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Second Brain: Microbiata

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ABSTRACT

A complex organ system formed by the combination of trillions of microorganisms is the intestinal microbiota. It has been known as the second brain because the enteric nervous system can operate independently of the central nervous system and works like a complex organ. By stimulating the immune system and central nervous system, the studies carried out show the physiological and psychological effects of commensal, symbiotic and pathogenic microorganisms living in the gastrointestinal system. It is seen that there is a special microflora for these diseases, especially when microbiota are examined in some diseases. Significant evidence has been presented that metabolic diseases such as obesity, diabetes, asthma, Crohn's, and neurodegenerative disorders such as schizophrenia, parkinson's, alzheimer's, depression/anxiety are correlated with the gut (bowel) microbiota. The impact on human health of intestinal microbiota and bacteria tend to be of greater interest in the coming years. The physiological and psychological effects of intestinal microbiota on human health are reviewed in this article as a result of changing diet and affecting the immune system and brain.

Keywords: *Brain, Bowel, Diet, Gastrointestinal System, Microbiota*

Introduction

Microbiota refers to communities of commensal, symbiotic and pathogenic microorganisms found in different parts of the body. By defining the microbiota, organisms such as bacteria, fungi, protozoa and viruses which live on the epithelial barrier surfaces of our body, or all of the special species we live with, they actively work on many physiological functions, especially the shaping, maintenance, absorption, digestion, intestinal motility and mucosal immunity of human physiology (Heintz-Buschart & Wilmes, 2018; Yoldaş & Türeyen, 2020). The organism community in various parts of the body such as mouth, pharynx, skin, respiratory system, gastrointestinal and urinary systems are the most vital creatures responsible for the maintenance of the host's homeostasis (Dominguez-Bello et al., 2019). When microbiota is mentioned, the first thing that comes to mind is the gastrointestinal system (GIS). The gut microbiota is called the second brain because it contains the largest number of bacteria and nerve cells with the presence of trillions of microorganisms and works like a complex organ system (Kalip & Atak, 2018). As a result of the studies, the human body is known to have microorganisms at least ten times the amount of its own cells, more than 75% of which are in the colon, and more than 35,000 species of bacteria live in the GIS. The composition of intestinal microbiota, such as Firmicutes, Bacteroidetes, Proteobacteria, Verrucomicrobia, Actinobacteria, Fusobacteria, Lentisphaerae, Spirochaet and Cyanobacteria, is dynamic and the main bacterial groups live (Khanna & Tosh, 2014). Gram-positive Firmicutes and

gram-negative Bacteroidetes are known as the most dominant groups of bacteria within these bacterial groups (Eckburg et al., 2005; Çelebi & Uygun, 2013).

However, human intestinal microbiota includes more than 1000 species and more than 7000 subspecies (Lozupone et al., 2012). Intestinal bacteria can produce active metabolites for human organ systems. For example, Lactobacillus and Bifidobacteria can synthesize gamma amino butyric acid from monosodium glutamate (Barret et al., 2012). While Escherichia, Bacillus and Sacromicesler norepinephrine, Candida, Streptococcus, Escherichia and Enterococcus produce serotonin, Bacillus and Serracia produce dopamine (Lyte, 2011). An increase in plasma tryptophan levels was observed in rats administered orally with Bifidobacterium infantis (Desbonnet et al., 2008). Lactobacillus acidophilus increases the expression of cannabinoid receptors in the brainstem (Muccioli et al., 2010). On the other hand, plasma serotonin levels were found to be high in germ free mice (Collins, 2009).

Under the influence of diet, medication and stress, intestinal microbiota diversity can change. A decrease in the levels of proteobacteria and actinobacteria and a rise in firmicute levels were identified after 21 days of olanzapine administration in rodents (Davey et al., 2013). Separation from the mother in rats has been shown to cause fecal lactobacillus levels to decrease even on the third day and its effect on the microbiota continues for a long time (O'Mahony et al., 2009; Evrensel & Ceylan, 2015).

The diversity of microbiota and its presence in the intestine vary depending on the diet. Since GIS is intensely innervated by neurons inside and outside the intestine, the intestinal microbiota regulates many functions in the body and works together with the central nervous system. The gut microbiota affects neurons in the central nervous system through enteric neurons by producing various metabolites, regulates the physiology and metabolism of the host, and also affects autonomic functions, brain function, motor coordination, affection, temperature regulation, behavior and cognition, and functions through the gut-brain axis.

Formation of Intestinal Microbiota and Immunity

The bacteria acquired by the mother and environmental factors during birth form the growth of the intestinal microbiota (Backhed et al., 2007; Round et al., 2010; Evrensel & Ceylan, 2015). In humans, immediately after birth, GIS starts to take shape and develop. Olszak et al., stated in their article published in Science magazine in 2012 that the diversity of microbiota produced in the perinatal period has a lifelong effect on natural killer Tlymphocytes (Olszak et al., 2012).

It has been known for many years that microorganisms in the gut can affect the synthesis of some vitamins or the degradation of some nutritional components, which is, the effects of the microbiota on nutrition. It is thought that a significant part of the differences in intestinal microbial patterns of individuals can be explained by the differences in their nutritional status. It is known that nutrition can affect both gut microbiota composition and function by affecting microbial diversity, microbial taxonomy, genetic information, gene expressions and enzyme activities.

Bacteria living in the intestines interact with human cells (Dinan & Quigley 2011). This interaction occurs with Toll-like receptors (TLR), one of the pattern recognition receptors (PRR) (Carvalho et al., 2012; Lucas & Maes, 2013). In addition, 10 TLR types have been defined in the immune system (Takeuchi & Akira, 2010). These receptors are the first step in the cytokine production pathway and are found commonly in neurons (McKernan et al., 2011; McCusker & Kelley, 2013).

It is known that inflammatory cytokines such as interferon alpha cause depression and can be prevented by antidepressant drugs (Udina et al., 2012; McNutt et al., 2012). In addition to the effect

of antidepressants on monoamines, it is thought to have an antidepressant effect by suppressing inflammation via the powerful immunoregulatory cytokine IL-10 (Maes et al., 2005). In addition, it is known that probiotics have an antidepressant effect by increasing the level of IL-10 (Levkovich, 2013).

Interest in microbiota and probiotic therapies in the formation and development of immunity has become popular in recent years. Toxins are bound by probiotics and inhibit their absorption from the intestines. To minimize complaints of diarrhea, indigestion and bloating, tablets and capsules are used. By binding to toxins secreted by the microbiota, it assists the GIS to relax (Fond et al., 2014). In the treatment of Clostridium difficile infection, Irritable bowel syndrome and ulcerative colitis/ Crohn's disease, fecal microbiota transplantation (FMT) has long been used successfully (Brandt, 2013). Studies on its efficiency have recently increased in the treatment of cardiometabolic and autoimmune disorders (Smits et al.,. 2013; Rook et al., 2015). Restoration of the microbiota with probiotics without the need for FMT should be the ideal approach.

The Role and Effects of Intestinal Microbiota on Brain Functions

GIS is defined as the biggest immune organ, and GIS-related metabolites may be neuropathogenic (Severance et al., 2014). The potential effects on the central nervous system of the effect of microbiota are summarized as: changes in microbial content, immune stimulation, neural pathways, metabolism of tryptophan, intestinal hormonal response, metabolites of bacteria (Collins & Bercik 2009; Borre et al., 2014; O'Mahony et al., 2015).

Significant effects on intestinal microflora are determined by long-term eating habits. For both our body and the microbial flora, carbohydrates are an essential source of energy. The production of short-chain fatty acids increases as a result of the fermentation of carbohydrate weighted diets in the intestines, and their mixing into the systemic circulation affects brain functions (MacFabe et al., 2012; Kimura et al., 2013). There are opinions that high carbohydrate nutrition produces autistic behaviors as a consequence of the studies (MacFabe, 2012).

The nervus vagus establishes a direct link between the brain and the stomach and intestines like a wide highway. Hormonal, neural and interestingly bacterial change in the intestines is transmitted to the brain via the nervus vagus (Borovikova et al., 2000, Perez-Burgos et al., 2013). Intestinal microbiota has been shown to have an effect on brain development and plasticity by secreting many neurotrophins and proteins such as brain derived neurotrophic factor (BDNF), synaptophysin, PSD-95 (Heijtz et al., 2011; Douglas-Escobar et al., 2013).

The microbiota is affected by stress from external factors, probiotics, antibiotics and nutrient content taken with the diet. Moreover, brain synapses are affected and reflected in our behaviour as a result of microbiota activities. The role of intestinal microbiota is very important in psychiatric disorders. In particular, there is a lot of research on microbiota schizophrenia, anxiety and depression, autism spectrum disorder, irritable bowel syndrome, cognitive disorders, alcohol dependency, obesity, and metabolic disorders.

It has been shown that minocycline, a second generation tetracycline, produces antipsychotic-like effects in rats, and is effective especially on negative symptoms in additional treatment of schizophrenia and treatment-resistant schizophrenia (Jhamnani et al., 2013; Khodaie-Ardakani et al., 2014, Dokuyucu et al., 2014; Liu et al., 2014; Qurashi et al., 2014).

Severance et al. clinically studied the impact of microbiota on schizophrenia and found that microbial products involved in systemic circulation caused immune imbalances in schizophrenia

when the serological immune markers were compared between schizophrenia, bipolar patients, and the control group (Severance et al., 2013).

The relationship between microbiota and anxiety/depression has been studied mostly in animal experiments (Lyte et al., 1998; Dinan et al., 2013; Desbonnet et al., 2010). In the study conducted in 2011 by Bravo et al., a decreasement was found in both anxiety and depression scores in mice given Lactobacillus rhamnosus for 28 days (Bravo et al., 2011).

Milk fermented with probiotic bacteria in healthy individuals has a beneficial effect on emotional centers. Berk et al. reported that in depression, there is a chronic, low-level inflammatory condition that may be related to intestinal permeability disorder. The critical role of unhealthy diets and depression is thought to be the microbiota (Dash et al., 2015).

We can clearly see the beneficial effects of probiotics, especially in nutritional habits, in irritable bowel syndrome. Bifidobacterium infanticin showed significant improvement in gastrointestinal symptoms in a parallel group placebo-controlled study (O'Mahony et al., 2005).

Dietary changes in mouse studies have been shown to affect the functions of learning and memory by leading to the diversity of gut microbiota differentiation (Kang et al., 2014). Whether cognitive dysfunctions occur directly or by inducing anxiety is not understood.

Muccioli et al. suggested that intestinal microbiota interacts with cannabinoid receptors in the brainstem, especially Lactobacillus acidophilus stimulates the production of cannabinoid receptors, and thus this bacterium may be associated with obesity (Muccioli et al., 2010). In a 2015 mouse experiment, stool was taken from mice on a high-fat diet and transplanted into the intestines of mice on a normal diet (fecal microbiota transplantation, FMT). In mice fed a normal diet, deterioration in intestinal wall continuity, increase in circulating endotoxins, increase in TLR-2 and TLR-4 levels, increase in neuroinflammation, deterioration in cerebrovascular homeostasis and behavioral changes were detected. It is an interesting evidence that obese type intestinal microbiota causes immunological and behavioral changes before obesity occurs (BruceKeller et al., 2015; Evrensel & Ceylan, 2015).

Conclusion

It is acknowledged that many diseases are predisposed to eating habits and the basis of this knowledge targets groups of microorganisms that are later involved in our gastrointestinal system. Since bacteria that reside in the intestines interact with human cells. By influencing our growing and living microbiota system, our diet, which has become our daily routine, forms the basis of our immune system and behavior. Metabolic diseases such as obesity, diabetes, asthma, and neuropsychiatric disorders such as schizophrenia, autism, anxiety, and depression are closely linked to the damaged or undeveloped gut microbiota, based on the hypothesis that all diseases start in the intestine. New research shows the stimulation of the immune system and central nervous system by friendly, harmful and probiotic microorganisms living in GIS. By improving our eating habits effectively, by reducing the triggers of many physiological and psychological diseases, we can enhance our quality of life.

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