

Breakdown in gut barriers to bacteria may promote inflammation and craving in alcoholics

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Bacteria in the gastrointestinal tract fulfill many vital functions and are critical for digestion. Yet, these same bacteria can induce strong inflammatory responses by the immune system if they penetrate the gut and enter the bloodstream.

Although acute inflammation is a natural response to protect the body, chronic or systemic inflammation is linked to numerous disorders and diseases. Prior research has established the involvement of <u>inflammatory processes</u> in the development of psychiatric disorders, including major depression and <u>alcohol</u> dependence, but the origins of such inflammation have remained unclear.

Now, researchers at Université Catholique de Louvain in Belgium, led by senior authors Dr. Philippe de Timary and Dr. Peter Stärkel, have found that inflammatory pathways are stimulated in alcohol-dependent patients by bacteria that escape the gut barrier, which correlated with alcohol craving. They report their findings in the current issue of *Biological Psychiatry*.

"In this study, we established a link between alcohol consumption, craving and activation of pro-inflammatory cytokines which contribute to a systemic inflammatory status in alcohol-dependent patients," said Stärkel.



To conduct this work, they recruited 63 actively-drinking alcohol-dependent patients who underwent testing both before and after alcohol detoxification. That data was compared with testing from 14 healthy volunteers.

When patients were exposed to alcohol, the researchers found that the inflammatory response originated from gut-derived bacterial products that crossed the gut barrier, which in turn, activated specific inflammatory pathways in blood mononuclear cells.

Prior to undergoing detoxification, the observed inflammation correlated with both <u>alcohol consumption</u> and alcohol craving among the alcohol-dependent patients. Following detoxification, some, but not all, of the altered inflammatory processes were either partially or fully recovered.

"This establishes a new concept where events having their origin at peripheral sites in the body could modify central brain mechanisms that ultimately influence behaviour in alcohol dependence," Stärkel explained.

Dr. John Krystal, Editor of *Biological Psychiatry*, commented, "This study suggests that there may be a link between inflammatory processes that develop when gut barriers to bacteria break down and risk for continued heavy drinking among people with <u>alcohol use disorders</u>. The findings suggest that it might be helpful to protect and restore gut integrity and to reduce inflammation when helping patients recover from alcohol use disorders."

Stärkel agreed, adding, "The study does not only open new areas for research but also identifies new targets for developing novel treatment and management approaches for <u>alcohol dependence</u>. Targeting the gutbrain axis either at the level of the gut itself or at the level of effector cells such as blood mononuclear cells in order to influence behaviour



could become a potential option in the care of alcohol-dependent <u>patients</u>."

More information: The article is "Role of Inflammatory Pathways, Blood Mononuclear Cells, and Gut-Derived Bacterial Products in Alcohol Dependence" by Sophie Leclercq, Christine De Saeger, Nathalie Delzenne, Philippe de Timary, and Peter Stärkel (DOI: 10.1016/j.biopsych.2014.02.003). The article appears in *Biological Psychiatry*, Volume 76, Issue 9 (November 1, 2014)

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