Understanding the Gut Brain

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Part 1: Understanding the Gut Brain

- What is the Gut Brain?
- The Gut-Immune System
- The Language of the Gut brain
1. What is the Gut Brain?

Nervous System (NS)
- Peripheral NS
  - Autonomic NS
  - Somatic NS
- Central NS
  - Brain
  - Spinal Cord

Enteric

Sympathetic NS
- Telencephalon
  - Cerebral Cortex
  - Basal Ganglia
  - Hippocampus
  - Amygdala

Parasympathetic NS
- Diencephalon
  - Thalamus
  - Hypothalamus
- Mesencephalon
  - Tectum
  - Tegmentum
- Metencephalon
  - Pons
  - Cerebellum
- Myelencephalon
  - Medulla
Central Nervous System

Brain & spinal cord – brain weighs 3 #

100 billion neuron
Trillions of glia (support cells)
Major Divisions

- **Central** – brain & spinal cord
- **Peripheral** – somatic & autonomic
  - **Somatic** – carries messages to muscles
  - **Autonomic** – internal processes
    - sympathetic (SNS), parasympathetic (PNS) & enteric
Enteric Nervous System

- **Enteric** – meshwork of nerve fibers that innervate the viscera (gastrointestinal tract, pancreas, gall bladder)
Role of Enteric NS

- Functions autonomously but is modified by PSN (vagus) & SNS
- When the **vagus nerve** is severed, the enteric nervous system still functions

  90% of messages that operate the gut, come from the enteric NS not the brain
Enteric Nervous System

Embedded in lining of gut

“Distinct Entity” it is a complete network of neurons, neurotransmitters, and special proteins responsible for communications, "thinking," "remembering," and even "learning"
ENS is autonomous
BUT also influences the brain!!
2. Gut Immune System

- **Immune system contains:** blood, organs & cells (0:39 – 2:26)

- **Epithelial cells:** central component of immune system in gut

http://www.youtube.com/watch?v=gnZEtge78_78 6 min
Gut Immune System

What triggers immune system development in gut?

- Gut sterile in uterus
- Birth canal, bacteria become signal to activate gut immune system
- C-section – pick up bacteria on skin surfaces & have different community of bacteria
  - More colic
  - Slightly ↑ rates of asthma & allergies, 2X more obese by age 3
The Gut Immune System

- **Macrophages**: secrete chemical mediators - cytokines

- **Cytokines**:
  - **Proinflammatory cytokines**: cytokines that coordinate inflammatory responses in the body
    - Tumor Necrosis Factor (TNF)-α
    - IL-1β, IL-6
Gut Immune System & Gut Flora

Work together:

- **Crowd** out bad bacteria – no place to hang on to
- **Symbiotic** relationship
- **Microbiota** allowed to grow, multiple & thrive, minimally being destroyed by host derived inflammatory mediators
- **Prototype peacekeeper** – *Bacteroides fragilis*
Gut Barrier

3 barriers that work together:

- **Mechanical barrier** - mucosal epithelial cells
  - 1. neurons (afferent)
  - 2. endocrine cells
  - 3. immune cells

- **Ecological barrier** - gut bacteria

- **Immune barrier** – like the blood brain barrier
Body Defenses

Mechanical Barrier

The GUT

70 - 90% immune cells are found in the gut

http://www.youtube.com/watch?v=5zlJ8CztFO8&feature=related

start 1:02 stop 2:32
How do we produce Serotonin?

- Tryptophan
- 5-HTP
- Serotonin
- Melatonin
Sources

Tryptophan - Amino acid mg

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<tr>
<th>Source</th>
<th>Amount</th>
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<tr>
<td>Seaweed</td>
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<tr>
<td>Soy nuts</td>
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<td>Cottage cheese</td>
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<tr>
<td>Chicken livers</td>
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<tr>
<td>Tofu</td>
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<td>310</td>
</tr>
<tr>
<td>Milk</td>
<td>(1c)</td>
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</tr>
</tbody>
</table>

Egg white 1000 mg

Crab, lobster

Seeds – sesame, sunflower, nuts (Cashews, almonds)

Cheese (cheddar, Swiss (320 mg/4 oz))

Oat bran, Chia seeds
Egg

Perfect food
High in tryptophan
High in choline 126 mg
(most foods 20 – 30 mg)
Serotonin Production

Two Steps: GUT and BRAIN

First Step – SMALL INTESTINE

Tryptophan → 5-Hydroxy-Tryptophan

Second Step - BRAIN

5-Hydroxy-Tryptophan → Serotonin
Enteric Nervous System

Breast milk

Supports development of neurons in gut & gut wall

So premature &/or none breast fed – high risk for diarrhea & necrotizing enterocolitis

Seems to have memory – not breast fed (trauma to gut wall) & being fed solid foods too soon leads to infection & gut diseases later in life
Hundreds of thousands of endocrine cells produce more than 20 hormones – all target other organs in GI system

- **CCK** – gallbladder
- **Gastrin** - stomach
So How Do Things Go Wrong???

Diet, environment, climate, stress, illness, drugs, aging
3. The Language of the Gut

Pain

• GI diseases are accompanied by pain
• Pain arises when CD4 from immune barrier
• As microbiota are disturbed, substance P mesenteric plexus
Visceral pain results from:

- Direct inflammation of visceral organ
  - inflammatory bowel disease
  - pancreatitis,
  - appendicitis,
  - occlusion of bile,
  - GERD, dyspepsia

- Functional visceral disorders
  - irritable bowel syndrome (IBS)
Visceral pain results from:

- Cardiovascular disease (CV) – clots
- Urinary syndromes - interstitial cystitis, kidney stones
- Female issues - endometriosis
Language of Gut – Gut Feelings

- The more signals leaving the viscera, the more likely to ‘feel’ something

- Messages carried by spinal cord to brain – often are not specific – referred pain
Visceral sensations include: nausea, bloating
All arrive at Insular Cortex in brain
Plays role in emotions & body homeostasis
Regulates the immune system
Conscious desires – food, drugs
Stress alters gut motor function:
- affects peristalsis
- experience more hypersensitivity to gut activity
Brain Actions of Corticotropin-Releasing Factor (CRF)

- CRF stimulates the Pituitary Gland to release ACTH and β-Endorphin.
- CRF also stimulates the Medulla Oblongata, which in turn activates the Sympathetic Nervous System.
- Sympathetic activation leads to increased Cardiac output, Stroke volume, Peripheral vascular resistance, Blood glucose, Heart rate, and Blood pressure.
- CRF stimulates the Adrenal Medulla to produce Epinephrine, which increases Gastric acid secretion and Gastric emptying.
- Behavioral response to stressors and Behavioral activation are indicated by arrows pointing upwards.
Stress

Activation of corticotropin releasing factor (CRF):

- Contributes to delayed gastric emptying
- Increased colonic activity
- Functional bowel disease (IBS)
- Increase in gut permeability
- Leaky gut – antigens leaking out
- Toxic liver overload
- Systemic disease
Cortisol receptors are located throughout the central nervous system.

- **Hippocampus** (limbic system), a structure involved in learning, memory and mood
- **Prefrontal cortex** (tries to shut down cortisol release during stress)
Healthy status

Healthy CNS function

Normal gut physiology

Physiological levels of inflammatory cells/mediators
Normal gut microbiota

Stress/disease

Alterations in behaviour, cognition, emotion, nociception

Abnormal gut function

Increased levels of inflammatory cells/mediators
Intestinal dysbiosis
ENS is autonomous BUT also influences the brain!!
70-90% immune system is in the gut
Need healthy gut for Serotonin production
Healthy gut begins at birth
Many thing can go wrong – diet, environment, stress, drugs, aging
Most times we are unaware of the gut’s language, BUT visceral sensations secondary to pain, inflammation, stress, dysbiosis can be felt by some!