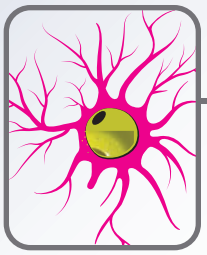

Neurobiological mechanisms of mental disorders and diet as a modulator

By Yoon Suh Moh

This article is the second in a three-part series on an intricate combination of determinants of mental health, with an emphasis on diet as a lifestyle factor. This month, we are covering major areas of the selective neurobiological pathways of mental disorders that are likely modulated by diet. In addition, we will address the effects of early life experiences on the development and functional health of the bidirectional gut-brain dialogue, as well as microorganisms residing on our skin and inside our guts. We will also examine the current state of the use of nutraceutical interventions for mental disorders and provide information regarding dietary assessment in practice.

Pathways in mental disorders and diet

Wolfgang Marx and colleagues noted in 2017 in *Proceedings of the Nutrition Society* that several neurobiological pathways are implicated in mental illness, including inflammation, oxidative stress, brain plasticity, the microbiota-gut-brain (MGB) axis and mitochondrial dysfunction. These authors addressed the importance of understanding that these pathways likely overlap synergistically and intricately interact with one another in relation to human functioning.

Despite the complexity of these mechanisms pertaining to mental disorders, the good news is that emerging evidence suggests these pathways can be modulated by diet. In this article, we will focus on the MGB axis. In 2018 in *OMICS: A Journal of Integrative Biology*, Stefanie Malan-Muller and colleagues described the MGB axis as the bidirectional communication between the brain and gut microbiota.

Microbiota, microbiome and the MGB axis

Our bodies consist of numerous host cells. These cells cohabit with a wide variety of commensal microorganisms such as bacteria, eukaryotes, archaea and viruses, collectively called the *microbiota*. Maneesh Dave and colleagues noted in *Translational Research* in 2012 that the *microbiome* is defined as the complete catalog of these microorganisms and their genes.

Counselors are familiar with Urie Bronfenbrenner's ecological systems theory that says humans are at the core of interrelating systems (i.e., micro-, meso-, exo-, macro- and chronological systems) operating as one organism, and that their development is influencing and influenced by the interrelations of each of those systems across the life course. From a cellular perspective, however, the human body itself is viewed as an ecosystem in which the host cells and microorganisms coexist in symbiosis across the life span. Furthermore, Ygor Parladore Silva and colleagues noted earlier this year in *Frontiers in Endocrinology* that the host microbiota colonize our skin and several of the body's mucosal cavities (e.g., nasal, oral, pulmonary, vaginal). The gastrointestinal track of the body is a habitat for the majority of these microorganisms.

The Human Microbiome Project was launched in 2007 by the National Institutes of Health to study microbial communities associated with the human body. Emerging evidence from this project supports the significant roles of gut microbiota in the human body. As described by Ilseung Cho and Martin J. Blaser in *Nature Reviews Genetics* in 2012 and Noah W. Palm and colleagues in *Clinical Immunology* in 2016, these roles include protecting against pathogens; regulating metabolic, endocrine and immune functions; and influencing drug metabolism and absorption. For more detailed information on milestones in human microbiota research, counselors are referred to the Nature.com webpage at *tinyurl.com/NatureMicrobiotaMilestones*.

Gut microbiota roles

Silva and colleagues also noted that growing evidence suggests the influence of the microbiota is not restricted to the gastrointestinal tract. Rather, it also plays a pivotal role in the bidirectional communication between the gastrointestinal tract and the central nervous system (CNS). In addition, Paul Forsythe and colleagues reported in *Advances in Experimental Medicine and Biology* in 2014 that there are varying potential pathways through which the gut microbiota can influence brain function.

Furthermore, microorganisms can influence CNS processes bidirectionally via the vagus nerve. This bidirectional communication can also occur through the modulation of the immune system, as described by Daniel Erny and colleagues in *Nature Neuroscience* in 2015.

Boushra Dalile and colleagues reported in 2019 in *Nature Reviews Gastroenterology & Hepatology*

that microbiota have the ability to synthesize a number of neurotransmitters and produce metabolites that possess neuroactive properties. In 2018, Hamid Said and colleagues described gut microbiota metabolites in the sixth edition of *Physiology of the Gastrointestinal Tract* as metabolic end products of the microbiome, whereas the microbiome is seen as an initial genetic programming of the gut microbiota.

Gut microbiota in mental disorders

Emeran Mayer reported in 2016 that the diversity and abundance of gut microbiota are implicated in gut health, and this intricately relates to brain health, leading to overall health and mental health. For instance, Johan Söderholm and Mary H. Perdue reported in the fourth edition of *Physiology of the Gastrointestinal Tract* in 2006 that commensal microorganisms stimulate the gastrointestinal outer lining (called the epithelium) to produce anti-microbial peptides that act as a first line of defense against invaders (e.g., pathogenic bacteria).

In contrast, in *Cellular Microbiology* in 2014, Charisse Petersen and June L. Round characterized microbial dysbiosis as a disturbance in gut microbiota, abnormal host-microbiota interactions, loss of beneficial microbiota, low microbial diversity and an increase in pathogens. Per Yuliya Borre and colleagues in *Trends in Molecular Medicine* in 2012, microbial dysbiosis has been implicated in behavioral, neurodevelopmental (e.g., autism spectrum disorder) and neurodegenerative (e.g., Alzheimer's and Parkinson's diseases) pathologies. According to Jane A. Foster and Karen-Anne McVey Neufeld in *Trends in Neurosciences* in 2013, it has also been implicated in neuropsychiatric conditions (e.g., depression and anxiety). Per Christina Casén and colleagues in *Alimentary Pharmacology and Therapeutics* in 2015, it has been implicated in bowel disease (e.g., irritable bowel syndrome (IBS)). Additionally, Marx and colleagues reported that the gut microbiota have been implicated in a variety of neurobiological pathways via the modulation of brain-derived neurotrophic factor (BDNF), serotonin neurotransmission, immune function, and the stress response mediated by the hypothalamic-pituitary-adrenal (HPA) axis.

In animal studies, Nobuyuki Sudo and colleagues reported in *The Journal of Physiology* in 2004 that germ-free mice with a deficiency in gut microbiota exhibited a heightened stress response. In addition, Gerard Clarke and colleagues noted in *Molecular Psychiatry* in 2013 that lower BDNF and serotonin receptor levels in the cortex and hippocampus of the brain were observed in germ-free mice that were microbiota deficient compared with normal gut-colonized mice. Also, Siobhain M. O'Mahony and colleagues reported in *Biological Psychiatry* in 2009 that the activation of the HPA axis was associated with the modulation of gut microbial composition in rats.

In clinical studies, John R. Kelly and colleagues reported in the *Journal of Psychiatric Research* in 2016 that there was a decrease in gut microbiota richness and diversity in rats with depression-related behaviors when compared with healthy counterparts. Furthermore, Peng Zheng and colleagues noted in *Molecular Psychiatry* in 2016 that the transplantation of microorganisms from depressed clients into rodents resulted in depression-related behaviors.

Early life experiences and the gut microbiota

The diversity and richness of gut microbiota are highly related to human health across the life span. Mayer reported in *The Mind-Gut Connection* in 2016 that the diversity in gut microorganisms is low during the first three years of life when a stable gut microbiome is being established. Fatemeh R. Kapourchali and colleagues wrote earlier this year in *Nutrition in Clinical Practice* that multiple factors are known to influence the development of the infant microbiota. Specifically, gut microbial composition initiates from the gestational period and is influenced by gestational age, mode of delivery and mode of feeding. According to these authors, maternal conditions (e.g., maternal body weight, diet, risky lifestyles) during gestation, lactation, and other factors (e.g., genetics, maternal vaginal and skin microorganisms) also influence the infant's microbial composition. In short, early life factors such as antibiotics and environmental exposure influence the trajectory of microbiota development.

According to Mayer, microbial diversity reaches its maximum level during adult life and declines as we age. The aforementioned low diversity during the early period of life puts us at high risk for developing neurodevelopmental disorders (e.g., autism spectrum disorder), whereas the late period of low diversity coincides with a higher risk of developing neurodegenerative diseases (e.g., dementia).

Furthermore, for healthy brain development, a period prior to birth also holds significance. Malan-Muller and colleagues reported that during the perinatal period, the functional development of the mammalian brain is susceptible to both internal and external environmental cues.

Additionally, L. Desbonnet and colleagues noted in *Neuroscience* in 2010 that the commensal bacterium (e.g., bifidobacterium infantis) has the ability to modulate tryptophan metabolism. This suggests that the gut microbiota can influence the precursor for neurotransmitters such as serotonin and various tryptophan metabolites. Malan-Muller and colleagues reported that these results underscore the importance of the gut microbiota in very early life developmental stages and their effects on neurodevelopment and mental health.

Early life adversity and gut-brain communication

Given the high prevalence rates of trauma exposure in the U.S. general population as reported by the Centers for Disease Control and Prevention, counselors should understand the

effects of early adversity on gut and brain health and their intricate dialogue with each other. Bridget Callaghan and colleagues reported in *Development and Psychopathology* in 2019 that exposure to early life adversity (e.g., stressful life events, parental neglect, community violence) was a potential risk factor for both gastrointestinal and health issues in children and adolescents. In addition, Kara Bradford and colleagues noted in *Clinical Gastroenterology and Hepatology* in 2012 that early adversity was associated with up to a threefold increase in risk of IBS symptoms. Katie A. McLaughlin and colleagues reported in the *Archives of General Psychiatry* in 2010 that this increased risk contributes to more than a third of lifetime mental illness diagnoses.

Interestingly, Natasha A. Koloski and colleagues noted in *Alimentary Pharmacology & Therapeutics* in 2016 that, in a prospective cohort study, IBS was shown to precede mood disturbances in over 60% of respondents, whereas the mood disturbance preceded IBS in only 30% of cases. According to Callaghan and colleagues, addressing gastrointestinal symptoms may be particularly important in treating elevated anxiety in populations with adversity exposure, especially early in life, because alleviating the gastrointestinal distress could mediate the adversity-anxiety relationship.

Additionally, Johanna Bick and colleagues in *JAMA Pediatrics* in 2015 and Jennifer A. Silvers and colleagues in the *Journal of Neuroscience* in 2016 reported that caregiver neglect was associated with a heightened risk for atypical functional and structural development of the prefrontal cortex and amygdala, prefrontal cortex connectivity, amygdala reactivity, and changes in the default resting state network. Not surprisingly, according to Howard Mertz and colleagues in *Gastroenterology* in 2000, these patterns overlap with the hubs of dysregulated neural activity seen in adults with IBS symptoms.

Counseling implications

Women during pregnancy: Particularly when counseling women during pregnancy, it is critical for counselors to provide education on the roles of diet and nutrition, especially given the impact of diet on women's mental health during pregnancy, their offspring's microbial development in infancy, and emotional behavior in childhood. In addition, it may be ideal for counselors to collaborate with other key professionals such as OB-GYNs and clinical dietitians for optimal care of female clients during the perinatal period. Marx and colleagues reported that women are more susceptible to nutrient deficiencies during pregnancy because of increased physiological stress on the body and increased nutrient demand from the growing fetus.

Furthermore, Tiffany Field reported in *Infant Behavior and Development* in 2011 that perinatal depression affects 1 in every 7 women and is one of the most common complications during pregnancy, resulting in negative consequences on developmental outcomes in their offspring. Similarly, in 2015, Rachel Baskin and colleagues, writing in the journal *Appetite*, noted an association between poor diet quality and antenatal depression, although evidence was inconsistent for an association between diet quality and postnatal depression and anxiety. Following the recommendation made by the U.S. Preventive Services Task Force in 2016 and again in 2018, it is recommended that counselors conduct depression screenings when working with perinatal women.

Dietary assessment: The 2014 *ACA Code of Ethics* recommends that counselors use assessment as one component of the counseling process. As mentioned in the first article of this series, diet as a modifiable lifestyle factor plays a pivotal role in our mental states (along with numerous other factors). Thus, incorporating diet into our usual practice of conducting a biopsychosocial assessment is important.

Whereas dietary guidelines provide a good road map for a healthy diet, conducting an intentional dietary assessment helps counselors identify both quantitative and qualitative characteristics of clients' diets. According to the online course on food and mood provided by Deakin University, the assessment of personal dietary intake can help us better understand eating habits, track down eating patterns, and map out areas for improvement. Among the popular assessment tools in practice and research are:

- Diet record: Recording all foods and beverages consumed over three days
- 24-hour dietary recall: Reporting all foods and beverages consumed over the past 24 hours in an interview
- Food frequency questionnaire: Reporting the frequency of consumption and portion sizes of a range of foods and beverages over a long-term period

In addition, a food diary that records when, what and how much food and beverage was consumed and a checklist that calculates a specific score for consumption of a specific food or food group (e.g., vegetables) are also good tools for dietary assessment in practice. For additional details on dietary assessment, counselors can review a resource guide published by the Food and Agriculture Organization (FAO) of the United Nations in 2018 (see *tinyurl.com/FAODietAssessment*).

Alternative interventions: Counselors may not directly provide the interventions described in this section unless they have additional training and education pertaining to this area. However, they may still find the following interventions helpful.

Emerging evidence indicates that some nutraceutical and dietary supplements could help manage mental health. The aforementioned food and mood course from Deakin University defines *nutraceuticals* as foods or food components with functional capacity to prevent or treat disorders, whereas *dietary supplements* are defined as products that contain dietary ingredients (e.g., herbs, vitamins, minerals). Specifically, Jerome Sarris and colleagues reported

in *The American Journal of Psychiatry* in 2016 that some nutraceuticals (e.g., S-adenosylmethionin, methylfolate, omega-3, vitamin D) used in combination with antidepressants reduced depressive symptoms. Felice Jacka reported in 2017, however, that diet and nutritional supplements are not equivalent, and data supporting the utility of such supplementation in mental illness are somewhat limited, with the exception of omega-3 supplementation.

Emerging evidence also supports the investigation of probiotics in health conditions, including mental illness. In the FAO and World Health Organization's 2002 guidelines for the evaluation of probiotics in food, a *probiotic* is defined as "a live microorganism which, when administered in adequate amounts, confers a health benefit on the host." However, Jacka noted in 2017 that the available data are preliminary at this time. To learn more about the current state of probiotics use in health care, counselors might consider watching an international forum titled Vital Cells of Existence: The Science of Your Microbiome, launched in 2019 via the World Science Festival (see *tinyurl.com/VitalCellsMicrobiome*). ❖

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