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## The New Approach to the Gut-Brain Axis Research and Possible Implications for the Rethinking of the Addiction Problem

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Over the years, research on the brain-gut system has led us to significant findings, which we believe are crucial for the study and understanding of addiction. A summarizing article detailing these findings has recently been published [1].

The most notable result of our experiments is the identification of p-cresol, a substance produced by the gastrointestinal bacteria *Clostridium difficile*, as playing a key role in the release of dopamine in specific brain regions and the activation of dopamine receptors. Additionally, our research suggests that the release of opioid substances by brain regions, in response to dopamine transportation to the brain cells, is necessary to neutralize dopamine's effects and facilitate synaptic connections.

A major conclusion from our seven-year study is the hypothesis that the primary cause of mental disorders is not an increase in dopamine levels or the over-production of p-cresol by gut bacteria, but rather a delay in the release of opioid substances in the brain. During this delay, dopamine continues to be released, leading to prolonged excitation of brain cells. Over time, this disrupts the development of synaptic connections and results in brain degradation.

This perspective challenges the current consensus on brain function, reframing the brain as a mechanism primarily driven by the pursuit of pleasure. From an evolutionary standpoint, this is plausible, given that the brain evolved from the enteric nervous system as a more efficient organ for acquiring food and, consequently, pleasure.

Viewing addiction through this lens a condition arising from a lack of pleasure-offers a novel approach to addressing addiction. If addiction (in any form) develops because an individual is unable to find a source of pleasure in their social environment to counteract dopamine-induced excitation, leading them to seek "mechanical" means (such as drugs), then a new strategy emerges for intervention. In addition to traditional therapies aimed at identifying and replacing the object of addiction, our research suggests that temporarily reducing through proper medication the bacterial colony responsible for producing p-cresol and thereby decreasing dopamine release-could be equally important. By reducing the size of this bacterial colony, dopamine release, and

consequently, the intensity of addiction, may decrease, enhancing the effectiveness of therapeutic interventions.

**References**

1. Gigi Tevzadze, Lali Shanshiashvili, David Mikeladze (2024) Besides the development of mental disorders, gut microbiome bacteria appear to play a major role in turning on cognitive activity: Outcomes of experiments, foreseen implications and hypotheses. *Journal of Biological Physics and Chemistry* 24: 70-77.

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