New research correlates inflammation in the brain and gut to negative emotional state during opioid withdrawal

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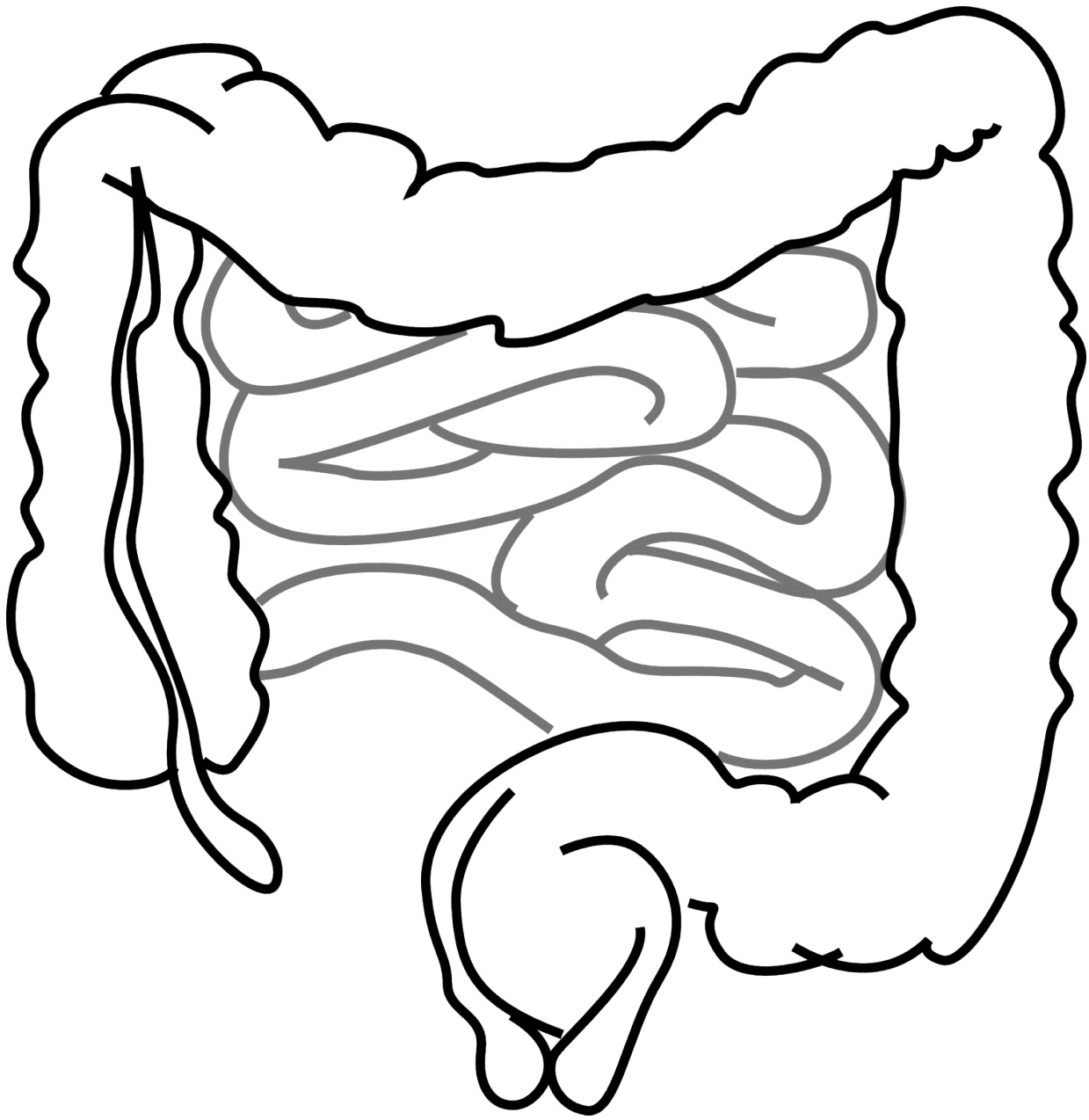

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Opioid dependence has become a national crisis with serious impact on economic and social welfare, and numerous casualties. A big goal of ongoing research in combating opioid use disorder is understanding drug

withdrawal. The physical and emotional symptoms of withdrawal can be life threatening and make up a powerfully negative experience; the fear of these symptoms strongly motivates addiction.

Researchers in the lab of James Schwaber at the Daniel Baugh Institute for Functional Genomics and Computational Biology at Thomas Jefferson University are studying how inflammation contributes to drug withdrawal and dependence. Their study was published in *Frontiers of Neuroscience* on July 3.

Opioids can cause inflammation in the brain by inducing immune cells to release inflammatory molecules called cytokines. The main immune cells in the brain are microglia and astrocytes. Inflammatory responses induced by opioids have been observed in the central amygdala, a brain region that has been strongly implicated in opioid dependence because of its role in emotion and motivation. The central amygdala can also be affected by inflammation in other parts of the body, like the gut. In fact, the communication between the gut and the brain can shape a variety of motivated behaviors and emotional states, including those associated with drug dependence and withdrawal.

The researchers including first author Sean O'Sullivan in Dr. Schwaber's lab isolated single neurons, microglia, and astrocytes from the central amygdala and studied their genetic profiles in normal, opioid-dependent, and withdrawn rats. They were surprised to find that the profile of astrocytes changed the most, shifting genetic expression to a more activated state. This shift correlated strongly with opioid withdrawal. Furthermore, all three cell types showed a considerable increase in an inflammatory cytokine called TNF alpha in withdrawn animals.

In addition, the researchers also assayed different types of bacteria in the gut of rats and found that certain anti-inflammatory bacteria were suppressed in withdrawn animals, shifting the ratio of gut microbiota and

causing a phenomenon called dysbiosis, which can cause inflammation in the digestive system. It is unclear how these changes influence opioid withdrawal, but the authors propose that the simultaneous inflammation in the gut and central amygdala may be linked to the negative emotional experience of withdrawal.

The findings underscore the highly complex relationship between the gut and the brain, and suggest that inflammation in the gut and brain may exacerbate symptoms associated with withdrawal. Targeting inflammation in these regions may alleviate the negative experience of drug withdrawal, and therefore prevent dependence.

More information: Sean J. O'Sullivan et al, Single-Cell Glia and Neuron Gene Expression in the Central Amygdala in Opioid Withdrawal Suggests Inflammation With Correlated Gut Dysbiosis, *Frontiers in Neuroscience* (2019). DOI: 10.3389/fnins.2019.00665

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