Human Microbiome
The Gut-Brain Axis

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**Human Microbiome**

- 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

- 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

- 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
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?

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

- 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 diagnostic of microbiomic diseases
  - therapies designed around disease
    - phychobiotics
    - transplant
  - new medical specialty, microbiomology, is being born
Intestinal Microbiome

- 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

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

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

- **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

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 as obesity and diabetes
- Allergic disease
- Neurodevelopmental illnesses
  - Gut brain axis
GUT-Brain Axis

- The gut–brain axis is the \textit{biochemical signaling} between the
  - gastrointestinal tract
  - central nervous system
- Includes the role of the gut flora in the interplay; the term \textit{microbiome-gut-brain} axis is used to describe a biochemical model \textit{that explicitly includes the gut flora}
GUT-Brain Axis – Four Networks

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

- 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

- 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
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

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

- 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

- 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

- 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

- Neuromuscular abnormalities result 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

- 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

- 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

- 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

- 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

- 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

- 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

- 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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