Next Level Functional Nutrition™

Susan Allen-Evenson, RDN, CCN

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

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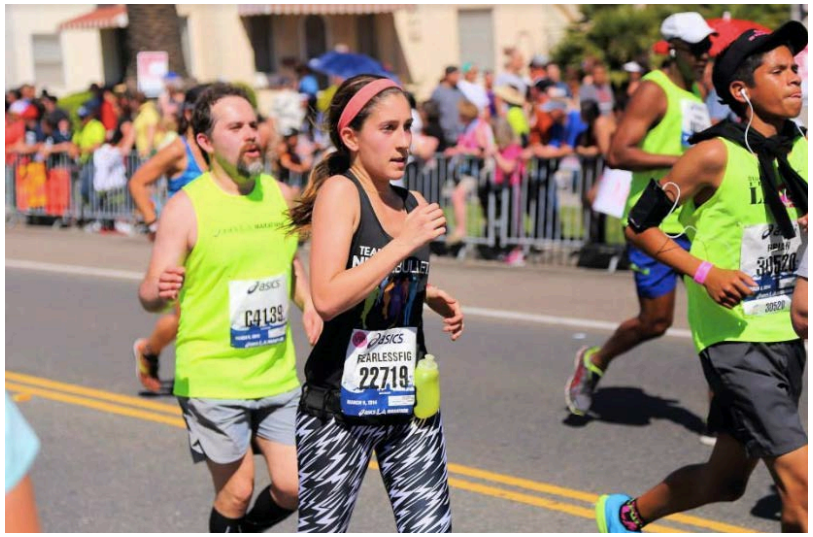
My Background

- 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



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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

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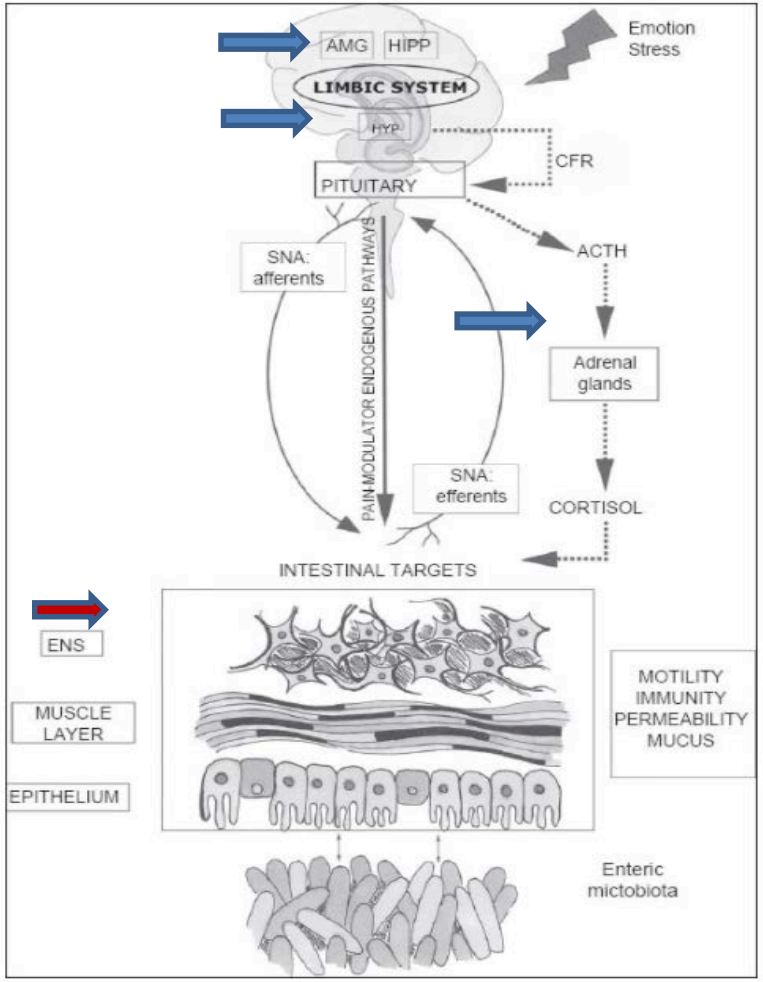
Communication Pathways

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



Carabotti, M, et al. "The gut-brain axis: interactions between enteric microbiota, central and enteric nervous systems". Ann Gastroenterol. 2015 Apr v.28 (2): 203-209

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Communication Pathways cont

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

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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

Deloose, E, et al. “The migrating-motor complex: control mechanisms and its role in health and disease”. Nat Rev Gastroenterol Hepatol. 2012 Mar 27;9(5): 271-85

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Communication Pathways - ENS

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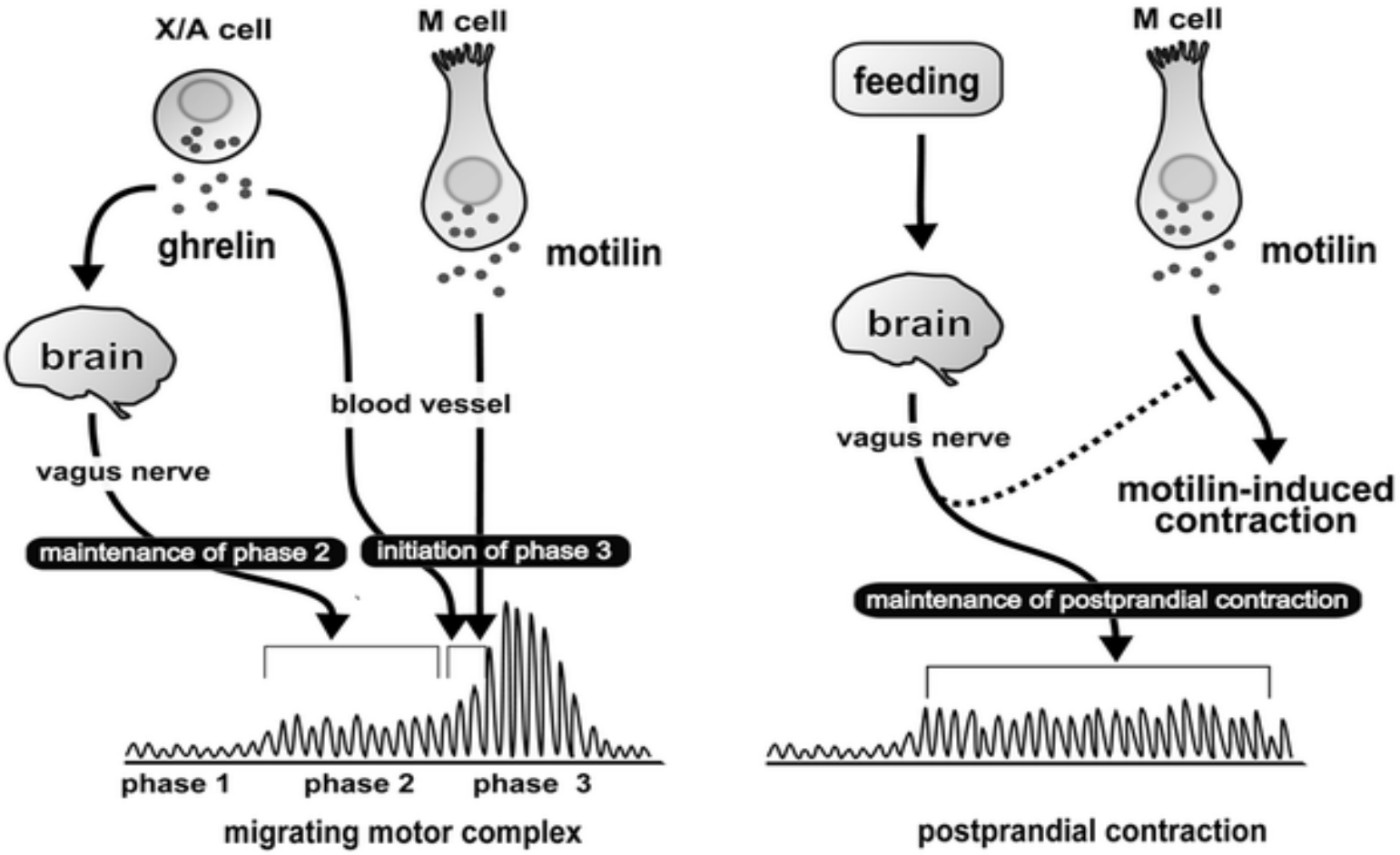
Communication Pathways



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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

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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

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Communication Pathways

CNS

- Brain and spinal cord
- Uses 20% of the total oxygen we breathe
- Receive information from the gut via the vagus nerve

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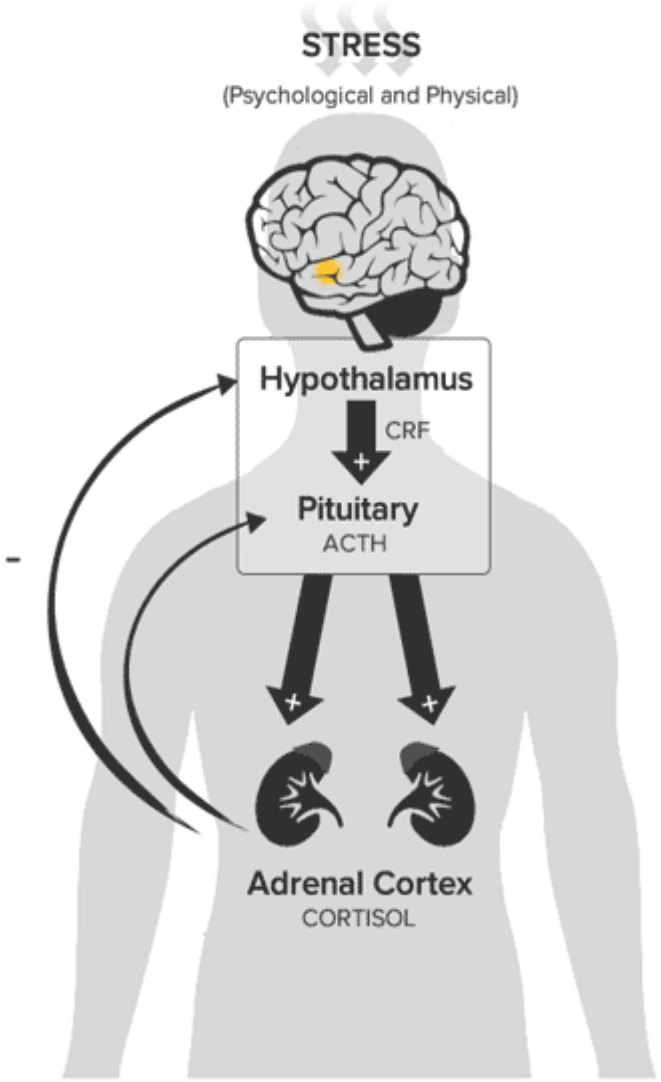
Communication Pathways
HPA Axis

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



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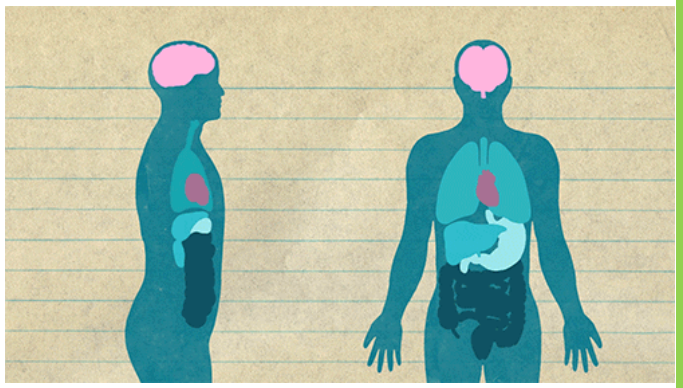
Communication Pathways

- 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



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Communication Mediators

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

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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

Mittal, R, et al. “Neurotransmitters: the critical modulators regulating gut-brain axis”. J Cell Physiol. 2017 Sep; 232(9): 2359-2372
Bravo, J A et al. “Ingestion of Lactobacillus strain regulates emotional behavior and central GABA receptor expression in a mouse via the vagus nerve”. Proc Natl Acad Sci USA. 2011 Sep 20; 108(38): 16050–16055.

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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

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Dysfunction

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

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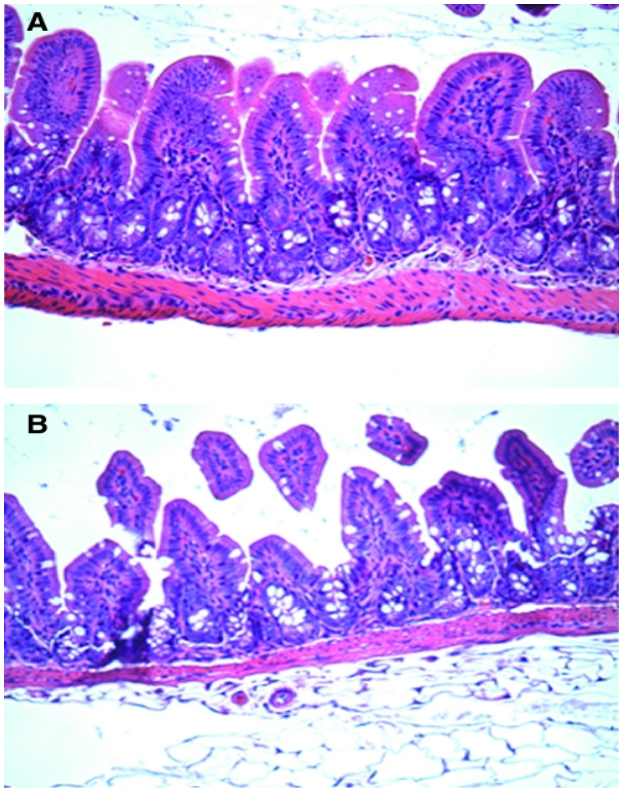
Physical Trauma

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



Bansal, V, et al. “Traumatic Brain Injury and Intestinal Dysfunction: Uncovering the Neuro-Enteric Axis”. BJ Neurotrauma. 2009 Aug; 26(8): 1353–1359.

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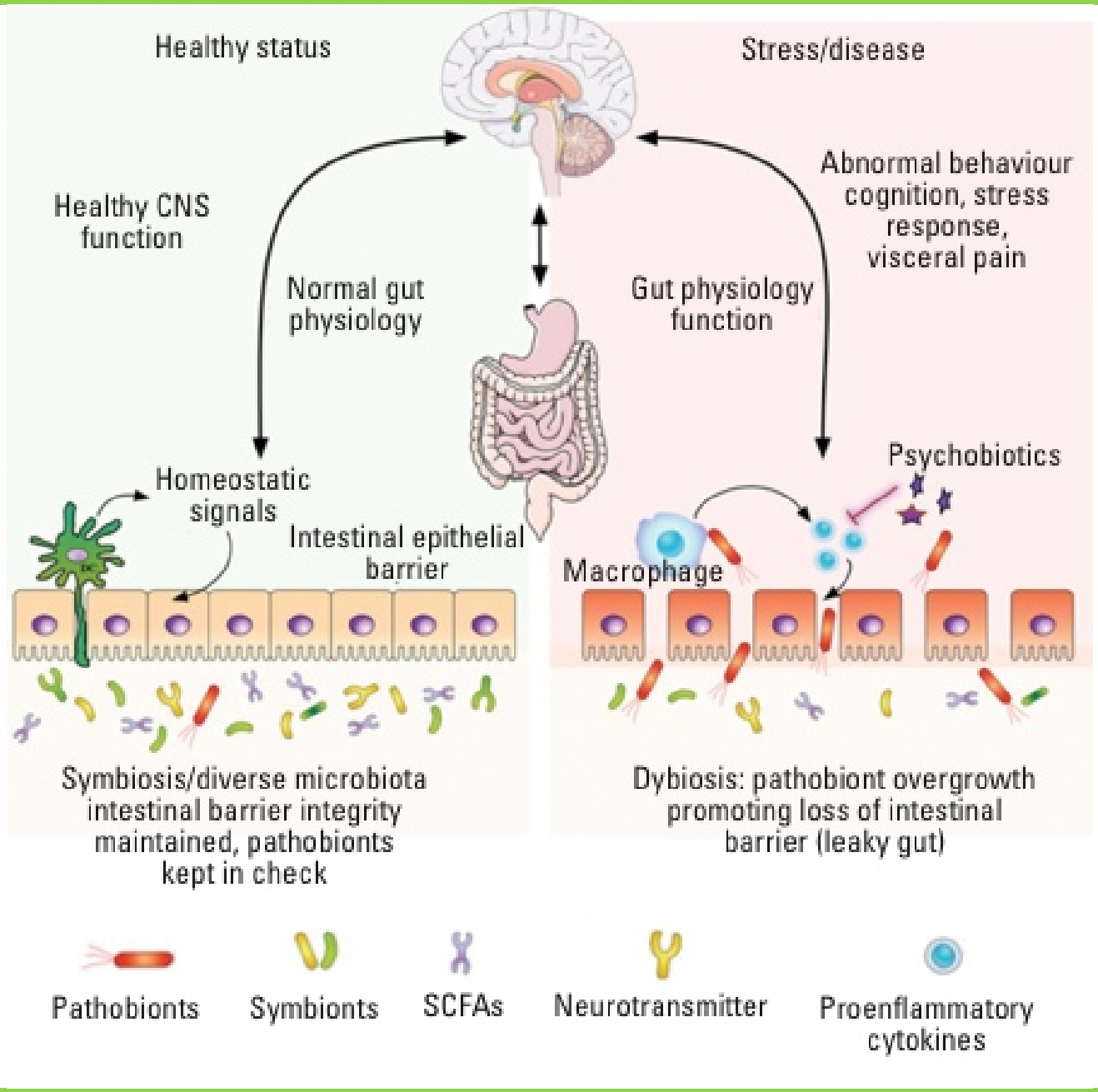
Impact of Stress



Graphic:The microbiota-gut-brain axis and cognitive function (M.G. Gareau, Microbial Endocrinology: The Microbiota Gut-Brain Axis in Health and Disease, Springer, 2014).

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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

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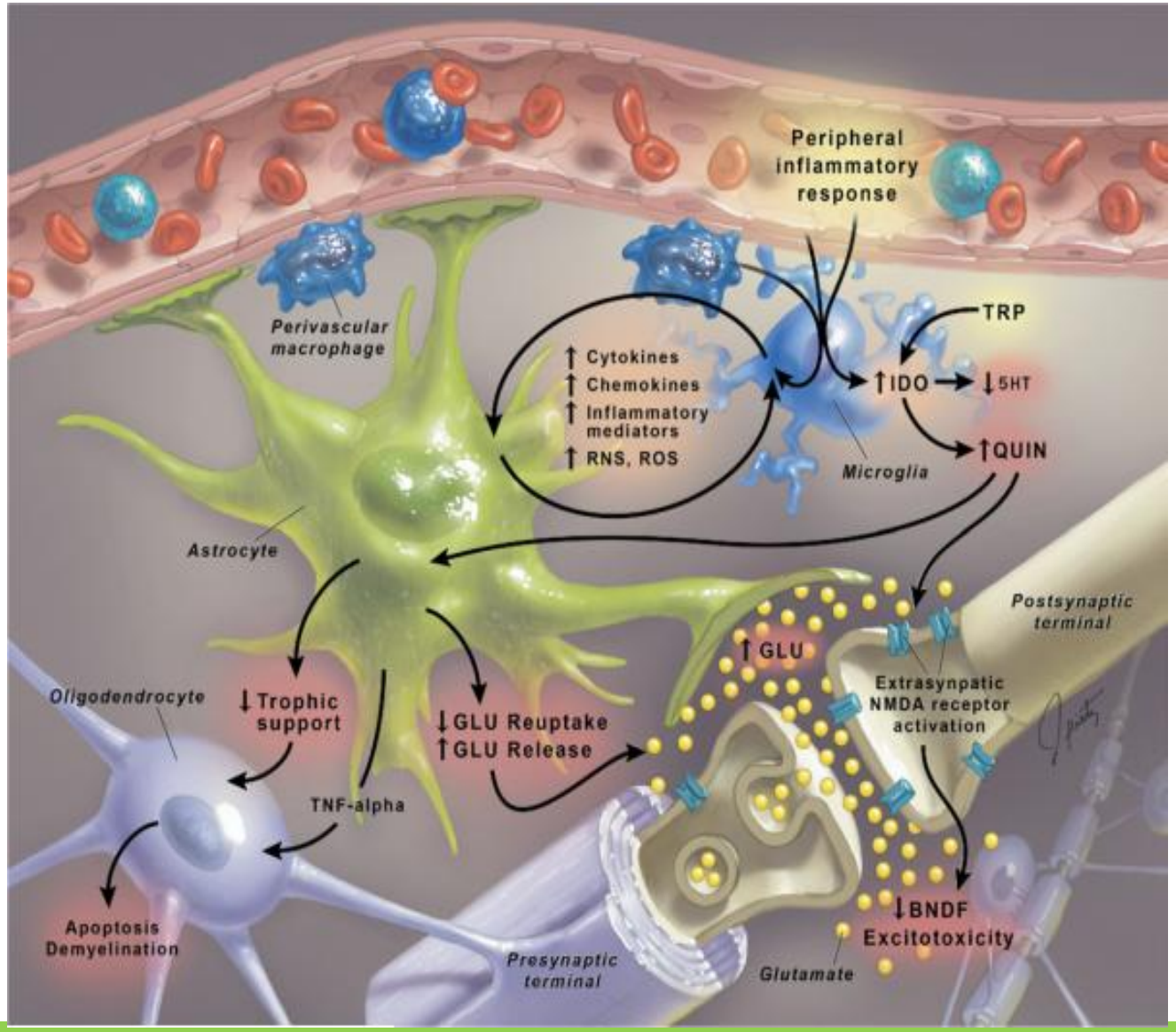
Impact of Inflammation



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:

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Impact of Inflammation

Inflammation kicks off immune response

- Mobilizing macrophages
- Upregulating cytokines
- Downregulates neurotransmitters
    - Glutamate
    - Catecholamines
    - Serotonin
        - Decrease BDNF

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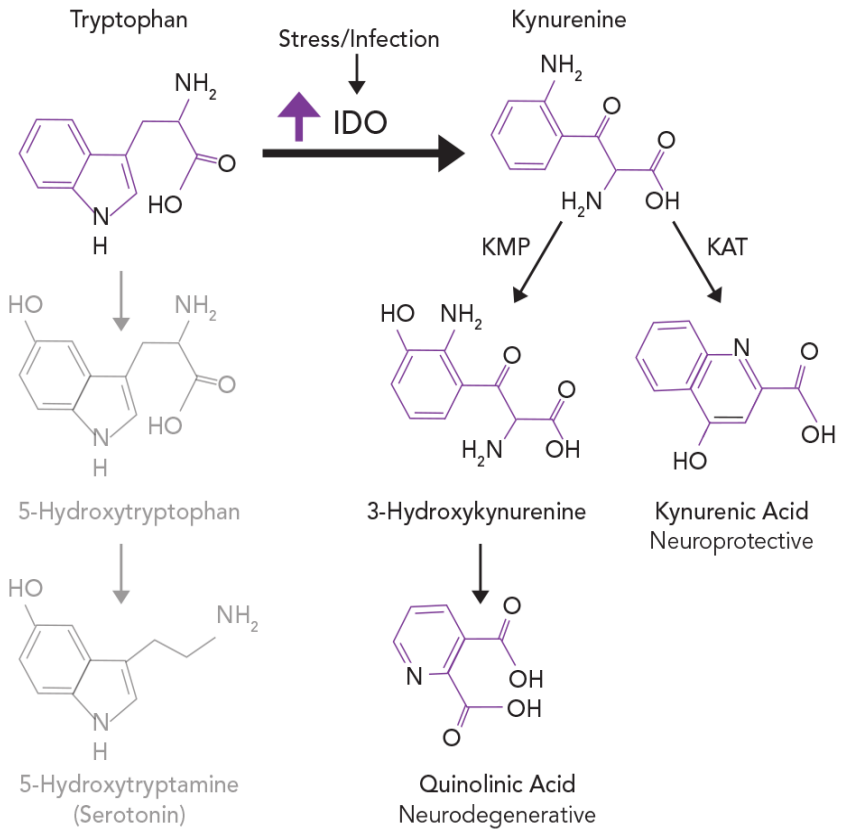
Impact of Inflammation

- 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/ Updated March 2014. Accessed July 14.

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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

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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

Carabotti, M, et al. “The gut-brain axis: interactions between enteric microbiota, central and enteric nervous systems”. Ann Gastroenterol. 2015 Apr v.28 (2): 203-209

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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

Selective Serotonin Re-uptake Inhibitors. Mayo Clinic. https://www.mayoclinic.org/diseases-conditions/depression/in-depth/ssris/art-20044825. Updated August 31, 2017. Accessed June 24, 2018.

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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

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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

JA, Foster, et al. “Gut-brain axis: how the microbiome influences anxiety and depression.”. Trends Neurosci. 2013 May;36(5):305-12.

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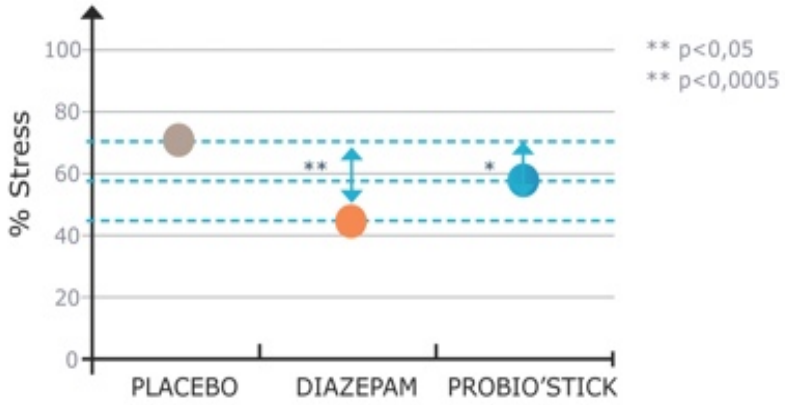
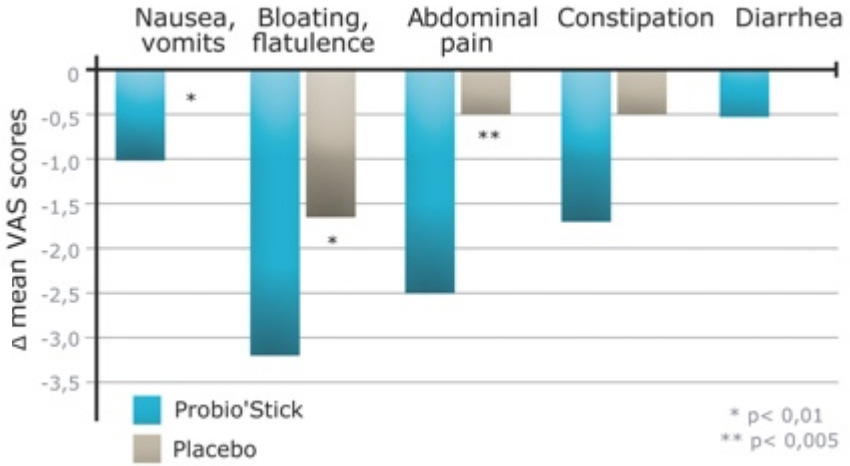
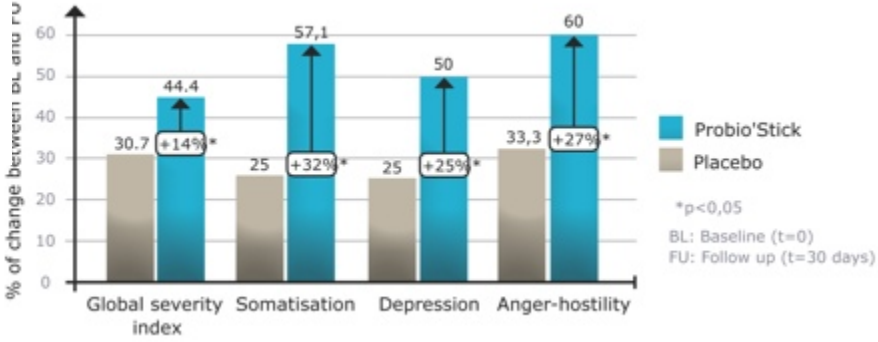
Impact of Gut Diversity







Diop, L. *et al*., "Probiotic Food Supplement Reduces Stress-Induced Gastrointestinal Symptoms in Volunteers: A Double-Blind, Placebo-Controlled, Randomized Trial," *Nutrition Research* 28(1), 1–5 (2008).

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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

Mudd, A, et al. “Serum cortisol mediates the relationship between fecal *Ruminococcus* and brain N-acetylaspartate in the young pig”. Journal Gut Microbes. Volume 8, 2017Issue 6 589600. Mayer, E, et al. “Altered brain-gut axis in autism: comorbidity or causative mechanisms?” Bioessays.2014 Oct;36(10):933-9.

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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

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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

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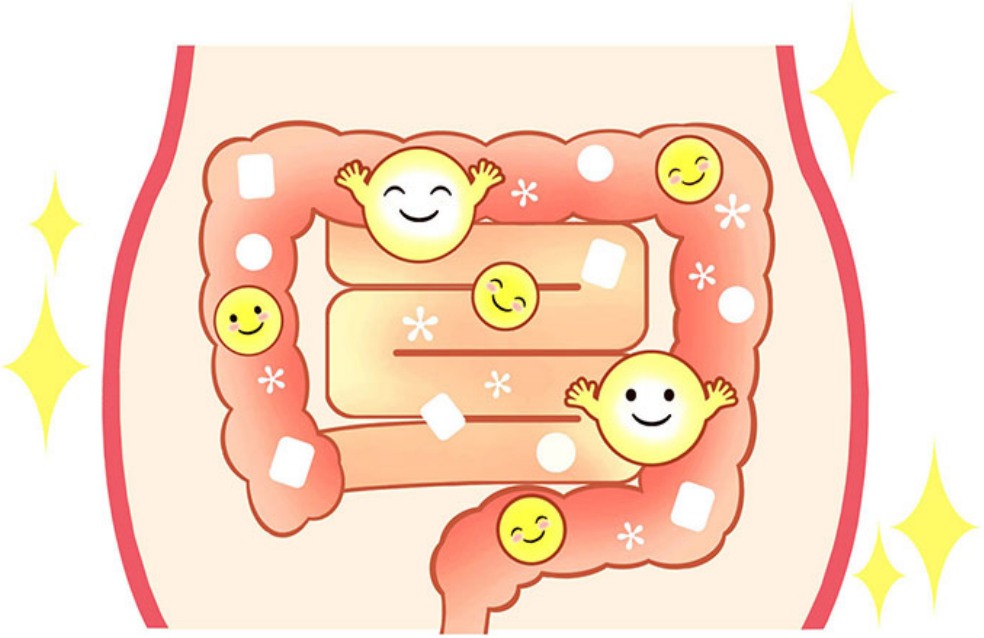
Nutrition and Lifestyle Interventions

- Nutrition
  - Food interventions
  - Supplements
  - Testing
- Lifestyle



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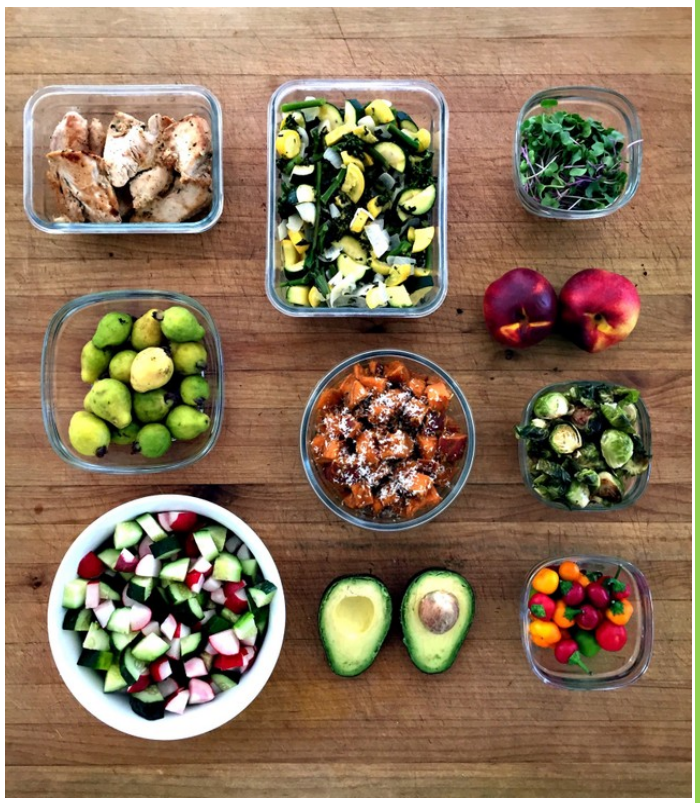
Nutrition

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



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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

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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

Distrutti, E, et al. “Modulation of Intestinal Microbiota by the Probiotic VSL#3 Resets Brain Gene Expression and Ameliorates the Age-Related Deficit in LTP”. Plos One. 2014; 9(9): e106503. Brave, J, et al. “Ingestion of Lactobacillus strain regulates emotional behavior and central GABA receptor expression in a mouse via the vagus nerve.” Proc Natl Acad Sci USA. 2011 Sep 20;108(38):16050-5. doi: 10.1073/pnas.1102999108. Epub 2011 Aug 29.

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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

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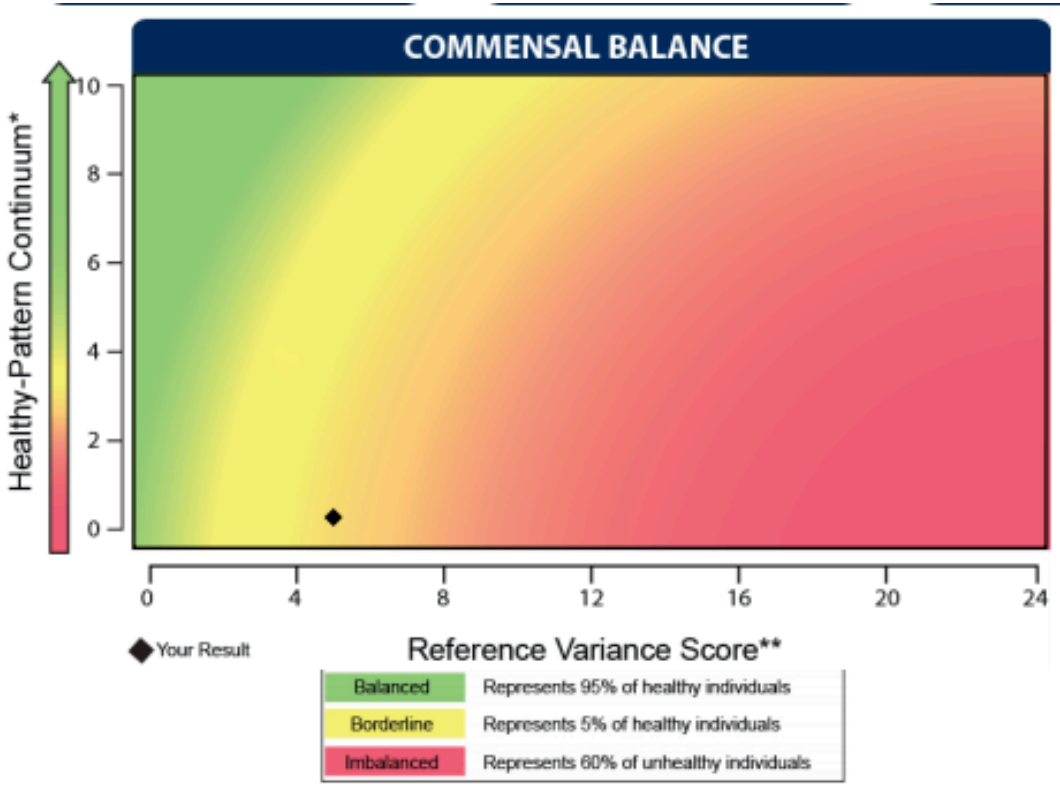
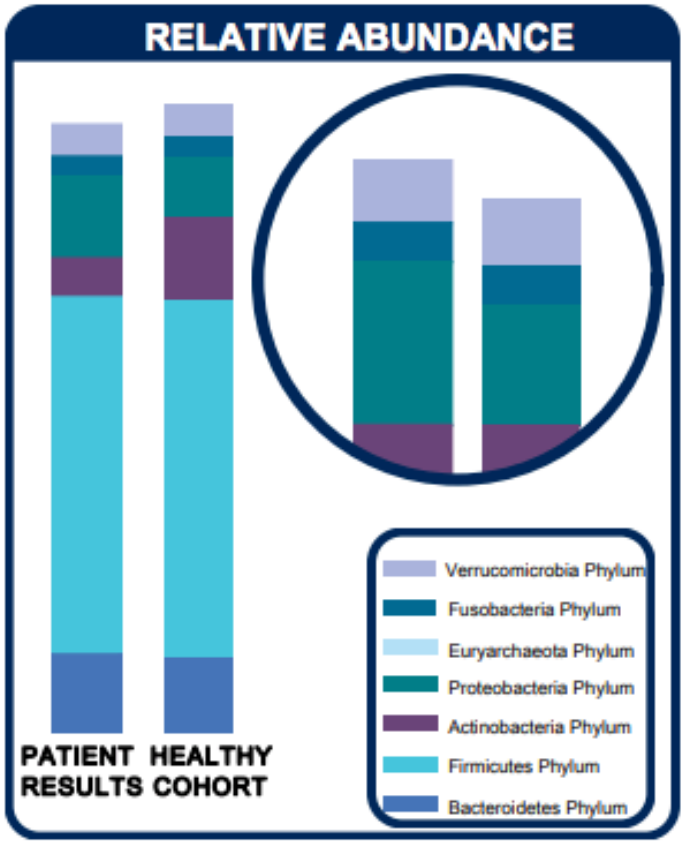
GI Testing



*A progressive ranking scale based on a Genova proprietary algorithm that differentiates healthy and unhealthy commensal patterns.

**The total number of Commensal Bacteria (PCR) that are out of reference ranges for this individual.



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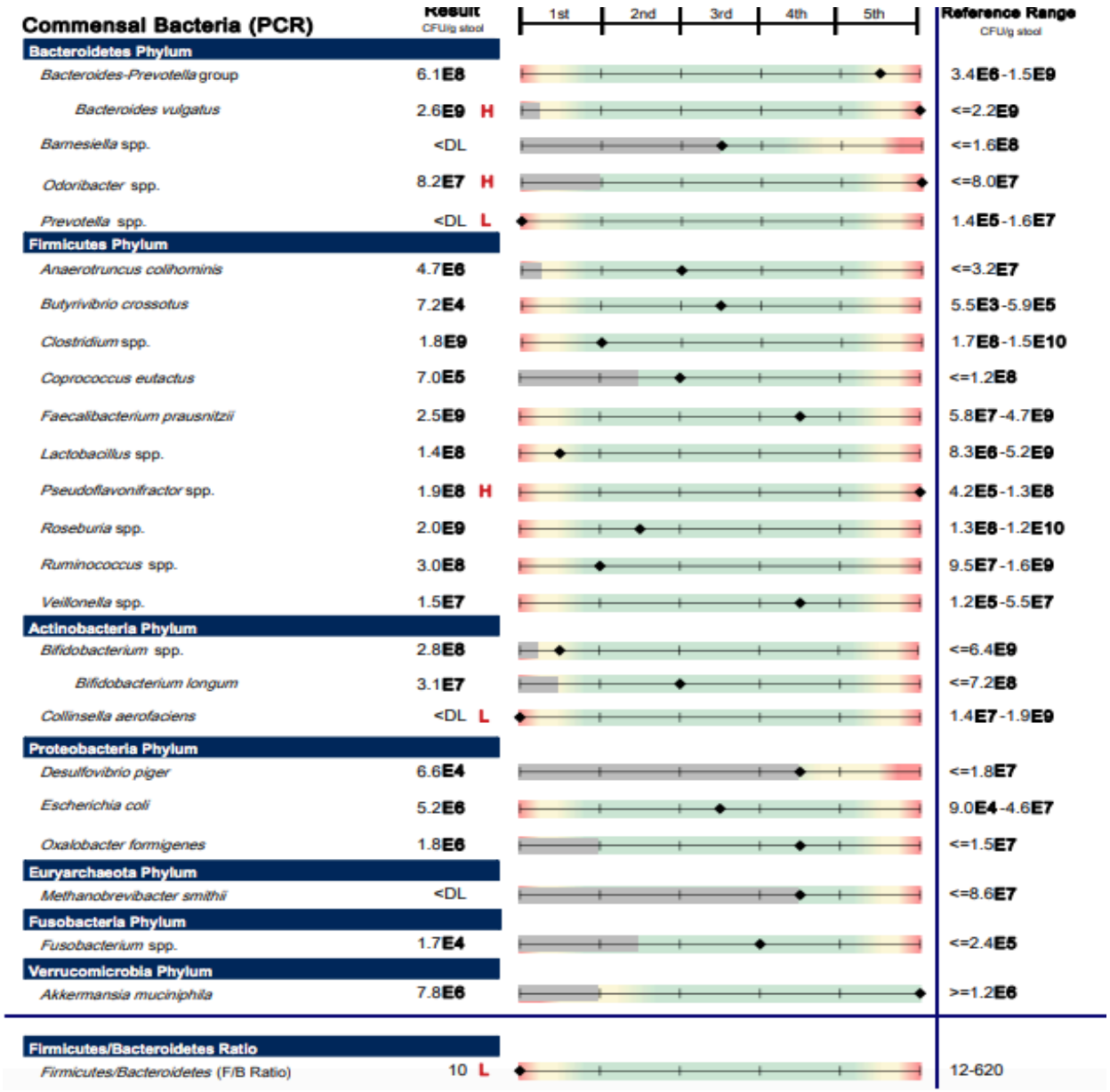
GI Testing



Commensal Bacteria (PCR)	Result CFU/g stool		Reference Range CFU/g stool
Bacteroidetes Phylum			
Bacteroides-Prevotella group	6.1E8		3.4E6-1.5E9
Bacteroides vulgatus	2.6E9	H	<=2.2E9
Barnesiella spp.	<DL		<=1.6E8
Odoribacter spp.	8.2E7	H	<=8.0E7
Prevotella spp.	<DL	L	1.4E5-1.6E7
Firmicutes Phylum			
Anaerotruncus colihominis	4.7E6		<=3.2E7
Butyrivibrio crossotus	7.2E4		5.5E3-5.9E5
Clostridium spp.	1.8E9		1.7E8-1.5E10
Coprococcus eutactus	7.0E5		<=1.2E8
Faecalibacterium prausnitzii	2.5E9		5.8E7-4.7E9
Lactobacillus spp.	1.4E8		8.3E6-5.2E9
Pseudoflavonifractor spp.	1.9E8	H	4.2E5-1.3E8
Roseburia spp.	2.0E9		1.3E8-1.2E10
Ruminococcus spp.	3.0E8		9.5E7-1.6E9
Veillonella spp.	1.5E7		1.2E5-5.5E7
Actinobacteria Phylum			
Bifidobacterium spp.	2.8E8		<=6.4E9
Bifidobacterium longum	3.1E7		<=7.2E8
Collinsella aerofaciens	<DL	L	1.4E7-1.9E9
Proteobacteria Phylum			
Desulfovibrio piger	6.6E4		<=1.8E7
Escherichia coli	5.2E6		9.0E4-4.6E7
Oxalobacter formigenes	1.8E6		<=1.5E7
Euryarchaeota Phylum			
Methanobrevibacter smithii	<DL		<=8.6E7
Fusobacteria Phylum			
Fusobacterium spp.	1.7E4		<=2.4E5
Verrucomicrobia Phylum			
Akkermansia muciniphila	7.8E6		>=1.2E6
Firmicutes/Bacteroidetes Ratio			
Firmicutes/Bacteroidetes (F/B Ratio)	10	L	12-620

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Nutrition Testing

SIBO Patterns (GI Effects Testing)

Biomarker pattern, along with associated symptoms suggest	Biomarkers	Next steps
Small Intestinal Bacterial Overgrowth (SIBO)	↑ Relative Abundance ↑ Products of Protein Breakdown ↑ SCFA ↑ n-butyrate ↑ Fecal Fat (total) ↓ PE1 (limited evidence) ↑ *Methanobrevibacter smithii*	• Confirm with SIBO Breath Test

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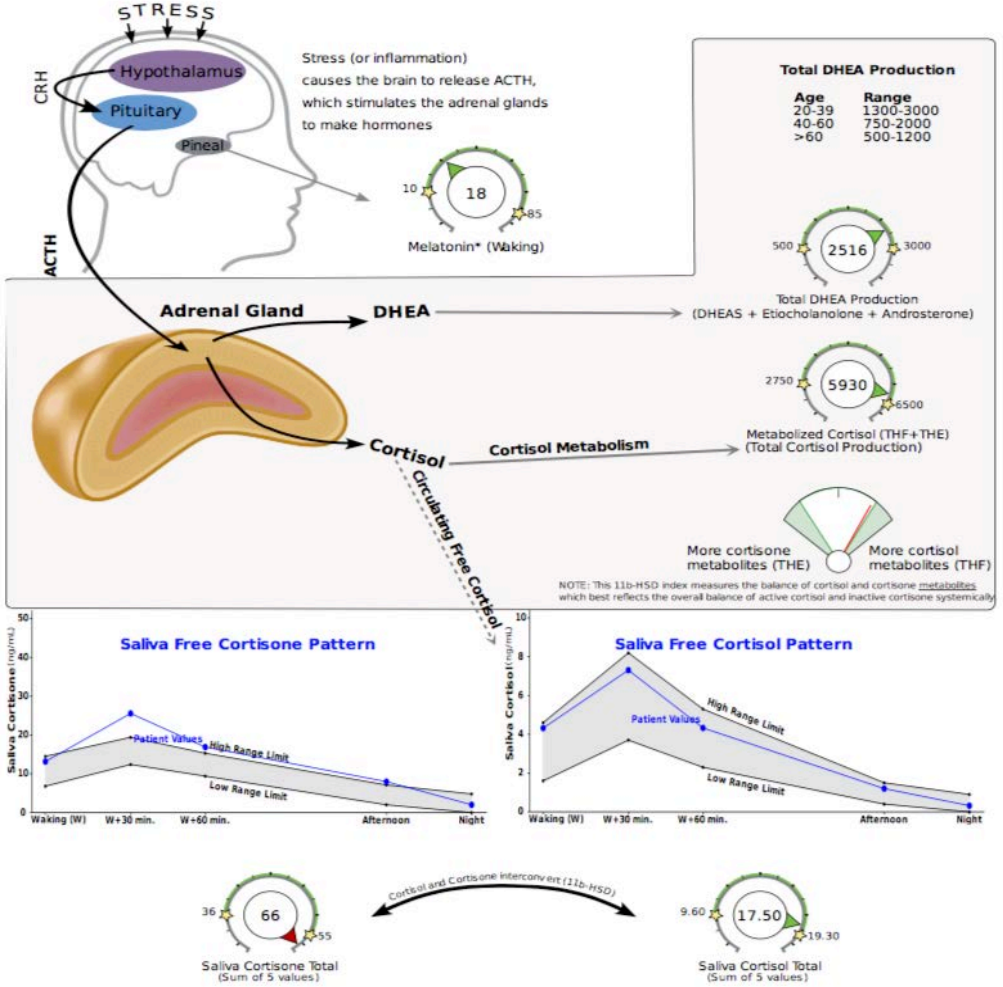
Nutrition Testing

- Dutch Test Plus
- ZRT
  - Diurnal cortisol
  - Neurotransmitters



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Nutrition Testing
(Dutch Test)

Neurotransmitter Metabolites				
Dopamine Metabolite - (Urine)				
Homovanillate (HVA)	Low end of range	5.6	ug/mg	4 - 13
Norepinephrine/Epinephrine Metabolite - (Urine)				
Vanilmandelate (VMA)	Within range	4.8	ug/mg	2.4 - 6.4
Serotonin Metabolite - (Urine)				
5-Hydroxyindoleacetate (5HIAA)	Above range	16.0	ug/mg	2.5 - 7.5
Melatonin (*measured as 6-OH-Melatonin-Sulfate) - (Urine)				
Melatonin* (Waking)	Low end of range	18.2	ng/mg	10 - 85
Oxidative Stress / DNA Damage, measured as 8-Hydroxy-2-deoxyguanosine (8-OHdG) - (Urine)				
8-OHdG (Waking)	High end of range	4.3	ng/mg	0 - 5.2

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Lifestyle

- Be mindful of medications
- Decrease binge drinking
  - Increase endotoxins in blood
- Remove toxic products in house hold
  - 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

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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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Upcoming Events

Get in on our Summer Savings Specials!

25% off all NLFN Membership packages

- All Members receive 10% off full training programs, exclusive partner discounts, and access to our private member networking Q & A forum.
- Upgrade to Gold and get 50% off hot-topic and 2017 archived webinars and 10% off Private mentoring and Grand Rounds series
- Upgrade to Platinum for FREE webinars, including unlimited access to 2017 archives.

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Summer Savings Specials!

10% off training (above member discounts!)

- IFMNT Foundations now available as a Fast-Track recorded series
- IFMNT Certificate of Training 15-mo intensive starts Monday, July 23rd
- IFMNT Advanced Topic 12-mo training started last month – there's still room to jump in!

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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.

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thank you!

Questions?

Sarah@fearlessfig.com