Title: Gut Microbiota and Neuropsychiatric Disorders

Authors: Reza Bidaki¹, Seyed Hossein Hekmati Moghaddam², Maryam Sadeh³*

1. MD, Associate Professor of Psychiatry, Research Center of Addiction and Behavioral Sciences, Diabetes Research Center, Shahid Sadoughi University of Medical Sciences, Yazd, Iran. Email: reza_bidaki@yahoo.com
2. MD, Associate Professor of Pathology, Department of Advanced Medical Sciences and Technologies, School of Paramedicine, Shahid Sadoughi University of Medical Sciences, Yazd, Iran. Email: shhekmati2002@yahoo.com
3. PhD, Assistant Professor of Microbiology, Department of Laboratory Sciences, School of Paramedicine, Shahid Sadoughi University of Medical Sciences, Yazd, Iran.

*Corresponding author: Maryam Sadeh, PhD, Assistant Professor of Microbiology, Department of Laboratory Sciences, School of Paramedicine, Shahid Sadoughi University of Medical Sciences, Yazd, Iran. Email: sadeh_m20@yahoo.com

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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, especially vagina. However; the gastrointestinal (GI) tract has the largest population of microbiota including bacteria, fungi, parasites and viruses that are symbiotic with the host and improve host metabolism (Erny, Hrabe de Angelis, & Prinz, 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, Van Oudenhove, Vervliet, & Verbeke, 2019; Sharon et al., 2019; Zhang et al., 2017). Due to vast usage of antibiotics in communities leading to altered gut microorganisms, and also due to unknown nature of many psychiatric and neurologic disorders are unknown, it is wise to consider studies relating these two dilemmas. Some of the most salient works so far are mentioned below. Each piece of data or information looks 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 by Finegold et al., it was found that several pathobionts such as Proteobacterium and Desulfovibrio were increased in the feces of children with ASD which produce hydrogen sulfide. The question is why the balance of microbial metabolites in these children was disturbed? (Finegold, 2011). Autism studies in animal models reported altered microbiota composition. In human patients with autism disorder and animal models, administration of a single bacterial strain (Bacteroides fragilis or Lactobacillus reuteri) could 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 increased, resulting in higher production of short-chain fatty acids (SCFAs) (He et al., 2018).
Administration of probiotics has been introduced as a suitable treatment for neurodegenerative diseases such as AD. Accordingly, treatment of 3xTg-AD mice with probiotics resulted 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 polysaccharide can be detected in the cerebral tissues of patients with AD using rabbit polyclonal antibodies. It has been hypothesized that CA may be a response to microbial infections in their brain (Pisa, Alonso, Rabano, Horst, & Carrasco, 2016).

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

Diversity (lack of uniformity) of microbiota in healthy people is allegedly greater than in patients with amyotrophic lateral sclerosis (ALS). The frequency of pathobionts (Firmicutes/Bacteroidetes and genus Methanobrevibacter) in these patients was more, while the beneficial microorganisms (Faecalibacterium and Bacteroides) were less (Zhai, Zheng, An, Huang, & Tan, 2019). Another study showed that transgenic 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).

The increases in gut permeability, colonic mucosal destruction, and colonic IL-1β expression due to chronic administration of morphine in a mouse model was prevented by an antibiotic cocktail which depleted gut microbiota. Morphine tolerance was also prevented by broad-spectrum
antibiotics. It shows that the GI microbiota can alter physiological responses in the nervous 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, neuroimaging 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).

Collectively, the current knowledge on the impact of gut microbiota on neuropsychiatric problems 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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