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Commentary Paper

Gut Microbiota and Neuropsychiatric Disorders

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ABSTRACT

Numerous studies in humans and animals hypothesize that gut microbiota dysbiosis is involved in the development of behavioral and neurological diseases such as depression, autism spectrum disorder, Parkinson disease, multiple sclerosis, stroke and Alzheimer's disease. Some of the most salient works so far regarding the brain-gut axis are mentioned below. The current knowledge on the impact of gut microbiota on nervous system diseases is far from being directly used for pharmacologic or nutritional advice toward restoration of normal bodily functions. It seems that a more comprehensive approach should be followed so that the individual effect of each kind of intervention on the patient's somatic or psychological status is determined. Future research must address global need for regimens which could re-establish normal composition of gut microorganisms after each neuropsychological disorder.

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Highlights

- Microbiota dysbiosis is involved in development of neuropsychological diseases
- Some of the salient works so far regarding the brain-gut axis are mentioned here
- Regimens are needed for re-establishing normal microbiota in nervous system diseases

Plain Language Summary

A population of commensal microorganisms called microbiota inhabit the human body. Microbiota colonizes various places including the skin, mouth, nose, pulmonary tract and genitourinary tract especially vagina. However; the gastrointestinal tract has the largest population of microbiota including bacteria, fungi, parasites and viruses that are symbiotic with the host and affect host metabolism. The interaction between the microbes living inside or outside of our body and our brain is important for our brain health, and this fact is shown in numerous past studies, some of which summarized in this paper. Nervous system diseases such as depression, autism spectrum disorder, Parkinson disease, multiple sclerosis, stroke and Alzheimer's disease are all affected by the composition of our commensal microorganisms. In many instances the diversity of the microbes is reduced or altered in neuropsychiatric disorders which needs hands-on dietary modifications to be used by people. The current knowledge on the influence of gut microbiota on neuropsychiatric problems is far from being directly used for pharmacologic or nutritional advice toward restoration of normal bodily functions. Here we emphasize the importance of future research toward finding the impact of each diet, medication or food supplement on various aspects of the relationship between body microbes and neurological, behavioral or developmental brain problems.

1. Commentary

The human body is covered by a population of commensal microorganisms called microbiota. Microbiota colonizes various places, including the skin, mouth, nose, pulmonary tract, genitourinary tract, and especially vagina. However; the gastrointestinal (GI) tract has the largest population of microbiota including bacteria, fungi, parasites, and viruses that are symbi-otic with the host and improve host metabolism (Erny et al., 2017; Lynch & Pedersen, 2016).

Numerous studies in humans and animals hypothesize that gut microbiota dysbiosis is involved in the development of behavioral and neurological diseases, such as depression, autism spectrum disorder (ASD), Parkinson's disease (PD), multiple sclerosis, stroke, and Alzheimer's disease (AD) (Borre et al., 2014; Dalile et al., 2019; Sharon et al., 2019; Zhang et al., 2017). Due to the vast usage of antibiotics in communities leading to altered gut microorganisms, and also due to the unknown nature of many psychiatric and neurologic disorders are unknown, it is wise to consider studies related to these two dilemmas. Some of the most salient works so far are mentioned below. Each piece of data or information seems encouraging toward finding hands-on treatments for a specific disorder.

In a pilot study, the use of a multivariate probiotic, including *Lactobacillus*, *Bifidobacterium*, and *Streptococcus* species twice a day for 2 months changed the microbiota and had anti-inflammatory properties (Tankou et al., 2018).

In a study conducted by Finegold et al., several pathobionts, such as *Proteobacterium* and *Desulfovibrio* were increased in the feces of children with Autism spectrum disorder (ASD) that produce hydrogen sulfide. The question is why the balance of microbial metabolites was disturbed in these children (Finegold, 2011). Autism studies in animal models reported altered microbiota composition. In human patients with autism disorder and animal models, the administration of a single bacterial strain (*Bacteroides fragilis* or *Lactobacillus reuteri*) can reverse many behavioral and GI changes (Buffington et al., 2016; Sgritta et al., 2019).

In another study on schizophrenic patients, the microbial community of *Clostridiales*, *Prevotella*, and *Lactobacillus ruminis* was found to increase, resulting in higher production of short-chain fatty acids (SCFAs) (He et al., 2018).

The administration of probiotics has been introduced as a suitable treatment for neurodegenerative diseases, such as AD. Accordingly, treatment of 3xTg-AD mice with probiotics re-sulted in a good reduction in inflammatory cytokines and cognitive deterioration. It appears to be due to reduced brain damage and reduced accumulation of amyloid beta aggregates (Bonfili et al., 2017). *Corpora Amylacea* (CA) is found in the brain of patients with AD or other neurodegenerative disorders. Two fungal proteins, anolase and b-tubulin, and chitin poly-saccharide can be detected in the cerebral tissues of patients with AD using rabbit polyclonal antibodies. It is hypothesized that CA may be a response to microbial infections in the brain (Pisa et al., 2016).

Sequencing the fecal microbiome of patients with PD revealed a decrease in the *Bacteroidetes* and *Prevotellaceae* but increased concentrations of short-chain fatty acids (SCFA) and *Enterobacteriaceae* compared to the control group (Unger et al., 2016). The presence of gut microbes is influential in eliciting pathophysiological alterations, especially motor dysfunction in PD in a mouse model of α-Syn overexpression, therefore eliminating the gut microbiota with antibiotics ameliorated the condition (Sampson et al., 2016).

The diversity (non-uniformity) of microbiota in healthy people is allegedly greater than in patients with amyotrophic lateral sclerosis (ALS). The frequency of pathobionts (Firmicu-tes/Bacteroidetes and genus *Methanobrevibacter*) was higher in these patients, while the beneficial microorganisms (*Faecalibacterium* and *Bacteroides*) were less (Zhai et al., 2019). Another study showed that transgenic amyotrophic lateral sclerosis (ALS) mice developed more severe disease when treated with antibiotics. Also, several species of bacteria have been identified associated with disease progression (Blacher et al., 2019).

The presence of gram-positive filamentous bacteria in the GI tract that activate Th17 cells significantly affects the severity of experimental autoimmune encephalitis (Berer et al., 2017).

Increased gut permeability, colonic mucosal destruction, and colonic IL-1β expression due to chronic administration of morphine in a mouse model were prevented by an antibiotic cocktail that depleted gut microbiota. Morphine tolerance was also prevented by broad-spectrum antibiotics. It shows that the GI microbiota can alter physiological responses in the nerv-ous system (Kang et al., 2017).

The role of gut clostridia in GI sensorimotor function via serotonergic pathways in patients with irritable bowel syndrome was shown in another study. Through network analysis, neu-roimaging and assessment of fecal RNA, they found that certain members of the order Clostridiales can modulate host 5-HT biosynthesis, and release, and influence some brain regions, including subcortical (and to a less degree cortical) neural connections (Labus et al., 2019).

The current knowledge on the impact of gut microbiota on neuropsychiatric problems is directly used for pharmacologic or nutritional advice to restore normal bodily functions. It seems that a more comprehensive approach should be followed to determine the individual effect of each kind of intervention on the patient's somatic or psychological status. Future research must address the global need for regimens that can restore the normal composition of gut microorganisms after each neuropsychological disorder.

Ethical Considerations

Compliance with ethical guidelines

All ethical principles are considered in this commentary.

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Authors' contributions

All authors equally contributed to preparing this article.

Conflict of interest

The authors declared no conflict of interest.

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