IJBPAS, December, 2021, 10(12): 4263-4268

ISSN: 2277–4998

International Journal of Biology, Pharmacy and Allied Sciences (IJBPAS)

'A Bridge Between Laboratory and Reader'

www.ijbpas.com

INTERACTION OF PROBIOTICS WITH GUT-BRAIN-AXIS AND ITS IMPACT ON HEALTH AND DISEASE

MANDAL M[1] AND MANDAL S[2*]

1: Department of Physiology, MGM Medical College, Kishanganj-855107, India

2: Laboratory of Microbiology and Experimental Medicine, Department of Zoology, University of Gour Banga, Malda-732103, India

***Corresponding Author: Prof. Shyamapada Mandal: E Mail: samtropmed@gmail.com; sam.micro11@ugb.ac.in**

Received 18th Feb. 2021; Revised 17th Mar. 2021; Accepted 16th April. 2021; Available online 1st Dec. 2021

https://doi.org/10.31032/IJBPAS/2021/10.12.5735

ABSTRACT

Recently, there have been advances in research on the role of probiotics in the improvement of interaction between enteric micobiota with gut-brain axis, important for the proper maintenance of gastrointestinal homeostasis and its association with emotional and cognitive functions of the brain. The neural, immune and hormone mediated communication exert its regulation on the brain to influence the activities of intestinal cells, which in turn, are affected by the gut microbiota. This communication, based on the available published information, represents an update the role of probiotics in brain-gut-axis functioning.

Keywords: Gut-brain-axis, microorganisms, probiotics, health and disease

INTRODUCTION

The gut-brain axis (GBA), refers to the two-way reciprocal connection between the emotional and cognitive centers in the brain and the gastrointestinal tract **[1]**. The GBA comprises the central nervous system (CNS), the autonomic nervous system (ANS), the enteric nervous system (ENS) and the hypothalamic pituitary adrenal (HPA) axis **[2]**. The sympathetic and parasympathetic division of the ANS, transmits afferent signals from the lumen to CNS via enteric, spinal and vagal

pathways, and efferent signals from CNS to the intestinal wall. The HPA axis, which is a part of the limbic system involved in memory and emotional reactions, is triggered by environmental stress and systemic pro-inflammatory cytokines that causes release of the corticotropin-releasing factor (CRF) from the hypothalamus, which stimulates adrenocorticotropic hormone (ACTH) secretion from pituitary gland that, in turn, causes the stress hormone, cortisol to be released from the adrenal glands **[3]**. The HPA acts as a coordinator through which exposure to psychological stress produce intestinal barrier dysfunction, changed composition of the gut microbial community, and behavioral anomalies of mood disorders and cognitive defects **[4]**.

INTERACTION BETWEEN COMMENSAL MICROBIOTA AND GBA

The microorganisms inhabiting the gut have a mutual association with their host that assist in the catabolism of food products into absorbable nutrients, function to maintain immune homeostasis, and defend against stress-induced upsurges in vulnerability to infection with enteric pathogens **[5]**. Besides microbial community in the gut affect brain neurochemistry that is relevant for memory, exploratory behavior, susceptibility to anxiety and depression **[4]**. The mechanism behind the interaction between microbiota and the brain-gut-axis is bidirectional, one from gut microbiota to brain and the other from brain to gut microbiota **[6]**. The former is mediated by formation, expression and turnover of neurotransmitters like serotonin, GABA and brain-derived neurotrophic factor (BDNF), protection of intestinal barrier and tight junction integrity, modulation of enteric sensory afferents, bacterial metabolites, mucosal immune regulation, while the latter is mediated by change in mucus and biofilm formation, motility, intestinal permeability, immune function **[2]**. The intestinal microbial dysbiosis is associated with the pathophysiology of chronic gut disorders, such as irritable bowel syndrome (IBS) and inflammatory bowel diseases (IBD) **[1]**, and the probiotic manipulation of gastrointestinal microflora exerts positive effects on IBS and IBD symptoms **[7]**.

EFFECT OF PROBIOTICS ON GBA

Probiotics are live microorganisms capable of providing favorable nutritional advantage and health benefits to their host when adequate amounts are administered

continuously **[7]**. As per the International Scientific Association for Probiotics and Prebiotics consensus statement probiotics are defined as the "live microorganisms that, when administered in adequate amounts, confer a health benefit on the host" **[8]**. Probiotics as microbial feed supplement function to improve the intestinal microbial balance and the properties of the indigenous microflora through their metabolic activities, competitive exclusionof medically significant pathogens, stimulation of the immune system, treatment and neutralization of the side effects of antibiotic therapy **[9]**. Probiotics functionality has been maintained through immune modulation, organic acid, mainly lactic acid, and antimicrobial (viz., hydrogen peroxide and bacteriocin) production, production of short chain fatty acids (acetate, butyrate and propionate), interaction with gut microbiota, and by colonization resistance and enzyme formation **[10]**.

Probiotics are being increasingly used as alternative treatment options and there are innumerable reports of probiotics with demonstrated beneficial effects in patients with infectious diarrhea, allergies, IBS and IBD cases **[7]**. An example of probiotic interaction with GBA through excitation of enteric sensory afferents is *Lactobacillus reuteri* that is reported to modulate gut motility and pain perception by impeding the opening of calcium-dependent potassium channels **[11]**. The gut microbiota and oral probiotics influence systemic inflammation, oxidative stress,glycemic control, tissue lipid content and mood **[12]**. *Lactobacillus*-containing probiotics have been reported to beuseful in both gut and the brainregion **[13]**. Supplementation of probiotics prevented chronic stress-induced bacterial translocation, colorectal hypersensitivity and repaired intestinal barrier dysfunction **[14]**. Probiotics cured and prevented the infection caused bybacterial pathogensas well as its associated anxiety-like behavior and stress-induced memory dysfunction **[15]**. *Bifidobacterium longum* showed anxiolytic effect in chronic colitis associated anxiety disorder, however this effect was absent in mice that were vagotomized before the induction of colitis **[16]**. Oral Bifido bacteria reduced systemic inflammatory cytokines and normalized brain levels of stress hormones, and Lactobacillus decreased anxiety-like behavior **[17]**. Administration of a combination of *L.helveticus* with *B. longum*

restored tight junction barrier integrity and decreased HPA axis and ANS activities, in terms of cortisol and catecholamine releases **[18]**. Prolonged usage of *L.rhamnosus* induced increase in $GABA_{B1b}$ in cortical cingulate and prelimbic regions and decrease $GABA_{B1b}$in the hippocampus, amygdala, and locus coeruleus, while a reduced $GABA_{A\alpha2}$ expression was found in the prefrontal cortex and amygdala, but increase in the hippocampus; thus *L. rhamnosus* regulated GABA expression in the brain causing decrease in the prefrontal cortex and increase in the hippocampus via vagus nerve apart from also reducing corticosterone, and exhibiting anxiolytic action and depression reducing activities **[19]**. The mitigation of antibiotic-induced visceral hypersensitivity and mucosal inflammation with *L. paracasei* supplementation **[20]**.

CONCLUSION

The gut microbiota exerts vital influence on bidirectional communications between the gut and the nervous system by regulating neural chemistry and neuro-endocrine systems. There has been comprehensive research on the modulation of gut microbiota through the administration of probiotics in health and disease, all of which have been studied in animal models. The evaluation of probiotics in man with respect to its influence on GBA in health and disease is required to be carried out through strain characterization **[21, 22]**, dosage optimization and formulation for large scale clinical trials. Elucidation of the mechanisms behind interactions between the brain-gut-microbiota axis and the significant role of probiotics has great therapeutic implications for a wide-ranging disorder of the gut and beyond.

Funding sources: nil

Conflict of interest: none

REFERENCE

[1] Koloski NA, Jones M, Kalantar J, Weltman M, Zaguirre J, Talley NJ. The brain-gut pathway in functional gastrointestinal disorders is bidirectional: a 12-year prospective population-based study. *Gut* 2012; 61: 1284-1290.

[2] Rhee SH, Pothoulakis C, Mayer EA. Principles and clinical implications of the brain-gut-enteric microbiota axis. *Nat Rev Gastroenterol Hepatol* 2009; 6: 306-314.

[3] Tsigos C, Chrousos GP. Hypothalamic-pituitary-adrenal axis, neuroendocrine factors and

stress. *J Psychosom Res* 2002; 53: 865-871.

[4] Foster JA, McVey Neufeld KA. Gut-brain axis: how the microbiome influences anxiety and depression. *Trends Neurosci* 2013; 36: 305-312.

[5] Chow J, Lee SM, Shen Y, Khosravi A, Mazmanian SK. Host-bacterial symbiosis in health and disease. *Adv Immunol* 2010; 107: 243-274.

[6] De Palma G, Collins SM, Bercik P, Verdu EF. The Microbiota-Gut-Brain axis in gastrointestinal disorders: Stressed bugs, stressed brain or both? *J Physiol* 2014; 592: 2989-2997.

[7] Floch MH, Walker WA, Madsen K, Sanders ME, Macfarlane GT, Flint HJ, *et al*. Recommendations for probiotic use-2011 update. *J Clin Gastroenterol* 2011; S168-S171.

[8] Hill C, Guarner F, Reid G, Gibson GR, Merenstein DJ, Pot B, *et al*. Expert consensus document. The International Scientific Association for Probiotics and Prebiotics consensus statement on the scope and appropriate use of the term probiotic. *Nat Rev Gastroenterol Hepatol* 2014; 11: 506–514.

[9] Sherman PM, Ossa JC, Johnson-Henry K. Unraveling mechanisms of action of probiotics. *Nutr Clin Pract* 2009; 24: 10–14.

[10] Sanders ME, Merenstein DJ, Reid G, Gibson GR, Rastall RA. Probiotics and prebiotics in intestinal health and disease: from biology to the clinic. *Nat Rev Gastroenterol Hepatol* 2019; 16: 605–616.

[11] Kunze WA, Mao YK, Wang B, Huizinga JD, Ma X, Forsythe P, *et al*. Lactobacillus reuteri enhances excitability of colonic AH neurons by inhibiting calcium-dependent potassium channel opening. *J Cell Mol Med* 2009; 13: 2261-2270.

[12] Bowe WP, Logan AC. Acne vulgaris, probiotics and the gut-brain-skin axis - back to the future? Gut Pathogens 2011, 3:1.

[13] Quigley EM, Shanahan F. The future of probiotics for disorders of the brain-gut axis. Adv Exp Med Biol. 2014; 817: 417-432.

[14] Zareie M, Johnson-Henry K, Jury J, Yang PC, Ngan BY, McKay DM, *et al*. Probiotics prevent bacterial translocation and improve intestinal barrier function

in rats following chronic psychological stress. *Gut* 2006; 55: 1553–1560.

[15] Gareau MG, Wine E, Rodrigues DM, Cho JH, Whary MT, Philpott DJ, *et al*. Bacterial infection causes stress induced memory dysfunction in mice. *Gut* 2011; 60: 307–317.

[16] Bercik P, Park AJ, Sinclair D, Khoshdel A, Lu J, Huang X, *et al*. The anxiolytic effect of *Bifidobacterium longum* NCC3001 involves vagal pathways for gut-brain communication. *Neurogastroenterol Motil* 2011; 23: 1132-1139.

[17] Desbonnet L, Garrett L, Clarke G, Kiely B, Cryan JF, Dinan TG: Effects of the probiotic *Bifidobacterium infantis* in the maternal separation model of depression. Neuroscience 2010, 170: 1179-1188.

[18] Ait-Belgnaoui A, Colom A, Braniste V, Ramalho L, Marrot A, Cartier C, *et al*. Probiotic gut effect prevents the chronic psychological stress-induced brain activity abnormality in mice. *Neurogastroenterol Motil* 2014; 26: 510-520.

[19] Bravo JA, Forsythe P, Chew MV, Escaravage E, Savignac HM, Dinan TG, *et al*. Ingestion of Lactobacillus strain regulates emotional behavior and central GABA receptor expression in a mouse via the vagus nerve. *Proc Natl Acad Sci USA* 2011; 108: 16050-16055.

[20] Verdu EF, Bercik P, Verma-Gandhu M, Huang XX, Blennerhassett P, Jackson W, *et al*. Specific probiotic therapy attenuates antibiotic induced visceral hypersensitivity in mice. *Gut* 2006; 55: 182-190.

[21] Mandal S, Mandal MD, Pal NK. Detection of intestinal colonization of probiotic *Lactobacillus rhamnosus*by stool culture in modified selective media. *Asian Pacific Journal of Tropical Disease* 2012; 2(3): 205-210.

[22] Halder D, Mandal M, Chatterjee SS, Pal NK and Mandal S. Indigenous probiotic *Lactobacillus* isolates presenting antibiotic like activity against human pathogenic bacteria. *Biomedicines* 2017; 5(2): 1-11.