



Gut - Brain Connection



Gut - Brain Connection

Discussion of:

- Diet influencing our Mental Health
- Gut Feelings
- Vagus Nerve Gut-Brain connection
- Microbiota
- Neurotransmitter influenced by diet, microbiome. Their causes of being deficient and what we can do.



Mental Health and Diet Connection

Fast-food and commercial baked goods consumption and the risk of depression

• Findings

 Fast food and processed pastries lead to a higher risk of depression

 Consumption lead to a 48% increased risk of depression

Association between dietary patterns and depressive symptoms over time: a 10-year followup study of the GAZEL cohort

- Findings:
- Western diet increased risk of depressive symptoms
- Traditional diet lowered risk of depressive symptoms



Dietary pattern and depressive symptoms in middle age.

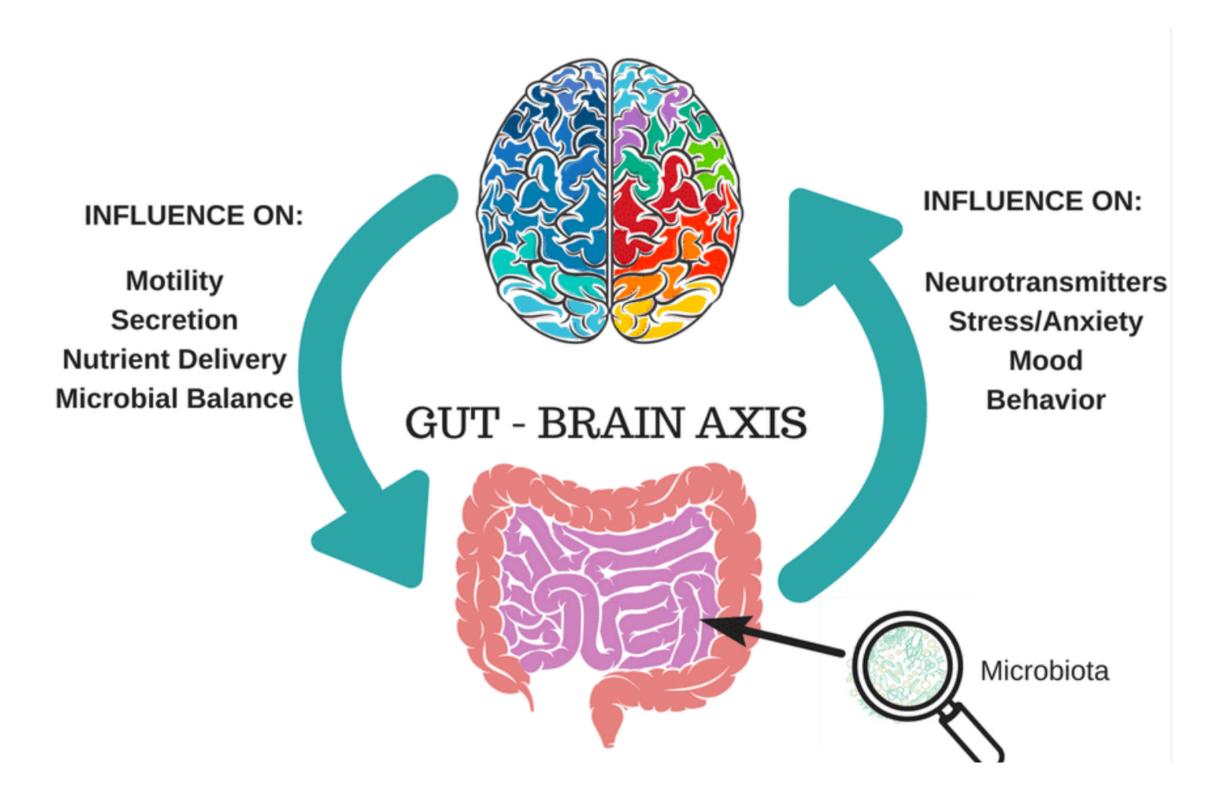
- Findings:
- Processed food increased risk of depression
- Whole food diet decreased risk of depression

Association of Western and traditional diets with depression and anxiety in women

- Findings:
 - Western diet increased risk of mental disorders
 - Traditional diet decreased risk of mental disorders.

Gut- Brain Connection

The connection between the gut and the brain is known to be bidirectional. This means messages from the gut affect brain function just as much as messages from the brain affect gut function.

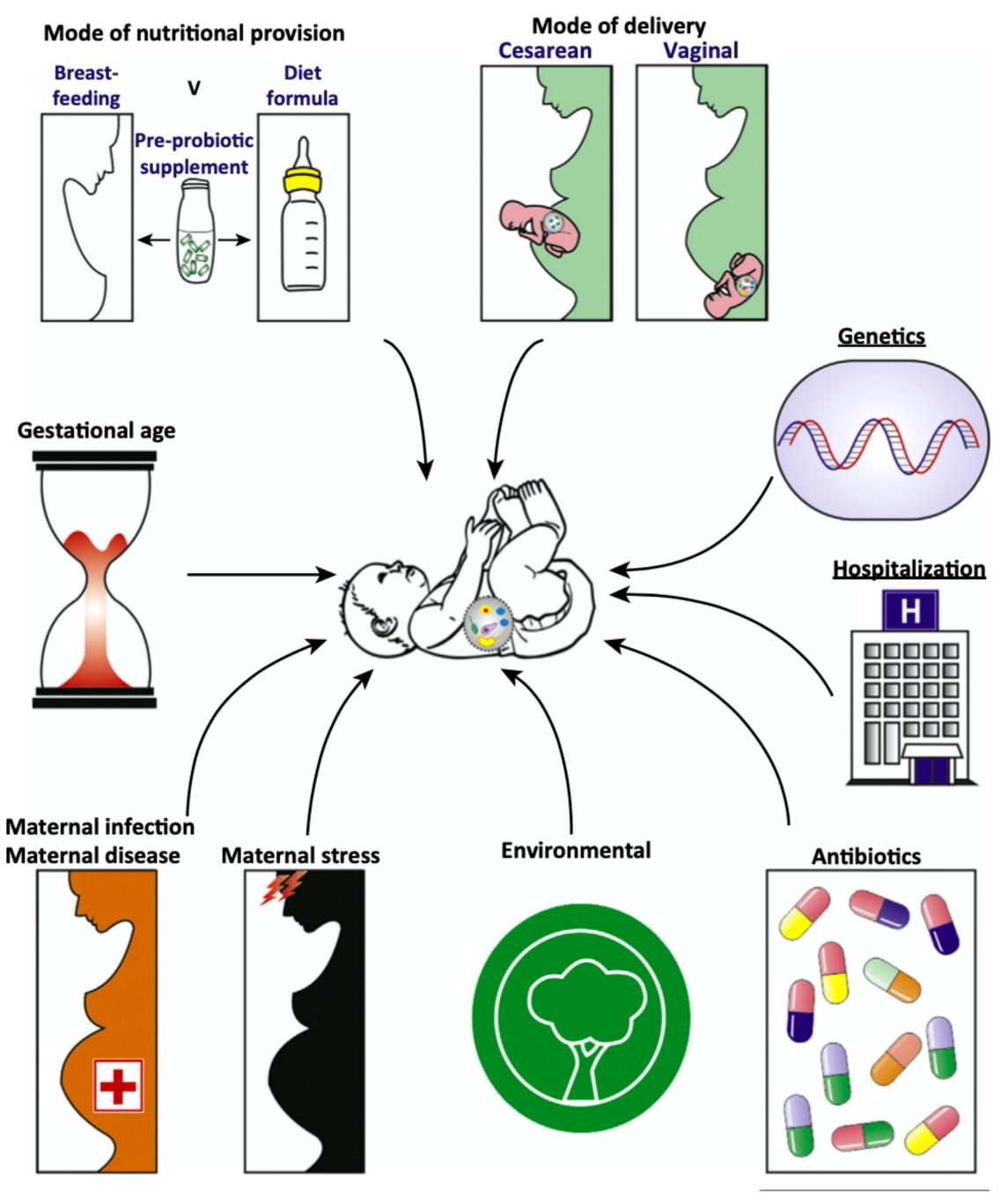




Gut-Brain Connection

Several factors play a role in shaping of the bacterial landscape in the development of the infant microbiota. In addition to mode of birth, mode of early nutrition, environment, other factors such as gestational age, genetics, and hospitalization, also influence the microbial composition of the infant. Infections (both maternal and infant) and antibiotic usage influence the trajectory of the developing microbiota as does the selective transient enrichment by probiotics and prebiotics.





TRENDS in Molecular Medicine

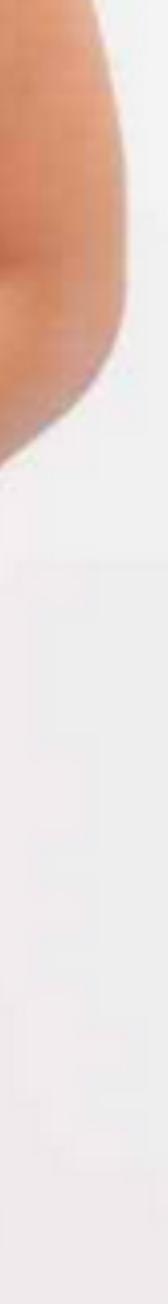


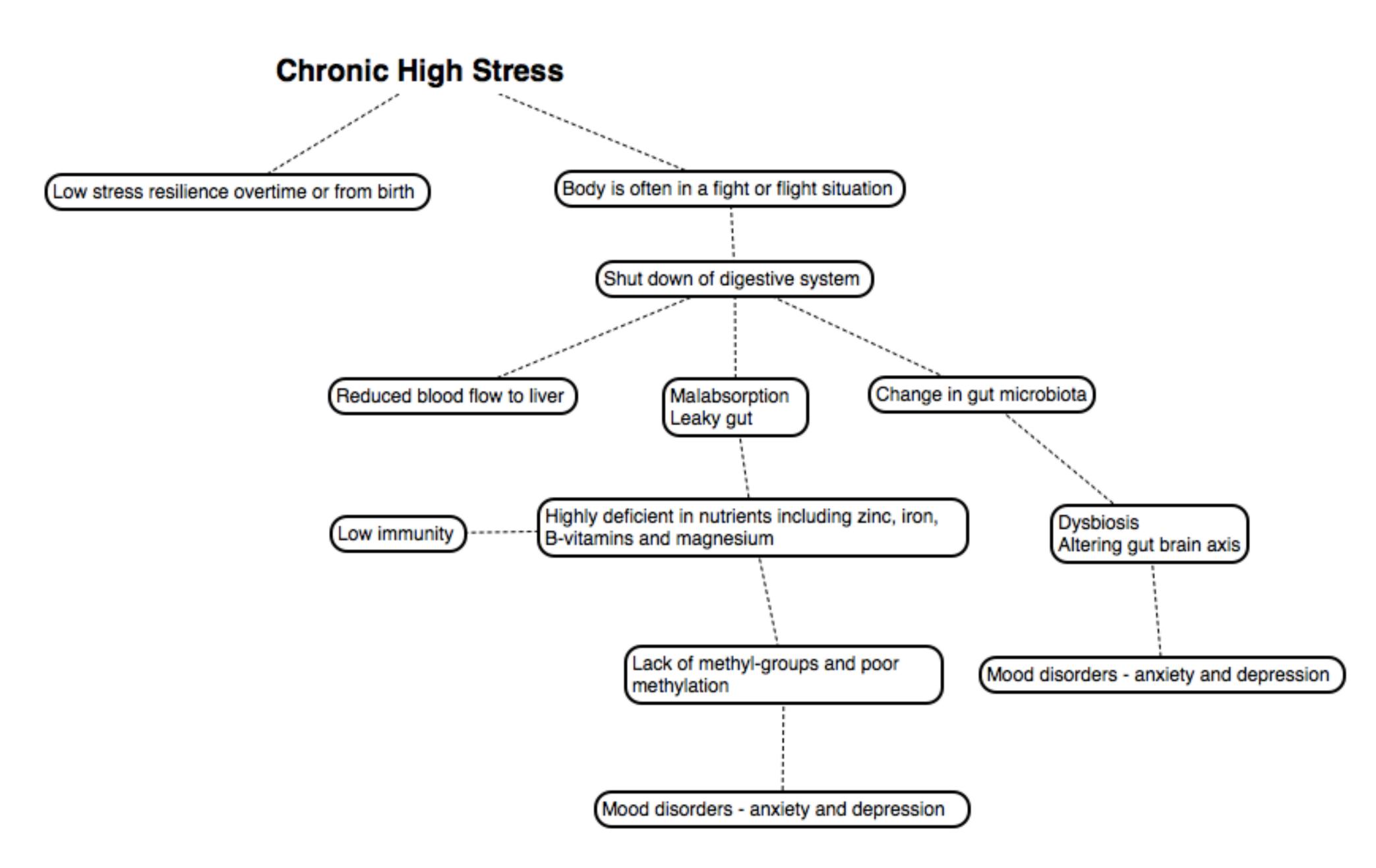
Chronic Stress

Stress affects every system of our body, including the gut- most commonly recognised by people with anxiety are GIT symptoms. When stressed, frightened or anxious our body has trouble digesting food, either constipation or diarrhoea, (IBS), bloating and pain. Stress affects our food choices and the makeup of out gut microbiome. Therefore our body is denied certain essential nutrients due to malnutrition, breakdown issues or inflammation (Leaky Gut)

Without a well functioning digestive system we become sicker in all areas of our body.

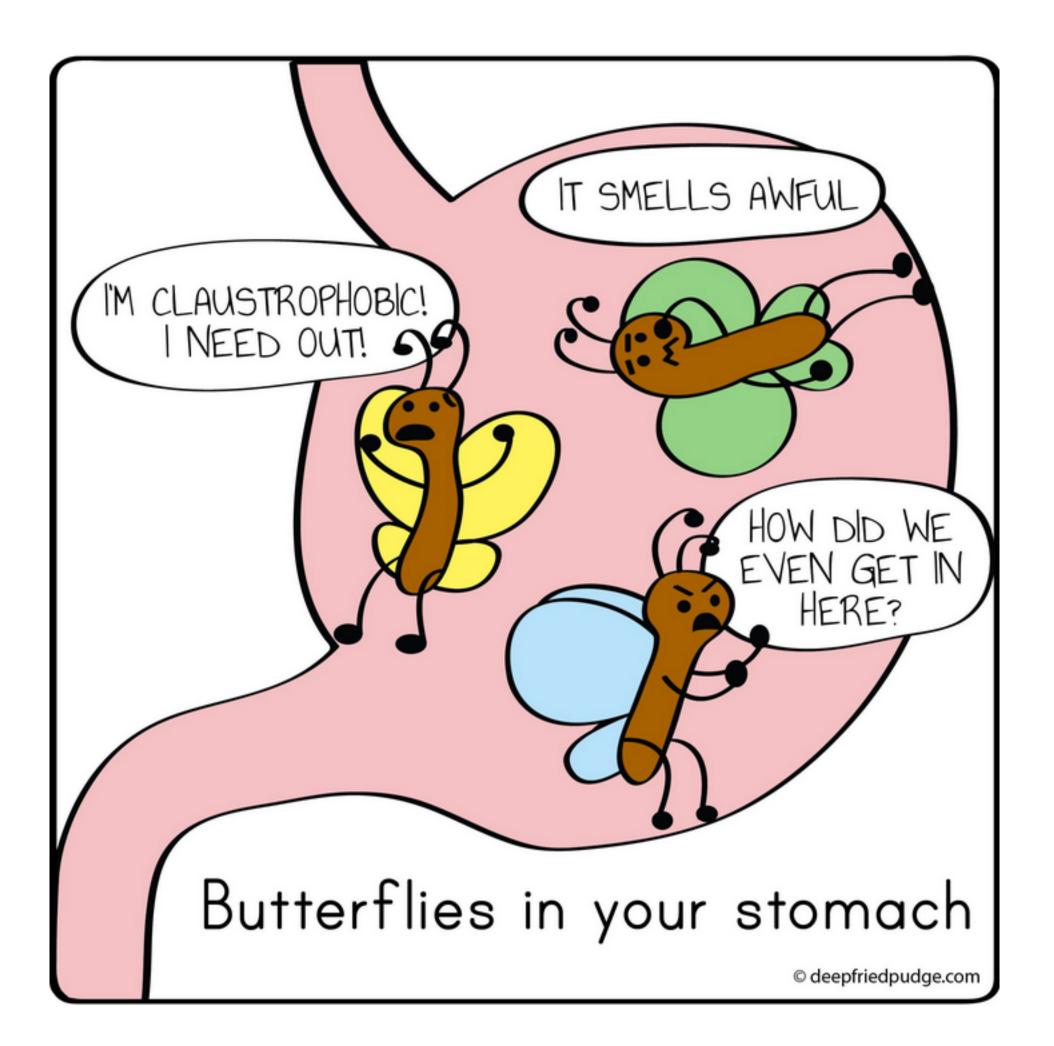








Enteric Nervous System ENS



The gut-brain connection is no joke; it can link anxiety to stomach problems and vice versa. Have you ever had a "gut-wrenching" experience? Do certain situations make you "feel nauseous"?

Have you ever felt "butterflies" in your stomach? We use these expressions for a reason. The gastrointestinal tract is sensitive to emotion. Anger, anxiety, sadness, elation — all of these feelings (and others) can trigger symptoms in the gut.





Enteric Nervous System ENS

When we think of our nervous system, we often think of the central nervous system (CNS): the brain, spinal cord and related neurons (nerve cells).

However, the gut contains as many neurons as the spinal cord!

20% of vagus nerve fibers send instructions from the brain to the stomach

These signals control:

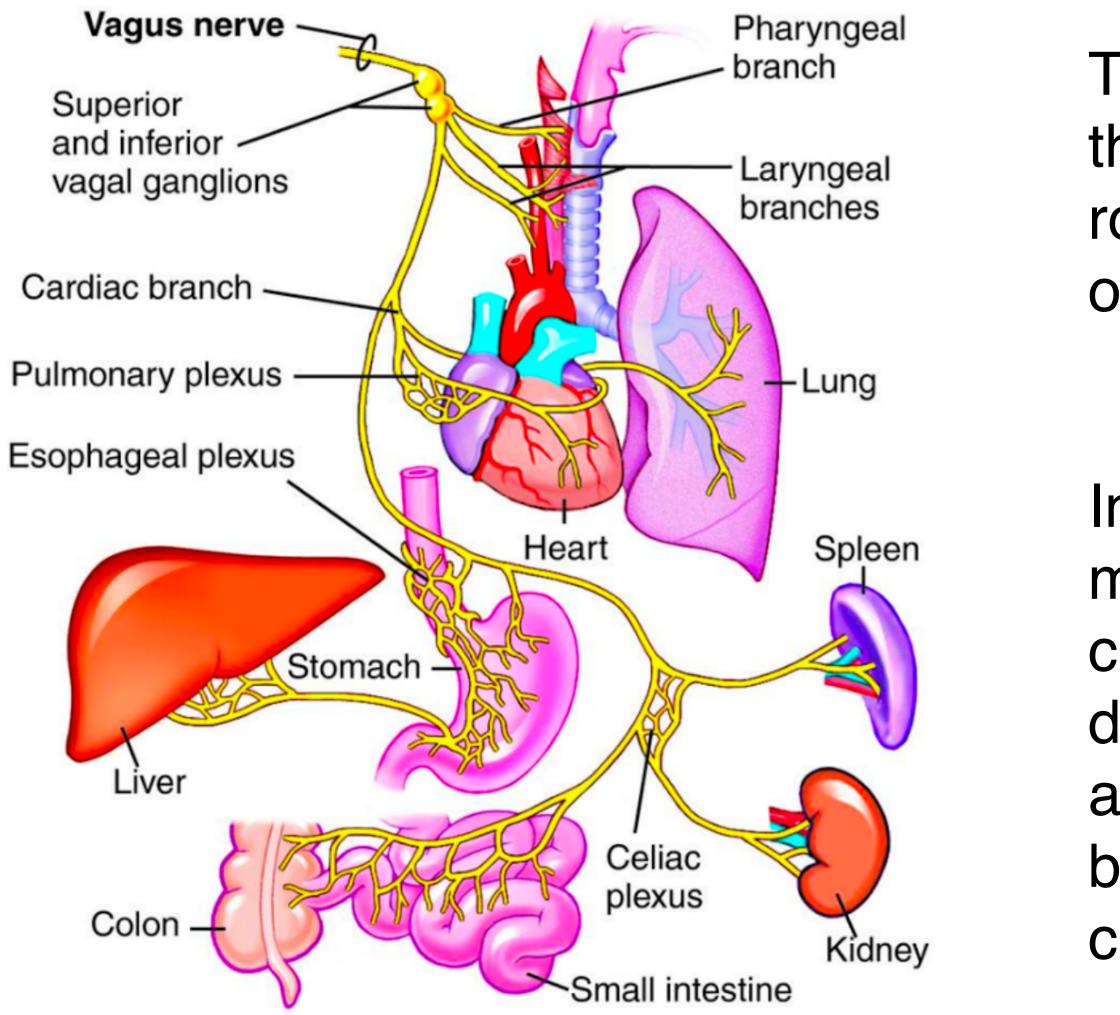
- Gastric acid secretion
- Digestive enzyme secretion
- Gastric capacity
- Blood glucose

80% of vagus nerve fibers send instructions from the stomach to the brain

These signals control: Satiety (Hunger) Satiation (Fullness) Energy Metabolism

More than 400 million neurons, present in the lining of the gut, are part of a network called the enteric nervous system (ENS), or your "gut brain" or "second brain," which is connected to the CNS via the vagus nerve. The vagus nerve connects the gut with the brain. TRULY HEAL .com





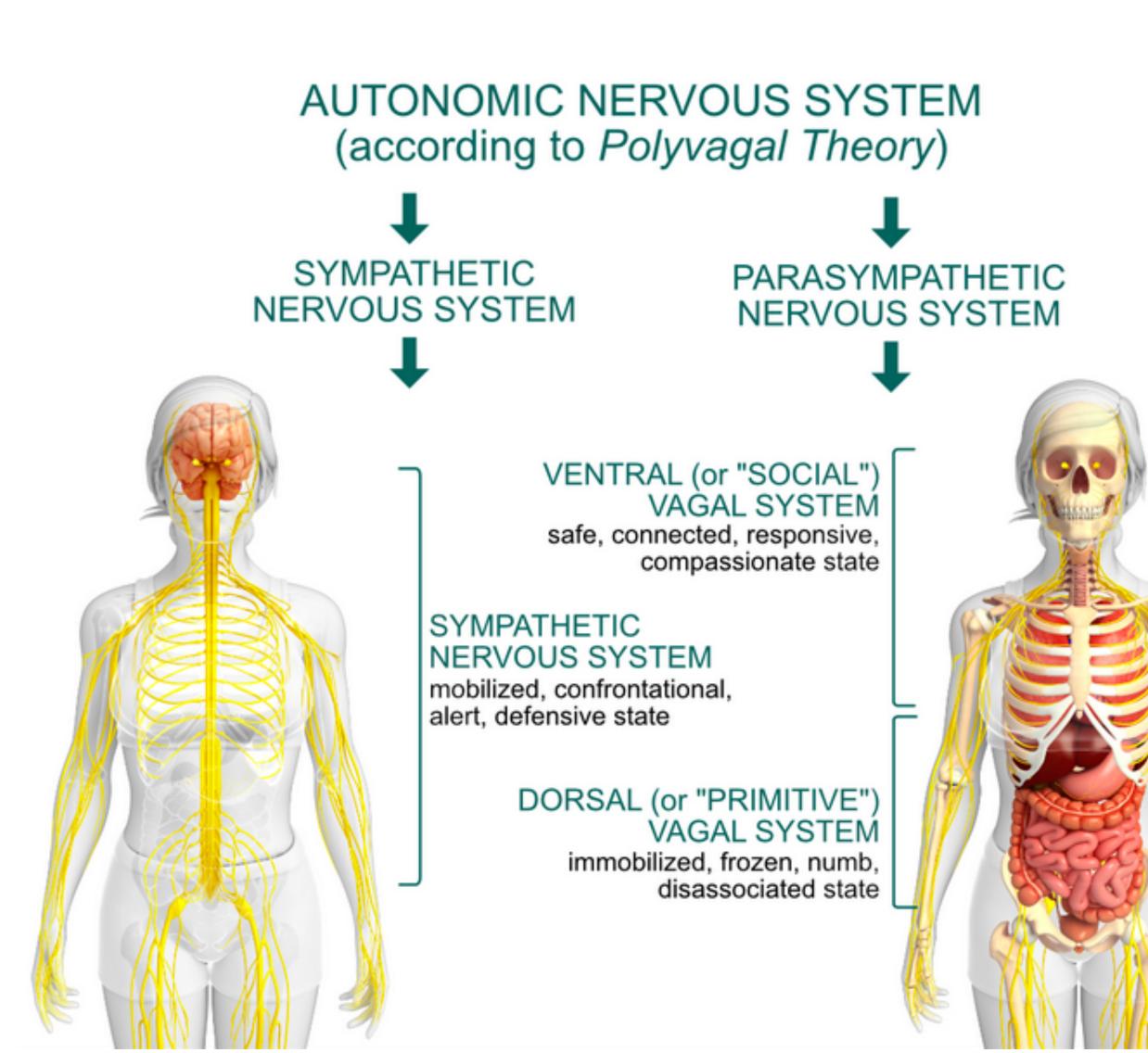
Vagus Nerve

The vagus nerve has a variety of functions throughout the body and plays an important role in stress response, for example slowing our heart rate and breathing.

In the gut, the vagus nerve serves to control muscle contraction (peristalsis), secretion of certain substances to aid in GI function and digestion of food, and blood flow to the gut. It also relays important messages from the gut brain to the brain via neurotransmitters, or chemical messengers.



Vagus Nerve



When we are in homeostasis the vagus nerve acts as a neutral break, keeping us calm and open, helping us be our most social selves.

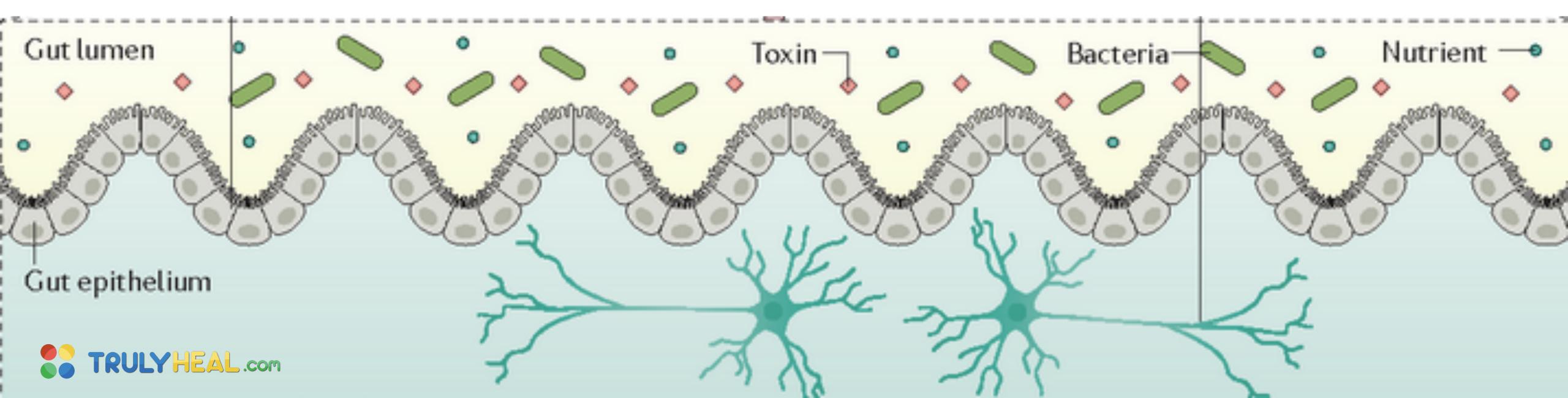
When the vagus nerve is activated and it enters its defence system, fight or flight responses can manifest themselves almost immediately.



Enteric Nervous System ENS

fungi and other microbes that live inside of our gut.

these microbial messages to our brain.



- The ENS gathers information from the microbiome, the divers array of bacteria,
- Gut microbes make neurotransmitters as they break down the food we eat, sending

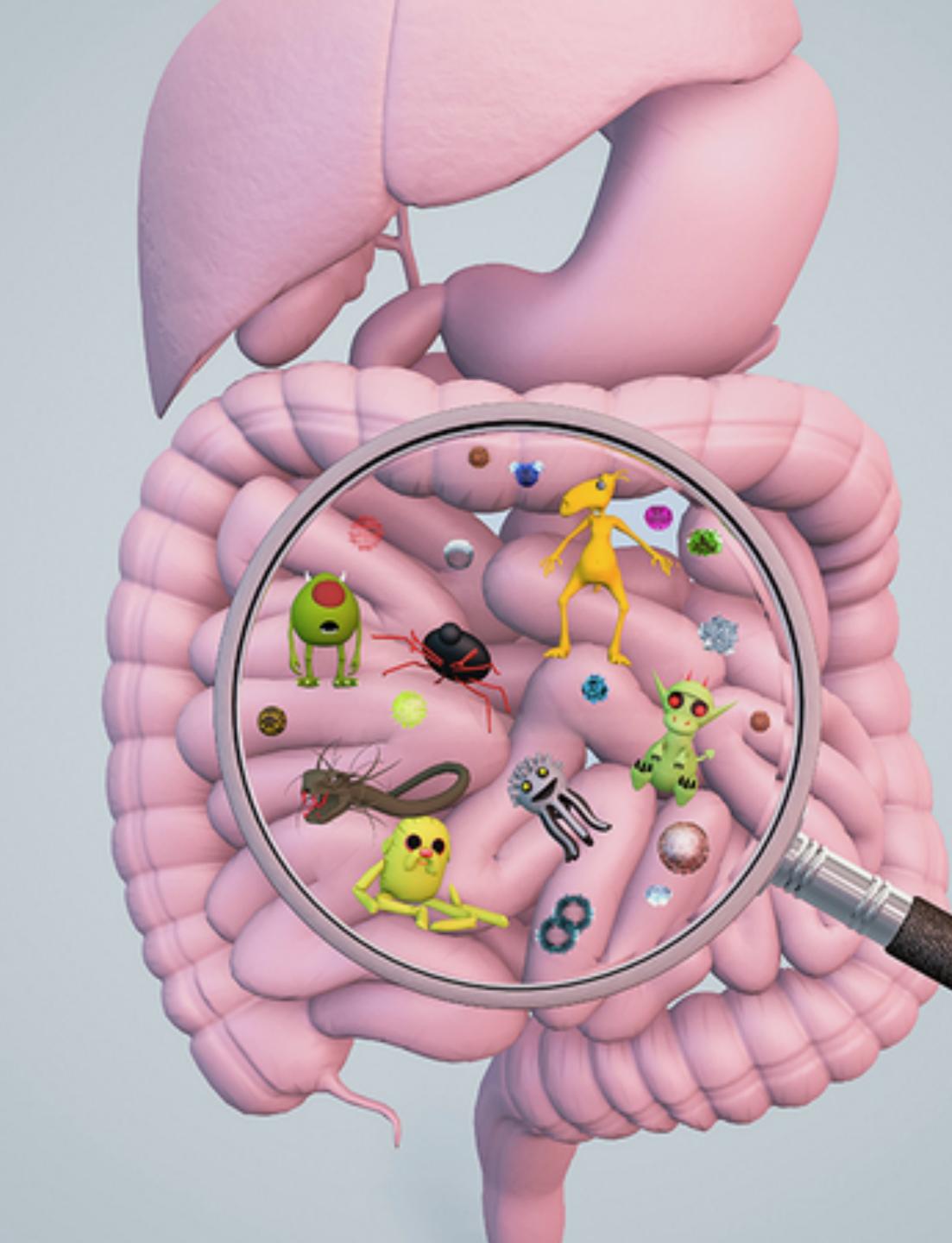
Gut Microbiota

The presence of certain types of gut bacteria can also positively or negatively affect the production of certain brain chemicals / neurotransmitters.

Dysbiosis is linked to a variety of brain-related disorders, including depression, anxiety, Parkinson's disease, autism and more.





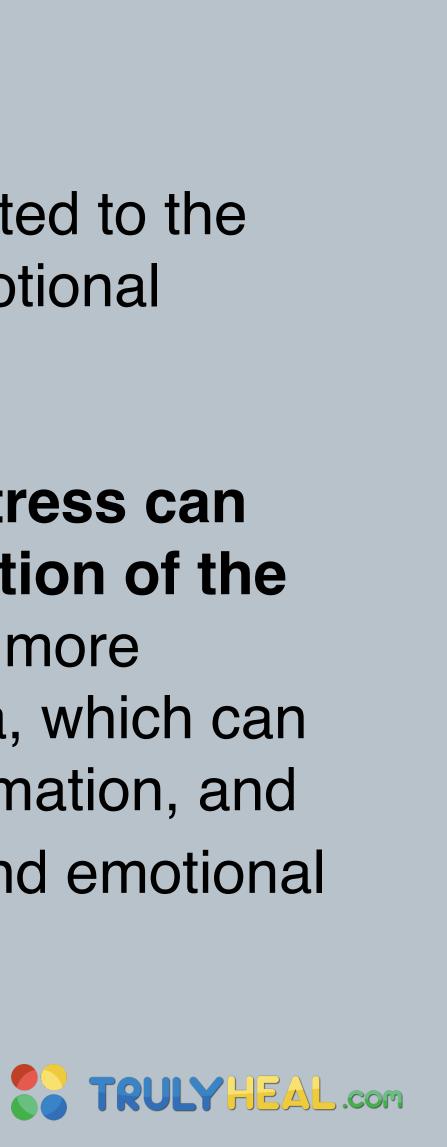


Gut Microbiota

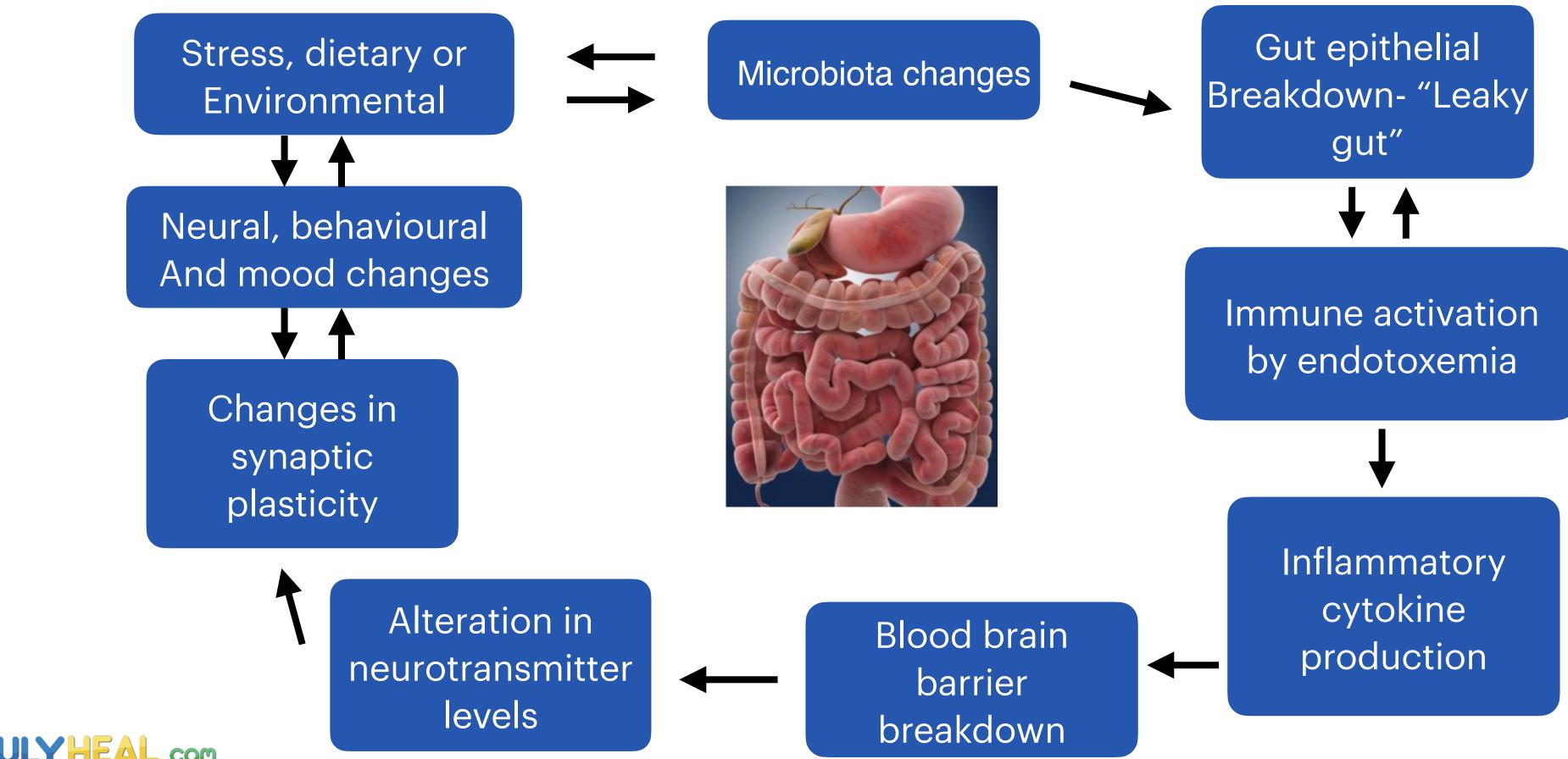
The role of our gut bacteria is increasingly important as related to the brain and our mental and emotional health.

For example, we know that stress can alter the microbial composition of the gut, making it less diverse or more vulnerable to harmful bacteria, which can then lead to increased inflammation, and

myriad physical and emotional symptoms.



The "GUT" Feeling How our GI tract can influence the CNS



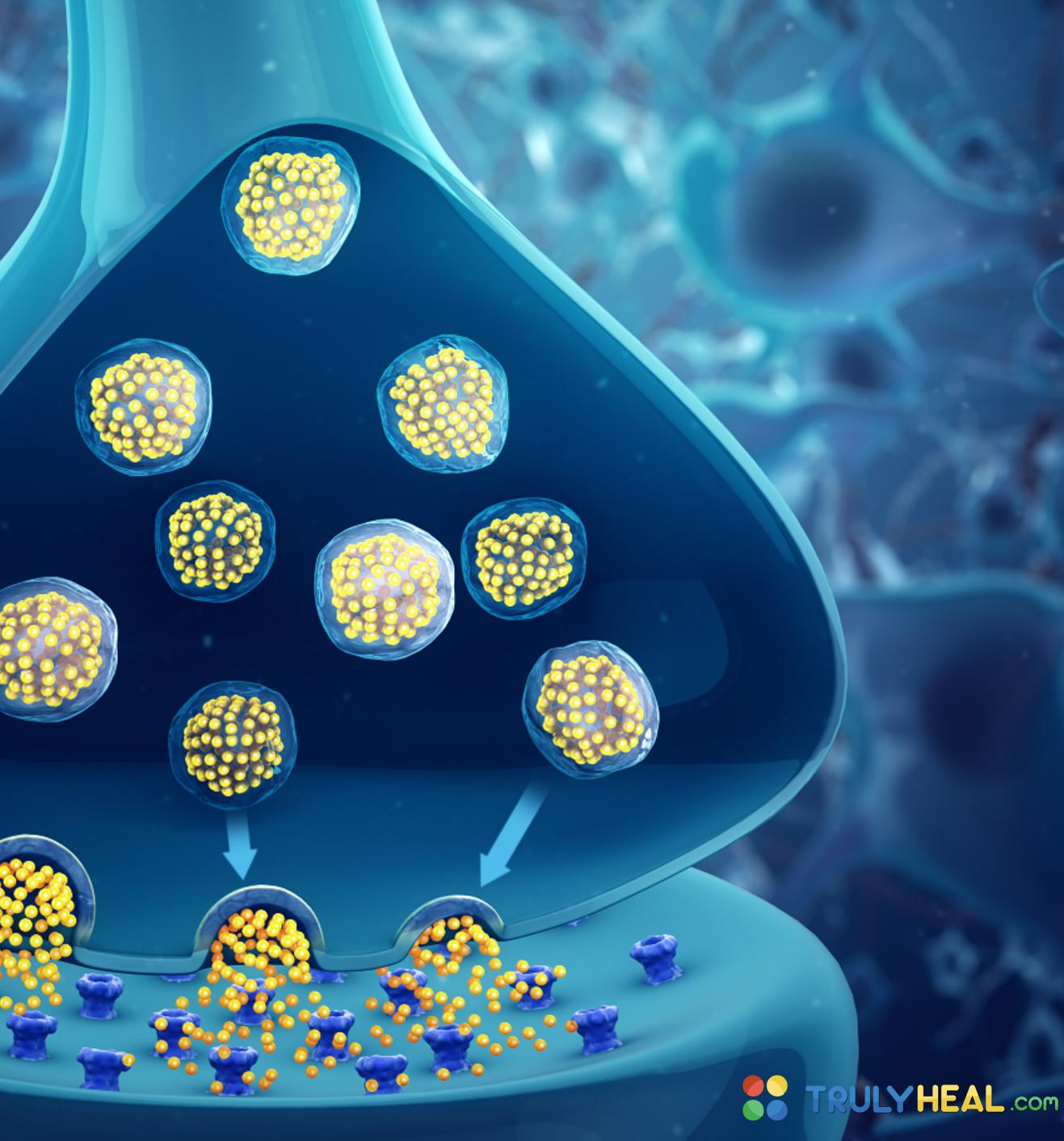


Neurotransmitter

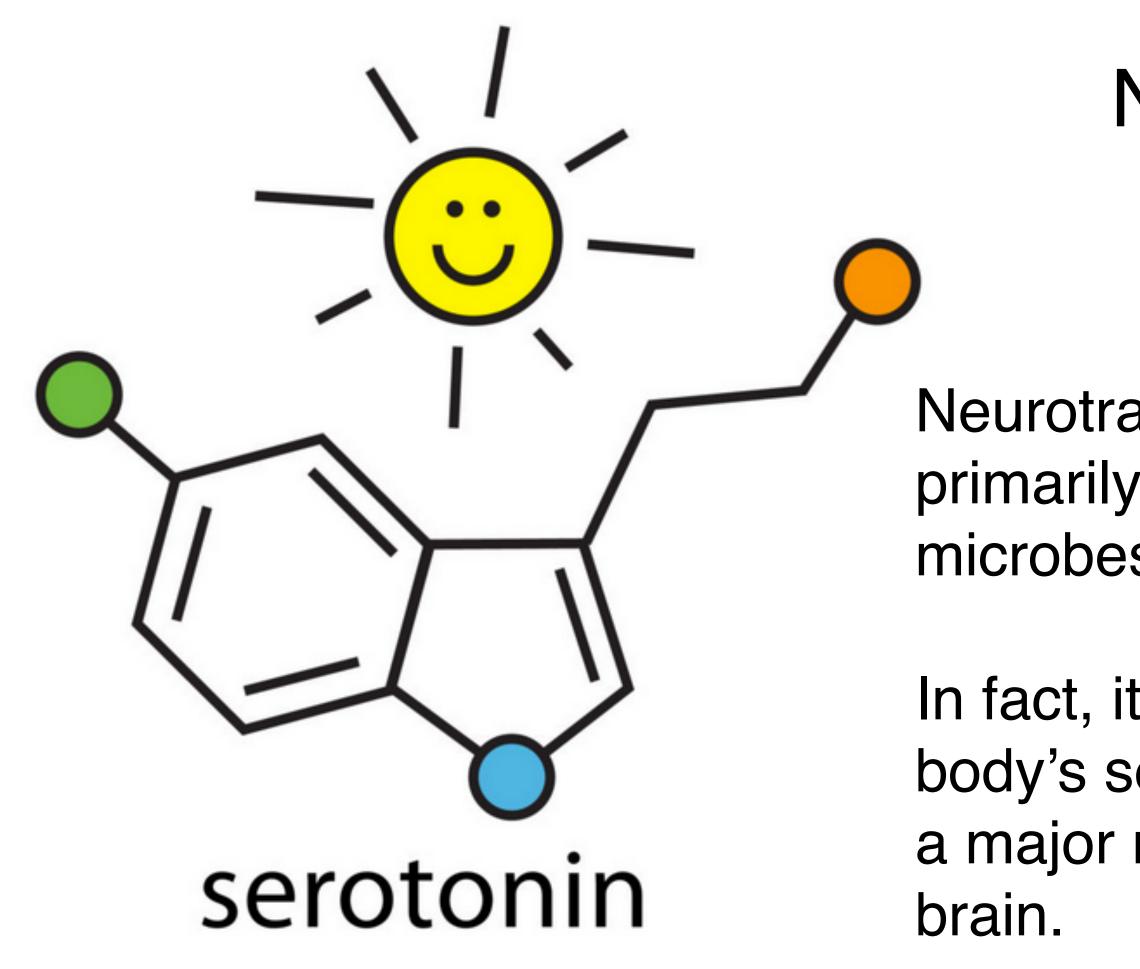
Basically are: Chemical Messengers that tell the body what to do and how to feel.

The most important neurotransmitter are:

- Serotonin
- Dopamine
- Norepinephrine
- Acetylcholine
- GABA









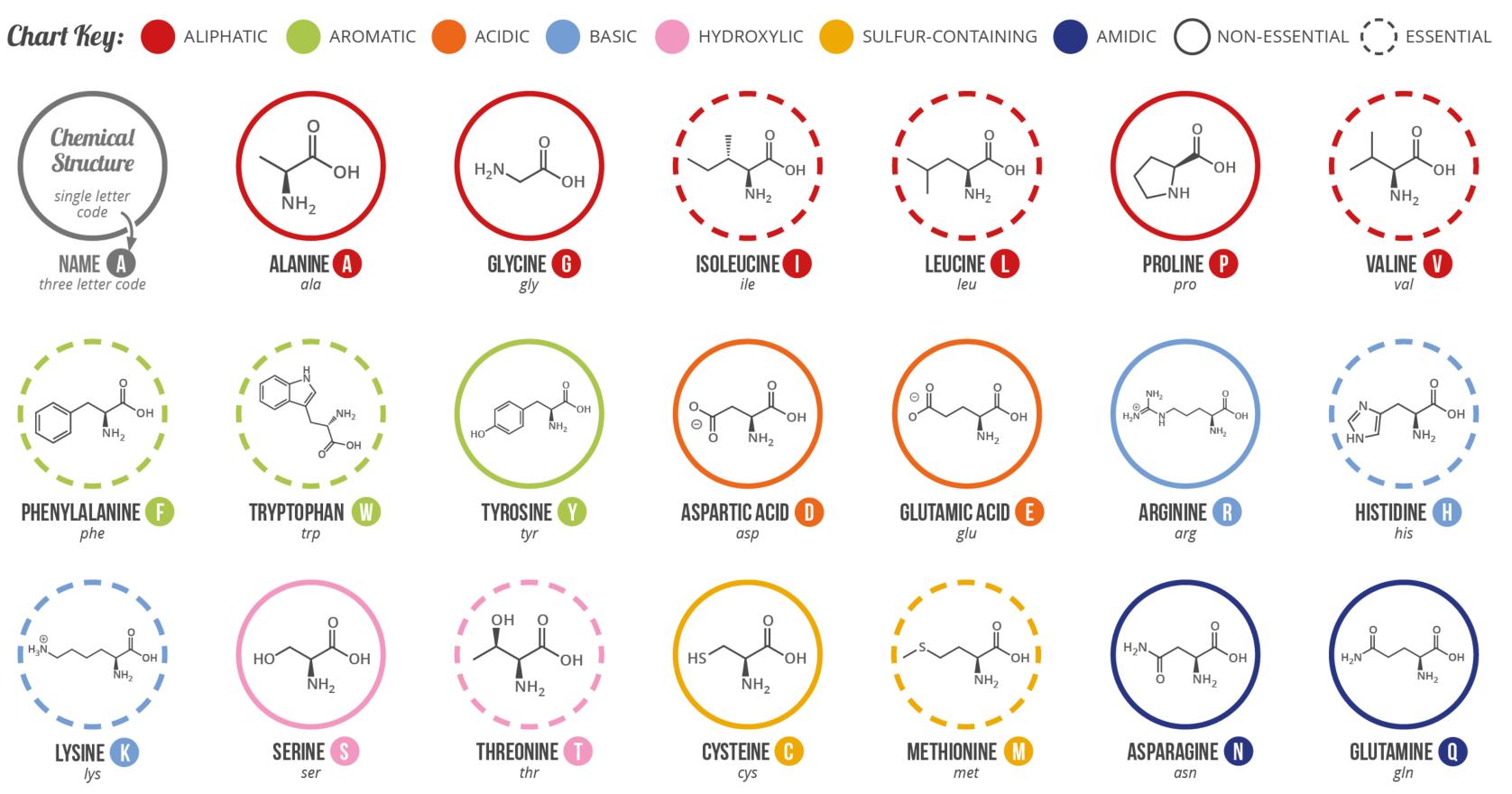
Neurotransmitter

Neurotransmitters, such as serotonin, are produced primarily in the gut with the help of the trillions of microbes that reside there.

In fact, it is estimated that more than 90% of the body's serotonin is produced in the gut, where it plays a major role in communication between the gut and

A GUIDE TO THE TWENTY COMMON AMINO ACIDS

AMINO ACIDS ARE THE BUILDING BLOCKS OF PROTEINS IN LIVING ORGANISMS. THERE ARE OVER 500 AMINO ACIDS FOUND IN NATURE - HOWEVER, THE HUMAN GENETIC CODE ONLY DIRECTLY ENCODES 20. 'ESSENTIAL' AMINO ACIDS MUST BE OBTAINED FROM THE DIET, WHILST NON-ESSENTIAL AMINO ACIDS IESISED IN THE BODY.



Note: This chart only shows those amino acids for which the human genetic code directly codes for. Selenocysteine is often referred to as the 21st amino acid, but is encoded in a special manner. In some cases, distinguishing between asparagine/aspartic acid and glutamine/glutamic acid is difficult. In these cases, the codes asx (B) and glx (Z) are respectively used.

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Amino Acids are the building blocks of proteins.

Amino acids are the building blocks of Neurotransmitters.

Essential Amino acids must be obtained from our diet.

Non-Essential Amino acids can be synthesised in the body.







Amino Acid Synthesis

Essential Amino Acids :

amino acids that cannot be synthesized by the organism at a rate sufficient to meet the normal requirements of growth, reproduction, and normal maintenance and therefore must be supplied by the diet

Non-Essential Amino Acids : amino acids that can be made from simpler precursors and are thus not required in the diet

Essential Amino Acids Arginine Histidine Isoleucine Leucine Lysine Methionine Phenylalanine Threonine Threonine Tryptophan Valine Non Essential Amino Acids Alanine Asparagine Aspartate Cysteine Glutamate Glutamine Glycine Proline Serine Tyrosine



Willmore 2003

Function of Essential amino acid:

These amino acids all have important functions in the body.

epinephrine and dopamine, which are important in the brain.

Similarly, the amino acid **tryptophan** is used to form serotonin in the brain.

tissue.

Connective tissue fibers are formed using the acid **threonine**.

immune system along with the amino acid lysine.

- **Phenylalanine**, for example, is needed to make various neurotransmitters such as
- Valine and leucine are both important in forming muscle and repairing muscle
- **Histidine** is the precursor molecule for histamine and functions as part of the



Serotonin (5HT) - feel good neurotransmitter

- Function
- Mood
- Bowel movements
- Nausea/Diarrhoea
- Blood clotting

- Deficiency signs
- Depression
- Anxiety
- Aggression
- Sugar cravings
- Constipation
- Obsessive thought
- Compulsive behaviours
- Suicide / aggression

 Production – Tryptophan (Essential Amino Acid)





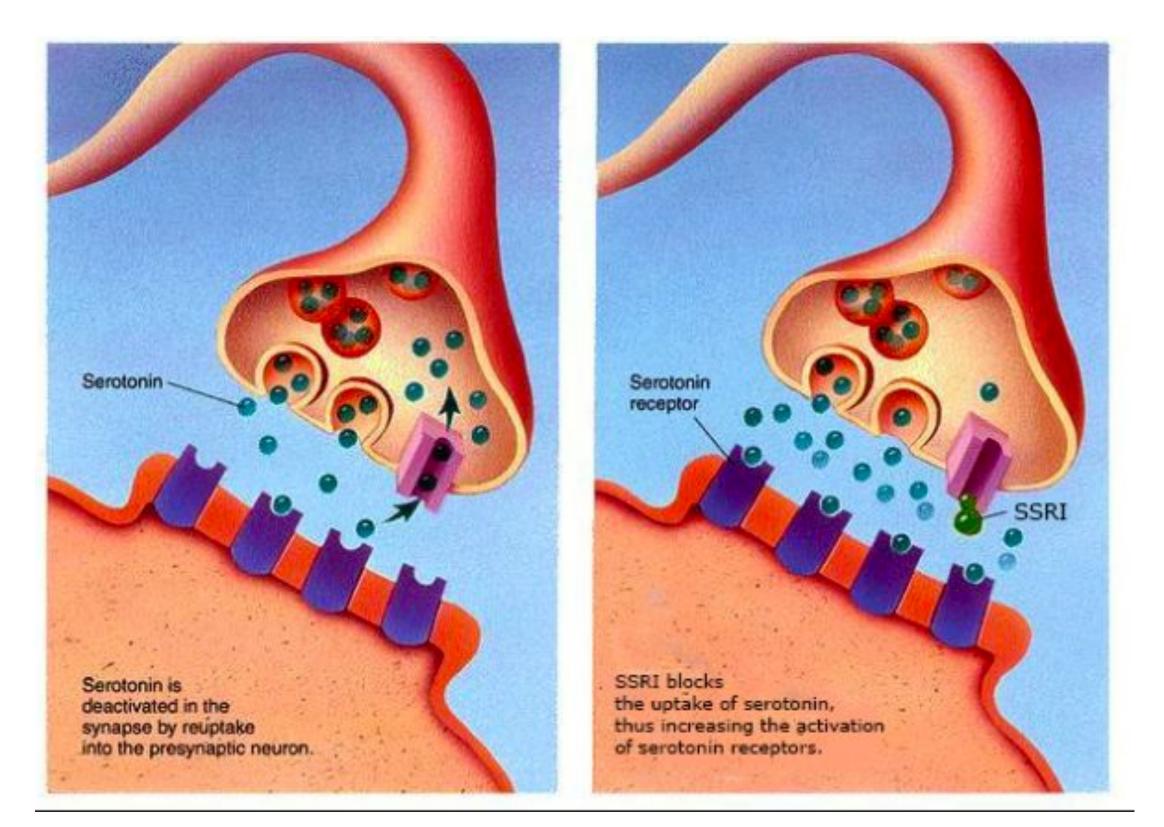
Serotonin (5HT) important facts:

Serotonin is the precursor to the sleep hormone melatonin. Individuals who struggle with insomnia but see improvement when they take melatonin are most likely deficient in serotonin.

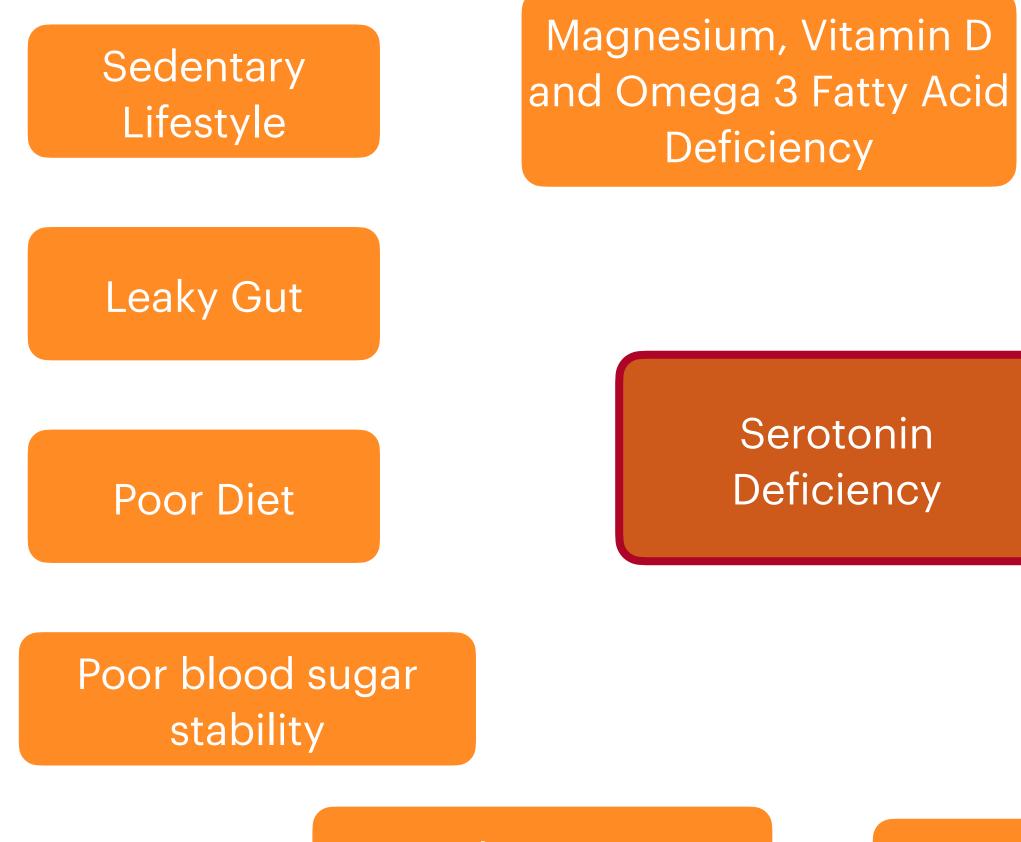
Anti-depressants are selective serotonin reuptake inhibitors which act to increase serotonin activity in the brain.

This NEVER gets to the cause of the low serotonin. SSRI's as a long-term health strategy have tremendous side effects and can be addictive and hard to wean off of.





Most Common Causes of Serotonin Deficiency



Inadequate or ineffective Sleep

Chronic Mental / **Emotional Stress** Vitamin B1, B2, B6 and Folate Deficiency Tryptophan Deficiency

> Drugs Antibiotics / Proton Pump Inhibitor /NSAIDs

> > TRULY HEAL.com

Dysbiosis



Drugs disturbing the gut microbiome

-ANTIBIOTICS: On average, 1 course of antibiotics disturbs the microbiota for 16 months.

-PROTON PUMP INHIBITORS: PPIs such as Prilosec and Nexium decrease populations of small bowel bifidobacteria within 7 days of commencing therapy.

NSAIDs like Aspirin and Ibuprofen reduce populations of beneficial flora including bifidobacteria and lactobacilli.







Serotonin (5HT) produced by gut bacteria

Escherichia coli (K-12) Hafnia alvei (NCIMB, 11999) Klebsiella pneumoniae (NCIMB, 673) Lactobacillus plantarum (FI8595) Lactococcus lactis subsp. cremoris (MG 1363) Morganella morganii (NCIMB, 10466) Streptococcus thermophilus (NCFB2392)



<u>Shishov VA, 2009</u> <u>Özoğul, 2004</u> <u>Özoğul, 2004</u> <u>Özoğul, 2012</u> <u>Özoğul, 2012</u> <u>Özoğul, 2004</u>



Serotonin Foods Tryptophan/100g

Nuts and Seeds

Pumpkin seeds 576mg Chia Seeds 437mg Sesame Seeds 388mg Sunflower Seeds 348mg Flaxseeds 297mg Cashew Nuts 287mg Pistachio Nuts 251mg Almonds 211mg Hazelnuts 55mg

Animal Products

Eggs 167mg



Chicken 507mg Beef 374mg Pork 376mg Crab 330mg Lamb 329mg Turkey 287mg Salmon 285mg

Beans

Edamane 242mg Tofu 235mg White beans 115mg Pinto beans 108mg Black beans 105mg Kidney beans 104mg Chickpeas 85mg



What can we do to boost Serotonin:

- Anti-inflammatory diet with adequate proteins
- Foods high in Tryptophan
- Improve Microbiome
- Regular Exercise
- Reduce Stress
- Regular sun exposure (sunlight stimulates serotonin production)

Supplementation:

- 5-HTP (It is easy for the body to convert 5-HTP into serotonin.)
- Omega 3 fatty acid
- Rhodiola (This adaptogenic herb acts as a monoamine oxidase inhibitor in that it blocks the enzymes in the body that break down serotonin.) 100-200mg up to twice a day
- L-Theanine (provides relaxation)
- B-complex
- Magnesium (modulates stress hormone levels)







Dopamine

- Function
- Reward and motivation
- Cognition, memory, learning
- Voluntary movement
- Precursor of Norepinephrine

- Production
- Phenylalanine (Essential
- Amino Acid)
- Tyrosine
- Non-Essential Amino Acid)

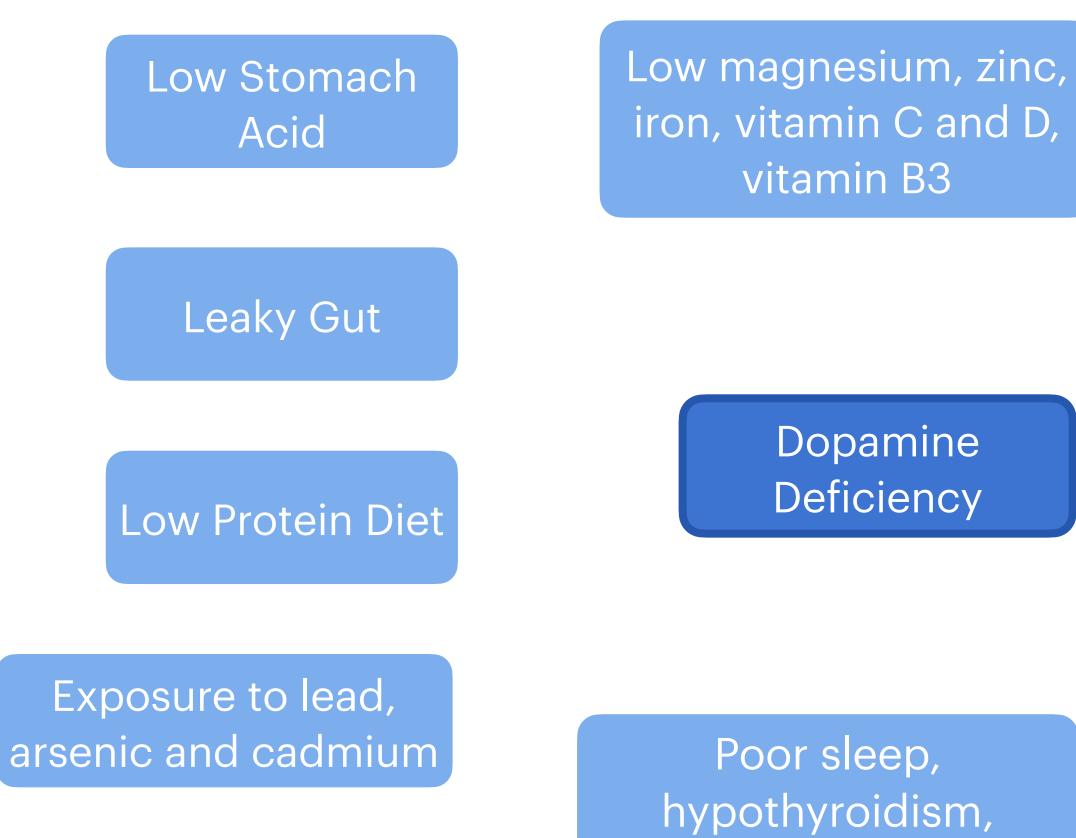


Deficiency signs
Addictive tendencies
Lacking motivation
Forgetfulness
Low libido
Slow reaction time
'Pleasure centre' dysfunction
Restless Leg syndrome

Co-factors
Iron
Active form of Vitamin B6
(Pyridoxal-5-phospahte)



Most Common Causes of Dopamine Deficiency



Dysbiosis

Chronic Stress Adrenal Fatigue

B6 Deficiency

Tyrosine and/or Phenylanaline Deficiency

hypoglycaemia (Increase dopamine

turnover)

Drugs Antibiotics / Proton Pump Inhibitor /NSAIDs





Dopamine produced by gut bacteria

	Bacillus cereus
	Bacillus mycoides
	Bacillus subtilis
	Escherichia coli
	Escherichia coli (K-12)
Dopamine	Hafnia alvei (NCIMB, 1
	Klebsiella pneumoniae
	Morganella morganii (N
	Proteus vulgaris
	Serratia marcescens
	Staphylococcus aureus



11999)

(NCIMB, 673)

NCIMB, 10466)

Tsavkelova et al., 2000 Tsavkelova et al., 2000 Tsavkelova et al., 2000 Tsavkelova et al., 2000 Shishov VA, 2009 Özoğul, 2004 <u>Özoğul, 2004</u> <u>Özoğul, 2004</u> Tsavkelova et al., 2000 Tsavkelova et al., 2000 Tsavkelova et al., 2000

Dopamine Foods

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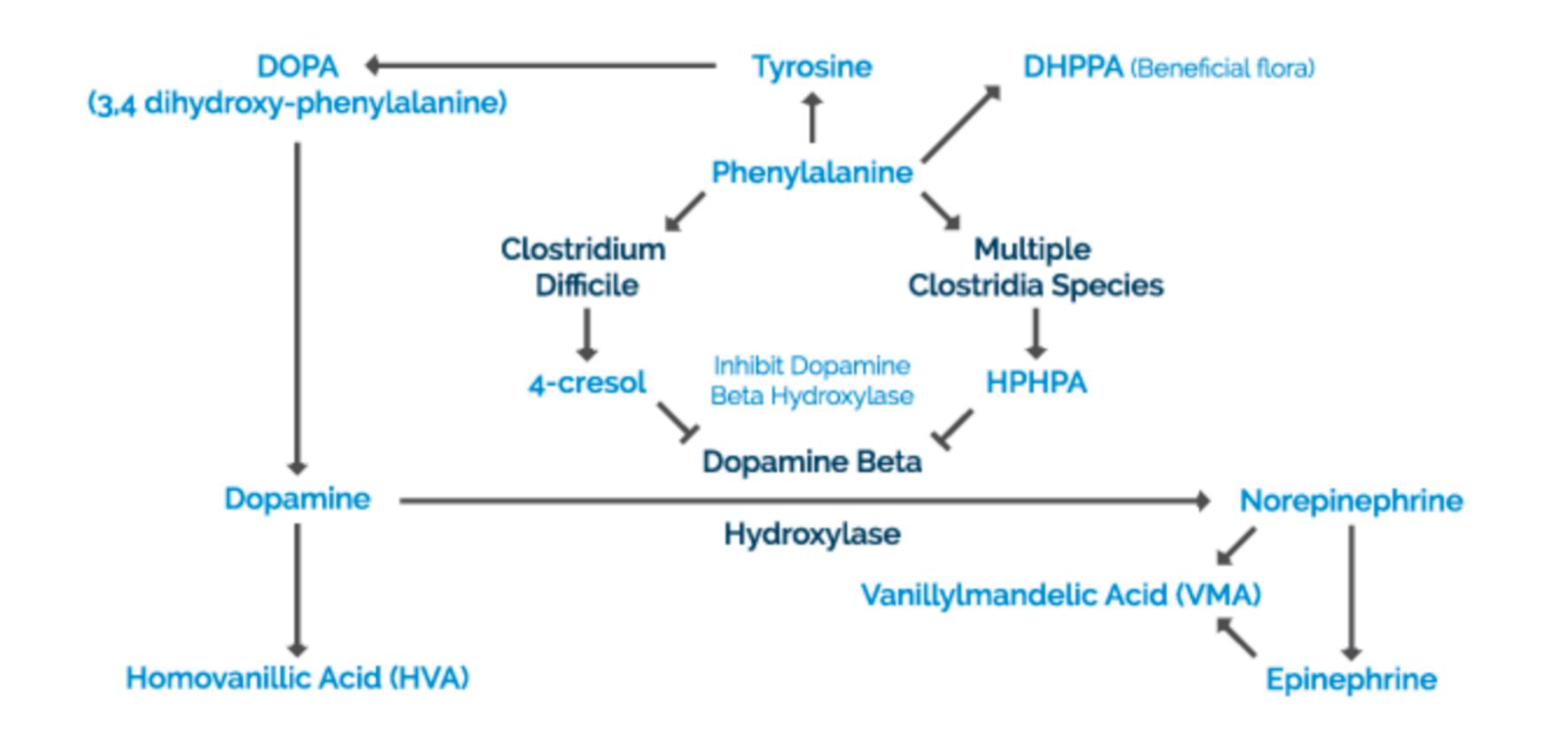
Phenylalinine mg/100g

- Soy Beans 2066mg
- Parmesan 1922mg
- Pumpkin seeds 1733mg
- Watermelon seeds 2031mg
- Beef 1464mg
- Chicken 1294mg
- Pork 1288mg
- Tuna 1101mg
- Eggs 680mg
- Pinto Beans 531mg
- White beans 526mg
- Kidney beans 511mg
- Lentils 445mg
- Cashews 270mg
- Almonds 319mg

Tyrosine mg/100g

- Parmesan 1995mg
- Soy Beans 1497mg
- Beef 1386mg
- Salmon 1157mg
- Chicken 1155mg
- Pumpkin seeds 1093mg
- Peanuts 963mg
- Sesame seed 743mg
- Oats 573mg
- Chia seeds 563mg
- Eggs 499mg
- Wild rice 277mg
- White beans 274mg
- Split peas 242mg
- Lentils 241mg
- Adzuki Beans 224mg

Dopamine produces Norepinephrine





What can we do to boost Dopamine:

- Anti-inflammatory diet with adequate proteins
- Foods high in Phenylalanine and Tyrosine
- Better sleep
- Improve Microbiome
- Regular Exercise
- Reduce Stress
- Reduction of toxins

Supplementation:

- L-Tyrosine (500-2500mg/ day)
- DL-Phenylalanine (1-2 grams/day)
- Vitamin B6 (50-100mg/day)
- Rhodiola (adaptogenic herb) 100-200mg up to twice a day
- Cordyceps (adaptogenic) 400-800mg up to twice a day

Rhodiola and cordyceps have the strongest effect on modulating dopa levels. Some other great adaptogens include ashwagandha, ginseng, holy basil and reishi mushroom among others.







GABA (Gamma-AminoButyric Acid)

Function
 Relieving anxiety
 Relieving pain
 Stabilising blood pressure
 Supporting sleep
 Decreasing blood sugar level
 Muscle stiffness

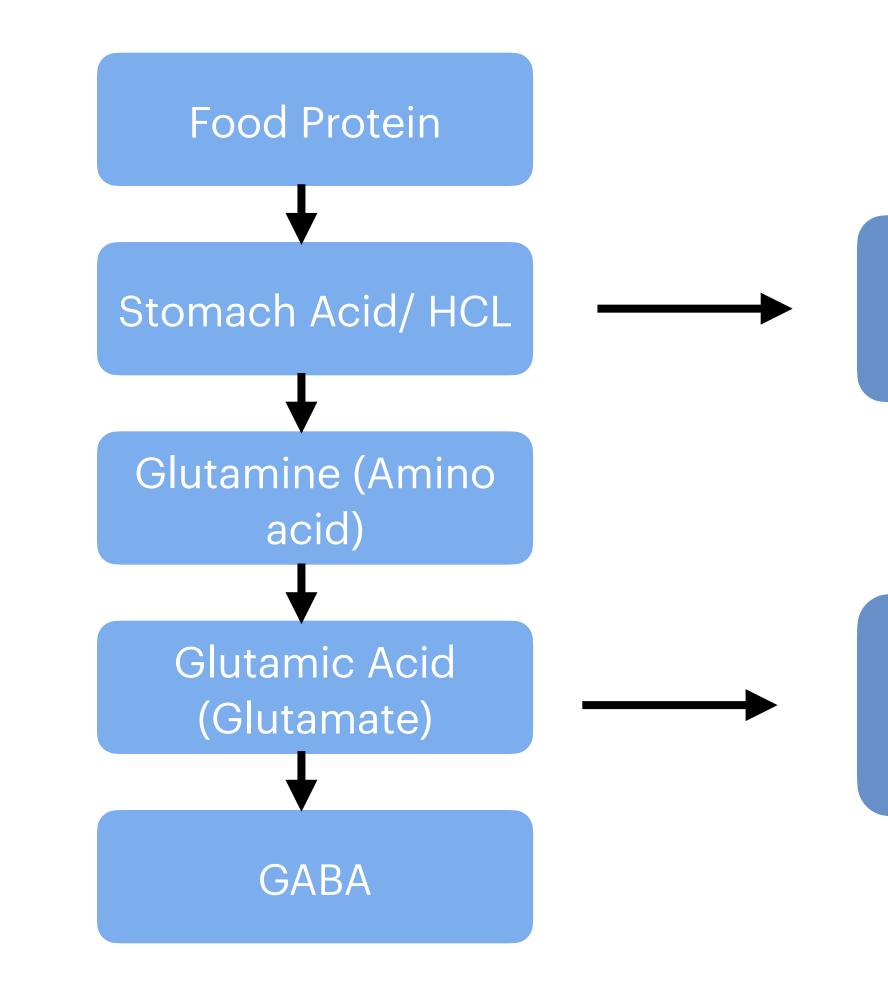
Production

Glutamine (Non Essential Amino Acid)
 Our gut microbiome plays an important role
 with GABA production and helps to convert
 glutamine and glutamic acid into GABA





The GABA Pathway

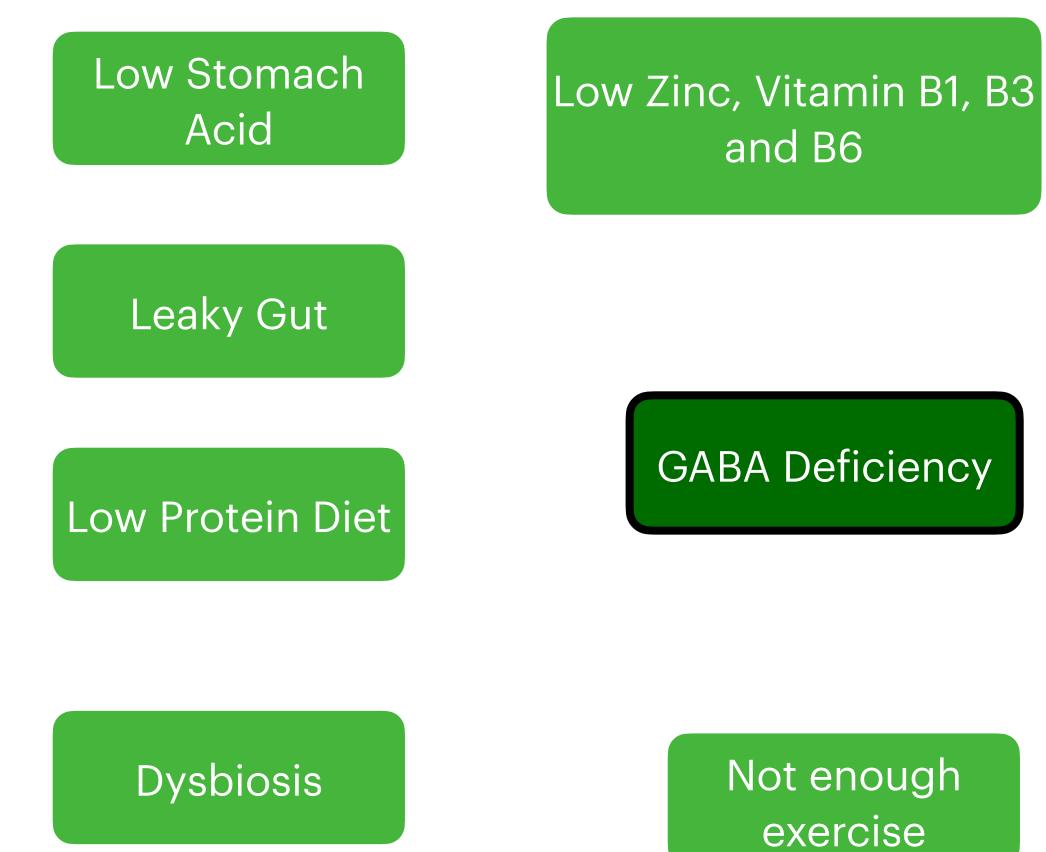


Zinc, Vitamin B1, B3 and B6 are needed to make stomach acid

Glutamate Decarboxylase converts Glutamic Acid to GABA and needs Vitamin B6 and Taurine.



Most Common Causes of GABA Deficiency



Chronic Stress Adrenal Fatigue

B6 Deficiency

Glutamine Deficiency

Drugs Antibiotics / Proton Pump Inhibitor /NSAIDs





Drugs disturbing the gut microbiome

-ANTIBIOTICS

-PROTON PUMP INHIBITORS: PPIs such as Prilosec and Nexium decrease populations of small bowel bifidobacteria within 7 days of commencing therapy.

Bifidobacteria is important for production of our chief inhibitory neurotransmitter, GABA, as well as for production of the short chain fatty acid (SCFA) butyrate, the main fuel for enterocytes which heals and seals the gastrointestinal lining, reinforcing gut barrier integrity.

-NON-STEROIDAL ANTI-INFLAMMATORY DRUGS: **NSAIDs** I







GABA produced by gut bacteria

Bifidobacterium adolescentis Bifidobacterium angulatum (A Bifidobacterium dentium (DP Bifidobacterium infantis (UCC Lactobacillus brevis (DPC610 Lactobacillus buchneri (MS) Lactobacillus paracaseiNFRI Lactobacillus plantarum (ATC Lactobacillus reuteri (100-23) Lactobacillus rhamnosus (YS) Lactobacillus. delbrueckiisubs Monascus purpureus (CCRC Streptococcus salivarius subsp

GABA



s (DPC6044)	Barrett et al., 2012
(ATCC27535)	Pokusaeva et al., 2017
PC6333)	Barrett et al., 2012
CC35624)	Barrett et al., 2012
08)	Barrett et al., 2012
	Cho et al., 2007
I (7415)	Komatsuzaki et al., 2005
CC14917)	Siragusa et al., 2007
3)	Pokusaeva et al., 2017
59)	Siragusa et al., 2007
osp. bulgaricus (PR1)	Siragusa et al., 2007
31615)	Su et al., 2003
sp. thermophilus (Y2)	Yang et al., 2008



Milk

Being rich in glutamine, milk promotes production of glutathione, an antioxidant that combats oxidative stress

Eggs

Loaded with glutamine, eggs strengthens the immune system and keeps diseases at bay

Nuts

Immense amounts of glutamine and healthy fats in nuts optimize cardiac health and lowers the risk of heart disease

Glutamine Foods

Beans

Excellent source of glutamine, beans heal wounds and speed up the recovery process after an injury

Red Cabbage

Bestowed with glutamine and vitamin C, red cabbage enhances eye health and fortifies bones





What can we do to boost GABA:

- Anti-inflammatory diet with adequate proteins
- Foods high in Glutamine
- Better sleep
- Improve Microbiome
- Regular Exercise
- Reduce Stress
- Taking Epsom salt bath

Supplementation:

- Magnesium (Magnesium L-threonate 1-2g / daily)
- Vitamin B complex
- GABA (100-200mg 1-2 daily)
- L-Glutamine 4-5 g up to 10-20g / daily
- Taurine (helps ton activate GABA receptors)
- without inducing drowsiness.)



- Probiotics (a variety of lactobacillus and Bifidobacterium strains help to raise up GABA levels.)

– L-Theanine (L-theanine improves GABA production and induces a state of relaxation of the mind



Testing of Neurotransmitter



Organic Acid Test (in urine):

– Dopamine: The metabolite homovanillic acid (HVA) is a breakdown product of dopamine metabolism. When HVA levels are very low it is an underproduction of dopa, typically due to adrenal fatigue and/or a deficiency in L-phenylalanine, L-tyrosine and/or vitamin B6.

– GABA: Biomarker B6 pyrodixic. Low levels can indicate that their isn't enough B6 to successfully convert glutamate to GABA. We may also see very high or very low levels of homovanillic (HVA), which is a dopamine biomarker and vanillymandelic (VMA), a biomarker of adrenaline.

– Serotonin: Biomarker called 5-HIAA (5-Hydroxyindoleacetic Acid). This is the metabolite of the neurotransmitter serotonin. High levels can result with serotonin supplements (5-HTP) and low levels can indicate a need for more serotonin production.

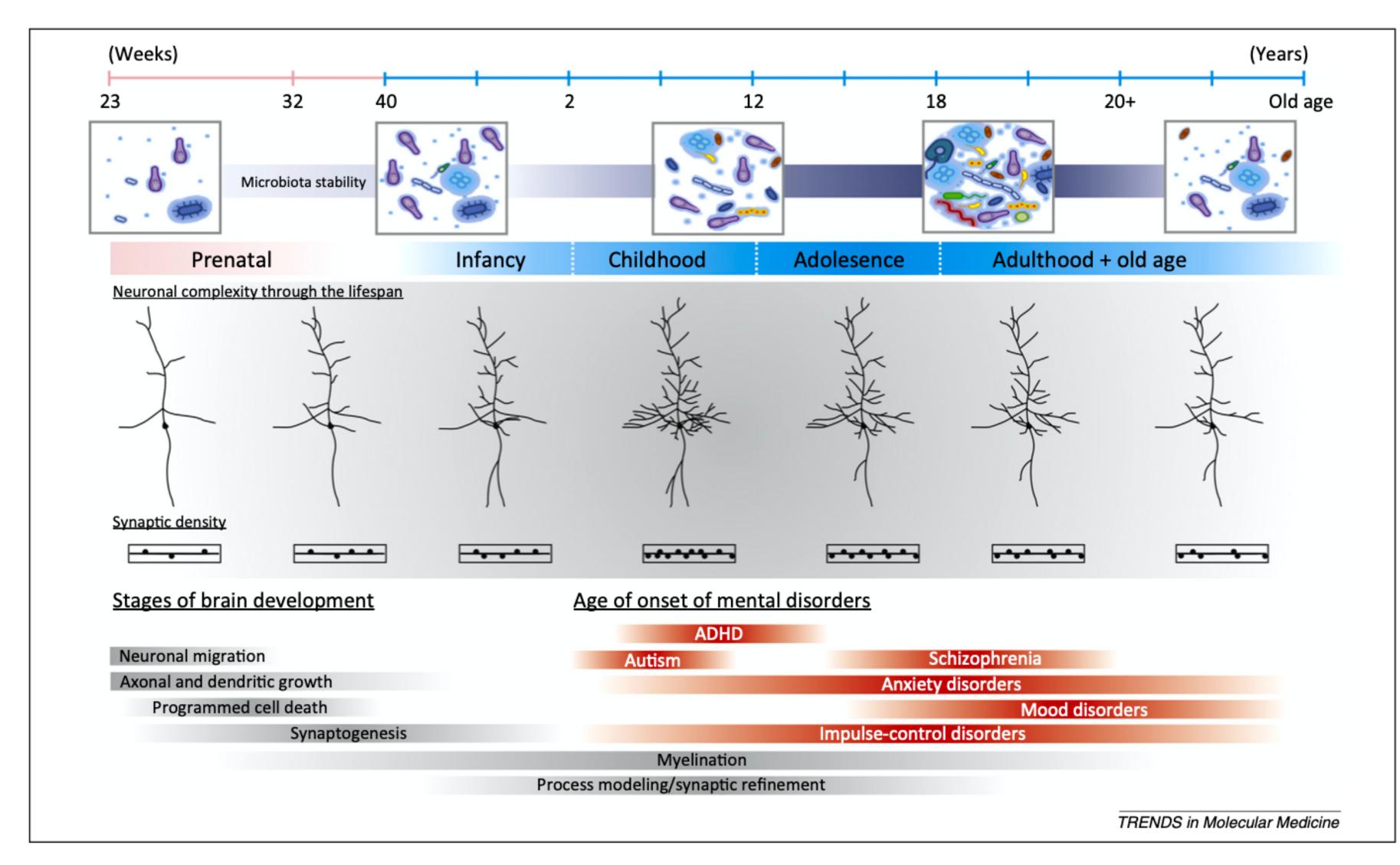


Tying it all back together

- Poor digestion causes food broken down incompletely
- Poor diet causes nutritional deficiencies
- Leaky Gut causes inflammation (brain) deficiencies
- Deficiencies in diet and due to GIT problems causes amino acid deficiencies neurotransmitter deficiencies
- Dysbiotic microorganism deficiencies in neurotransmitter can create toxins that affect brain function
- Stress causes activation of vagus nerve Dysbiosis activation of ENS......



Tying it all back together

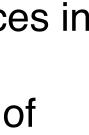


This diagram shows the neurodevelopmental sequences in relation to the age of onset of mental disorders and degree of microbiota stability/diversity throughout life.

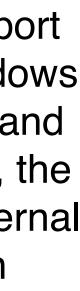
Gut microbiota is essential to human health and is a key player in the bidirectional communication between the gastrointestinal tract and the central nervous system.

The microbiota dynamically changes throughout lifespan, establishing its symbiotic rapport with the host with critical windows during infancy, adolescence, and aging. During these windows, the organism is vulnerable to external stressors, which may result in mental disorders.

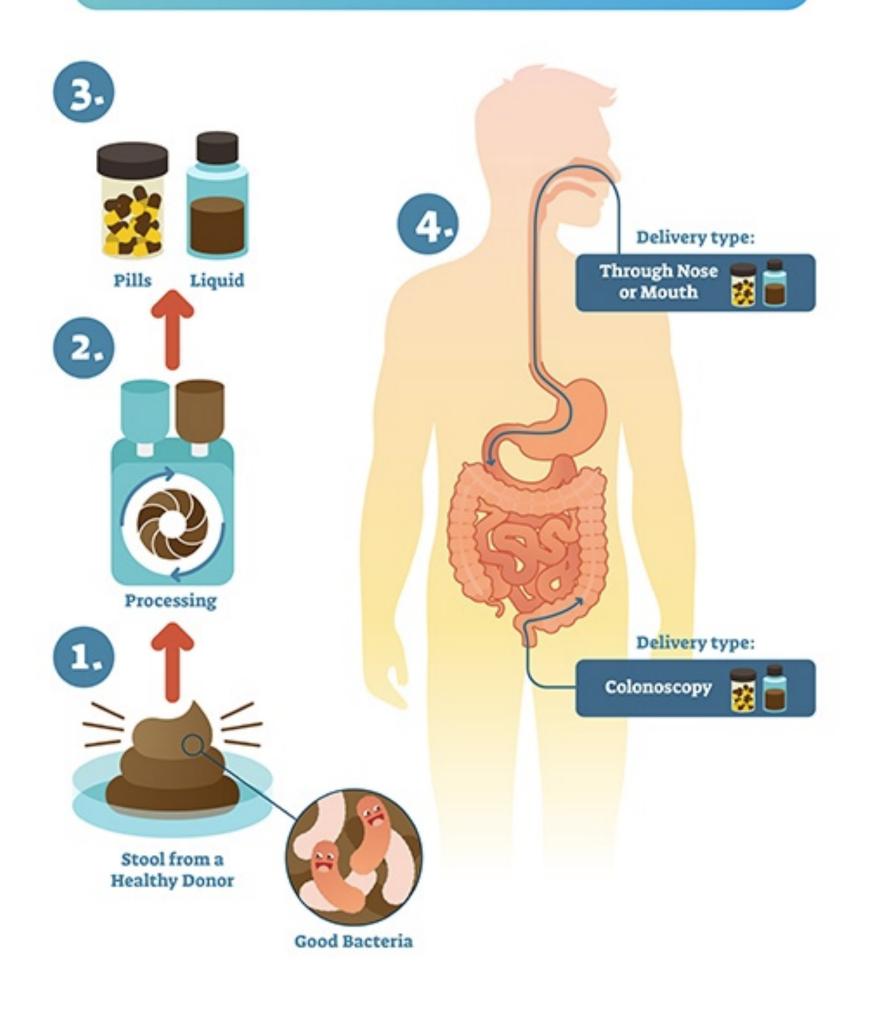








FECAL TRANSPLANT THERAPY



Definition: Faecal microbiota transplantation involves transplanting faecal material from a healthy person to a patient, with the aim of treating disease.

Stool donors have to be healthy and are screened for a range of diseases. A faecal material is usually transplanted during colonoscopy / enema or special pills.

https://no autism/

Faecal transplant

https://nourishinghope.com/fecal-transplant-



Faecal transplant / thoughts??

Do children with food allergies have different intestinal microbiota than healthy children? At Brigham and Women's Hospital, they analyzed 240 stool samples from 59 babies with food allergies and 97 healthy controls. To identify the bacteria, they used a highly sensitive technique known as 16S rRNA gene sequencing. The results, soon to be published, revealed 77 microbial species whose presence differed between food-allergic babies and controls across age groups





CASE STUDY

CLIENT: 21-year-old female: diagnosed with severe general anxiety disorder, PTSD and depression.

Client is under the supervision of a general practitioner (GP) and psychologist. She came to me to pursue alternatives before committing to the SSRI prescribed by her GP.

PRESENTING COMPLAINT: Anxiety, depression and gastrointestinal complaints

BRIEF HISTORY: Childhood trauma as an infant which resulted in chronic stress and whole body dysregulation.

The client experiences severe anxiety since 15 years, presenting with malaise, nausea, headaches, dizziness, stomach pain and emesis. The duration of these symptoms range from 5-hrs to 30mins. Her diagnosis of depression correlated to the progression of anxiety attacks.

The client also suffers from poor digestive function. Client experiences flatulence, nausea, pain and bloating with consumption of foods. Evacuates her bowels 5-6 times per day, stool is loose, pale, and steatorrhea (contains fat). The client has a low immunity and gets sick regularly. Recovery is slow and often the infection is recurring. Energy levels are low and she wakes feeling unrefreshed and fatigued.



An imbalanced gut microbiome in early years can result in poor immune function all through adulthood. Psychological stress activates the HPA-axis, elevates cortisol levels and causes gut permeability Chronic stressors can lead to downregulation of the immune system also evident in the client

The diagnosis of PTSD and a history of anxiety since 5 years of age indicate that the client's nervous system and digestive system has been impacted from an early age. Traumatic incidences have been proved to instantly alter the gut microbiota. As a result of stress, intestinal dysbiosis and leaky gut can adversely influence gut physiology resulting in unfortunate gut-brain-axis signaling These particles enter the bloodstream, increasing pro-inflammatory cytokines and altering metabolism of tryptophan. In turn this leads to alterations in serotonin (5HT) and glutamine neurotransmission. This mechanism impairs CNS functioning altering neurochemistry, cognition, behavior and stress response Chronic stress further compromises the pancreas this results in a dysregulation of enzyme secretion, induction of inflammatory response Specific to this case, deficiencies could be caused by, malabsorption is caused from inflammation, lack of pancreatic enzymes, low bile salt production, liver congestion, low HCL, leaky gut, stress and food sensitivities. Tryptophan is the direct precursor for serotonin synthesis and requires several cofactors to function optimally. A cofactor deficiency in this pathways can directly lead to depression, behavioral changes and mood disorders

Chronic stress results in methyl-group depletion resulting in bile dysfunction and the aforementioned gut dysbiosis. This feeds into interference with methylation, liver phase 2 dysregulation and toxic overload.



CASE STUDY

Improve:

- Gut function and lining integrity to support healthy digestion, absorption and assimilation of nutrients
- Down-regulating inflammation
- Supporting bile acid function and enzyme production to improve malabsorption
- Supporting the hypothalamus-pituitary-adrenal-axis (HPA)- Stress reduction
- Facilitate healthy nervous system response Vagus nerve
- Improve gut microflora
- Support detoxification pathways to ensure proper elimination
- Support neurotransmitter function
- Improving nutrient status
- Supporting and facilitating methylation
- Regulating immune response
- Optimising serotonin levels and production to stabilise moods

Addressing diet, food sensitivities and lifestyle changes

Supplements: magnesium, taurine, zinc, glutamine, vitamin C, A, E and activated B's, NAC, digestive enzymes, herbal formula, probiotics, 5-Hydroxytryptophan (5HTP) (derived from tryptophan)







