

THE GUT–BRAIN AXIS:

IT'S ALL CONNECTED!





All diseases begin in the gut ~ Hippocrates

Many people experience some gut-related symptoms like abdominal discomfort or diarrhea due to changes in their emotions. Is that by chance?

Or maybe there is an actual connection between the gut and the brain? Well, recent studies confirmed a connection between GI function and emotions. But is this a brand-new science?

Well, not quite. The father of medicine, Hippocrates, once said: “all diseases begin in the gut.” The brain and gut communicate via immune, endocrine, and neural connection. This connection is becoming increasingly evident. More importantly, studies recognized that gut bacteria play a role in this connection and even detected a correlation between dysregulation of gut bacteria and some diseases.

These include mood disorders (depression and anxiety), type 1 diabetes, irritable bowel syndrome, celiac disease, and many more! (1)

Let’s dive into some of the nitty-gritty details regarding this marvelous connection and what diseases might happen if things go wrong.

YOUR GUT CONTROLS YOUR EMOTIONS!

Our stress response is regulated by the hypothalamic-pituitary-adrenal (HPA) axis. This is a complex system, but its end result is the production of the hormone cortisol, which affects every corner of our body, like digestion, immune function, and, undoubtedly, emotions.

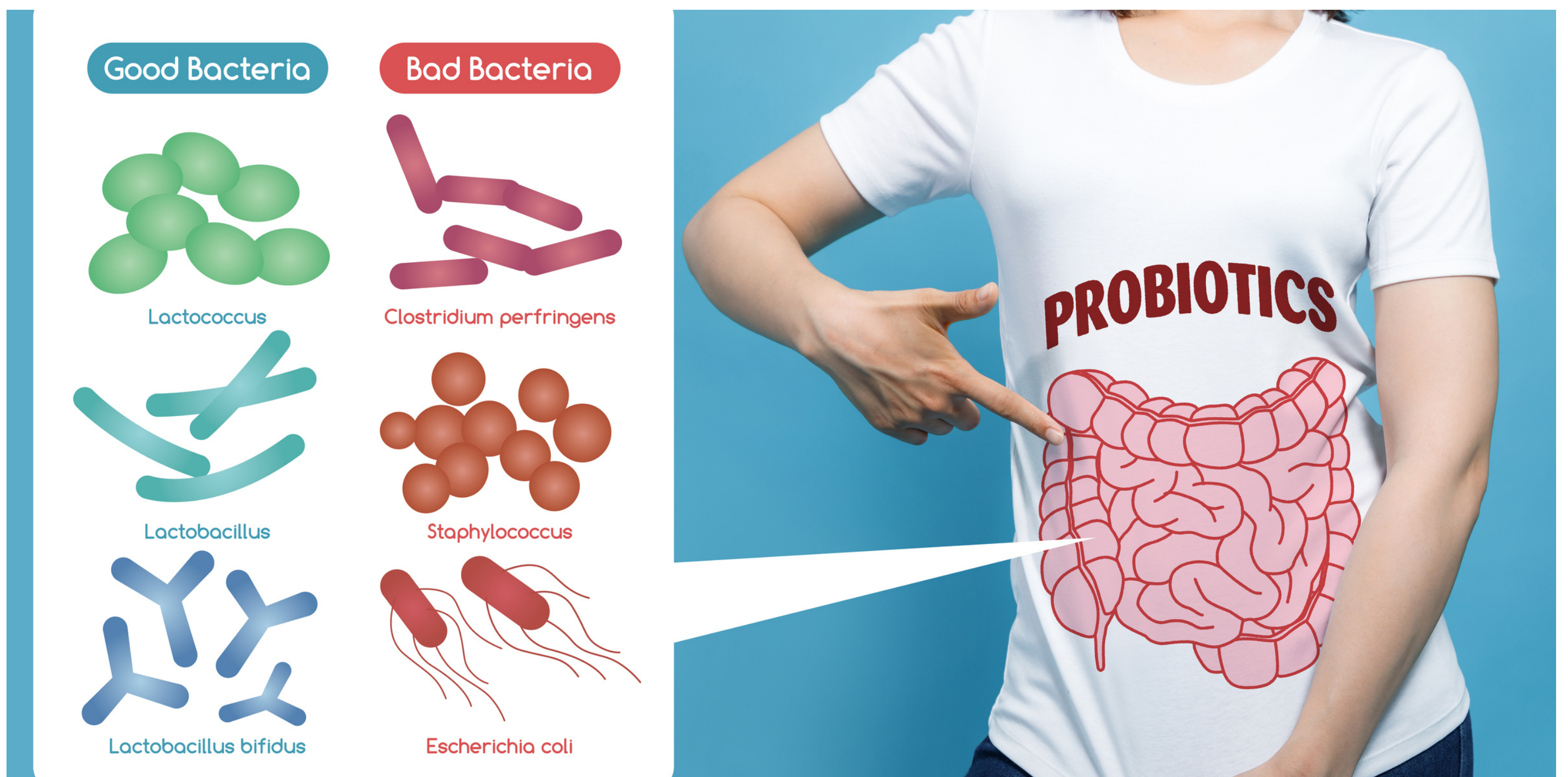
Studies found that dysregulation of the HPA axis is associated with more severe depression symptoms. (2)

Interestingly, many studies demonstrated that the lack of gut bacteria exacerbates the behavioral responses to stress and increases cortisol levels.

It is believed that altered gut bacteria negatively influences gut physiology and leads to the inappropriate gut-brain axis and associated consequences like depression (3).

Conversely, stress at the level of the brain can alter the gut bacteria and disrupt the intestinal barrier, increasing the permeability of our gut to bacteria, also known as leaky gut.

So, it seems like the connection is bidirectional (1).



These findings highlight the importance of a healthy microbiome for the appropriate development of the stress response.

Supporting these facts, studies on humans found that supplementation with some healthy gut bacteria like *Lactobacillus helveticus* demonstrated anxiolytic-like activity and reduced cortisol effects (4).

But wait, how exactly can gut bacteria alter brain function? Some theories explain that: (1)

- 1- Healthy bacteria in our gut can produce tryptophan. Tryptophan is used by our brain to create serotonin, the happiness neurotransmitter!
- 2- In people with leaky gut, harmful bacteria can produce endotoxins that travel via the blood until it reaches the brain. This can lead to inflammatory response and negatively impact the mood

Now comes a critical question...

WHAT ARE THE PRACTICAL IMPLICATIONS?

Short answer: take care of your gut.
But how?

Well first, we need to understand 2 basic concepts: probiotics and prebiotics.

- 1- Probiotics are living strains of healthy gut bacteria. They can be taken as a supplement or from certain foods. Their consumption is associated with numerous health benefits.
- 2- Prebiotics are fibers consumed by gut bacteria and support their growth. Also, their consumption by bacteria results in producing some healthy substances that nourish our gut lining.

Here is a guide to help you understand how to incorporate them into your diet

PROBIOTICS

Whether you take them through diet (discussed below) or as a supplement, probiotics can have a tremendous impact on your health. This includes:

- Weight loss (5)
- Controlled blood cholesterol (6)
- Blood pressure control (7)
- Reduce symptoms of anxiety and depression (8)
- Improve immune function (9)

Nevertheless, if you want to consume them through diet, there is a good list of food that you can find. Still, you will be getting a similar benefit as if you take them as a supplement. Foods include:

- Yogurt
- Sauerkraut
- Kefir
- Miso soup
- Soft cheese
- Sourdough bread
- Acidophilus milk
- Sour pickles
- Tempeh



Note that yogurt, specifically, is very rich in probiotics (healthy gut bacteria). Many studies found that it can benefit many gastrointestinal diseases like diarrhea, constipation, colon cancer, and inflammatory bowel disease (10) (11)

PREBIOTICS

Alright, with probiotics discussed, now let's move on to prebiotics, shall we?

Resistant starches

Resistant starches can act as prebiotic fibers (meaning that they can feed the gut microbiome); they also facilitate the health and diversity of the gut microbiome. Moreover, they increase the production of short-chain fatty acids within the gut, which can have anti-cancer effects on our colon.

A recent meta-analysis found that resistant starches significantly affect bowel function by increasing fecal weight content and butyrate production. This substance can have an anti-cancer, anti-inflammatory, and antioxidant effect on our gut (12).

Less than 5% of Americans meet the Institute of Medicine recommendation for 25 to 38 grams of fibers/day, which has been a concern for decades. According to some economic models, consuming fibers, including resistant starches, would reduce the direct medical costs by \$12.7 billion per year if all adults in the USA consume their daily recommended intake of fibers (12).

Here is a list of some foods high in resistance starch: (13)

- Lentils (25.4 g/100g)
- Corn (25.2/100g)
- Red kidney beans (24.6/100g)
- Barley (18.2g/100g)
- Black-eyed peas (17.7g/100g)

THE GUT: IS IT THE ONE TO BLAME FOR CERTAIN DISEASES?

Our gastrointestinal tract harbors bacterial cells that outnumber all of our body's cells by a factor of 10.

The genes expressed by these bacteria exceed their host's genes by more than 100 times.

Therefore, our gut and microbiome seem to play a huge role in other diseases and mechanisms in our bodies.

In fact, problems related to intestinal permeability and imbalance of our gut microbiome have been linked to many gut-related issues like celiac disease, inflammatory bowel disease (IBD), irritable bowel syndrome (IBS), type 1 diabetes, and even heart disease.

Let's switchgear and learn more about these diseases and how our gut could be guilty when it comes to certain conditions!



IRRITABLE BOWEL SYNDROME

Irritable bowel syndrome (IBS) affects around 10-20% of adults and adolescents worldwide! Clearly, this is a prevalent condition, with many people ending up having this diagnosis after their physicians could not explain their symptoms by any other disease.

Wondering whether you have IBS or not? IBS is diagnosed if the following criteria are present: Recurrent abdominal pain on average at least 1 day/week during the last 3 months.

Pain could be in the form of bloating, flatulence, and urgency. It must be associated with at least 2 (or more) of the following:

- Change in stool appearance or form
- Change in stool frequency
- Pain-related to defecation

If someone meets these criteria, they are officially diagnosed with IBS.

Although IBS is not a dangerous disease, it can negatively impact the quality of life, resulting in reduced work productivity, missed workdays, and anxiety. It is believed that several mechanisms play a role in developing IBS. These mechanisms include impaired brain-gut interaction and gastric motility, stress, dietary allergies, intestinal infections, alteration in gut microbiota, and intestinal permeability (14). Among all of these, gut microbiota variations are thought to play a role in intestinal inflammation in IBS.

Usually, in a healthy gut, healthy intestinal bacteria either have a direct killing effect of pathogens or prevent the adherence of pathogens to the gut wall. Imbalance in gut bacteria, scientifically known as dysbiosis, facilitates the adhesion of pathogens that could initiate inflammation and cause IBS pathogens (15).

Supporting this idea, a systematic review and meta-analysis found that the administration of probiotic supplements (discussed above) seems to have beneficial effects in treating the overall symptoms of IBS and improving symptoms like abdominal pain, bloating, and flatulence (16).

IF YOU ARE AN IBS SUFFERER, HERE IS AN EXTRA TIP FOR YOU:

Eating a low Food FODMAP diet has been shown to significantly decrease the symptoms related to IBS.

Interestingly, it has the potential to be the first line of treatment utilized by evidence-based physicians.



BUT WHAT IS THE LOW- FODMAP DIET?

FODMAP stands for Fermentable, Oligosaccharides, Disaccharides, Monosaccharides, and Polyols.

These are carbohydrates that are poorly absorbed and digested in the small intestine. As a result, they travel to the large intestine, where they are fermented by the bacteria, leading to the formation of gases that can exacerbate IBS symptoms (17).

HERE IS A SUMMARY OF LOW FODMAP DIETS:

Celiac, gliadin, and your gut permeability: a hole in the bucket

Celiac disease affects around 1% of healthy adults. Even though the number may sound small, you will find that millions of people have the disease if you do the math.

Although the exact mechanism is unknown, it is believed that celiac disease occurs when the immune system in our intestine creates an immune reaction against the protein gluten. This leads to damage of the intestinal lining, leading to the inability to absorb nutrients necessary for health.

It has been suggested that there is a problem related to intestinal barrier function.

Typically, our gut is impermeable to large molecules such as gluten because of the presence of normally functioning tight junctions that seal off the gap between intestinal cells.

A recent study found that exposure to gluten leads to increased intestinal permeability in patients with celiac disease.

Nevertheless, among participants, those who had been on a gluten-free diet for at least 12 months experienced minor changes in intestinal permeability (18).

Here comes a question: Why do people with celiac disease have that increased gut permeability when exposed to gluten?

The exact answer is unknown, but it is believed that gluten influences tight junctions and gut inflammation in some genetically predisposed people.



Take-home point: gut permeability most likely plays an essential role in celiac disease. Eating a gluten-rich diet increases gut permeability and leads to the manifestations of the disease. This is why people with celiac are recommended to avoid gluten-rich foods. They include:

- Wheat
- Spelt
- Rye
- Barley
- Bread
- Pasta
- Cereals
- Beer

The gut microbiota and type 1 diabetes mellitus (T1D)

Type 1 diabetes mellitus is a disease common in children. The condition is characterized by insufficiency of insulin production.

This happens due to an autoimmune attack of the pancreas, leading to the destruction of beta cells, which are responsible for insulin production. Now you start wondering, what is the relation between gut microbiota and insulin production (from the pancreas)? They seem to be completely different organs. Well, not quite. Studies comparing gut microbiota in healthy children and children with T1D found that gut microbiota is different in T1D children from healthy ones.

These alterations are associated with short-chain fatty acid butyrate production, leading to a weak intestinal barrier and increased permeability (19).

Okay great. But how will increased permeability make the immune system attack our pancreas?

This was answered in a study showing that increased gut permeability leads to some gut bacteria sneaking into our blood.

If these bacteria mimick our body's own beta cells, our immune system will recognize the beta cells as a pathogen and start attacking them (18).

Interestingly, a randomized control trial found that fecal microbiota transplantation halts the decline in insulin production in recently diagnosed patients with T1D 12 months after disease onset (20).

Note that research in this area is still in its early phase. So why do we bother covering it?

This is just to show you that there is a shred of solid evidence between gut microbiota and several autoimmune diseases like T1D.



Final tip: Don't confuse Type 1 diabetes with type 2 diabetes. They are entirely different conditions. Unlike Type 1, type 2 is common in adults and is not associated with beta cell destruction and insulin deficiency. Instead, it happens when our cells are no longer responsive to insulin, formally known as insulin resistance.

Bugs love hugs: your gut bacteria and heart disease

Gut bacteria and the heart?! Our gut continues to impress us with how sly it is! The sad thing is that the research in this area is still in its infancy, and clinicians can't apply these studies to their patients since the evidence is not strong enough.

Congestive heart failure is a common condition associated with high mortality and morbidity.

Although the pathophysiology of heart failure is complex and beyond the scope of this Ebook, having an overview is helpful.

Basically, what happens in heart failure is that your heart can no longer pump blood to your organs. This happens for various reasons, but heart attacks and valve disease seem to be the most common causes.

When your heart cannot pump blood, blood accumulates in veins, leading to lower limb edema, pulmonary edema, and many other symptoms.

Studies found that heart failure is a multisystem disease that affects the heart and other systems like the immune system, neuroendocrine, and musculoskeletal.

It is also associated with a chronic inflammatory state in the whole body. Inflammation is believed to result from toxins and bacteria entering the circulation from the gut due to increased gut permeability.

The reason behind this increased permeability is accepted to be due to insufficient blood flow to the gut (due to heart failure).

This inadequate blood flow causes the gut wall to become leaky and causes some bacteria to enter the blood through it.

This hypothesis was supported by a clinical study that found that patients with heart failure have increased intestinal permeability compared to normal people, contributing to the chronic inflammatory state in the condition (21).



TAKE-HOME POINT

I am impressed by how motivated you are! You are so motivated that you completed the full eBook. This was a long, exciting journey full of new scientific information.

In this Ebook, we learned about the role of gut bacteria and intestinal permeability in many diseases like celiac, IBS, diabetes, and heart disease.

We also had a look at the gut-brain axis and how it could affect our mood and stress. Also, we learned that the connection is bidirectional, and our stress response impacts our gut bacteria as well.

It affected organs that we never thought of and played a role in many autoimmune disorders as well.

It controlled our mood and level of stress. This is marvelous. I have no idea if that doesn't blow your mind what else would!

Anyway, thank you for sticking to the end. I hope that was enjoyable!

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