

Depression & Illness Syndrome

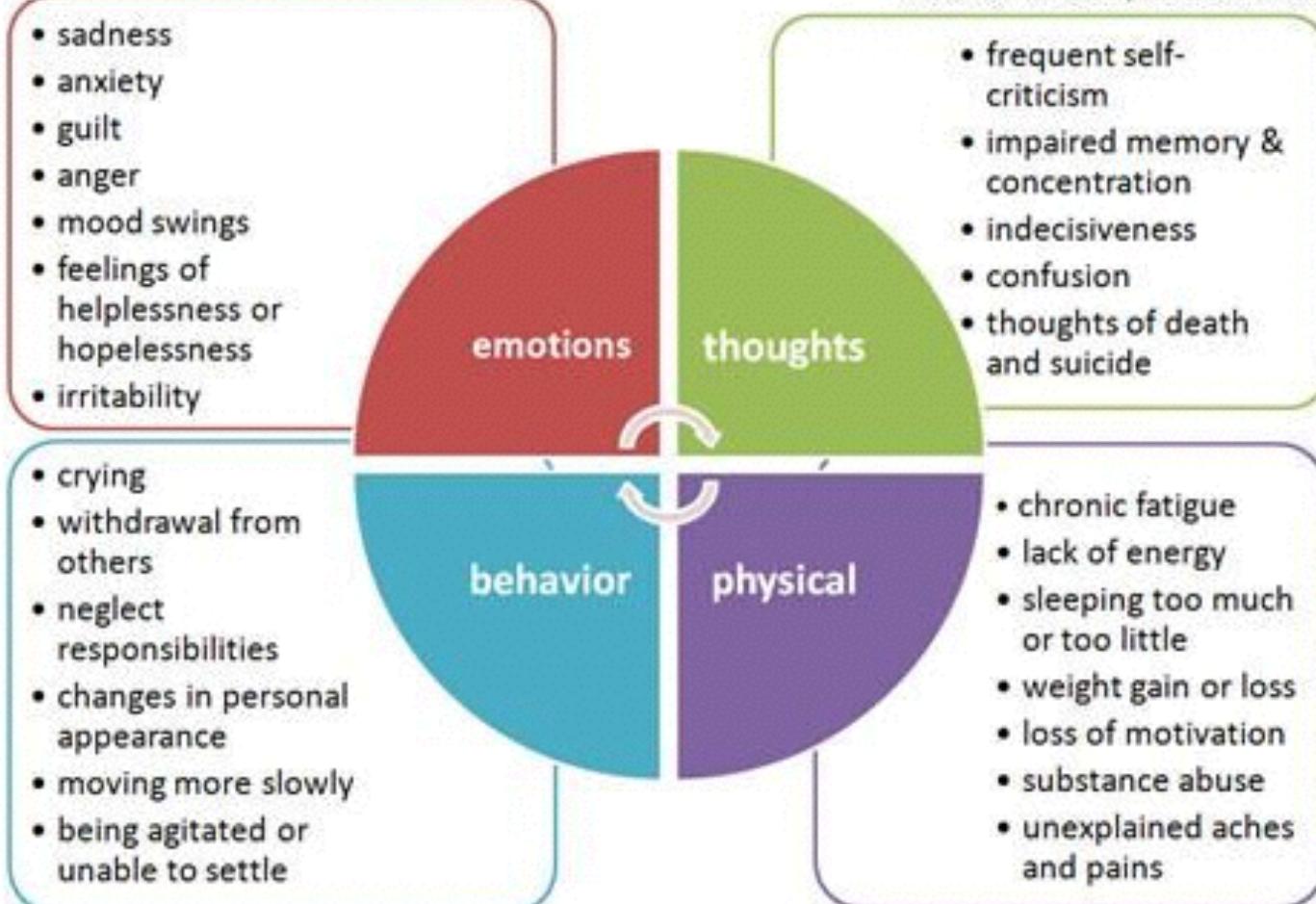
Utilizing the Organic Acid Test and Pathway Planners

Dr Eric Balcavage



Symptoms of Depression

--Mental Health First Aid, mentalhealthfirstaid.org



"Depression is not a genetic disease.
It is an epigenetic syndrome."

Dr. Kelly Brogan

thebestbrainpossible.com



CHRONIC CONDITION
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BEST PRACTICE



Metabolic features of the cell danger response.

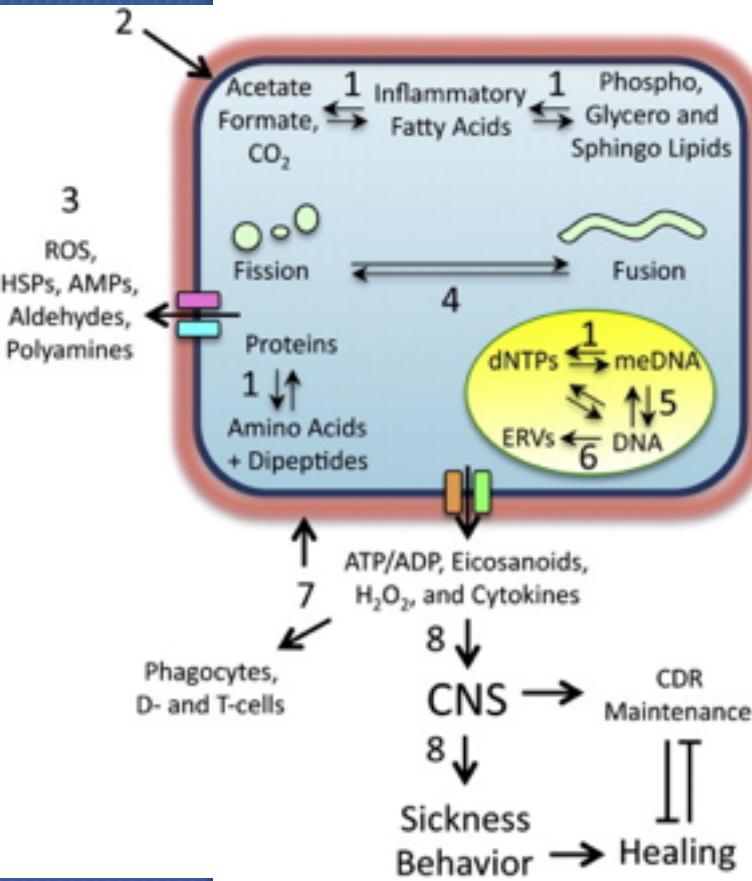
Naviaux RK¹.

Author information

Abstract

The cell danger response (CDR) is the evolutionarily conserved metabolic response that protects cells and hosts from harm. It is triggered by encounters with chemical, physical, or biological threats that exceed the cellular capacity for homeostasis. The resulting metabolic mismatch between available resources and functional capacity produces a cascade of changes in cellular electron flow, oxygen consumption, redox, membrane fluidity, lipid dynamics, bioenergetics, carbon and sulfur resource allocation, protein folding and aggregation, vitamin availability, metal homeostasis, indole, pterin, 1-carbon and polyamine metabolism, and polymer formation. The first wave of danger signals consists of the release of metabolic intermediates like ATP and ADP, Krebs cycle intermediates, oxygen, and reactive oxygen species (ROS), and is sustained by purinergic signaling. After the danger has been eliminated or neutralized, a choreographed sequence of anti-inflammatory and regenerative pathways is activated to reverse the CDR and to heal. When the CDR persists abnormally, whole body metabolism and the gut microbiome are disturbed, the collective performance of multiple organ systems is impaired, behavior is changed, and chronic disease results. Metabolic memory of past stress encounters is stored in the form of altered mitochondrial and cellular macromolecule content, resulting in an increase in functional reserve capacity through a process known as mitocellular hormesis. The systemic form of the CDR, and its magnified form, the purinergic life-threat response (PLTR), are under direct control by ancient pathways in the brain that are ultimately coordinated by centers in the brainstem. Chemosensory integration of whole body metabolism occurs in the brainstem and is a prerequisite for normal brain, motor, vestibular, sensory, social, and speech development. An understanding of the CDR permits us to reframe old concepts of pathogenesis for a broad array of chronic, developmental, autoimmune, and degenerative disorders. These disorders include autism spectrum disorders (ASD), attention deficit hyperactivity disorder (ADHD), asthma, atopy, gluten and many other food and chemical sensitivity syndromes, emphysema, Tourette's syndrome, bipolar disorder, schizophrenia, post-traumatic stress disorder (PTSD), chronic traumatic encephalopathy (CTE), traumatic brain injury (TBI), epilepsy, suicidal ideation, organ transplant biology, diabetes, kidney, liver, and heart disease, cancer, Alzheimer and Parkinson disease, and autoimmune disorders like lupus, rheumatoid arthritis, multiple sclerosis, and primary sclerosing cholangitis.

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Functions of the acute cell danger response.
The acute CDR includes 8 functional changes in cell structure, physiology, metabolism, and gene expression. These are:

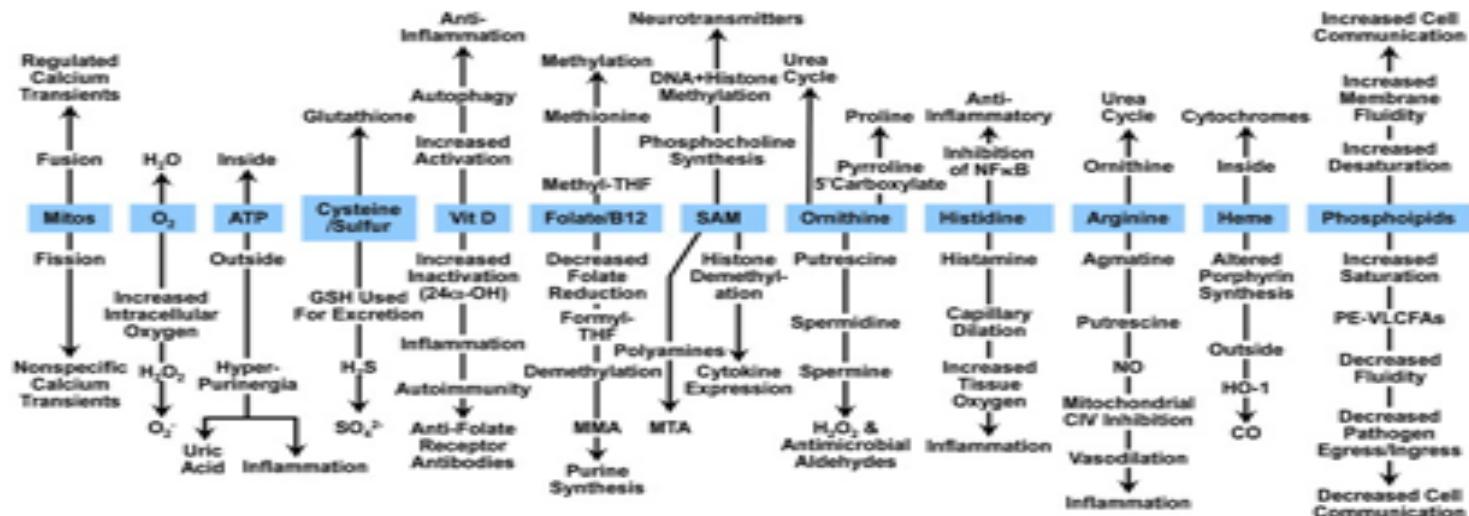
- 1) Shift cellular metabolism from polymer to monomer synthesis to prevent the hijacking and assembly of cellular resources by intracellular pathogens
- 2) Stiffen the cell membranes to limit superinfection and pathogen egress
- 3) Release antiviral and antimicrobial chemicals into the pericellular environment,
- 4) Increase autophagy, mitochondrial fission, and mitophagy to facilitate removal of intracellular pathogens and biogenesis centers
- 5) Change DNA methylation and histone modification to alter gene expression
- 6) Mobilize endogenous retroviruses and LINEs to produce genetic variations
- 7) Warn neighboring cells and distant effector cells of the danger with extracellular nucleotides, H₂O₂, eicosanoids, metabolites, and cytokines
- 8) **Alter the behavior of the host to prevent the spread of infection to kin, and sleep patterns to facilitate healing.**

Abbreviations:

- HSPs: heat shock proteins
- AMPs: antimicrobial peptides
- D-cells: Dendritic Cells
- ERVs: endogenous retroviruses
- LINEs: long interspersed nuclear elements
- meDNA: methylated DNA
- dNTPs: deoxynucleoside triphosphates
- CNS: central nervous system.

A

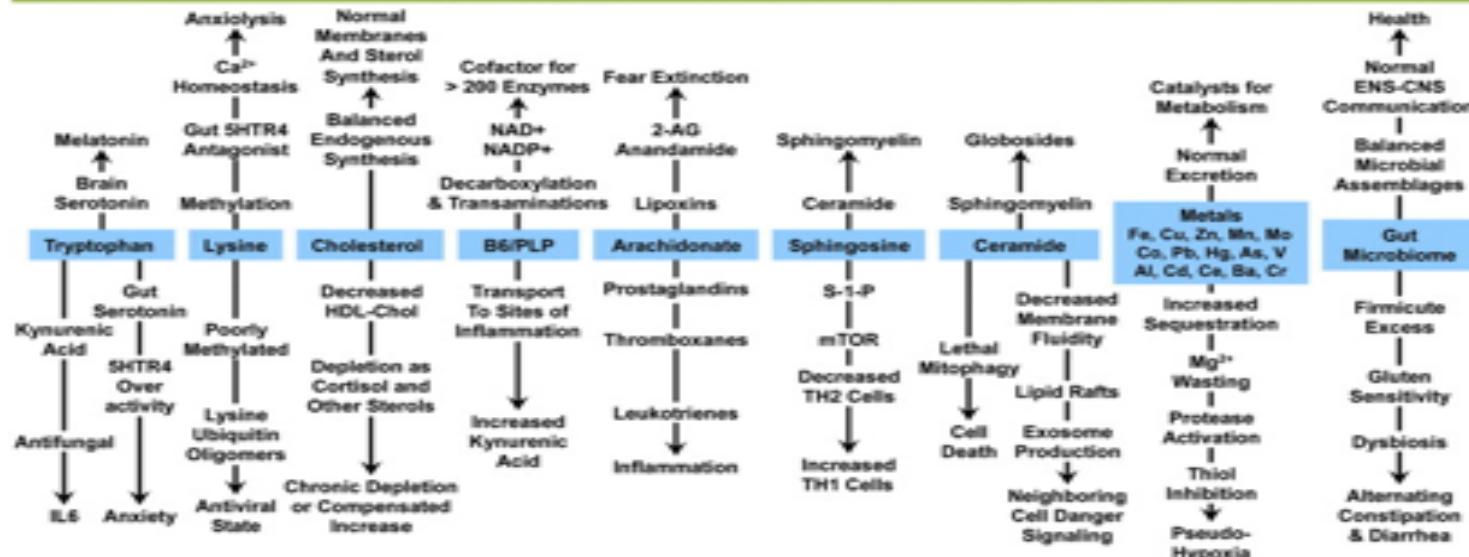
Healthy Development—Winter Maintenance Metabolism



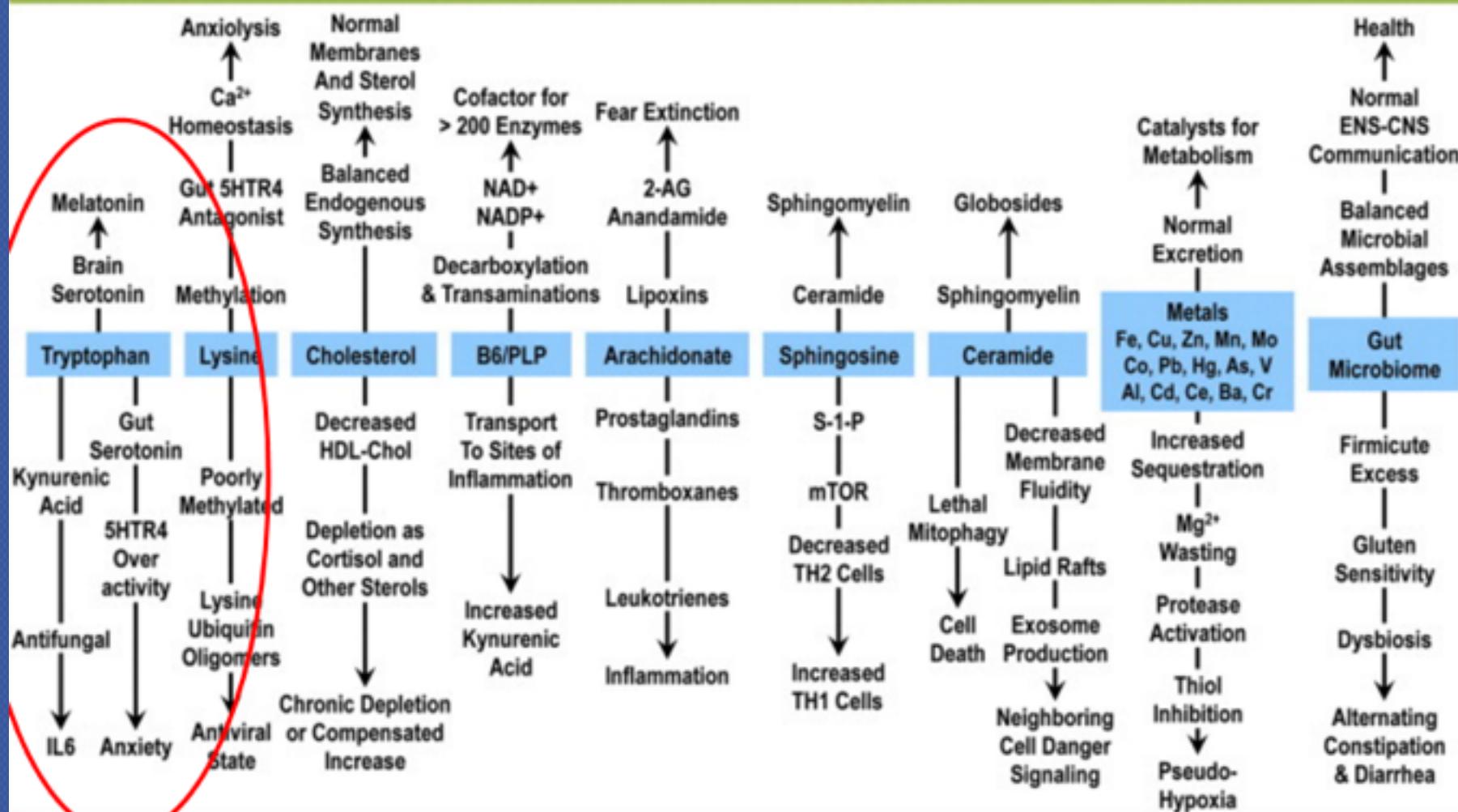
Innate Immunity, Inflammation—Summer Growth Metabolism

B

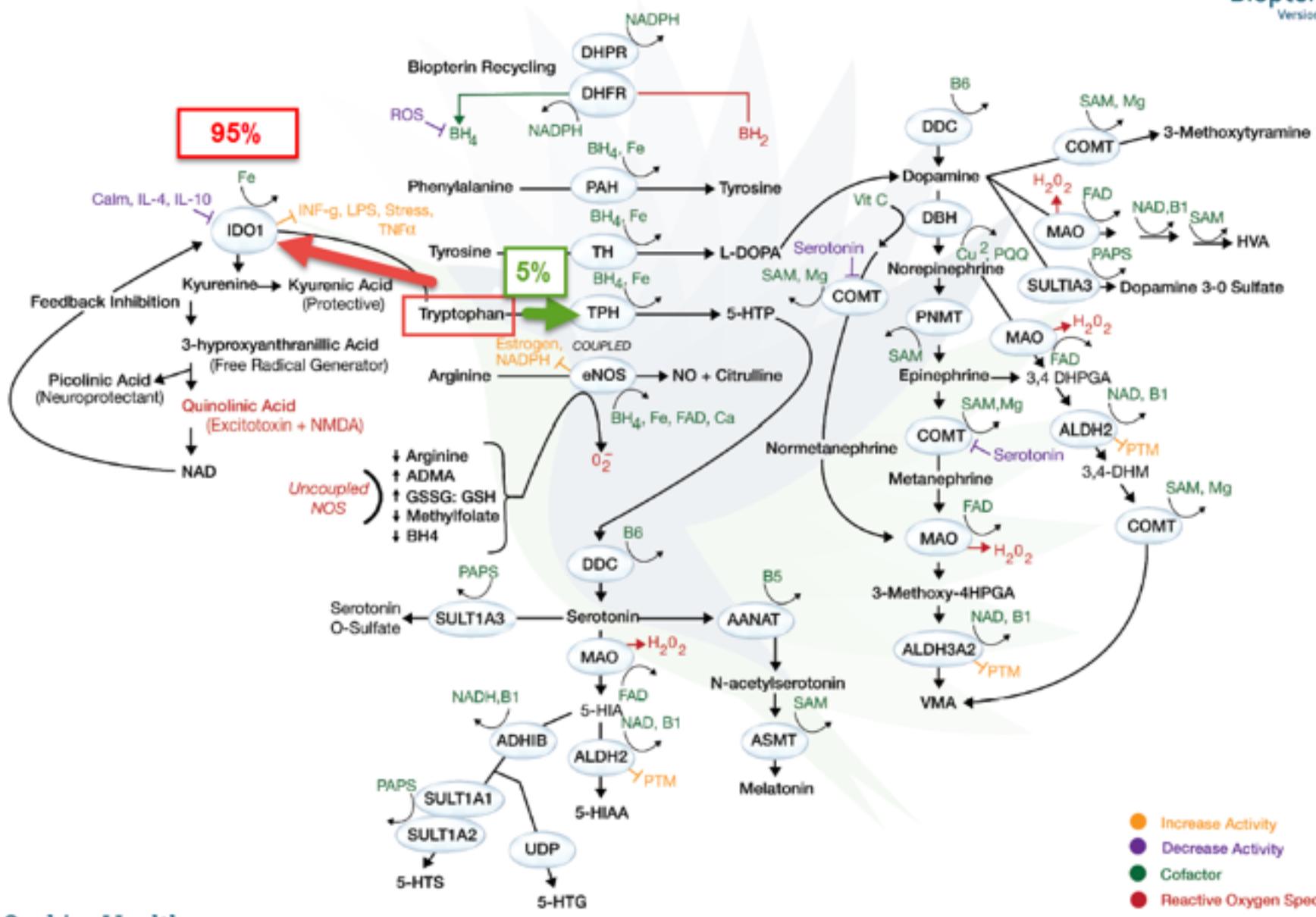
Healthy Development—Winter Maintenance Metabolism



Healthy Development—Winter Maintenance Metabolism



Innate Immunity, Inflammation—Summer Growth Metabolism



Kynurenine Pathway

[Expert Rev Neurother.](#) 2015;15(7):719-21. doi: 10.1586/14737175.2015.1049999. Epub 2015 May 24.

What is the tryptophan kynurenine pathway and why is it important to neurotherapeutics?

Davis J¹, Liu A.¹

 Author information

Abstract

The kynurenine pathway has received increasing attention as its connection to inflammation, the immune system and neurological conditions has become more apparent. It is the primary route for tryptophan catabolism in the liver and the starting point for the synthesis of nicotinamide adenine dinucleotide in mammals. Dysregulation or overactivation of this pathway can lead to immune system activation and accumulation of potentially neurotoxic compounds. These aspects make the kynurenine pathway a promising target for therapeutic development to treat inflammation and disease with neurological aspects, especially in cancer patients undergoing chemotherapy.

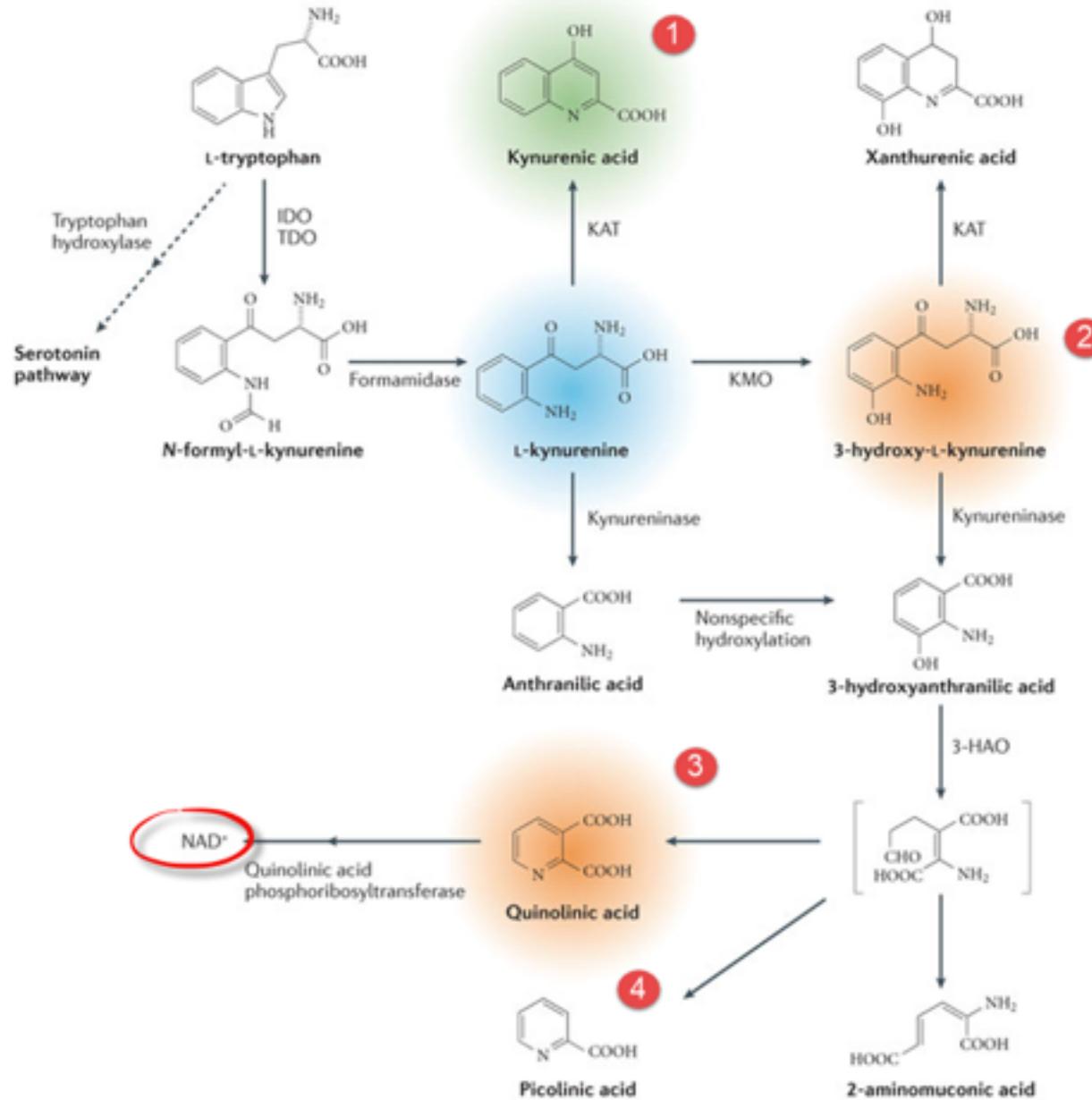
KEYWORDS: excitotoxicity; inflammation; melatonin; quinolinic acid; serotonin

PMID: 26004930 PMCID: [PMC4482796](#) DOI: [10.1586/14737175.2015.1049999](#)

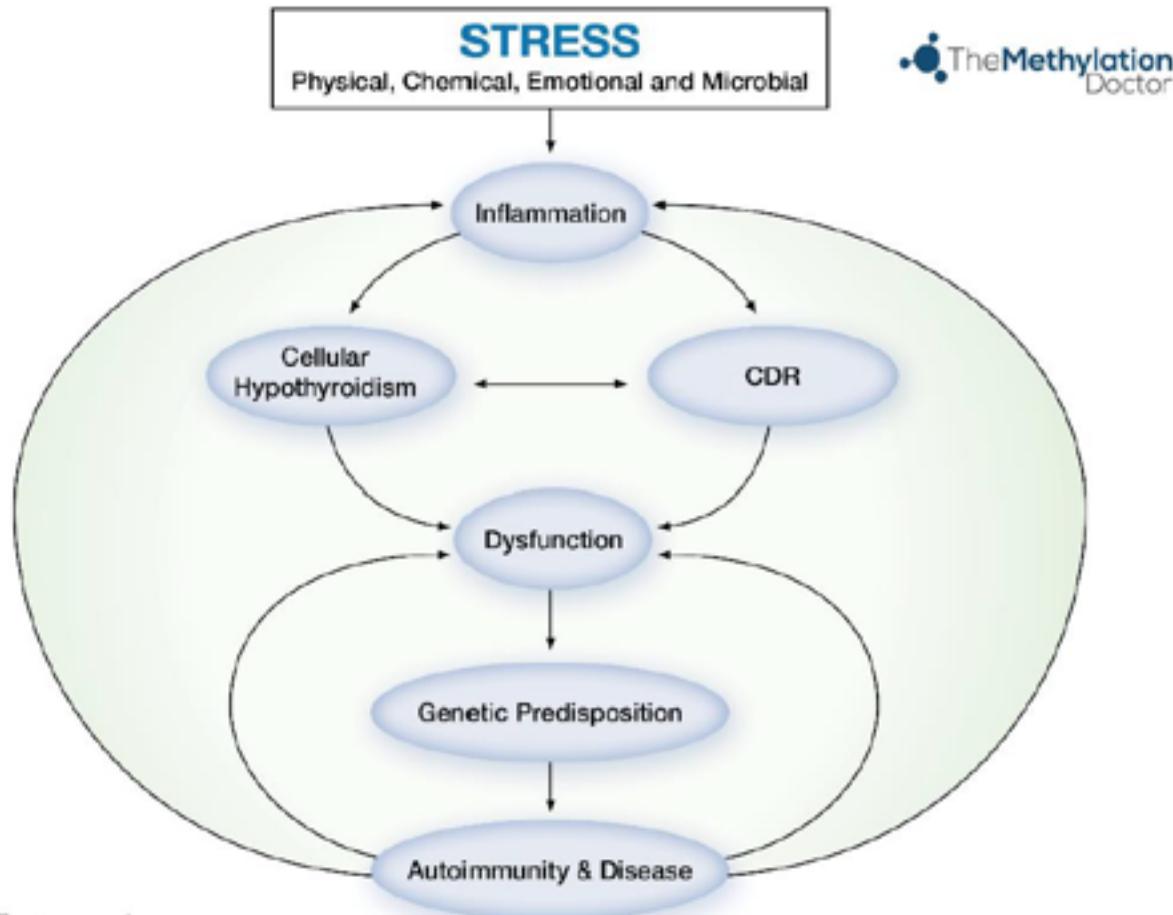
[PubMed - indexed for MEDLINE] [Free PMC Article](#)



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Sickness Syndrome



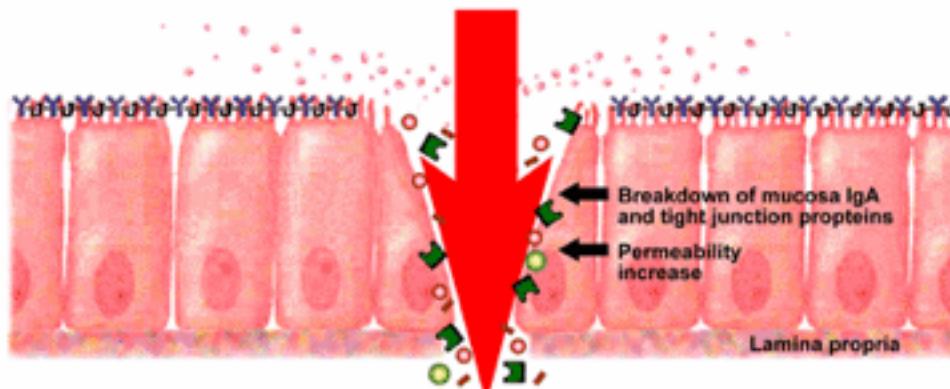
TheMethylation
Doctor



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Factors affecting mucosal immune system resulting in intestinal barrier dysfunction, autoimmunity and nervous system abnormalities



INTESTINAL BARRIER DYSFUNCTION

FOOD ALLERGY & INTOLERANCE

IMMUNE SYSTEM ABNORMALITIES

AUTOIMMUNITY

**INFLUENCE ON THE BLOOD-BRAIN BARRIER
AND NEUROAUTOIMMUNITY**



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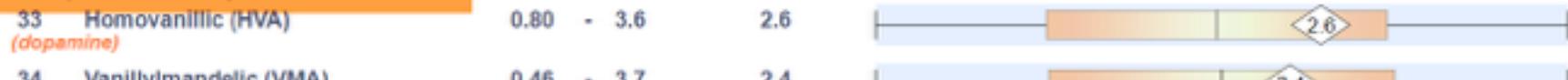
Metabolic Analysis Profile



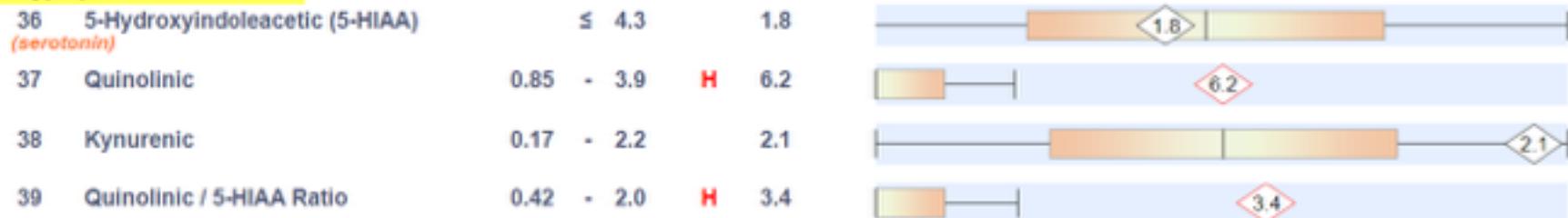
Neurotransmitter Basics

Neurotransmitter Metabolites

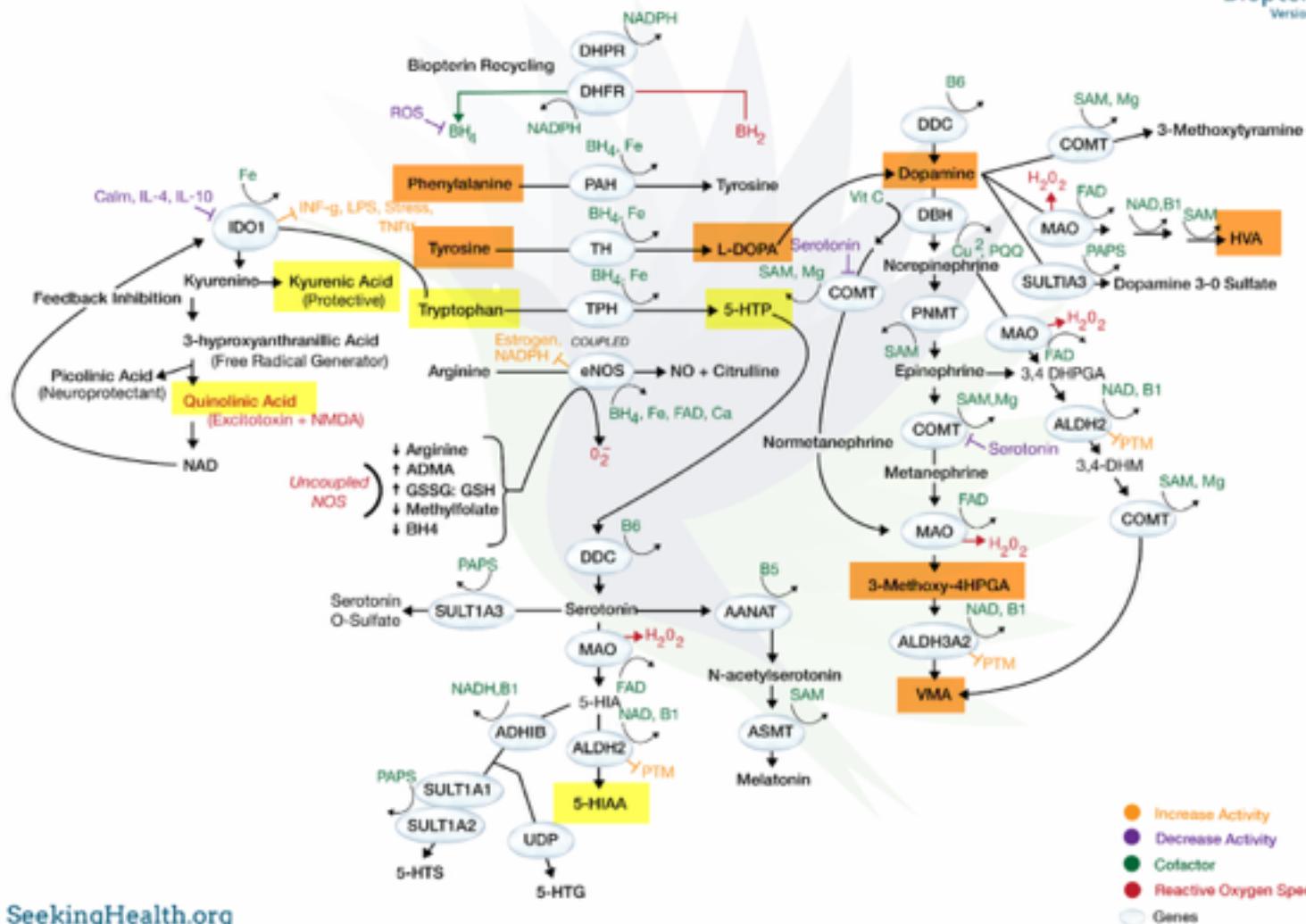
Phenylalanine and Tyrosine Metabolites



Tryptophan Metabolites



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The Patient

- 72 yof
- Primary complaints: Hypothyroidism, diabetes, excessive weight gain, fatigue, chronic pain, depression, insomnia, sinus problems, high blood pressure and anxiety
- Medications: Losartan, Levothyroxin, Metformin, Fenofibrate

Initial Symptoms

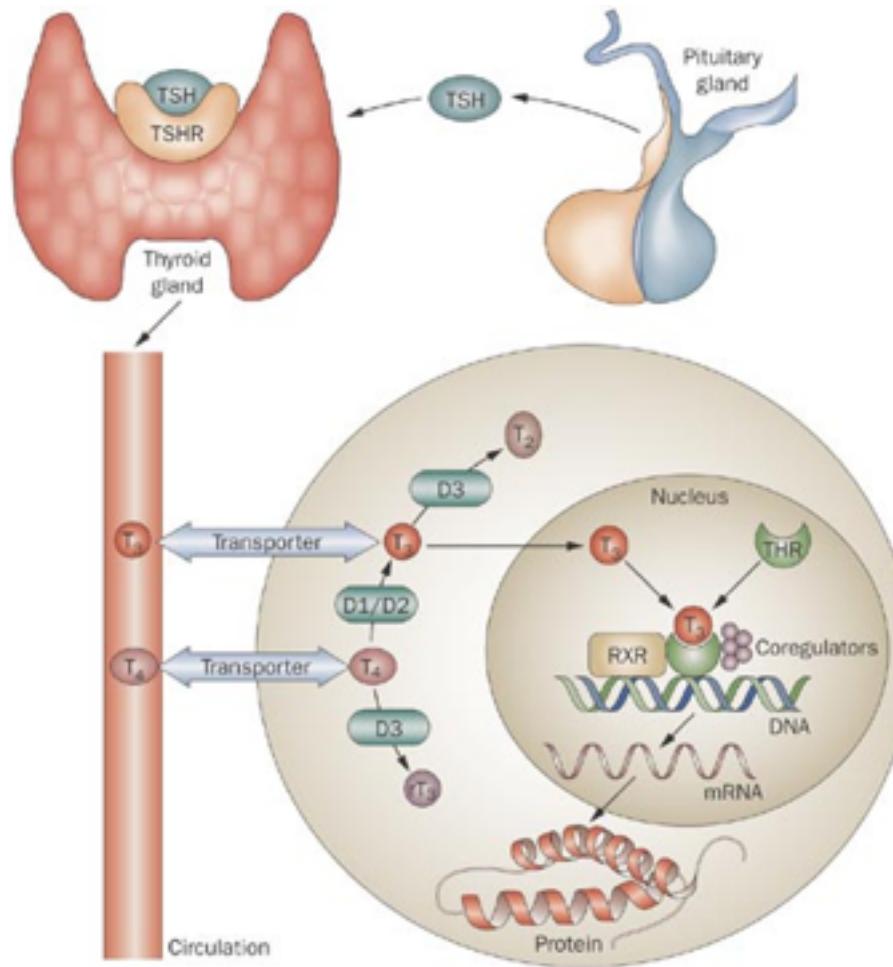
SYMPTOMS	10/28
SLEEP	9
FATIGUE	9
IRRITABILITY	9
DEPRESSION	8
SINUS	6
PAIN	6
FREQ URINATION	5
WEIGHT	182
BLOOD PRES	141/75



Initial Labs

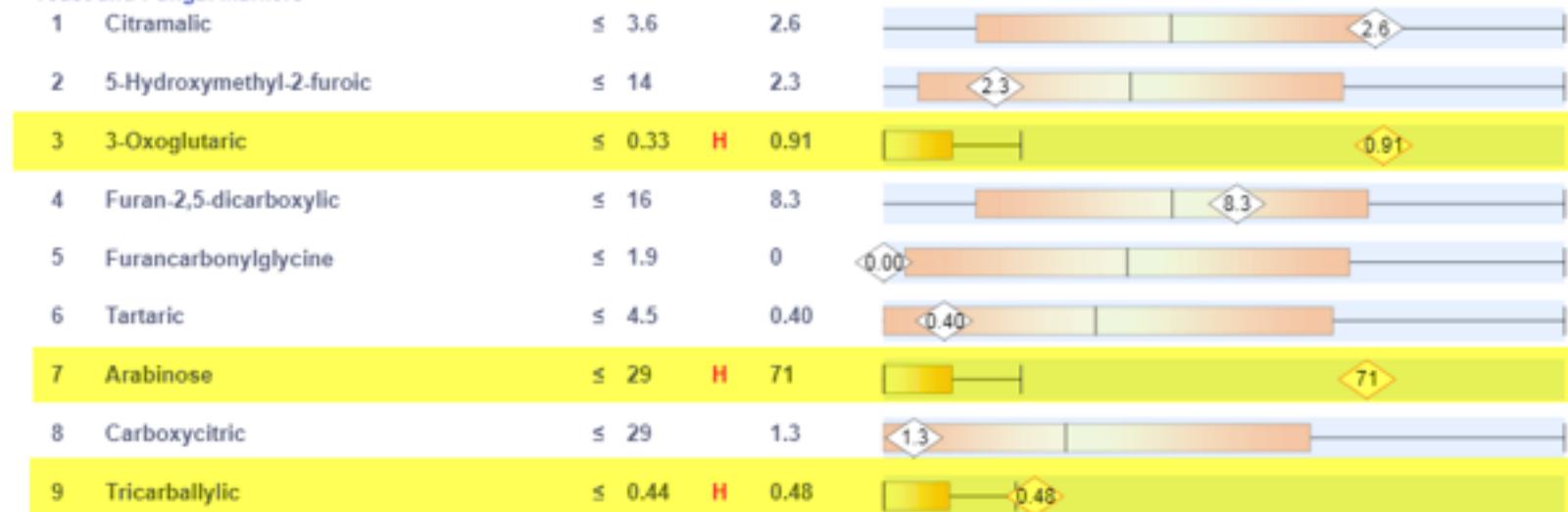
- HA1C: 6.7 H
- BUN: 24 H
- ALK Phos: 29 L
- Trig: 160 H
- CHOL: 205 H
- LDL: 127 H
- HCY: 18.8 H
- CRP: 1.11 FH
- TSH: 3.8 FH
- T4: 8.5
- T3: 84 FL
- fT4: 1.21
- fT3: 2.4 FL
- rT3: 16.7
- $T3/rT3 = 5.02$ L
- $fT3/rT3 = .14$ L

Cellular Hypothyroidism

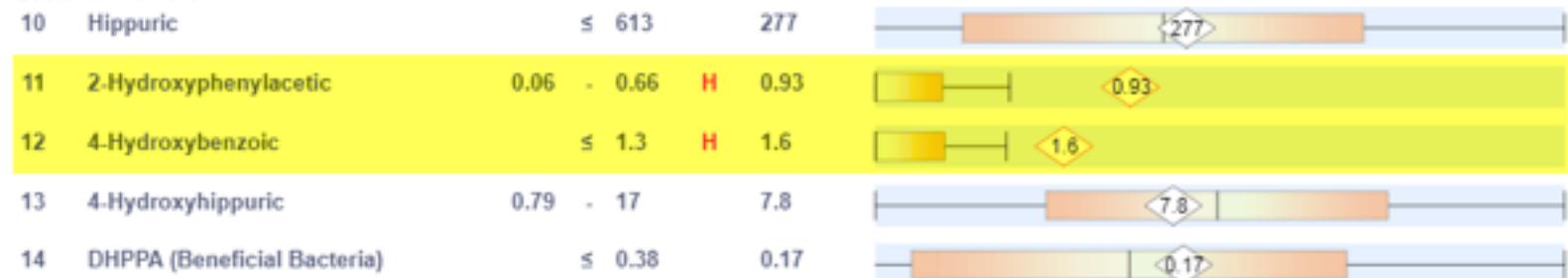


Intestinal Microbial Overgrowth

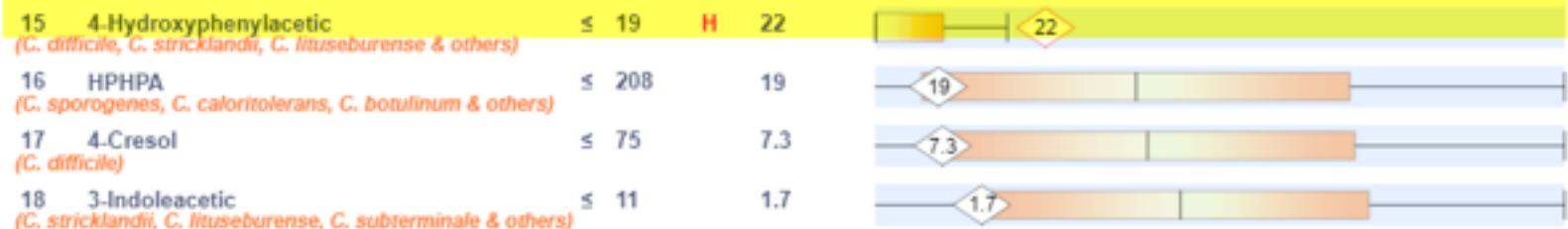
Yeast and Fungal Markers



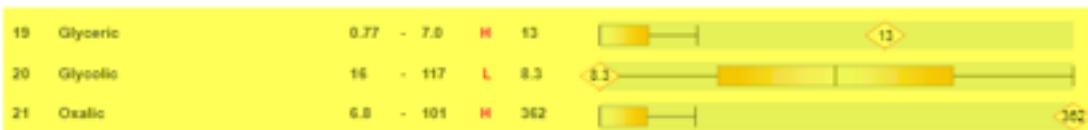
Bacterial Markers



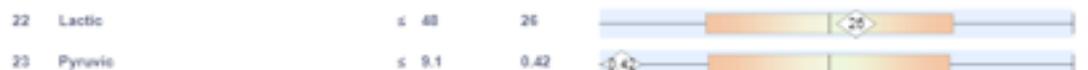
Clostridia Bacterial Markers



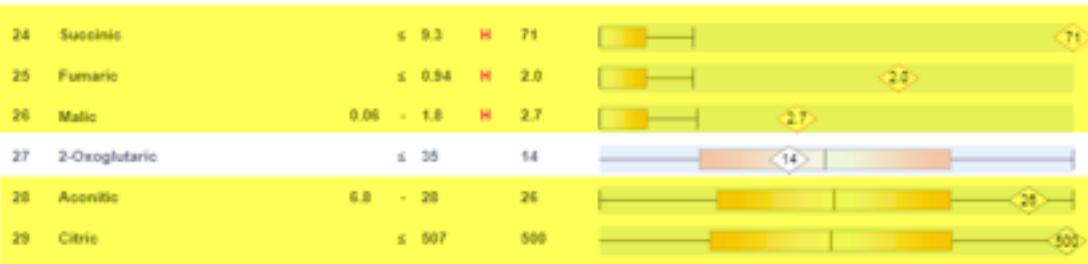
Oxalate Metabolites



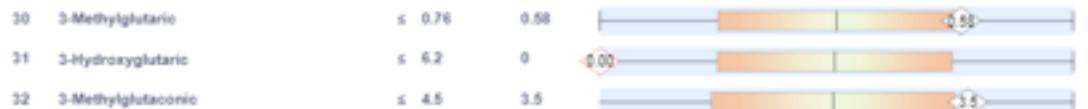
Glycolytic Cycle Metabolites



Mitochondrial Markers - Krebs Cycle Metabolites

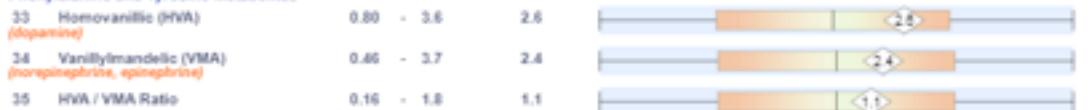


Mitochondrial Markers - Amino Acid Metabolites

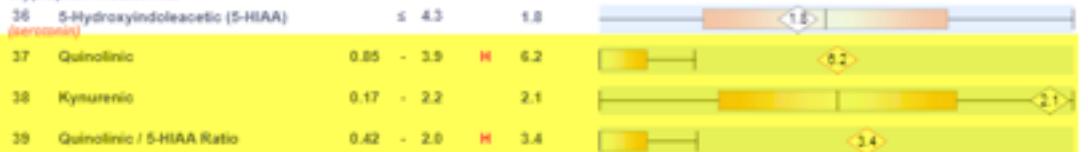


Neurotransmitter Metabolites

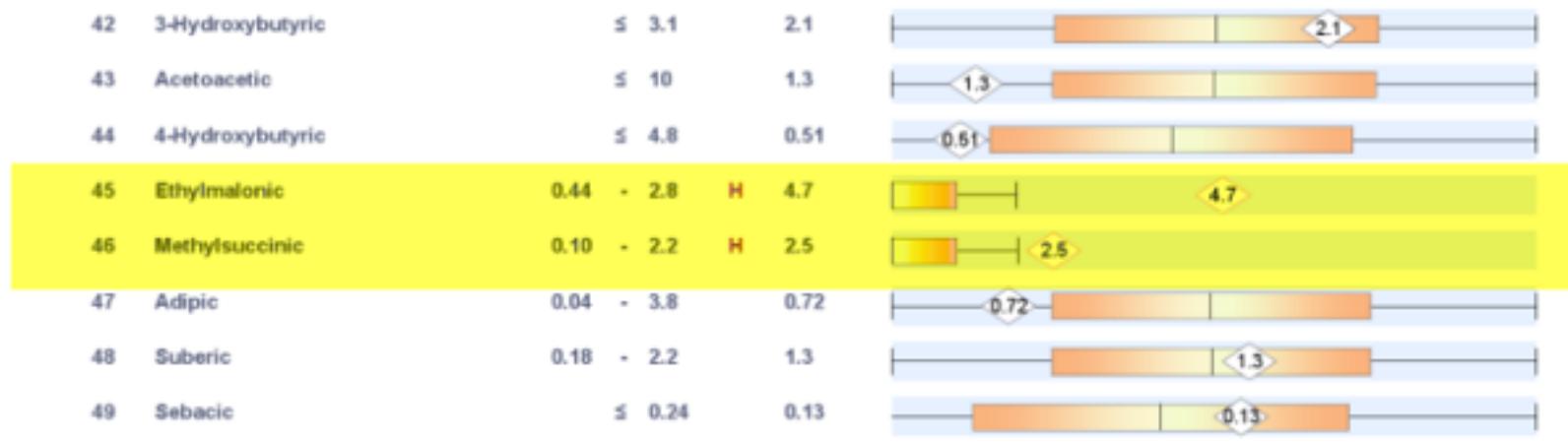
Phenylalanine and Tyrosine Metabolites



Tryptophan Metabolites



Ketone and Fatty Acid Oxidation



● Abnormal values are indicated.

Indicators of Detoxification

Glutathione

58	Pyroglutamic ●	10 - 33	H 35	
59	2-Hydroxybutyric ●	0.03 - 1.8	H 4.0	

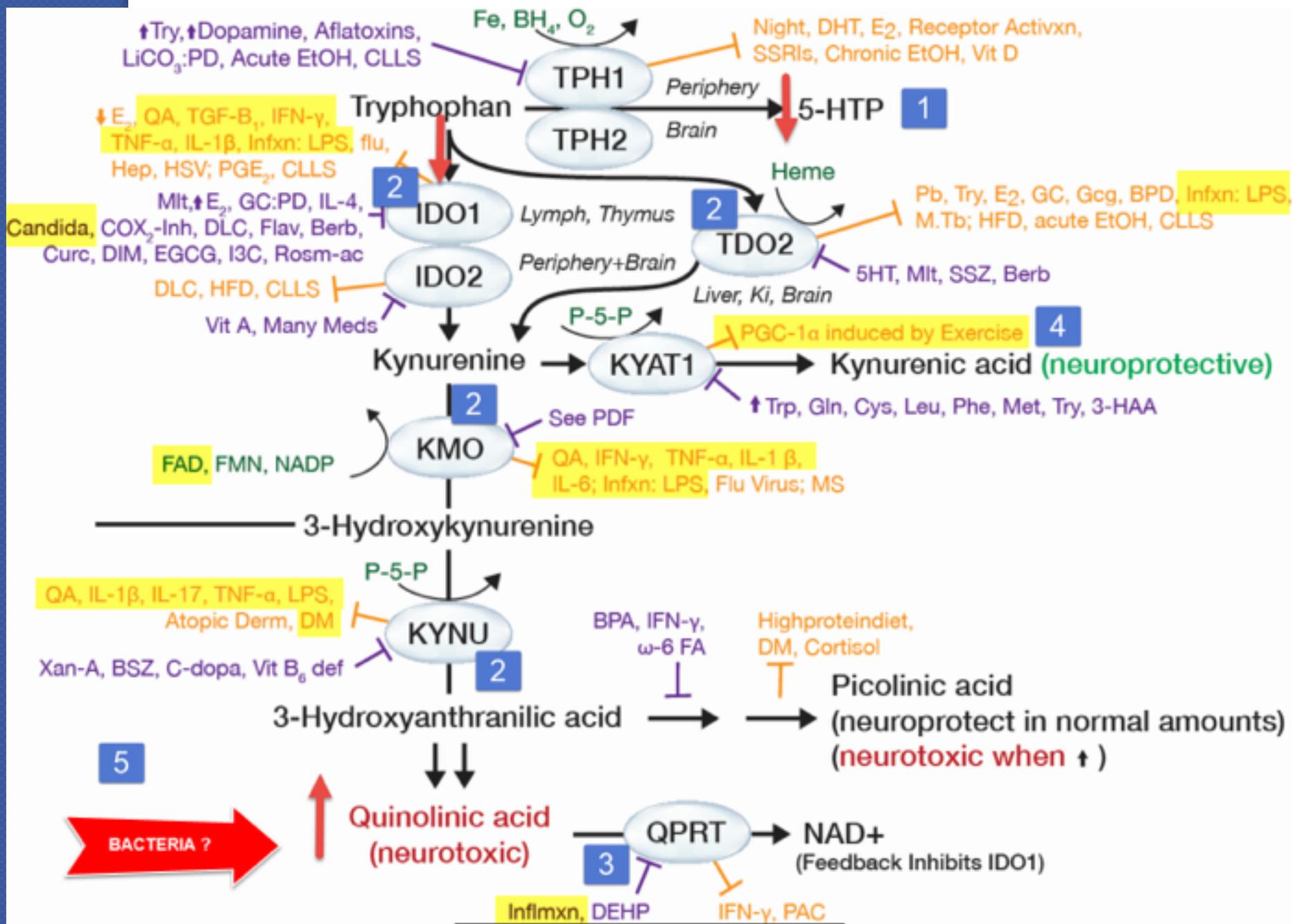
Ammonia Excess

60	Orotic	0.06 - 0.54	0.18	
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Aspartame, salicylates, or GI bacteria

61	2-Hydroxyhippuric	≤ 1.3	H 1.6	
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● A high value for this marker may indicate a Glutathione deficiency.



Systemic lipopolysaccharide-mediated alteration of cortical neuromodulation involves increases in monoamine oxidase-A and acetylcholinesterase activity.

Abstract

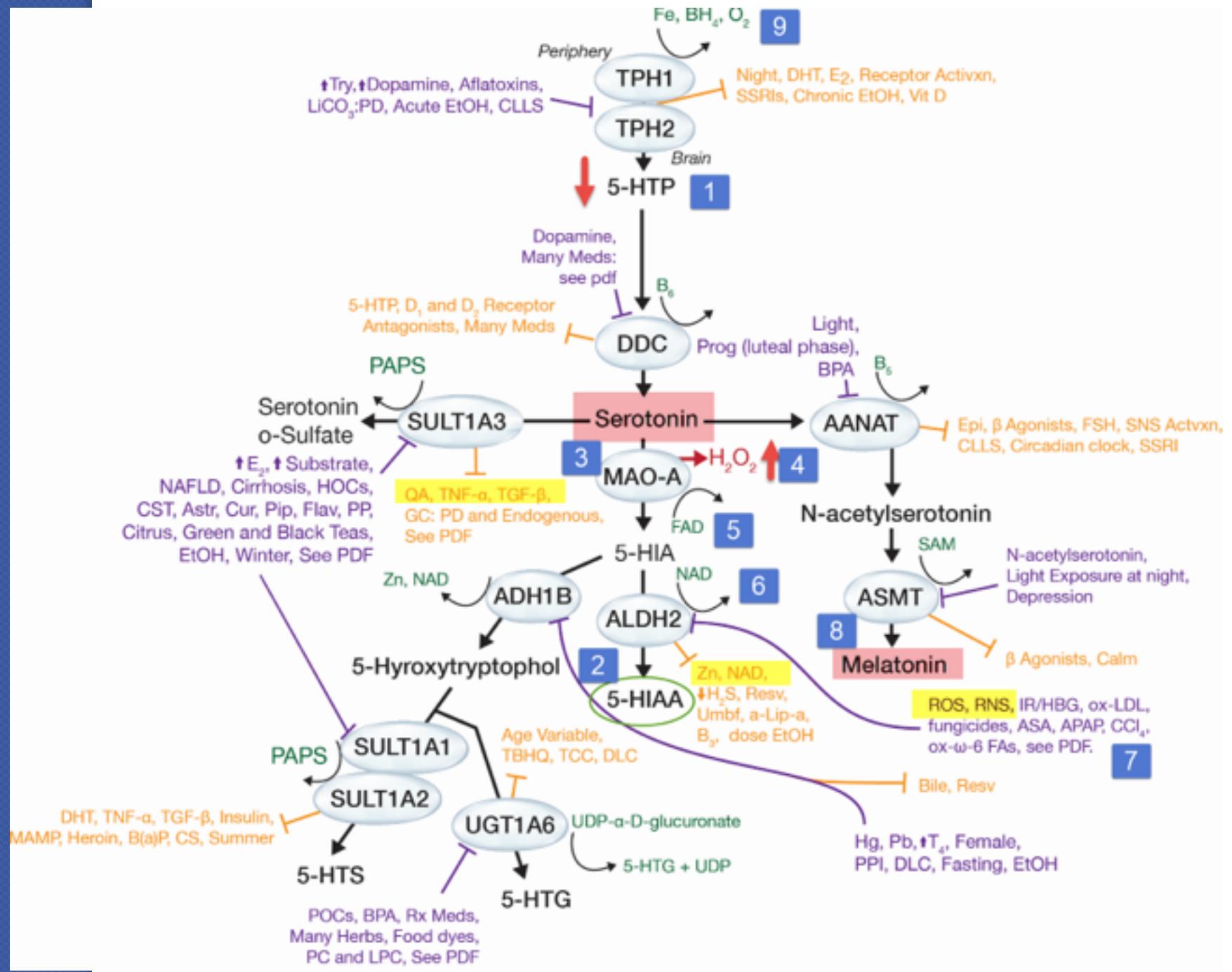
Background: Lipopolysaccharide (LPS)-mediated sickness behaviour is known to be a result of increased inflammatory cytokines in the brain. Inflammatory cytokines have been shown to mediate increases in brain excitation by loss of GABA_A-mediated inhibition through receptor internalization or inactivation. Inflammatory pathways, reactive oxygen species and stress are also known to increase monoamine oxidase-A (MAO-A) and acetylcholinesterase (ACh-E) activity. Given that neuromodulator actions on neural circuits largely depend on inhibitory pathways and are sensitive to alteration in corresponding catalytic enzyme activities, we assessed the impact of systemic LPS on neuromodulator-mediated shaping of a simple cortical network.

Methods: Extracellular field recordings of evoked postsynaptic potentials in adult mouse somatosensory cortical slices were used to evaluate effects of a single systemic LPS challenge on neuromodulator function 1 week later. Neuromodulators were administered transiently as a bolus (100 μ l) to the bath perfusate immediately upstream of the recording site to mimic phasic release of neuromodulators and enable assessment of response temporal dynamics.

Results: Systemic LPS administration resulted in loss of both spontaneous and evoked inhibition as well as alterations in the temporal dynamics of neuromodulator effects on a paired-pulse paradigm. The effects on neuromodulator temporal dynamics were sensitive to the Monoamine oxidase-A (MAO-A) antagonist clorgyline (for norepinephrine and serotonin) and the ACh-E inhibitor donepezil (for acetylcholine). This is consistent with significant increases in total MAO and ACh-E activity found in hemi-brain samples from the LPS-treated group, supporting the notion that systemic LPS administration may lead to longer-lasting changes in inhibitory network function and enzyme (MAO/ACh-E) activity responsible for reduced neuromodulator actions.

Conclusions: Given the significant role of neuromodulators in behavioural state and cognitive processes, it is possible that an inflammatory-mediated change in neuromodulator action plays a role in LPS-induced cognitive effects and could help define the link between infection and neuropsychiatric/degenerative conditions.

Keywords: Inflammation, Phasic neuromodulator release, Cortical network, Cortical inhibition





SYMPTOMS	10/28	11/30	1/4	3/24
SLEEP	9	9	6	3
FATIGUE	9	8	6	3
IRRITABILITY	9	8	5	2
DEPRESSION	8	6	4	2
SINUS	6	5	4	2
PAIN	6	6	4	1
FREQ URINATION	5	5	3	3
WEIGHT	182	169	166	162
BLOOD PRES	141/75		126/62	122/70



Treatment

- We worked on diet, breathing, movement, lifestyle / behaviors, sleep routine, reduced screen time
- We worked on 4R protocol for her gut
- We addressed kept her focused on a real food, low processed food diet
- We supported her phase 1 and phase 2 detoxification pathways, methylation – via creatine and PC, and supported with glutathione and glutathione recycling products
- She was able to reduce her blood pressure medication
- She dropped her HA1C to 6.0 from 6.7
- Her HCY dropped from 18.8 to 12.8



References

- <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4457461/pdf/nihms688821.pdf>
- <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4482796/>
- https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4344755/pdf/12974_2015_Article_259.pdf
- <http://www.sciencedirect.com/science/article/pii/S1567724913002390>
- <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3195227/pdf/ijtr-2-2009-001.pdf>
- PMC3400832

FEELING DEPRESSED?

Have you experienced most of the following symptoms
during the past two months or longer?

Sadness
Lack of energy
Apathy
Sleep Problems

Appetite or weight changes
Lack of concentration
Feelings of worthlessness or guilt
Thoughts of death or suicide

If you are between the ages of 18 and 65, you may qualify to participate
in a research study involving an investigational medication
for the treatment of depression.



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