



# Centre de Neurosciences Psychiatriques

## CNP SEMINARS

### ANNOUNCEMENT

Friday, February 7, 2020, 11:00 – 12:00

## Role of the gut microbiota in the modulation of the gut-liver-brain axis in alcohol use disorders: proof of concept with the fecal microbiota transplantation

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It is well established that alteration of the gut microbiota composition can disturb many aspects of host physiology, including metabolism, immunity and peripheral and central nervous system with consequences for brain functions and behavior. In a previous study, we found that alterations of the gut microbiota composition of alcohol-dependent (AD) patients were associated with high scores of depression, anxiety and alcohol craving, as well as low score of sociability, suggesting the existence of a gut-brain axis in AD patients.

In this new experimental study, we demonstrated the causal role of the gut microbiota in the development of the psychological symptoms associated with alcohol dependence, by using fecal microbiota transplantation. The microbiota of AD patients and healthy controls (CT) were transferred into two groups of mice which were subsequently tested for behavior. We found that mice transplanted with the gut microbiota of AD patients exhibited increased depression-like behavior and decreased social behavior compared to CT-recipient mice. Furthermore, AD-recipient mice showed alterations of brain functions such as myelination, neurotransmission and neuroinflammation. Blood metabolomics analysis revealed, in AD-recipient mice, elevated ethanol concentration and decreased levels of a ketone body, the b-hydroxybutyrate (BHB). Raising the levels of BHB through nutritional approach (ketogenic diet) improved sociability and brain functions in mice, thereby supporting the hypothesis that BHB is a key metabolite in the gut-liver-brain axis. The involvement of these two metabolites, ethanol and BHB, and their links with the psychological symptoms were confirmed in a cohort of AD patients.

The results of this study confirm the production of ethanol by intestinal bacteria that consequently impacts liver and brain metabolism, and reinforce the existence of a gut-liver-brain axis in alcohol use disorders.

Invited by Benjamin Boutrel

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**Salle de séminaires 1<sup>er</sup> étage CNP  
Hôpital Psychiatrique de Cery-Site de Cery, CH-1008 Prilly-Lausanne**

#### Related publications

Leclercq, S. *et al.* *The Gut Microbiota Drives Metabolic Disorders Which Compromise Sociability in Alcoholic Patients.* <https://papers.ssrn.com/abstract=3461778> (2019).

Leclercq, S., Stärkel, P., Delzenne, N. M. & de Timary, P. The gut microbiota: A new target in the management of alcohol dependence? *Alcohol* 74, 105–111 (2019).

Leclercq, S. *et al.* Intestinal permeability, gut-bacterial dysbiosis, and behavioral markers of alcohol-dependence severity. *Proc. Natl. Acad. Sci. U. S. A.* 111, E4485–E4493 (2014).

Leclercq, S., De Saeger, C., Delzenne, N., de Timary, P. & Stärkel, P. Role of inflammatory pathways, blood mononuclear cells, and gut-derived bacterial products in alcohol dependence. *Biol. Psychiatry* 76, 725–733 (2014)