GUT AND BRAIN SPEECH: GAIN IN BIFIDOBACTERIA ALTERS THE HIPPOCAMPAL GABAERGIC PLASTICITY IN HEALTHY MALE RATS

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Introduction: The new concept in health and disease about the ability of gut microbiota to regulate some brain functions and behavior is emerging as interesting and exciting essential studies in neuroscience, focusing the gut microbiota (GM) as a powerful regulator of brain physiology and behaviour in humans and rodents. Ingestion of specific live bacteria (probiotics) therefore appear to be a potential treatment for several neurological disorders. Administration of adequate and specific probiotics may confer, in animals, a benefit for health affecting behaviour and several brain functions. A large plethora of studies suggested the hippocampus as a possible target for this fine tuning. Recent evidences highlighted that structural integrity of the hippocampal formation is contingent on the presence of a healthy GM.

Material and methods: The study was performed using adult male Sprague-Dawley rats treated intragastrically with TRIBIF (Bifidobacterium longum BB536, Bifidobacterium breve M-16V, Bifidobacterium infantis M-63). Western blot, immunohistochemistry and pach-clamp techniques were used to measure $GABA_A$ subunit expression and receptor function in hippocampus. Hormones were detected with IBL ELISA kits and dendritic spine density were measured with a modified Golgi-Del Rio Hortega protocol. Here we studied in adult male rats the long-lasting effect of a 1-2months chronic treatment with a mixture (TRIBIF) of three different Bifidobacteria (Longum, Breve, Infantis) on GABAergic system and hippocampal plasticity as well as HPA axis responsiveness to acute stress in adult naïve rats measuring the plasma levels of hormones such as allopregnanolone (AP) and corticosterone (CTS).

Results: TRIBIF treatment induced a decrease in basal plasmatic content of AP with no changes in CTS amount. Furthermore, the treatment failed to change foot-shock-induced increase of CTS levels when compared to vehicle group. Western blot analysis showed that two months of TRIBIF treatment reduced the expression of a1, a3, a4, a5and d $GABA_A R$ subunits while increased g2subunit. Patch-clamp experiments performed in dentate gyrus granule cells (DGGC) showed no change in GABA-mediated synaptic currents whereas significantly decreased the tonic component of GABAergic inhibition. The lack of TRIBIF towards the response to an acute stress worth to be further investigated given that treatment was carried out in healthy animals suggesting that beneficial effects of TRIBIF could well manifest themselves in organisms with an altered microbiota.

Discussion/Conclusion: The mechanism involved in the ameliorating action of GM on brain, behavioral and cognitive functions, has not yet fully understood. Recent studies demonstrate that germ-free mice display alterations in stress-responsivity and behavior indicative of a reduction in anxiety in comparison to conventional mice. Moreover, it has been recently proposed that changes in GM alter the stress responses to the hypothalamic-pituitary-surrenal (HPA) axis, an effect that may involve the GABA inhibitory system, one of the first candidates in the modulation of emotions. Our data demonstrate that chronic treatment with a mixture of three different strain of Bifidobacteria induces a parallel positive changes in brain plasticity and cognitive behavior in male adult healthy rats. Our results, together with recent findings show the potential effect of probiotics ingestion and the possible role in the treatment of patho-physiological mechanisms for major depressive disorder (MDD), including the immune system and hippocampal HPA axis regulation. Further supports are necessary to understand the crucial role of the microbiota on the synaptic plasticity and brain function. Founded by VALEAS.