Cheese, Please! Depression Curing Cultures

How Diet Can Alter Your Mood

by Julia Borys

The human body is made up of about 30 trillion eukaryotic, or animal, cells.[1] It also contains about 38 trillion bacterial cells. This means that a typical human has as many, if not more, bacteria in and on them as they do actual human cells. Despite this, medicine is largely focused on how we can affect our human cells to cure disease, heal wounds, and prevent sickness. These questions are very important in understanding human health, but less focus is placed on how our bacteria may be altered by our actions. In order to understand the full picture of human health and how it can be optimized, we need to better understand the function of our bacterial communities as well.

The bacteria in and on the human body are organized based on their location and function into groups called microbiomes.[2] This includes the skin microbiome, the oral microbiome, the lung microbiome, and the gut microbiome. The gut microbiome, which is the collection of bacteria and other microorganisms found in the gastrointestinal tract, has recently been under greater observation. This is because in addition to its main role of extracting key nutrients that the host is unable to digest, the gut microbiome has also been found to largely impact other areas of the body.[3] Although the brain itself is considered a sterile organ and does not have a microbiome, bacteria have been found to indirectly impact its function.

Some common foods contain bacterial strains that are able to affect the function of the brain. They are referred to as probiotics, or live microorganisms with health benefits, and may improve much more than just the health of a person's gut. Yogurt is probably the most well known probiotic, but there are plenty of others as choices since different people like different kinds of food.[4] European cheeses are another major source of probiotics, with different cheeses containing unique combinations of microorganisms. The specific effects that these foods have on the brain will be discussed, but is it possible that something as simple as eating some yummy cheeses every day could cure depression?

Disorders of the Brain

The brain's proper function is necessary for the well-being of its host organism. If the brain is not functioning properly, various problems may arise. Some of these problems involve mood and cognition. Major depressive disorder, or depression, is a disease of the brain where the affected individual experiences a lowered mood state. Depression is very prevalent in the United States today, with 13.8% of adults using antidepressants.[5] This has increased since 2010 by 3.2%. While it is unknown whether the cases of depression itself are increasing, insurance companies have reported an increased rate of diagnosis for depression in addition to the increased use of antidepressants.[6,7] The use of antidepressants to treat depression poses many problems, however. Antidepressants are not a guaranteed treatment for individuals with depression. Because there are so many different compounds that respond uniquely to each individual, it can be difficult to find one that works well for a patient. Additionally, they may not ameliorate the patient's symptoms at all.

In addition to depression, another common disorder of the brain is Alzheimer's disease (AD).[8] AD is a neurodegenerative disease where the individuals experience dementia, memory loss, and alterations in metabolism, which is the body's maintenance of energy. This disease is heart-breaking for loved-ones, as they see their friends and family lose their sense of self, effectively erasing all the experiences they had together. Age is the greatest risk for acquiring this disease. Because AD involves brain cells dying, memory loss and a reduced ability to concentrate occur. While there are some drugs that are used to treat the cognitive symptoms, unfortunately no cure for AD currently exists. To avoid both the issues in prescribing antidepressants and to find a better treatment option for individuals with AD, and perhaps allow them to retain memories of their loved ones, it is clear that additional therapeutic approaches should be explored.

In order to develop better treatment for brain disorders like depression and AD, the factors that affect the brain and its function must first be explored. Recently, more focus has centered around alterations to the gut microbiota as a way of affecting the brain and its behavior. This relationship has been dubbed the gut-brain axis.[9] Depending on the species of bacteria that are present within an organism's gut, the brain might function differently (Figure 1). Some physical adverse effects of an improperly functioning gut-brain axis include obesity and stomach pain. While the exact mechanism of how this occurs is unknown, communication is thought to occur via the vagus nerve—the nerve running from the brain to the abdomen that is responsible for organ functions—and results in the modulation of various structures withThe gut-brain axis is thought to affect mood through the HPA axis of the brain.[10] The HPA axis, or hypothalamic-pituitary-adrenal axis, is the system responsible for an organism's response to stress. For example, say a student

receives a failing grade. The student sees the grade and the brain tells the adrenal glands on top of the kidneys to produce the stress hormone cortisol. Cortisol signals the body to change, which we experience as stress. These changes include a lowered mood, increased blood pressure, and a decreased sensitivity to pain.[11] Depending on the bacterial species that are in the gut, the function of the HPA axis may be altered.[10] One study performed on rats removed all of the microorganisms from their gut.[12] These rats, when electrically shocked, showed an increased stress response than those who had a healthy gut microbiome. If this could be applied to humans, it would mean that certain strains of bacteria, as acquired through food, could decrease the reaction experienced from a stressful situation. In the situation above, the failing grade would not seem as scary to a student eating cheese and yogurt, and the pain from stress would be diminished.

Experimental Treatments Using Probiotics

Because of their ability to potentially alleviate the negative emotions, many researchers are exploring the potential for probiotics as treatment for various brain disorders, like depression, generalized anxiety disorder (anxiety), and AD. Probiotics deliver certain species of bacteria to an individual's gut, altering its composition. As seen, the changes in composition may also change the way a brain functions.

To assess the effects of bacteria supplementation, via probiotics, on depressive and anxiety-like behaviors, researchers used rats. Germ-free rats, or rats without any microbes or bacteria in their gut, were given either a probiotic containing the species *Lactobacillus rhamnosus* or no probiotic (Figure 2).[13] *L. rhamnosus* is a relatively rare bacteria naturally found in human gut microbiomes.[14] The rats that were given this probiotic showed a decrease in anxiety-like and depressive behaviors. This was tested by forcing the rats to swim and observing their reaction, such as trying to swim or giving up. If the rat acts as though it is not worth it to continue swimming, this is seen as a potentially depressive behavior, where hope is seemingly lost. The bacteria was determined to be communicating through the vagus nerve. Upon severing the rats' vagus nerves, the rats who were given the probiotics exhibited the same depressive behaviors as the rats without probiotic supplementation.

The anti-depressive effects of probiotics were also tested in humans. As opposed to *L. rhamnosus*, another *Lactobacillus* strain, *L. helveticus*, and *Bifidobacterium longum* were given to individuals for 30 days.[15] Like *L. rhamnosus*, these strains naturally occur in the human gut. These bacteria were seen to alleviate anxiety-like and depressive behaviors as revealed by the test scores of the patients, which self-reported the patients' mood and depressive emotions. We know that the increased mood in the patients was due to the probiotics, because another group was given a placebo, or a treatment with no effect. If the patients thought that they would be happier, so then became happier, the test scores would have increased in the placebo group as well. This was not true, however, so we can assume that the increase in mood is indeed a result of the probiotic. Additionally, no adverse effects were observed from taking the probiotic. In order to consider probiotics as a standard treatment, more studies would need to be done on different populations using different strains. This is because people from varying parts of the world may require the bacteria

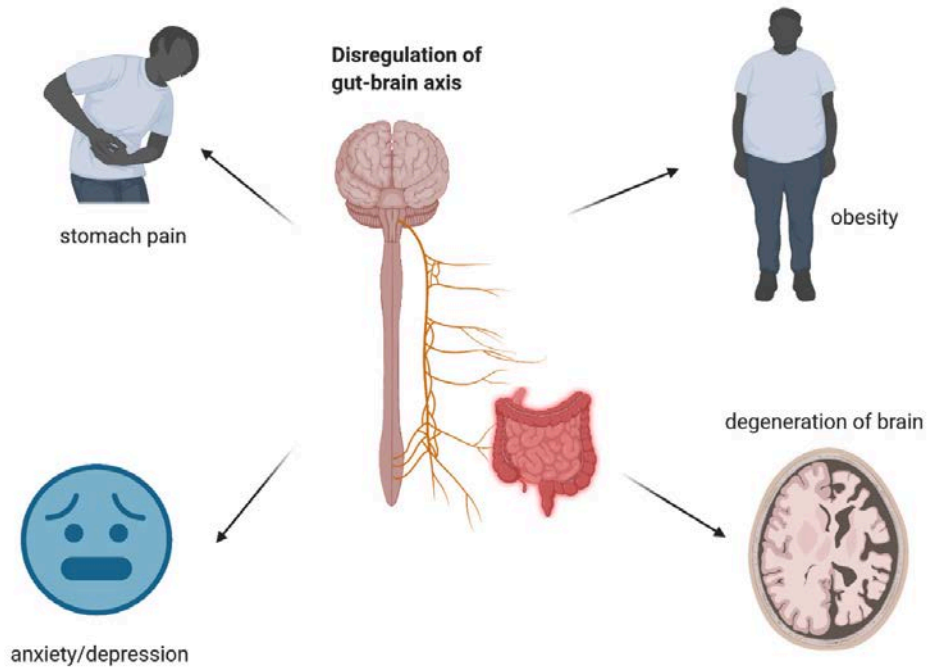

Figure 1. The adverse effects that may result from an imbalanced gut-brain axis. Image created with Biorender.com by Julia Borys, licensed CC BY 4.0.

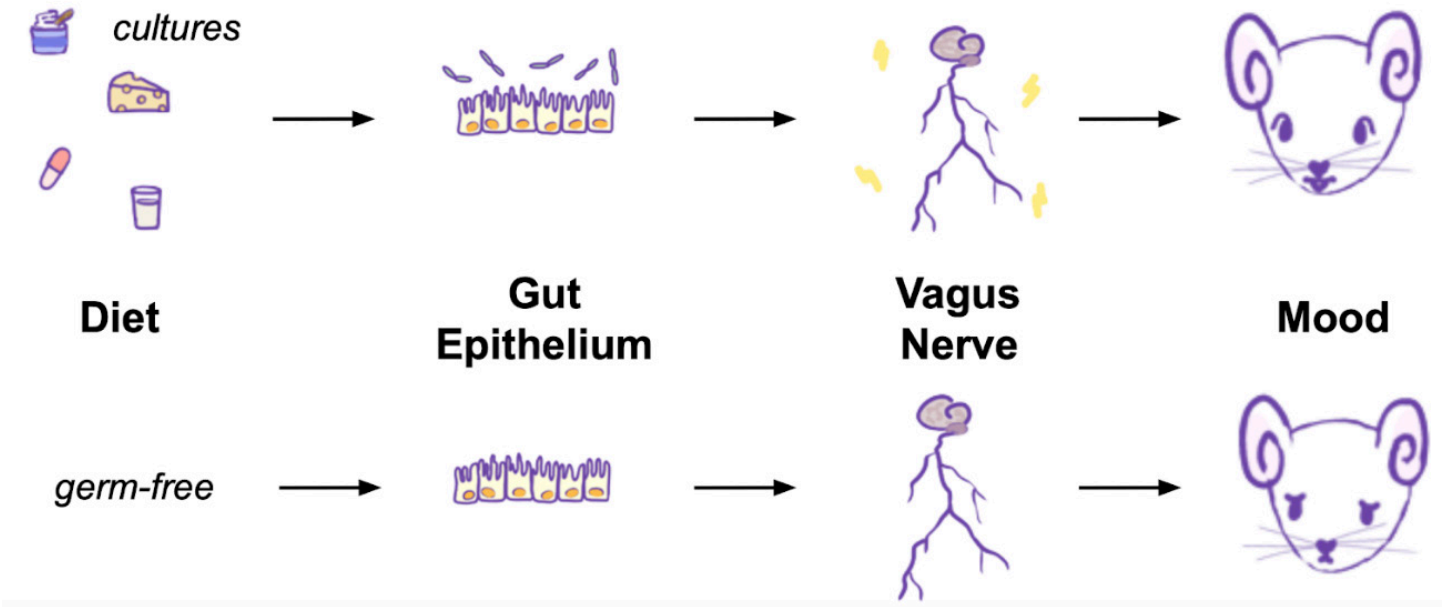

Figure 2. Illustration for the effect probiotic cultures have on mood. Arrows represent the cause and effect. Gut epithelium is the lining in the intestines, where bacteria reside. Figure by Julia Borys, licensed CC BY-NC 4.0.

from their local foods to have a functional gut microbiome.

In addition to testing the antidepressant effects of probiotics, the cognitive effects were also observed in humans. This was done in an attempt to alleviate some of the unfortunate effects of AD, whose patients are known to experience decreases in cognition as mentioned previously. Alzheimer's patients were divided into two groups. They were either given plain milk, which acts as the placebo control, or a probiotic mixture (containing *L. acidophilus, L. casei*, *B. bifidum*, and *L. fermentum*) for 12 weeks.[8] Their score from a test to assess mental state was recorded before and after. In the AD patients that received the probiotic treatment, a significant improvement in their test scores was observed. Some alterations in the patients' metabolisms, such as insulin, a hormone/signalling substance that affects cognition, also were observed in the treated group. Because metabolism is another issue resulting from AD, these results suggest the wide benefit probiotics may have. If something as simple as feeding an older person yogurt or sourdough bread allows them to remember their grandchildren without any side-effects, probiotics absolutely should be implemented as a treatment option.

Incorporation of Probiotics in Diet

One of the attractive characteristics of probiotics is that they tend to be more accessible than medications, which may require insurance or other additional expenses. Many of the probiotic species included in the study can be found in supermarket foods. The relative affordability of probiotics, when incorporated simply into diet, could help poorer families self-treat mood or cognition disorders. Especially because those in lower socioeconomic classes experience the stress of caring for themselves and their families, probiotic treatment may help ease this burden while also fulfilling their need for food. Not only do these foods have the potential to improve mood and cognition, they are also simply delicious! *L. rhamnosus* is used as a flavoring agent in the Italian cheese parmigiano reggiano, a favorite cheese of many.[16] In fact, parmigiano reggiano is so tasty and desired that a black market for the cheese exists in Italy. This cheese can be expensive, but there are other tasty probiotics that are more affordable. *L. helveticus* is also naturally found in other Italian and Swiss cheeses, as well as kefir, a fermented milk drink.[17,18] Kefir and yogurt also include *B. longum*. Yogurt is a very popular and affordable probiotic, and many different varieties and flavors exist to tailor to every individual's taste. *L. helveticus* and *B. longum* are the species that were seen to have anti-anxiety and antidepressant effects in the previous research. *B. longum* and another species that improved cognition in AD patients can also be found in fermented fruits and vegetable-containing foods. This includes sauerkraut, kimchi, miso, and others.[19,20,21] Sourdough bread also includes *L. fermentum*, another strain that alleviated AD symptoms, within its microbial cultures.[22] Although current research has not yet isolated the specific bacterial species or combinations of species that affect the brain in their studies, especially as the effective probiotic combination may vary between different people, it seems generally as though a combination of probiotic-containing foods assists

in a healthy, brain-supporting diet.

Potential Side Effects of Probiotics

As with any drug treatment, treatment using probiotics has the potential to cause some side effects, but don't throw out all of your yogurt and cheese yet! Since probiotic cultures introduce microbial species into the body, there is a risk for the host to contract infection if the host's immune system, which is the body's protection against infection, is not able to protect itself. However, since many of these strains are naturally found in fruits and vegetables, which are part of a healthy diet, as well as the human gut, the patients' risk should be assessed based on how their immune system typically responds to such foods. This is why more research into the body's response to varying probiotics is especially important if probiotics are to be used as widespread treatment. The immune system may react to the probiotics in other ways as well. Autoimmune responses, which is when the immune system attacks the host body rather than the foreign microbes, may occur. However, only one case of an autoimmune response after probiotic supplementation has been reported to occur in humans, and these responses typically have only been seen in rats.[23]

Future of Medicine and Microbes

Probiotics could be implemented as treatment, or in conjunction with existing treatments, for various mental disorders. They not only present few risks, but are relatively affordable and may be more accessible than prescriptions. However, to better understand their effects and how they may uniquely affect each individual patient, more research needs to be dedicated to understanding each strain, as well as their effects on different populations of individuals. This way, medical professionals would be able to best recommend treatment options to their patients while keeping them safe. In general, probiotics can become a very powerful tool for many of the common disorders that the population experiences today, and more effort should be put towards establishing probiotics as a common treatment. ■

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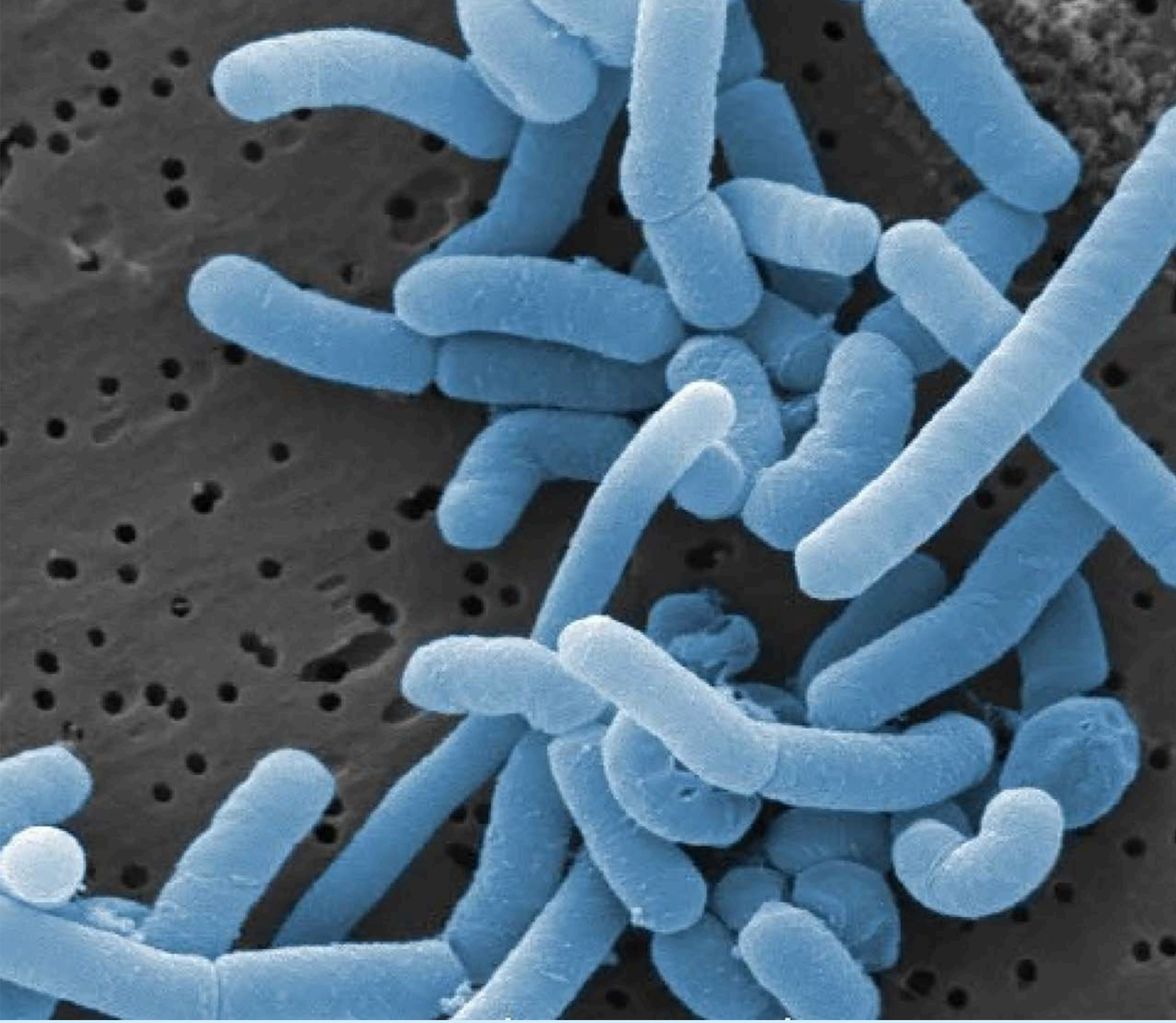

Lactobacillus paracasei. Adapted from an image by Wdwdbot, licensed CC BY-SA 3.0.

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