Veteran and Soldier Populations

Part III

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Disclosure

This certifies that I, Jennifer M. Williams, have not, nor has my spouse/partner or any immediate family member have had in the past 12 months or expect to have in the upcoming months, any financial relationship or gift-in-kind with industry that is relevant to the subject matter of the presentation.

Outline

- Military Culture
  - Training Resources
  - Area Health Education Center Presentation
- Pain Comorbidities
  - Microbiome
  - Microbiota-Gut-Brain axis
  - Gut Health
  - Immune System
  - Pain Dysregulation
- Therapy
  - Dietary Therapy
  - Nutritional Therapy

Military Culture

- A 2014 RAND report noted that many community providers are not trained or experienced in treating the Veteran community
- In early 2015, the American Medical Association issued guidelines for assessing a patient's military experience and duty assignments
- Free training resources to introduce community providers to the unique needs of veterans

Military Culture Fact Sheet

VA | U.S. Department of Veterans Affairs | **Fact Sheet**

Office of Public Affairs
Media Relations
Washington, DC 20420
(202) 461-7600
www.va.gov

April 2015

Military Culture Training for Community Providers

It's important that all who care for Veterans have a basic understanding of military culture. With the new Choice Program, the signature initiative of the Veterans Access, Choice and Accountability Act of 2014, eligible Veterans have increased access to health care from community-based medical care providers.

Many community providers are not trained or experienced in treating this unique Veteran patient community, according to a 2014 RAND report. In early 2015, the American Medical Association issued guidelines for assessing a patient's military experience and duty assignments.

In the interest of the highest quality, most compassionate health care for our Nation's Veterans, the Department of Veterans Affairs (VA) is providing a number of accredited training resources at no cost to *all* Veteran care providers. Click the course title hyperlink to learn more and to access the training resources:

- **Military Cultural Awareness**
  Note: Click "OK" to move past the pop-up notice

- **Military Culture: Core Competencies for Healthcare Professionals**
  Module 1: Self-Assessment/Intro to Military Ethos
  Module 2: Military Organization and Roles
  Module 3: Stressors and Resources
  Module 4: Treatment, Resources, and Tools

Note: The four modules listed are delivered via VHA TRAIN, a new service to share valuable Veteran-focused continuing medical education at no cost to community health care and public health providers. Dozens of additional Veteran-care training courses will be added to VHA TRAIN throughout 2015.

To learn more about opportunities to care for our Nation's Veterans, please visit the Veterans Choice Program and the Non-VA Medical Care Program websites. If you are interested in becoming a Patient-Centered Community Care and/or Choice Program provider, please contact one or both of the Third Party Administrators below:

Health Net
- Provider Customer Service: 1 (800) 979-9620
- HNFSProviderRelations@Healthnet.com

TriWest
- Provider Services Contracting: 1 (866) 284-3742
- TriWestDirectContracting@triwest.com

AHEC VETERANS MENTAL HEALTH PROJECT

Robert P Dick, SSG USARMY NG PAARNG (US)

There’s nothing normal about war.

There’s nothing normal about seeing people losing their limbs, seeing your best friend die.

There’s nothing normal about that, and that will never become normal…”

Lt. Col. Paul Pasquina, MD, from the movie "Fighting For Life"

SCOPE OF THE ISSUE

Survey of 2.2 million **Soldiers and Marines in Iraq and Afghanistan**

- Over ***75%*** being in situations where they could be seriously injured or killed;
- ***62-66%*** knew someone seriously injured or killed;
- more than ***1/3*** described an event that caused them intense fear, helplessness or horror

(Office of the Army Surgeon General Mental Health Advisory Team [MHAT] IV, Final Report, Nov 06)

In war, there are no unwounded soldiers.

Jose Narosky

BASIC TRAINING – MILITARY CULTURE

BASIC TRAINING – MILITARY CULTURE

Understanding the nature of the military culture, combat and the stresses of living and working in a war zone are critical to establishing credibility with your patients or clients.

BASIC TRAINING – MILITARY CULTURE

The military has its own laws, its own clothes and its own language. To serve them better and help ease their fears about treatment, we first need to understand what being a veteran is all about and be familiar with all things military.

Scott Swain, 15-year Gulf War veteran,
Senior Director Veterans Services
Valley Cities Counseling and Consultation
Auburn, WA

BASIC TRAINING – MILITARY CULTURE

- High standard of discipline
- Distinct ceremony and etiquette
- Creates shared rituals and common identities
- Emphasis on group cohesion & esprit de corps

BASIC TRAINING – MILITARY CULTURE

- Army/Army National Guard
- Navy/Naval Reserves
- Marine Corps/Marine Corps Reserve
- Air Force/Air National Guard/ Air Force Reserves
- Coast Guard*

WHY WE SERVE

-Loyalty to Nation
-Upbringing
-Family members in the Military
-A paycheck
-College benefits
-Persuaded by a Recruiter
-Adventure

WHY WE STAY

-Loyalty to Nation

-Loyalty to Unit, Branch

-Loyalty to one another, bond

-Personal Pride

THE BOND

-”All in this together”

-”We are the few the proud…”

-Embedded in our “Soldier” upbringing

-Part of a time honored organization, spans generations

-…for the group

-Mission first, Soldiers always

THE BOND, CONT

-More than a 9-5/partime job

-We are friends, teammates, supervisors, mentors, leaders, buddies, big bothers/sisters, peers, parents, coaches

-Die for the person to our left and right

-We realize and understand the big picture, but when it is “real” it is about each other

-Taught to REALLY know each other

BASIC TRAINING – MILITARY CULTURE

- Lingo…
  - DoD = Department of Defense
  - VA = Department of Veterans Affairs
  - IED = Improvised Explosive Device
  - VBIED = Vehicle Born IED (car or suicide bomb)
  - FOB = Forward Operating Base
  - TDY = Temporary Duty
  - ROE = Rules of Engagement

BASIC TRAINING – MILITARY CULTURE

- Connects service members to each other
- Continued into retirement
  - Wearing of service uniforms - parades and military unit apparel

BASIC TRAINING – MILITARY CULTURE

- Guard and Reserve culture
- Formally a Strategic Reserve
  - Backfill the Active Duty force
  - Train one weekend a month
  - Two weeks a year

HOW THIS RELATES TO YOU

- Guard and Reserve culture
- Now an Operational Reserve
  - Some units deploy as often as Active Duty
  - Families often see themselves as Military Families
  - May lack community supports

HOW THIS RELATES TO YOU

- Dependents of deployed service members use Tricare
- Active duty members and dependents use Tricare
- Veterans and retirees have Tricare
- The VA is not always the answer

"I learned early that war forms its own culture. The rush of battle is a potent and often lethal addiction, for war is a drug, one I ingested for many years....

War exposes the capacity for evil that lurks not far below the surface within all of us.

And this is why, for many, war is so hard to discuss once it is over."

Chris Hedges, Veteran War Correspondent,
War is a Force that Gives Us Meaning

Behavioral Health Issues

MENTAL HEALTH NEEDS OEF/OIF VETS (2014 PROJECTIONS)

• PTSD only	4.7%	113,978
• MDD only	4.7%	113,978
• PTSD and MDD	9.1%	220,680
• Other MH Dx	11.6%	281,307
• TOTAL	30.1%	729,943

National Council for Behavioral Health
"Meeting the Behavioral Health Needs of Veterans: Operation Enduring Freedom and Operation Iraqi Freedom"
November 2012

Behavioral Health Issues

- Ideally problems are picked up within DoD or VA continuum of care

BUT…

- Only 50% of all OEF/OIF Veterans eligible for VA care have come to VA
- *Where are the other 50%?*
- "Silent majority" OEF/OIF veterans not coming to VA

Post Deployment Issues – Active And Reserve Components

- Study - 88,235 US soldiers returning from Iraq
- Active duty (AD) and Reserve component (RC)
- Completed Post Deployment Health Assessment (PDHA)
- Completed Post Deployment Health Reassessment (PDHRA) 6 months later

Milliken, Auchterlonie & Hoge (2007). JAMA 298:2141-2148

Changes Active Duty And Reserve Component At PDHRA

Results…

- Roughly ½ with PTSD symptoms

  PDHA improved by PDHRA

BUT…

- Twice as many <u>new</u> cases of PTSD at

  PDHRA

Milliken, Auchterlonie & Hoge (2007). JAMA 298:2141-2148

Changes Active Duty and Reserve Component at PDHRA

Results…

- Depression rates at PDHRA
  - Doubled in AD to 10%
  - Tripled in RC to 13%
- Identified as needing MH treatment post deployment
  - AD 20.3%
  - RC 42.4%

Milliken, Auchterlonie & Hoge (2007). JAMA 298:2141-2148

Changes Active Duty and Reserve Component at PDHRA

Results…

- 4-fold increase in concerns about interpersonal conflict
- Alcohol abuse rate high
  - AD 12%
  - RC 15%
  - Only 0.2% referred for treatment

Milliken, Auchterlonie & Hoge (2007). JAMA 298:2141-2148

Post Deployment Issues – Active And Reserve Components

- Why RC is at greater risk than AD…
- **AD** - have on-going access to healthcare
- **RC** situation -
  - DoD health benefits (TRICARE) expire 6 months after deployment ends
  - Pay for coverage
  - **S**pecial VA benefits end at 60 months unless a service-connected condition identified)

Post Deployment Issues – Active And Reserve Components

Why RC is at greater risk than AD…

- May be geographically separated from military and VA facilities
- 1/2 service members beyond standard DoD benefit window by PDHRA
- Lack of day-to-day contact with Battle Buddies
- Added stress transition back to civilian life

Posttraumatic Stress Disorder (PTSD)

PTSD

- Characterized by a constellation of symptoms
- Follows exposure to an extreme traumatic event
- Involves actual or threatened death or serious injury

PTSD

- Response to the event must include
  - Intense fear, helplessness or horror
  - Symptoms persist more one month
  - May involve
    - Re-experiencing the traumatic event through intrusive recollections, dreams or nightmares
    - Avoidance of trauma-associated stimuli, such as people, situations, or noises

PTSD

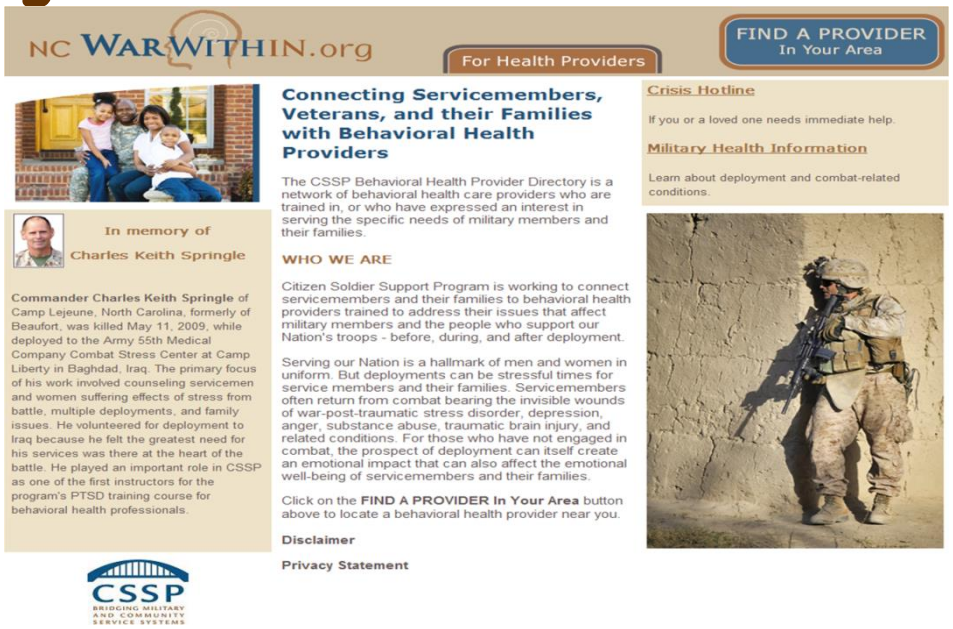
- Response to the event may involve
  - Persistent symptoms of increased arousal
    - Sleep disturbance
    - Hyper vigilance
    - Irritability
    - Exaggerated startle response

PTSD

- Diagnosis must be accompanied by clinically significant distress or impairment in
  - Social area
  - Occupational situations
  - Other important areas of function
- Problems must persist at least one month after the event

A National Demonstration Project

- Citizen Soldier Support Program Directory of BH Providers
- http://www.warwithin.org/
  - Validated licenses
  - Lists special interests and relevant training
  - Specifies insurances accepted including TRICARE
  - Google mapping to site of care



Combat/Operational Stress Reactions And Injuries

Combat Stress Injury

- Happens *to* a person (not chosen)
- Involves loss of normal integrity
- Causes loss of function at least temporarily
- Provokes predictable self-protective or healing symptoms
- Cannot be undone (though it usually heals)

Capt. Bill Nash in Combat Stress Injury

COMBAT STRESS INJURY - TRAUMA

Participant in or witness to event(s) involving

- Horror
- Feelings that you or someone close to you will die
- Helpless
- Powerless

Capt. Bill Nash in Combat Stress Injury

Public Health Model

- Most war fighters/veterans *do not* develop a mental illness
- All war fighters/veterans and their families face important readjustment issues

Public Health Model

- Problems are more ***functional*** than ***clinical***
- ***There is a difference between having a problem and being disabled***

Common Themes/Presenting Problems

- Marriage, relationship problems
- Medical issues
- Financial hardships
- Endless questions from family and friends
- Guilt, shame, anger
- Lack of structure
- Feelings of isolation
- Nightmares, sleeplessness
- Lack of motivation
- Forgetfulness
- Anger
- Feeling irritable, anxious, “on edge”

"He's been to war…and war is a place where you lose who you were. And then if you get back, you don't have any idea who you are, and you're scared to death of what you might become"

November 27, 2012

episode of TV show *Parenthood*

(In reference to a man who served 2 tours of duty in Iraq.
Spoken to his girlfriend by her grandfather, a veteran of Vietnam)

Assessment Measures

- Primary Care PTSD Screen (PC-PTSD)
- Combat Exposure Scale (CES)
- PTSD Checklist – Civilian Version (PCL-C)
- Trauma Symptom Checklist - 40 (TSC-40)
- Other measures as appropriate

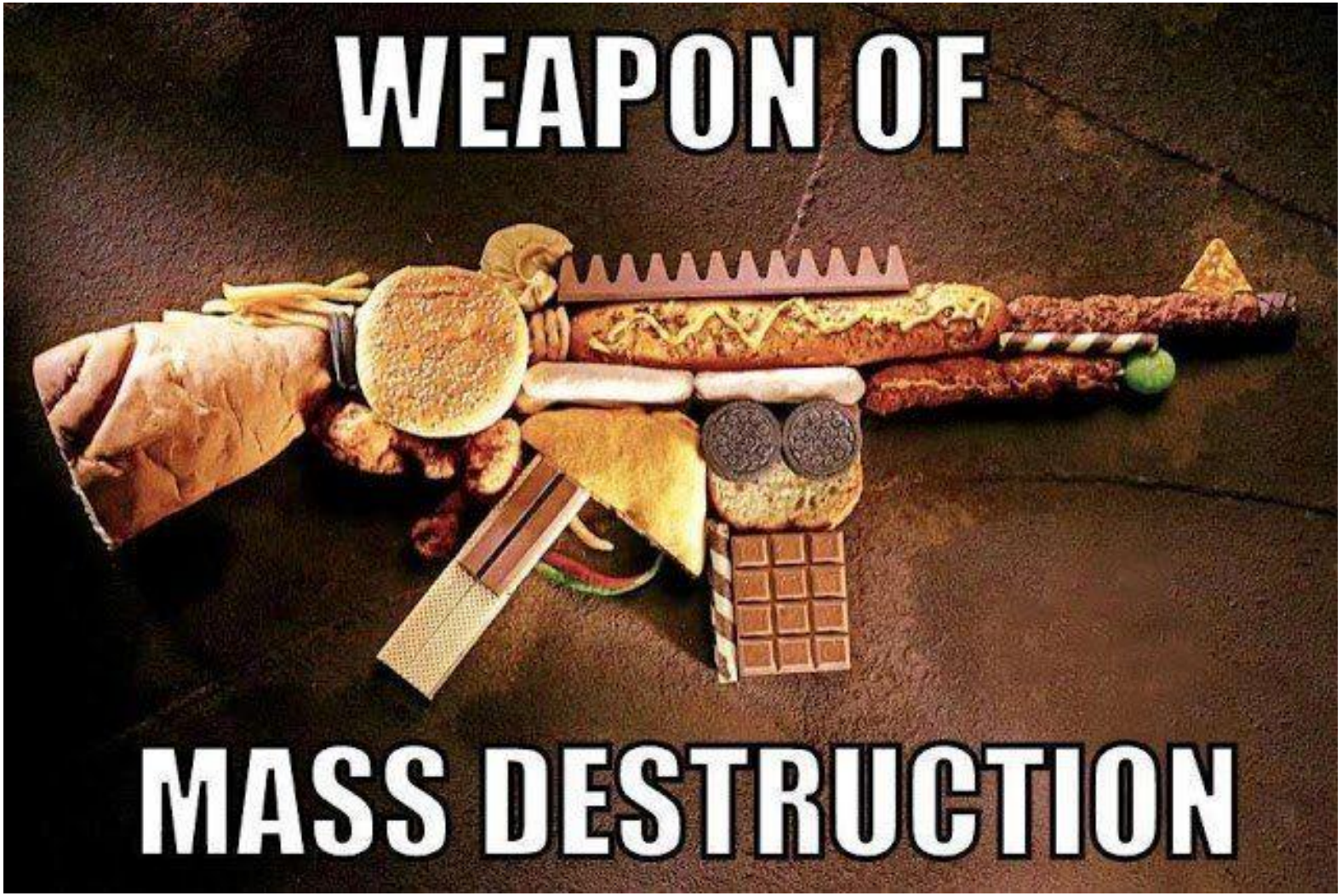
Take Home Points…

- No wrong door to enter to seek help
- Know something about military culture
- Post deployment MH is not just PTSD
- Issues of service members & family are more functional vs. clinical
- **Ask all patients about military service**

Pain Comorbidities

- What does trauma, stress reactions, poor sleep, poor mental health, and chronic pain have in common?
- **What could possibly make it worse?**

Pain Comorbidities



Pain Comorbidities

- Chronic Pain Factors
  - Predisposition
    - Physical Health
    - Psycho-emotional Health
  - Go through each date of service individually
- Microbiome
- Gut Health
- Trauma

Chronic Pain Factors

- Soldiers can be predisposed to pain
  - Changes in sleep
  - Feelings of stress
  - Feeling of anxiousness
  - Changes in diet
  - Cravings/addictions
    - » Effects Physiological Health
    - » Effects Phyco-emotional Health

Chronic Pain Factors

- **Physical Health**
  - ❑ Poor sleep
  - ❑ Poor digestion
  - ❑ Irregular bowels
  - ❑ Weight gain
  - ❑ Other Illness
- **Mental Health**
  - ❑ Feelings of Stress
  - ❑ Anxiety
  - ❑ Frustration
  - ❑ Depression
  - ❑ Cravings/Addiction

Chronic Pain Factors

- Physical Health and Mental Health
  - Can be influenced by microbiome and gut health
- Microbiome and Gut health
  - Can influence mood
  - Can influence how one processes trauma
- Trauma
  - Can be Physical or Emotional
  - Can cause pain
- Chronic pain and factors share connection to gut health
  - Gut as a secondary brain has a complex connection to the brain

Evidence-Informed Practice

John Hopkins Medicine (2016). **Anxiety and depression have been thought to contribute to gastro conditions like irritable bowel syndrome (IBS).** The Brain-Gut Connection.

If you've ever "gone with your gut" to make a decision or felt "butterflies in your stomach" when nervous, you're likely getting signals from an unexpected source: your second brain. Hidden in the walls of the digestive system, this "brain in your gut" is revolutionizing medicine's understanding of the links between digestion, mood, health and even the way you think.

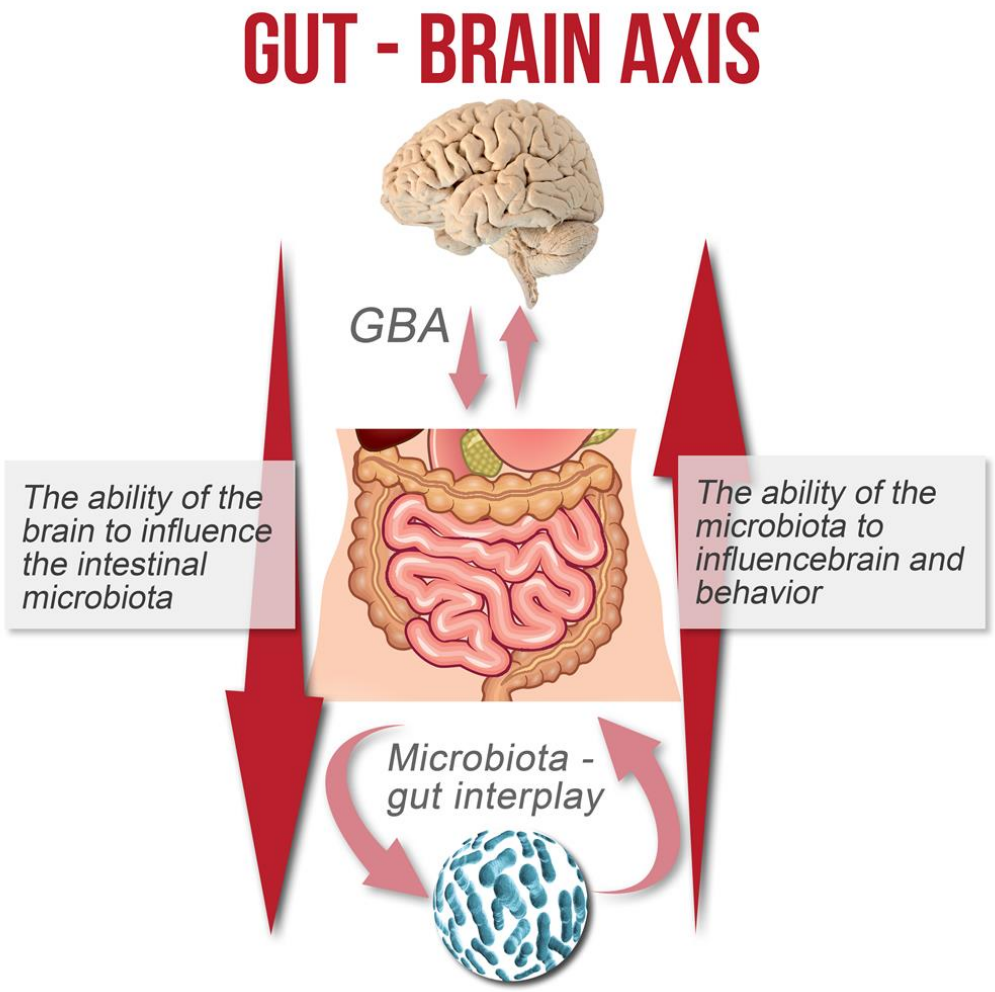
Scientists call this little brain the enteric nervous system (ENS). And it's not so little. The ENS is two thin layers of over 100 million nerve cells lining gastrointestinal tract from esophagus to rectum.

What Does Your Gut's Brain Control? Unlike the big brain in your skull, the ENS can't balance your checkbook or compose a love note. "Its main role is controlling digestion, from swallowing to the release of enzymes that break down food to the control of blood flow that helps with nutrient absorption to elimination," explains Jay Pasricha, M.D., director of the Johns Hopkins Center for Neurogastroenterology, whose research on the enteric nervous system has garnered international attention. "The enteric nervous system doesn't seem capable of thought as we know it, but it communicates back and forth with our big brain—with profound results."

Researchers are finding evidence that irritation in the gastrointestinal system may send signals to the central nervous system (CNS) that trigger mood changes.

Gut-Brain Connection

- Links emotional and cognitive centers of brain with peripheral intestinal functions.
- Recent research describes importance of gut microbiota in influencing these interactions.



Evidence-Informed Practice

Mayer, E., Tillisch, K., Gupta, A. (2015). **Gut/brain axis and the microbiota**. JCI, February 17, 2015, http://dx.doi.org/10.1172/JCI76304

Tremendous progress has been made in characterizing the bidirectional interactions between the central nervous system, the enteric nervous system, and the gastrointestinal tract. A series of provocative preclinical studies have suggested a prominent role for the gut microbiota in these gut-brain interactions. Based on studies using rodents raised in a germ-free environment, the gut microbiota appears to influence the development of emotional behavior, stress- and pain-modulation systems, and brain neurotransmitter systems. Additionally, microbiota perturbations by probiotics and antibiotics exert modulatory effects on some of these measures in adult animals. Current evidence suggests that multiple mechanisms, including endocrine and neurocrine pathways, may be involved in gut microbiota–to–brain signaling and that the brain can in turn alter microbial composition and behavior via the autonomic nervous system.

Gut-Brain Connection

- These interactions are not possible without **microbiota**
  - We will look deeper at Microbiota-Gut-Brain Axis
- ***Why should we be interested?***
  - Emerging science provides a framework for *Gu*
  - Help express etiology of CM and WM pain presentations
- ***How do we get started?***
  - Get deeply upset, deficient, and destroy gut health
    - Throw in a latent virus and add auto-immunity
  - Review biomedical framework

Microbiota-Gut-Brain Axis

- A framework for *Gu*
  - May append esoteric ideologies
    - Pathogenic microbiota in *Phlegm*
    - Significantly effects mood and behavior
    - Many ghost/inner-outer dragon points for parasites
  - May fill a gap in current Western research
    - Similar to Biofilm
      - Phlegm type substance for microbiota to hide
      - Recent research suggests pathology and movement

Evidence-Informed Practice

Macfarlane S., Bahrami B., & Macfarlane G. (2011). Mucosal biofilm communities in the human intestinal tract. Adv Appl Microbiol, 75:111-43. doi: 10.1016/B978-0-12-387046-9.00005-0

Until relatively recently, the majority of our information on intestinal microbiotas has come from studies on feces, or aspirates from the upper gut. However, there is evidence showing that mucosal bacteria growing in biofilms on surfaces lining the gut differ from luminal populations, and that due to their proximity to the epithelial surface, these organisms may be important in modulating the host's immune system and contributing to some chronic inflammatory diseases. Over the past decade, increasing interest in mucosal bacteria, coupled with advances in assessing microbial diversity, has begun to provide insight into the complexity of mucosa-associated communities. In gastrointestinal conditions it has been shown that a dysbiosis exists in microbial community structure, and that there is a reduction in putatively protective mucosal organisms. Therefore, manipulation of mucosal communities may be beneficial in restoring normal functionality in the gut, thereby improving the immune status and general health of the host. Biofilm structure and function has been studied intensively…modulation of biofilm composition by antibiotics, prebiotics, and probiotics.

Evidence-Informed Practice

Song, T., Duperthuy, M., & Wai, S. N. (2016). Sub-Optimal Treatment of Bacterial Biofilms. *Antibiotics*, *5*(2), 23. http://doi.org/10.3390/antibiotics5020023

Bacterial biofilm is an emerging clinical problem recognized in the treatment of infectious diseases. Appearance of microbial biofilm in clinical settings is steadily increasing due to increased use of quality of life-improving artificial devices. In contrast to infections caused by planktonic bacteria that respond relatively well to standard antibiotic therapy, biofilm-forming bacteria tend to cause chronic infections that persist despite seemingly adequate antibiotic therapy. This review describes responses of biofilm matrix components towards sub-lethal concentrations of antimicrobial agents…

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https://www.uptodate.com/contents/joint-infection-beyond-the-basics

Artificial joint infections are hard to treat, partly due to development of “biofilm” within joint. A biofilm develops when bacteria adhere to solid surface of artificial joint and can act as shield to some bacteria, making it difficult for the bacteria to be found and destroyed by the body's defenses or by antibiotic medications…2017

Gut-Brain Overview

- Microbiome
  - Brain
  - Digestive tract
  - Gut epithelial lining
  - CNS
- Microbiota
  - Gut Associated Bacteria
  - Parasites
  - Fungus
- Neurotransmitters
  - GABA
  - Serotonin
  - Dopamine
- Communication
  - Gut Health
  - Wei Qi

Gut-Brain Axis

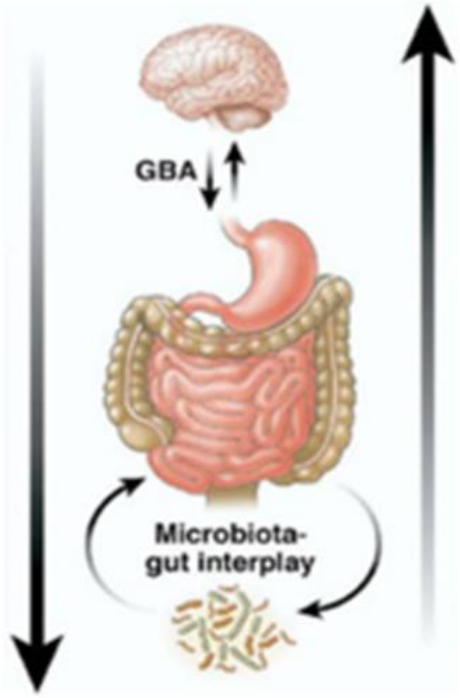
The Bidirectional Gut-Brain Axis

The ability of the brain to influence the intestinal microbiota

Perturbation of your normal habitat via stress-induced changes in gastrointestinal:

- Physiology
- Epithelial function
- Mucin production
- EE cell function
- Motility

Release of Neurotransmitters



The ability of the microbiota to influence brain, behavior, and mood

Activation of neural pathways to the brain

Activation of musosal immune responses

Production of metabolites that directly affect the CNS

Grenham S, Clarke G, Cryan JF, Dinan TG. Brain-gut-microbe communication in health and disease. Front Physiol. 2011;2:94. Epub 2011 Dec 7. PubMed PMID: 22162969; PubMed Central PMCID: PMC3232439

Gut Brain Simple View

- Microbiome
  - Environment of Microbiota
- Microbiota
  - Commensal, symbiotic, pathogenic microorganisms
- Neurotransmitters
  - Chemical Messengers
- Communication
  - Microbiota-Gut-Brain Axis

Microbiome and Microbiota

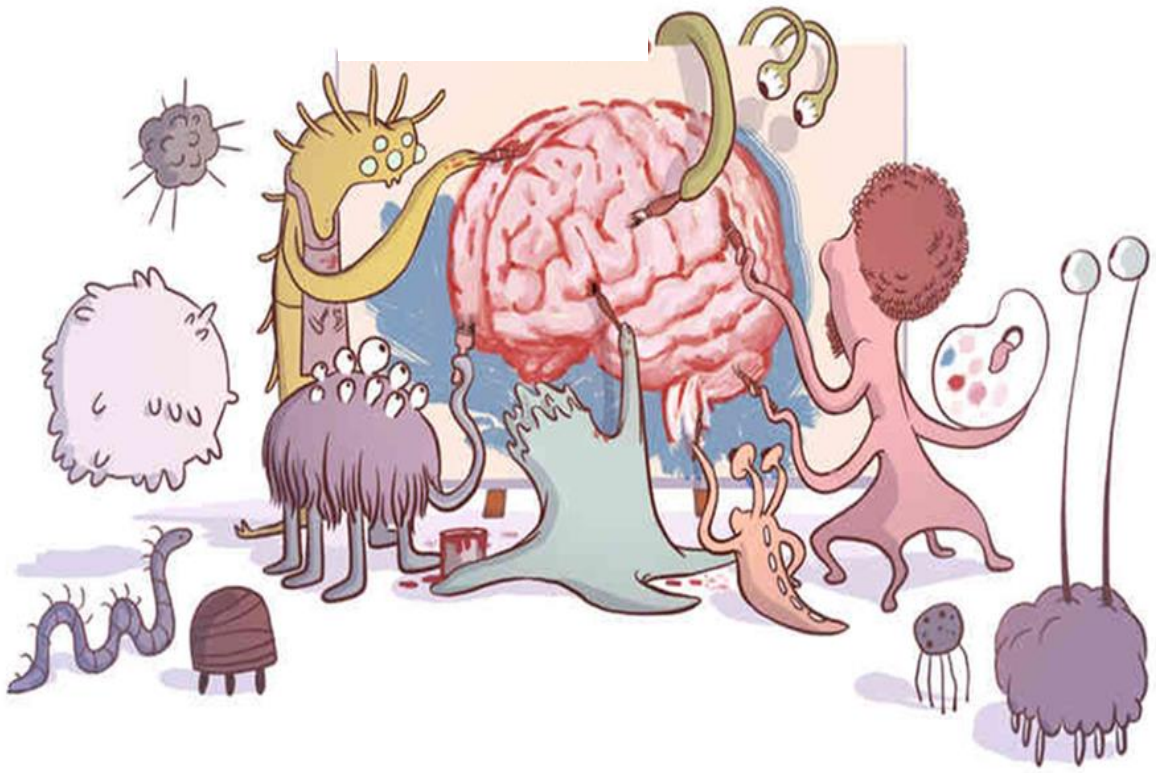
- Microbiome
  - Environment and Function of Microbiota
    - Brain
    - Gut epithelial lining
    - Digestive Tract
    - CNS
- Microbiota
  - Commensal, symbiotic, pathogenic microorganisms
    - Gut Associated Bacteria
    - Fungus
    - Archaea
    - Eukaryome
    - Virome
    - Protozoa

Microbiota

- Commensal, symbiotic, and pathogenic microorganisms
  - Gut Associated Bacteria
  - Eukaryotes
  - Mycobiota
  - Viruses
  - Archaea

Microbiota Significance

- Disruption of gut microbial community may impair mental health



Bacteria

- Over 35,000 Bacterial Species
  - Lactobacilli
  - Bifidobacteria
  - Clostridia
  - Enterococci
- Symbiotic Role
  - Control PH
  - Digestion of Proteins and Carbohydrates
  - Support immune cells

Eukaryotes

- Commensal Parasites
  - Protozoans
    - Common in healthy microbiomes
    - Blastocystis
      - Common parasitic infection in U.S.
  - Helminths
    - Evolved pathogen
    - Infects quarter of population
    - More morbidity than death
      - May reduce inflammatory diseases

Mycobiota

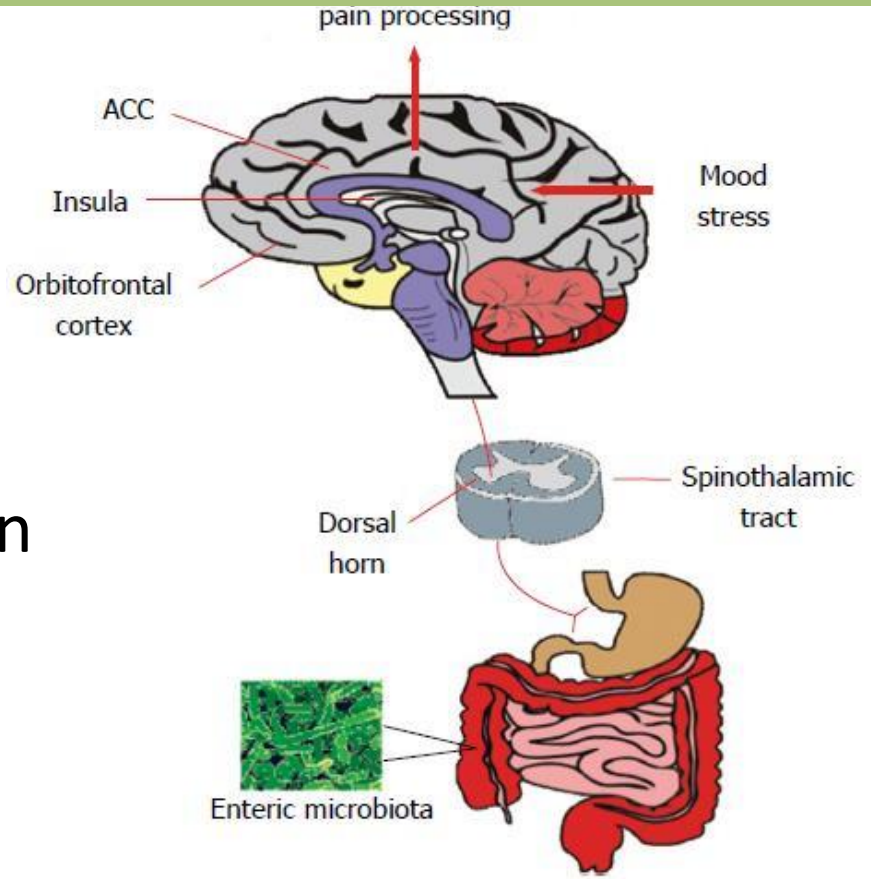
- Commensal Fungi
  - Relationship to host immune system
  - Saccharomyces Boulardii
    - Yeast from lychee and Mangosteen
      - Treats Cholera
- Pathogenic Fungi
  - Candida
  - Malassezia
    - Seborrheic Dermatitis
    - Tinea Versicolor

Microbiota Pathology

- Small Intestine Bacterial Overgrowth (SIBO)
  - Translocated Bacteria
    - Impaired microvilli function
- Candidiasis
  - Opportunistic overgrowth of candida albicans
    - Dimorphic fungus that can grow as yeast or fungus
- Dysbiosis
  - Microbial imbalance
  - Maladaptation in digestive tract

Microbiota Pathology

- Studies indicate gut microbiota appears to influence development of emotional behavior, stress-and pain-modulation systems, and brain neurotransmitter systems



Neurotransmitters

- Chemical Messengers
- Many Produced in Gut
  - Serotonin
  - Dopamine
  - GABA
  - Norepinephrine

Serotonin

- Estimated 90% made in digestive tract
  - Microbes stimulate intestinal cells to produce
- Found in GI tract, platelets, and CNS
- Made from Enterchromaffin cells
  - Epithelium of Stomach
  - Small Intestine
  - Colon

Dopamine

- Estimated 50% made in digestive tract
- Produced in response to psychosocial stress
  - Prompts food-reward behavior
  - Induces hyperphagia
  - Intake of high energy/low nutrient foods
    - ➢ Increase body weight and obesity

GABA (Gamma-aminobutyric acid)

- Helps regulate anxiety level and mood
- Crucial for calming brain
  - inhibits signals from nerve cells
- Low levels linked to mood disorders
  - gut bacteria can alter GABA activity in brains of mice and influence response to stress

Evidence-Informed Practice

Dinan, T. and Cryan, J. (2016). Mood by microbe: towards clinical translation. Genome Medicine 20168:36. DOI: 10.1186/s13073-016-0292-1

There is a growing realization that gut–brain axis plays a key role in maintaining brain health and the stress response. Recently, gut microbiota has emerged as a master regulator of this axis. Thus, opportunities to exploit the microbiome to treat stress-related psychiatric disorders are materializing. Clinical validation of such strategies is now warranted.

The only effective pharmacological therapies developed so far for the treatment of common psychiatric disorders target the monoaminergic systems within the brain. The paradigm giving rise to such therapies dates back to the 1950s. More recently, gut microbiota has emerged as a master regulator of this [gut-brain] axis. Preclinical studies have shown that the microbiome is key to normal neurodevelopment and behavior raising the potential of targeting this microbiota–gut–brain axis in the development of novel psychotropics. This approach offers a promising new avenue for treating conditions such as major depression or anxiety disorders.

Microbiota Influence on Mood

- Recent research has suggested that the gut microbiota has an influence on mood.
- Poor diet is a risk factor for depression.

Microbiota Influence on Mood

- Fecal Microbiota Transplant (FMT) is an emerging treatment for depression and other chronic illness.
- FMT is the transference of bowel from a healthy donor to a patient.

Neurogastroenerology

- Enteric Nervous System (ENS)
  - Operates independent of ANS and CNS
  - Communicates directly with CNS
- Central Nervous System (CNS)
- Autonomic Nervous System (ANS)
  - Parasympathetic
    - Vagus nerve
      - Most signals pass through from ENS

Microbiota-Brain-Gut Communication

- From Gut Microbiota to Brain
  - Production and expression of neurotransmitters
  - Bacteria metabolites
  - Mucosal immune regulation
- From Brain to Gut Microbiota
  - Alteration in motility
  - Alteration in intestinal permeability
  - Alteration of immune function

Microbiota-CNS Communication

- Microbiota Communication with Central Nervous System
  - The brain can sense gut bacteria
  - Bacterial signals are delayed to the CNS
  - Neuroendocrine signaling
  - Neural, endocrine and immune pathways
    - influences brain function and behavior*

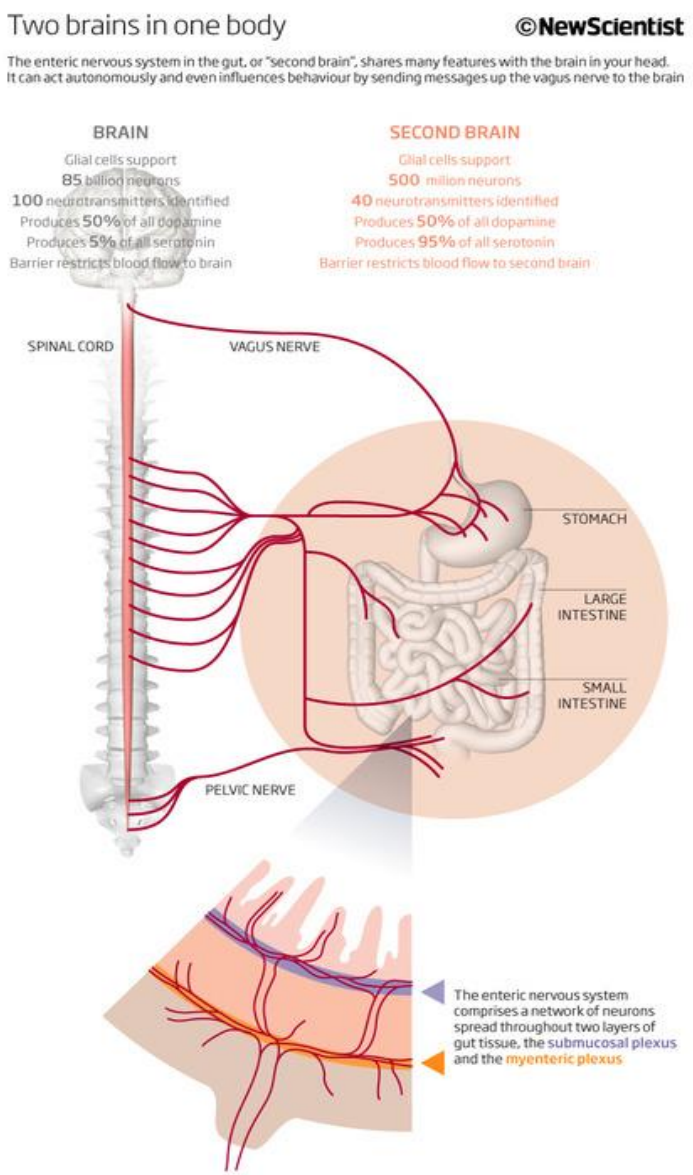
Evidence-Based Practice

Cryan, J. and Dinan, T. (2012). **Mind-altering microorganisms: the impact of the gut microbiota on brain and behavior.** Nature Reviews, Neuroscience. doi:10.1038/nrn3346

Recent years have witnessed the rise of the gut microbiota as a major topic of research interest in biology. Studies are revealing how variations and changes in the composition of the gut microbiota influence normal physiology and contribute to diseases ranging from inflammation to obesity. Accumulating data now indicate that the gut microbiota also communicates with the CNS — possibly through neural, endocrine and immune pathways — and thereby influences brain function and behaviour. Studies in germ-free animals and in animals exposed to pathogenic bacterial infections, probiotic bacteria or antibiotic drugs suggest a role for the gut microbiota in the regulation of anxiety, mood, cognition and pain. Thus, the emerging concept of a microbiota–gut–brain axis suggests that modulation of the gut microbiota may be a tractable strategy for developing novel therapeutics for complex CNS disorders.

Microbiota-Brain-Gut Axis

- Constant Bidirectional communication
- Specialized cells in gut wall interface between microbiota and host lumen
- Brain modulates specialized cells via autonomic nervous system and hypothalamic–pituitary–adrenal axis
- Neural, endocrine, immune, and humoral links



Evidence-Informed Practice

Carabotti, M., Scirocco, A., Antonietta, M., & Severia, C. (2015). **The gut-brain axis: interactions between enteric microbiota, central and enteric nervous systems**. Ann Gastroenterol, 2015 Apr-Jun; 28(2): 203–209, PMCID: PMC4367209

The gut-brain axis consists of bidirectional communication between the central and the enteric nervous system, linking emotional and cognitive centers of the brain with peripheral intestinal functions. Recent advances in research have described the importance of gut microbiota in influencing these interactions. This interaction between microbiota and GBA appears to be bidirectional, namely through signaling from gut-microbiota to brain and from brain to gut-microbiota by means of neural, endocrine, immune, and humoral links. I n this review we summarize the available evidence supporting the existence of these interactions, as well as the possible pathophysiological mechanisms involved. In clinical practice, evidence of microbiota-GBA interactions comes from the association of dysbiosis with central nervous disorders (i.e. autism, anxiety-depressive behaviors) and functional GI disorders. In particular, IBS can be considered an example of the disruption of these complex relationships, and a better understanding of these alterations might provide new targeted therapies.

Ancient Wisdom

“Man has no permanent and unchangeable I. Every thought, every mood, every desire, every sensation, says "I".”

“Man has no individual I. But there are, instead, hundreds and thousands of separate small "I"s, very often entirely unknown to one another, never coming into contact, or, on the contrary, hostile to each other, mutually exclusive and incompatible.”

“Each minute, each moment, man is saying or thinking, "I". And each time his I is different. Just now it was a thought, now it is a desire, now a sensation, now another thought, and so on, endlessly.”

-George Ivanovich Gurdjieff

Evidence-Informed Practice

Temko J., Bouhlal, S., Farokhnia, M., Lee, M., Cryan, J., Leggio, L. (2017). The Microbiota, the Gut and the Brain in Eating and Alcohol Use Disorders: A 'Ménage à Trois'? *Alcohol Alcohol*, Jul 1;52(4):403-413. doi: 10.1093

Accumulating evidence for the influence of the gut microbiota on the bidirectional communication along the gut-brain axis suggests a role of the gut microbiota in eating disorders (EDs) and alcohol and substance use disorders. The potential influence of altered gut microbiota (dysbiosis) on behaviors associated with such disorders may have implications for developing therapeutic interventions. Some studies suggest that dysbiosis and gut microbial byproducts may influence the pathophysiology of EDs via direct and indirect interference with peptide hormone signaling. Additionally, dysbiosis was shown to be correlated with alcohol use disorder-related symptoms, i.e. craving, depression and anxiety.

Ancient Wisdom

“Most people are walking corpses animated by the needs of the parasites within them that direct their desires” – Wang Ming Yi

Gut Health and Mental Health

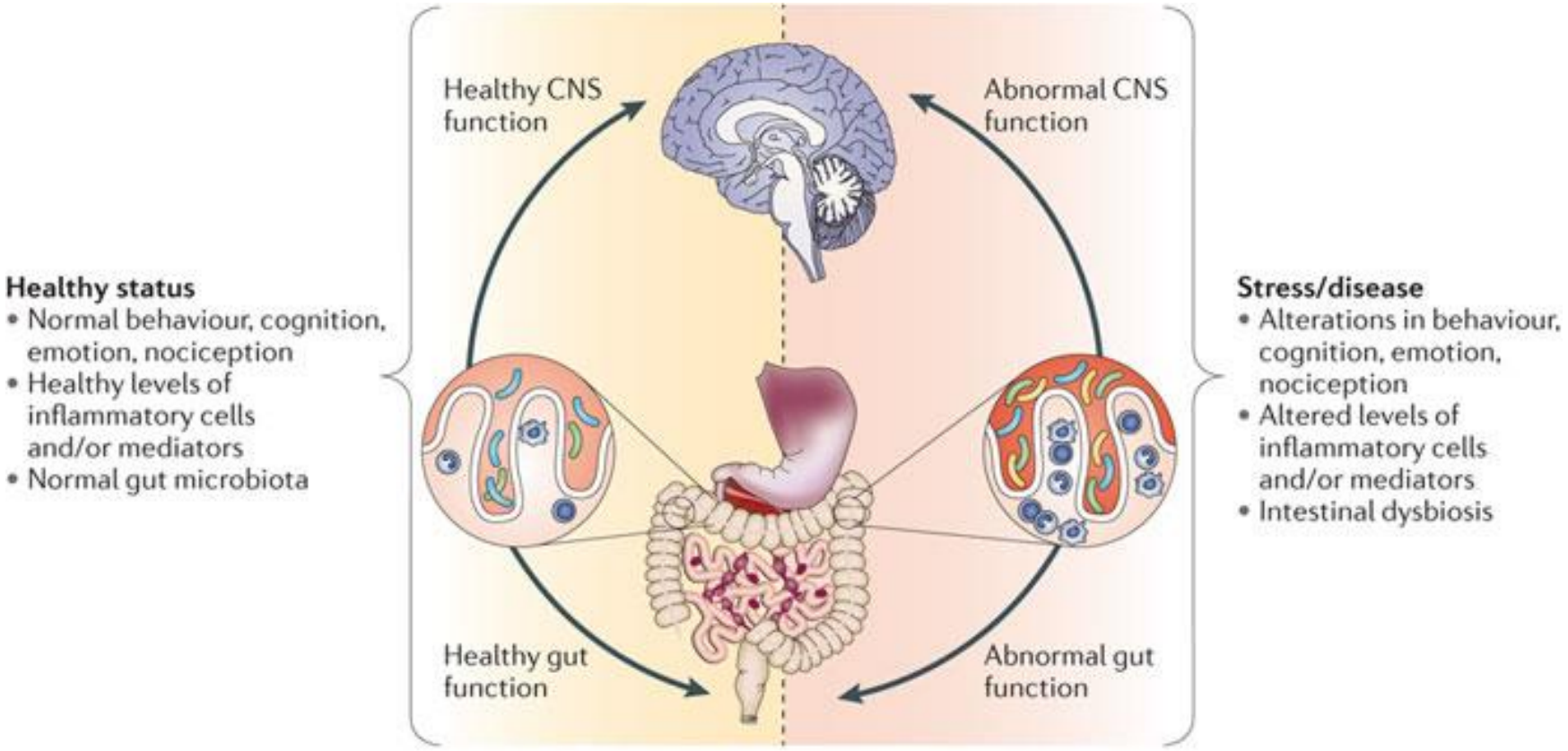
- Recent studies have shown a link between digestive health and mental health.
- Anxiety and depression are frequent comorbidities in gut disorders.
- There is also evidence that indigestion is correlated to low mood and anxiety.

Evidence-Informed Practice

Torres C., Economou, P. (2016). **Probiotics can Improve Mood: A Correlational Study Investigating the Relationship between Probiotics and Overall Mental Health**. J Prob Health 4:143, doi:10.4172/2329-8901.1000143

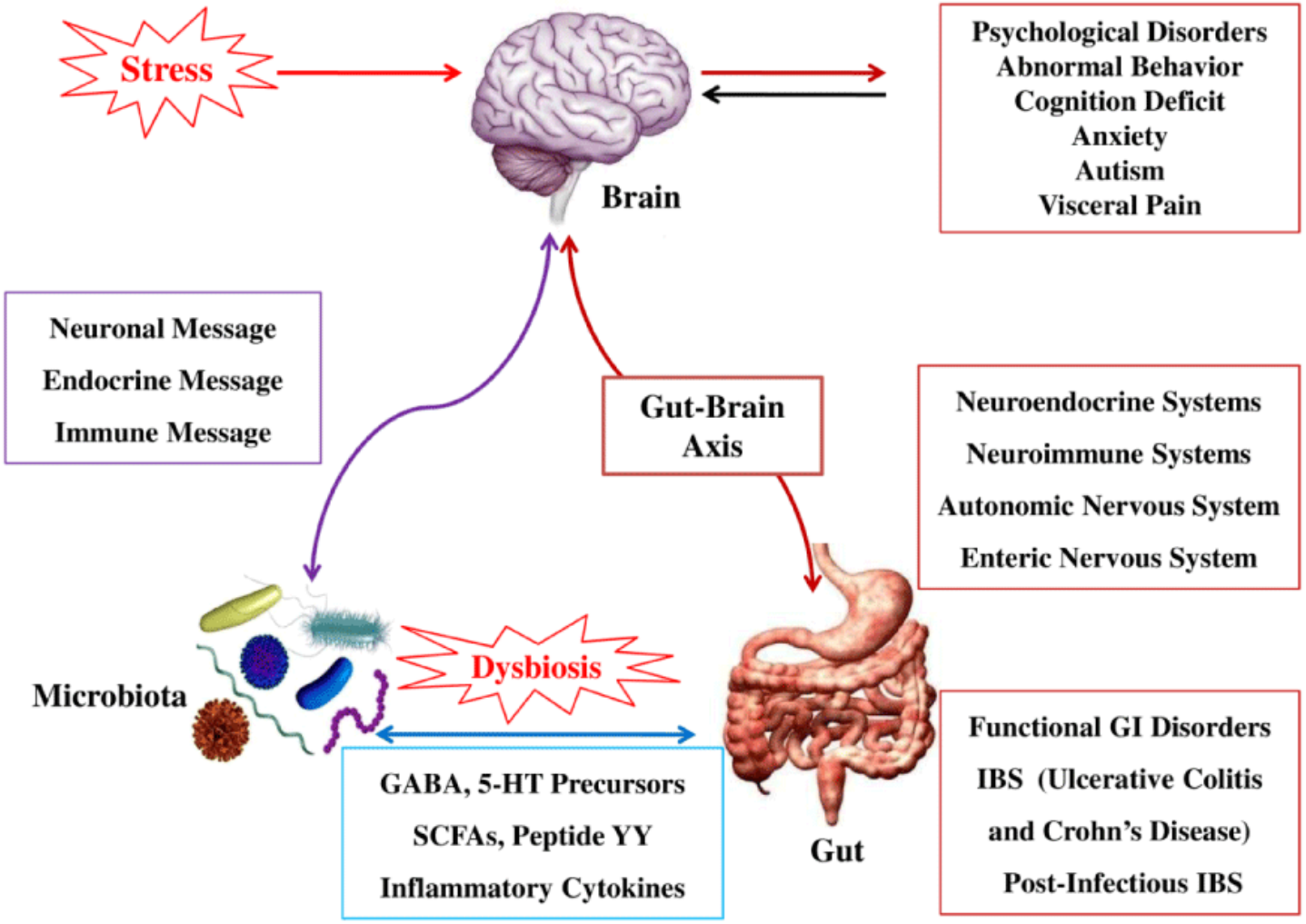
Recent studies have shown a link between the efficiency of the digestive system and mental health symptoms such as anxiety and depression. There is also evidence that when individuals suffer from indigestion (e.g., acid reflux or other stomach related ailment), there is a significant likelihood that those individuals have also experienced various mental health symptoms. These symptoms include low mood and anxiety. Additional studies have found that the use of a daily probiotic can improve mood, improve one's overall mental health, and alleviate symptoms that are often linked with depression. Another fact to consider is that anxiety and depression are among the most common psychiatric disorders and often comorbid. Anxiety and depression are frequent comorbidities in gut disorders, including inflammatory bowel disease (IBD).

Gut Health and Mental Health



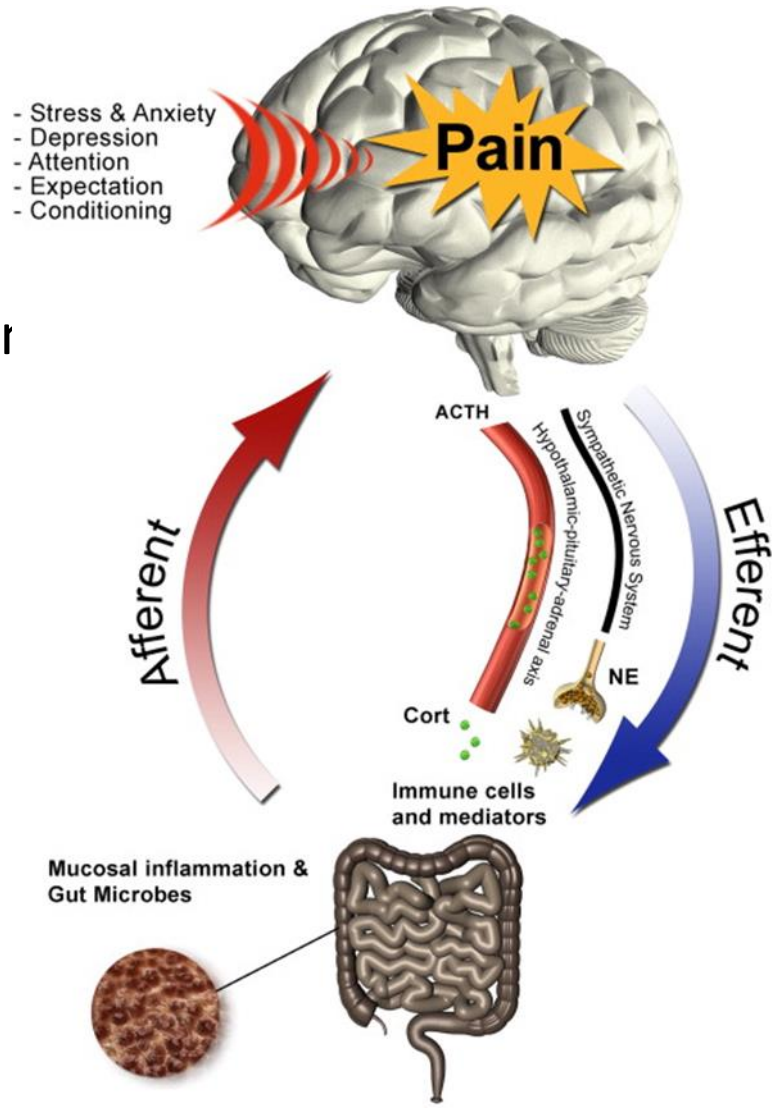
Nature Reviews | Neuroscience

Gut Health and Mental Health



Gut Health and Pain

- Significant research of the microbiota-gut-brain axis can link chronic pain and many chronic pain factors to poor gut health.
- Describes functions and interactions between gut microbiome, endocrine, immune, nervous systems, and the brain



Evidence-Informed Practice

Forsythe, P., Kunze, W., & Bienenstock, J. (2016). **Moody microbes or fecal phrenology: what do we know about the microbiota-gut-brain axis?** BMC Medicine, 14, 58. http://doi.org/10.1186/s12916-016-0604-8

Recent years have witnessed the rise of the gut microbiota as a major topic of research interest in biology. Studies are revealing how variations and changes in the composition of the gut microbiota influence normal physiology and contribute to diseases ranging from inflammation to obesity. Accumulating data now indicate that the gut microbiota also communicates with the CNS — possibly through neural, endocrine and immune pathways — and thereby influences brain function and behavior. Studies in germ-free animals and in animals exposed to pathogenic bacterial infections, probiotic bacteria or antibiotic drugs suggest a role for the gut microbiota in the regulation of anxiety, mood, cognition and pain.

Gut Health and Pain

Gut Health and Pain

- Chronic pain factors can be worsened by poor gut health
- Poor gut health effected by:
  - Medications
  - Digestive Disruptors
  - Toxin Environment

Gut Health and Pain

- Medications
  - Antibiotics - Kills all microbes ⟹ yeast overgrowth
  - PPIs- Malabsorption, leaky gut ⟹ bacteria overgrowth
  - NSAIDS - Mucosal damage ⟹ leaky gut, ulcers, bleeding
  - Opioids – Inflammation ⟹ chronic widespread pain

Evidence-Informed Practice

Dethlefsen, L., Huse, S., Sogin, M., and Relman, D. (2008). **The pervasive effects of an antibiotic on the human gut microbiota, as revealed by deep 16S rRNA sequencing.** http://dx.doi.org/10.1371/journal.pbio.0060280

The intestinal microbiota is essential to human health, with effects on nutrition, metabolism, pathogen resistance, and other processes. Antibiotics may disrupt these interactions and cause acute disease, as well as contribute to chronic health problems.

Several recent studies have characterized uncultured and complex microbial communities. Consistent with previous results, we found that the microbiota of these individuals was similar at the genus level, but interindividual differences were evident at finer scales. Ciprofloxacin reduced the diversity of the intestinal microbiota, with significant effects on about one-third of the bacterial taxa.

Evidence-Informed Practice

Williams, C. and McColl, K. (2006). **Review article: proton pump inhibitors and bacterial overgrowth. Alimentary Pharmacology & Therapeutics.** 23: 3–10. doi: 10.1111/j.1365-2036.2006.02707.x

ABSTRACT - Proton pump inhibitors are potent drugs producing profound suppression of gastric acid secretion. Consequently, they are highly effective at treating acid-related disorders. There have been concerns that the suppression of gastric acid will alter the bacterial flora of the upper gastrointestinal tract and lead to complications such as cancer, enteric or other infections and malabsorption. Studies have confirmed that proton pump inhibitors do alter the bacterial population but present evidence indicates that this only rarely leads to clinical disease. As with all drugs, proton pump inhibitors should only be used for disorders shown clearly to benefit from the therapy and where the benefits will outweigh the small risks associated with them. Further research to more fully quantify the risk associated with PPI therapy is required

Evidence-Informed Practice

Somasundarama, S., Hayllara, H, Rafia, S., Wrigglesworthb, M., Macphersonc, A., and Bjarnasona, I. (2008). **The Biochemical Basis of Non-Steroidal Anti-Inflammatory Drug-Induced Damage to the Gastrointestinal Tract: A Review and a Hypothesis**

Non-steroidal anti-inflammatory drugs (NSAIDs) are amongst the most successful group of drugs ever marketed. The gastrointestinal tract bears the brunt of NSAID-related toxicity. The gastro-duodenal side effects have attracted most attention because of the frequency, severity, and ease of documentation of the damage. Point prevalence studies suggest that 10-30% of patients on NSAIDs have gastroduodenal ulcers, but the clinical implications of these findings have been played down by suggestions that definitions of ulcer in these studies included a substantial number of large erosions of little clinical consequence as opposed to clinically significant ulcers, which have increased potential to perforate or bleed because of NSAIDs. There are, on the other hand, ample experimental data demonstrating NSAID-induced ulcers in all of the intestinal tract of animals and some erosions may be transitory lesions in the development of ulcers in man and hence markers of unacceptable mucosal damage.

Evidence-Informed Practice

Banerjee, S., et al (2016). **Opioid-induced gut microbial disruption and bile dysregulation leads to gut barrier compromise and sustained systemic inflammation.** *Mucosal Immunology*, doi:10.1038/mi.2016.9

Morphine and its pharmacological derivatives are the most prescribed analgesics for moderate to severe pain management. However, chronic use of morphine reduces pathogen clearance and induces bacterial translocation across the gut barrier.

The enteric microbiome has been shown to have a critical role in the preservation of the mucosal barrier function and metabolic homeostasis. Here, we show that chronic morphine treatment significantly alters the gut microbial composition and induces preferential expansion of Gram-positive pathogenic and reduction in bile-deconjugating bacterial strains.

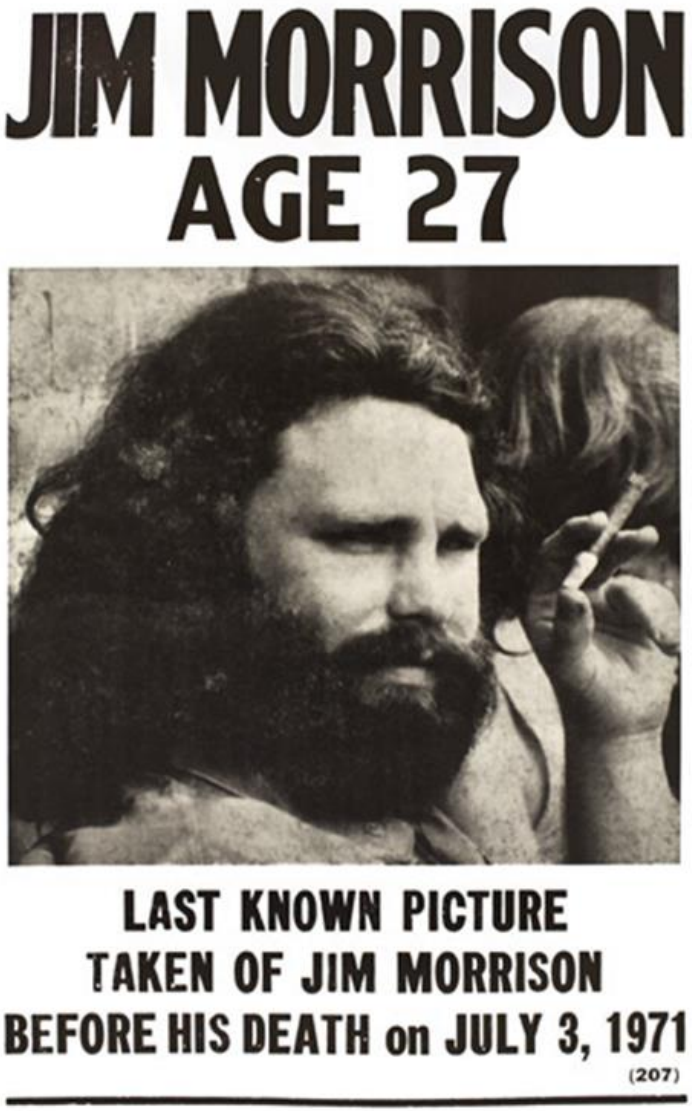
Morphine-induced microbial dysbiosis and gut barrier disruption was rescued by transplanting placebo-treated microbiota into morphine-treated animals, indicating that microbiome modulation could be exploited as a therapeutic strategy for patients using morphine for pain management.

Gut Health and Pain

Pain as Described by Jim Morrison

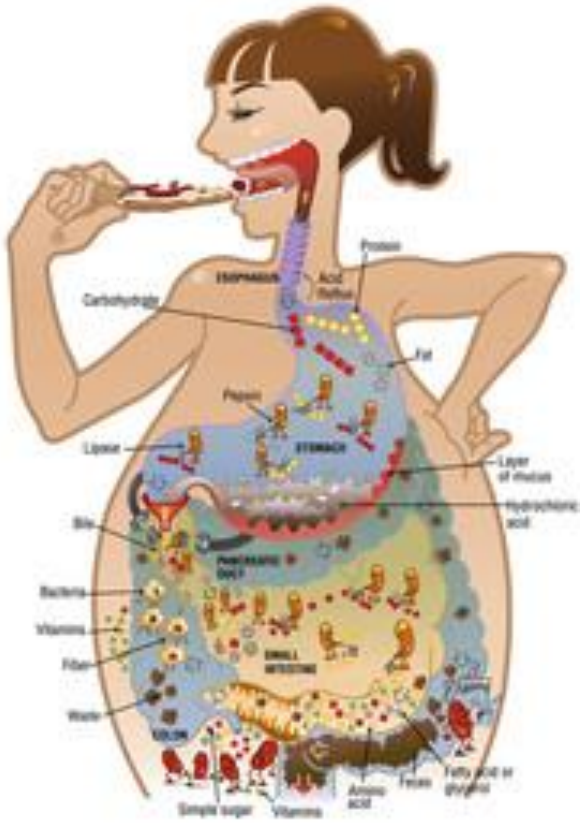
This is the end
Beautiful friend
This is the end
My only friend, the end
Of our elaborate plans, the end
Of everything that stands, the end
No safety or surprise, the end
I'll never look into your eyes...again
Can you picture what will be
So limitless and free
Desperately in need...of some...stranger's hand
In a...desperate land
Lost in a Roman...wilderness of pain

Gut Health and Pain



Gut Health and Pain

- Modern digestive disruptors
  - Altered food supply
  - Stress
  - Worry
  - Overwork
  - Lack of sleep
  - Toxic environment



Gut Health and Pain

- Toxic Gut Environment
  - Antibiotics, NSAIDs, alcohol, antacids, chlorine, over eating, anti-depressant drugs, soda, tobacco, processed foods, additives, coloring, preservatives, artificial sweeteners, excess sugar
- Toxic Environmental Pollutants
  - Solvents, cleaning agents, pesticides, herbicides, fungicides, plastics, paints

Gut Health and Pain

- Human gut represents largest surface area in direct contact with external environment (200m2).
- Human intestinal tract homes up to 100 trillion microorganisms, outnumbering human cells x 10.
- Human gut houses 60-70% of immune system

Immune System

- Organs of Immune system
  - **Primary**: Thymus and bone marrow where lymphocytes mature
  - **Secondary**: Lymph nodes, spleen, mucosal associated lymphoid tissues (MALT) and gut associated lymphoid tissues (GALT)
  - **Tertiary**: Cutaneous associated lymphoid tissues (CALT)

Immune System

- Mucosa-associated lymphoid tissue (MALT) contains 80% of all immune cells within the body and constitutes the largest lymphoid organ system.
  - Specialized immune barrier
  - Gut-associated lymphoid tissue
  - Bronchial-associated lymphoid tissue
  - Urogenital system

Immune System

MALT has three main functions:

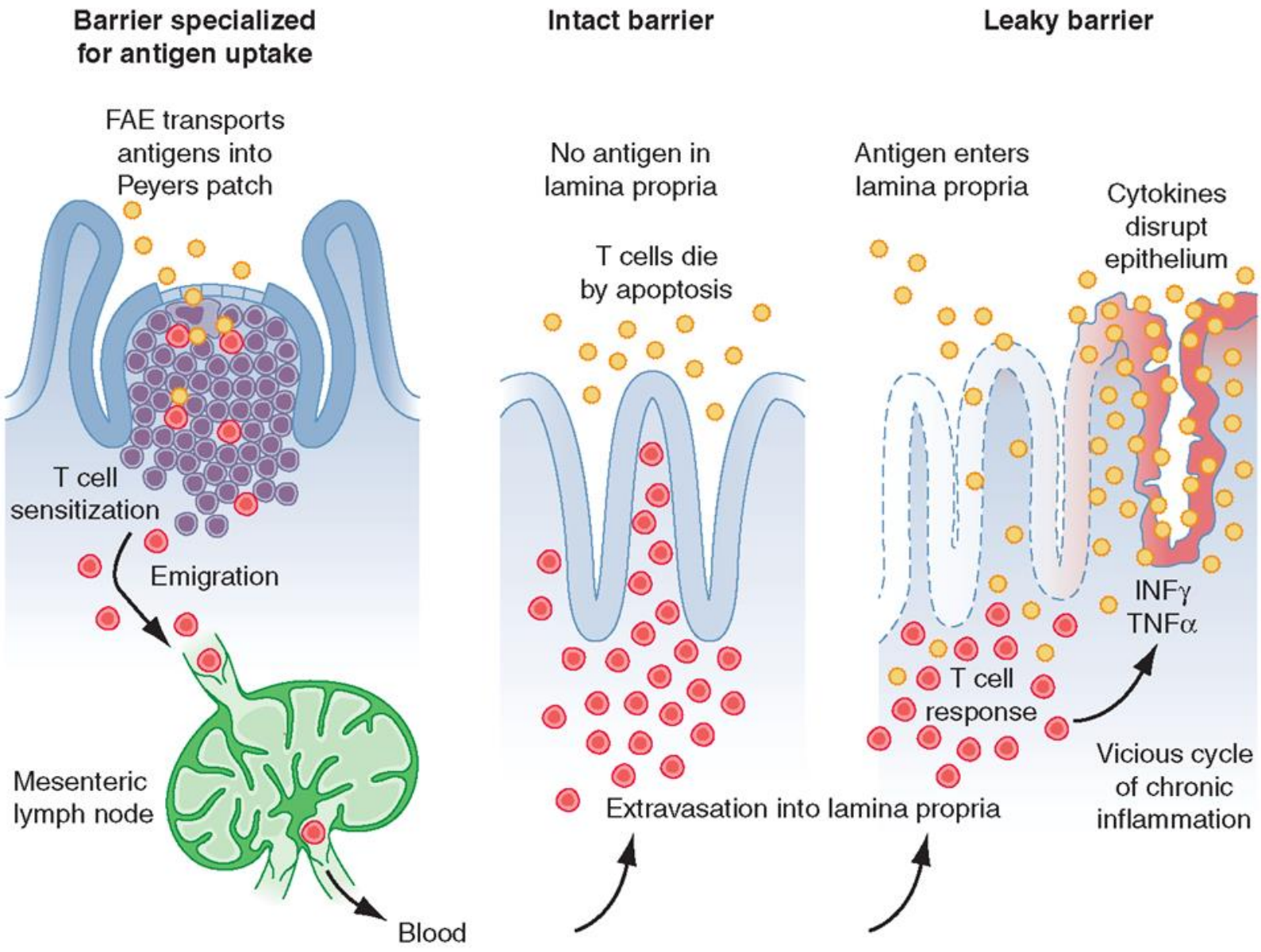
- protect mucous membranes from invasive pathogens
- prevent uptake of foreign antigens from food, organisms, airborne pathogens, and particulate matter
- prevent pathologic immune responses from foreign antigens if they do cross mucosal barriers
  - When gut barrier breaks down, immune responses to antigens can cause inflammatory bowel diseases
  - Uncontrolled MALT immune responses to food antigens, such as gluten, can cause celiac disease

Immune System

- GALT
- Plasma cells, macrophages, lymphocytes located in lamina propria and submucosa
- Intraepithelial lymphocytes – specialized T cells found between columnar epithelial cells
- Lymph nodules; aggregations of lymphocytes that may extend to submucosa

Immune System

- When gut is depleted of normal commensal flora, immune system becomes abnormal with decline of TH1 T cell function.
- Restoration of normal gut flora can reestablish balance in T helper cells.
- When gut barrier is intact antigens do not transverse the gut epithelium


Barrier specialized for antigen uptake
Intact barrier
Leaky barrier
FAE transports antigens into Peyers patch
No antigen in lamina propria
Antigen enters lamina propria
Cytokines disrupt epithelium
T cells die by apoptosis
T cell sensitization
Emigration
INFγ
TNFα
T cell response
Vicious cycle of chronic inflammation
Mesenteric lymph node
Extravasation into lamina propria
Blood

Immune System

- Increased epithelial permeability may contribute to development of chronic gut T cell-mediated inflammation
- Increased epithelial permeability may allow antigens to penetrate junctions
- Pro-inflammatory cytokines further increase epithelial permeability
  - Sets up vicious cycle of chronic inflammation

Inflammation

- Leading to the dis-regulation of such things as food intake, energy expenditure and glucose and fatty acid metabolism

- Over-weight people have higher circulating levels of pro-inflammatory cytokines and C-reactive protein

Inflammation

- Abdominal Obesity
  - Associated with low-grade chronic inflammation
    - Appears to be an adaptive response to overfeeding
- Adipose tissue
  - Secretion of pro-inflammatory cytokines TNF-alpha, IL-6, IL-1 beta
    - C-Reactive Protein which initiates inflammatory pathway signaling

Inflammation

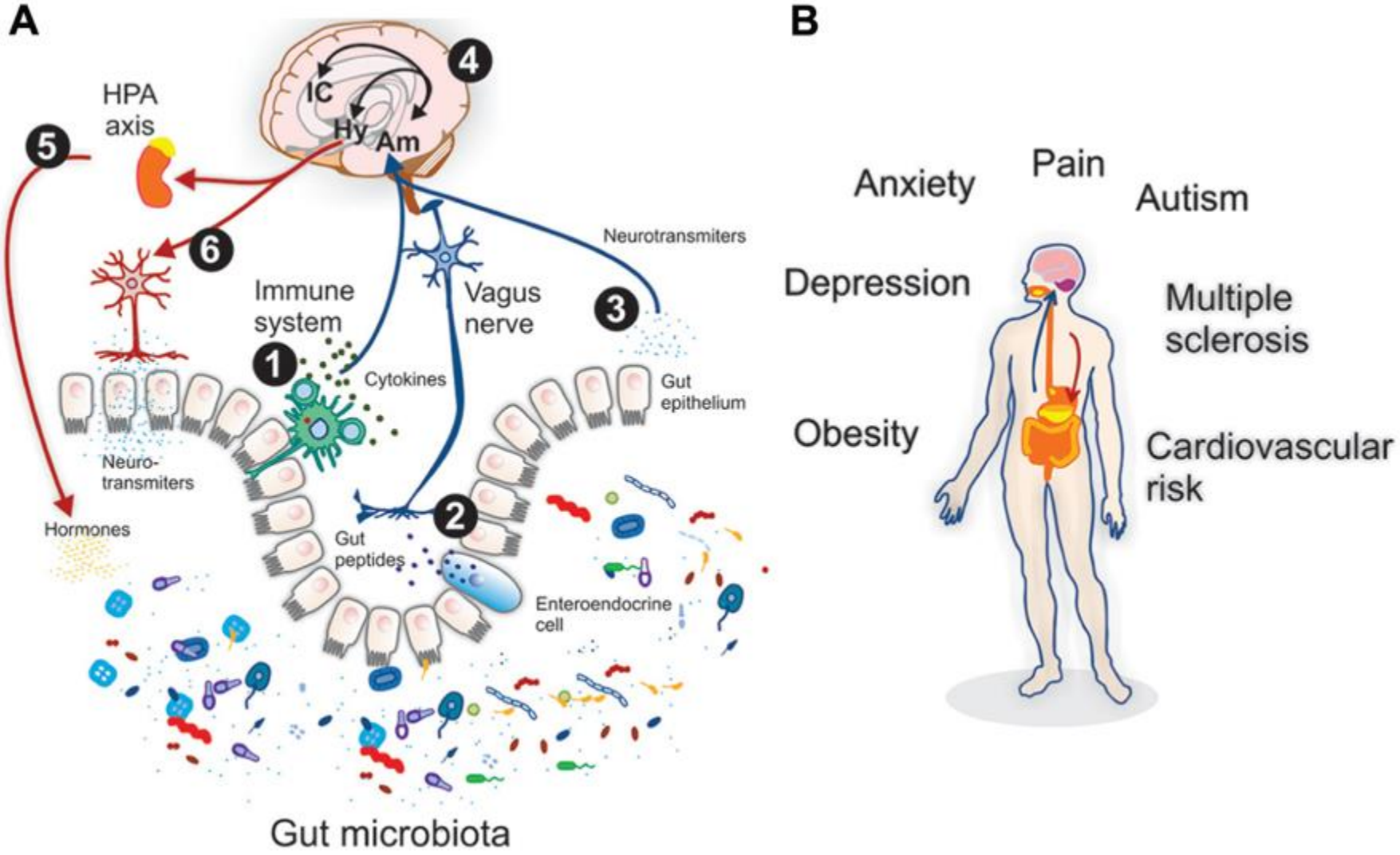
DESSERTS

is

STRESSED

spelled backward

Pain Dysregulation



Glial Cells

- Multiple functions and physiological processes
  - CNS development
  - Pathogen recognition, phagocytosis, cytotoxicity
  - Extracellular matrix remodeling, repair,
  - Stem cell regulation
  - Regulation of tumor cell proliferation
  - Modulation of inflammation

Glial Cells

- Participate initiation and maintenance of pain
- Applied in development of neuropathic pain
- Central sensitization and pain dysregulation
  - Release neuroactive substances
    - Disrupt and elevate neuronal excitability
      - Heighten and prolong pain
  - Glia/astrocyte response in acute pain, migraine, inflammatory pain, neuropathic pain, bone cancer pain, and peripheral neuropathy

Glial Cells

- Gut microbiota may affect enteric glial cells
- Glial cells are components of ENS, CNS, and PNS
- Enteric glial cells are link in gut–brain axis
  - Enteric glial cells link microbial cues with NS
- Microglia cells are macrophages of CNS
  - Neurodegenerative, brain inflammatory diseases
- Satellite astrocytes in PNS
  - Precursor molecules to neurotransmitters

Evidence-Informed Practice

Sajja, V., Hlavac, N., & VandeVord, P. J. (2016). Role of Glia in Memory Deficits Following Traumatic Brain Injury: Biomarkers of Glia Dysfunction. *Frontiers in Integrative Neuroscience*, *10*, 7. http://doi.org/10.3389/fnint.2016.00007

Historically, glial cells have been recognized as a structural component of the brain and now intimately involved in the complexities of neural networks and memory formations.

Astrocytes, microglia, and oligodendrocytes have dynamic responsibilities which substantially impact neuronal function and activities. The importance of glia following brain injury has come to the forefront in discussions to improve axonal regeneration and functional recovery.

This review outlines the pathological states of glial cells which evolve from their positive supporting roles to those which disrupt synaptic function and neuroplasticity following injury.

Evidence suggests that glial cells interact extensively with neurons both chemically and physically, reinforcing their role as pivotal for higher brain functions such as learning and memory.

Therapy

"All disease begins in the gut."

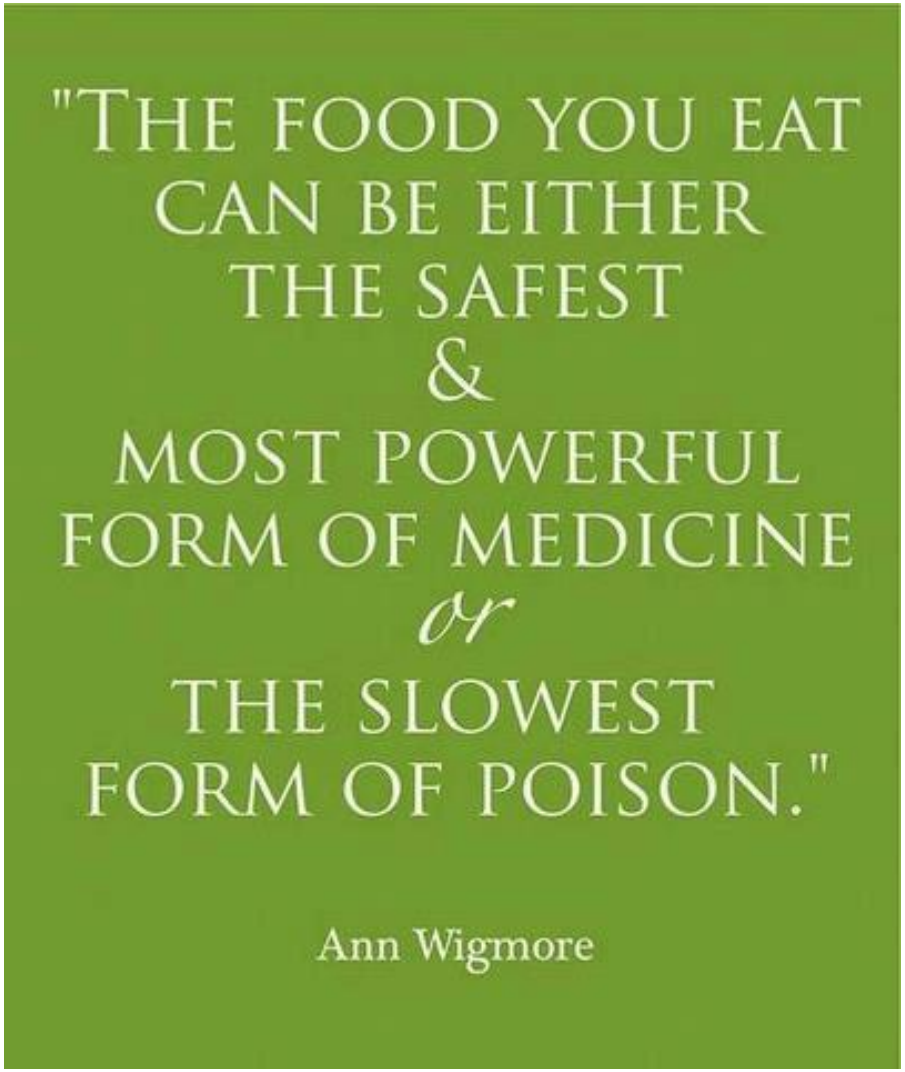
- Hippocrates

"What is sweet now turns so sour."

- George Harrison

"The road to health is paved with good intestines!"

- Sherry A. Rogers


"THE FOOD YOU EAT
CAN BE EITHER
THE SAFEST
&
MOST POWERFUL
FORM OF MEDICINE
or
THE SLOWEST
FORM OF POISON."
Ann Wigmore

Therapy

- Chronic pain and related factors can be improved with food, herbs, and supplements
- Improving gut health can help body absorb nutrients in food, herbs, and supplements
- Improving gut health can further:
  - reduce inflammation
  - improve mood
  - benefit sleep

Therapy

- **Boost Gut Health**
  - Essential fatty acids
  - Apple cider vinegar before meals for hypo-acidity
  - Bentonite clay for leaky gut
  - Saccharomyces
  - Glutamine
  - Red Krill Oil

Therapy

- **GAPS Diet**
  - Known to heal gut and boost microbiota
    - Boost communication in gut brain axis
  - Avoid all processed foods in packages and tins
  - Avoid grains, dairy, starchy veggies, refined carbs
  - Eat meats and veggies; balanced alkaline-acid foods
  - Consume butter, coconut oil, cold pressed olive oil
  - Bone broths, EFAs, fermented foods, probiotics

Therapy

- **Boost Gut Microbiota**
  - High quality prebiotics and probiotics
    - Water Kefir
    - Fermented Foods
    - Digestive Enzymes
    - Avoid Commercial Yogurt – HFCS, red dye, low probiotics
  - Supplements / Nutrients - GABA

Therapy

- **Pre-biotic Foods**
  - Raw asparagus
  - Jerusalem artichoke
  - Both raw and cooked onion
  - Raw bananas
  - Unrefined barley
  - Whole wheat flour
  - Jicama
  - Raw Garlic
  - Beans
  - Legumes
  - Raw oats
  - Raw honey

Therapy

- **Fermented Foods and Drinks**
  - Pickled vegetables
  - Sour dough bread
  - Cheese
  - Kraut
  - Yogurt
  - Kombucha
  - Pu-erh Tea
  - Vinegar
  - Miso
  - Water Kefir

Kombucha

- Fermented tea with probiotic health benefits
- Symbiotic colony of bacteria and yeast (SCOBY)
  - Microbial colony in SCOBY cultures vary
  - Generally includes various bacteria that oxidize yeast-producing alcohols to an acid
- Asian, Russian, and European cultures trace history of kombucha use back thousands of years

Kombucha

- Health benefits are much like quality probiotic
  - Digestive aid
  - Enhance mood
  - Balance PH
  - Can be used to reduce alcohol cravings

Water Kefir

- Also a probiotic drink
- Made from crystal grains
- Unlike milk kefir, it thrives on sugar not lactose
- The grains grow rapidly and need minerals
- Water ferments rapidly, even in the fridge
- May become alcoholic if fruit juices are used
- Can be used in place of soda for children

GABA and Serotonin

- GABA (Gamma-aminobutyric acid) and Serotonin
  - Help regulate anxiety level and mood
  - A molecule crucial for calming the brain
  - Inhibits signals from nerve cells, calming brain activity
  - Low GABA levels linked to depression/mood disorders

GABA and Serotonin

- Increase GABA and Serotonin via Diet
  - Stimulate production with foods rich in chemical precursors
    - glutamic acid and glutamate for GABA
    - tryptophan for serotonin

GABA

- **Increase GABA through Diet**
  - Foods rich in glutamate and glutamic acid
    - Provides raw material needed to synthesize GABA
    - Combine with complex carbohydrates

• almonds	oats	beef liver
• walnuts	halibut	lentils
• brown rice	potato	broccoli
• spinach	bananas	oranges

Serotonin

- **Increase Serotonin through Diet**
  - Foods rich in tryptophan
    - Chicken
    - turkey
    - beef
    - Lamb
    - nuts
    - beans
    - Salmon
    - tuna
  - Foods rich in complex carbohydrates
    - Bananas
    - beets
    - brown rice
    - Fennel
    - figs
    - pasta
    - Pineapple
    - spinach
    - radishes

Clearing Candida

- **Clearing Candida**
  - Avoid sugar or sweet foods, including fruit
  - Increase Probiotics and Fermented Foods
  - Berberines (quaternary ammonium salt – alkaloid)
    - Oregon grape Barberry
    - Goldenseal Yellow root
  - Caprylic acid, Lauric acid (saturated fatty acids)
    - High quality organic virgin coconut oil (3 tbsps. Daily)

FODMAPS Diet

FODMAPS

- **F**ermentable
- **O**ligosaccharides (eg. Fructans and Galacto-oligosaccharides (GOS))
- **D**isaccharides (eg. Lactose)
- **M**onosaccharides (eg. excess Fructose)
- **A**nd
- **P**olyols (eg. Sorbitol, Mannitol, Maltitol, Xylitol and Isomalt)

- Molecules found in food that may be poorly absorbed in small intestine
- Become food source to the bacteria that normally live in large intestine
- Bacteria then digest/ferment these FODMAPs can cause symptoms of IBS
- Limiting dietary FODMAPs is said to be a dietary treatment for symptoms of IBS

FODMAPS Diet

- **Foods high in FODMAPS**
  - **Fructose** - honey, apples, mango, pear, watermelon, HFCS
  - **Stone Fruits** - peaches, avocadoes, plums, apricots, cherries
  - **Fructans** - wheat, onions, garlic, artichokes, rye, barley
  - **Lactose** - milk, yogurt, unripe cheese (brie, cottage, ricotta)
  - **Galactans -** beans, lentils, chickpeas, legumes
  - **Polyols** – apples, mushrooms, pears, prunes

Omega 3

- **Omega 3**
  - Polyunsaturated Fatty Acids for heart, brain, eye health; joint mobility; and immune response
  - Promotes joint mobility and flexibility
  - Promotes positive mood and well-being
  - **EPA** - eicosapentaenoic acid – found in marine plants
  - **DHA** - docosahexaenoic acid – found in marine plants
  - **ALA** - α-linolenic acid - found in plant oils

EPA, DHA, ALA

- **Omega 3**
  - **EPA** and **DHA**
    - marine algae
    - Fish oils
    - phytoplankton
    - krill oil
  - **ALA**
    - walnuts
    - flaxseed oil
    - clary sage oil
    - edible seeds
    - hemp seed oil
    - algal oil

Evidence-Based Practice

Robertson, R., et al (2016). **Omega-3 polyunsaturated fatty acids critically regulate behavior and gut microbiota development in adolescence and adulthood.** Brain Behav Immun, pii: S0889-1591(16)30339-7. doi: 10.1016/j.bbi.2016.07.145

Neurodevelopment is strongly influenced by maternal and early-postnatal diet.

Omega-3 polyunsaturated fatty acids (n-3 PUFA) are vital structural and functional components of the developing brain.

The gut microbiota is also influenced by n-3 PUFA status.

Neurobehavioral development related to cognitive, anxiety and social behaviors, is highly dependent upon in utero and lifelong n-3 PUFA availability.

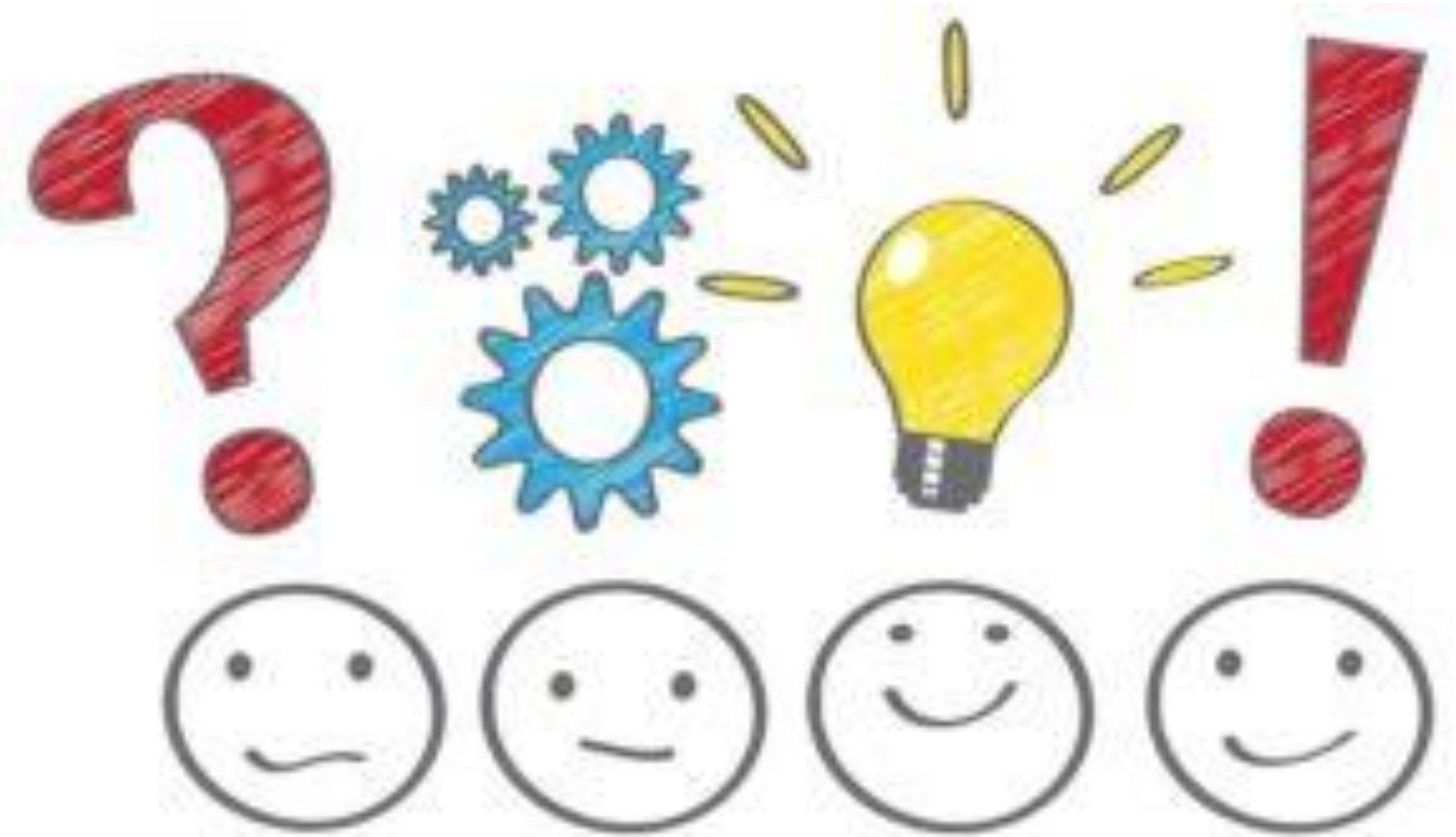
In addition, neurobehavioral changes induced by altering n-3 PUFA status are closely associated with comprehensive alterations in gut microbiota composition, HPA-axis activity and inflammation.

Food For Thought

Responsibility of Wellness

- Are there burdens to being well?
- Is there an investment in illness?
- How can this influenced practice?
- Does one seek cure or management?
- Can comorbid pain factors contribute to a culture of accepted malingering?

Questions, ideas, thoughts?



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