Gut Microbiota-Brain Axis and Mental Health

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Abstract

Gut microbiota-brain axis is the two-way information communication network between intestinal microbiota and brain, whose composition includes gut microbes and their metabolite, intestinal tract, enteric nervous system and the sympathetic and parasympathetic branch of the autonomic nervous system, neural immune system, neuroendocrine system and central nervous system. Gut microbiota-brain axis has become one of the hotspots in the field of neuroscience. A growing body of evidences have revealed that gut microbes not only play an important role in maintaining normal healthy homeostasis, but also can affect the individual’s mental health through inflammation, immune system, stress reaction and HPA axis. Dietary changes gut microbes associated with the risk of suffering from mood disorders. Probiotics supplementation not only plays an important role in the treatment of mental disease and regulating gut microbes, but also is a valuable therapy pathway for developing the new treatment methods to treat the brain disorder.

Keywords: Gut microbiota; Inflammation; Immune system; Stress; HPA axis; Dietary; Antibiotics; Probiotics; Mental health

Abbreviations

HPA: Hypothalamic Pituitary Adrenal; CRH: Corticotrophin Releasing Hormone; ACTH: Adreno Cortico-tropic Hormone

Introduction

Many studies have shown that gut microbiota affect brain’s physiological, behavioral and cognitive functions [1-5], and its precise mechanism has not yet been fully understood, with possible 5 routes including the gut-brain’s neuroanatomical pathway, neuroendocrine-HPA axis (hypothalamic-pituitary-adrenal axis, HPA axis) approach, gut immune system approach, path of many neurotransmitters and neural regulators synthesized by gut bacteria and path by intestinal mucosal barrier and blood-brain barrier [6] (see Figure 1). Both clinical and prenatal research show that the gut microbiota plays an important role in maintaining homeostasis of normal health, and if the gut microbiota is damaged, there will be high risk factors for suffering from mental illness and other central nervous system disorders [7].

Gut Microbiota

In human gut, it is estimated to have about 100 trillion “symbiotic” bacteria [7], the total number of cells is at least 10 times that of human cells, over 100 varieties, and the gene is 150 times that of human genome [8,9]. More than 99% of microbiota are anaerobic bacteria in gut, the rest are fungi, protozoa, archaea, and other microbiota. Gut microbiome refers to bacterial colonies and their genes in the gut [10], which also includes human host evolving archaea, protozoa, fungi and viruses. Gut microbiome are mainly determined by 2 major bacterial colonies of firmicutes (about 51%) and bacteroidetes (about 48%), and proteobacteria, actinomycetes, fusobacterium and verrucomicrobia are relatively small in number [11].

Human and gut microbiota are of “mutually beneficial and symbiotic relationship” [12]. The human body provides habitat and nutrition for gut microbiota, and gut microbiota play an important function of human body via immune system, intestinal system, endocrine

system, and nervous system, such as food processing, digesting complex and difficult-to-digest polysaccharides, synthetic vitamins and inhibition of pathogen.

Figure 1: Gut microbiota-brain axis.

Gut Microbiota-Brain Axis

Gut microbiota-brain axis refers to two-way information flow network between gut microbiota and brain, with its components including gut microbiota and their metabolic products, enteric nervous system, sympathetic and parasympathetic branch within autonomic nervous system, neural immune system, neuroendocrine system and central nervous system [6].

Through this network, the brain affects gut movement, sensory and secretion function. On the contrary, viscera information from the gut also affects brain function. For example, incoming and outgoing branches of vagus nerve allow information to transfer in and out of gut. Activation of the vagus nerve has anti-inflammatory effect. Positive effects of many gut microbiota and probiotics on brain function are dependent on the activity of vagus nerve. But other independent mechanism also plays a role.

Gut, inflammation and immune system

Development of gut immune system depends on gut microbiota [13,14]. Segmented filamentous bacterium in gut can restore the full functions of gut B and T lymphocytes [15-17]. Bacteria communicate with the host through a variety of ways, and the receptor-TLRs of host cell plays a key role in this communication between bacteria and host [18]. These receptors are the first step to produce cytokine reaction and is also widely distributed on neurons [19] So, intestinal epithelial cells can transport microbial composition or metabolites into inner environment, and the nervous system also interacts with these bacterial and viral components [20]. The balance of gut microbiota may change the regulation of inflammatory response and this mechanism may also get involved in the regulation of emotion and behavior.

Gut, stress reaction and HPA axis

Depressive disorder involves inflammation [26,27] and HPA [27,28]. Gut microbiota affect the hypothalamus function via pro-inflammatory factors and anti-inflammatory factors [29]. Among them, pro-inflammatory factors stimulate release of corticotrophin releasing hormone (CRH) which is the main polypeptide regulator of HPA axis [30]. HPA stimulates the adrenal glands to release adreno-cortico-
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Tropic-hormone (ACTH), and ACTH is necessary component to the normal stress. However, over-expression of CRH promotes stress overreaction. The system disorder is associated with depression and anxiety [31]. The germ-free mice study indicates that the symbiotic microbiota plays a key role of healthy and balanced immune system [32].

Damage of gut microbiota stimulates HPA activities to release stress hormones, and exogenous stress source direct stimulates HPA. At the same time, HPA also has devastating effects on gut microbiome. Stress leads to changes of intestinal motility and secretion function, which have negative effect on regeneration ability of intestinal mucosa and gut microbiota [33]. Stress reaction releases neuro-transmitters and pro-inflammatory factors, and these neuro-transmitters and pro-inflammatory factors affect intestinal physiology.

**Influence of diet on gut microbiota**

Gut microbiota is a dynamic entity, which is influenced by factors such as gene, diet, metabolites, age, and treatment with antibiotics [7]. Among above the influencing factors, gene, geography and age can't be changed, but other factors can be artificially adjusted so as to change the balance of gut microbiota.

Many studies have shown that diet is associated with the risk of suffering from affective disorder [34,35]. Imbalance of gut microbiota is also known as intestinal imbalance. Imbalance of gut microbiota is a biological pathway for regulating the relationship between diet and risk of suffering from affective disorder. Diet with high fat and high level of refined sugar are an important factor of gut imbalance [36]. Compared with diet with high fat and high level of refined sugar, diet rich in complex carbohydrates can reduce the variety of gut pathogenic bacteria [37], and complex carbohydrates also increases the variety of beneficial bacteria. Too many dietary fibers help to increase production of short chain fatty acid to prevent the growth of potentially pathogenic bacteria. Refined sugar can also mediate overgrowth of bacteria.

**Influence of antibiotics on gut microbiota**

Clinically, people use antibiotics to change the gut colonies to improve brain function of certain diseases. For example, to remove metabolites of gut colonies by regulating intestinal bacteria with application of antibiotics to improve the brain function of hepatic encephalopathy [38,39]. However, rarely to evaluate the role of antibiotics in gut microbiota-the brain axis [4].

In addition, antibiotic treatment can also affect gut balance by eliminating intestinal beneficial bacteria. Probiotics in food such as yogurt, kefir of Russia, kimchi, sauerkraut, and miso etc. can regulate the symbiosis of gut microbiota again, and make gut microbiome rebalancing.

**Effect of probiotics on treating mental disease**

Probiotics are not only good for treatment of antibiotic, but also can prevent and offset attack and damage by high fat and/or high protein diet on gut microbiota. So food containing probiotics should be introduced into food guide as well [40].

Probiotic supplementary treatment not only plays an important role in the treatment of mental diseases and regulating gut microbiota, but also is valuable treatment way of treating brain disorder [41,42]. Research shows that these bacteria can secrete neural active substances, such as gamma-aminobutyric acid and serotonin, and these neural active substances have an effect on gut microbiota-brain axis [43]. It is likely that these probiotics will become a new variety of psychobiotics or antipsychotics in the future [43]. Therefore, it, for patients with mental diseases, may be a reasonable way to improve or reverse their mental diseases via altering their diet and their life way.

**Conclusion**

It can be predicted in the foreseeable future that, study on regulating gut microbiota to affect the brain will be an important achievement and significant progress in the field of neuroscience and will change people’s concept of "stop-gap responses". With the deepening of
research, there will be more evidences to support the concept of altering the brain’s physiology, function and behavior via administering gut microbiota, and to provide a new way for people to "know the brain, protect the brain and exploit the brain", including treating patients with mental disorders.

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Conflict of Interest

The author declares no conflict of interest associated with this manuscript.

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