



# Human Microbiome The Gut-Brain Axis

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# Human Microbiome

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- The human microbiota is the collection or mass of microorganisms
- The ecological community of
  - commensal (coexist)
  - symbiotic ( naturally dependent)
  - pathogenic microorganisms that share our body space



# Human Microbiome

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- The human body contains over 10 times more microbial cells than human cells
- Entire microbiome only weighs about 200 grams, with some weight estimates ranging as high as 3 pounds
- Certain microbiota perform tasks that are known to be useful for the human host yet the role is not well understood.
  - expected to be present
  - under normal circumstances do not cause disease
  - are deemed normal flora or normal microbiota



# Human Microbiome

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- Includes bacteria, fungi, and archaea
- Distinguished as "microbiome" and "microbiota" to describe
  - collective **genomes** of the microorganisms that reside in an environmental niche
  - the microorganisms themselves
  - Joshua Lederberg coined the term, arguing the importance of microorganisms inhabiting the human body in health and disease



# Human Microbiome

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- A microbiome that resides on or within a number of tissues and biofluids
  - skin,
  - mammary glands
  - placenta
  - seminal fluid
  - uterus, ovarian follicles
  - lung
  - saliva, oral mucosa,
  - conjunctiva
    - the mucous membrane that covers the front of the eye and lines the inside of the eyelids
  - gastrointestinal tracts\*\*\*\*



## Microbiome An Organ?

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- A "newly discovered organ"
  - not recognized until the late 1990s
  - understood to have potentially overwhelming impact on human health



## Microbiome – A New Organ?

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- Like any other organ, the microbiome has physiology (structure) and pathology (behavior of disease), and the overall health might be damaged when its collective population structure is altered
  - the diagnosis of microbiomic diseases
  - therapies designed around disease
    - phycotherapeutics
      - [http://www.cell.com/trends/neurosciences/fulltext/S0166-2236\(16\)30113-8](http://www.cell.com/trends/neurosciences/fulltext/S0166-2236(16)30113-8)
    - transplant
  - new medical specialty, microbiology, is being born

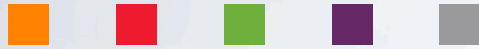


## Intestinal Microbiome

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- The normal gut microbiota imparts specific function in host
  - nutrient metabolism
  - xenobiotic and drug metabolism
  - maintenance of structural integrity of the gut mucosal barrier
  - Immunomodulation
  - protection against pathogens





## Intestinal Microbiome

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Several factors play a role in shaping the normal gut microbiota

- Mode of delivery (vaginal or caesarean)
- Diet during infancy (breast milk or formula feeds)
- Adulthood (vegan based or meat based)
- Use of antibiotics or antibiotic like molecules that are derived from the environment or the gut commensal community



## Intestinal Microbiome Antibiotic Use

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A major concern of antibiotic use

- long-term alteration of the normal healthy gut microbiota and **horizontal transfer of resistance genes** that could result in **reservoir of organisms with a multidrug resistant gene pool**



## Intestinal Microbiome Antibiotic Use

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- Disrupt the microbial community in healthy infants (Gevers et al., 2014)
- Amplifies the microbial dysbiosis in pediatric patients with Crohn's disease (Gevers et al., 2014)
- Several reports have shown that **dysbiosis alone as may result from antibiotic treatment** is sufficient to drive intestinal inflammation (Hooper et al., 2012).
- Alterations of the microbial composition are often associated with **changes in brain development and plasticity and alterations in motor, anxiety and social behavior** (Sudo et al., 2004; Diaz-Heijtz et al., 2011; Neufeld et al., 2011; Clarke et al., 2013; Desbonnet et al.,



## Intestinal Microbiome

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The gut microbiota have been associated with a large array of human diseases

- Luminal diseases such as inflammatory bowel diseases (IBD) and irritable bowel syndrome (IBS)
- Metabolic diseases such obesity and diabetes
- Allergic disease
- Neurodevelopmental illnesses
  - Gut brain axis



## GUT-Brain Axis

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- The gut–brain axis is the **biochemical signaling** between the
  - gastrointestinal tract
  - central nervous system
- Includes the role of the gut flora in the interplay; the term **microbiome-gut-brain** axis is used to describe a biochemical model that **explicitly includes the gut flora**



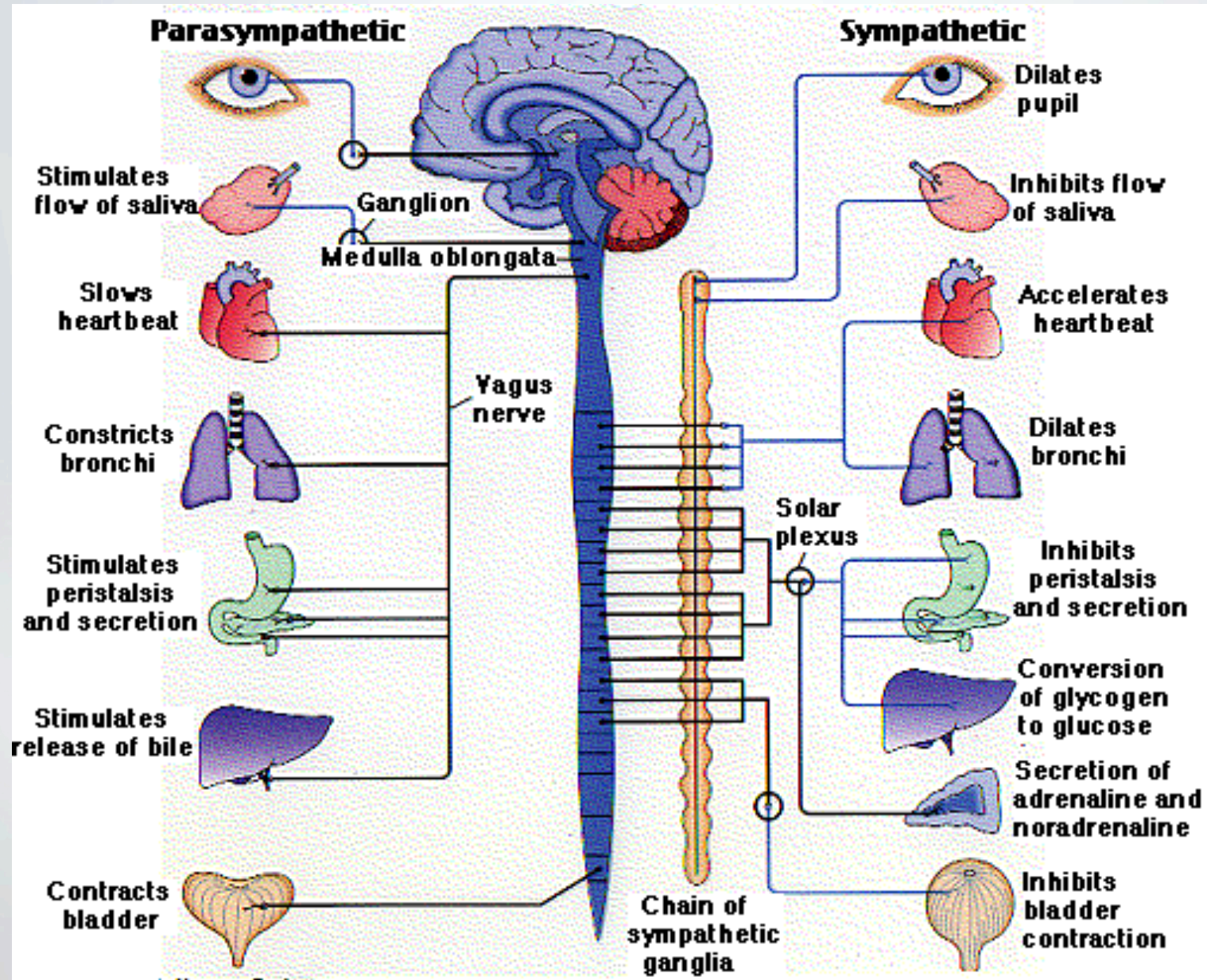
## GUT-Brain Axis – Four Networks

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This bidirectional communication network

- central nervous system (CNS), both brain and spinal cord
- autonomic nervous system (ANS)
  - evidence indicates that microbiota communication with the brain involves the vagus nerve
- the enteric nervous system (ENS)
  - “the guts brain”
- hypothalamic pituitary adrenal (HPA) axis







## Gut Brain Axis

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- Bidirectional communication from gut microbial between the central and the enteric nervous system
  - linking emotional and cognitive centers of the brain with peripheral intestinal functions
- Signaling from gut-microbiota to brain and from brain to gut-microbiota by means of neural, endocrine, immune, and humoral links ( antibodies in body fluids)





## Gut Brain Axis

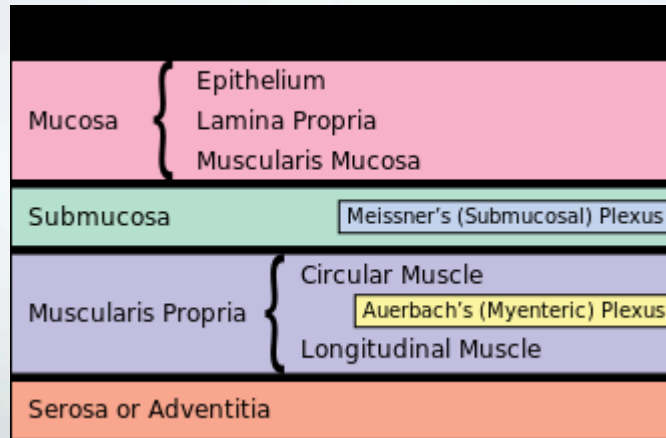
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- Central nervous system communicate with different intestinal targets
  - enteric nervous system (ENS)
  - muscle layers and gut mucosa
  - modulating motility, immunity, permeability and secretion of mucus.



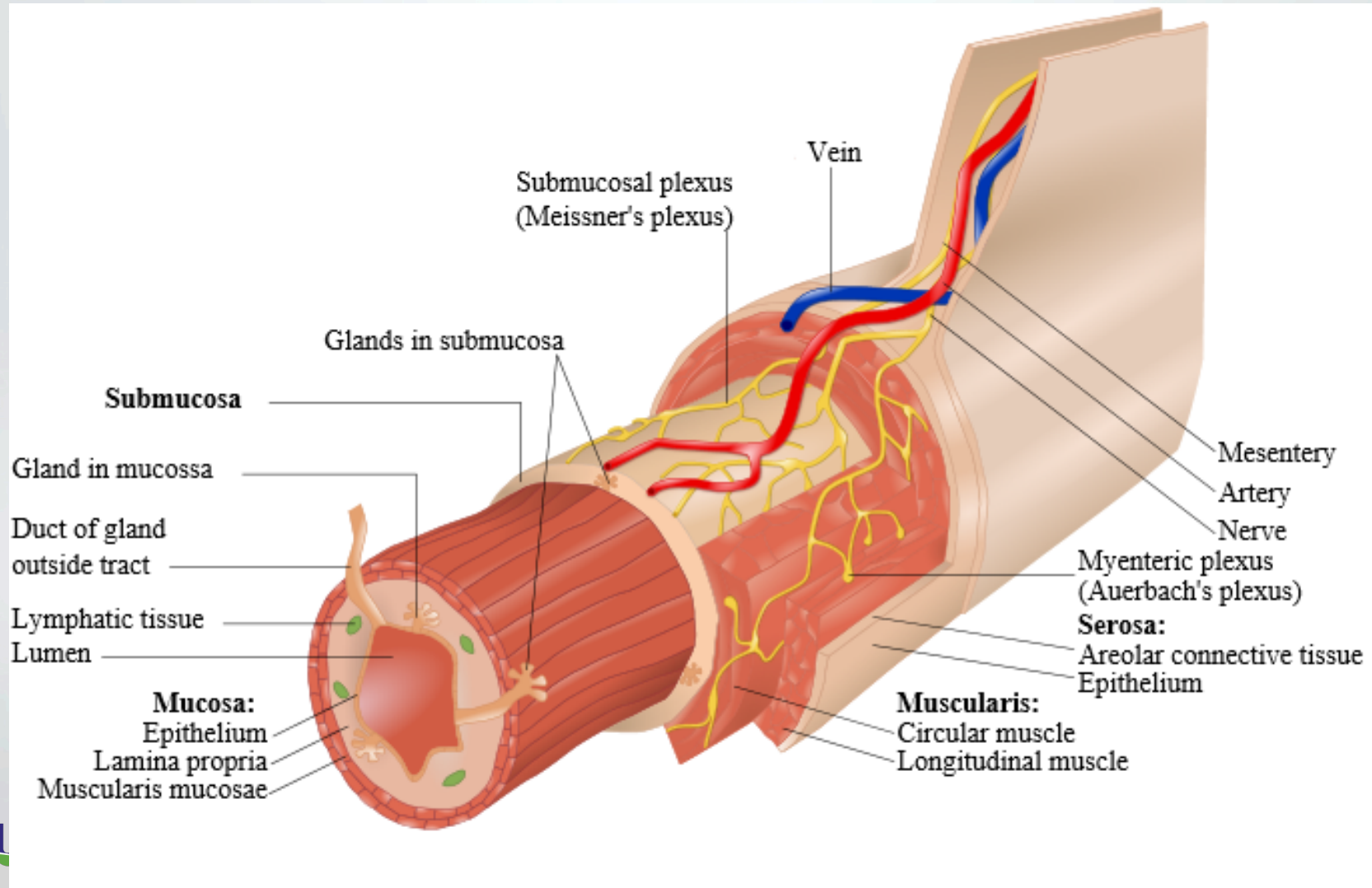
# Enteric NS

- The enteric nervous system (ENS) or intrinsic nervous system is one of the main divisions of the nervous system and consists of a mesh-like system of neurons that governs the function of the gastrointestinal system
- Separate from the autonomic nervous system since it has its own independent reflex activity





# Enteric NS





# Enteric NS

## The Brain in Your Gut

The gut's brain, known as the enteric nervous system, is located in sheaths of tissue lining the esophagus, stomach, small intestine and colon.

### SMALL INTESTINE CROSS SECTION

#### Submucosal plexus

Layer contains sensory cells that communicate with the myenteric plexus and motor fibers that stimulate the secretion of fluids into the lumen.

#### Myenteric plexus

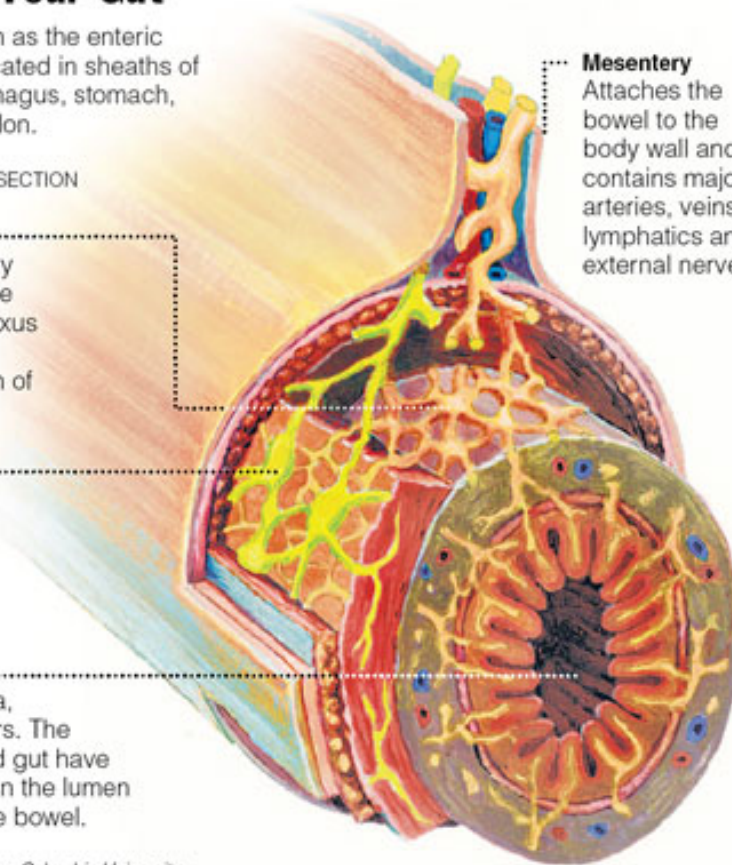
Layer contains the neurons responsible for regulating the enzyme output of adjacent organs.

#### Lumen

No nerves actually enter this area, where digestion occurs. The brains in the head and gut have to monitor conditions in the lumen across the lining of the bowel.

#### Mesentery

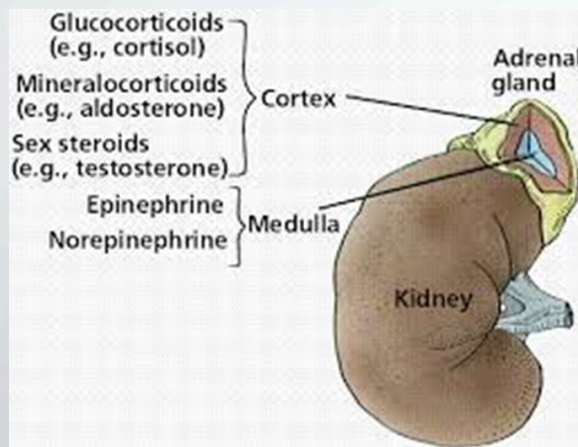
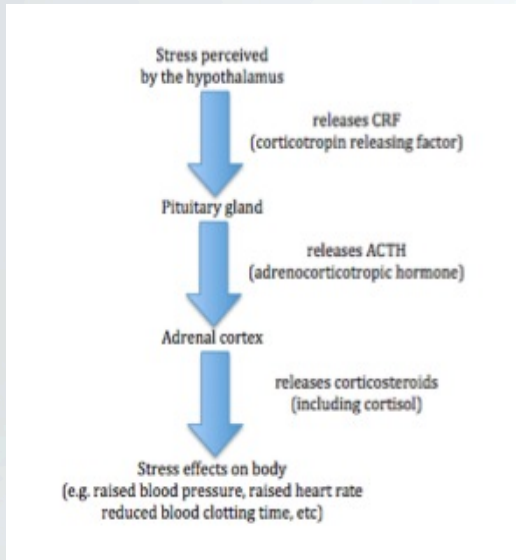
Attaches the bowel to the body wall and contains major arteries, veins, lymphatics and external nerves.



Source: Dr. Michael D. Gershon, Columbia University



# Hypothalamic–pituitary–adrenal axis (HPA)



- The **Brain** – perceives stress
- Sends message via hormones (ACTH) to
  - Adrenal cortex which in turn
    - releases cortisol
  - Cortisol increases the availability of the body's fuel supply of carbohydrate, fat and glucose which is needed to respond to stress.
  - Excessive, ongoing cortisol has profound health consequences
    - weight
    - cardiovascular
    - emotional /neurobiological





## Regulating HPA Axis- Excess Cortisol

SUPPLEMENTS

Several neurotransmitters are important in regulating the HPA axis particularly dopamine, serotonin and norepinephrine

Serotonin receptors modulate the release of many neurotransmitters



## Stress and Neurobiological Disorders

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- The HPA axis is involved in the neurobiology of mood disorders and functional illnesses
  - anxiety disorder, bipolar disorder, insomnia, posttraumatic stress disorder, borderline personality disorder, ADHD, major depressive disorder, burnout, chronic fatigue syndrome, fibromyalgia, irritable bowel syndrome, and alcoholism
- Treated with antidepressants

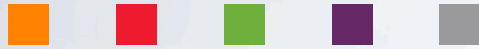


## Nutritive Support to Reduce Stress Response

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- Chronic overstimulation of HPA (cortisol) due to stress
- Course of action; multifaceted protocol based on three phases
  - adaptogens
  - B vitamins
  - vitamin C
  - lavender (*Lavandula angustifolia*)
  - amino acids

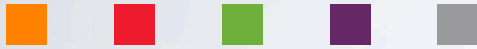




## Gut Bacteria

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- Bacterial colonization of the gut is central to development and maturation of both ENS and CNS
- The absence of microbial colonization is associated to an **altered expression and turnover of neurotransmitters in both nervous systems**
- Alterations of gut sensory-motor functions, consisting in **delayed gastric emptying** and intestinal transit



## Gut Bacteria

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- Neuromuscular abnormalities results in **reduction in gene expression of enzymes** involved in the synthesis and transport of
  - neurotransmitters
  - muscular contractile proteins - muscle contraction
- **All these anomalies are restored,**
  - After re colonization in a bacteria



## Intestinal and Neurological Health Issues

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- In clinical practice, evidence of microbiota-Gut Brain Axis interactions is associated with
  - dysbiosis of gut microbial with central nervous disorders
    - autism, anxiety-depressive behaviors
    - memory dysfunction
  - functional gastrointestinal disorders
    - irritable bowel syndrome
    - heartburn
    - acid reflux
    - chronic gas
    - dysphagya – ( swallowing)



## Probiotic Influence

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- Microbiota affects anxiety and HPA system by influencing brain neurochemistry
- Chronic treatment with *Lactobacillus rhamnosus* (JB-1) induced region-dependent alterations in GABA mRNA (messenger RNA) in the brain
- Probiotic reduced **stress-induced release of cortisol**, anxiety- and depression-related behavior



## The Gut Brain Axis and Immunity

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- Separated domains
  - neurology,
  - endocrinology
  - immunology
  - microbiology
- With their various organs
  - the brain
  - glands, gut
  - immune cells
  - Microbiota
- Are joined to each other in a multidirectional network of communication, **in order to maintain homeostasis**



## The Gut Brain Axis and Immunity

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- The gut microbes greatly impact the immunological, psychological, and overall well-being of the host
  - (Collins and Bercik, 2013; El Aidy and Kleerebezem, 2013a; Wang and Kasper, 2013; Moloney et al., 2014)



## Products

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- NOW80690 C-1000 with 100mg Bioflavonoids 100vcap
- NOW80692 C-1000 with 100mg Bioflavonoids 250vcap
- NOW80680 C-1000 Sustained release (citrus free) 100tab
- NOW80682 C-1000 Sustained release (citrus free) 250tab
- NOW86425 Apple Pectin 700mg 120cap
- NOW86512 Glucomannan 575mg 180cap
- NOW85966 Organic Psyllium Husk Powder 340g
- NOW85968 Organic Psyllium Husk Whole 340g
- NOW85970 Psyllium Husk 500mg 200cap





## Products

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- NOW85975 Psyllium Husk Powder 340g
- NOW85980 Psyllium Husks Whole (bottle) 340g
- NOW85981 Psyllium Husks Whole (bag) 454g
- NOW80330 Vit A 10,000 IU 100gel
- NOW84750 Slippery Elm 400mg 100cap
- NOW82120 MSM 1000mg 120cap
- NOW82121 MSM 1000mg 240cap
- NOW82125 MSM Pure Pwd 227g
- NOW83342 Relora 300mg 60vcap
- NOW84754 Rhodiola (ArcticRoot) 500mg 60vcap





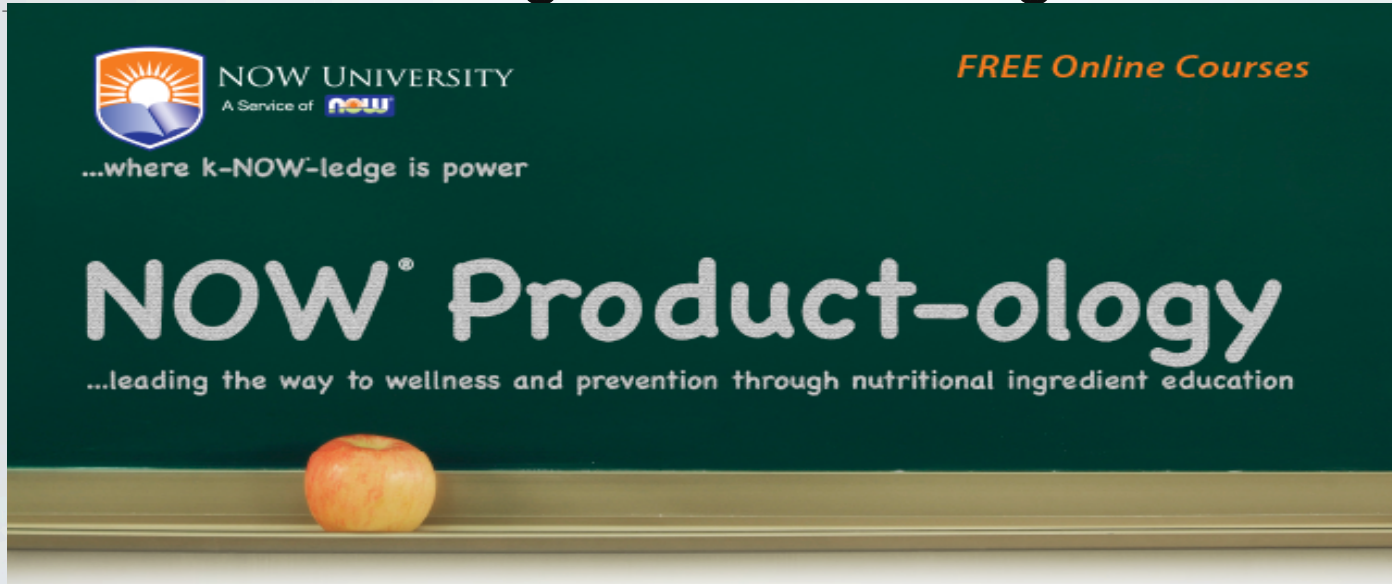
## Products

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- NOW82919 GI Probiotic 10Bill 9Strain 60vcap (RR)
- NOW82912 Gr8-Dophilus, Enteric Coated 60vcap
- NOW82926 Probiotic-10™ 25 Bill (10 Strains) 50vcap
- NOW82934 S. Boulardii 5 Billion (Diarrhea aid) 60vcap
- NOW82944 Org Inulin 100% Pure Pwd 227g
- NOW83345 Ulcetrol w/PepZinGI, Carnosine, Mastic, Zinc 60tab



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  4. The name of the tele-training session i.e. Nutritional Fats, Cognitive Health etc.
  5. The name of the product that you are requesting
  6. Password given by Marva Ward during the presentation



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