You are what you eat: Mental health and the microbiome

As humans, much of what we assume about reality is based on our senses. In particular, if we can't see it, hear it or feel it, then it is not likely to occupy a place in our consciousness.

In this world of the senses, humans tend to have an "us versus them" view of nature. *Homo sapiens*, in our mind's eye, exists as an elegant, self-sustaining species quite distinct from the rest of the plant and animal kingdom. Of course, we at times rely on other species to provide energy and the materials we need to sustain healthy growth, development and maintenance of our own protoplasm. However, once we have eaten and digested a good salad, the relationship with the spinach, tomatoes and cucumbers often ends, and we move back to being autonomously functioning units, responsible for our own survival and dependent on clever ways of reaping the nutritional benefits of other living things.

But the reality we have constructed of ourselves as autonomously functioning is startlingly inaccurate. Enter the world of microbes — an ancient and diverse collection of organisms including bacteria, fungi and other microscopic organisms, which for the purposes of this discussion, we will limit to bacteria.

Although we are generally unaware of bacteria (with the possible exception of the sights and smells of some of our longer refrigerator "experiments" and occasional bouts of strep throat), their presence is ubiquitous. Their sheer numbers leave the remaining life on the planet in a thick cloud of dust. Justin and Erica Sonnenburg, authors of *The Good Gut,* offer an astounding description of the bacterial world as consisting of 5 nonillion (5×10^{30}) tiny earthly citizens whose biomass exceeds that of the totality of all of the planet's animals and plants combined.

Any illusion of human autonomy must be adjusted to accommodate the notion that bacteria are amazingly proficient at finding places to put down roots and "raise a family." This includes covering every possible surface of the human body, from ear canals to navels. However, in the context of the human (or other mammalian) body, the preferred spot for setting up residence is in the gut, with the large intestine being home to the largest population of bacteria in the body. With estimates that the human intestine harbors 100 trillion bacteria, the Sonnenburgs tell us that the contents of the large intestine can serve up something on the order of 500 billion bacteria per teaspoon. Thus, the number of bacterial cells that we harbor as humans far exceeds the number of other cell types in our bodies. The name that we give to this massive collection of bacteria that we harbor is the *microbiome*.

The biologists among us know, from years of observing the laws of nature, that having a large intestine with 500 billion bacteria per teaspoon is not a condition that would persist through time by accident. As microbiologists unravel the mystery of gut bacteria, it is indeed apparent that the bacteria that colonize our intestines can actually be considered an essential extension of our functional beings.

The diverse ecology of bacteria that humans harbor (up to 1,600 species) are engaged in a wide array of healthy physiological functions that maintain our physical and mental health. Failing to foster a healthy microbiome can have far-reaching consequences. In the realm of physical health, these bacteria have a relationship to, among other things, obesity, diabetes, inflammatory bowel disease and certain cancers. Among the mental health challenges that can ensue from an unhealthy bacterial composition are anxiety, depression and a dysregulated stress response. It is rather difficult to imagine where humans end and bacteria begin — we are a symbiotic, collective unit showcasing mutual dependence for survival.

The composition of the microbiome is, to some extent, very individualized. The types of bacteria harbored by a given individual are dependent on a number of factors, including:

- Whether that individual had a vaginal or cesarean birth
- Whether the individual was breast-fed as an infant
- The degree to which the individual has been administered antibiotics
- The individual's level of exposure to stress
- The presence or absence of animals (including pets and farm animals) in the person's living environment
- The amount of food in the person's diet containing bacteria-friendly, water-soluble fiber that is not digestible by humans (found in bananas, dandelion greens, onions, leeks and garlic) and gut-friendly live-culture foods (e.g., yogurt)

- The amount of optimal sleep the person gets
- The individual's genes

When the bacterial health and composition is optimal, immune, nervous and hormonal function can maintain homeostasis. However, stress, poor diet, unnecessary use of antibiotics and other antimicrobial products, and infection with unhealthy (i.e., pathological) bacteria can affect this equilibrium and, in doing so, impact mental health. For an in-depth look at this fascinating topic, both *The Good Gut* (previously mentioned) and *I Contain Multitudes,* by Ed Yong, are excellent sources. An especially interesting topic covered in these books, but beyond the scope of this article, relates to the role that gut microbiota play in certain critical periods in human postnatal nervous, endocrine and immune system development.

The microbiome and mental health

Certain idioms in the English language, such as "I have a gut feeling," reveal that humans have instinctively known that an important connection exists between the brain and the gut. A close anatomical study of the gut reveals two important clues regarding the centrality of gut function to human mental health. First, the enteric nervous system (commonly known as the gut) has a collection of nervous tissue that gives it the distinction of being termed the "second brain." Second, key neurological connections exist between the gut and the brain, including the very prominent vagus nerve and an elaborate, multimodal complex of connections. These include nerve fibers, gut-generated neurotransmitter precursors, gut immune system-generated substances that communicate with nervous tissue, and hormonally mediated gut-brain communication.

This rich network of connections is called the microbiome-gut-brain axis (MGBA). Most importantly for our discussion, the health and composition of bacteria that make up the microbiome portion of this axis have been implicated in anxiety, depression, increased stress reactivity, autism and other disorders. The remainder of this article will focus primarily on the anxiety, depression and stress reactivity, but readers interested in the area of autism are encouraged

to explore the work of Jennifer Mulle, William Sharp and Joseph Cubells in the February 2013 issue of *Current Psychiatry Reports*.

As is the case for much of the contemporary cutting-edge work in mental health, our current understanding of the microbiome comes largely from what we have learned in animal studies. Breakthrough animal experimentation suggesting a link between the microbiome and mental health harkens back to a 2004 study by Japanese scientist Nobuyuki Sudo and colleagues. They were able to demonstrate that mice raised free of germs from birth had a greater output of stress hormones under stressful situations than did mice with a normal bacterial composition. Since 2004, a number of scientists using other types of mouse models have looked more closely at microbiome-mediated, brain-based neurophysiological changes that are reliable indicators of anxiety and depression.

One substance that has received considerable attention in experimental models of the microbiome-mental health connection is brain-derived neurotrophic factor (BDNF). This substance has major implications for mental health. Neuron viability, neuroplasticity and growth of synapses are all dependent on BDNF, and its depletion in the hippocampus and cortex are associated with anxiety and depression.

Based on the literature, one would expect higher levels of BDNF to be present in the hippocampus and cortex of less anxious mice. In one revealing experimental model devised by scientist Premysl Bercik and colleagues from McMaster University, the gut bacteria of particularly anxious mice were introduced into the sterilized gut of a markedly courageous strain of mouse. In this clever experiment, the nervous mice, with newly implanted bacteria from their courageous counterparts, became less anxious and showed increased hippocampal BDNF production. The formerly courageous mice, having received bacteria from nervous mice, became more anxious and showed decreased BDNF activity.

Other MGBA studies investigating serotonin, a neurotransmitter important in depression and anxiety, have also had promising results. Studies have looked at microbiome-related control of circulating serotonin and regulation of serotonin receptors in the hippocampus and other locations in the brain. Although scientists are still uncovering the details concerning the microbiome-serotonin connection, it is clear that gut microbiota have an important role in its regulation. Because serotonin is the primary neurotransmitter at both ends of the MGBA and is central to mental health, this regulatory function of the microbiome makes it a potential future target for treating anxiety and depression, including possible use of adjunctive dietary interventions.

The neurotransmitter GABA (gamma-aminobutyric acid), which has an inhibitory effect on the central nervous system and whose regulation is important in anxiety and depression, was implicated as a target of microbiome action by a collaboration of scientists from McMaster University and the University of Cork, led by Javier Bravo. This group took a suspected anxiolytic probiotic consisting of the bacterium *Lactobacillus rhamnosus* and administered it to mice. (A probiotic is a substance consisting of live microorganisms that are ingested with the expectation of some degree of health benefit. It is not to be confused with a prebiotic, which is a type of water-soluble fiber that is not digestible by humans but is digestible by bacteria and promotes their healthy growth.) Evidence of decreased anxiety was observed, and GABA production was seen to simultaneously increase in various brain regions, including the hippocampus, amygdala and locus coeruleus.

This experiment also elucidated the mechanism by which the probiotic was able to bridge the divide between the gut and the brain. Scientists were able to demonstrate that when the vagus nerve was severed, the mice showed no changes in behavior or any increase in GABA production, thus underscoring the importance of this major neurological connection between gut and brain.

Chronic stress, the immune system and the microbiome

Scientists have known for some time that certain types of immune responses are implicated in depression. More specifically, clear connections have been made linking chronic stress to inflammation and, in turn, linking circulating mediators of inflammation called proinflammatory cytokines (PICs) to the symptoms of depression, including social withdrawal, anhedonia, dysphoria and fatigue.

The gut is a major source of PICs and helps to regulate circulating levels of these substances. In turn, high levels of circulating PICs regulate functioning of both the stress response and neurotransmitters such as serotonin, thus explaining their relationship to depression. Many brain cells have receptors for PICs, including areas in the hippocampus and hypothalamus.

The condition known as "leaky gut," which Alessio Fasano, director of the Center for Celiac Research and Treatment at Massachusetts General Hospital, has studied extensively, points to a relationship between the microbiome, inflammation and depression. In the face of some controversy, Fasano and other scientists contend that certain conditions increase the permeability of the intestinal wall, allowing bacteria and certain bacterial products to penetrate it and trigger harmful inflammatory responses that lead to increases in circulating PICs. These conditions include chronic stress, infection by particular gut pathogens, excessive alcohol consumption, high doses of non-steroidal anti-inflammatory drugs and some cases of antibiotic use. As explained, this proinflammatory state is associated with symptoms of depression.

Applications to clinical practice

As science continues to elucidate the connection between the microbiome and psychological health, counselors will need to keep pace in translating this knowledge to their own scope of practice. Referring clients to experts in nutrition and diet, alongside psychotherapy, aligns with counseling's growing interest in integrative health care teams, wellness models and holistic practice. The gut is a much more accessible organ than the brain; targeting the *gut* portion of the gut-brain axis with complementary nutritional therapies may offer promising new avenues for mental health intervention.

Our earlier discussion concerning GABA and the use of *Lactobacillus rhamnosus* as a probiotic provides a window to a much larger question: Can pre/probiotics act as the new antidepressants? The term *psychobiotics*

has been applied in particular to the use of probiotic preparations that, through administration of specific bacteria, draw on the therapeutic potential of a healthy gut microbiome to influence psychological health.

Randomized, controlled studies of probiotic interventions have demonstrated significant reductions in depression and anxiety symptoms, sad mood and rumination in as few as four weeks of treatment. Other studies have shown positive effects on brain activity in regions central to emotional processing and suppression of overreactive stress responses. Finally, in one study, infants given a probiotic intervention in the first six months of life had lower rates of neuropsychiatric diagnosis than did their study control counterparts at age 13. Counselors aware of this literature might consider referral for dietary recommendations as a simple and low-risk intervention option in treating a host of mental health challenges, including mood disorders, anxiety disorder and attention-deficit/hyperactivity disorder.

Although probiotics may provide accessible strategies to promote a healthy gut, other potential microbiome interventions could be … tougher to swallow. Fecal microbiota transplants (FMTs) are the safe transfer of fecal samples from a donor with a healthy microbiome to a patient needing to replenish bacterial balance. John Kelly and colleagues recently demonstrated that taking an FMT from depressed humans and transferring it to rats could induce behavioral and physiological features of depression in the rats (e.g., anhedonia). This has led to speculation that an FMT from a healthy patient might generate an antidepressant effect.

As counselors learn more about the relationship between mental health and the MGBA, we can foresee drawing on therapies related to mind-body issues such as insomnia to develop a multicomponent cognitive behavior therapy framework that could complementarily target the gut-brain axis and the various mental health challenges associated with the microbiome. For example, in the case of depression, such a framework might begin with didactic psychoeducation regarding the gut-brain axis and its association with depression. Subsequently, the counselor, in conjunction with a nutritionist or a medical professional, could provide dietary education based on the empirical effectiveness of specific foods that treat depressed mood. This antidepressant diet could then be behaviorally monitored with food journaling. Concurrently, cognitive therapy could target maladaptive coping patterns and introduce healthy coping alternatives (e.g., exercise, mindful eating, mindfulness practices more generally) that positively affect both the gut and the brain.

A multicomponent approach of this nature may have the potential to interrupt cyclical patterns of depressed or anxious clients in which an unhealthy gut microbiome contributes to the development or exacerbation of depression or anxiety. Clients who are stressed or sad and who engage in maladaptive coping behaviors such as unhealthy eating may in turn be negatively impacting their gut microbiome and exacerbating mental health problems.

Finally, we would be remiss if we did not discuss the integral role of diet in gut-brain mental health and the degree to which poverty unjustly contributes to poor gut health. Urban and rural food deserts, and the high cost of probiotic and fresh high-fiber foods, may contribute to mental health issues in these underresourced populations. Through advocacy and activism, counselors can exert efforts to support clients in transforming unjust social arrangements that deprive individuals of healthy nutritional resources and impede positive MGBA functioning. ❖

Kathryn Z. Douthit is chair and associate professor of counseling and human development at the University of Rochester's Warner Graduate School of Education. In the past decade, she has given numerous presentations and produced publications addressing applications of biomedical science to counseling, with a particular interest in how biological processes affect health and well-being in late life. Contact her at *kdouthit@warner.rochester.edu*.

Justin Russotti is a doctoral student in counselor education and supervision at the University of Rochester's Warner Graduate School of Education. He is also a clinician and researcher at the Mt. Hope Family Center, specializing in the developmental sequelae of trauma. His primary interest is bridging the worlds of counseling and the biological sciences to inform practice. Contact him at *justin_russotti@urmc.rochester.edu*.

Letters to the editor: *ct@counseling.org*