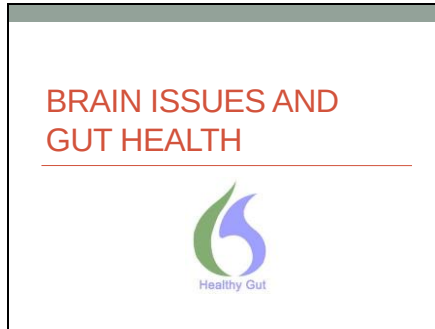


Slide 1

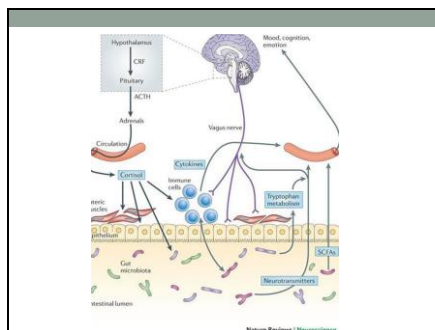


Slide 2

- The brain and gut are connected by an extensive network of neurons, chemicals and hormones which allow communication back and forth between the brain and the gut (brain-gut axis)
- Known as the enteric nervous system (the second brain)
- Messages go back and forth between the brain to the gut and gut to the brain
- What is not known is which comes first - does the brain initiate the communication or does the gut
- Does it go brain-gut-brain
- or gut-brain-gut



Slide 3



Slide 4

Issue With Sterile Mouse Model

- A lot of research on the gut-brain is based on germ-free mice or rats and the introduction of manipulated microflora
- There is some evidence that that maternal gut microbial metabolites migrate from the mother's microbiome to influence fetal brain development.
- This may mean babies are not as sterile when born as was presumed
- This means that the circumstances of the lab with this type of research may not be a true representation of what would happen in normal animals or us



Slide 5

Gut To Brain

- The gut microflora appears to influence the development of emotional behavior, stress and pain-modulation systems, and brain neurotransmitter systems.
- Additionally, microflora-related mood changes by probiotics and antibiotics exert modulatory effects on some of these aspects in adult animals.
- Current evidence suggests that multiple mechanisms, including endocrine and neuroendocrine pathways, may be involved in gut microflora-to-brain signaling and that the brain can, in turn, alter microbial composition and behavior via the autonomic nervous system.
- Why? It may be part of the process for the bacteria to get the food it wants

Slide 6

Gut To Brain

- Animal model research has found:
- Anxiety increases in animals with depleted microflora and that anxiety decreases when good bacteria is added
- One study found a reduction in depression in normal rats with the addition of probiotics
- Improvement of memory in diabetic rodents supplemented with probiotics
- Probiotics also improved social interactions
- Some studies indicated the microflora influences digestive behavior such as taste, satiety etc.



Slide 7

Gut To Brain

- In a randomized, placebo-controlled study of healthy men and women, psychological distress and anxiety improved after taking *Lactobacillus* and *Bifidobacterium* compared with those taking a placebo
- One study has shown that chronic ingestion of a probiotic combination improved functional brain responses in healthy women
- However, the change in brain mechanisms in response to changes in the gut bacteria is not clear but may include some of the gut/brain signaling systems
- Vagus nerve is one the key signaling system but elements that enter the blood stream can also make their way to the brain

Slide 8

Gut To Brain

- Increases in HPA axis activity (including increased cortisol) can be reduced by probiotics
- Several studies showed reduced expression of brain-derived neurotrophic factor (BDNF) (helps support the survival of neurons in the brain and differentiation of new neurons and synapses) in animals with altered flora
- 2011 study concluded intestinal microbiota influences brain chemistry and behavior independently of the autonomic nervous system, gastrointestinal-specific neurotransmitters, or inflammation.
- It also concluded: Intestinal dysbiosis might contribute to psychiatric disorders in patients with bowel disorders.



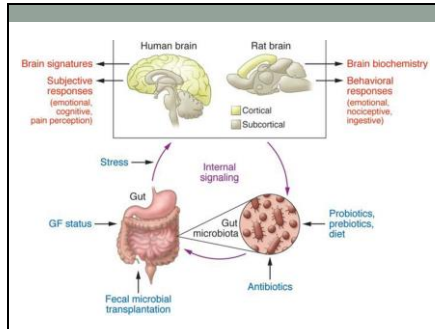
Slide 9

Gut To Brain

- A diet supplemented with *Bifidobacterium breve* was associated with increased fatty acid concentrations in the brain; however, the mechanisms underlying these effects are not known
- Evidence indicates that not only is our brain "aware" of our gut microbes, but these bacteria can influence our perception of the world and alter our behavior
- Also, research demonstrates an association between gut bacteria alterations and IBS, liver issues, infant colic, cravings in alcoholic, depression, and Parkinson's disease



Slide 10



Slide 11

Brain-Gut

- There are many issues of the brain that have a gut connection.
 - This means that new strategies exist to help with conditions
 - There is still a lot of research to be done to find all the pieces but a few interesting facts have been discovered that can help with these conditions.
- 



Slide 12

Migraines

- Migraines have been associated with both IBS and celiac disease
- Food allergies, especially IgG may also be connected
- Slower emptying of the stomach has been linked to migraines
- Inflammatory products such as lipopolysaccharides (LPS) (triggers a strong immune response when it enters through leaky gut) and inflammatory conditions such as asthma, obesity and metabolic syndrome have been linked to migraines



Slide 13

Migraines

- More importantly, in one study, 60 % of people with migraines, who took specific strains of good bacteria along with vitamins, minerals and herbs saw a total remission
- Strains: *Lactobacillus acidophilus*, *Lactobacillus bulgaricus*, *Enterococcus faecium*, and *Bifidobacterium bifidum*
- Leaky gut and inflammation have also been connected to migraines



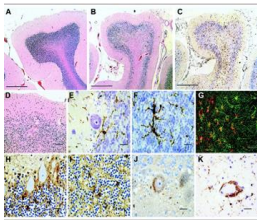
Slide 14

Autism

- Originally 1:10,000 (1950's) Now 1 in 68 persons (males>females)
- Abnormal Social Interaction- object fixation
- Speech and Language Difficulties
- Repetitive Stereotyped Movements
- Self-Injurious Impulsive Behavior
- Sensitivity to Sensory Input
- Savant Syndrome (rare)/restricted interests
- "picky eating" carb craving
- Comorbidities:
 - Seizure disorder
 - Gastrointestinal dysfunction

Slide 15

Brain Images

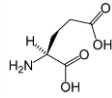


Neuropathology of Human Autism—Neuroinflammation/mild cell loss

Slide 16

Autism

- More research is looking to altered gut microflora as the key to understanding the disorder
- Autistic kids definitely have alter gut microflora – whether issues with the brain causes the altered flora or altered flora causes changes to the brain is not known
- It has been link to an excess of pathogenic bacteria creating dangerous metabolites that alter the brain-gut connection and brain function
- Autistic kids have an altered ratio of glutamate (a primary excitatory neurotransmitter and glutamine in favour of glutamate)



Slide 17

Autism

- A rat study found a connection to prenatal exposure to LPS leading to autism-like effects such as social issues, cognitive inflexibility and communication issues
- LPS also lowers glutathione levels important for detoxing heavy metals
- Correlations between gut bacteria and neurotransmitter-related metabolites are involved in the crosstalk between gut bacteria and the brain
- This is an current focus of research for autism but specific mechanisms are not understood



Slide 18

Autism

- Bacterial metabolites- symbiosis/dysbiosis
- Opportunistic Infections- key risk factor
- i.e clostridia, yeast (chronic antibiotics)
- Cell wall- LPS
- Fermentation products of dietary carbohydrate - Short chain fatty acids*
- Gut lining issues
- Dose & Timing of exposure



Slide 19

Autism

- Digestive system issues in autism – initially poorly studied
- But now renewed interest/technology (Horvath, Williams, Fasano)
- Focusing on an intestinal pathology on a subset of autistic patients
- Associated with regressive onset (autism occurs later) and GI symptoms
- Impaired carbohydrate digestion, inflammation, unique bacteria-carbohydrate craving



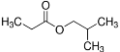
Slide 20

Autistic Children

- Factors occur while brain is growing
- Autistic kids have reduced carnitine (antibiotics deplete it), low levels of methyl B12, poor glutathione metabolism (from NAC)
- Higher LPS – found in the outer membrane of gram-negative bacteria and elicits a strong immune response
- Plus exposure to infections, antibiotics – dybiosis – clostridium produces higher levels of propionate (SFCA) – low levels are good – high levels are not
- All of this affects cell-to-cell communication and is very significant when synapses are being formed
- Poor carb metabolism causes carb cravings

Slide 21

Propionic Acid



- Used as a preservative – usually as calcium propionate or sodium propionate
- Prevents bacteria from producing energy
- Inhibits mold and bacteria
- Both have been linked to gastritis
- In rodent studies – it produced reversible behavior changes, hyperactivity, dystonia (muscle spasms and posture issues – may be involved in repetitive movement), neuroinflammation, glutathione depletion, social impairment, repetitive behavior

Dr. Derrick MacFabe, M.D., neuroscientist and director – Kilee Patchell-Evans Autism Research Group, Western University

Slide 22

Social Behavior

- After one dose of propionic acid

Before

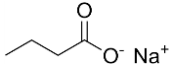
After



Slide 23

Propionate

- Time of exposure of excess propionic acid is critical (when brain developing)
- Autistic kids produce more propionate
- It is used in bread, dairy products and is sprayed on fruits.
- Interestingly – broad spectrum antibiotics temporarily improved autistic symptoms
- Inulin and resistant starch can produce more butyrate which can counter the propionate – however, dysbiosis needs to be considered



Slide 24

Bread

Ingredients: Dumpsters: 100% whole wheat
Whole grain whole wheat flour including the germ, water, glucose-fructose / sugar, yeast*, vegetable oil (canola or soybean), wheat gluten, salt, vinegar, acetylated tartaric acid esters of mono and triglycerides, **calcium propionate** sodium stearoyl-2-lactylate, sorbic acid, monoglycerides.
*Order may change.



Slide 25

Alzheimer's

- Bacteria biofilm and beta amyloid are similar in structure and trigger the same immune inflammatory response
- Precursor protein for beta amyloid has been found in intestinal epithelial tissue
- Beta amyloid has also been linked to irregular sleep and lack of sleep
- The gut bacteria inhibit production of cytokines when we wake in the morning, signaled by cortisol, and they define the transition between non-REM and REM sleep.
- Gut bacteria regulate circadian rhythms - disruption of the gut bacteria can have significant negative effects on sleep. Sleep also helps balance the gut flora



Slide 26

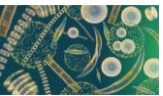
Alzheimer's

- Glutamate pathway may also be a factor in Alzheimer's
- Glutamine levels are low in Alzheimer's patients
- Sulfur (MSM) is low and is a key nutrient for detoxification
- Vitamin D and Magnesium also low in Alzheimer's patients
- Phosphatidyl choline and phosphatidyl serine help support memory (not by themselves)
- Supporting gut health aids nutrient absorption.
- Autistic kids show similar low levels
- [Study](#) - Novel diet and lifestyle program – 10 patients who had quit work due to memory decline – 6 returned to work

Slide 27

Alzheimer's Disease

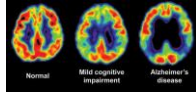
- Lack of diversity is linked to AD
- The more parasitic stress the lower the levels of Alzheimer's disease
- This has been linked to cultures with greater parasitic stress and lower incidence in those countries as compared to westernized cultures
- Conclusions: Variation in hygiene may partly explain
- Global patterns in AD rates: Microorganism exposure may be inversely related to AD risk. These results may help predict AD burden in developing countries where microbial diversity is rapidly diminishing



Slide 28

Alzheimer's

- Chronic intestinal inflammation suppresses hippocampal neurogenesis (re-populating with neurons). Increased levels of pro-inflammatory cytokines have detrimental effects on proliferation of elements that stimulate neurons.
- Deficient hippocampal neurogenesis may underlie increased rate of mood disorder and cognitive impairment observed in IBD patients.
- IBD and AD have some correlation



Slide 29

Prebiotics

- Prebiotics encourage the production of BDNF, especially GOS – lower BDNF is associated with lower cognitive function and anxiety
- Recent study found proof in principle that prebiotics can modify brain chemistry in same manner that other studies have shown probiotics can
- Rats who were fed FOS and GOS have stimulated neuroendocrine responses compared to controls – based on their ability proliferate gut bacteria
 - Did not alter glutamine or glutamate



Slide 30

Prebiotics

- Study tested 45 healthy individuals' emotional responses to stimuli after three weeks of taking either prebiotics or a placebo.
- Participants given the prebiotics had decreased levels of cortisol and were less reactive to negative information than placebo group.
- Were also more prone to focus on the positive and reported less anxiety



Slide 31

Probiotics

- One study found that women who ate yogurt twice a day for four weeks were calmer, with less reactions to stress and better cognitive ability
- Lactobacillus, and other Bifidobacterium help convert glutamate to GABA
- Probiotics also lower inflammation which is another factors for Alzheimers



Slide 32

Glutamine

- It is the precursor for neurotransmitters GABA and glutamate in the brain and helps with memory, focus and concentration
- GABA is also regulates many functions of the GI tract such as intestinal motility, gastric acid production, gastric emptying
- Glutamine regulates nitric oxide synthesis by endothelial cells - critical for lowering inflammation in the blood vessel walls and maintaining the blood vessels
- Low glutamine is a factor in dysbiosis and yeast overgrowth



Slide 33

Nutrients

- Probiotics and prebiotics
- Glutamine – is recommended even for those with autism
- Glutathione (NAC or cysteine) to bio transform toxins
- Epsom salt bath for magnesium and sulfur
- Vitamin D (time should be spent outside)
- Reduce stress and get proper sleep
- Other gut health nutrients as needed.
- Consider strategies for helping get clients to take the nutrients



In Conclusion

- Limited information is available on how these findings may translate to healthy humans or to disease states involving the brain or the gut/brain axis.
- Future research needs to focus on confirming that the rodent findings are translatable to human physiology and to diseases such as irritable bowel syndrome, autism, anxiety, depression, and Parkinson's disease.
- However, there is a definite link for all these conditions