

Role of Microbiome-gut-brain axis in Depression

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The Microbiota-gut-brain axis is an emerging belief pertaining to the way the microbial population in the gut corresponds with the human brain and alters neuropsychiatric functions and mood. This bilateral communication occurs through neural (vagus nerve), hormonal, immunological and neuroendocrine networks [1]. The 10⁴ Microbiota harboring the human intestinal tract confer a symbiotic relationship, the most numerous of which are the Firmicutes and Bacteroides, with Proteobacteria, Actinobacteria, Fusobacteria, and Verrucomicrobia following soon after [2]. Depressive episodes associated with the link between microbiota and Hypothalamic-pituitary- adrenal (HPA) axis were demonstrated by comparing Germ-free mice having increased levels of corticosterone and adrenocorticotrophin (ACTH) levels, and House specific-Pathogen-free mice with reduced stress hormones due to probiotic effects [3,4]. The hygiene hypothesis states that the normal maturation of HPA needs exposure to commensal colonialism during early life to ensure normal development of the stress signaling pathway. Inhabited commensal microbiota produces mood-stabilizing neurotransmitters gamma-aminobutyric acid (GABA) from monosodium glutamate, norepinefrin, serotonin, and dopamine. On the contrary, GF mice have raised plasma serotonin levels which had negative mood stabilizing effects [4,5]. Additionally, it was observed that 50% of patients with Irritable Bowel syndrome were also diagnosed with clinical depression; the underlying adverse mechanism explained by the diminished density of commensal microbiota and increased harmful bacteria. Similarly, mice exposed to chronic social defeat and overcrowding had increased depression, anxiety, and acute colitis. The data of this report revealed the cause to be remodeling of gut microbiomes with decreased commensal bacteroides and increased clostridium and cytokines (IL-6, MCP-1) [6]. A greater density of detrimental microbiota led to hampered synthesis of Brain-derived neurotrophic factor (BDNF) from the hippocampus leading to depression and stressed behavior. This was alleviated by restoring normal levels of BDNF and administration of antidepressants [7]. Mice treated with antibiotics neomycin and bacitracin, combined with antifungal pimarin, demonstrated altered microbiota and reduced anxiety and depression levels. Dysbiosis was induced in

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neonatal mice by Vancomycin which lead to continual negative behavioral changes in adult life [8]. Randomized controlled trials have exhibited the efficacy of probiotics in the treatment of depression. The HPA stress response can be reversed by a psychobiotic known as Bifidobacterium infantis having antidepressant effects. *Lactobacillus helveticus R0052* and *Bifidobacterium longum* were associated with decreased stress and depression scores. *Lactobacillus rhamnosus* showed similar results in a separate report. In another trial, patients diagnosed with major depressive disorder (MDD) were administered probiotics for a time period of eight weeks and later on showed positive outcomes on the Beck Depression Inventory scores [9].

These remarkable findings point towards the new implication, that these seemingly petty gut bacteria might have a greater role in controlling our behavior and decisions, than what we would like to admit. Additionally, it provides scientific light on the fact that the term 'gut feeling' is not merely a phrase but has a deeper-lying understanding to it.

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