Healthy brain
healthy Gut

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Gut-brain axis

The gut-brain axis (GBA) consists of bidirectional communication between the central and the enteric nervous system.

linking emotional and cognitive centers of the brain with intestinal functions.

Recent advances in research have described the importance of gut microbiota in influencing these interactions.

Gut-brain axis

The mechanisms underlying GBA communications involve neuro - immuno- endocrine mediators.

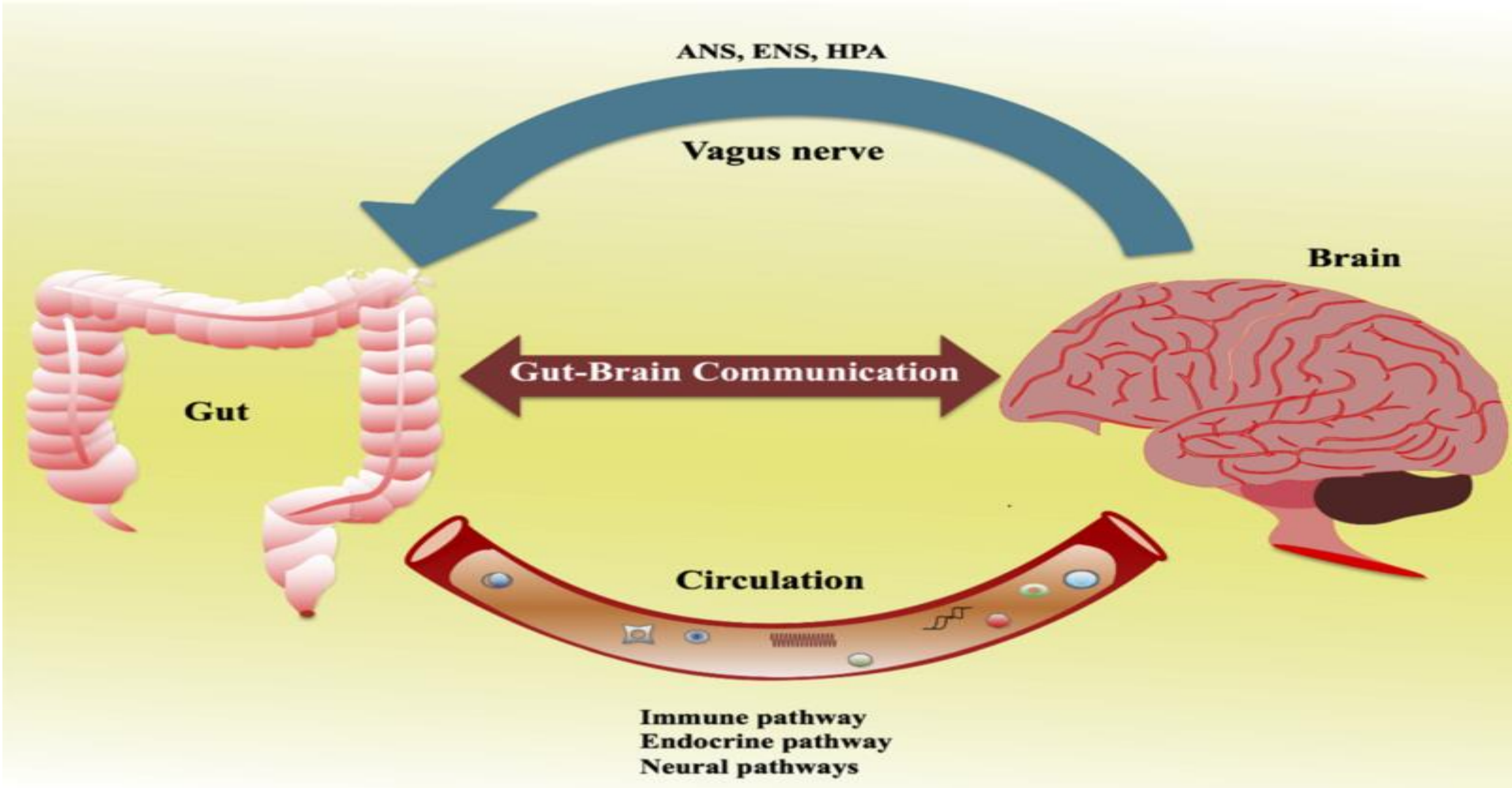
This bidirectional communication network includes:

Central nervous system (CNS) (brain and spinal cord)

Autonomic nervous system (ANS)

Enteric nervous system (ENS)

Hypothalamic pituitary adrenal axis (HPA)


ANS, ENS, HPA
Vagus nerve
Brain
Gut-Brain Communication
Gut
Circulation
Immune pathway
Endocrine pathway
Neural pathways

Autonomic nervous system

The autonomic system: (sympathetic and parasympathetic limbs)

drives both afferent signals, arising from the lumen and transmitted though enteric, spinal and vagal pathways to CNS, and efferent signals from CNS to the intestinal wall.

Enteric Nervous Systems

The enteric nervous system (ENS) is the largest component of the autonomic nervous system and is uniquely equipped with intrinsic microcircuits that enable it to orchestrate gastrointestinal function *independently* of central nervous system (CNS) input.

Hypothalamic pituitary adrenal axis (HPA)

Is a part of the limbic system, a crucial zone of the brain predominantly involved in memory and emotional responses.

Environmental stress, as well as elevated systemic pro-inflammatory cytokines, activate this system:

corticotropin-releasing factor (CRF) from the hypothalamus, stimulates adrenocorticotropic hormone (ACTH) secretion from pituitary gland that, in turn, leads to cortisol release from the adrenal glands.

Hypothalamic pituitary adrenal axis (HPA)

- Cortisol is a major stress hormone that affects many human organs, including the brain.
- Thus, both neural and hormonal lines of communication combine to allow brain to influence the activities of intestinal functional cells, such as:

immune cells, epithelial cells, enteric neurons, smooth muscle cells, interstitial cells of Cajal and enterochromaffin cells.

- These same cells, on the other hand, are under the influence of the gut microbiota , whose contributing role in brain-gut reciprocal communications has recently been assessed.

Who and what is in the gut

Microbiota in the gut weigh 1-2kg (similar to weight of adult human brain)

Microbiome consists of genetic material of bacteria, viruses, fungi, archae inhabiting the gut. Estimated 100 trillion organisms. Co-exists with gut pathogens.

Regulates the immune and endocrine system. Stress and sleep deprivation are known to increase cortisol which causes overgrowth of bad bacteria.

70% serotonin produced in the gut by the microbiome (Candida,Streptococcus, Escherichia, Enterococcus)

GABA, Dopamine, Acetylcholine and Noradrenaline are all made by gut bacteria

The gut microbiome

The gut microbiome serves numerous functions in the human body and is so crucial to our survival that it has been dubbed "**our forgotten organ**."

Some of the roles it serves include:

digestion of polysaccharides

development of the immune system

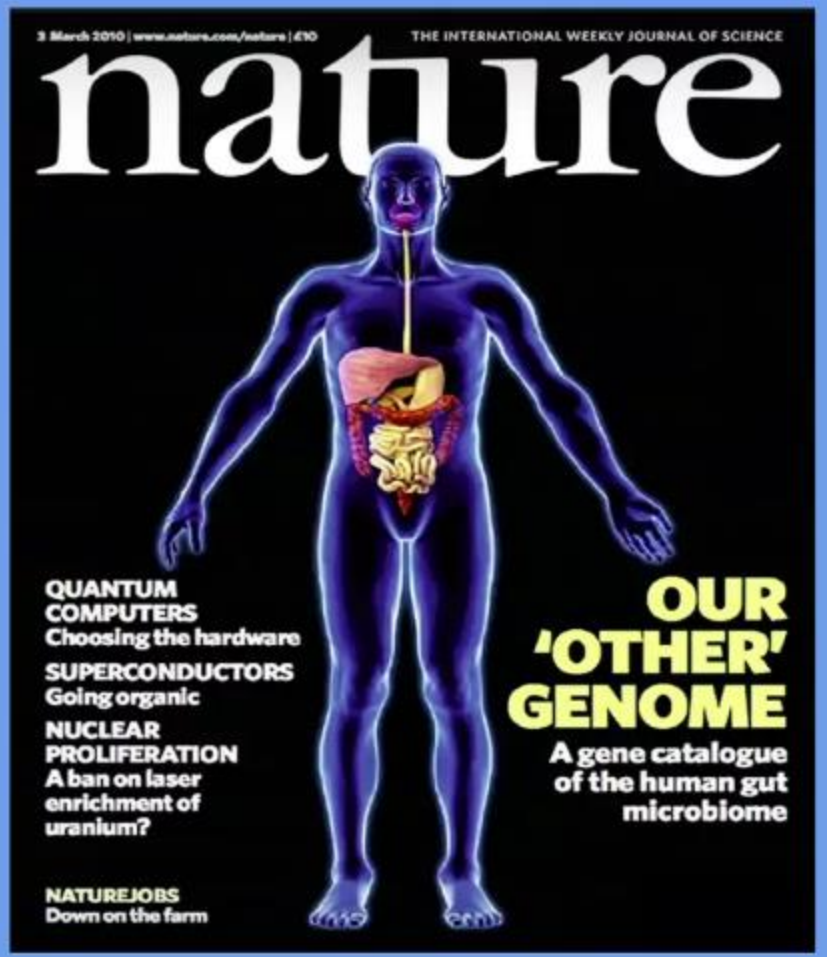
defence against infections

regulation of angiogenesis

production of essential proteins that our genes do not encode

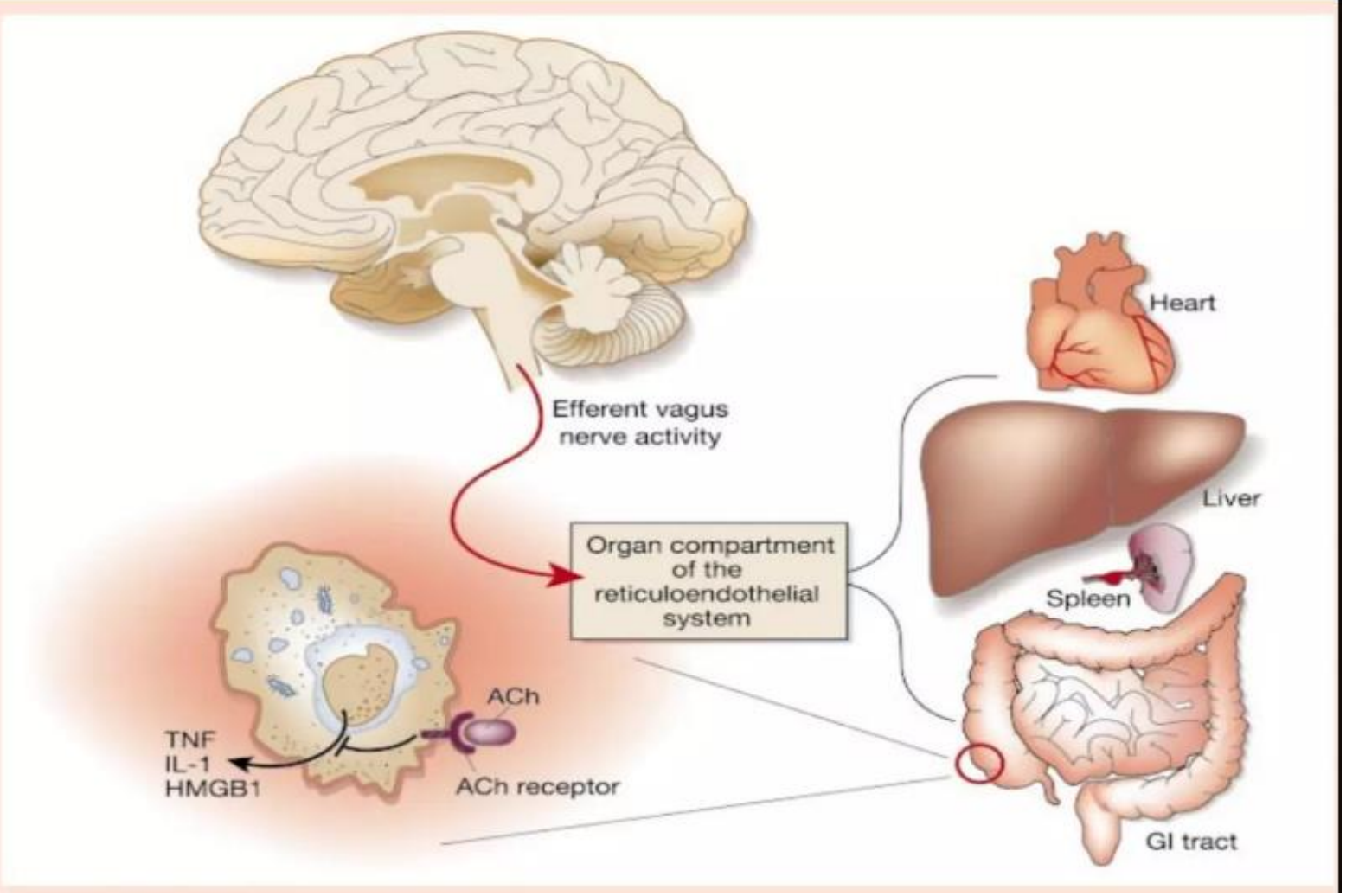
Our Microbiome = we live in a symbiotic relationship with bugs; we are ostensibly a community supporting each other

- **Our microbiome...**
  - Is inhabited by 100 trillion microorganisms
  - This is 10x the number of cells in the human body
  - Has 150x as many genes than we have
  - Co-exists with gut pathogens
  - Regulates the immune system
  - Regulates the endocrine system
  - Modulates digestion (Vitamin K2, single chain fatty acids, and fructose)
  - Weighs 2-6 pounds



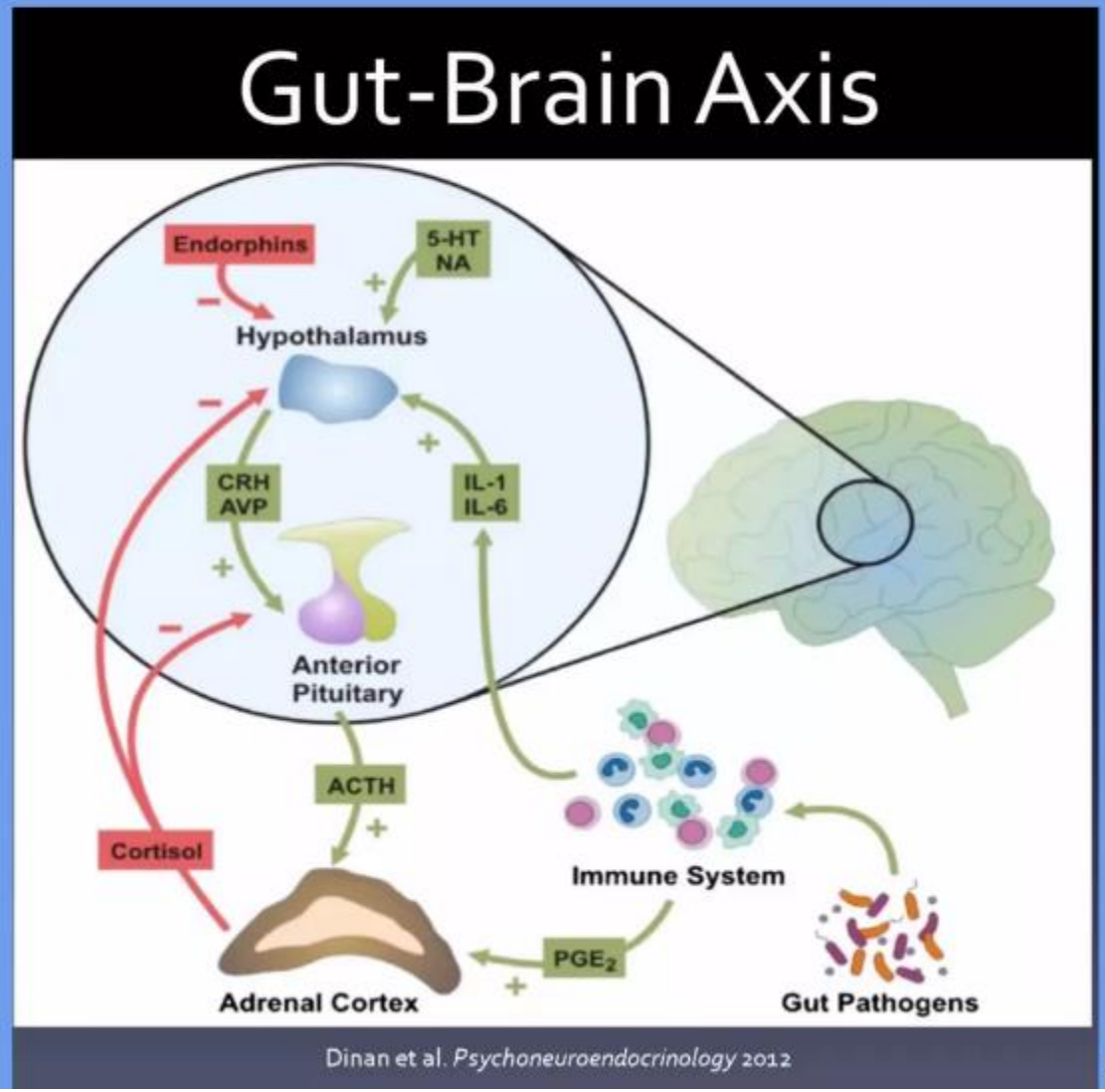
Motor Neural/Vagus Connection from Brain to Gut

Figure 1 The cholinergic anti-inflammatory pathway. Efferent activity in the vagus nerve leads to acetylcholine (ACh) release in organs of the reticuloendothelial system, including the liver, heart, spleen and gastrointestinal tract. Acetylcholine interacts with α-bungarotoxin-sensitive nicotinic receptors (ACh receptor) on tissue macrophages, which inhibit the release of TNF, IL-1, HMGB1 and other cytokines.

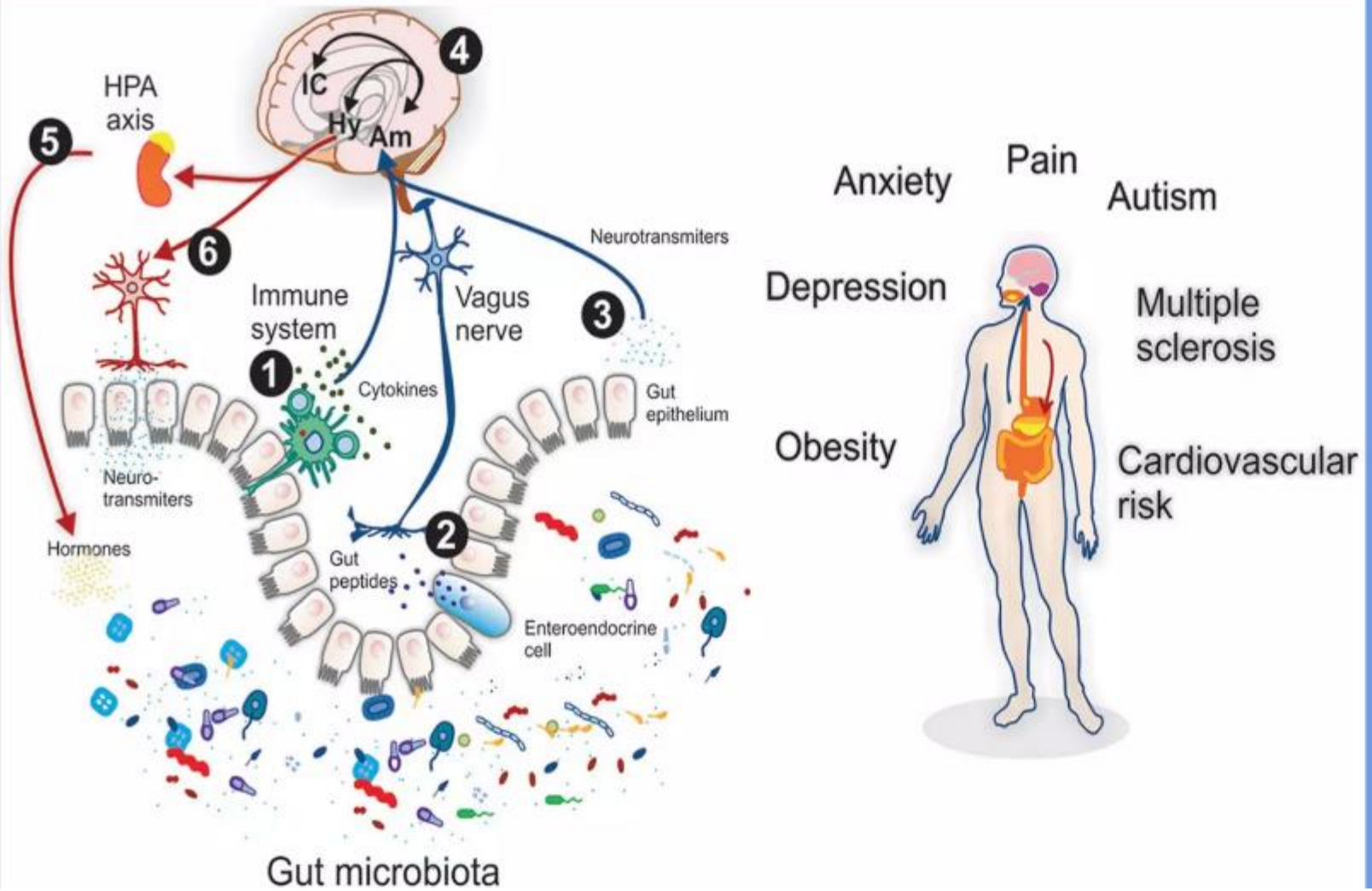


Communication with the Gut Brain Axis is Bi-directional

- ENDOCRINE CONNECTION
  - Take a mouse away from its mother, the gut flora is altered in the baby mouse
  - Stress and sleep deprivation are known to increase cortisol which causes overgrowth of bad bacteria
  - Overgrowth of gut pathogens triggers the immune system to release cortisol, and prostaglandins



Gut/Brain is Bidirectional
Blue= afferent, Red= Efferent



1. Immune system= via endocrine/cytokines
2. Neural Sensory (primarily Vagus Nerve)
3. Neurotransmitters made by microbiome =endocrine to brain
4. Solitary Nucleus brainstem + amygdala (Am), Insular Cortex (Ic), Hypothalamus (Hy)
5. Corticosteroids via HPA axis affect Microbiome
6. The cholinergic anti-inflammatory pathway.Efferent activity of the vagus nerve leads to acetylcholine (ACh) release in organs

Intestinal Permeability (leaky gut)

Gut injury: Gluten, Glyphosate (RoundUp), Lipopolysaccharides, medications (antibiotics, NSAIDs), stress

Zonulin released, tight junctions open

Systemic release of zonulin opens multiple tight junctions:

Gut

Blood brain barrier

Vascular system

Kidney tubules

Consequences of intestinal permeability

Diseases associated with Tight Junction Permeability:

Type 1 Diabetes

Multiple Sclerosis

Rheumatoid arthritis

Can also be associated with development of:

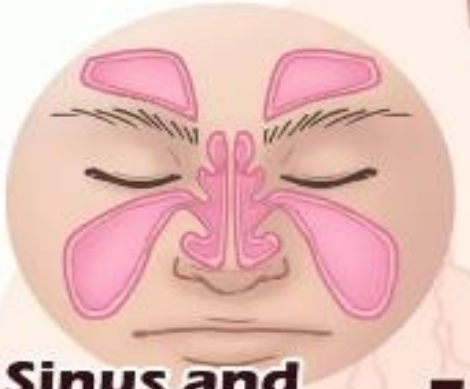
Cancer

Allergies

Infections

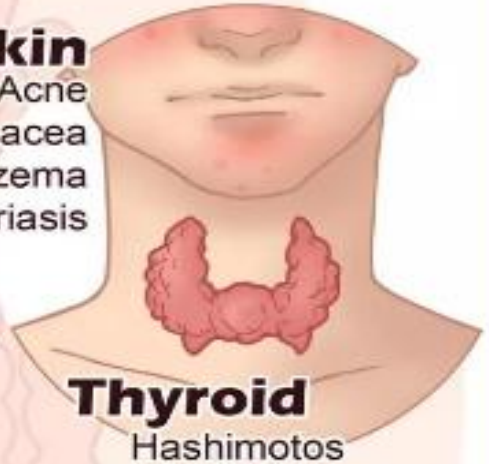
Leaky Gut Affects the Whole Body

Brain
Depression
Anxiety
ADHD



Sinus and Mouth
Frequent Colds
Food Sensitivities

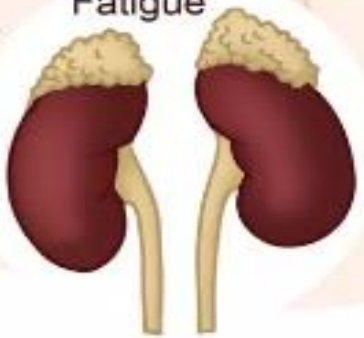
Skin
Acne
Rosacea
Eczema
Psoriasis

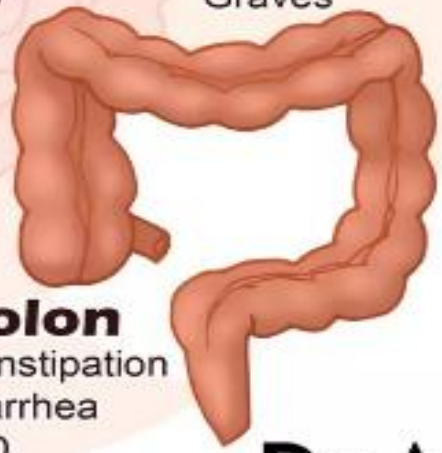


Thyroid
Hashimotos
Hypothyroidism
Graves

Joints
Rheumatoid Arthritis
Fibromyalgia
Headaches

Adrenals
Fatigue





Colon
Constipation
Diarrhea
IBD

Dr. Axe
FOOD IS MEDICINE

IBS

IBS is the most common disorder of brain-gut interaction, occurring in up to 4.8 % of the population worldwide.

up to 50% of individuals who meet diagnostic criteria for an anxiety disorder have IBS, and

individuals with IBS have a greater than three-fold risk of meeting diagnostic criteria for an anxiety disorder.

IBS

in the majority of IBS patients, CNS-related precipitants in early and adult life (e.g., psychological trauma, stress, abuse, maternal neglect) have been identified,

about half of IBS patients present after an intestinal trigger.

individuals with higher baseline levels of anxiety and depression were significantly more likely to develop IBS.

In recent years, there have been an increasing number of studies showing that patients with IBS and also Major Depressive disorder (MDD) have an altered gut microbiome compared to healthy controls.

transferring the microbiome of a depressed individual into a healthy rodent can induce depressive-like behaviors in the murine recipient suggesting the possibility of a causal role for the microbiota in pathophysiology of depression.

From brain to gut microbiota

psychological stressors modulate the composition and total biomass of the enteric microbiota,independently from duration.

exposure to social stressor for only 2 h significantly able to change the community profile and proportions of the main microbiota phyla

From brain to gut micro biota

Direct influence :

is mediated by the secretion, under the regulation of brain

signaling molecules by neurons ,immune cells and enterocromaffin cells, which might affect microbiota

bacteria have neurotransmitter receptors.

High affinity for GABA system has been reported in *Pseudomonas fluoresce.*

Escherichia coli O157:H7 has a receptor for host-derived epinephrine/norepinephrin

brain has a prominent role in the modulation of gut functions

such as motility, secretion of acid, bicarbonates and mucus, intestinal fluid handling and mucosal immune response,

all important for the maintenance of the mucus layer and biofilm where individual groups of bacteria grow

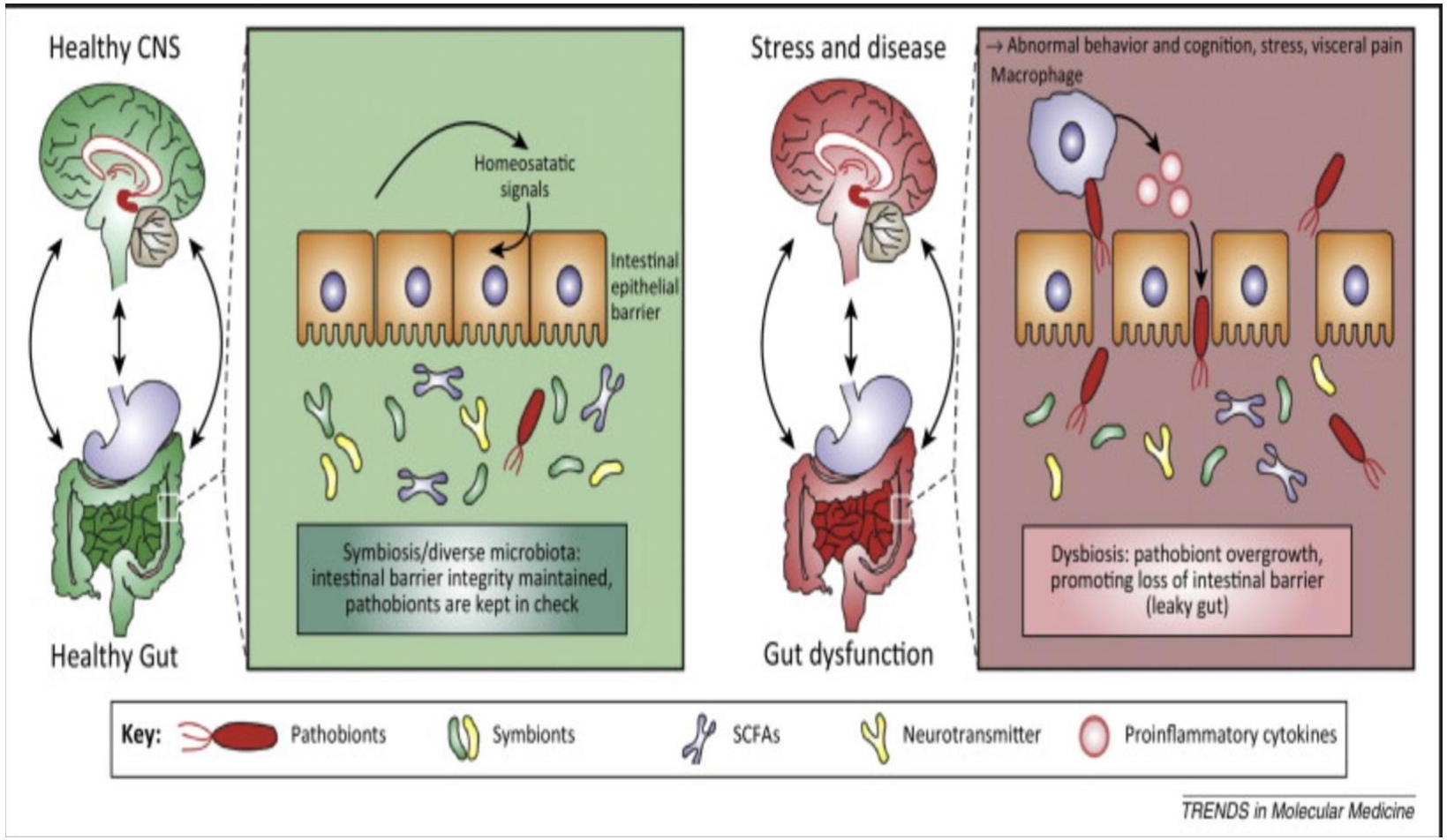
Brain might also affect microbiota composition and function by alteration of intestinal permeability, allowing bacterial antigens to penetrate the epithelium and stimulate an immune response in the mucosa.

Acute stress increased colonic paracellular permeability involving overproduction of interferon-γ

gut alterations associated to stress facilitate the expression of virulent bacteria.

Norepinephrine released during surgery induces the expression of *Pseudomonas aeruginosa*, which might result in gut sepsis .

Norepinephrine can also stimulate proliferation of *Campylobacter jejuni* and *Escherichia coli* 0157:H7



Healthy gut ⟺ Healthy brain