

***L. helveticus* R0052 and *B. longum* R0175 PRODUCE GABA AND ANTI-INFLAMMATORY CITOKYNES OF PATIENTS WITH ANXIETY: MICROBIOME MODEL**

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Objective: The aim of this work was to evaluate the effect of *Lactobacillus helveticus* R0052 and *Bifidobacterium longum* R0175 on the gut microbiota of mild anxious adults using microbiome model (Simulator of Human Intestinal Microbial Ecosystem- Shime®).

Methods: The experimental period in SHIME® was 4 weeks, divided into: Stabilization = 2 weeks, Control Period = 1 week, Intervention = 2 weeks [*Lactobacillus helveticus* R0052, 3.0×10^9 cfu.log/pill and *Bifidobacterium longum* R0175, 3.0×10^8 cfu.log/pill, (Lallemand Health Solutions Inc., Montreal, Canada)]. The composition of the intestinal microbiota obtained by sequencing the 16S rRNA gene, gamma-aminobutyric acid (GABA) and cytokines were analyzed. Statistical analyzes were performed by ANOVA and Tukey's multiple comparison test, as well as bioinformatics analyzes for microbiota diversity.

Results: The results showed a statistical difference ($p=0.01$) in bacterial communities regarding beta diversity, by unweighted Unifrac. The predominant

phyla before the probiotic treatment were *Actinobacteria*, *Firmicutes*, *Bacteroidetes* and *Proteobacteria*. Although after dosing of probiotic the increase ($p < 0.001$) of *Firmicutes* was observed. At the genus level, taxonomic assignment performed in the ascending colon in the SHIME® model showed that probiotics (7 and 14 days) increased ($p < 0.005$) the abundance of *Lactobacillus* and *Olsenella* and decreased ($p < 0.005$) *Lachnospira* and *Escheria-Shigella*. After 14 days of probiotic treatment, the results showed an increase ($p < 0.001$) of GABA and anti-inflammatory cytokines (IL-6 and IL-10) and decreased ($p < 0.001$) pro-inflammatory cytokines (TNF-alpha) when compared to the control period.

Conclusions: The gut-brain axis plays an important role in the gut microbiota, producing GABA and anti-inflammatory cytokines. Finally, the microbiota signature in anxiety disorders provides a promising direction for the prevention of mental diseases and opens a new perspective of the use of psychobiotics as a main player of therapeutic targets.