

What is the Gut-Brain Axis?

The gut-brain axis is a bidirectional communication between the enteric and central nervous system thought to have influence on affect, motivation, and higher cognitive functions as well as many other biochemical processes. The gut-brain axis includes the central nervous system (brain and spinal cord), the autonomic nervous system, the enteric nervous system, and the hypothalamic-pituitary-adrenal axis.

Alterations in our gastrointestinal (GI), central nervous system (CNS), autonomic nervous system (ANS), and immune systems by microbiota may lead to alterations in (a) fat storage and energy balance; (b) GI barrier function; (c) general low-grade inflammation (GI and systemic); and (d) increased stress reactivity.

The Role of Gut Microbiota:

Our “old-friends”: There has been a historic symbiotic relationship between humans and the commensal microbiota over millions of years of evolution and adapted to hunter-gatherer life. This microbiota was or used to be humans’ “old friends,” which include microorganisms and helminths found in pollution-free water, soil, and food. However, in modern society, dramatic changes in health care, lifestyle, and diet have greatly diminished exposure to these friends, which has resulted in abnormalities in immune development.

The gut is a microbial organ with 90–95% of its total cell number consisting of microorganisms. The gut provides living space and food for microorganisms, while the microbiota influences the development and function of the gut. The gut and gut microbiota work together to perform the tasks of digestion, immune and endocrine functions, and neurotransmission.

- Our gut microbiota plays an important role in nutrition (synthesize vitamin K, B vitamins; produce digestive enzymes that help us break down and absorb; ferment/break down prebiotics in the large intestine)
- Our gut microbiota maintains integrity of epithelial lining and produces energy from carbohydrates to fuel the cells of the intestinal lining
- Secretes IgA
- Keeps the gut barrier sealed so food/microbes don’t get in to bloodstream/chelates toxins and heavy metals (more on this on the “Leaky Gut” section)
- Produces neurotransmitters like serotonin (90%!), dopamine, GABA, glutamate, ACh

The Role of the Enteric Nervous System:

The Enteric Nervous System (ENS) is an independent, intrinsic innervation of the GI tract. The ENS is derived from neural crest cells and composed of neurons and glial cells. The ENS receives input from the CNS as well as ANS and communicates bidirectionally with the brain via the vagus nerve as well as neurochemicals, etc. Amazingly, there are over 400-600 million neurons in the ENS...the ENS contains more neurons than the spinal cord! The ENS functions autonomously, and is called the “2nd brain” even though it can be influenced by CNS. The ENS has been classified as the 3rd component of the ANS.

Our enteric bugs:

The two most prominent phyla in our gut are *Firmicutes* and *Bacteroides*, which comprise $\frac{3}{4}$ of the gut microbiome in healthy individuals. These microbiota interact locally as well as with CNS. Interestingly, there is evidence that dysbiosis is associated with IBS, neurodevelopmental disorders such as ASD, as well as mood disorders.

The Gut Immune System:

A healthy Gut-Immune system prevents harmful microbes or break-down products from digestion from entering our bloodstream as well as allowing for synthesis of lymphocytes. The gut epithelium and the mucosa form an important mechanical barrier that protects the body from microbial invasion. Amazingly, **70-90% of our immune system is found in the gut**, found in GALT (Gut associated lymphoid tissue) or in groups of cells called Peyer's patches (PP). Peyer's patches can be considered as the immune sensors of the intestine and coordinate immune responses to pathogens. The gut's Peyer's Patches allows beneficial bacteria to grow.

When Gut Microbiota is Out of Balance and Epithelial Lining is Compromised:

An abnormal microbiota leads to an unhealthy epithelial lining. When the balance of bacteria is altered (i.e., we need adequate *Bifidobacteria*) and the lining is compromised, there is decreased lymphocyte production as well as decreased neurotransmitter synthesis. With decreased lymphocyte production, unable to defend itself against microbes. Epithelial lining is compromised and toxins can pass through (toxic metabolites and inflammatory cytokines from opportunistic bacteria) into the bloodstream to the “Blood Brain Barrier (BBB)”.

What is this “Leaky gut”?

The gut barrier regulates the flow of nutrients and signal molecules in the body and prevents the entry of microorganisms, food residue, and harmful substances. The BBB controls the entry and exit of substances in the circulatory system, and its key components are tight junctions (TJs). Thus, the integrity of the barriers is critical for human health. Many factors, such as stress, alcohol use, unhealthy diet, and heavy metal, damage the gut barrier, increase intestinal permeability, and allow biomacromolecules and microorganisms to pass through to the body that could not do so before; this syndrome is called leaky gut.

When the gut barrier is broken, the BBB is also impaired, and proinflammatory chemicals can even pass through the BBB, reaching the brain and inducing neuroinflammation. These are thought to be key contributors to many inflammatory diseases, metabolic diseases, mental disorders, and neurological diseases.

Gut Microbiota & Our Health: Cause Vs Effect Vs Association

The gut-brain-microbiota connection functions not just as a digestive organ, but has a complex interplay between neuroendocrine and immune functions as well. There is growing research demonstrating the association between dysbiosis and inflammation, metabolic diseases, mental disorders, and neurological diseases. There is quite a bit of research as well looking at prebiotics, probiotics, fecal transplants and other ways to manipulate and encourage “healthy bacteria.” While we don’t yet have specific recommendations on which probiotic strains to use for treatment of certain diseases, making diet recommendations for patients to include anti-inflammatory foods and prebiotic foods (like beans, legumes, oats, barley, bananas, berries, onions, garlic, leeks, apples, flax seed, asparagus) may have beneficial effects for encouraging a healthy microbiota and healing a leaky gut.

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