GI Health: Digestion and Probiotics – Focus on Mood Support and Brain Health

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OBJECTIVES

- Define the GI’s “second brain” influences on mood and well-being
- Identify the impact of the microbiome in GI health and brain function
- Discuss the influence of probiotics on moods
- Understand serotonin’s positive influence on GI function
- Tying it all together: A case study
POLYPHARMACY

- The list of psychotropic medications considered potentially inappropriate in adults has grown.
- 2004 to 2013, CNS polypharmacy more than doubled.
- The FDA recently ordered a black-box warning to alert patients of serious risks, including death, caused by opioids co-prescribed with CNS depressants.
POLYPHARMACY

- While it was most common at visits with anxiety, insomnia, or depression, there was not a significant increase at such visits.

- Polypharmacy significantly increased for patients with a pain diagnosis resulting in opioid prescribing.

- Visits without pain, insomnia, or other mental health diagnoses accounted for nearly half (45.9%) of CNS polypharmacy visits and grew significantly from 2004 to 2013.
THE GI’s

“SECOND BRAIN”

INFLUENCES ON MOOD & WELL-BEING
TWO BRAINS

- Central nervous system (CNS) is composed of your brain and spinal cord.
- Enteric nervous system (ENS) is the intrinsic nervous system of your gastrointestinal tract (GI).
- Connected by the vagus nerve, the tenth cranial nerve, that runs from your brain stem down to your abdomen.
- The vagus nerve is the primary route your gut bacteria uses to transmit information to your brain.
The vagus nerve’s path connects from the brain to the intestines.

Allows the brain and multiple organs to “talk” to one another.
THE SECOND BRAIN

- 29.5 feet from esophagus to abdomen
- 100 million neurons
- More neurons than spinal cord or peripheral nervous system!
Well-Being

• Functional HPA axis
• Normal behavior
• Normal nociception

• Balanced microbiota
• Normal gut function
• Balanced immune system
• Normal gut morphology

Homeostasis

Stress

• Dysfunctional HPA Axis
• Altered behavior
• Increased pain perception

• Dysbiosis → Gut dysfunction
• Low-grade or overt inflammation
• Tissue damage

Disease

Catecholamines or other neurotransmitters (eg. GABA)
IRRITABLE BOWEL SYNDROME (IBS)

- Common disorder: 1/5 adults
- 50% begin before the age 35
- Twice as many women as men
- 25% with GI infections develop IBS
- Not contagious, inherited, or cancerous
- Bowel is not functioning properly
- Link between dysbiosis and inflammation, IBS and mood disorders

1 Bercik, et al., 2011
CAUSES OF IBS

- IgG food intolerance
- Gluten sensitivity
- Neurotransmitter imbalances
- Low beneficial bacteria
- Infections
- 78% test positive for small intestine bacterial overgrowth (SIBO)
GUT-BRAIN AXIS

- A dysfunction in the gut-brain axis is linked to neuropsychological, metabolic disorders such as obesity, immune, and endocrine disorders.¹

- Dysbiosis has been linked to depression and autism spectrum disorder (ASD), and GI disorders including IBD and IBS.²

- More than 90% of over 4,000 articles on the microbiome were published in PubMed in the last 5 years!

¹Tougas G. Gut. 2000
²Zhou and Foster. Neuropsychiatr Dis Treat. 2015
What influences from the brain affect the gut microbiota?¹

- The HPA axis
- The CNS regulating areas of satiety
- Neuropeptides released from sensory nerve fibers

¹Petra et al. *Clin Therapeutics*. 2015
Gutsy move... for a brain!
What influences from the gut affect the brain?

- Antibiotics and infections
- Environmental influences:
  - Toxins
  - Food and gluten sensitivities
  - Genetic predisposition
  - Nutrition and physical activity
- GI neurotransmitters
- Cytokines
- Mode of delivery at birth
Gut microbiota may be modulated with the use of probiotics, antibiotics, and fecal microbiota transplants as a prospect for therapy in microbiota-associated diseases.

It is clear that the gut microbiota can be a key regulator of mood, cognition, pain, and obesity.¹

¹Burokas et al. Advances in applied microbiology (Ch 1). 2015
MOOD DISORDERS

- The microbiota-gut-brain (MGB) axis and the neuroimmune system provides understanding and management of anxiety, ADHD, autism, cytokines, depression, stress, and neuroimmune conditions.¹

- Major depression and anxiety states are common in patients presenting with IBS.

¹Dinan and Cryan. *Neuropiastroenterol. Motil.* 2013
"Researchers have known that the brain sends signals to your gut, which is why stress and other emotions can contribute to gastrointestinal symptoms."

Cytokines

Neurotransmitter Hormones

Immune System

Microbiome

Central Nervous System

Retrieved from: http://www.drjaudy.com/organ-remaping/ (all rights reserved)
NEUROPLASTICITY

- Microbes influence neuroplasticity.¹
- Stimulator of neuroplasticity is brain-derived neurotrophic factor (BDNF).
- Studies have shown that germ-free mice have decreased levels of BDNF.
- BDNF is also decreased in normal mice following antibiotic administration.²

¹ Olsen. *Neuropharm.* 2011
² Bercik et al. *Gasteronenterol.* 2011
THE MICROBIOME & IMMUNITY

- Gut microbiota and some probiotics can regulate immune functions.
- Benefits may be anti-inflammatory actions of certain bacteria and a capacity to affect HPA axis activity.
- Most physical and mental disease have inflammation as their root cause.
- Our immune system, about 70%, is located in the gut microbiome.

- 70% of our immune cells reside in the GI tract.
- The development of the intestinal immune system is largely dependent upon exposure to microorganisms.
- The gut produces \( \frac{3}{4} \) of the body’s neurotransmitters.
- The gut has greater metabolic activity than the liver.
GLUTEN & DYSBIOSIS

- Gluten sensitivity is a result of dysbiosis, not a genetic disorder.
- Dysbiosis is most prominent in the digestive tract or on the skin, but can also occur on any exposed surface or mucous membrane.
- Dysbiosis creates inflammatory factors responsible for developing insulin resistance and body weight gain.¹

¹Cenit et al. *Nutrients*. 2015
DIET & MICROBIOME

- Poor mental health has been associated with an increased likelihood of eating unhealthy foods.\(^1\)
- Different diets create different gut flora.
- Study showed rural African children eating polysaccharide-rich diet had more Bacteroidetes and diversity than EU children eating the Western diet.\(^2\)
- In a 2014 study in *Nature*, it was indicated that these changes can happen in the human gut—within three or four days of a big shift in what one eats!

\(^1\)Oliver et al. *Psychosom Med.* 2000
\(^2\)Proc Natl Acad Sci. 2010
SPECIALTY TESTS

- **Sanesco NeuroLab®**
  - Neurotransmitters
  - Adrenal Function (ASI: Cortisol/DHEA)

- Comprehensive GI stool testing
THE IMPACT OF THE MICROBIOME IN GI HEALTH & BRAIN FUNCTION
OUR MICROBIOME

- The microbiome is inhabited by 100 trillion microorganisms
- 10x the number of cells in the human body
- 150x as many genes than we have
- Co-exists with gut pathogens
- Regulates the immune system
- Regulates the endocrine system
- Modulates digestion
- Weighs 2-6 pounds
MICROBIOME

- **Body:**
  - 10 Trillion cells
  - 23,000 genes (the fruit fly has 16,000 genes)

- **Microbiome:**
  - 100 Trillion cells
  - 3.3 million genes

- **Good bacteria** 80-90%
- **Bad bacteria** 10%
DYSBIOSIS

- Dysbiosis is a state in which the microbiome becomes altered in composition.

- Antibiotics, radiation, altered peristalsis, dietary changes and psychological and physical stresses.

- The close relationships between gut microbiota, health and disease has led to great interest in using probiotics and/or prebiotics to prevent or treat disease.¹

¹Prakash et al. *Biologics*. 2011
THERAPEUTIC LIFESTYLE CHANGE

Food          Activity Level          Stress
THE INFLUENCE OF PROBIOTICS ON MOOD
BENEFICIAL BACTERIA OVERVIEW

- Brain development, mental health, and memory
- Genetic expression
- Immune system
- Weight management
- Risk of numerous chronic and acute diseases, from diabetes to cancer
PSYCHOBIOTICS

- ‘Psychobiotics’ is an emerging class of probiotics of relevance to psychiatry.¹
- A psychobiotic is a live organism that produces a health benefit in patients suffering from mood disorders.
- Such “mind-altering” probiotics act via their ability to produce various biologically active compounds.

¹Dinan et al. J Biopsych. 2013
PSYCHOBIO蒂ICS

- Microbes produce neurotransmitters.
- More than 50 percent of your body’s dopamine and 95 percent of your body’s serotonin are produced in your gut, along with about 30 other neurotransmitters.\(^1,2\)
- These molecules are critical for signaling between cells of the nervous system.
- Dopamine and serotonin in the brain and the GI have both been shown to be involved in the regulation of eating behavior.\(^3\)

MICROBIOME & CNS

- Microbiota influence brain chemistry and consequently behavior.

- Clostridium difficile (CD), the hospital-based gut infection that kills 14,000 people each year in the U.S., is associated with depression and dementia.

- Two antidepressants, mirtazapine (Remeron) and fluoxetine (Prozac), are linked to a nearly 50 percent increased risk for CD infection.¹

¹Rogers, et al. BMC Medicine. 2013
PSYCHOBIOBIOTICS

- Bacteria are capable of producing and delivering GABA and serotonin, which act on the brain-gut axis.\(^1\)
- Microbes that actively secrete GABA in the gut are strains of Lactobacillus and Bifidobacterium.
- Psychobiotics produce psychotrophic effects on behavior, affect the HPA axis and neurochemicals in the brain.

\(^1\)Dinan et al. *J Biopsych.* 2013
“Two varieties of Bifidobacterium were more effective than escitalopram (Lexapro) at treating anxious and depressed behavior in a lab mouse strain known for pathological anxiety.”

— John F. Cryan, PhD

¹Foster and Neufeld. Trends Neurosci. 2013
Alterations in microbiota influence stress-related behaviors.

GI tract bacteria, including commensal, probiotic, and pathogenic bacteria can activate neural pathways and CNS signaling systems.¹

The MGB axis may provide novel approaches for prevention and treatment of mental illness, including anxiety and depression.¹

¹Foster and Neufeld. *Trends Neurosci*. 2013
Anxiety

Impaired Social Function

Cognitive Dysfunction

Depression

Disrupted Intestinal Barrier

LEAKY BRAIN

- A molecule, called “microRNA-155” is responsible for cleaving epithelial cells to create microscopic gaps that let material through.¹

- Acute stress increased GI and blood brain barrier (BBB) permeability through activation of mast cells (MCs), which express high affinity receptors for cortisol releasing hormone (CRH).

- Chronic stress disrupted the intestinal barrier through MC activation and permitted penetration of luminal antigens, microflora metabolites, toxins and lipopolysaccharide (LPS) in the systemic circulation and the CNS.²

¹Petra et al. Clin Ther. 2015
²Federation of Am Societies for Experimental Biology Research. June 2014
LEAKY BRAIN & ALZHEIMER’S DISEASE

- Correlations between microglial immunoreactivity and neuronal viability in AD brain tissue.
- Immunohistochemical analysis demonstrated AD, brain tissue expressed areas of diffuse fibrinogen indicative of a weakened BBB.

WHAT IS GOING ON NOW IS DIFFERENT

- Toxins
- Too much sugar
- Too many antibiotics, and given too young = leaky gut
- C-sections, no breast feeding, no skin-to-skin with parents
- Too many medications = leaky gut
- Low fat diets
- Amalgam fillings
- GMO = leaky gut
- Poor methylation = epigenetics

ADHD

- Food allergies, eczema, and asthma are associated with behavioral problems and neuropsychiatric disorders, including ADHD.

- Many children with Autism Spectrum Disorders (ASD) present with GI systems and altered GI flora.

- ASD may involve brain inflammation.

- 30% of children with ASDs have auto-antibodies against brain proteins.

Petra et al. Clin Ther. 2015
PSYCHOBIOLOGICS: L. PLANTARUM

- Tests revealed that chronic ingestion of probiotic Lactobacillus plantarum (Lp) significantly reduced anxiety-like and depression-like behaviors.\(^1\)
- It also reduced ELS (Eaton-Lambert's Syndrome) - induced elevation of serum corticosterone

\(^1\)Liu, et al., *Brain Res.* 2016.
PSYCHOBIOTICS: L. PLANTARUM

- Lactobacillus plantarum (Lp) also reduced inflammatory cytokine levels and increased anti-inflammatory cytokine levels in the serum.
- Furthermore, the dopamine levels in the brain were significantly increased.
- The psychotropic properties of certain bacteria have great potential for improving stress-related symptoms.¹

¹Liu, et al., Brain Res. 2016.
PSYCHOBIO蒂CICS: L. RHAMNOSUS

- Lactobacillus rhamnosus is a bacterial strain that has been shown to reduce anxiety and depression in anxious mice.\(^1\)
- L. rhamnosus markedly increased GABA levels.
- A number of microbes can produce other neurotransmitters, such as norepinephrine, serotonin, and dopamine.
- Bifidobacterium infantis, taken as a probiotic, alters serotonin levels just like Prozac but without the undesirable side effects.\(^2\)

\(^1\)Collins, et al. *Nat Rev Gastroenterol and Hepatol*. 2013
\(^2\)Davidson. *Psychology Today*. 2014
INFLAMMATION & PROBIOTICS

- Probiotics protect the inflamed intestinal epithelium.
- Competition for binding sites and inhibition of pathogen growth stimulate immune system including the stimulation of anti-inflammatory cytokines and enhancement of barrier function.

1Laukotter et al. *World J Gastroenterol.* 2008
PROBIOTIC RESEARCH

- From 2010 to 2013 10 RCT have been carried out using probiotics (L rhamnosus GG, L gasseri SBT2055, L acidophilus, L bulgaricus, L casei, L bifidum) and prebiotics.

- Studies ranged from 4 weeks to 24 weeks

- Key Findings:
  - Decrease in abdominal fat/decrease in weight gain
  - Decrease in triglycerides and insulin resistance
  - Decrease in IL-6, IL-8, TNF
Neurotransmitters

Microbiome

Lifestyle

Hormones

Diet
STRESS

- Stress induces a dysbiosis, which in turn can trigger anxiety and depression.
- Commensal bacteria modulates brain biochemistry and behavior through the vagus nerve affecting NTs.
- Prolonged stress triggers unfavorable shifts in bacterial composition and diversity.
- Populations of beneficial microbes die off, dysbiosis flourishes.

Bravo et al. *Proc Natl Acad Sci USA*. 2011
MICROBIOME & STRESS

- In dysbiosis, it’s easy for health to degrade, as the bacteria are no longer capable of supporting our optimal immune function.

- Stress can impact the structure and function of the intestine itself slowing down gut motility, leading to constipation, digestive disorders, toxic build-up and SIBO.¹

STRESS & DYSBIOSIS

- Chronic psychological stress is associated with a greater risk of depression, CVD, diabetes, autoimmune diseases, upper respiratory infections, and poorer wound healing.¹

- Stress induces leaky gut and increases mucosal immune response, which in turn alters the composition of the microbiome and leads to enhanced HPA drive.

¹Cohen et al. Proc Natl Acad Sci U S A. 2012
SEROTONIN’S POSITIVE INFLUENCE ON GI FUNCTION
SEROTONIN & THE GUT

- Motility patterns and gastric emptying
- Secretion
- Immune system
- Pain and discomfort
- Nausea and vomiting
- Alters microbiome
- Circulating 5-HT has the potential to impact many other tissues

Mawe and Hoffman, Nat Rev Gastroenterol Hepatol, 2013
SEROTONIN

- Promotes homeostasis
- Influences bone development
- Receptor sites on immune cells B and T lymphocytes
- Mast cells, macrophage and T-cells synthesize 5-HT

And there is more…..tune in to next month’s webinar!
TYING IT ALL TOGETHER: CASE STUDY
CASE STUDY

- 51 year old female presents with multiple symptoms:

  - Anxiety
  - Depression
  - Insomnia
  - Brain Fog
  - Fatigue
  - IBS
  - Daytime sleepiness
  - Inflammation
  - Low libido
  - Migraines
  - GERD
  - Infections

- Symptoms present for more than 5 years.

- Routine chemistry panels, colonoscopy & endoscopy were normal.

- History: Zoloft, Lexapro, Celexa
CASE STUDY ASSESSMENT

- Food intolerances
- GI dysfunction
- Neurotransmitter imbalance
- Adrenal fatigue
CASE STUDY EVALUATION

- Comprehensive stool analysis
  - Low diversity
  - High IgA
  - Impaired digestion and absorption
  - Beneficial bacteria – no growth

- IgG food sensitives
  - Dairy
  - Eggs

- Gluten sensitivity

- Sanesco NeuroLab® HPA
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Creatinine is used to calculate results and is not intended to be used diagnostically. (L) and (H) are based on optimal ranges.

![Cortisol Graph](image)
CASE STUDY PLAN

- Prolent™: 1-2 qd p.m.
- Lentra™: 1 po BID
- Procite-D™: add after 10 days – 1 in a.m.
- Contegra™: add after 14 days – 1 in a.m.
- Adaptacin™: add after 21 days – 1 in a.m.
CASE STUDY PLAN

- Discontinue dairy, eggs, and gluten
- Medical foods for repairing GI health
- Probiotics - 450 billion qd
- Digestive enzymes + betaine
- EPA DHA - 1000mg x 2
- DHEA – 25mg
3 weeks later…..

- GI symptoms improving, less bloating and C&D
- Mood improvement
- Less insomnia
- More energy
- No migraines
- GERD relieved
GI Health: Digestion and Probiotics – Focus on Mood Support and Brain Health

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THANK YOU
IMPORTANT REMINDERS FROM SANESCO

• Sign up for a complimentary Clinical Consultation or let us know if you would like more information about Sanesco by selecting the Contact Us Widget to learn more about incorporating the Communication System Management (CSM) clinical model into your practice.

• We’d love to hear your feedback – complete the brief survey after the webinar so we can continue to improve our webinars to you in the future.

• Connect with us on Social Media and join our Quarterly Practitioner E-Newsletter.
IMPORTANT REMINDERS FROM SANESCO

• Upcoming Events:
  – WEBINAR: Stay Tuned for our next webinar on April 20th
    The Happy Gut: Serotonin and the Microbiome
  – CONFERENCE: Northwest Naturopathic Physicians Convention in Vancouver

• Open enrollment for the Neuroendocrine Clinical Analysis Program (NCAP). Get your NCAP Accreditation. Visit www.SanescoHealth.com/ncap or select the URL Widget.
IMPORTANT REMINDERS FROM SANESCO

Must-Have Resources (Free Downloads):

- Copy of Presentation Slides
- Neurotransmitter & Hormone Interactions Handout
- Impacting Quality of Life For Over a Decade – Data Monograph
Q & A
GI Health: Digestion and Probiotics – Focus on Mood Support and Brain Health

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