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Study Identifies Link Between High-Salt Diet and Depression

A new study published in *The Journal of Immunology* found that a high-salt diet (HSD) induces depression-like symptoms in mice by driving the production of a protein called IL-17A. This protein has previously been identified as a contributor to depression in human clinical studies.

“This work supports dietary interventions, such as salt reduction, as a preventive measure for mental illness. It also paves the way for novel therapeutic strategies targeting IL-17A to treat depression,” shared Dr. Xiaojun Chen, a researcher at Nanjing Medical University who led the study. “We hope these findings encourage discussions on salt consumption guidelines,” said Dr. Chen.

The researchers also identified a type of immune cell called gamma-delta T cells (γδT cells) as an important source of IL-17A in HSD-fed mice, accounting for ~40% of IL-17A-producing cells. Depleting γδT cells significantly alleviated HSD-induced depressive symptoms, identifying another possible treatment method.

High-salt intake is ubiquitous in the Western diet, with fast foods often containing 100 times more salt than a home-cooked meal. HSD is already an important public health concern as it is linked to cardiovascular, autoimmune, and neurodivergent diseases. Furthermore, major depression disorder is also a significant public health concern with a lifetime prevalence of 15-18% and a place in the top 10 causes of death in the United States. HSD has long been associated with the occurrence and development of depression, but its role in the causation of depression was unclear.

In this study, mice were fed a normal diet or HSD for 5 weeks, a common timeframe used to study excessive dietary salt intake. After five weeks, the mice fed the HSD showed less interest in exploring and more inactivity in various scenarios compared to mice fed a normal diet, suggesting depression-like symptoms in mice

Given the already established role of IL-17A in the development of depression, the research team also investigated whether HSD induced IL-17A production in mice. HSD increased IL-

17A levels in the spleen, blood, and brain, correlating with anxiety- and depression-like behaviors. However, when mice that could not produce IL-17A were fed an HSD, depression-like symptoms were not observed, confirming the role of IL-17A in developing depression-like symptoms.

These findings corroborate epidemiological evidence that HSD correlates strongly with more severe depression and studies in people demonstrating that low sodium intake is closely associated with good mood.

The researchers hope these findings encourage further research into immune-mediated mechanisms of depression and pave the way for novel therapeutics targeting IL-17A or γδT cells. Dr. Chen and their team plan to validate these findings in humans while also investigating the mechanisms by which HSD activates γδT17 cells leading to increased HSD.

The research article is available on *The Journal of Immunology* website, or you can read more on AAI News.

Requests for interviews with authors, *The Journal of Immunology*, or the American Association of Immunologists can be made to kpalmer@aai.org.

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