Premier Online Education in Integrative and Functional Medical Nutrition Therapy (IFMNT)

Navigating The Gut-Brain Superhighway

Hosted by: Susan Allen-Evenson RDN, CCN, FMN
Presented by: Sarah Greenfield RDN, CSSD
My Background

• Grew up in a family with a variety of digestive issues
  – IBS, Crohn's, Allergies, SIBO
• Became a dietitian and was very frustrated with the approach to digestive care
• Started running marathons and coaching runners
  – Tons of digestive issues
• Became fixated with the gut
  – Formulated Probiotics
  – Worked with the top integrative GI doc in LA, functional medicine practices
  – Utilize consumer facing and third party labs tests on gut diversity
  – Started treating clients with gut dysfunction
Objectives

• Understand the communication pathways and mediators that make up the gut brain axis
• Identify causes of gut-brain axis dysfunction and the impact it has on mood
• Review tests that can help uncover imbalances
• Learn actionable nutrition and lifestyle interventions to improve gut dysfunction
Communication Pathways

The gut-brain axis

– Enteric Nervous System
  • Oversee the functions of the GI tract
    – Neuroendocrine
    – Microbiome
    – Migrating Motor Complex

– Autonomic Nervous System
  • Parasympathetic and sympathetic
    – Digestion (peristalsis), heart rate, respiratory rate, urination, and sexual arousal

Communication Pathways cont

– Central Nervous System
  • Brain and Spine
– HPA – hypothalamic pituitary adrenal
  • Stress response
– Vagus Nerve
  • Connect ENS and CNS
**Communication Pathways - ENS**

- Has more neurons acting than anywhere else in the body
- Moves smooth muscles, activates glands for secretion to lubricate and digest food
- Migrating Motor Complex
  - Mechanical and chemical cleansing of the stomach and small intestines during fasting
  - Happens about 3-5 hours between meals
  - Cleans out undigested food and excess bacteria
    - Divided into 4 phases
      - Phase 3 - most active, with a burst of contractions from the antrum or duodenum (5-15 minutes)
      - Can be induced by motilin and ghrelin

Communication Pathways - ENS

• Migrating Motor Complex
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Communication Pathways
Communication Pathways - ENS

Contains the gut microbiome

– Makes neurotransmitters, vitamins, upregulated immune system, interacts with hormones, modulates permeability

– Make SCFA that can stimulate the sympathetic nervous system, mucosal serotonin release and impact memory
  • We have about 5 main phyla of bacteria in our gut
    – 30-40 species make up the bulk of our gut
  • more diverse the better
Communication Pathway - ANS

- Parasympathetic and Sympathetic
  - The rest and digest and the fight or flight
- Regulates heart rate, digestion, respiratory rate, pupillary response, urination, and sexual arousal
- Two specific neurotransmitters
  - Acetylcholine
  - Norepinephrine
Communication Pathways

CNS

• Brain and spinal cord
• Uses 20% of the total oxygen we breathe
• Receive information from the gut via the vagus nerve
Communication Pathways
HPA Axis

• Stress response
• Communicates with the limbic part of the brain linked to emotions
• Activates cortisol

Communication Pathways

• Supplies tissues that are involved in the digestion, absorption, and metabolism of nutrients
  – Communication pathway from the ENS to the CNS
  – Vagal activation influences metabolic responses to food as well as inflammation
Communication Mediators

• Neurotransmitters made in ENS
• Immune modulators
  – Cytokines
• Hormones
  – Cortisol
• Bacterial by products
  – Lipopolysaccharides - in the structural makeup of gram negative bacteria
Communication Mediators - Neurotransmitters

• Serotonin
  – Made in the gut by enterochromaffin cells which depend on microbes to function
  – Also made through conversion of tryptophan
  – 90% of serotonin found in gut

• Acetylcholine
  – Increases GI motility when it acts on a smooth muscle

Communication Mediators - Neurotransmitters

• **GABA**
  - Calms down the body and mind
  - Alterations in GABA receptors and expression can be linked to depression and anxiety
    - Lactobacillus rhamnosus bacteria found to upregulate GABA receptors in the brain

• **Catecholamines**
  - Dopamine
    - Stimulates T-cell activity, regulating electrolyte activity
  - Epinephrine
  - Norepinephrine
Dysfunction

• Physical trauma - brain injury
• Stress
• Inflammation
• Poor Gut Diversity
  – Standard American Diet
• Medications
Physical Trauma

Alterations in the ANS

- Dysmotility, abnormal peristalsis
- Study found that mice with Traumatic Brain injury had a measurable difference in intestinal microvilli 6 hours after brain injury
  - Increase intestinal permeability
- Breakdown blood brain barrier
  - Inflammatory compounds can access the brain

Impact of Stress

Impact of Stress

• Types of stress
  – Physical and Emotional
  – Environmental
    • Toxic Burden
  – Excessive Exercise
  – Undereating

• HPA axis is stimulated
  – Cortisol released
    • Revs up immune system increasing cytokines and inflammation
      – Increasing permeability
    • Impacts serotonin
Impact of Inflammation

Miller, AH, et al. "Inflammation and its discontents: the role of cytokines in the pathophysiology of major depression". Biol Psychiatry. 2009 May 1;65(9):732-41. doi:
Impact of Inflammation

Inflammation kicks off immune response

• Mobilizing macrophages
• Upregulating cytokines
• Downregulates neurotransmitters
  • Glutamate
  • Catecholamines
  • Serotonin
    – Decrease BDNF
Impact of Inflammation

• Impact on Serotonin
  – IDO enzyme is upregulated
  – Tryptophan steal or Kynurenine pathway
    • Downregulates BDNF
• Root cause of depression

Is oxidative stress stealing your serotonin? The NEI Connection. https://neuroendoimmune.wordpress.com/2014/03/04/is-oxidative-stress-stealing-your-serotonin/
Impact of Gut Diversity

• Studies with germ-free mice
  – Gut
    • Delayed gastric emptying and intestinal transit
    • Reduced migrating motor complex
    • Decreased immunity
  – Brain
    • Altered expression and turnover of neurotransmitters
    • Reduction in gene expression of enzymes involved in the synthesis and transport of neurotransmitters
    • Increases anxiety and function of HPA
    • Memory dysfunction
    • Decrease in brain-derived neurotrophic factor (BDNF)
      » All functions restored when bacteria re-introduced
Impact of Gut Diversity

Studies with germ-free mice

- Delayed gastric emptying
- Reduced migrating motor complex
- Altered expression and turnover of neurotransmitters
- Reduction in gene expression of enzymes involved in the synthesis and transport of neurotransmitters
- Impaired immune response
- Memory dysfunction
  - Decrease in brain-derived neurotrophic factor (BDNF)
  - All functions restored in an age-dependent manner

Impact of Gut Diversity

IBS

- Linked to abnormal microbiota
  - activates mucosal innate immune responses
  - increase epithelial permeability
  - activate nociceptive sensory pathways inducing visceral pain
  - dysregulates the enteric nervous system

Impact of Gut Diversity

In those with IBS, antidepressants have been found to have a positive effect on motility and visceral hypersensitivity

- **SSRI**
  - SSRIs improve depression through increasing serotonin but also help relieve constipation

- **Tricyclic**
  - Interact with serotonin and norepinephrine
  - Treatment for IBS-D, diarrhea prone IBS
Impact of Gut Diversity

Anxiety

— commensal, probiotic, and pathogenic bacteria, in the gastrointestinal (GI) tract can activate neural pathways and central nervous system (CNS) signaling systems

• Impact GABA receptors
• Yeast can increase inflammation

Impact of Gut Diversity

Impact of Gut Diversity

Autism

- Probiotics have been found to be helpful in several observed abnormal behaviors
- Certain bacterial strains impact certain compounds in the brain

Impact of Gut Diversity

- *Bacteroides* - higher levels of myo-inositol, predicted higher levels of creatine, but an abundant presence of
- *Clostridium* - higher levels of myo-inositol
- *Ruminococcus* bacteria was associated with lower n-acetylaspartate, NAA
- *Butyricimonas* - higher levels of n-acetylaspartate (NAA).
  - These altered levels of compounds have been found in individuals diagnosed with autism spectrum disorder.
- Ketogenic diet has also been found to improve behavioral abnormalities
Medications

• Antibiotics
  – Decreases diversity
  – Children with lots of abx intake, harder to rebuild gut because strains have been wiped out

• PPI
  – Chronic use, decrease diversity

• NSAIDS
  – Decrease diversity, encourage growth of gram neg bacteria and can damage the gut
Nutrition and Lifestyle Interventions

• Nutrition
  – Food interventions
  – Supplements
  – Testing
• Lifestyle
Nutrition

Food Shifts

- Increasing whole foods in diet, decreasing sugar / artificial sweeteners, using herbs
- Eat lots of raw foods
- Easy ways for a busy lifestyle
  - Using frozen vegetable blends
  - Growing herbs in a windowsill
  - Utilizing a food delivery or grocery delivery service
  - Photo-journaling
  - Meal prep
- Adjusting for sensitivities and allergies
Nutrition

Supplements

• Omega-3 fatty acids
  – Boost mood and vagal tone
  – Decrease NF-κB activation

• Prebiotics
  • Increase gut diversity, SCFA production which can impact sympathetic nervous system, mucosal serotonin release and impacts our memory
Nutrition

• Probiotics
  – *Lactobacillus helveticus* R0052 and *Bifidobacterium longum* R0175 restored tight junction barrier integrity and attenuated HPA axis and autonomic nervous system activities
  – *Lactobacillus rhamnosus* interacting with GABA
    • Improving anxiety
    • VSL#3 leads to an increase in BDNF expression

Nutrition Testing

Get to root cause of permeability / inflammation

– GI Effects Test, GI mapping
– SIBO Testing
  • Understanding microbial balance
  • Can see patterns for SIBO in the GI Effects test
– MRT Test
  • Looking at mediators for sensitivities
GI Testing
<table>
<thead>
<tr>
<th>Phylum</th>
<th>Result</th>
<th>1st</th>
<th>2nd</th>
<th>3rd</th>
<th>4th</th>
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<td>Firmicutes Phylum</td>
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<td>5.5E3 - 5.9E5</td>
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<td>Clostridium spp.</td>
<td>1.8E9</td>
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<td>1.7E8 - 1.5E10</td>
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<td>Coprococcus eutactus</td>
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<td>Faecalibacterium prausnitzii</td>
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<tr>
<td>Lactobacillus spp.</td>
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<td>8.3E8 - 5.2E9</td>
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<td>Actinobacteria Phylum</td>
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<td>Bifidobacterium spp.</td>
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<td>Proteobacteria Phylum</td>
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<td>Desulfovibrio piper</td>
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<td>Escherichia coli</td>
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<td>9.0E4 - 4.6E7</td>
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<td>Oxalobacter formigenes</td>
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<td>Euryarchaeota Phylum</td>
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<td>Fusobacteria Phylum</td>
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<td>Verrucomicrobia Phylum</td>
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<td>Akkermansia muciniphila</td>
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</table>

| Firmicutes/Bacteroides Ratio |        |     |     |     |     |     | 12 - 620                 |

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# Nutrition Testing

## SIBO Patterns (GI Effects Testing)

<table>
<thead>
<tr>
<th>Biomarker pattern, along with associated symptoms suggest</th>
<th>Biomarkers</th>
<th>Next steps</th>
</tr>
</thead>
<tbody>
<tr>
<td>Small Intestinal Bacterial Overgrowth (SIBO)</td>
<td>Relative Abundance, Products of Protein Breakdown, SCFA, n-butyrate, Fecal Fat (total), PE1 (limited evidence), <em>Methanobrevibacter smithii</em></td>
<td>Confirm with SIBO Breath Test</td>
</tr>
</tbody>
</table>
Nutrition Testing

- Dutch Test Plus
- ZRT
  - Diurnal cortisol
  - Neurotransmitters
# Nutrition Testing
(Dutch Test)

<table>
<thead>
<tr>
<th>Neurotransmitter Metabolites</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Dopamine Metabolite - (Urine)</strong></td>
</tr>
<tr>
<td>Homovanillate (HVA)</td>
</tr>
<tr>
<td><strong>Norepinephrine/Epinephrine Metabolite - (Urine)</strong></td>
</tr>
<tr>
<td>Vanilmandelate (VMA)</td>
</tr>
<tr>
<td><strong>Serotonin Metabolite - (Urine)</strong></td>
</tr>
<tr>
<td>5-Hydroxyindoleaceta (5HIAA)</td>
</tr>
<tr>
<td>*<em>Melatonin (<em>measured as 6-OH-Melatonin-Sulfate) - (Urine)</em></em></td>
</tr>
<tr>
<td>Melatonin* (Waking)</td>
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<tr>
<td><strong>Oxidative Stress / DNA Damage, measured as 8-Hydroxy-2-deoxyguanosine (8-OHdG) - (Urine)</strong></td>
</tr>
<tr>
<td>8-OHdG (Waking)</td>
</tr>
</tbody>
</table>
Lifestyle

• Be mindful of medications
• Decrease binge drinking
  – Increase endotoxins in blood
• Remove toxic products in household
  – EWG. Think Dirty
• Exercise Moderately
• Meditation
• Reducing stress
• Sleep!
• Self-care
  – Reframing negative thought patterns
  – Finding alternative ways to change mood that are not food related
  – Gratitude journaling
Conclusion

• The brain and the gut are in constant communication via vagus nerve using neurotransmitters
• Decreased gut diversity can lead digestive and mood related disorders
• Finding root cause of inflammation and gut permeability can shift health outcomes especially related to mood dysfunction
• Implement lifestyle, nutrition interventions and specific testing to help clients feel better
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Also Starting Soon....

• Advanced Culinary for IFMNT Application with Amanda Archibald, RDN
  – Starts Tuesday, July 24th
  – 5-session series

• Functional Nutrition Grand Rounds
  – An on-line, small group, interactive “think-tank” series for clinicians wanting to integrate their evidenced-based learning into practice.
thank you!

Questions?

Sarah@fearlessfig.com