Bugno at Biol.Psych@sobp.org. Journalists wishing to interview the authors may contact David Stacey, PhD, at +61 8 8302 8339 or david.stacey@unisa.edu.au.

The authors' affiliations and disclosures of financial and conflicts of interests are available in the article.

John H. Krystal, MD, is Chairman of the Department of Psychiatry at the Yale University School of Medicine, Chief of Psychiatry at Yale-New Haven Hospital, and a research psychiatrist at the VA Connecticut Healthcare System. His disclosures of financial and conflicts of interests are available [here](#).

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The journal publishes novel results of original research which represent an important new lead or significant impact on the field, particularly those addressing genetic and environmental risk factors, neural circuitry and neurochemistry, and important new therapeutic approaches. Reviews and commentaries that focus on topics of current research and interest are also encouraged.

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