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Health Psychology Open
July-December 2017: 1–5
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sagepub.com/journalsPermissions.nav
DOI: 10.1177/2055102917724335
journals.sagepub.com/home/hpo


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Abstract

The microbial environment of the human gut has powerful influence on immunity, metabolism, and obesity. There is now emerging evidence that the microbiome of our gastrointestinal system may also be a key factor impacting our emotional and behavioral health. The purpose of this article is to elucidate how this emerging area of science can further educate and encourage mental health professionals to explore an additional means to treatment. Since much of this research is found in the biological and neuroscientific literature, it can be quite cumbersome for clinicians to digest and apply, who would critically benefit from a concise discussion of the gut–brain connection.

Keywords

gastrointestinal microbiome, mental health, microbiota, probiotics, psychotherapy

Introduction

The past decade has brought with it a substantial interest in exploring the connection between the microbial world of our gut and other important aspects of health, including immune functioning, chronic gastrointestinal (GI) dysfunction, metabolism, and obesity (Bravo et al., 2012; Collen, 2015; DeSalle and Perkins, 2015; Lynch and Pedersen, 2016; Mayer, 2011). An expanding branch of this research—of particular interest to mental health professionals—is providing evidence that supports a strong link between the microbial state of our gut and our emotional functioning, particularly in relation to stress, anxiety and depression (Dinan and Cryan, 2012; Foster and McVey Neufeld, 2013; Wang and Kasper, 2014). Furthermore, the microbial functions of our gut may also have significant influence on more profound disorders, such as autism (Mayer et al., 2014). Since much of the research is found in the biological and medical literature, published work can prove to be quite cumbersome to digest and apply for those trained in the behavioral sciences. The purpose of this article can be described in three parts. One, regardless of training or theoretical orientation, the information provided here will hopefully inform all mental health practitioners that a previously untapped domain may better assist in understanding and

treating patients. Second, some general information pertaining to gut health is provided. Along with this information, it must be understood that individual dietary treatments are best provided by professionals who are adequately trained in such areas. Third, since most of the literature in this area can feel quite foreign and overwhelming for clinicians, this topic will be succinctly broached from a stance that is more user-friendly to clinicians not directly trained in biology or medicine.

The conventional practice in therapy has been to focus on the more established variables known to underlie mental health—childhood experiences, relationships with significant others, our individual history of learning, and nervous system functioning. The *process* of psychotherapy most often focuses on two aspects. From a psychological approach, we work with clients through listening, reflecting, acknowledging

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insights, trying to address their past and understand current thoughts and behaviors. Although the work of therapy can vary greatly based on the theoretical orientation of the therapist, all can be viewed as a form of “talk therapy,” where various aspects of the psychological domain are understood as the cause for distress. It is this traditional focus on behavioral and psychological variables that can be understood as the first tier in treatment.

The second area that is often addressed in mental health comes from biology and the medical sciences. Psychiatrists have provided us invaluable science and medication to understand and assist patients who are in need of treatment. The strength of the medical world is so great—that the notion of chemical connections in the brain—and its relation to a patient’s emotional state and behavior is often addressed even by practitioners who are not specifically trained in medicine. Antidepressants, anxiolytic medication, and other powerful psychotropic medications are widely accepted by practitioners, patients, and the public as an important factor in treatment. Building on the traditional aspects of therapy aforementioned, use of psychotropic intervention would be considered the second tier in the healing process.

However, in addition to the psychological and neurochemical variables that contribute to our emotional state and behavior, there is mounting evidence that the state of our digestive system—our gut—may be a key factor significantly influencing our mental health (Cryan and Dinan, 2012; Dinan and Cryan, 2013). This rapidly emerging domain is providing powerful indications that a new piece of the puzzle must be added as the third tier toward a more comprehensive understanding and treatment of patients.

A bit of biology

Our body is not uniquely human. It is estimated that the number of uniquely human cells in one person ranges from nearly 10 trillion to over 30 trillion cells (Bianconi et al., 2013; Mayer, 2016). In addition to our “own” cells, an estimated additional 100 trillion “foreign” cells reside in and on us (Collen, 2015; Gill et al., 2006; Mayer, 2016). Collectively, these organisms, predominantly classified as bacteria and largely residing in our gut, are referred to as a *microbiome* (DeSalle and Perkins, 2015). By definition, a microbiome is the entirety of microscopic organisms and their genetic material that inhabit a particular environment (Lynch and Pedersen, 2016). Rather than comparing the number of human versus non-human cells in and on a person, differences in genetic material may be compared. Humans have an estimated 20,000 different genes. This pales in comparison with the additional eight million different genes that comprise our microbiome (National Institutes of Health (NIH), 2012). Thus, we are harboring within us over 360 times more genetic material than is our own.

The organisms of our microbiome, having co-evolved with us for millennia, interact with our body in intricate and

balanced ways, to powerfully assist and influence our metabolic, immune, behavioral, and numerous other functions (DeSalle and Perkins, 2015). In turn, we provide them a home to survive, reproduce, and evolve. The relationship between “us” and “them” is predominantly balanced, providing countless commensal and mutualistic exchanges (Wang and Kasper, 2014). Health problems arise when dysbiosis, an unhealthy imbalance of such bacteria, occurs. Illnesses, a course of antibiotics, a change in location, poor diet, and various other factors can cause the natural state of our microbiome to become imbalanced (Collen, 2015). Although dysbiosis can be corrected over time, research suggests that chronic states of dysbiosis may be a key factor leading to many serious ailments, including obesity, allergies, psychiatric, and behavioral problems (Chutkan, 2015; Collen, 2015; Logan et al., 2016).

Putting our microbiome aside for a moment, how does communication between two seemingly separate parts of the body occur? The vagus nerve is the main communication link between the brain and the gut. What is most interesting, even when the vagus nerve is severed, and the link is broken, the gut continues to function. This is due to the fact the human gut is the only organ that has a nervous system that is functionally separate from the autonomic nervous system. Biologically classified as the enteric nervous system (ENS), consisting of nearly 100 million neuronal connections, and the ability to function independently, it is often referred to as the *second* brain (Carpenter, 2012). Adding the trillions of actions and interactions of the gut bacteria back into the communication network, evidence is supporting the existence of a powerful and three-factor link known as the microbiota–gut–brain axis, working in complex ways to affect a host of behaviors, emotional experiences, and disease (Cryan and O’Mahony, 2010; Foster and McVey Neufeld, 2013; Mayer et al., 2015; Wang and Kasper, 2014). One example of the microbiota–gut–brain axis is in the production and use of serotonin, a neurotransmitter whose imbalance is strongly correlated with depression. Although serotonin is commonly associated with location in the central nervous system (CNS), it is found not only in the brain but is also created in the gut. Strikingly, about 95 percent of our serotonin is synthesized by bacteria in the gut! (Carpenter, 2012). Thus, complex communication pathways involving production and adequate levels of serotonin, the ENS, the vagus nerve, and CNS serve to provide solid basis to infer that the microbiome of our gut should act as a critical variable concerning depression. Although no studies to date have specifically investigated the effect of chronic dysbiosis on serotonin synthesis in the human gut, based on what we know regarding this three-factor link, it can be hypothesized that a state of microbial imbalance in the gut may have a direct adverse effect on the functions of both the ENS and CNS and subsequent experience of depression (Mayer, 2016).

Probiotics and prebiotics

A discussion about the impact of our gut health on our behavior and emotional well-being cannot occur without addressing two very important players: probiotics and prebiotics. The World Health Organization (WHO, 2002) defines probiotics as “live microorganisms which when administered in adequate amounts confer a health benefit on the host” (p. 8). Dietary supplements aside, probiotics are found in fermented foods, such as yogurt, kefir, and certain fermented vegetables to name a few (Chutkan, 2015). Some of these microorganisms, many of which reside in our gut, were initially obtained moments after birth (Collen, 2015; Se Jin Song et al., 2013). Others have hitched a ride from contact with people, animals, and objects in our environment and have set up a home inside and on us over the course of our lifetime (DeSalle and Perkins, 2015). However, the details of specific strains of bacteria and their potential effects on our body are beyond the scope of this article. This omission is intentional, as one aim of this article is to serve as a contribution for clinicians to become better aware of this growing area of therapeutic potential. However, it should not be inappropriately or prematurely used as a treatment tool for patients. As stated earlier, referrals should be made to GI and nutritional professionals for patients who may benefit from the emerging science.

Prebiotics are the nutritional substances that probiotics require in order to survive, reproduce, and thrive. Simply stated, prebiotics can be understood as the food upon which probiotic microbes feast. Without proper nutrition, no organism great or small can thrive. The same holds for the microorganisms that reside in and on the human body. Prebiotics that are naturally occurring in our diet are simply special forms of indigestible fiber that are obtained from food such as bananas, asparagus, onions, and many others (Chutkan, 2015). A critical problem is that the modern Western diet, of which most Americans have become accustomed, fails in its ability to provide prebiotics and adequately nourish the microbiota of the human gut (Chutkan, 2015; Collen, 2015). The irony lies in the fact that we are eating more than ever at any point in history. However, the foods we *are* consuming are potentially starving and destroying the microbiome that is crucial to our physical and mental health. Thus, comprehensive understanding of the vitality of the human microbiome and its effect on measures of health would have proper nutrition at its core.

Implications for practice and research

The emerging evidence indicating that the state our gut can have a significant impact on our behavior and emotion is something that should be received and evaluated with serious consideration for those providing mental health treatment. Traditionally, the field of psychology has separated the mind from the body. However, the strong bi-directional impacts

that our body and mind have on one another are becoming ever increasingly clear. For example, we know that a stressful event, such as an interview, an exam, or an argument, can often lead to a whole host of physiological effects in the gut, ranging from “butterflies” to nausea, and bouts of diarrhea, in cases of irritable bowel syndrome (IBS). Furthermore, the stressed states of our mind may even be able to adversely impact the composition of our vital gut microbiome. O’Mahony et al. (2009) examined the effects of daily maternal separation—a commonly accepted operationalization of stress—in rats. Rats that experienced separation compared to a control group demonstrated numerous stress-related outcomes. One of the most notable outcomes was a reduction in the diversity of the GI microbiome among rats in the experimental group, compared to those in the control condition. Conversely, as the mounting research is uncovering, communication is also occurring from the bottom up, with the gut microbiome “talking to” the brain, consequently affecting behavior. In a groundbreaking study, Sudo et al. (2004) provided evidence that germ-free mice have an exaggerated physiological response to a stressful stimulus, as evidenced by abnormal functioning of the hypothalamic–pituitary–adrenal axis. Once such mice were colonized with a particular strain of bacteria that is commonly found in the GI tracts of infants, as well as in many fermented milk products, the stress response was reversed. Moreover, results from this study point to the important influence that the gut microbiome has on appropriate stress responses. Bercik et al. (2011) also demonstrated the powerful effects of gut microbes on exploratory behavior as a measure of anxiety, in two strains of germ-free mice. Bagg Albino/c (BALB/c) mice are naturally more timid and inhibited, compared to NIH Swiss mice, which are much more exploratory in nature. Under controlled conditions, each group of mice were bred germ-free and subsequently colonized with microbiota from their counterparts. Results indicated that after the microbial transplants from NIH Swiss mice, BALB mice demonstrated behaviors much more characteristic of their Swiss peers, including greater exploratory behavior as well as an increase in the expression of brain-derived neurotrophic factor (BDNF) in the hippocampus. In contrast, Swiss mice demonstrated a behavioral profile similar to their anxious donors, as evidenced by an inhibition in exploratory behavior. It is of note that the changes were not permanent in nature but clearly demonstrated how alterations in gut microbiota directly affect brain and behavioral functioning. It is evident that with studies such as these, the combined efforts of biology, neuroscience, nutrition, psychology, and psychiatry will undoubtedly provide a more profound understanding of communication between our “first” and “second” brain.

Nearly all clinicians will work with patients suffering from some form of anxiety or depression during their career. It is not uncommon for both patients and clinicians to feel frustrated during the therapeutic process when nearly every psychotropic option has been exhausted, and psychological

areas of exploration appear to no longer provide valuable insight and change. We now know there is real possibility that something as simple as a patient's diet, history of GI illness, or chronic use of antibiotics may have significantly imbalanced an intricate system, with direct influence on emotion and behavior. Building on psychotherapy, and pharmacotherapy, this third domain to treatment, involving precise nutritional evaluation and therapy may prove to be an *additional*, powerful, and natural tool to help us better understand and aid in the healing process of patients. Dinan et al. (2013) discuss the potential for the development of a specific novel class of probiotics, known as *psychobiotics*. They suggest that these live organisms, when properly administered, have the ability to act upon the gut–brain axis through the production of substances that are strongly correlated with depression and anxiety, thus aiding patients with psychiatric conditions. Neef and Sanz (2013), as well as Bravo et al. (2012), further support the notion that targeted food and probiotic supplement usage are important areas for future clinical application. The promise of psychobiotic and specialized nutritional prescriptions may strongly resonate for clinicians as an innovative and important aspect to treatment. However, it is important to note that such substances and interventions are still in the early stages of development and are not readily available for clinical use as of yet. Undoubtedly, this area could prove to be of great utility, as it would affect biological processes, but without the sometimes severe and chronic side-effects of traditional psychotropic medication.

Although not specifically employed as a psychobiotic, Messaoudi et al. (2011) examined the effects of a probiotic formula on several measures of behavioral and psychological functioning, in both rat and human samples. The pre-clinical trial demonstrated reduced anxiety-like behavior, among rats after a 2-week ingestion of the probiotic formula. However, what is more striking are the results of the clinical trial, involving 66 human participants. In the double-blind, placebo-controlled trial, subjects were given a fruit bar that either contained the probiotic formula or a placebo, for 30 days. Both the experimental and control bars tasted the same. Results indicated that those in the experimental condition reported significantly lower levels of anxiety, anger, depression, and somatization, on a number of self-report measures. Lower levels of cortisol were also evident in the experimental condition compared to the control group. Tillisch et al. (2013) also demonstrated the effect of a fermented milk product containing probiotics, with significant impact on brain activity in regions controlling emotional and sensory processing, in healthy women. Although researchers used a placebo-controlled design, sample size of each condition was relatively small.

The work of Messaoudi et al. (2011), as well as Tillisch et al. (2013), should be lauded for its inclusion of human, as opposed to solely animal subjects, as most research in this area lacks such a design. However, it is crucial not to oversimplify the idea that nutritional intervention and a healthy

gut will be the panacea for profound psychological difficulties. Severe mood and paralyzing anxiety disorders are not going to be cured with probiotic yogurt and prebiotic fiber, alone. Additional, well-controlled, double-blind, studies are needed to investigate what particular strains of bacteria might directly confer mental health benefits, which strains of bacteria are directly related to specific emotional problems, and how to best nourish our gut as a means to creating holistic treatment plans for different disorders. Furthermore, as a way to strengthen the generalizability of future findings, research designs employing human participants will be crucial.

Conclusion

The brain–gut connection is no longer an abstract concept. Neurobiological research has demonstrated a strong, bidirectional communication pathway whereby two seemingly independent organs influence each other in profound ways. Evidence from medical science has strongly supported the notion that unchecked stress levels exacerbate GI illnesses, such as IBS and other digestive disorders. What is becoming increasingly clear is that a third factor—the microbiome of our gut—is playing a powerful role in this connection. Mounting evidence supporting the notion of a microbiome–gut–brain axis is not only helping us better understand the complex underpinnings of GI illnesses, allergies, metabolic functioning, and obesity but also providing additional clues into untangling multifaceted psychological problems such as depression, anxiety-based illnesses, and autistic disorders. As both interest and technology advance, we are well on our way to developing innovative research designs that will potentially lead to nutritionally based and psychobiotic treatments, in addition to traditional psychological and psychotropic intervention. It is important to note that pure research alone will not be enough to advance this newly discovered territory. Practitioners must embrace the burgeoning science not simply as an adjunct to the healing process but as a vital third tier to the treatment they provide.

Declaration of conflicting interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The author(s) received no financial support for the research, authorship, and/or publication of this article.

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