



Emerging Neurological Disorders A Path to Solutions

Dr Suzanne K Gazda

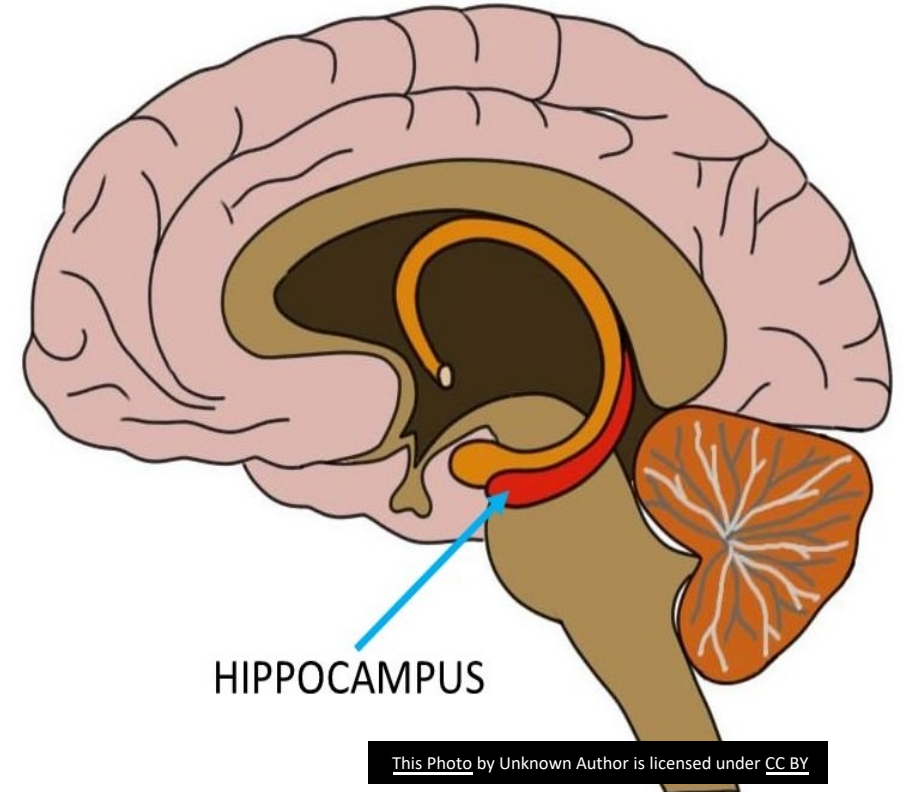
Medicine in the Post 2020 Era: What is Surging to the Top of the Iceberg

- Medicine is forever changed
- Millions if not billions are suffering, and the mounting toll continues to rise
- The brain and the nervous system are under siege
- Montalvan V et al showed 36.4% of LC patients have neurological problems
- 80% of vaccine injuries are neurological (React 19 survey 2021)
- We are facing a crisis of brain health



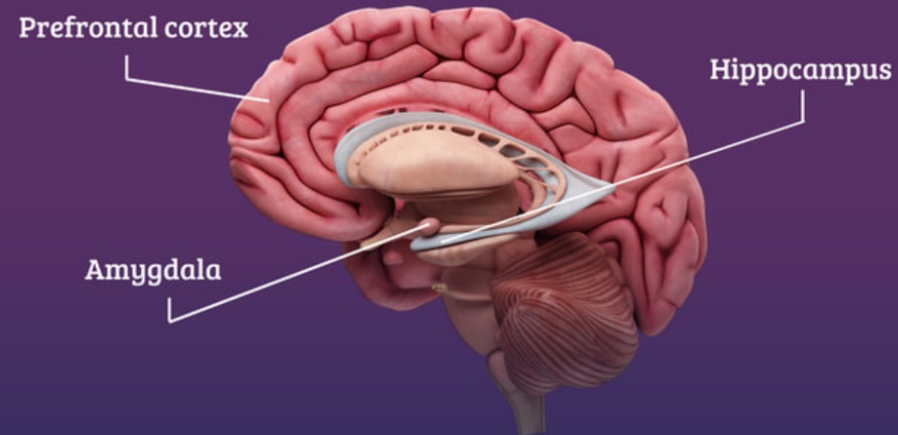
The Hippocampus May Have Been Hit the Hardest

- Stores and recalls memories , curiosity, learning and mood.
- New neurons are being formed here (neurogenesis)
- Spike protein, isolation and fear can cut off the frontal brain from the hippocampus by activating microglia that release proinflammatory cytokines
- Alzheimer's disease can be initiated or deteriorated in COVID-19 patients due to reduced hippocampal neurogenesis.
- Children who witnessed Hurricane Irma had distorted memory decreased HC neurogenesis (vs non-exposed children)



How does isolation affect our brain?

Scientists looked at both human and animal (rodent) models to learn more about the effects of isolation and how it may negatively impact our brains.*



Prefrontal cortex: guides social behaviors and decision-making

- Changes to the signaling processes were observed in study animals.
- People who identify as lonely showed reduced brain volume.

Amygdala: part of the limbic system, it plays an important role in emotions & behavior.

- In people who express loneliness, scientists have observed smaller amygdala.
- Prior studies have shown that fewer personal relationships correlate to a reduced-size amygdala.

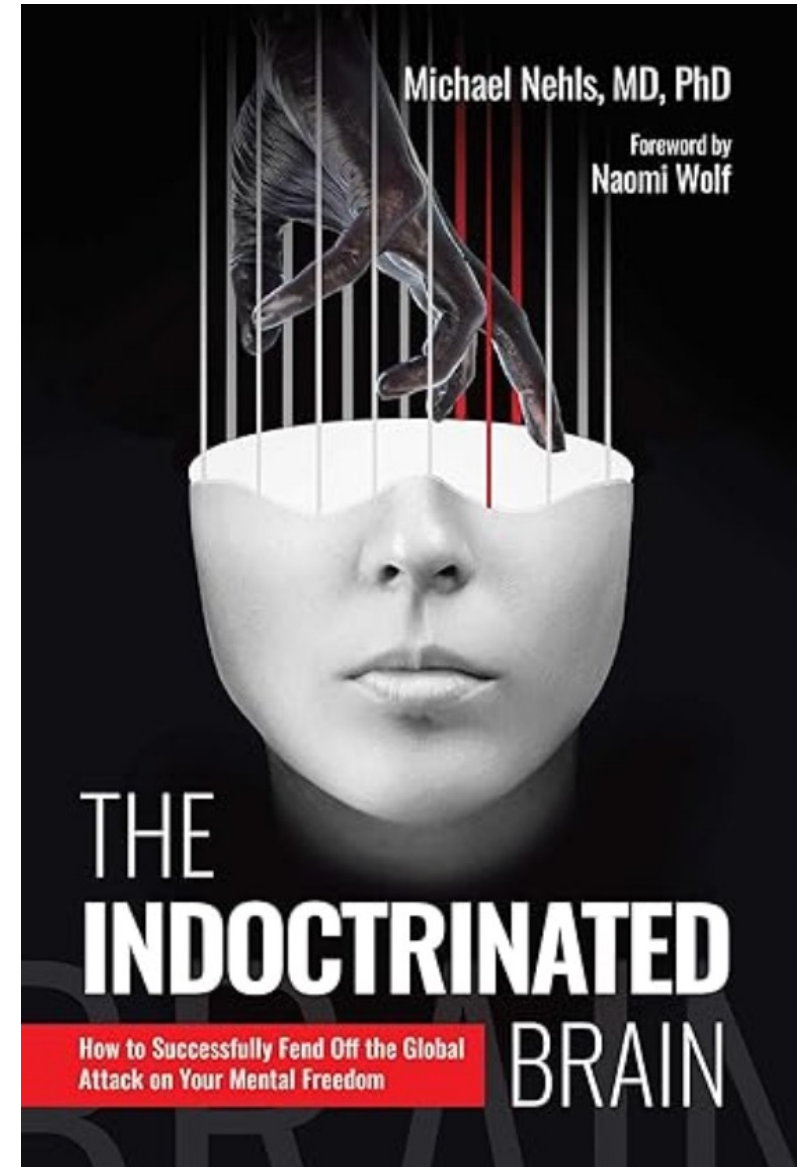
Hippocampus: regulates hormones including cortisol, the stress hormone, and is the primary memory center of the brain.

- Humans and animals in isolation may have a smaller hippocampus and reduced brain-derived neurotrophic factor resulting in poor learning and memory.
- Isolated animals exhibited higher levels of cortisol.

*From The Scientist, by C. Offord (July 13, 2020). "How Social Isolation Affects the Brain." • <https://www.the-scientist.com/features/how-social-isolation-affects-the-brain-67701>

“A Mind is a Terrible Thing to Waste”

- Spike protein from the mRNA vaccine, causes a neuropathological attack on our autobiographical memory (hippocampus)
- Rational thinking, psychological resilience, and natural human curiosity have been shown to be severely impaired
- Without curiosity, we might become stagnant, complacent, less open to new ideas and experiences
- He infers this was all designed to alter brain function and “mind control”



References on the Vulnerable hippocampus

- The functional and structural changes in the hippocampus of COVID-19 patients Nouraeinejad A Acta Neurologica Belgica 2023
- Larger gray matter volumes in neuropsychiatric long-COVID syndrome Besteher B Psychiatry Research 2022
- SARS-CoV-2 spike protein induces cognitive deficit and anxiety-like behavior in mouse via non-cell autonomous hippocampal neuronal death Oh, J et al Nature Scientific reports March 2022
- The functional and structural changes in the hippocampus of COVID-19 patients Nouraeinejad A Acta Neurologica Belgica 2023
- Mild respiratory COVID can cause multi-lineage neural cell and myelin dysregulation Monje M et al Cell July 2022
- Dysregulation of brain and choroid plexus cell types in severe COVID-19. Yang AC et al Nature (2021)
- COVID-19 induces neuroinflammation and loss of hippocampal neurogenesis Klein R et al Res Squ October 2021
- Neuroinflammation After COVID-19 With Persistent Depressive and Cognitive Symptoms Braga J et al JAMA Psychiatry May 2023

References on the Vulnerable Hippocampus

- Changes in Brain Activation Pattern During Working Memory Tasks in People With Post-COVID Condition and Persistent Neuropsychiatric Symptoms Chang L Neurology April 2023
- SARS-CoV-2 invades cognitive centers of the brain and induces Alzheimer's-like neuropathology Shen W et al bioRxIV Sept 2022
- Cortical Grey matter volume depletion links to neurological sequelae in post COVID-19 “long haulers” Rothstein T BMC Neurology
- Accelerated Brain Volume Loss Caused by Anti- β -Amyloid Drugs: A Systematic Review and Meta-analysis Alves F et al Neurology 2023
- Post-traumatic stress symptoms in COVID-19 survivors: a self-report and brain imaging follow-up study. Tu Y et al Mol Psychiatry 2021

References on the Vulnerable Hippocampus

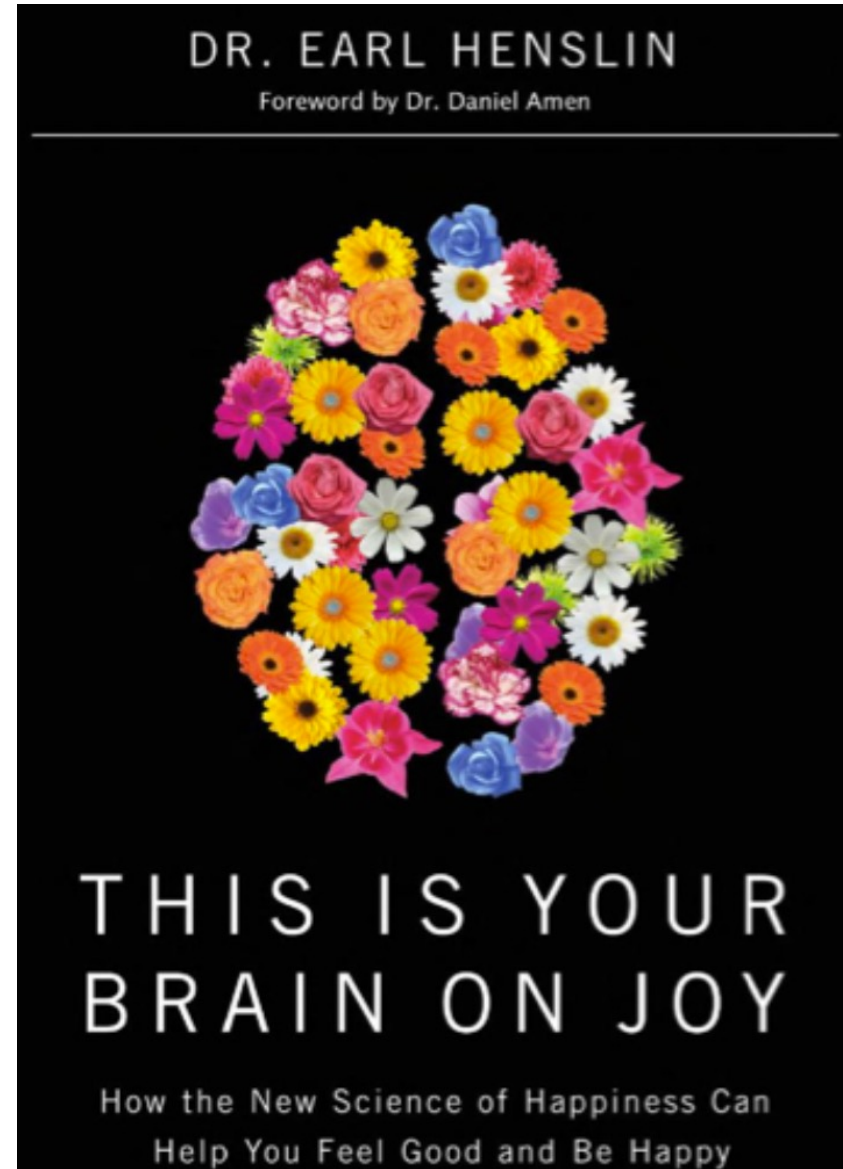
- “SARS-CoV-2 Is Associated with Changes in Brain Structure in UK Biobank.” Fidel Alfaro-Almagro Nature 2022
- Gray Matter Changes Following Mild COVID-19: An MR Morphometric Study in Healthy Young People Perlaki G et al JMRI August 23, 2023
- One-year trajectory of cognitive changes in older survivors of COVID-19 in Wuhan, China: a longitudinal cohort study. Liu YH et al JAMA Neurol. 2022
- Cerebral blood flow in patients recovered from mild COVID-19 Sen S J of Neuroimaging June 2023
- Susceptibility-Weighted Magnetic Resonance Imaging Highlights Brain Alterations in COVID Recovered Patients Mishra S et al medRxiv preprint Nov 2022
- Gray Matter Thickness and Subcortical Nuclear Volume in Men After SARS-CoV-2 Omicron Infection. Du Y et al JAMA Network Open 2023

References on the Vulnerable Hippocampus

- Cerebral micro-structural changes in COVID-19 patients—an MRI-based 3-month follow-up study Lu Y et al EClinicalMedicine 2020
- COVID-19 induces neuroinflammation and loss of hippocampal neurogenesis Klein R et al Res Square 2021
- COVID-19 causes neuronal degeneration and reduces neurogenesis in human hippocampus. Bayat AH 2022 Apoptosis
- Mild respiratory COVID can cause multi-lineage neural cell and myelin dysregulation. Fernandez-Castaneda A et al Cell 2022
- COVID-19 induces CNS cytokine expression and loss of hippocampal neurogenesis Soung A et al Brain 2022

How Do We Treat Long COVID Neurological Injuries

- Case by Case
- Address retained spike protein, reduce inflammation and oxidative stress, enhance immune function, upregulate autophagy, address micro-clotting, mitochondrial dysfunction, mast cell stabilization and gut health
- Diet/ Intermittent fasting/Non-GMO diet
- Exercise/ movement/ strength training
- Neuroplasticity training
- Vagal nerve retraining
- Targeted supplements
- Never ever lose hope, Love and Joy

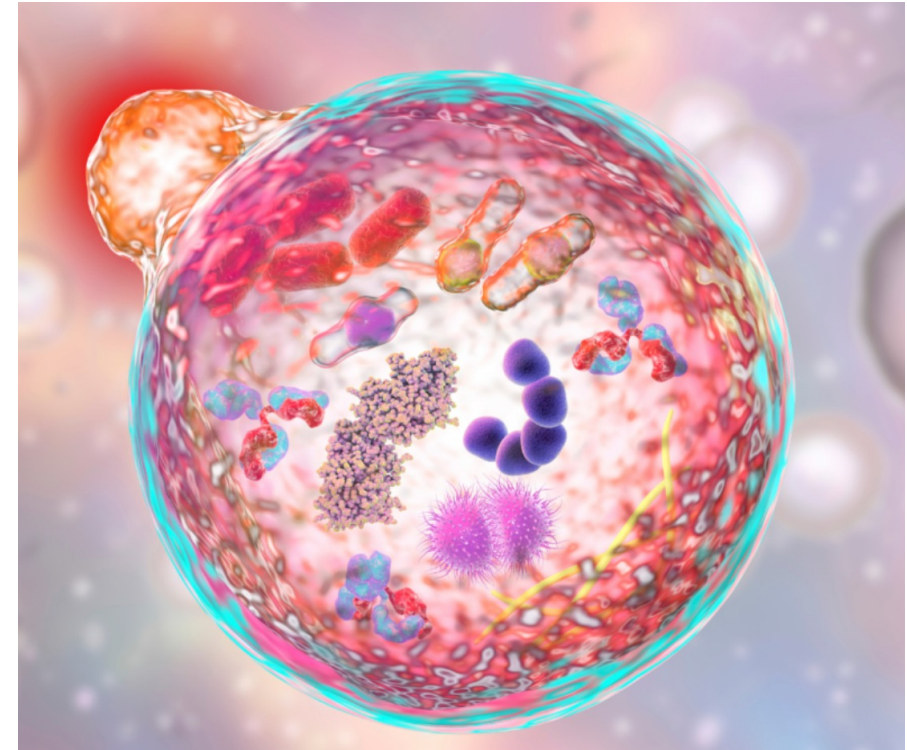


Autophagy is a Promising Strategy for Treating Neurodegenerative Disease

- “If we started IF in mid-life, we would dramatically delay the onset of neurodegenerative disease and slow down aging” (Mark Mattson PhD)
- **Neurons are particularly vulnerable to malfunction of autophagy** which helps enhance the removal of prions like tau, amyloid, alpha synuclein, etc.
- Numerous studies suggest S1 drives senescence

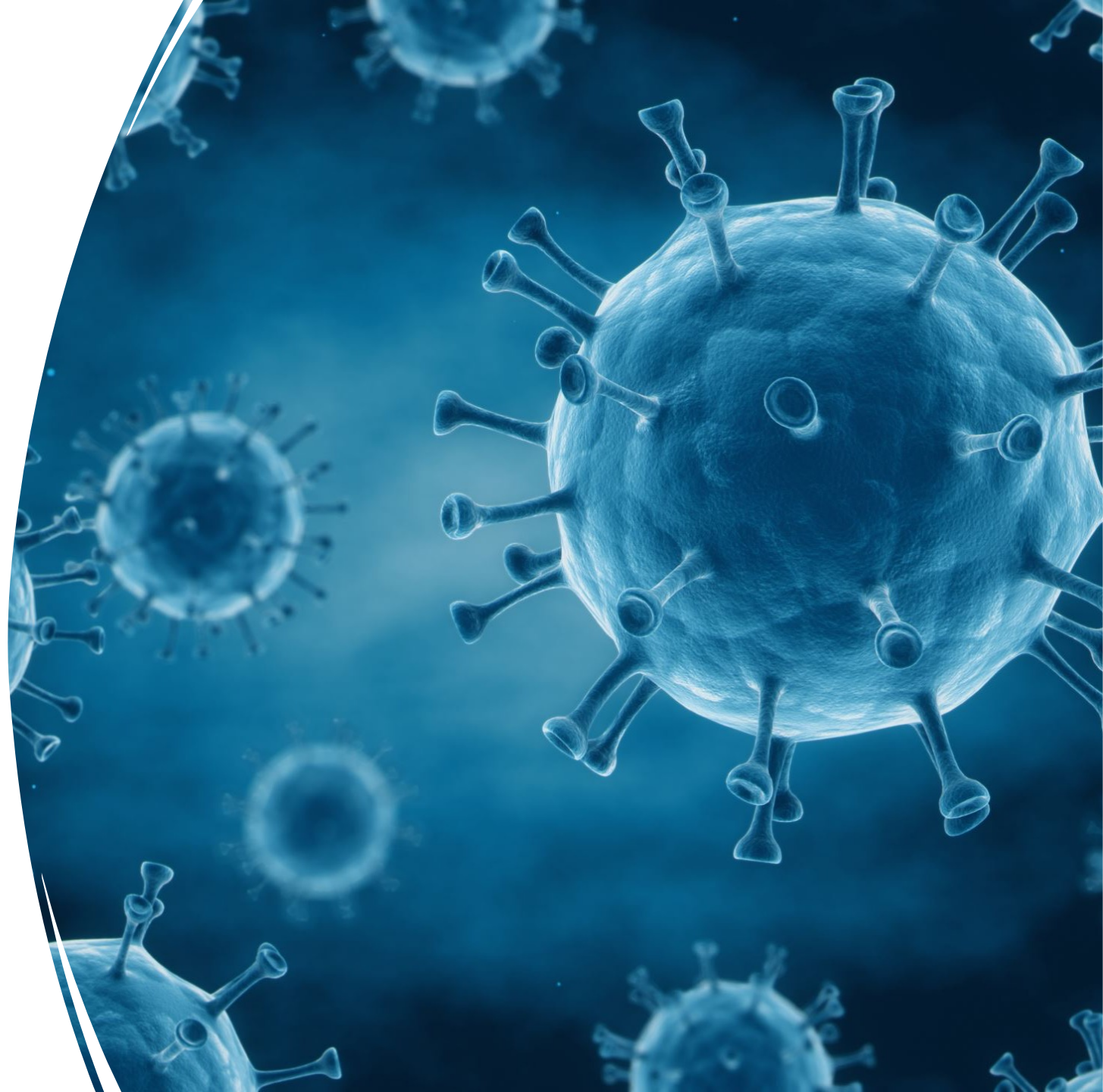
Autophagy in Neurodegenerative Diseases: A Hunter for Aggregates
Park H et al International J of Molecular Science 2020

Manipulation of autophagy by SARS-CoV-2 proteins. Koepke L et al
Autophagy. 2021



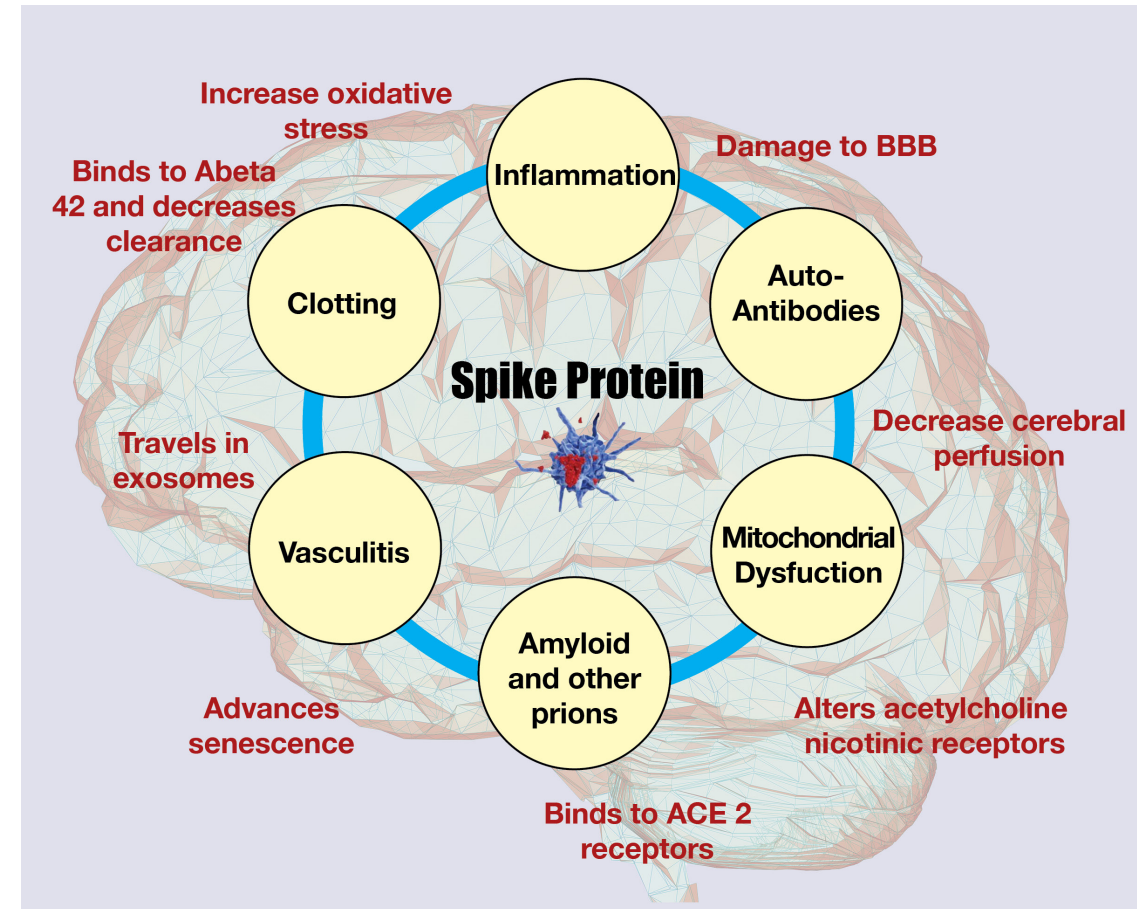
What Causes Neuro-COVID and Post Vaccine Injury?

Multiple Mechanisms of
Harm



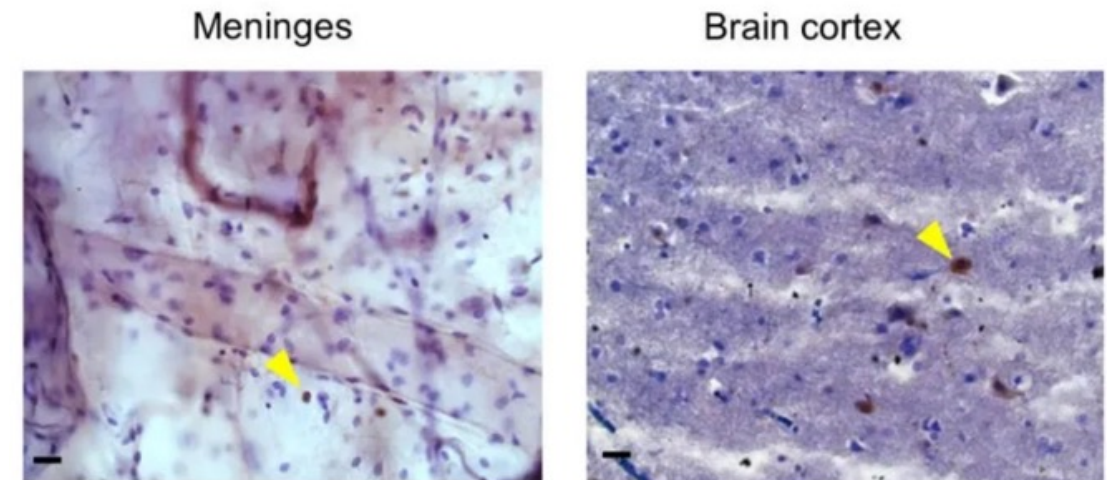
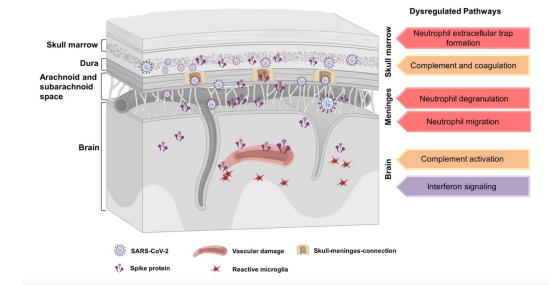
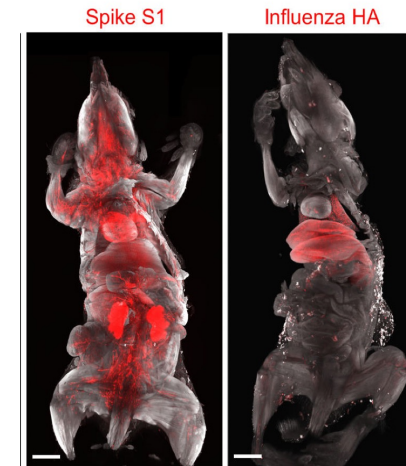
Spikeopathy Mechanisms of Injury

- High levels of inflammation
- Alteration of the innate and adaptive immune system
- High levels of Oxidative Stress
- Damage to the BBB
- Autoimmune/molecular mimicry
- Prion's forming
- Micro-clotting / vascular/ low CBF
- Neurotoxins affecting the cholinergic system
- Mast Cell Activation
- Mitochondrial dysfunction
- Advances Senescence and Apoptosis
- Viral Reactivation
- Low Serotonin
- Gut Dysbiosis
- Damage to the Vagus nerve
- Neurons fusing



We Have Only Begun to See Long-Term Effects of Spike Protein Linger

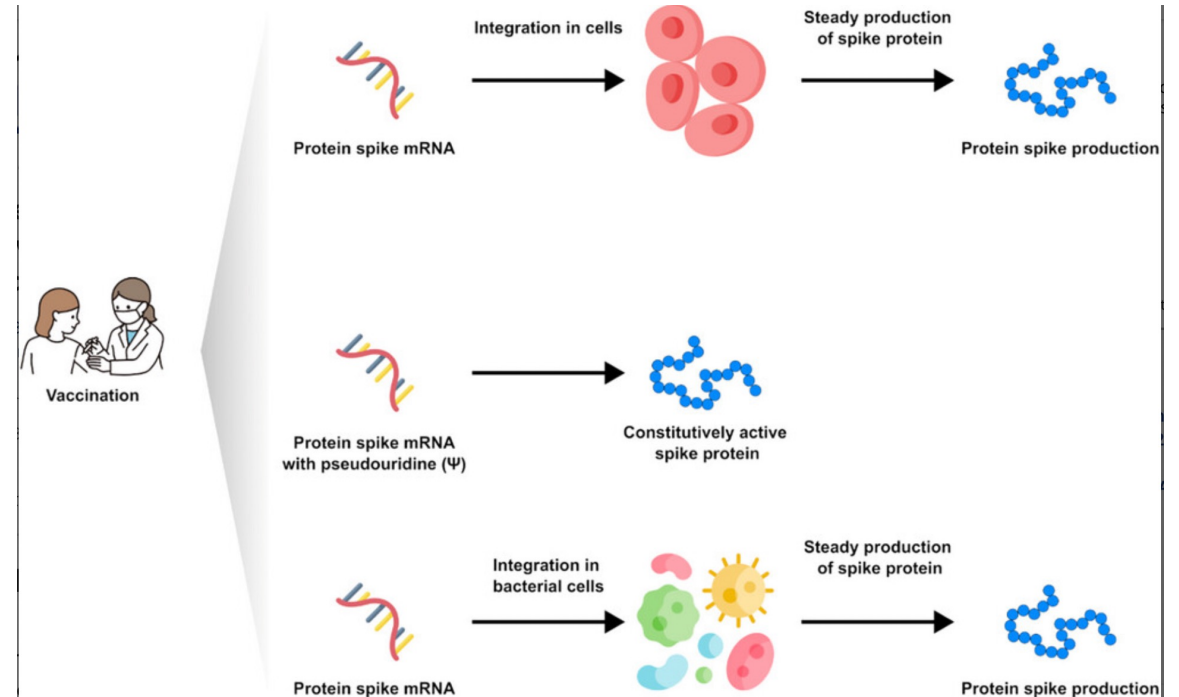
- IV injection of spike and then optical transparency clearing and imaging using light-sheet microscopy (all organs took up S1)
- S1 protein accumulated in the skull marrow and in the long bones, the tibia, and femur, indicating it reaches bone marrow niches
- Spike protein may linger for a long time
- It was also found in the meninges and brain cortex in a subset of individuals who recovered from COVID-19 and died due to non-COVID-related causes
- In the brains, only spike, no nucleocapsid and all were PCR negative



Spike Protein Lingers for up to 6 months Only in the Vaccinated

- A study by Brogna C et al 8-2023, found persistence of spike protein in the blood of 50% people who received mRNA COVID-19 vaccines at up to six months after vaccination

Detection of recombinant Spike protein in the blood of individuals vaccinated against SARS-CoV-2: Possible molecular mechanisms Brogna C et al Journal of Proteomics Clinical Applications August 31 2023



Most Common Things We See Today

- Dysautonomia/POTS/Exercise Intolerance/HR variability/Post Exertional Malaise
- Fatigue
- Brain Fog and Cognitive Decline
- Numbness/Neuropathy/ Muscle pain/Spasms/ Weakness
- Movement disorders
- Weakness
- Dizziness
- Headaches
- New onset or worsening Neurodegenerative Disease and or Autoimmune disease
- "Functional Neurological Disorder"

Brain fog and Cognitive disorders

Cognitive impairment (CI) is regarded as one of the most disabling long-term consequences of LC and PVI

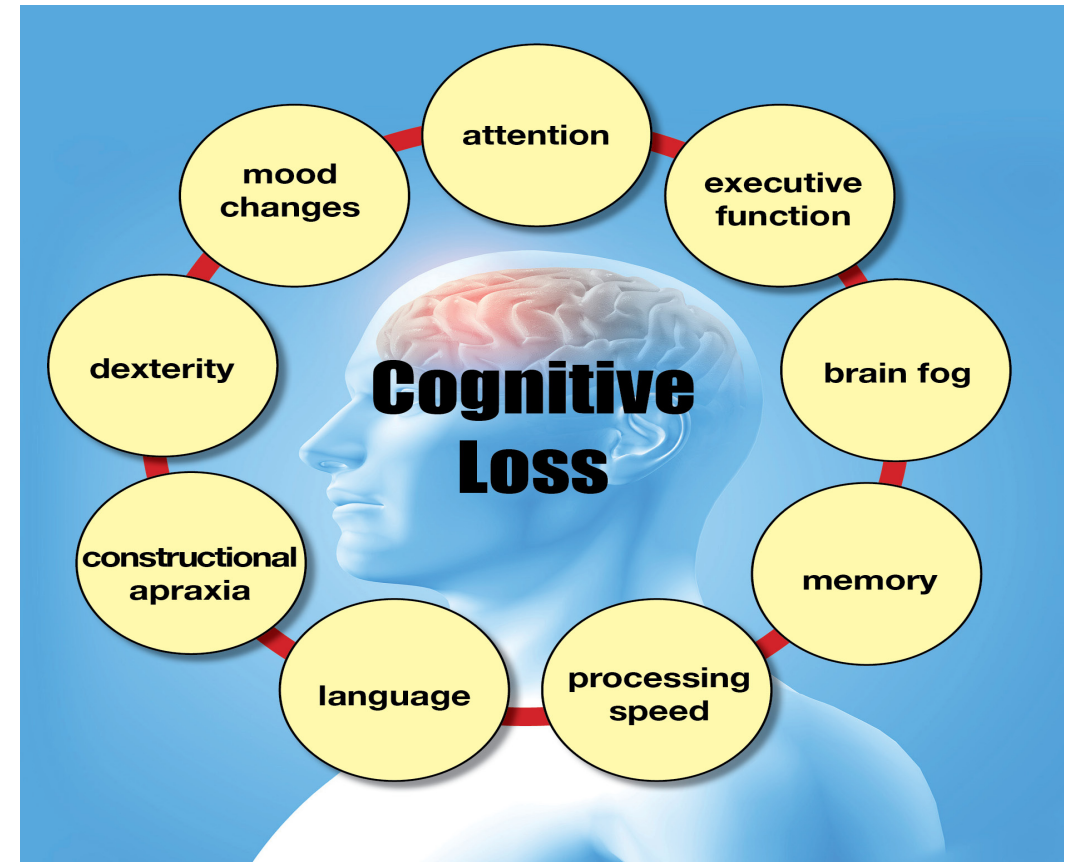


The prevalence of Cognitive COVID, ranges from 12% to 80% across studies

- Symptoms include deficits in attention, executive function, memory, language, and learning (Taquet M) (Miskowiak KW)
- Pronounced cognitive slowing in people with PCC (Zhao S 2024)
- More than 50% of long-COVID patients failed to improve 1.5 years after their initial diagnosis (Agergaard J)

Long-term Prognosis at 1.5 years after Infection with Wild-type strain of SARS-CoV-2 and Alpha, Delta, as well as Omicron Variants Agergaard J et al Journal of Infectious Disease October 2023

Long COVID is associated with severe cognitive slowing: a multicentre cross-sectional study Zhao L et al The Lancet Jan 2024

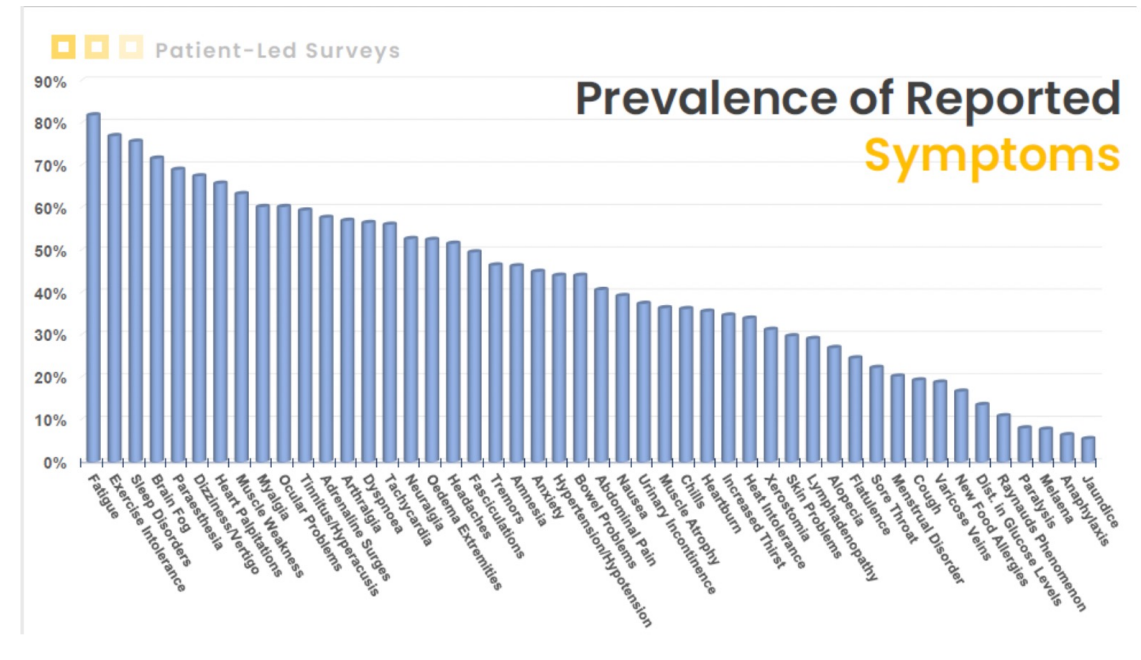


Brain Fog and Cognitive Impairment in Over 70% of Vaccine Injured

- 50% were no better a year post shot

[React19 Research: Persistent Symptoms Survey #2 - React19](#)

Cognitive deficits and memory impairments after COVID-19 vaccination
Chaurasia, A et al Brain Behav Immun Health. 2022



Be Careful Out There

- NYT reported in 2021 that MVA and deaths — began surging
- The U.S. Secretary of Transportation Pete Buttigieg announced in January 2023 it a “national crisis of traffic deaths”
- Could this be because drivers are not perceiving & processing information the way that they used to ?
- An astounding 45% of subjects had cognitive impairment 11 months post infection but were not reporting memory problems (Golderisi et al)

Cognitive impairment after recovery from COVID-19: Frequency, profile, and relationships with clinical and laboratory indices Golderisi S et al European Neuropsychopharmacology Feb 2024



Our Mental Sticky Note Is Lost

- Medical students with no cognitive complaints were studied after recovery from mild COVID-19 (avg age 20 y/o).
- **Auditory working memory** performance was significantly impaired in patients compared with controls
- AWM is a virtual 'workspace' in our mind & is crucial for learning, solving problems, keeping track of info until we need to use it
- Academic performance and day to day function will be affected

Preferential Impairment of Auditory Working Memory in Long COVID: An Observational Study of Undergraduate Medical Students Manna S et al Cureus Jan 2024



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The eighth COVID-19 wave is here. Could catching it trigger Alzheimer's, Parkinson's or autoimmune disorders?

By [Catherine Taylor](#)

Posted Tue 21 Nov 2023 at 12:00pm, updated Tue 21 Nov 2023 at 1:28pm



Is Long COVID Related to Alzheimer's?

- Studies point to a concerning risk of Alzheimer's 6-12 months post infection (Taquet M) (Liu YH) (Wang L) (Davis H) (Xu E) (Douadad G) (Zhao S)
- Even mild covid can lead to an overall reduction in the size of the brain equivalent to 10 years of aging (UK Biobank 2022)

NEWS

Alzheimer's and Long Covid, could they be related?

by: [Brooklynn Norris](#), [Stuart Price](#)

Posted: Aug 13, 2022 / 02:23 PM CDT

Updated: Aug 13, 2022 / 02:23 PM CDT

PRESS RELEASE

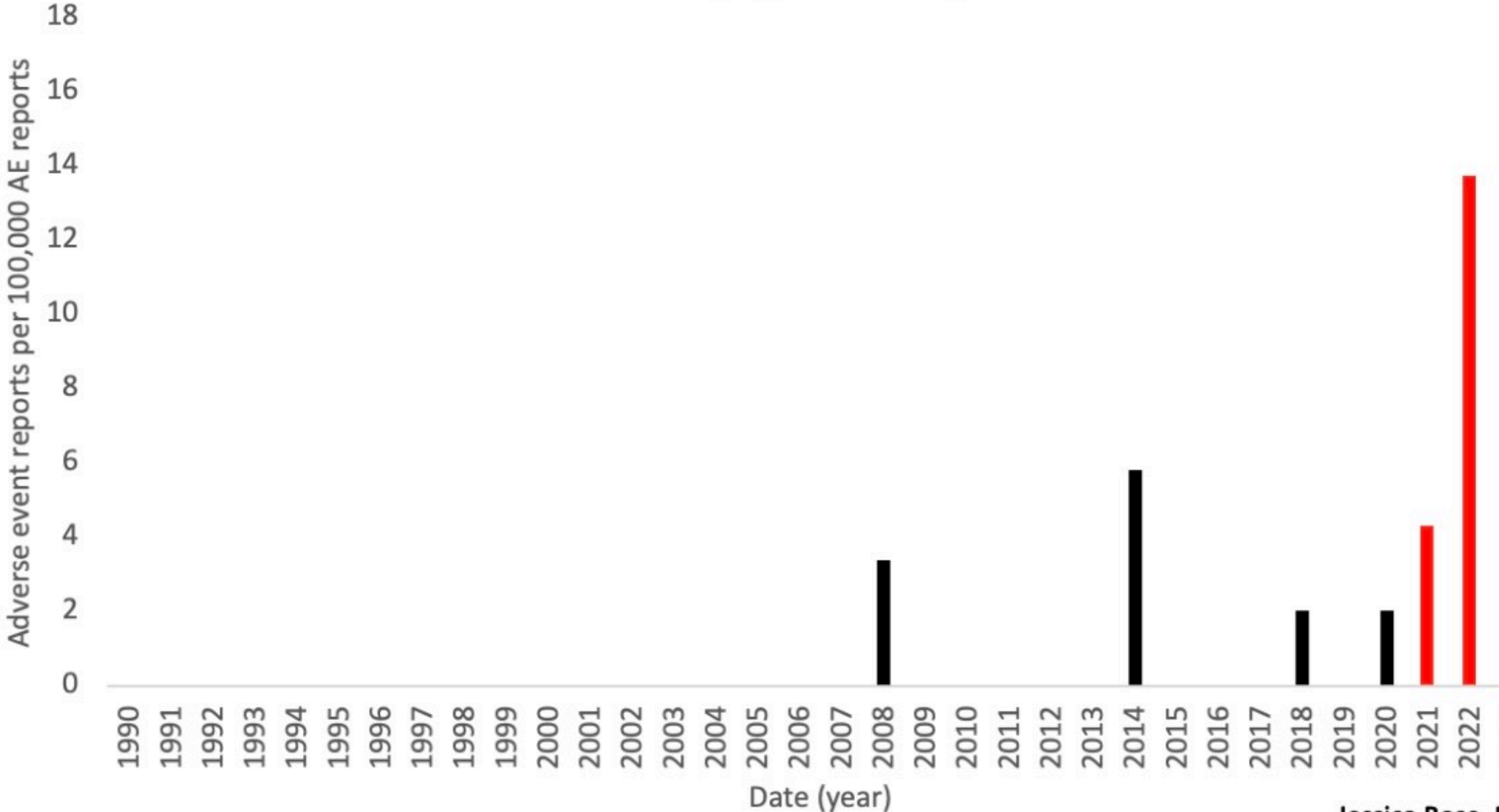
COVID-19 Associated with Long-Term Cognitive Dysfunction, Acceleration of Alzheimer's Symptoms

Press release from
Alzheimer's Association
International Conference
(AAIC®) 2021

- Cumulative data points to disturbing trends showing COVID-19 infections leading to lasting cognitive impairment and even Alzheimer's symptoms
- Alzheimer's Association International Conference (AAIC) report the presence of brain fog was proposed as a high risk of having AD

Annual VAERS Alzheimer's reports

Source: <https://vaers.hhs.gov>



How One Crisis Worsens Another

- A recent publication, observed a substantial increase in spike protein post COVID whenever amyloid plaques are present (primate model)
- Spike proteins and the pathological proteins fuel neuroinflammation
- They found memory centers particularly vulnerable (entorhinal cortex and the hippocampus)
- *“I believe we are going to see, in a few decades, an epidemic of early demented people, especially the ones that had COVID-19 several times. I also believe that older people who accumulate amyloid plaques in normal aging will shift to dementia and Alzheimer's much faster than the normal progression we often observe”. Dr Danielle Beckman*



Fiona Phillips, 62, blames her early dementia diagnosis on 11 years of 3am starts for breakfast television as the former GMTV host reveals her symptoms might be slowed by a groundbreaking drug trial

By Katie Hind Consultant Editor Showbusiness
00:03 02 Dec 2023, updated 07:21 02 Dec 2023



Biomarkers for Alzheimer's

- Ratio of AB 42 to 40 : Higher risk of AD: < 0.160 **AD Detect**
- **APO E genotype** 4 indicates the highest risk
- **pTau-181**: reference range: 0-55 years: 0.00–0.95 pg/mL and >55 years: 0.00–0.97 pg/mL
- p tau-217 (ALZPath test) as good as PET/CSF (Ashton N 2024)
- GFAP (glial fibrillary acidic protein)

Bollinger, J, et al. Validation of plasma amyloid- β 42/40 for detecting Alzheimer disease amyloid plaques. *Neurology* Dec 2021

Prediction of Longitudinal Cognitive Decline in Preclinical Alzheimer Disease Using Plasma Biomarkers Mattson-Calgren N *JAMA Neurology* 2023

Diagnostic Accuracy of a Plasma Phosphorylated Tau 217 Immunoassay for Alzheimer Disease Pathology Ashton N et al *JAMA Neurology* Jan 2024

What if You Knew Alzheimer's Was Coming for You?

Simple blood tests may soon be able to deliver alarming news about your cognitive health.

AD Biomarkers Predict future Decline

- Two blood-based serum biomarkers, $A\beta_{42/40}$ ratio and phosphorylated tau181 were followed in middle aged women over 14 years.
- Higher levels of p-tau 181 were linked to accelerated cognitive decline and, lower AB 42/40 levels were associated with faster cognitive decline

Blood-based biomarkers for Alzheimer's disease and cognitive function from mid- to late life Wang X et al Alzheimer's and Dementia J of Alzheimer's Disease Dec 2023

Midlife blood test may predict cognitive decline, Alzheimer's in later life



December 21, 2023

Contact:
[Kim North Shine](#)

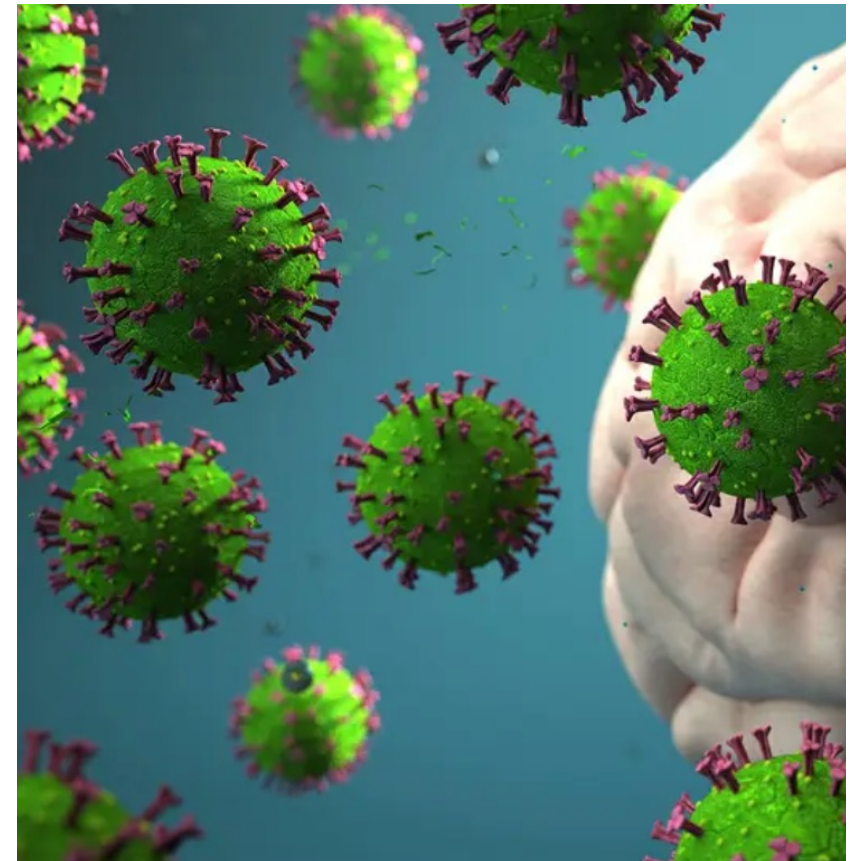
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Long-Term Brain Injury Markers in COVID-19 Survivors: A Looming Shadow of Neurological Peril

- Studies reveal a disturbing pattern: elevated levels of brain injury markers **tau**, **GFAP** (Glial fibrillary acidic protein) and **NfL** (**Neurofilament light chain**) remained present in the blood of a significant portion of patients (Benedict M)
- Multiple other studies have shown the same but up to a year (Boutajangout A) (Frontera JA) (Bark L) (Sun B)

Para-infectious brain injury in COVID-19 persists at follow-up despite attenuated cytokine and autoantibody responses Michael BD et al Nature Communications (2023)

Post-COVID cognitive deficits at one year are global and associated with elevated brain injury markers and grey matter volume reduction: national prospective study Benedict M et al Research Square 2024



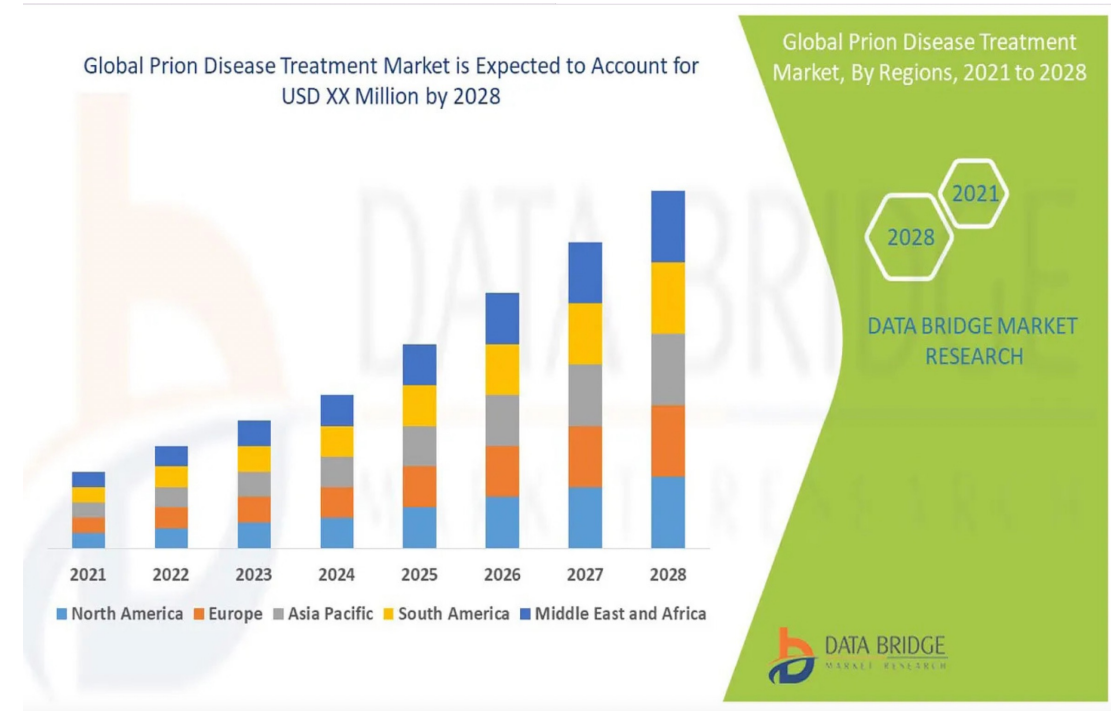
Prion Involvement in Long COVID

Is This Why Some Patients Are Not Getting Better?

Big Pharma is Planning for a 300% Global Rise in Prion Disease

- Brain fog, confusion, cognition and memory issues, etc., may be associated with the symptomology, onset, and development of human prion disease (PrD) (Stefano et al)
- S1 drives prions (Nystrom S) (Zha0) (Larrsen et al)

Potential Prion Involvement in Long COVID-19 Neuropathology, Including Behavior
Stefano G et al Cell Mol Neurobiol. 2023




Case # 1

- 48 y/o PhD who developed severe brain fog, insomnia, fatigue & GI symptoms after COVID in the spring of 2020. Her symptoms dramatically worsened after shot 1 & 2 (Dec 2020 and Jan 2021) & after shot 2 she developed erythromelagia, POTS and severe PEM. She began working with the Patterson group in 2021 but was not helped. Statin caused high LFT's.
- I saw first saw her in Spring 2022. Exam muscle loss in hands/normal EMG / Routine Lab negative. COVID spike antibodies greater than 25000, AD detect .17 Micro-clot 3.5/4 MRI Brain normal but NQ with high levels of neuroinflammation
- We instituted the FLCCC recovery protocol + The Bredesen Protocol



NeuroQuant Is the Gold Standard for MRI Brain Volume

- Values in red shading indicate that the reported value brain tissue: less than the 5th percentile for normative data of healthy individuals and
- Values in blue shading indicate that the reported value brain tissue: greater than the 95th percentile for normative data of healthy individuals
- Send a message <https://www.cortechs.ai/contact/> to ask for a Coretech MRI near you



NeuroQuant®
Triage Brain Atrophy Report

HI and EI
-
Preferred contact info

Version 3.0.0

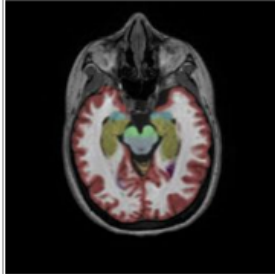
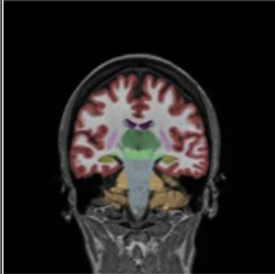
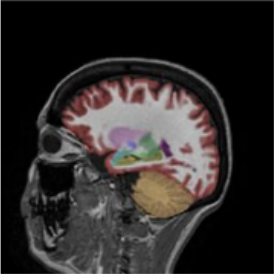
PATIENT INFORMATION

Patient ID: ENV3850671	Patient Name:	Sex: F	Age: 47	Referring Physician: GAZDA, SUZANNE
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SCAN INFORMATION


Scan Date: 2022-04-14	Accession Number: PLA9918876
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MORPHOMETRY RESULTS

Structure	Total Volume (cm ³)	Percentile			Cortical Brain Regions	Percentiles		
		Left	Right	Total		Left	Right	Total
Intracranial Volume	1406	-			Frontal Lobes	49	49	49
Whole Brain	1155	82			Superior Frontal	50	68	75
Forebrain Parenchyma	996	70			Middle Frontal	31	1	6
Total Volumes					Inferior Frontal	59	68	62
Cerebral White Matter	90	74	84	Lateral Orbitofrontal	80	79	81	
Cortical Gray Matter	31	34	32	Medial Orbitofrontal	41	31	33	
Ventricles	18	14	15	Paracentral	99	93	98	
Cerebral WM Hypointensities*	55	71	74	Primary Motor	20	64	39	
Subcortical Structures					Parietal Lobes	53	35	44
Cerebellar White Matter	99	99	99	Primary Sensory	13	63	46	
Cerebellar Gray Matter	44	64	55	Medial Parietal	33	42	36	
Brainstem	-	-	63	Superior Parietal	91	61	69	
Thalamus	99	99	99	Inferior Parietal	41	2	8	
Ventral Diencephalon	90	91	92	Supramarginal	76	31	57	
Basal Ganglia				Occipital Lobes	51	27	37	
Putamen	99	99	99	Medial Occipital	63	74	80	
Caudate	5	6	5	Lateral Occipital	27	9	13	
Nucleus Accumbens	13	50	26	Temporal Lobes	9	45	21	
Pallidum	2	1	1	Transverse Temporal + Superior Temporal	9	26	14	
Cingulate	87	82	85	Posterior Superior Temporal Sulcus	1	62	73	
Anterior Cingulate	69	38	50	Middle Temporal	10	53	24	
Posterior Cingulate	86	92	90	Inferior Temporal	11	10	8	
Isthmus Cingulate	79	95	90	Fusiform	10	65	34	
				Parahippocampal	59	65	63	
				Entorhinal Cortex	27	19	20	
				Temporal Pole	56	64	61	
				Amygdala	77	99	98	
				Hippocampus	99	99	99	

*White matter hypointensities are abnormally low signal intensity regions within white matter as observed on a T1-weighted MRI scan.



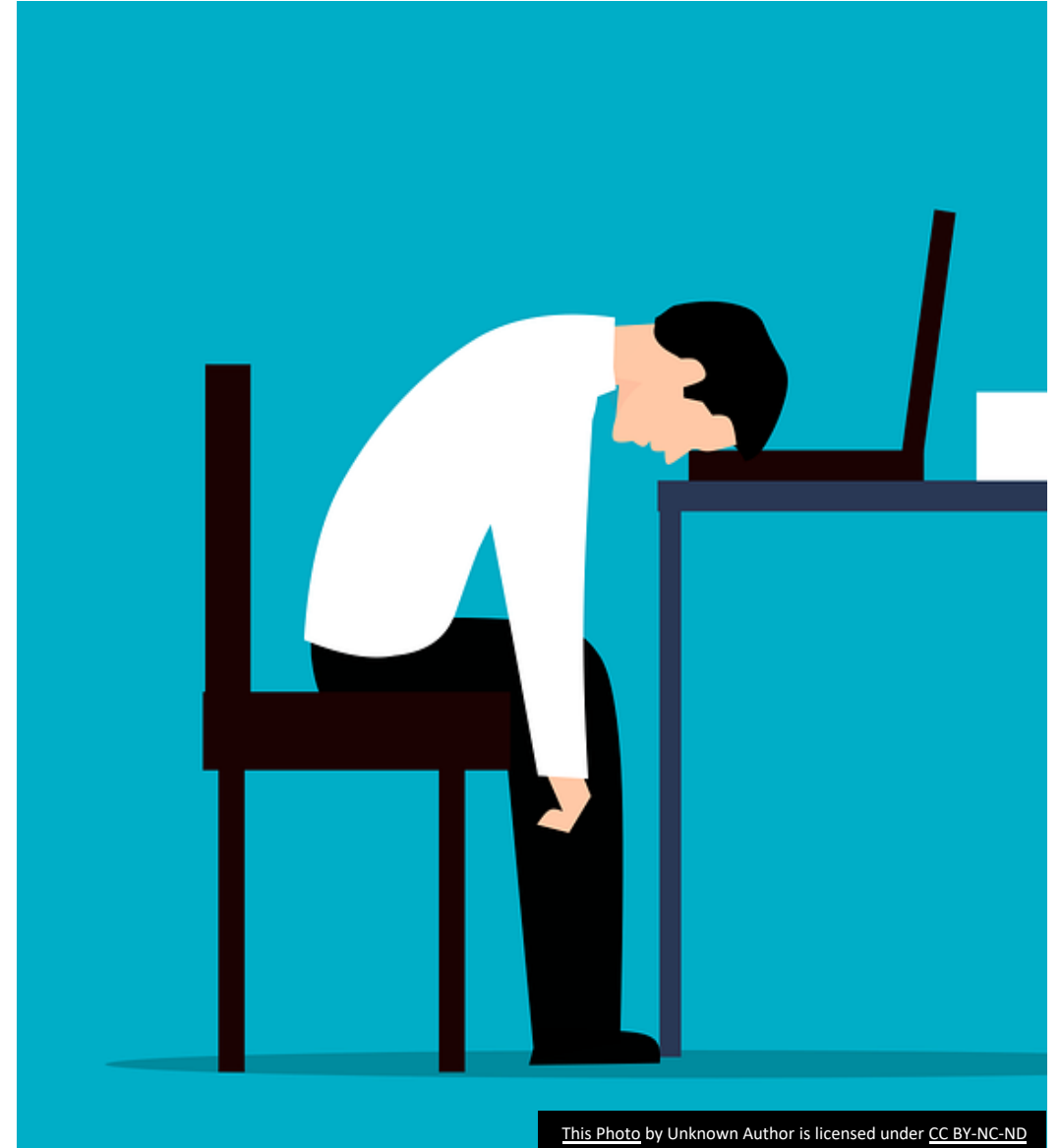
What Worked

- **Intermittent fasting and anti-inflammatory diet , Bredesen and FLCCC protocol**
- **Gut healing**
- **Optimizing Sleep** (Melatonin/L Theanine)
- **Slow return to exercise (yoga, stretching, vibration plates)**
Now walks 3-4 miles and adding strength training) Stretching and low-level resistance exercises were used at first since aerobic exercise worsened PEM
- **Organic green tea q day**
- **Mindfulness and behavioral modification, strong social support**
- **Vagal nerve retraining (breath work, meditation)**
- **Optimized hormones**
- **Neuroplasticity training w Brain HQ**
- **Optimized her hearing**
- **Manual lymphatic drainage**
- **Hope**
- **LDN**
- **IVM X first 6 months**
- **Montelukast 10mg at hs**
- **Vit D3/K2**
- **CDP Choline**
- **Fluvoxamine low dose**
- **Nattokinase, 81 mg ASA**
- **Methylene Blue troche w PBM**
- **Trans-resveratrol**
- **Omega 3**
- **Augmented NAC**
- **Neuroprotect**
- **Nadovim**
- **Acetylcarnitine 1500 mg / day**
- **Vit E**
- **Cardio Miracle**
- **Creavitalis® 4 grams/ day**
- **Oxytocin**
- **Plasmalogens**
- **Vielight 5 X/week**

What Was Not Helpful

- Maraviroc, Statin, Tolovid, Paxlovid
- Guanfacine+NAC (caused sedation, dizziness, decreased BP) and at DC caused rise in BP and extreme nervousness “Tired and wired”
- Nicotine patch
- Ketotifen (too drowsy)

Clinical experience with the α_2A -adrenoceptor agonist, guanfacine, and N-acetylcysteine for the treatment of cognitive deficits in “Long-COVID19” Feshariki-Zehh A et al Neuroimmunology Reports Dec 2022



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The Nicotine Effect

- Farsalinos et al. (2020) examined and identified neurotoxin sequences in the S1 RBD similar to snake venom that interact with nACh receptors and block the cholinergic system
- The nAChRs are the principal structures of central and autonomic neuromodulation and very important for sleep, cognition, skeletal muscle and many other things
- Nicotine patch was helpful for many LC symptoms (Letzke M)

What is the impact of nicotine on the Post-COVID-19 syndrome - a severe impairment of acetylcholine-orchestrated neuromodulation: A case series Letzke M Research Sq 2022

Editorial: nicotine and SARS-CoV-2: COVID-19 may be a disease of the nicotinic cholinergic system: Farsalinos K et al Toxicology Report 2020

What is the impact of nicotine on the Post-COVID-19 syndrome - a severe impairment of acetylcholine-orchestrated neuromodulation: A case series Letzke M et al Research Square 2022

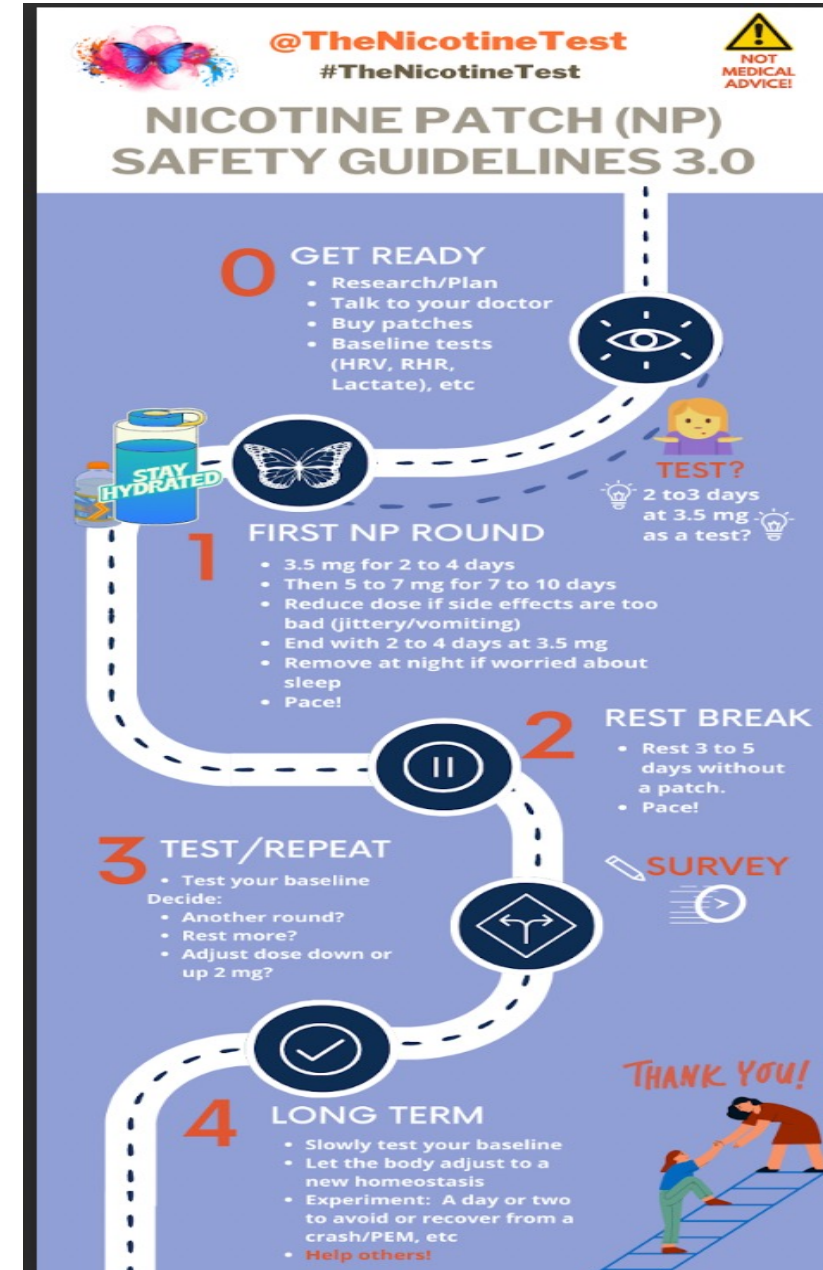


Nicotine

- <https://linktr.ee/thenicotinetest> Is a Great resource
- Nicotine has 30x the affinity for the nicotinic acetylcholine receptors (nAChR) than acetylcholine. The continuous dose of nicotine thereby liberates/blocks S1 from the receptor
- "Herx" is not uncommon
- The Mind Study is the longest study using Nicotine for Memory finding no increased risk of cancer or addiction

<http://mindstudy.org/faq>

Renegade Research: The Nicotine Test : Over 6000 members on Facebook





Ways to Increase Acetylcholine

Donepezil ,Rivastigmine, Galantamine, Mestinon

Vagal Nerve Stimulation (cold showers, breath work, yoga, Gupta protocol, Annie Hopper protocol)

Choline

Bacopa may block acetylcholine breakdown and increase the activity of the enzyme that produces acetylcholine

Huperzine A is described as a strong acetylcholinesterase inhibitor.

Caffeine might increase acetylcholine in the brain, especially in the “memory hub” – the hippocampus

Ginkgo extract increased acetylcholine in the brain of rats

Luteolin enhances cholinergic signaling and acetylcholine levels in brain cells

EGCG improved cholinergic signaling and protected the brain in animal studies

Curcuminoids are hypothesized to be strong inhibitors of acetylcholinesterase

Rosemary, Grape Seed Extract, Cinnamon , Propolis, Ginseng, Licorice, Sulphoraphane

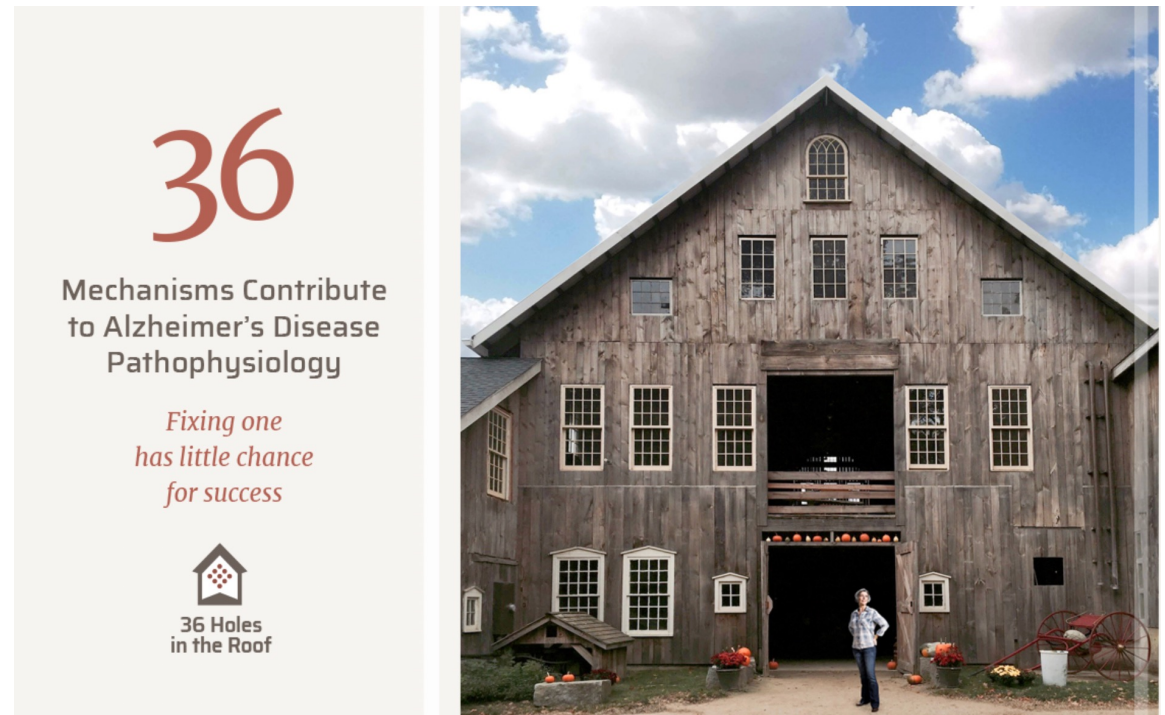
<https://selfhacked.com/blog/cholinergic-activity-natural-boosters/>

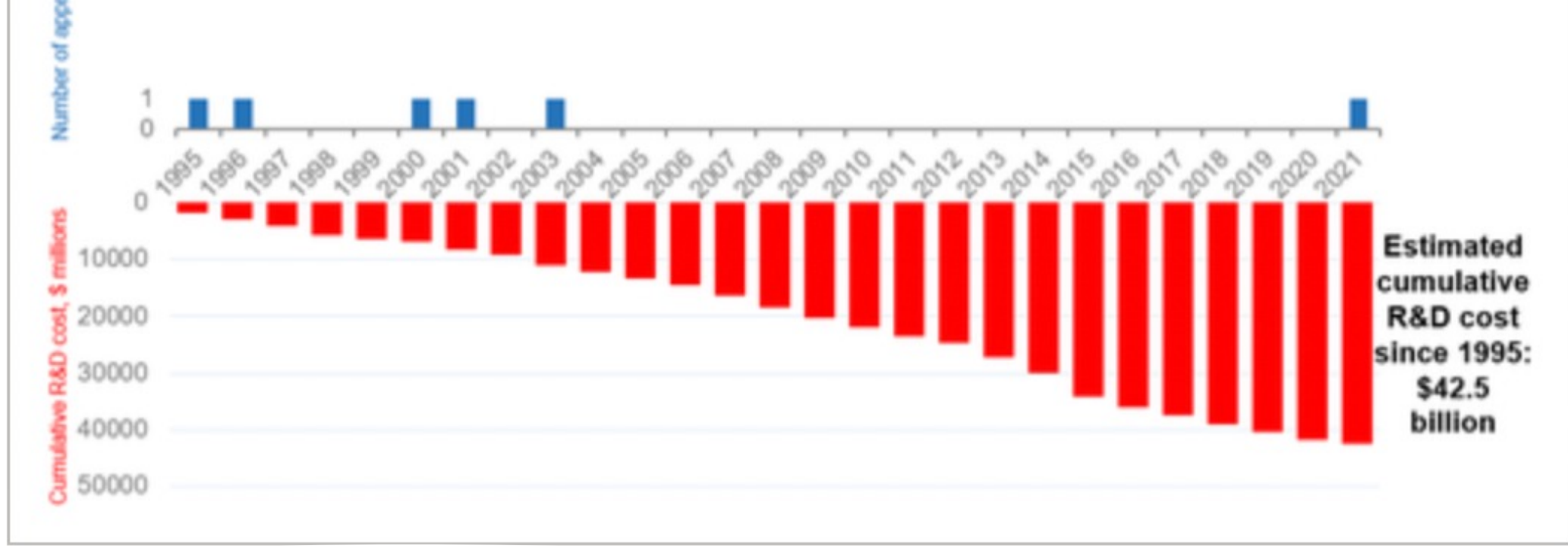
The Bredesen Protocol

Restoring Balance to the Brain by Addressing Multiple Mechanisms

- Neuropathology with AD begins years before presentation
- In their pilot study, 74% of patients with showed improvement or stabilization of cognition
- They had a 145% improvement in risk factors, and an 80% improvement in quality of life compared to the control group
- Alzheimer's is treatable and preventable

ReCODE: A Personalized, Targeted, Multi-Factorial Therapeutic Program for Reversal of Cognitive Decline Bredesen D et al Biomedicines September 2021





Verses The Pharma Approach

- Amyloid drugs have failed miserably
- Amyloid is not the problem
- The number of people living with the disease doubles every 5 years beyond age 65. This number is projected to nearly triple to 14 million people by 2060 (projections BEFORE COVID)

The costs of developing treatments for Alzheimer's disease: A retrospective exploration Cummings J et al J of Alzheimer's Association 2021

The Bredesen Seven For All

- **Exercise** upregulates autophagy, increases cerebral blood flow and brain-derived-neurotrophic factor (BDNF), helps to improve oxygenation, the BBB, improves sleep, reduce overall stress, optimize BMI (body mass index), & improves insulin sensitivity
- **Sleep** is vital for memory consolidation and optimal functioning of the glymphatic system to clear cerebral toxins, including amyloid-beta and promotes metabolic health, reduces inflammation, and up-regulates the immune system.
- **Stress** (mindfulness, meditation, breath work, Yoga, on-line programs)



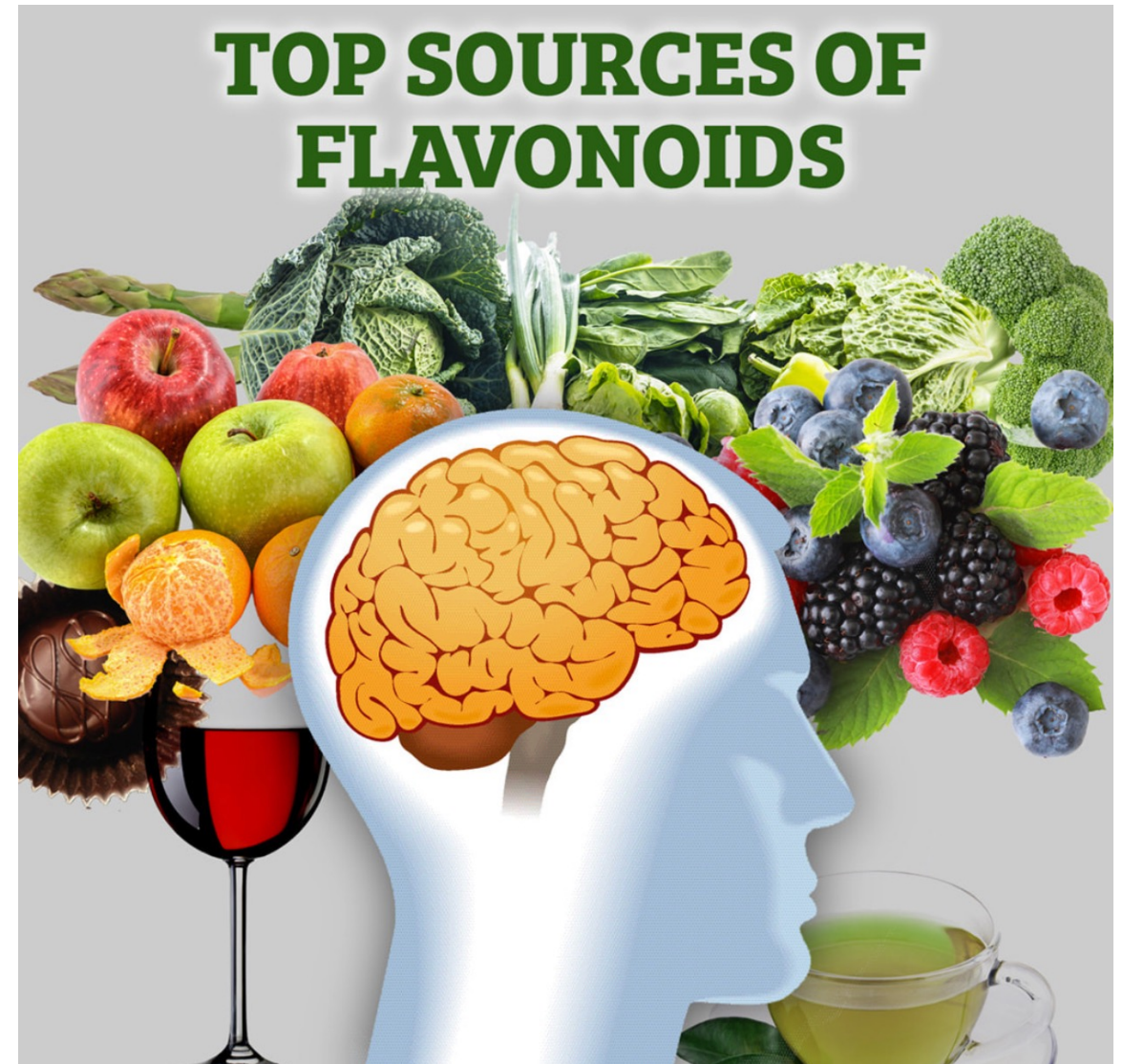
Food Is Medicine

- Higher consumption of ultra-processed foods was associated with a higher rate of global and executive function decline after a follow-up of eight years. (Goncalvas N)
- Ultra-processed food, is called “thoughtless food” because of its potentially negative effect on our thinking abilities.
- Other studies have concluded higher flavonoid use can reduce the risk of dementia

Association Between Consumption of Ultraprocessed Foods and Cognitive Decline Goncalvas N et al JAMA Neurology Dec 2022

Long-term Dietary Flavonoid Intake and Subjective Cognitive Decline in US Men and Women. Neurology Jul 2021

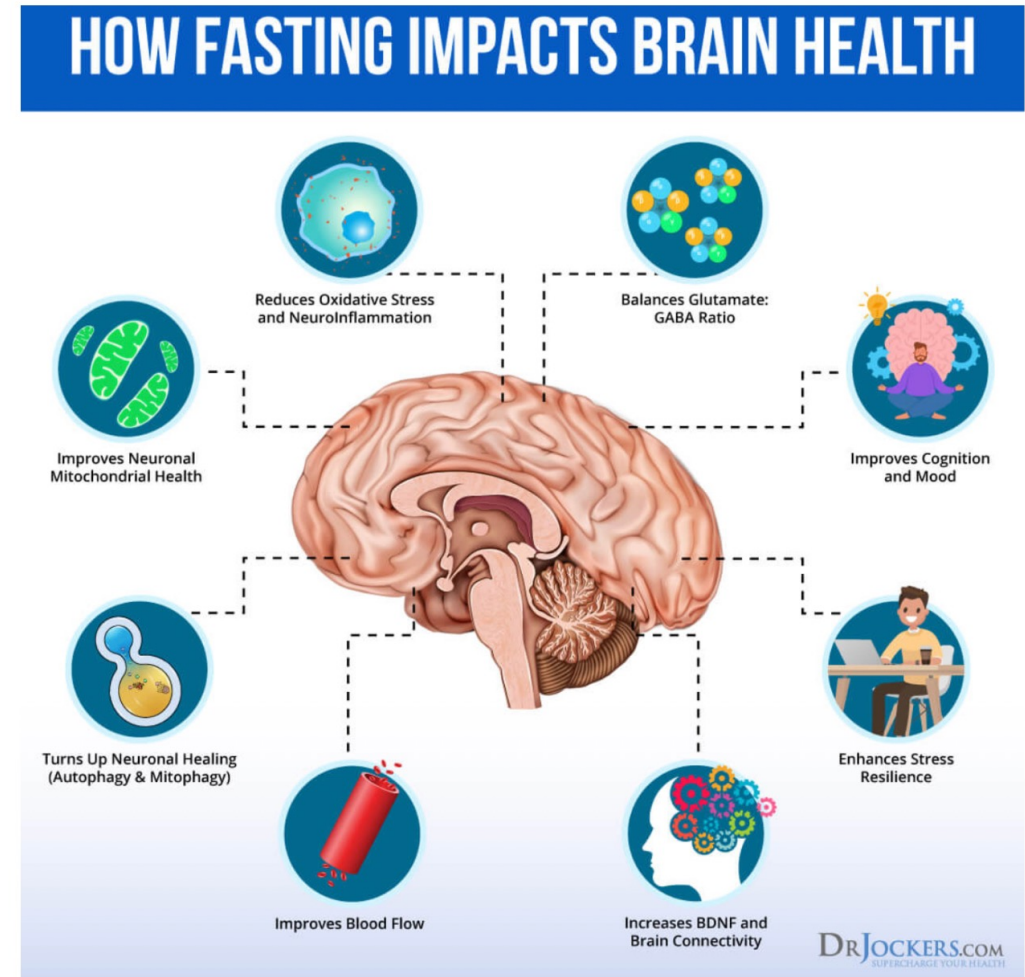
Dietary flavonols and risk of Alzheimer dementia Holland T et al Neurology 2021



Intermittent Fasting

- IF becomes a lifestyle/most 12 hours (ApoE 4 need 14-16 hours)
- Fasting reduces inflammation, increases BDNF, improves insulin sensitivity, metabolic and vascular health and upregulates autophagy
- In a study, published **Cell Metabolism**, mice that were fed on a time-restricted schedule showed improvements in memory and reduced accumulation of amyloid proteins in the brain.

Circadian modulation by time-restricted feeding rescues brain pathology and improves memory in mouse models of Alzheimer's disease Whitiaker D et al Cell August 2023



Autophagy: The "Fountain of Youth" For Your Cells

- **Trans-Resveratrol** induces autophagy by inhibiting mTOR, increases cerebral blood flow, boosts BDNF, protects mitochondria, lowers inflammation and reduces glutamate. Resveratrol is associated with A β clearance from the AD brain and neurons. Resveratrol can deactivate the TLR-4-related pathway which was found to be activated by spike protein which caused cognitive impairment in mice (Fontes-Dontes 2023)
- **Methylene Blue w/PBM:** enhances autophagy, clears prions and delays senescence and markedly enhances mitochondrial function, increases levels of acetylcholine, catecholamines and boosts serotonin and norepinephrine affecting anxiety, depression and memory (10-30mg / day)

Natural Products as Modulators of the Proteostasis Machinery:
Implications in Neurodegenerative Diseases Cuanolo-Contreras Int J Mol
Sci. 2019 Oct



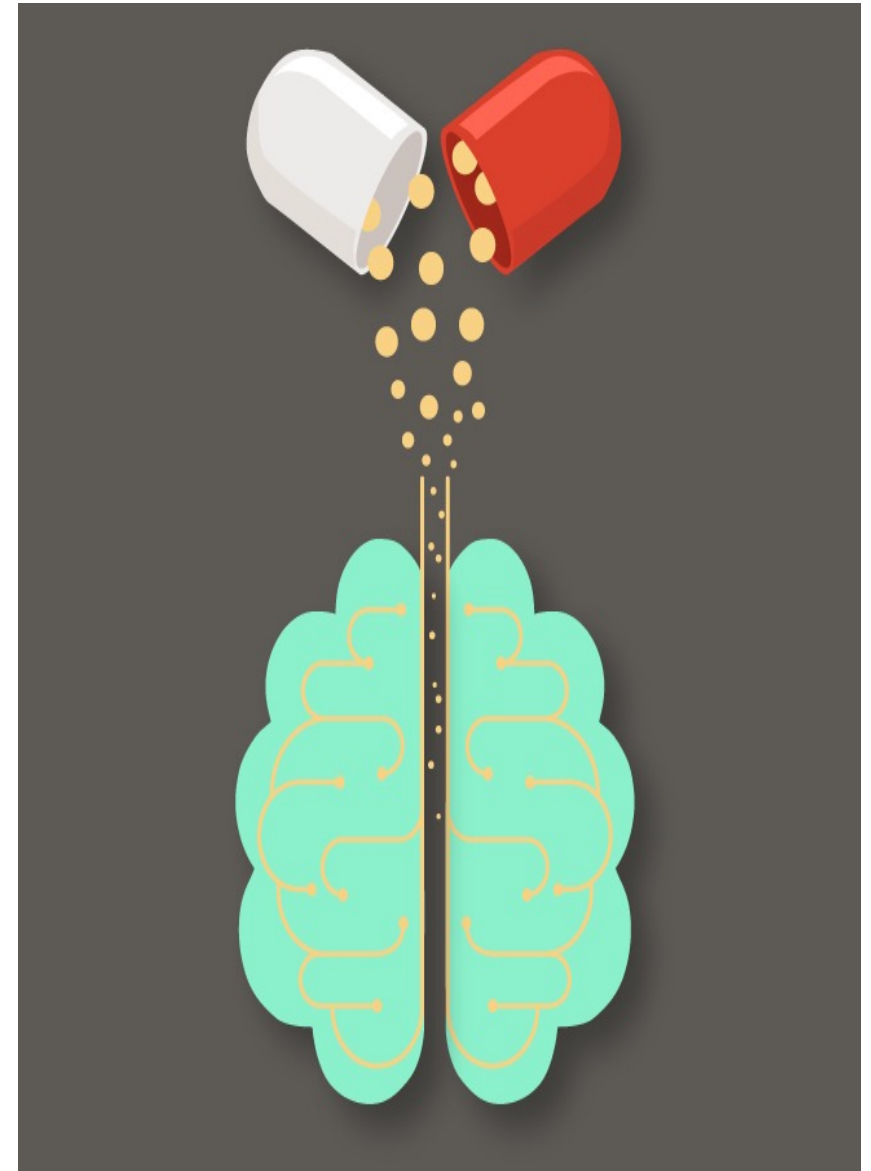
Autophagy: The "Fountain of Youth" For Your Cells

- **Ivermectin** also induces autophagy through an intracellular signaling pathway named "AKT/mTOR."/clears S1/immunomodulating
- **Fluvoxamine** induces autophagy/inhibits platelets/activates sigma 1 receptors with **neuroprotectant properties** and even promoting neurogenesis.
- **Melatonin** reduces oxidative stress, inflammation, regulates the immune system, raises BDNF and activates the autophagy pathway
- **Fisetin** has anti-oxidant, anti-inflammatory activities and is neuroprotective. In preclinical models it was shown to be effective at preventing the development and/or progression of multiple neurological disorders including Alzheimer's disease, Parkinson's disease, Huntington's disease etc.
- **Quality sleep**
- **Meditation** was shown (Epel et al) to lower serum levels of A β 40, which implies increased autophagy in brain nerve cells and a reduced risk of dementia.
- **Sauna therapy**
- **Photo-biomodulation**



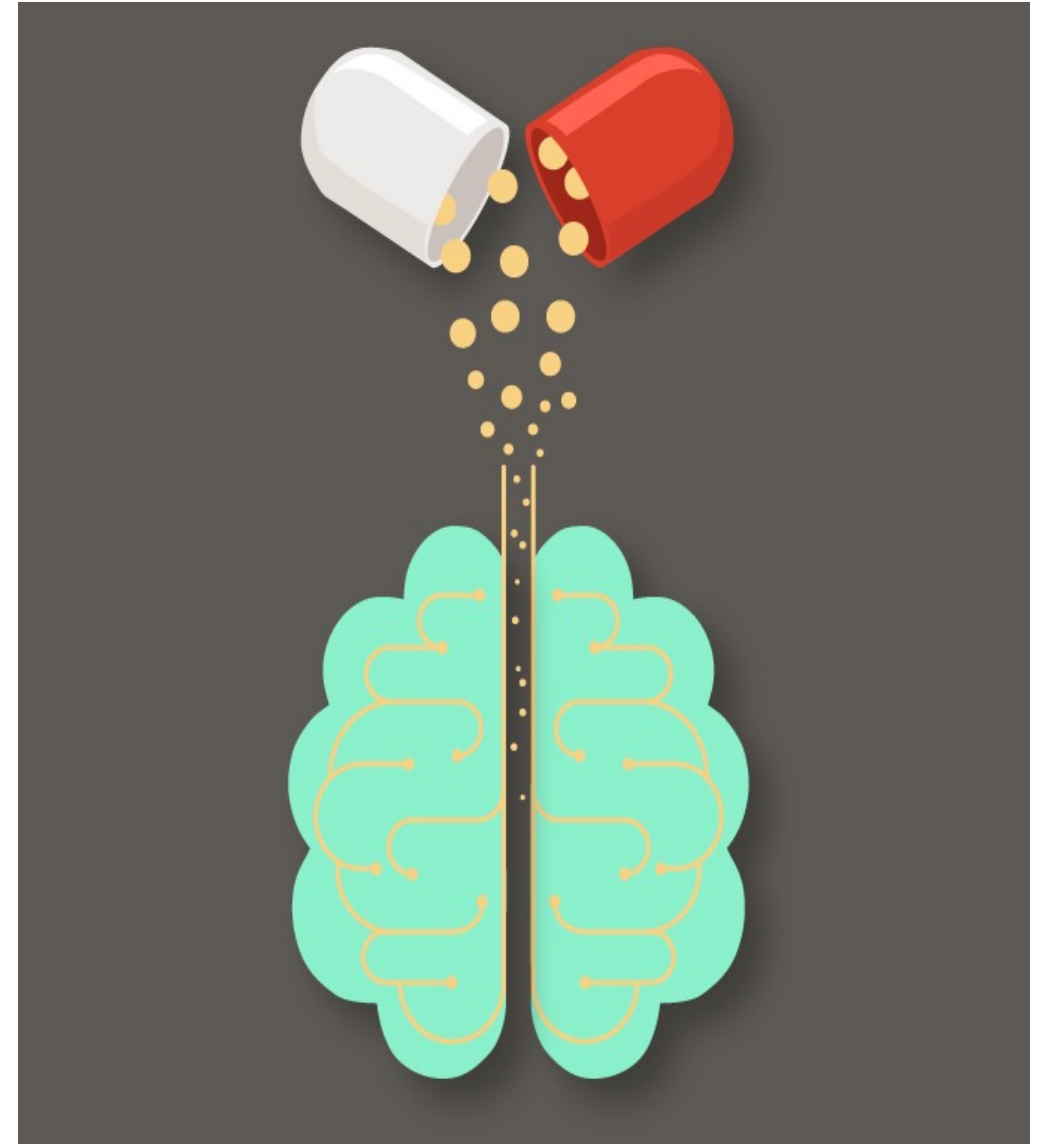
Healing the Brain

- **OMEGA 3** high brain concentration of DHA can optimize synaptic plasticity and efficiency and help maintain homeostasis in the synapses It enhances the glymphatic system /shown to help prevent AD (2000-3000mg/ day) Good for the heart and the brain
- **Vit D & Sunlight** (get levels 60-100) boosts immune status low linked to schizophrenia and psych problems. Low D affects astrocytes and BBB and can inhibit TLR-4 which drives microglial activation. Low Vit D is linked to brain volume loss (Terak J 2022) A recent UK Biobank study showed Low D increased risk of dementia in young (Hendriks S Dec 2023)
- **CDP Citicoline** is a naturally occurring choline source for the synthesis of acetylcholine, enhances the release of dopamine, norepinephrine and serotonin significantly reduces blood-brain barrier dysfunction, and is neuroprotective . It is an intermediate in the synthesis of phospholipids, which are essential components in the assembly and repair of cell ,mitochondrial & neuronal membranes.



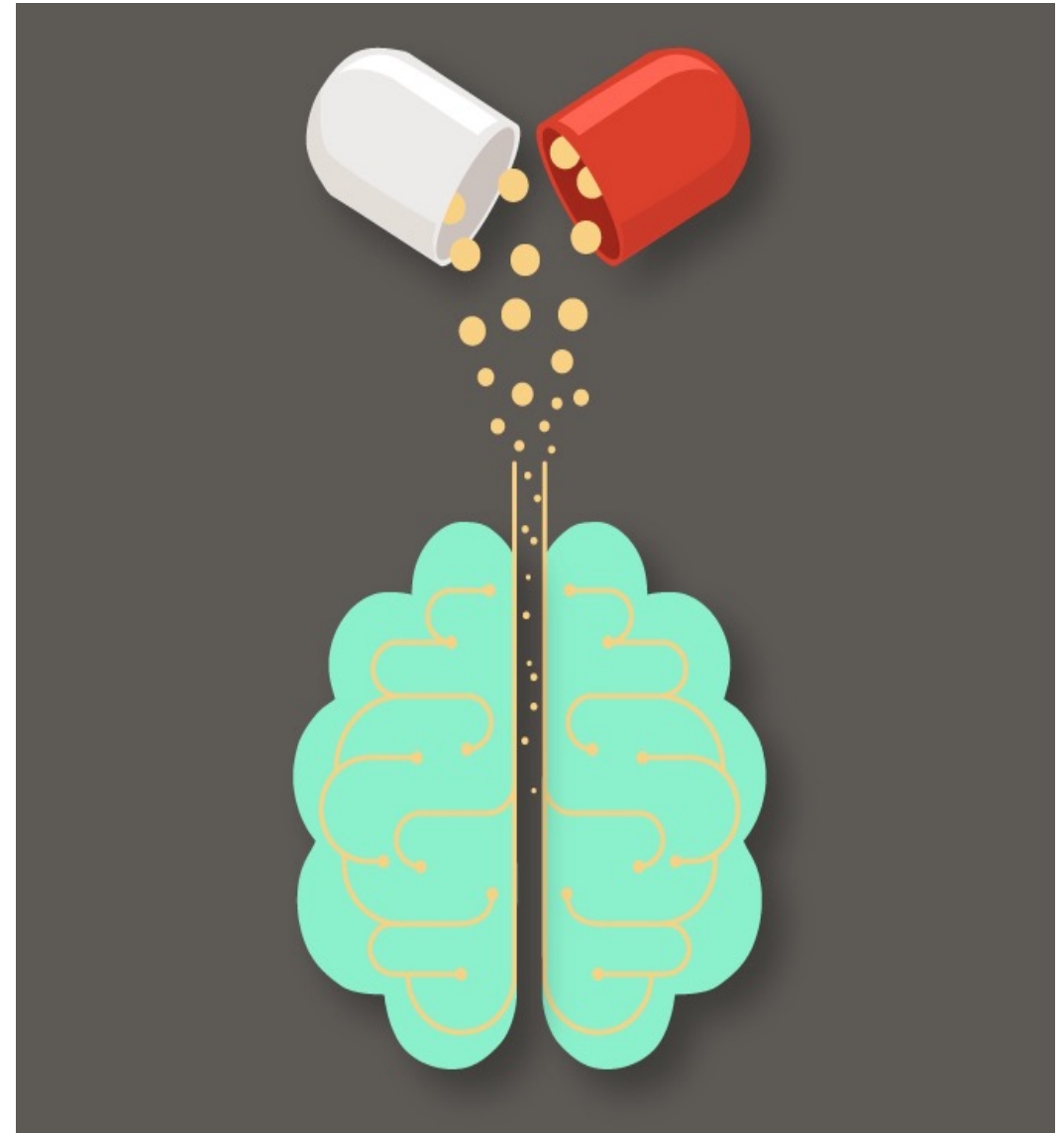
Healing The Brain

- **Vitamin E** is a proven antioxidant that protects cells from oxidative stress and interacts with cellular processes, particularly those involved in neuroprotection and the maintenance of cognitive function (400-800 IU/ day)
- **Flavonoids** have antioxidant/anti-inflammatory effects & also can inhibit acetylcholinesterase (AChE) and help restore acetylcholine. They can help boost NGF (nerve growth factor) and BDNF (neurotrophic factors for the brain Examples Quercetin, baicalin, EGCG) A 2020 study showed higher intake less AD
- **Curcumin** increases BDNF, reduces oxidative stress and has anticoagulant, antiplatelet and fibrinolytic properties, upregulates autophagy. Most do not cross the BBB
- **Magnesium threonate** blocks the NMDA receptor/ modulates glutamate and is essential for maintaining brain neural plasticity. Mg deficiency has been shown in NDG disease. It crosses the BBB better than Mg glycinate



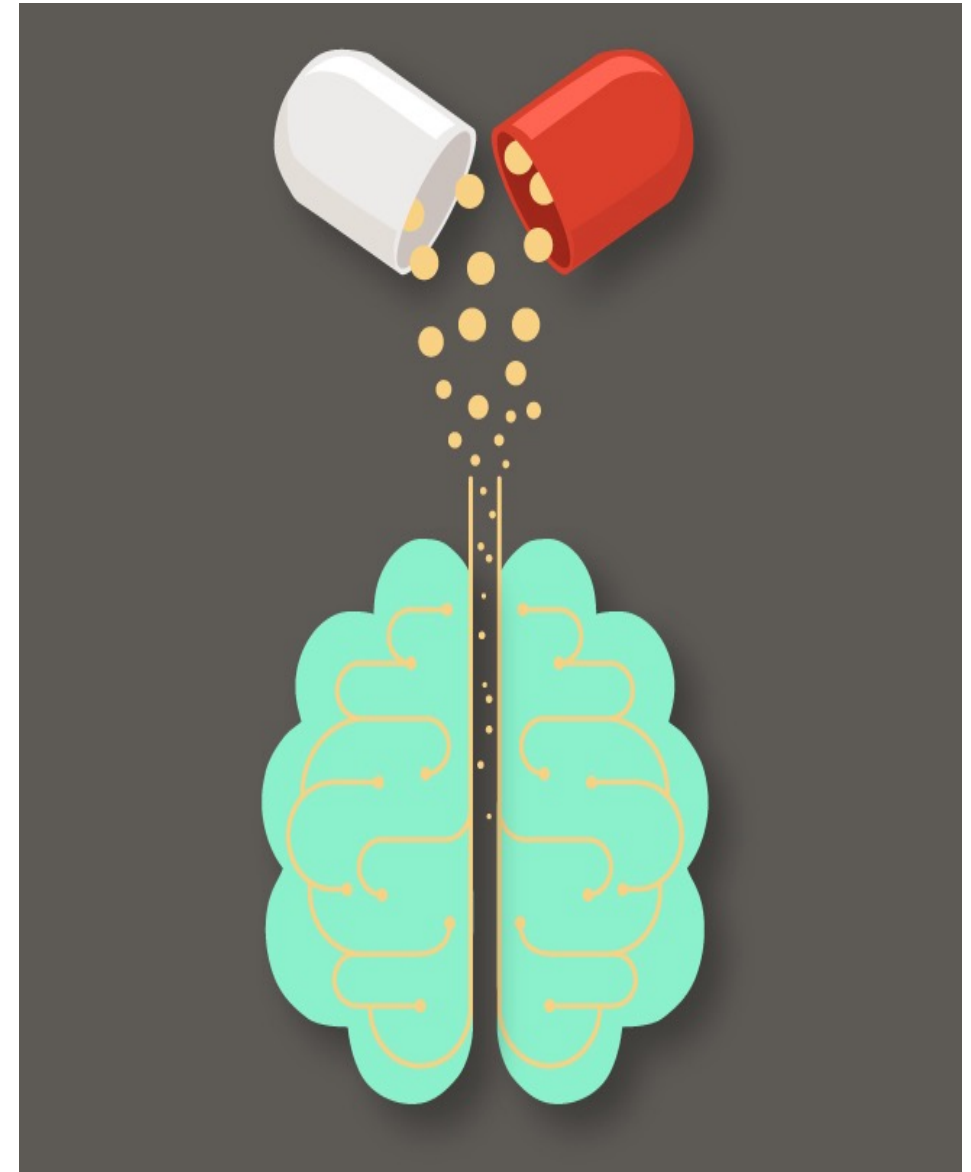
Healing the Brain

- **Berberine:** can shear up the BBB, lowers inflammation, upregulates autophagy raises BDNF and neurotransmitters in the brain: acetylcholine, norepinephrine, and serotonin.
- **Beta hydroxybutyrate** blocks the activation of NLRP3 inflammasome and can shear up the BBB. It also inhibits histone deacetylase (HDAC), is an activator of G protein-coupled receptor (GPCR) & can increase NGF and BDNF
- **NAC** has been shown to successfully cross the BBB and raise glutathione levels in the brain –in turn reducing oxidative stress and protecting the brain from free neuronal damage.
- **B vitamins** : B12, B6, and B9 (folate) can restore the integrity of the blood-brain barrier in adults with mild cognitive impairment and elevated homocysteine. They may be protective against excitotoxicity, oxidative stress, and neuroinflammation (**B complex will work**)
- **MVI** showed significant reduction in memory loss and cognitive aging (American J of Nutrition Jan 2024)



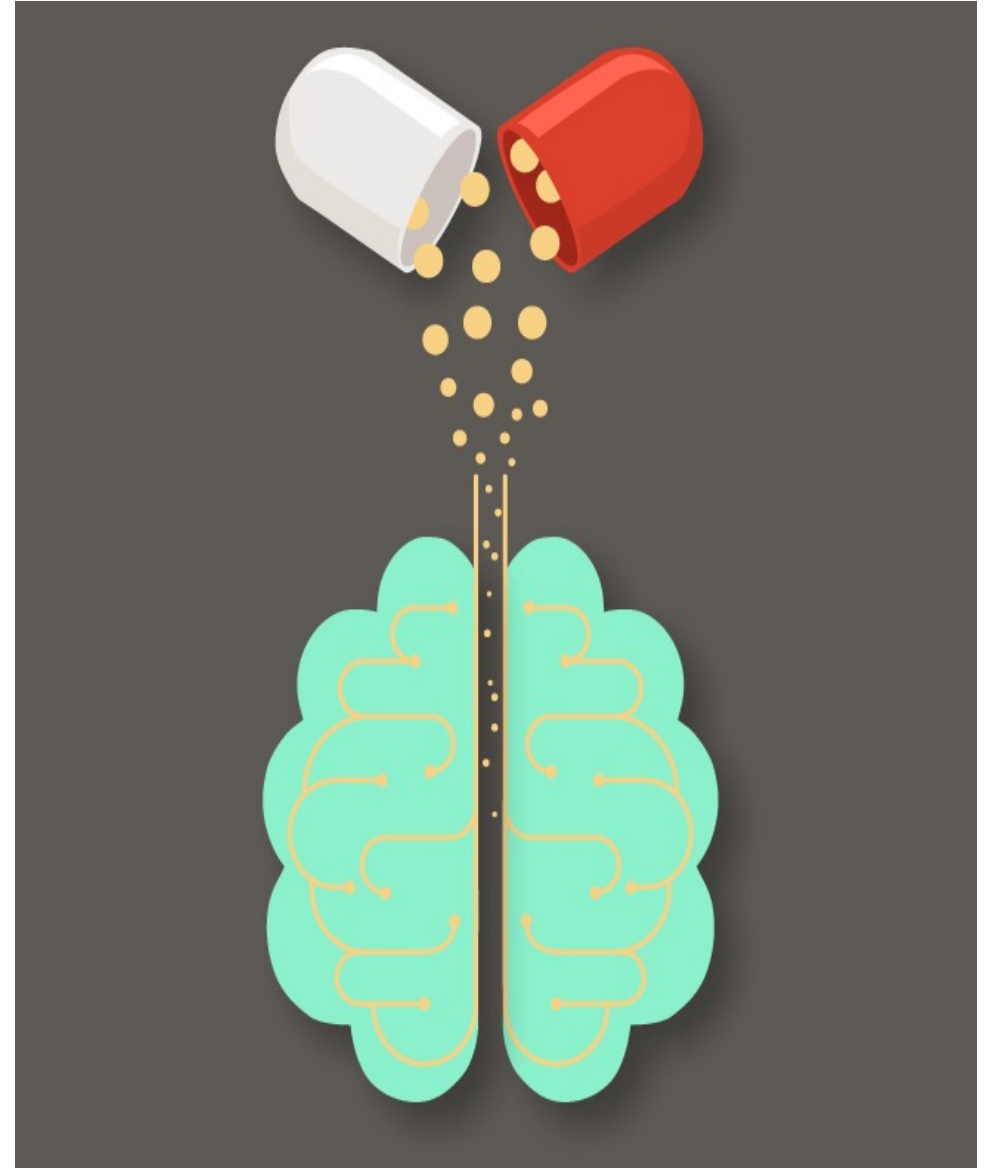
Others / So many More

- **VIT K2:** is a fat-soluble vitamin with many benefits including to the heart, bone, gut and brain health. It promotes mitophagy. The brain is high in K2/ reduces oxidative damage, inflammation and protects myelin. Studies strongly suggest that it could play an important role in AD prevention and therapy. (Popescu A).
- **Vitamin C** has important anti-inflammatory, antioxidant, and immune-enhancing properties, including increased synthesis of type I interferons and improves gut function
- **Hydroxy methyl butyrate (HMB)** used by body builders was shown to reduce plaques and increases factors for neuronal growth to protect learning and memory.(mice) Dose: 400-800mg/ day Also helps prevent muscle loss
- **L theanine** is found in green tea and increases GABA, crosses the blood-brain barrier, and can modulate inhibitory neurotransmitters, selective serotonin, and dopamine to bring calming effects.



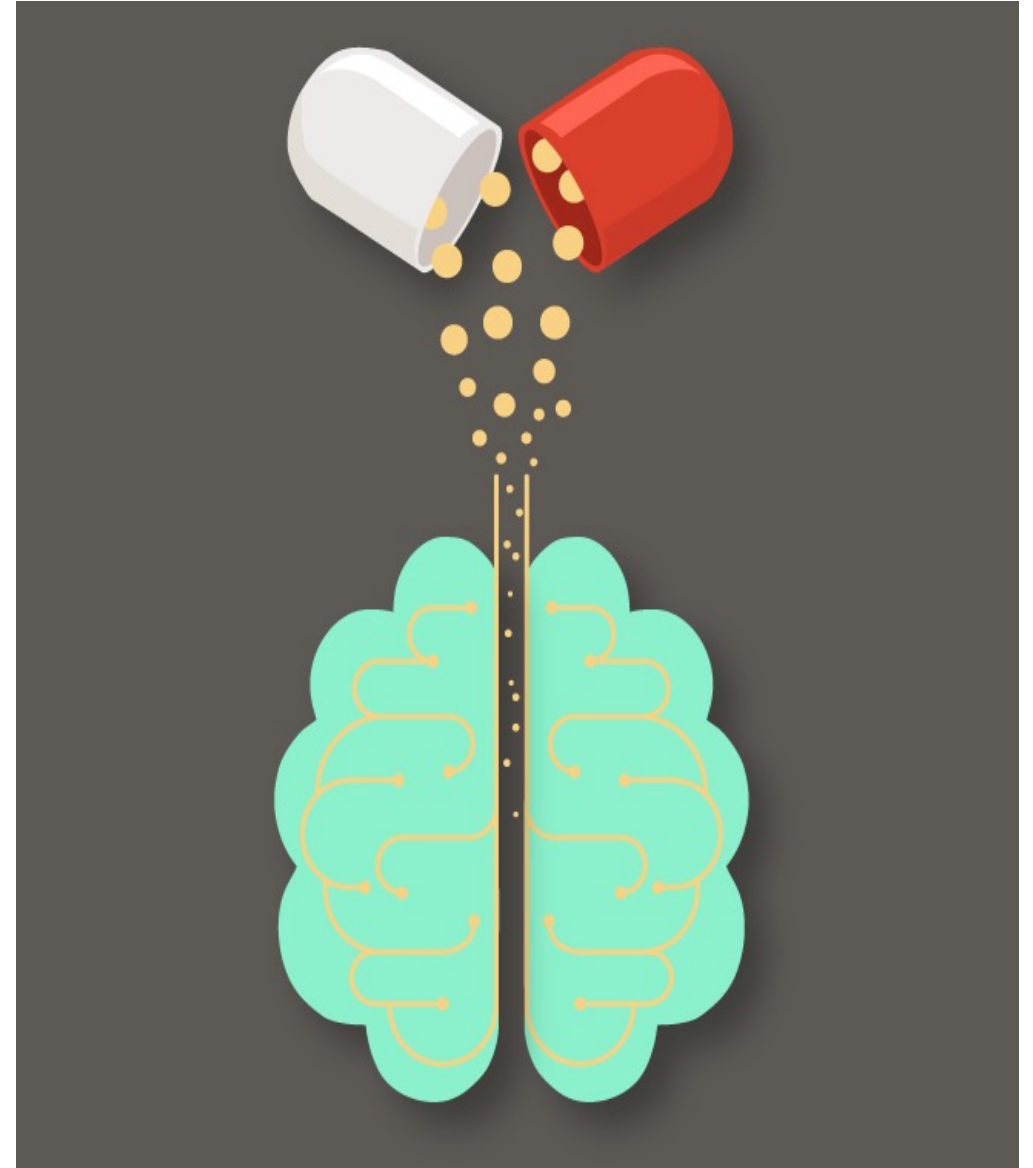
And More

- **GlyNac:** a study showed that older humans taking GlyNAC for 16-weeks improved defects of aging. (Kumar P)
- **PQQ** raises blood flow to the cerebral cortex, improves mitochondria and protects nerves from the degradation caused by neurotoxins (Zhang Q)
- **PEA** targets neuro-inflammation, MCAS, pain, depression, anxiety and supports neurogenesis and synaptic pruning. (Collzi P)
- **Luteolin** anti-oxidant, anti-inflammatory and inhibits mast cells, inhibits microglial IL-6 release, serves as a neuroprotectant, mimics BDNF,& inhibits endothelial inflammation
- **Neuroprotek:** Luteolin, Quercetin and Rutin
- **Taurine** taken earlier in life is associated with better cognitive function in the elderly/deficiency may be a driver of aging (Singh 2023)



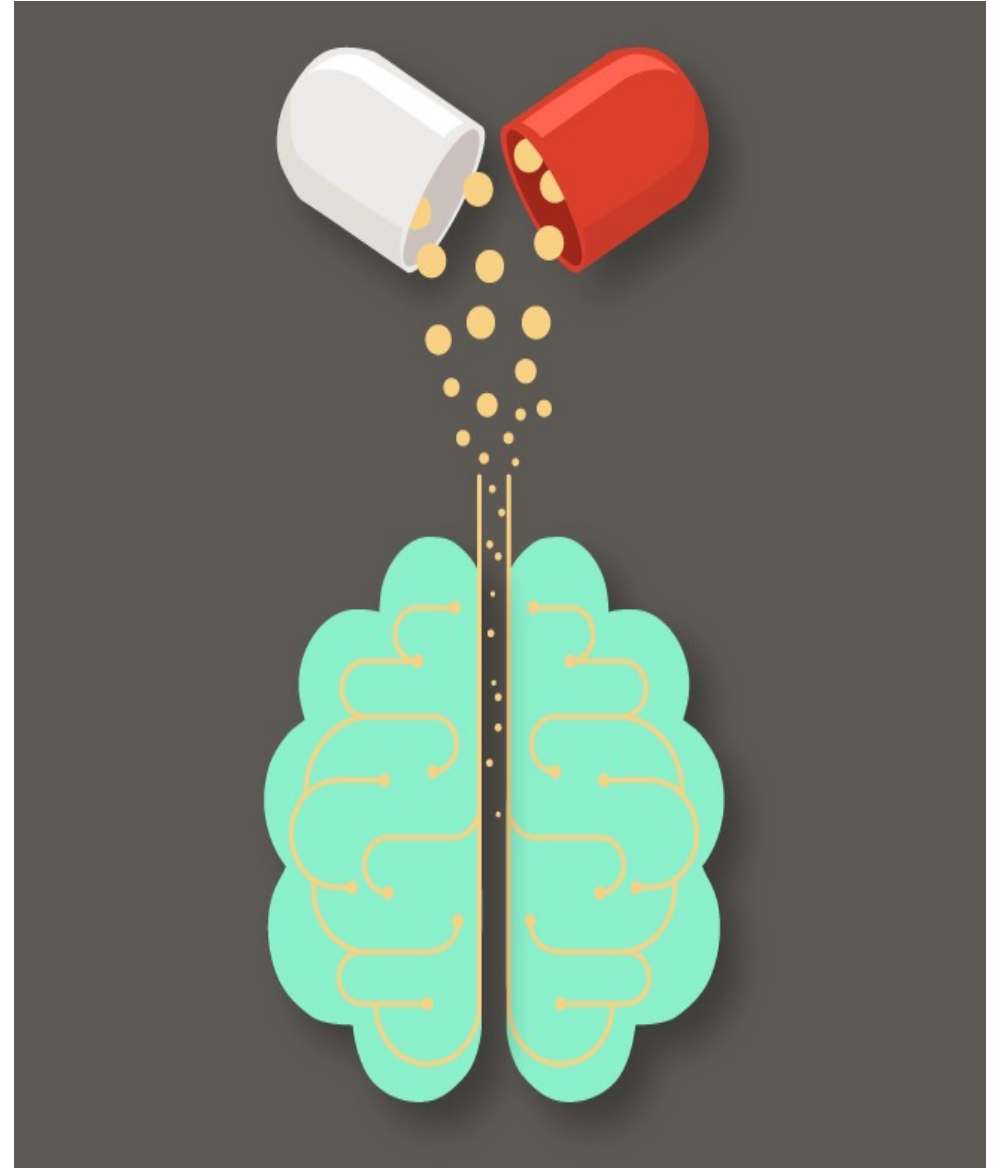
And More 😊

- **HCQ** targets multiple pathogenic mechanisms in AD including synaptic dysfunction, neuroinflammation, A β & tau clearance. (Varma V 2022)
- **Metformin** promotes autophagy, has anti-inflammatory, antioxidative, and anti-apoptotic effects on the nervous system, and exerts neuroprotective effects.
- **Probenecid** has neuroprotective, antiepileptic, and anti-inflammatory properties, as evidenced by its effect against neurological and neurodegenerative diseases. It helps block neuroinflammation and can help transport meds across the BBB/ may stabilize the kynurene pathway to be more protective
- **Sulphoraphane** enhances detox systems, can prevent breakdown of the blood-brain barrier, reduce permeability and improve cognitive function after stroke and traumatic brain injuries



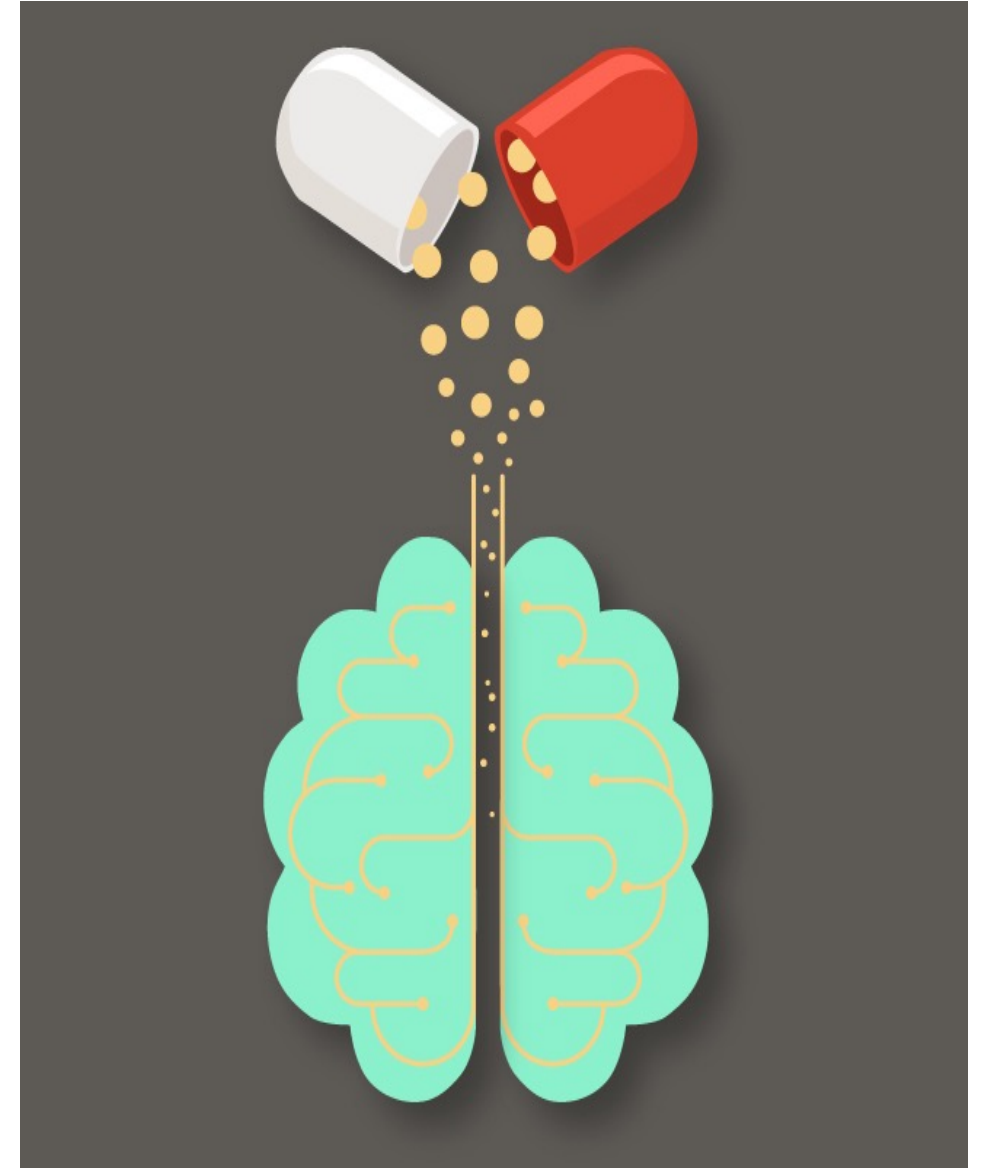
More

- **Luvox** helps with inflammation, autophagy, and platelet activation. It activates Sigma 1 receptors and may be a neuroprotectant and even promoting neurogenesis (Hindmarch I) (Daniels W)
- **Memantine** binds to NMDARs and prevents the influx of calcium ions, thereby preventing the disruption of synaptic plasticity and blocks the effects of glutamate. (Li P) (Scampoli C) May help pain
- **Sildenafil** crosses the blood brain barrier & improves cerebral blood flow. (Sanders O)One study found a 69% reduction of AD in those that use Viagra (Fang J)
- **Monteleukast** lowers TNF Alpha and IL 6, increases glutathione and has been reported to reduce microglia activation, increase neurogenesis, be neuroprotective and restore cognitive function (Marschallinger J 2015)



Mast Cell Stabilizers

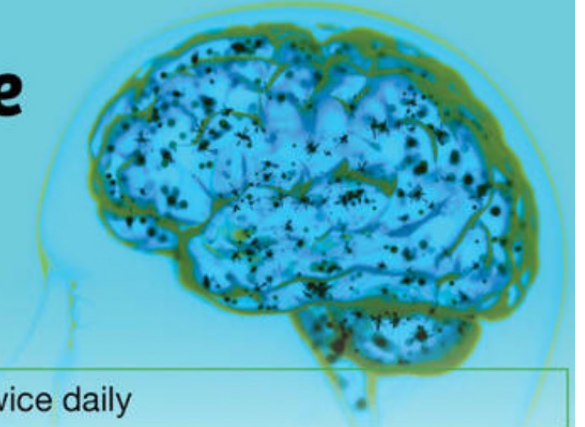
- **Luteolin** is a potent antioxidant, anti-inflammatory, inhibits mast cells, inhibits microglial IL-6 release, is a neuroprotectant, mimics BDNF, inhibits endothelial inflammation, macrophage activation, alleviates neuroinflammation and in animal models reduces amyloid deposition
- **NeuroProtek[®]** is a mixture of Luteolin, Quercetin and Rutin with olive pomace oil used to maximize the effects of these flavonoids by overcoming any absorption
- **Montelukast** is a leukotriene receptor antagonist (LTRA) and has antiviral activity, lowers TNF Alpha and IL 6, MCAS, increases glutathione and has been reported to reduce microglia activation, increase neurogenesis, and restore cognitive function (Marschallinger J 2015) Black box warning
- **Ketotifen** is a MC stabilizer, inhibits MC degranulation may also prevent the direct effect of histamine on microglial activation. Crosses the BBB
- **Others** Quercetin, vitamin C, local raw honey, curcumin, bromelain, probiotics, astragalus, butterbur, PEA, LDN, Pepcid, Zyrtec



Reducing Glutamate

- Glutamate and GABA are integrally related in both form and function. Memantine, Topamax, Lamotrigine, Ketamine, Amantadine, Zonisamide
- Don't forget diet, lower stress, exercise, avoid MSG, aspartame

Reducing glutamate –naturally.



Recommended supplements:

Taurine	500mg, twice daily
Ginger	1 to 3 capsules of a high quality product daily
Vitamin C	500mg, twice a day.
Coenzyme Q10	once daily
L-theanine	100-200mg, once daily
PQQ	10-20mg, once daily
B6	250mg, once per day
Magnesium glycinate	250mg, twice daily
Spore-based probiotic to optimize gut health and support the microbiome	
Vitamin B6 (pyridoxine). P5P is the active coenzyme form of Vitamin	
Other supplements that increase GABA include the traditional relaxing herbs: Kava, valerian, lemon balm, chamomile, and passionflower.	

Support Your Mitochondria



- **Mg glycinate** improved mitochondrial ATP synthesis, and thus greater ATP availability
- **Melatonin** protects mitochondria by scavenging for ROS and improves mitochondrial function
- **Benfotamine** is a highly available form of thiamine which is used for mitochondrial production of ATP. It decreased cognitive decline in Alzheimer's by 43%, (Xu C 2018) Helps neuropathy too/ 300mg / day
- **Acetylcarnitine** can decrease the risk of free radical damage within mitochondria /X's the BBB / increases Ach
- **D Ribose** Studies have looked at D Ribose in neurodegenerative diseases such as early ALS and MS with promising results)
- **NAD** Levels decrease w/age. Animal studies show that nicotinamide supplementation reduces neuronal death and brain edema and attenuates BBB disruption in TBI. NAD is primary fuel for sirtuins (longevity proteins that become depleted with age) /helps integrity of BBB
- **L Carnitine** for muscle
- **Ubiquinol or CoQ10, ATP 360, MitoQ**
- **PQQ** pyrroloquinoline quinone boosts mitochondria, increase CBF and protects nerves from the degradation caused by neurotoxins. It can also reduce prions.
- **CoQnol** (Designs for Health) a unique combination of ubiquinol and trans-geranylgeraniol
- **Alpha Lipoid Acid** has mitochondrial, antioxidant effects, can stabilize the BBB improves glucose control and insulin sensitivity, boosts acetylcholine, and easily crosses the BBB
- **Mitopure** promotes mitophagy which cleans up defective mitochondria and allows the mitochondria to repair themselves and improve their performance
- **Oxaloacetate (BENAGENE)** is a ketone that can dramatically impact cellular energy production In a ME/CFS study : 500 mg bid to tid up to 1000 mg tid All got better (Kaufman et al)
- **Glycine** impacts mitochondria epigenome/has been found to have neuroprotective benefits in animal models (Ullah R et al)

Neuroprotective Effects of Herbs



- **Ashwagandha** (Indian ginseng) is one of the most prominent herbs prescribed as a brain rejuvenator for AD :inhibits acetylcholinesterase, reduces oxidative stress, regenerates neurons and synapses, reduces amyloid, reverses mitochondrial dysfunction, improves auditory–verbal working memory, executive function, processing speed, and cognition
- **Gotu Kola** has been used for centuries to enhance memory and cognitive functioning and to combat the effects of aging in the brain. It has calming properties (500 mg twice a day)
- **Bacopa** (take at night) improves stress, memory, and learning
- **Lions Mane:** Increases NGF
- **Rhodiola** increases neurotransmitters (DA and serotonin/ calming
- **Whole coffee fruit extract (WCFE)**, dramatically increases BDNF
- **Ginko Biloba** protects against glutamate excitotoxicity/mitochondrial damage
- **Scutellaria Baicalensis** is an antioxidant, attenuates microglial activation & may improve neurogenesis in the hippocampus
- **Huperzine A** inhibits the breakdown of the neurotransmitter acetylcholine

Brain photo-biomodulation holds the potential to enhance mitochondrial function, increase CBF and reduce neuroinflammation

- Mitochondrial function declines with age within neurons and CBF decreases
- Near-infrared light (NIR) stimulates mitochondrial respiration in neurons by donating photons that are absorbed by cytochrome oxidase and this energy is converted into ATP for cellular use
- PBM creates mild oxidants (ROS), which leads to gene transcription and then to cellular repair and healing
- PBM improves endothelial dysfunction via increasing bioavailable NO
- Helps clear proteins and waste

Advances in photobiomodulation for cognitive improvement by near-infrared derived multiple strategies Pan W et al J of Translational Med 2023

Shining light on the head: Photobiomodulation for brain disorders Hamblin M BBA Clinical 2016

“The Ultimate Guide to Red Light Therapy.” Ari Whitten

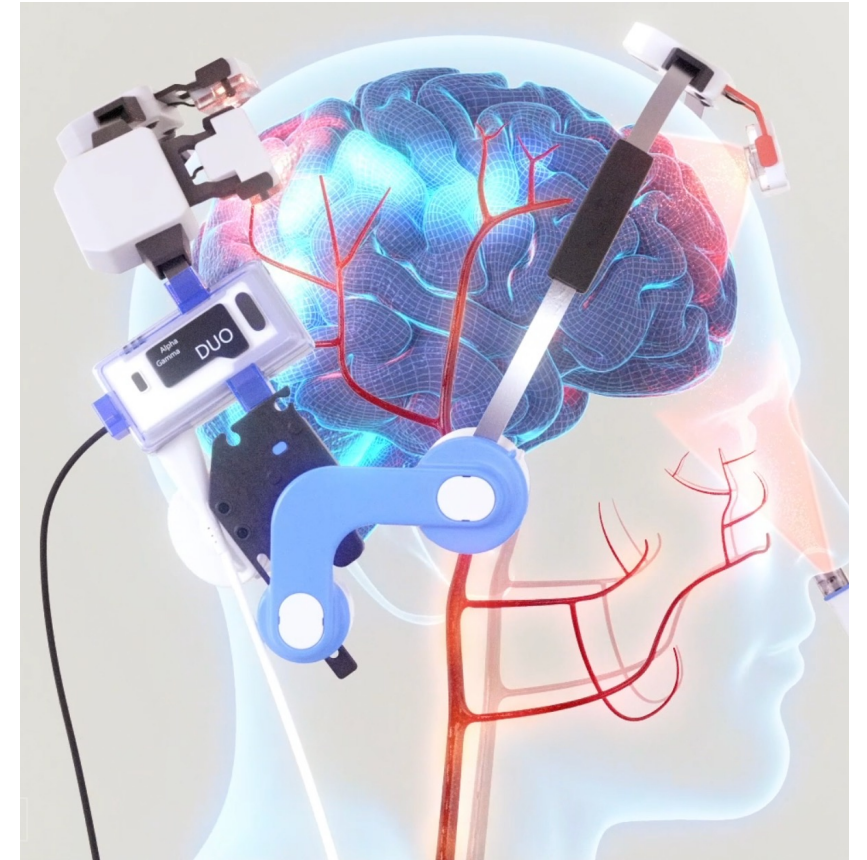


Vielight: Now Being Tested in Long COVID

- The Neuro Gamma PBM device exposes the default mode network to stimulation with 810 nm NIR light pulsed at 40 Hz.
- Many studies show near-infrared PBM could positively cognition, memory consolidation and mental energy.
- The 40hz Gamma improves brain energy (ATP), boost the functioning of microglia, enhances cerebral blood flow, and plays a role in neuronal protection and regeneration

References at <https://www.vielight.com/devices/vielight-neuro-gamma/>

Distinct BOLD variability changes in the default mode and salience networks in Alzheimer's disease spectrum and associations with cognitive decline Zhang L et al Nature Scientific Reports 2020



Auragen Light and Sound Photobiomodulation

- Auragen's Gamma stimulation utilizes the optimal signaling mechanisms based on research studies with delivery of synchronized 40hz via the visual and the auditory cortex (Liu J 2022)
- Theta brain stimulation that provides deep rest and stress relief
- Use a massage pillow, lay on stomach to reach back of the brain

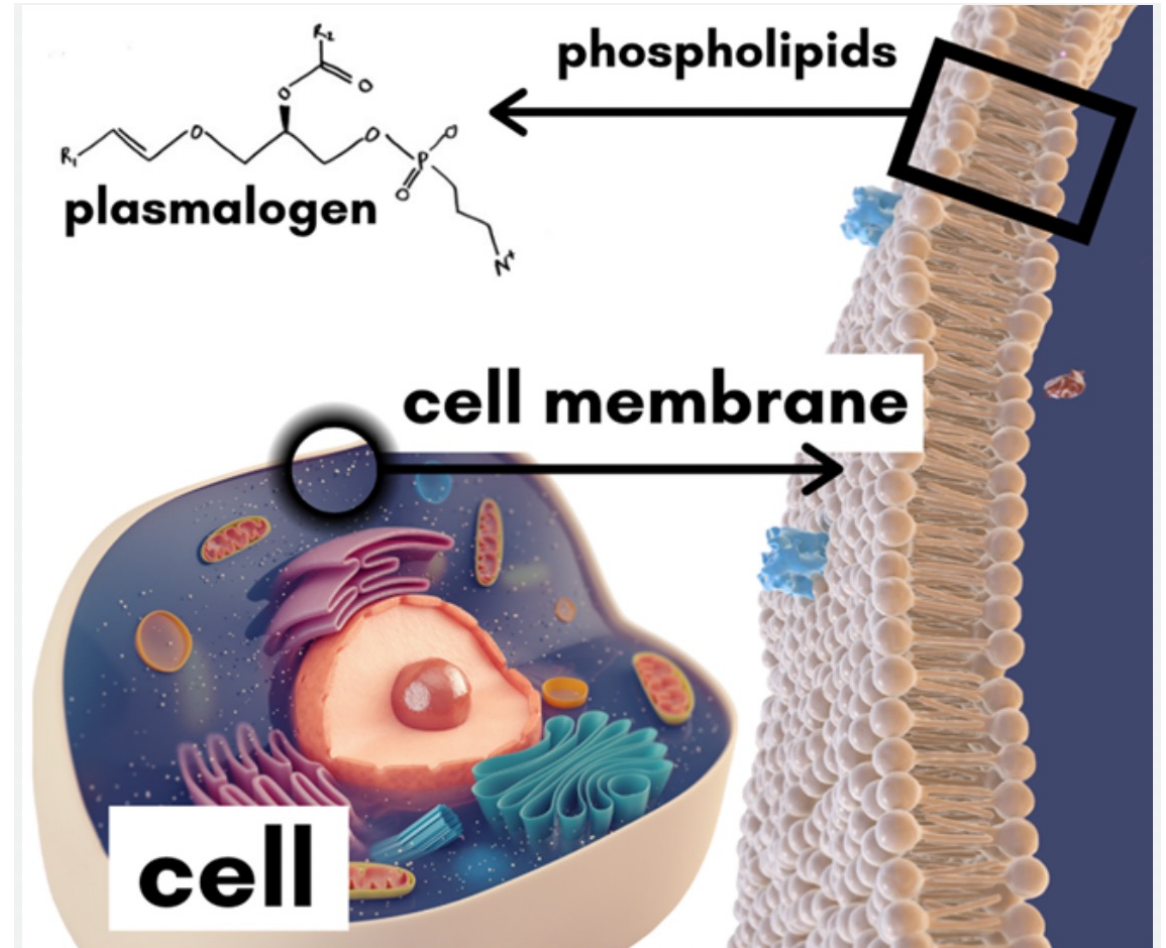
<https://reversalsolutions.com/pages/auragen-light-therapy>

The anti-inflammatory effects of photobiomodulation are mediated by cytokines: Evidence from a mouse model of inflammation Shimoo S Frontiers Neuroscience 2023



Plasmalogens: The Secret Tool?

- Plasmalogens are a special type of phospholipid found on cell membranes
- They are found in high concentrations in the brain and heart. They build as much as 20% of the brain
- Plasmalogen levels begin to decrease after age 50.
- Persons with dementia exhibit a more rapid decrease in plasmalogens – especially omega-3 plasmalogens.



Plasmalogen deficiency and neuropathology in Alzheimer's disease: Causation or coincidence? Goodenowe D et al Alzheimer's Dementia 2019

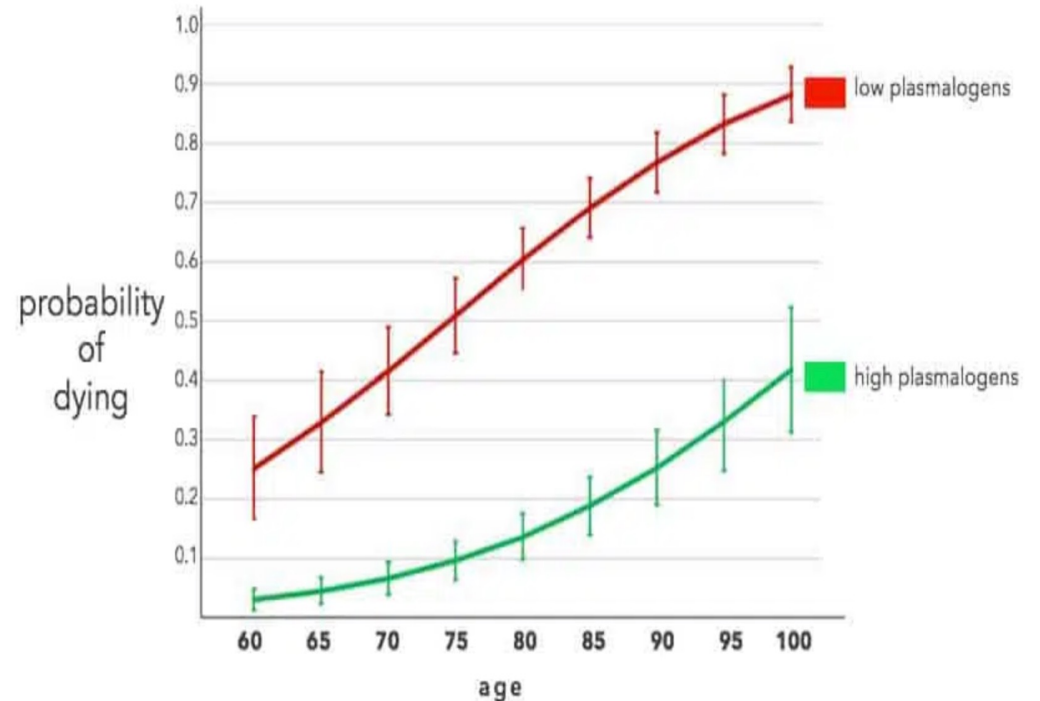
Plasmalogens and Chronic Inflammatory Diseases Bozell J et al Front. Physiol., 21 October 2021

Plasmalogens: The Secret Tool?

- Plasmalogen deficiency is associated with cognitive impairment and Alzheimer's disease and all cause mortality.
- 5-year mortality was directed correlated with plasmalogen level
- ProdromeNEURO™ is designed to elevate omega-3 plasmalogens. (Prodome Science) \$550.00/3 months.
- Plasmalogens and Alzheimer's disease: a review Su X et al Lipids in Health and Disease 2019

Plasma metabolomic profiles associated with mortality and longevity in a prospective analysis of 13,512 individuals Wang F et al Nature Communications 2023

<https://newsinnutrition.com/2023/01/autism-may-be-a-plasmalogen-deficiency-syndrome>



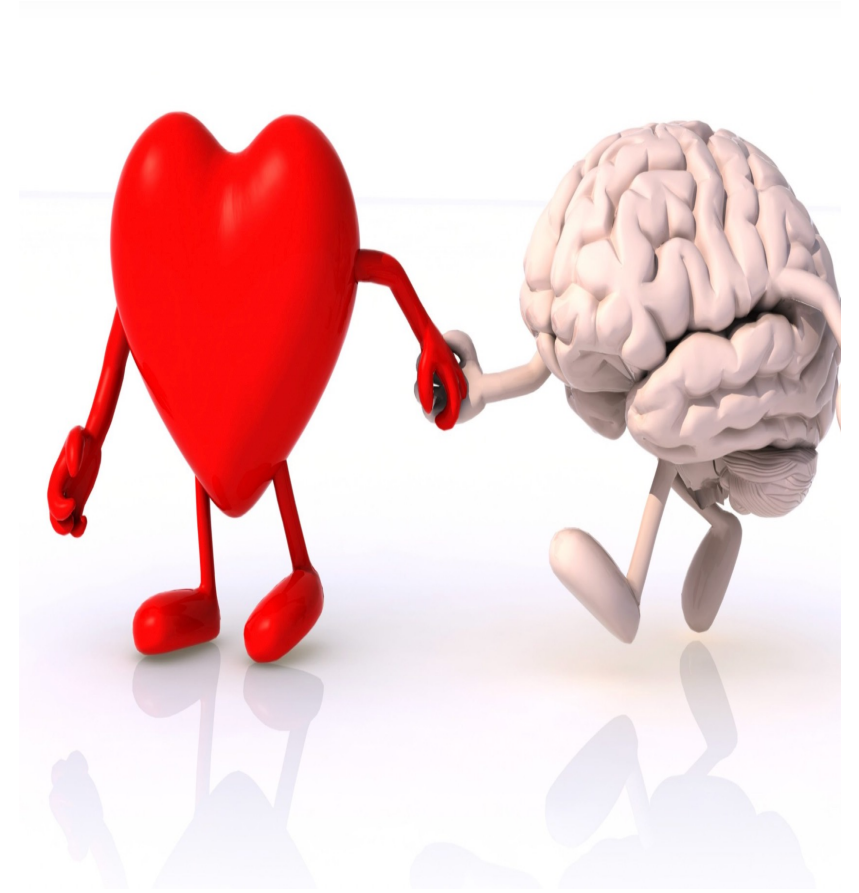


Oxytocin: The Love Hormone Biological Metaphor for Safety

- Oxytocin is a hormone responsible for bonding behaviors and romantic attachment.
- Oxytocin receptors are spread widely though out the body and the brain/ hippocampus.
- Imbalances in the oxytocinergic system are implicated in neuropsychiatric diseases like autism spectrum disorder, clinical depression, NDG disease , some cancers and eating disorders.
- OXT promotes bone , cardiovascular, metabolic health, improves nocturnal frequency, calms MCAS, is profoundly anti-inflammatory & has anti-aging properties with telomere lengthening
- May help taste and smell

Effects of Oxytocin are Probably Modulated by the Autonomic Nervous System

- Modulation of the ANS improves cardiovascular and inflammatory response, leading to increased vascularization (Norman G) (Jakowski M)
- Peripherally administered **oxytocin can stimulate the vagus nerve**, and then this VNS is able to modulate neural pathways (Everett N)
- **Oxytocin improves cerebral blood flow** (Martins D)





The Power of Love

- OXT has important roles in the hippocampus, by modulating neuronal excitability, network oscillatory activity, synaptic plasticity, and social recognition memory (Talpo F)
- OXT effectively reverses some of the damage caused by amyloid plaques in the hippocampus in AD mouse (Selles M 2023) (Jiang G 2023)
- OXT increases gray matter in hippocampus (Riem M 2019)
- The neuromodulation by Oxytocin is due to the presence in many brain regions of G-protein coupled receptor complexes (Borroto-Escuela et al)

Safety

- FDA approves the use of oxytocin for pregnant women who have complications of childbirth, such as:

Cardiovascular-Renal Disease

Eclampsia

Preeclampsia

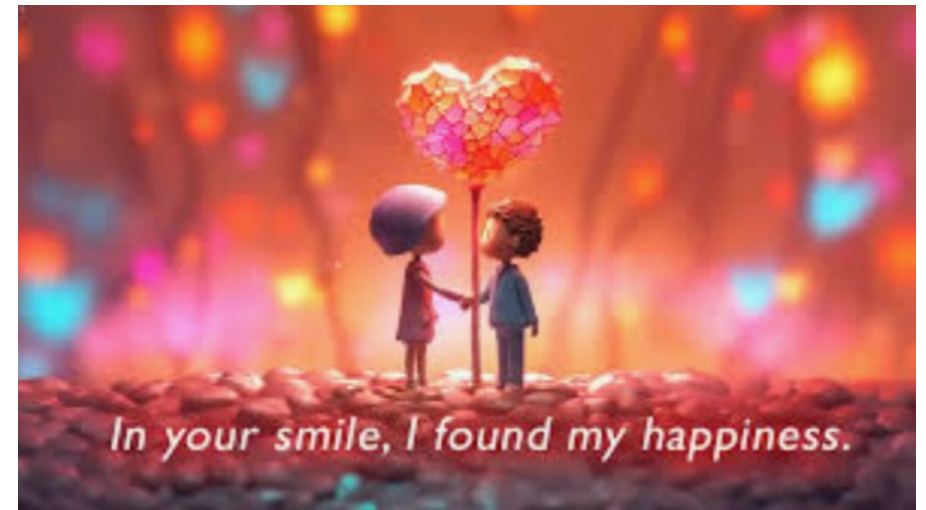
Premature Rupture of Membranes (PROM)

* May be associated with prostate cancer correlation (not causation)

- Very rarely patients may have increased nightmares or anxiety. Stopping further administration resolves side effect

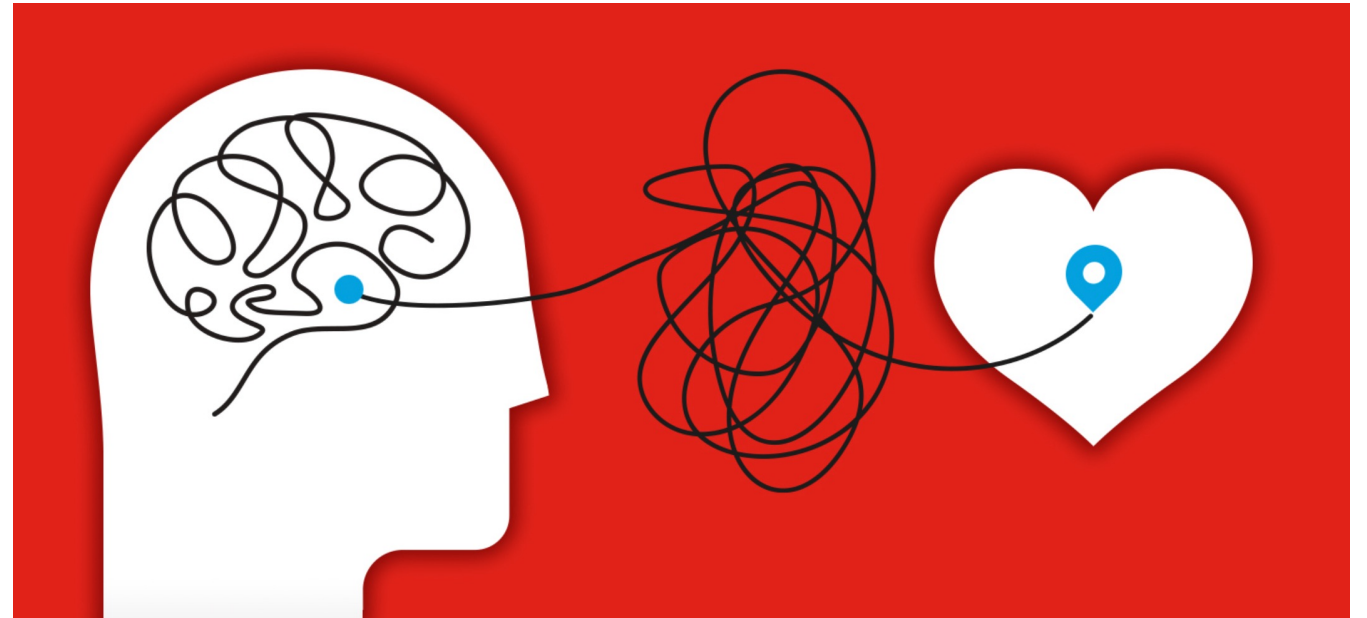
Oxytocin and cancer: An emerging link. Lerman B et al World J Clin Oncol. 2018

A review of safety, side-effects and subjective reactions to intranasal oxytocin in human research McDonald E Psychoneuroendocrinology 2011



Oxytocin Dosing

- SL troche or CR tablet
- Start 50 IU for most and can increase to 100 IU hs
- Can go higher to 100 bid (this has been used in PTSD and POTS with no ill effect)



Now....Think of
Someone or
Something that You
Really Love/Loved

*Eventually, you will come to understand
that love heals everything, and love is all
there is.*

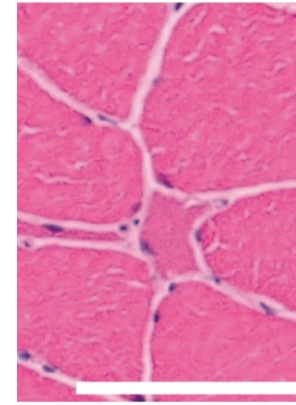
Gary Zukav



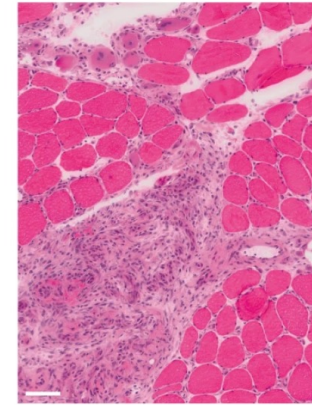
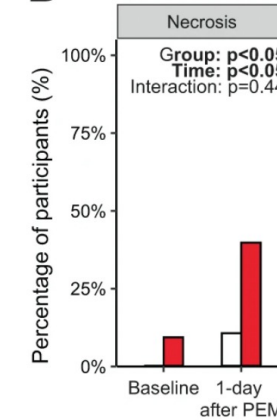
Sarcopenia, Mitochondrial Damage and Amyloid in Muscles

- ACE-2 is expressed in skeletal/ cardiac muscle and plays an integral role in muscle pathology
- Appleman et al found mitochondrial damage, small atrophic fibers and focal necrosis along with amyloid deposits in muscle which worsened with exercise
- The amyloid deposits could be provoking autoantibodies
- Other studies have found this too plus capillary injury in muscle (Ashman T) (Hejbol EK) (Ramirez-Velez) and there the inability to extract O₂ from the vasculature during exercise (Kahn P)
- Endothelial damage and micro-clotting don't help either

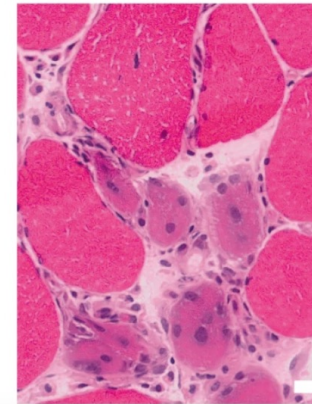
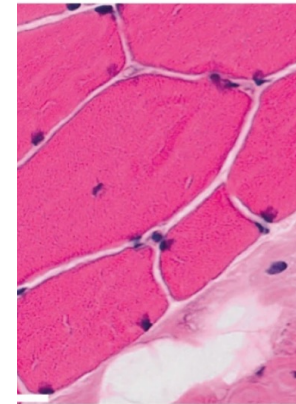
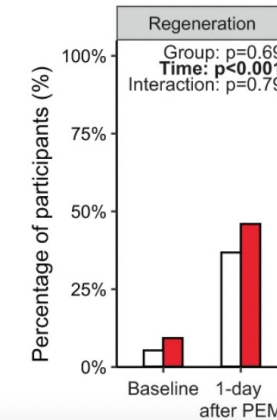
Muscle abnormalities worsen after post-exertional malaise in long COVID Appleman B et al Nature Communications Jan 2024



B



D



Is the EMG Really Normal? It is If You Don't Look

- Myopathic changes in quantitative EMG and/or increased jitter in small fiber EMG were seen in 63% of 84 patients with Long COVID neuromuscular symptoms.
- Electron microscopy showed damage of terminal nerves and motor endplate.

Myopathy as a cause of Long COVID fatigue: Evidence from quantitative and single fiber EMG and muscle histopathology
Agergaard J et al Clinical Neurophysiology 2023



Measure to address PEM/muscle wasting

- **Creatine** can increase phosphocreatine stores in muscles which have been found to be low in LC. It can cross the BBB and has been found to be helpful in various NDG diseases (Rochel H) Taking dietary creatine for three months substantially improved feelings of fatigue, and by six months, had produced improvements in body aches, breathing issues, loss of taste, headaches, and problems concentrating — or “brain fog” — compared to people given a placebo. Creavitalis 4 grams/day (Slankamena J)
- **Serotonin** significantly promoted longitudinal growth of skeletal muscle fibers in vitro. Increased branching, differentiation, and fusion of myoblasts into myotubes were also observed
- **L Carnitine** for muscle mitochondrial function and energy production and competes with the ACE 2 receptor (Bellamine A)
- **L-arginine** is an amino acid that helps the body build protein & stimulates nitric oxide production, improves collagen synthesis in tenocytes, improves tendon function and accelerates healing of damaged tendons.
- **Argivit** with 3 g of arginine associated with creatine, L-carnitine, aspartic acid, magnesium, selenium and vitamins C and E (Bologna C)
- **Magnesium** is a cofactor of different enzymatic reactions involved in anabolic and catabolic processes that affect muscular performance during exercise
- **Cardio Miracle** is a supplement with over 50 ingredients formulated to increase nitric oxide (NO) production
- **Vitamin E** twice a day, subjects experienced accelerated muscle recovery (Cannon et al, 1990)
- **Selenium** supplementation augments calcium release from the sarcoplasmic reticulum thus improves skeletal muscle performance
- **Blood flow restrictive therapy**
 - Address endothelial damage and micro-clotting
 - Physical activity focused on progressive **resistance-based strength training/ LiveO2/EWOT**
- **Nutritional counseling** to address protein needs
- **Upregulate autophagy/ intermittent fasting** with time restricted eating should not cause muscle wasting (Philips M 2024)

Evaluation for Brain Fog / MCI/ Cognitive



- Chem 12, CBC, Vit D, Vit B12, ESR , IgG and IgG subsets, ANA, TFTs, free T 3 and free T 4, thyroglobulin antibody, Hgba1C, fasting insulin, homocysteine, APOE genotype, MTHFR, heavy metals, Copper, TGF beta, VEGF, Western blot, hormone levels, EBV early antigen and viral panel, HHV6 IgG and IgM, Fibrinogen, D dimer, SARS-CoV-2 Antibody (IgG), Spike, Semi-Quantitative, SARS-CoV-2 Antibodies, IgG, Spike, GAD 65
- Biomarkers: Amyloid beta 42/40, serum tau 181
- Consider Autoimmune Dementia/Paraneoplastic panel
- MRI Brain with and without GAD and Neuroquant
- Bedside MoCA
- Neuropsychological evaluation
- Some need EEG, LP CSF, RPR, HIV and some will need further integrative workup

A photograph of a woman with dark hair, wearing a black t-shirt and blue jeans, sitting in a black wheelchair. She is holding a young girl with red hair, wearing a black top and blue shorts, in her arms. They are in a home setting with a wooden floor and a blue table in the background. The text is overlaid on the image.

Is Long COVID and Spike-opathy a New Form of Autoimmune Disease

More research suggests spike protein looks eerily like the body and brain

Mallory Stanislawczyk sits with her daughter Olivia, 3, while receiving a saline infusion at her Walkersville,

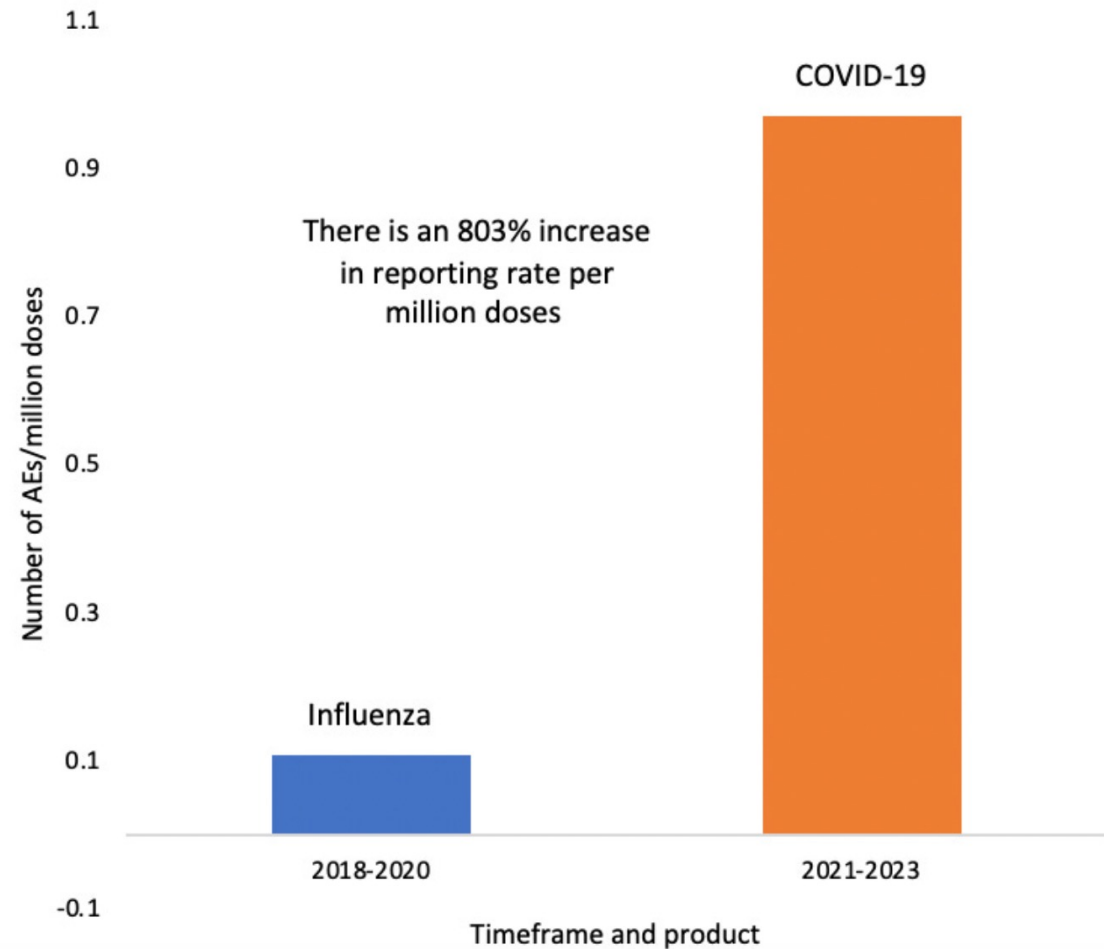
Megan Kelly
Regrets
Getting the
COVID vaccine



Rise in Autoimmune Disease

VAERS reports of "Autoimmune disorder" per 1 million doses of Influenza vaccine (2018-2020) (blue) or COVID modmRNA injectable product (2021-2023) (orange)

Source: <https://vaers.hhs.gov>



Ribosomal Frameshifting, Glitches & Off Target Protein Garbage

- Scientists discovered that in addition to the toxic “spike protein,” mRNA vaccines introduce “read errors,” making vaccinated individuals produce nearly random proteins with unknown and unpredictable effects.
- They found that 25-30% of vaccinated people experience unintended immune response from this ‘glitch’
- The damage comes from pseudouridine substituted for uridine
- Experts are calling this a massive “developmental and regulatory failure.”

N1-methylpseudouridylation of mRNA causes +1 ribosomal frameshifting
Mulrony T et al Nature December 2023

The Telegraph

One in four who had Pfizer Covid jabs experience immune response

Joe Pinkstone

Wed, December 6, 2023 at 11:17 AM CST · 4 min read

↑ 4.2k



Up to 30% of people receiving mRNA vaccines suffered unintended immune responses - LEON NEAL/PA

Case # 3 Autoimmune Encephalitis

- 54y/o executive w h/o DB/mild depression who after a series of 2 Covid vaccines in 2021 and then getting COVID (mild) in Jan 2022 developed HA, accelerated cognitive impairment, depression, anxiety, tremor, PEM, POTS muscle pain, mild tremor and had to stop working in early 2023. He got 3 more shots in 2022.
- Lab 12-2022: **Vit D low**, Mayo AE and Paraneoplastic panel negative, **Sars Cov 2 IgG spike greater than 25000**, **Amyloid 42/40 .17**, **Elevated Nfl**, E3/E3, CSF MS panel negative X mild **increase in TP**, no cells /normal EEG, MoCA 28 Incell DX sCD40L 53000, VEGF 151 **but S1 in monocytes**
- MRI scattered subcortical white matter changes new from 2019
- Neuroquant: Very high diffuse neuroinflammation
- EMG: normal but SFN positive

NeuroQuant[®] TBA

Triage Brain Atrophy Report

Patient Information

Patient ID: PPI6692
 Sex: M
 Age: 53
 Referring Physician: GAZDA, SUZANNE

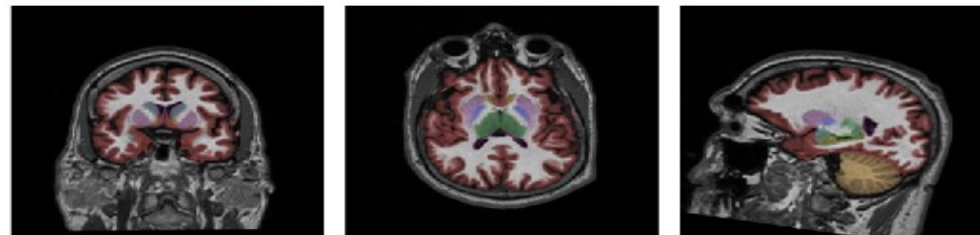
Report Information

Scan Date: 2022-11-28
 Scan Accession: 100/0490
 Report Date: 2022-11-28
 Software Version: 3.1.2

Site Information

Paesanos Parkway Imaging
 3603 Paesanos Pkwy, Suite 110
 San Antonio, Texas 78231

Brain Structure Visualization



Brain Structure Volumes

Brain Structure	Volume (cm ³)	Normative Percentile
Intracranial Volume	1470	-
Whole Brain	1209	99
Forebrain Parenchyma	1040	98

Brain Structure	Normative Percentiles		
	Left	Right	Total
Cerebral White Matter	61	57	59
Cortical Gray Matter	98	97	98
Ventricle	16	3	8
Cerebral WM Hypointensities*	94	96	97
Subcortical Structures			
- Cerebellar White Matter	98	92	96
- Cerebellar Gray Matter	96	96	96
- Brainstem	-	-	99
- Thalamus	88	97	95
- Ventral Diencephalon	99	99	99
Basal Ganglia			
- Putamen	86	95	91
- Caudate	72	33	54
- Nucleus Accumbens	64	35	38
- Pallidum	83	96	92
Cingulate	85	97	96
- Anterior Cingulate	67	93	89
- Posterior Cingulate	96	98	98
- Isthmus Cingulate	60	75	67

*White matter hypointensities are abnormally low signal intensity regions within the white matter as observed on a T1 weighted MRI scan.

Color Code Key:

Pink: A tissue is below the 5th percentile OR a ventricle that is above the 95th percentile OR WM hypointensity that is above the 50th percentile.
 Blue: A tissue is above the 95th percentile OR a ventricle is below the 5th percentile

Prior scan not compatible with change analysis

Brain Structure	Normative Percentiles		
	Left	Right	Total
Frontal Lobe	76	83	80
- Superior Frontal	50	99	89
- Middle Frontal	79	16	48
- Inferior Frontal	61	81	73
- Lateral Orbitofrontal	47	37	41
- Medial Orbitofrontal	37	24	27
- Paracentral	96	86	94
- Primary Motor	83	86	87
Parietal Lobe	99	98	99
- Primary Sensory	98	72	94
- Medial Parietal	95	97	97
- Superior Parietal	44	87	72
- Inferior Parietal	99	97	99
- Supramarginal	74	82	82
Occipital Lobe	50	36	42
- Medial Occipital	69	94	85
- Lateral Occipital	38	5	14
Temporal Lobe	99	99	99
- Transverse Temporal / Superior Temporal	99	99	99
- Posterior Superior Temporal Sulcus	60	35	42
- Middle Temporal	94	95	97
- Inferior Temporal	45	56	50
- Fusiform	86	51	72
- Parahippocampal	92	93	94
- Entorhinal Cortex	99	99	99
- Temporal Pole	83	85	88
- Amygdala	74	95	89
- Hippocampus	99	99	99

Treatment

- We started the Bredesen protocol & the FLCCC recovery protocol I but over time he was not improving
- He continued Lamotrigine, Xanax prn, Cymbalta, Adderall and DB meds per other doctors
- Memantine, LDN, NAC, NK, LD ASA, IVM, Vit E/ B complex/ D3/K2, Melatonin, Megaspore, BCM Curcumin, Trans-Resveratrol, Omega 3, Ashwagandha, Bacopa, Mg Threonate, ALCAR, Brain HQ, Healthy Diet/IF ,Light stretching, some resistance training
- Seen in the ER NOV 2023 with psychosis , he was started on Ketamine NS by psychiatry which seemed to help
- Based on careful observation, the fact that antibody panels in AE have limited accuracy, his white matter changes on MRI, elevated CSF TP, a **Brain PET was ordered and showed findings c/w AE**
- Early Jan, DC Ashwagandha, Bacopa & IVM: added Oxytocin, Probenecid, breath work, daily meditation
- The patient dramatically improving now on above plus IVIG

Treatment of Cognitive Deficits and Behavioral Symptoms Following COVID-19-Associated Autoimmune Encephalitis With Intravenous Immunoglobulin: A Case Report and Review of the Literature Naeem S et al Cureus Dec 2023

The Laboratory Diagnosis of Autoimmune Encephalitis Lee S et al J of Epilepsy Res 2016

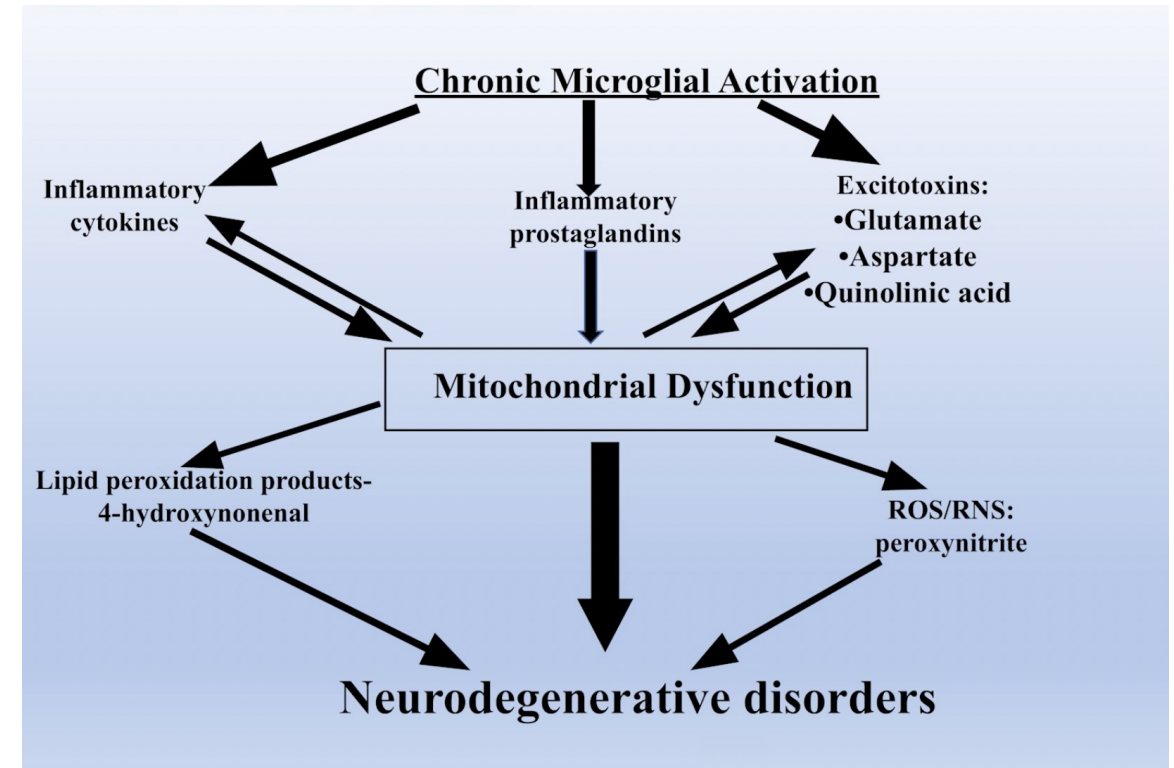
A possible case of autoimmune encephalitis after mRNA COVID-19 booster vaccine: a case report. Abu-Abaa M et al Cureus. 2022;

Chronic Neuroinflammation is the Downfall of the Brain

- Neuroinflammation is a key pathophysiological mechanism in Neuro-COVID (Monje M) (Talla A) (Vonderheiden A) (Braga J)
- Lingering viral fragments are damaging the vasculature, the BBB, stimulating a dysregulated immune response in the brain causing neuroinflammation, autoantibodies & in some prions

Neuroinflammation: the devil is in the details Disabato D et al J of Neurochemistry 2016

Long COVID is associated with extensive in-vivo neuroinflammation on [18F]DPA-714 PET Pre-print June 2022



Autoimmune Encephalitis: Over 50% are Autoantibody Negative

- AE is characterized by new onset seizure, cognitive impairment, and or psychiatric symptoms
- Now cases are different and more challenging
- If MRI and CSF are negative and you strongly suspect AE , PET scan is indicated in all patients
- Workup for these patients should include MRI, Neuroquant, CSF , Mayo AE and Paraneoplastic panel, IgG and IgG subsets, NfL, AD 42/40, serum tau 181, ESR, metabolic and conventional lab & in some eval for malignancy , EEG

Treatment of Cognitive Deficits and Behavioral Symptoms Following COVID-19-Associated Autoimmune Encephalitis With Intravenous Immunoglobulin: A Case Report and Review of the Literature Naeem S et al Cureus Dec 2023

The Laboratory Diagnosis of Autoimmune Encephalitis Lee S et al J of Epilepsy Res 2016

A Case Report: Multifocal Necrotizing Encephalitis and Myocarditis after BNT162b2 mRNA Vaccination against Covid-19. Vaccines Morz M 2022

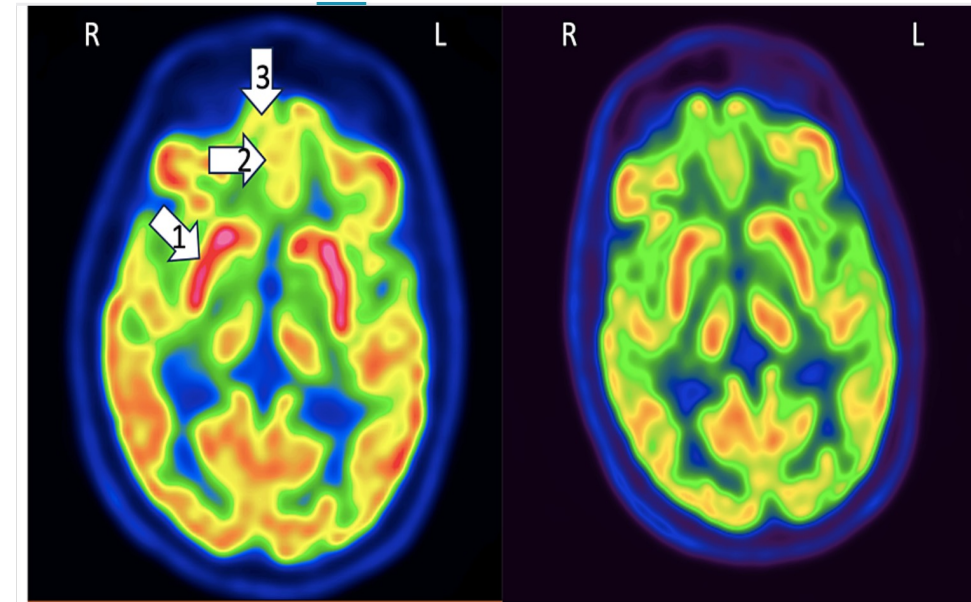


Figure 1a

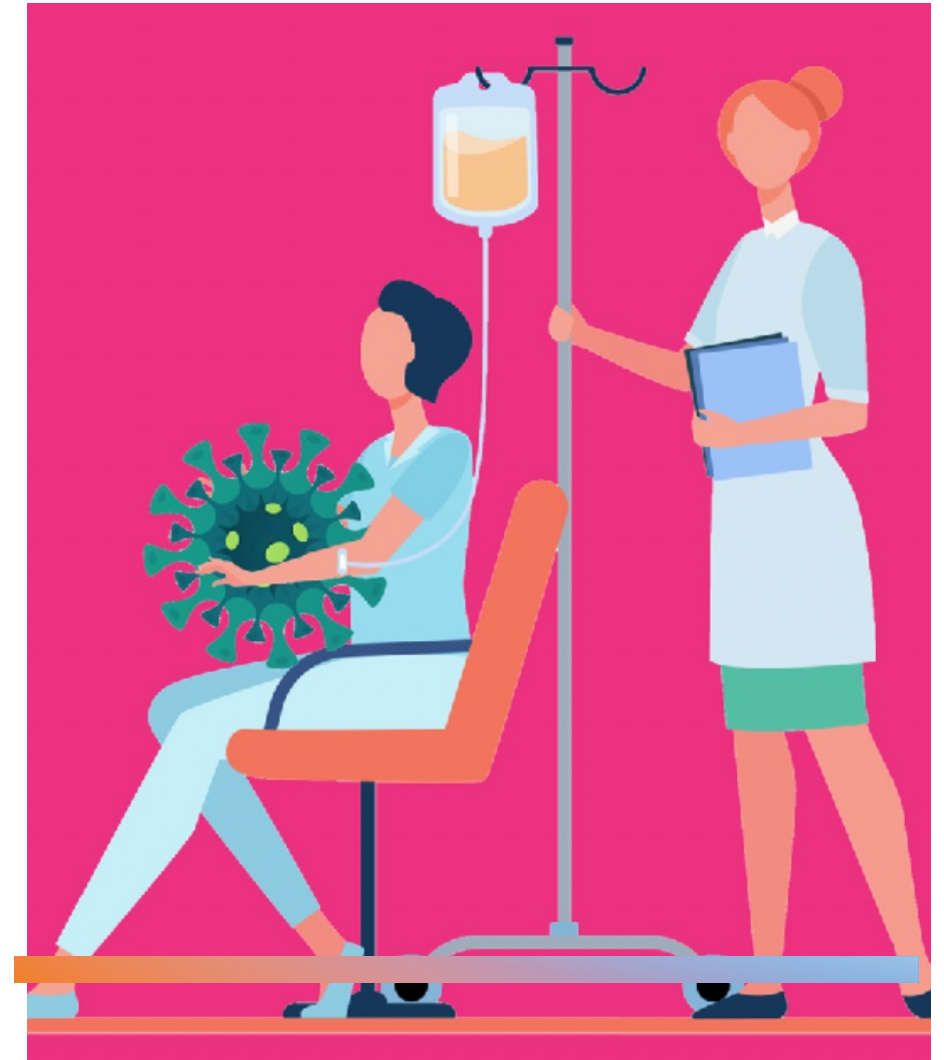
Figure 1b

Figure 1: PET FDG Scans

In a PET scan, colors showing decreasing order of metabolic activity are red, yellow, green, and blue. 1a shows areas of hypermetabolism, indicated by red/red-white shade for the basal ganglia (1), yellow shade for the olfactory cortex (2), and superior/middle frontal gyri (3) leading to the diagnosis of autoimmune encephalitis. Following the five-day course of IVIG, these areas (1b) showed hypometabolism (trending towards normal) as indicated by a decrease in the intensity of red shade for basal ganglia (1), green shade for olfactory cortex (2), and green-yellow shade for superior and middle frontal gyri (3).

The Many Wonders of IVIG

- Multiple papers show benefit of IVIG in Long Covid
- IVIG reduces inflammasome/cytokines driving microglial cell activation and promotes autophagy
- IVIG was beneficial in a mouse model of TBI (Willis et al March 2023)
- Inactivates auto-reactive T-cells by competing for and interrupting their interaction with antigen presenting cells
- Downregulates antibody production by B-cells, interferes with B-cell proliferation via a blockade of cell surface receptors and prevents the activation of certain subtypes of B-cell
- Affects innate immunity by interrupting the steps in the complement activation cascade and blocking Fc-receptor mediated activity
- May help sheer up the BBB and **induces autophagy**
- IVIG can be helpful in many autoimmune diseases including small fiber neuropathy



IVIg Protocol

- IVIG can trigger MCAS therefore the needs for pre-meds like H1 and H2 blockers (famotidine 20 mg twice daily or ranitidine 150 mg twice daily), and steroids . Some patients with severe mast cell activation syndrome take up to 8 doses of a histamine 1 receptor blocker on the day of infusion and for 2-3 days after
- One liter of normal saline over 1 h, warmed to body temperature for patients with severe autonomic dysregulation and/or mast cell activation syndrome as temperature change is often a trigger for mast cell activation. If needed, a second liter can be given at the end of the IVIg infusion for patients with prolonged headaches despite the above treatments. Note: should not run concomitantly with the IVIg due to the risk of precipitation of the antibody molecules
- Start slowly and increase as tolerated

0.25 g/kg weekly x 4 infusions within 28 days then

0.33 g/kg approximately every 10 days × 3 infusions within 28 days then

0.50 g/kg approximately every 14 days × 2 infusions within 28 days then

0.75 g/kg approximately every 21 days × 1-2 infusions then

1.0 -2 g/kg approximately every 28 days thereafter.

Atypical Guillain Barre Cases Rising

- There are multiple case reports of GBS after the vaccines
- GBS is an acquired demyelinating polyneuropathy that often begins in the lower extremities and ascends over time with loss of reflexes, causing muscle weakness
- 806 VAERS reports of which “verified” 295 cases of GBS from the mRNA vaccine (Abara W 2023)
- GBS incidence went down during 2020 (Keddie S 2021)
- This patient: Tetra-paresis/B/B dysfunction Jan 2021: DG FND/sent home unable to move



Functional Neurological Disorder: A Dangerous Diagnosis A Failure of Western Medicine

- At one large US tertiary care movement disorder clinic, the number of newly referred patients who received a diagnosis of FND increased by 60.1% (Hull M et al 2021)

The onset of functional movement disorders after COVID-19: A case series
Rodion S Indian Journal of Psychiatry Sept 2022

Functional Neurological Disorder After SARS-CoV-2 Vaccines: Two Case Reports and Discussion of Potential Public Health Implications Butler M et al J of Psychiatry and Clinical Neurosciences July 2021



Nerves in the Line of Fire

- 59% of LC patients and over 70% of the vaccine injuries have neuropathy symptoms.
- Neuropathic pain, sensory disturbances, neurovascular dysregulation and autonomic dysfunction
- Need SFN BX/ EMG will be normal
- MOA: Antibody mediated damage to key receptors, molecular mimicry, MCAS and/or smoldering inflammation

Prevalence Data React 19 2021

Peripheral Neuropathy Evaluations of Patients With Prolonged Long COVID Oaklander A et al Neurology 2022

SYMPTOMS OF SMALL FIBER NEUROPATHY

Pain and Burning In The Lower and Upper Extremities

“Pins and Needles”

Loss Of Feeling In The Hands and Feet

Feet and Hands are Tender and Sore

Cramping In Feet, Ankles, Calves, and Hands

Numbness

Fatigue

Inability To Sweat

Dry Eyes

Skin Discoloration

Dizziness, Lightheadedness

Difficulty Breathing

Increased Heart Rate

Difficulty With Bowel and Bladder Functions

Pussycat Doll Member Shares Vax Injury

- Jessica Sutta recently spoke out about her vaccine injury occurring in 2021 after her Moderna shot with unremitting pain, uncontrollable movements and weight loss.
- DG with Small Fiber Neuropathy
- Small fibers are every where and these presentations can be varied and atypical (Nath A) (Khokhar F) (Tandia R)
- In 50% of the patients, pain and sensory disturbances from small fiber neuropathy affect the entire body and can be very severe (McAlpine L)
- Autonomic nerve fibers are usually involved



More POTS in the COVID-19 and Vaccine Era

- A high percentage of people with long COVID have symptoms of autonomic dysfunction and most will have SFN
- A study in Nature, (284,592 vaccinated individuals), found a **33 percent** increase in POTS. (Kwan A)
- **55%-85%** of long COVID patients c/o post-exertional malaise, brain fog, palpitations, fatigue, and dizziness (Thaweethai T)
- The vasculature is dysregulated with SFN

Apparent risks of postural orthostatic tachycardia syndrome diagnoses after COVID-19 vaccination and SARS-Cov-2 Infection Kwan A et al Nature Cardiovascular Research December 2022

POTS Subtypes

Neuropathic POTS

Characterized by decreased sympathetic innervation, particularly in legs

- Loss of sweating in extremities
- Blood pooling
- Blue/red/purple feet when standing or warm



Hypovolemic POTS

Characterized by low blood volume, both plasma and red blood cells

- Weakness
- Decreased exercise tolerance



Hyperadrenergic POTS

Characterized by elevated plasma norepinephrine and rise in systolic blood pressure when standing

- Extreme tachycardia
- Heart palpitations
- Tremor
- Migraine headaches
- Nausea/vomiting



Dysautonomia contributes to fatigue, brain fog, autonomic and neuropathic symptoms

- Patients w ME/CFS and LC had inappropriate tachycardia at rest, with a high percentage of patients with POTS.
- Lower parasympathetic activation was associated with **worse cognitive performance**

Dysautonomia and small fiber neuropathy in post-COVID condition and Chronic Fatigue Syndrome Azcue N Research Square 2023



Multiple Mechanisms in POTS Post COVID

- **Damage to the Vagus nerve** (Woo M)
- **Autoimmune/Molecular mimicry:** antibodies to adrenergic and muscarinic receptors, ganglionic acetylcholine receptor, NMDA receptor and Spike protein shares molecular mimicry with GPCR's (Wallukat G)
- **Low Serotonin** (Wong A) (Rinker L)
- **Ach Nicotinic Receptors blocked** (Leitzke M)
- **Small Fiber Neuropathy**
- **Mitochondrial dysfunction** (Chen CH)
- **Downregulation of ACE2** by SARS-CoV-2 increase angiotensin II (AngII), which activate release of pro-inflammatory cytokines (PC) & fuel the SNS (Khazaai S)

Case 3: Dysautonomia/EDS

- 41 y/o WF previously healthy after second shot in 2021 had a sore R arm and then developed crushing body pain, intractable vomiting, choking, cold extremities, feels like has rubber gloves on, extreme fatigue, severe insomnia, urinary incontinence, R side weak, neck pain, joint pain/whole body itches, No brain fog/NO cardiac SX
- One night: found unresponsive, intubated, negative eval in hospital: DG FND /depression
- Lab : high ferritin/ **spike antibodies greater than 25000**/ MTHFR double mutation
- Exam: Low BP/ mild tremor / hypermobile (new) /brisk reflexes/ red/ purple discoloration of hands and feet
- MRI Brain and C spine and NQ OK/ EMG normal but **Syn One skin BX showed alpha synuclein**
- F/u one month later: on class 2 narcotic, progressing, no control over body, bobble head, extreme joint laxity, muscle and joint pain can not control his muscles, L side weak now, loss of proprioception, balance worse, “body has been taken over by an alien”



Syn One

- Levine et al found 7 of 22 neuropathic POTS patients had cutaneous alpha-synuclein deposition
- Miglis et al report the presence of p-syn in five young patients with Long-COVID POTS (LC-POTS) but without prodromal features of neurodegenerative disease.

Trans-synaptic spreading of alpha-synuclein pathology through sensory afferents leads to sensory nerve degeneration and neuropathic pain Ferreira N et al Acta Neuropathologica Communications 2021

Microscopic Description	
Phosphorylated Alpha-Synuclein Abnormal Phosphorylated alpha-synuclein deposition was observed in the posterior cervical biopsy.	Intraepidermal Nerve Fibers Normal Intraepidermal nerve fiber density was normal in all biopsies.
Amyloid Deposition (Congo Red) Normal Modified Congo red staining shows no evidence of apple-green birefringence under polarized light in any of the biopsies.	Skin Histology (Hematoxylin and Eosin) Normal Routine hematoxylin and eosin staining show no histopathologic abnormalities in any of the biopsies (see page 2).

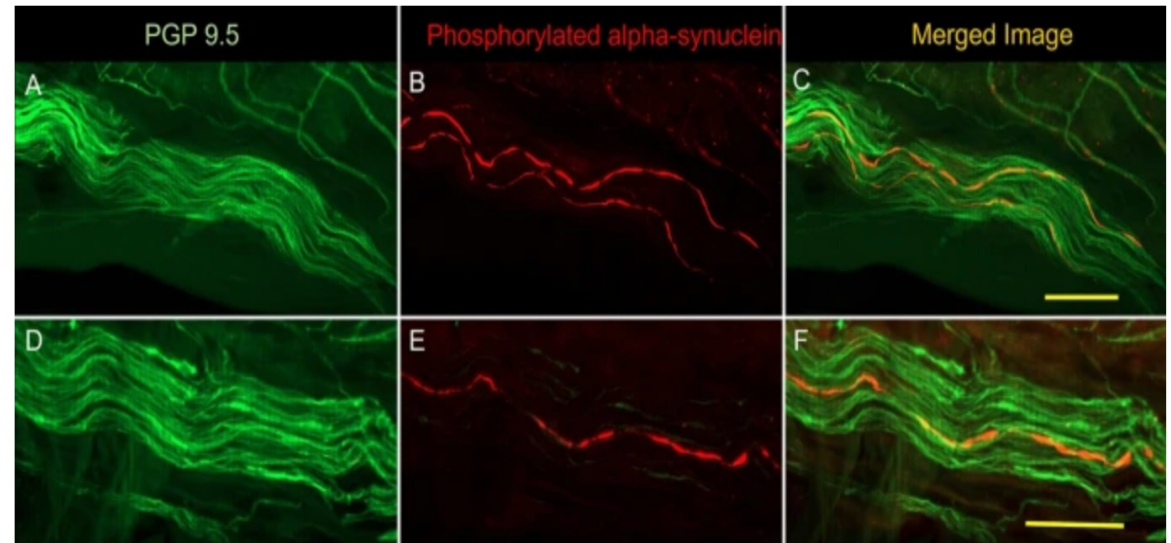
Synucleinopathies Diagnosed with the Syn One Skin Punch Biopsy CND Life Sciences

- Parkinson's disease
- Dementia with Lewy bodies
- Multiple system atrophy
- Pure autonomic failure
- REM sleep behavior disorder
- Dysautonomia w POTS or in Long COVID

Alpha-Synuclein in Skin Nerve Fibers as a Biomarker for Alpha-Synucleinopathies. Kim JY et al J Clin Neurol. 2019 Epub 2019

The Synuclein-One Study: Skin Biopsy Detection of Phosphorylated alpha-synuclein for Diagnosis of the Synucleinopathies. Presented at: AAN Annual Meeting; April 2023 Gbbions C et al

Fig. 1



Examples of nerve fibers from two patients (A–C and D–F). On the left (A and D), nerve fibers surrounding a blood vessel are shown in green through immunostaining with protein gene product 9.5 (PGP9.5). In B and E, the presence of phosphorylated α -synuclein (P-SYN) is seen in red. In C and F, the merged image reveals the presence of intra-axonal phosphorylated α -synuclein in orange

EDS: Be Vigilant

- The outcomes of five women, ages 33 to 51, **who did not have a history of a hypermobility disorder were recently reported** (Logarbo B Dec 2023) and were found to have new onset EDS
- Up to 15 months after getting COVID-19, all patients developed persistent and debilitating fatigue, accompanied by cognitive dysfunction, joint pain, and dysautonomia
- All had MCAS and were homozygous for MTHFR
- EDS often have high MCAS and SFN
- Musculoskeletal complications and hypermobility are reported in Long COVID (Swarnaker R)(Hakim A) (Gavrilova M)
- This is due to misdirected immune response to connective tissue post COVID or PVI (Logarbo B)

<https://www.midwesterndoctor.com/p/the-hidden-link-between-hypermobility>

<https://www.midwesterndoctor.com/p/how-to-improve-zeta-potential-and>

What Will Her Future Hold?

- A large and long of study suggests a phenotype conversion rate of 6.25% per year, with 73.5% of the cohort developing a neurodegenerative disease, most commonly an alpha-synucleinopathy, over 12 years of follow up (Postuma RB)

Risk and predictors of dementia and parkinsonism in idiopathic REM sleep behavior disorder: a multi-center study Postuma RB Brain 2019



Treatments initiated

- Zyrtec, Pepcid, Zafirlukast (Accolate) bid
- Quercetin one twice a day
- Luvox 25 mg once a day X one week then one twice a day
- Baby ASA /NTK
- LDN/IVM
- NAC one twice a day
- Vitamin C and manganese to help produce collagen
- Methylated B vitamins +Zinc ((Vitamins B6 and B12, zinc also play a role in the production of collagen and B for MTHFR)
- Omega 3 one twice a day
- BCM Curcumin one to two twice a day
- Sunlight every day to help increase liquid crystalline water and increase VIT D
- Divinia water (deuterium depleted water in recyclable glass bottles)
- Vegetable juicing every day (benefits of juicing is the presence of liquid crystalline water, DDW, and possibly some type of electrical charge from the plants plus nutrients)
- Kachava 2 scoops/ day one a scoop of Collagen Peptides in smoothie or other
- Physiotherapy for ligament and joint strengthening

Celine Dion announced she has SPS in 2022

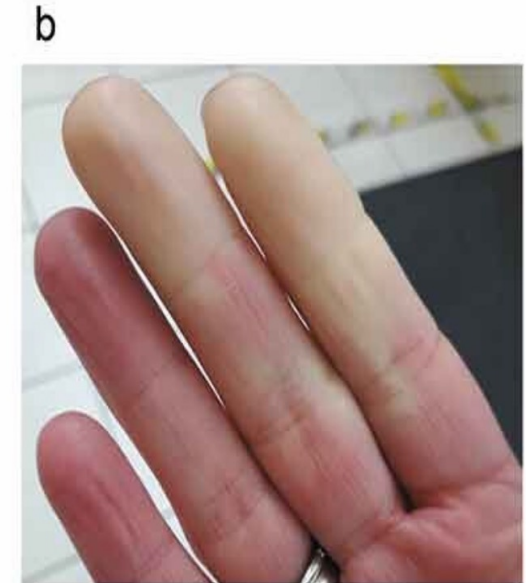


28 out of 55 Human
Tissues Reacted to Viral
Fragments
GAD was One of Them
Vojdani et al Frontiers
Immunology 2021

Antigens	Spike protein OD	% reactivity
SARS-CoV-2	3.40	100 ++++
Actin	0.74	17.6 +
Mitochondrial antigen (M2)	1.52	41.8 +++
ENA	0.85	21.0 +
NA	1.34	36.2 ++
Histone	0.65	14.8 +
S100B	0.46	9.0 +
MBP	0.53	11.1 +
NFP	1.98	56 ++++
Synapsin	0.81	19.8 +
Beta-amyloid P	0.83	20.4 +
Tau protein	0.41	7.4 +
Collagen	0.45	8.6 +
Alpha-myosin	0.72	17.0 +
Tropomyosin	0.21	1.2 -
TPO	0.98	25.1 ++
Liver microsome	1.00	25.7 ++
PDH peptide	0.91	22.9 +
GAD-65	1.35	36.5 ++
Insulin	0.25	2.5 -
Insulin-R	0.72	17.0 +
Phospholipid	0.93	23.5 +

Case 4 SPS

- 43y/o WF with new onset severe muscle spasms, startle phenomena, dystonic spasms, severe fatigue and brain fog, neuropsychiatric symptoms, Raynaud's, uncontrollable tremor and other bizarre movements a few weeks after vaccine # 2 in 2021
- **DG FND**
- MRI / all labs normal except **GAD 65, Nfl high, and EMG c/w SPS**
- NeuroQuant: High levels of neuroinflammation
- Not much help from initial protocol **but now back working after IVIG X 6 months**





GAD65-Ab Associated Neurologic Syndromes Are On A Continuous Disease Spectrum

- GAD is the rate-limiting enzyme to produce GABA (the main inhibitory neurotransmitter in the CNS)
- Anti-GAD antibodies are classically seen with SPS, cerebellar ataxia, limbic encephalitis (LE) and overlap syndromes (GAD 65 greater than 10000)
- Neurological syndromes with **low GAD 65** (atypical PKD, Myasthenia, MS, Movement disorders, Myelopathy, Immune-mediated neuropathies, Autoimmune encephalitis) (Thevarkalam M)
- GAD may be a marker of autoimmune issues but may not actually mediating disease ; it may be a marker for response to immunotherapy
- **Neurofilament light chain (NfL)** is a marker of axonal damage and is elevated early in the course
- IVIG is the mainstay of RX for GAD illness, and **these atypical syndromes can also respond to IVIG**

Early Neuroaxonal Damage in Neurologic Disorders Associated With GAD65 Antibodies Eisenhut K et al Neurology October 2023

Neurologic syndromes related to anti-GAD65 Amaia Muñoz-Lopetegi et al Neurology 2020

Neurological Manifestations of Glutamic Acid Decarboxylase Autoimmunity in Indian Patients Thevarkalam, Meena et al Annals of Indian Academy of Neurology 2023

Clinical spectrum of glutamic acid decarboxylase antibodies in a Taiwanese population. Kuo WC et al Eur J Neurol 2019

Take Home List for All

- Eat Real Food
- Intermittent Fasting
- Never go to bed without learning one new thing
- Value Sleep
- Keep your body active/ keep moving
- Immerse in Nature/ Sunshine
- Be present, be aware, be mindful



Thank you

Each and Everyday Work to Build a Better Brain

The BRAIN That
CHANGES
ITSELF





“

To the people still choosing their own safety, security, and emotional comfort over saving lives and protecting freedom for posterity,
**it's not too late to do the right thing—
but someday it will be.**

”

From Jenna McCarthy's 'Here's a Thought...'

Additional Resources

Dr Suzanne K Gazda

Improve the Immune Terrain

- LDN is immunomodulation , reduces IL-6 and TNF α & activity of toll-like receptor 4 (TLR4) Toll-like receptors recognize conserved molecular patterns and nucleic acids as part of the innate immune response
- CBD can help modulate or suppress the functioning and secretion of cytokines
- Omega 3: omega-3 and omega-6-derived metabolites have important immune-regulatory functions.
- SPM's
- Pro-resolving mediators
- Peptides like Thymosin α 1 could restore the T cells by enhancing their maturation and inhibiting apoptosis In addition, it also could prevent a proinflammatory cytokine storm by increasing regulatory T cells
- HBOT increases telomere length and decreases immuno-senescence
- PLEX
- IVIG



Improve the Immune Terrain: SPM's

- Specialized pro-resolving mediators (SPMs) are endogenous small molecules produced mainly from dietary omega-3 polyunsaturated fatty acids by both structural cells and cells of the active and innate immune systems
- Pro-resolving mediators signal the immune system to stop actively responding to pro-inflammatory signals, and instead to accelerate the return to homeostasis and promote clearance of damaging byproducts, microbes, and debris by enhancing macrophage phagocytosis
- SPMs promote resolution by binding to G-protein coupled receptors that can modify cellular behaviors such as mediating pro-inflammatory chemokine, cytokine, and adipokine regulation, microRNA transcription and translocation, and cell traffic
- SPM Active 2 / day

The Resolution Code of Acute Inflammation: Novel Pro-Resolving Lipid Mediators in Resolution Serran C et al Semin Immunol. 2015 May

Ligand-specific conformational change of the G-protein–coupled receptor ALX/FPR2 determines proresolving functional responses Cooray S et al Proc Natl Acad Sci U S A. 2013

Dissolving Prions

- Quercetin disaggregates prion fibrils and decreases fibril-Induced cytotoxicity and oxidative Stress (Lee C 2020)
- Methylene blue: binding of methylene blue to a surface cleft inhibits the oligomerization and fibrillization of prion protein (Cavaliere 2018)
- Doxycycline was reported as an antiprion agent in different experimental models (Varges D 2006)
- Epigallocatechin-gallate (EGCG) interferes in different steps of amyloid formation (Fernandes L 2021)
- Most Flavonoids
- Curcumin inhibits amyloid (Ivanov F 2020)
- Intranasal Oxytocin (El-Ganainy S 2022) showed with Galantamine , reduced β -amyloid, Tau accumulation, and neuronal death/ may lengthen telomeres
- Serrapeptase and Lumbrokinase (Metkar S 2022)
- Fisetin is a natural substance found in strawberries and apples and has anti-amyloid properties (Ahmad A 2017)
- TUDAC reduces ER stress by regulating of Akt-dependent cellular prion protein (Cortez L 2015)
- HBOT reduced amyloid burden by reducing the volume of pre-existing plaques and attenuating the formation of new ones
- NanoVi produces the same biological signal your body makes to repair cell damage brought on by free radicals (eng-3)

HCQ for Alzheimer's Disease and Stolen Memories

- Using longitudinal insurance claims data from Medicare beneficiaries they found a reduced risk of AD in those on HCQ vs MTX(over 100000 patients followed)
- HCQ targets multiple pathogenic mechanisms in AD including synaptic dysfunction, neuroinflammation, A β clearance, and tau phosphorylation
- Rescues impaired hippocampal synaptic plasticity prior to amyloid accumulation, enhances microglial clearance of A β 1-42, inactivates STAT3 in microglia, neurons, and astrocytes and lowers neuroinflammation

Hydroxychloroquine lowers Alzheimer's disease and related dementias risk and rescues molecular phenotypes related to Alzheimer's disease Varma V et al Molecular Psychiatry Nature Dec 2022



Metformin

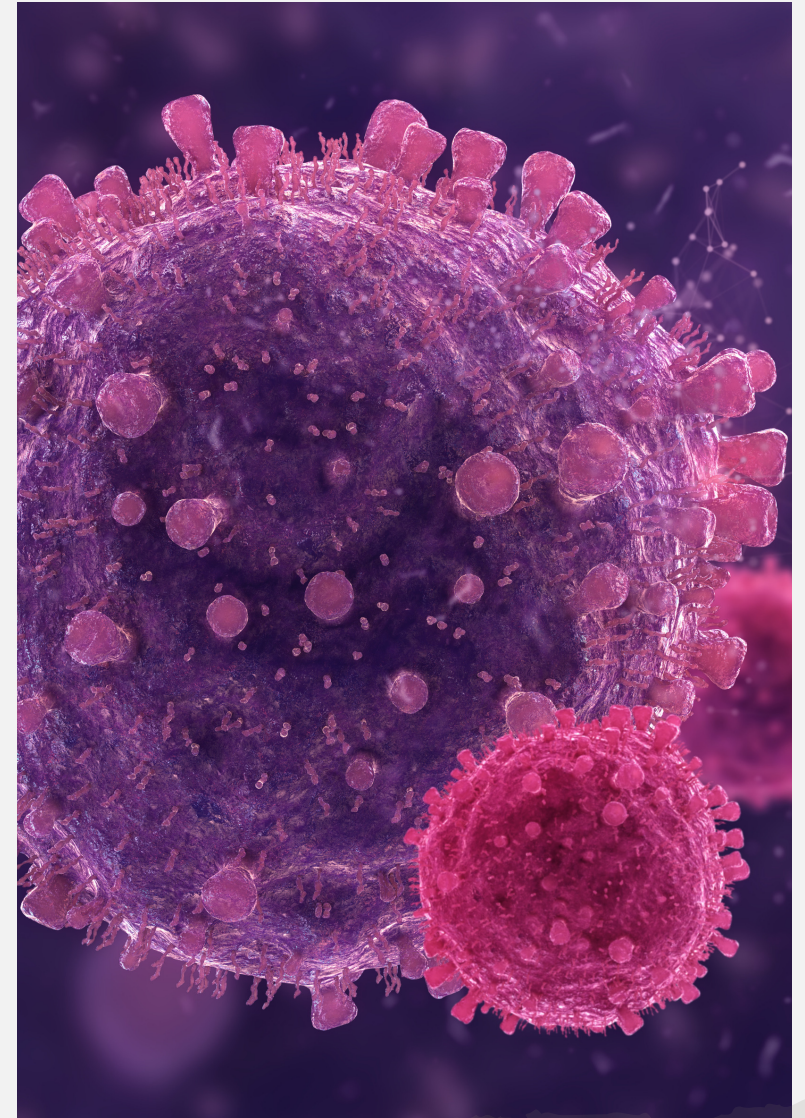
- Metformin can regulate synaptic transmission & plasticity in pathological conditions but also to regulate the balance of excitation and inhibition (E/I balance) in neural networks
- Improves insulin signaling and enhances neuritic growth and has been shown to play many different roles within the brain, ranging from neuroprotective effects to positively influencing higher cognitive processes.
- Promotes autophagy in vivo and in vitro, to reduce Tau hyperphosphorylation and improve cognition
- Is a HDAC inhibitor and downregulates proinflammatory pathways
- Inhibits intracellular inflammatory pathways, activates AMPK, and increases inhibition of mTOR, which may be a major target for regulating aging
- Metformin can improve synaptic defects, memory problems and enhance cognition in animal models of AD (Pilipenko et al 2020; Saffari et al 2020).
- Metformin's ability to inhibit mTOR expression may be helping it regulate the activity of out-of-control sensory neurons that are causing so much pain in FM and other diseases.

Metformin: A Prospective Alternative for the Treatment of Chronic Pain Baeza-Flores C et al *harmacol* 2020

Exploring the Pharmacological Potential of Metformin for Neurodegenerative Diseases Du M et al *Front. Aging Neurosci.*, 26 April 2022

Mast Cell Stabilization

- **Montelukast (brand name Singulair)** has antiviral activity, lowers TNF Alpha and IL 6 or **Zafirlukast (Accolate)** 20mg bid
- **Supplements** including **luteolin, quercetin, vitamin C**, local raw honey, **bromelain**, probiotics, astragalus, butterbur, **D-HIST, PEA** may reduce microglial activation
- **Luteolin**: calms/inhibits the mast cell response; has anti-inflammatory, anti-carcinogenic, and anti-viral properties; “inhibits interleukin (IL)-6, IL-8 and VEGF
- **H1 and H2 blockers**
- A low histamine diet
- **LDN (Low Dose Naltrexone)** .5-4.5 mg per day



Address Microclotting

- **Nattokinase, Streptokinase, Lumbrokinase**
- **Pycnogenol** (protects the endothelium) 100-180mg/ day
- **ASA/ Plavix / Eliquis**
- **Pentoxifylline** PTX ER, 400 mg three times daily . PTX is a non-selective phosphodiesterase drug that has anti-inflammatory and antioxidant effects
- **Arterosil:** The endothelial glycocalyx is a microscopically thin gel-like layer that coats the entire luminal side of the vascular endothelium.
- **Curcumin** lowers fibrinogen ,Vitamin B6 exerts several effects on preventing excessive platelet aggregation & Butyrate can reduce platelet growth factor
- **Resveratrol:** A dose-dependent inhibitory effect of resveratrol on platelet aggregation has been observed in cellular and animal models.
- **Vitamin C 500mg Quercetin,500mg ,Lutein 40mg** all increased nitrous oxide very effectively
- **Vit D** may have anti-fibrotic properties
- **L Arginine, Agmatine, Cardio-Miracle** (all work to increase nitrous oxide). L-arginine improves endothelial dysfunction by being the substrate of NO generation in endothelial cells
- **SSRI** like Luvox can inhibit platelet activation (sigma-1 receptor (S1R) agonist which, on the one hand, reduces the expression of IL-6, while increasing that of eNOS).
- **HBOT**
- **Flow Therapy**

Nattokinase: The Heart of the Matter

- NK has potent fibrinolytic/antithrombotic activity & also has antihypertensive, anti-atherosclerotic, lipid-lowering, antiplatelet/anticoagulant, and neuroprotective actions
- NK enhanced fibrinolysis through cleavage and inactivation of PAI-1
- NK can degrade amyloid fibrils therefore the neuroprotective effect of NK are due to its proteolytic, anti-inflammatory, and antiapoptotic effects

Nattokinase: A Promising Alternative in Prevention and Treatment of Cardiovascular Diseases Chen H et al. Biomark Insights. 2018 Jul

Amyloid-Degrading Ability of Nattokinase from Bacillus subtilis Natto. Hsu et al | Journal of Agricultural and Food Chemistry, 2009

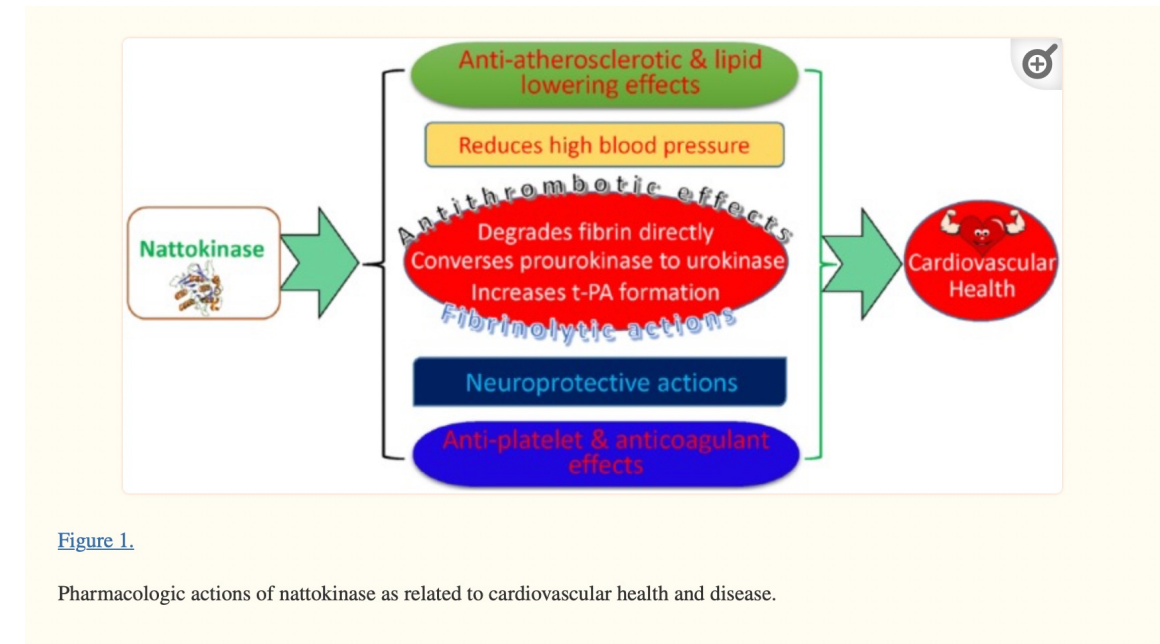


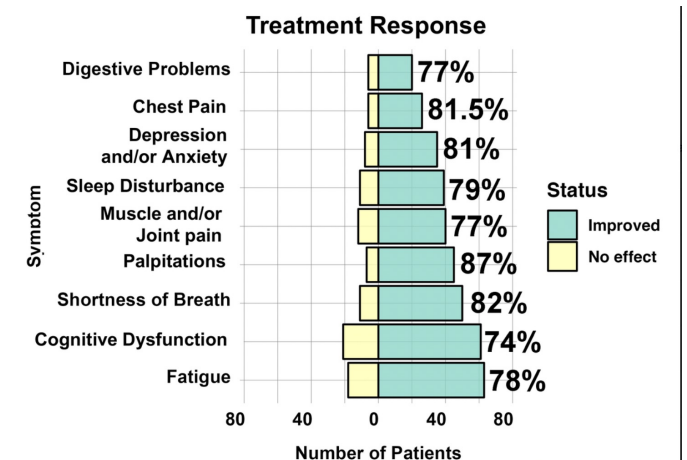
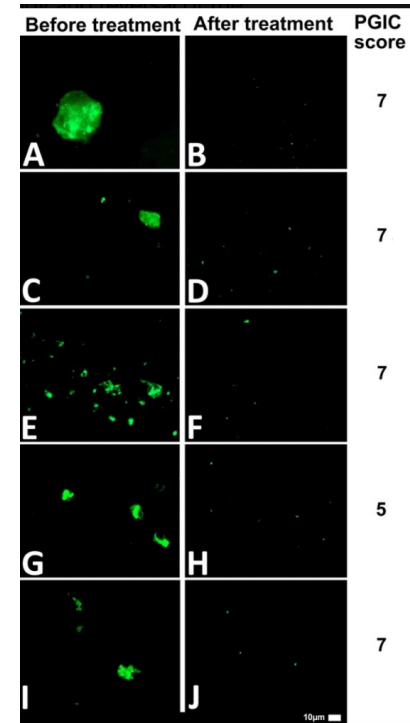
Figure 1.

Pharmacologic actions of nattokinase as related to cardiovascular health and disease.

Triple Therapy in Long COVID

- A dramatic reduction in Long COVID symptoms and microclotting was found with triple anticoagulation therapy (Pretorius R)
- The pathophysiology of Long COVID starts with damage to the endothelium (endothelialitis)
- LC symptoms are a result of a combination of microclot formation, platelet aggregates and endothelialitis a defect in oxygen transfer at a capillary level arises, leading to tissue hypoxia
- The anticoagulant regime included dual antiplatelet therapy (Clopidogrel 75mg + Aspirin 75mg) once a day, and a direct oral anticoagulant Apixaban 5mg twice a day w/ a PPI 40mg/ day

Treatment of Long COVID symptoms with triple anticoagulant therapy
 Pretorius R et al Research Square March 2023



Vit D and Brain Health

- Patients at Rush Memory and Aging Project had vitamin D concentrations measured in four brain regions.
- Higher brain 25(OH)D3 concentrations were associated with a 25% to 33% lower odds of dementia or mild cognitive impairment (MCI) at the last visit before death
- Low Vit D is associated with reduced gray matter
- V D deficiency affects 35 percent of adults in the United States & is among 15 adjustable lifestyle factors that appear to drive up a person's early dementia risk by 40% (UK biobank Dec 2023)

Brain vitamin D forms, cognitive decline, and neuropathology in community-dwelling older adults Shea M et al The J of Alzheimer's Dec 2022

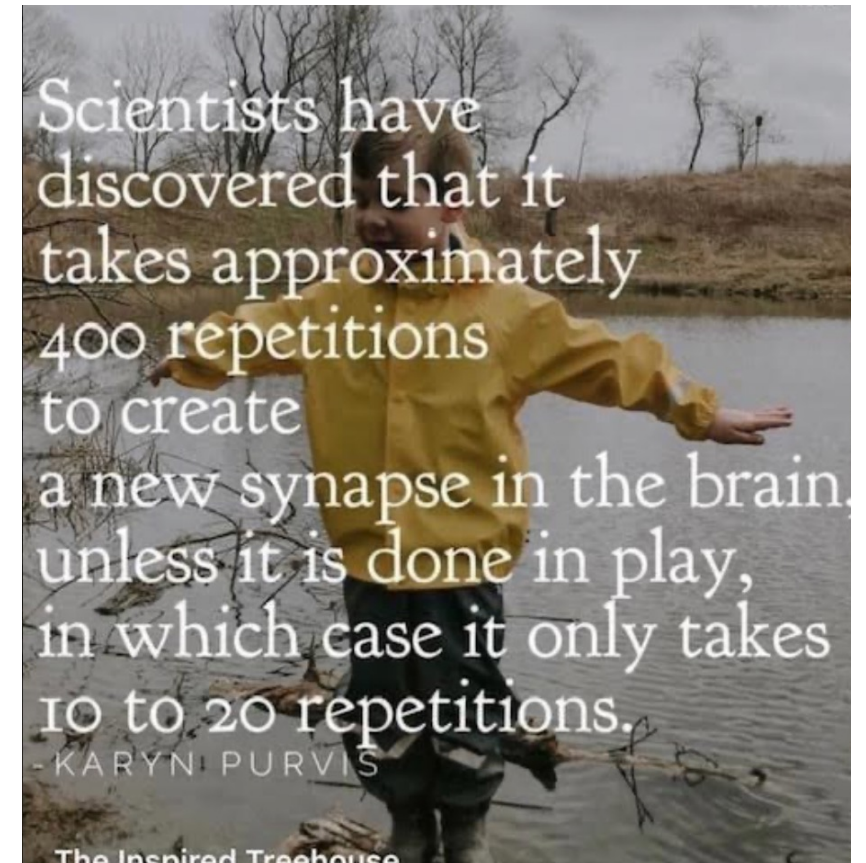
Risk Factors for Young-Onset Dementia in the UK Biobank Hendriks S et al JAMA Neurology Dec 2023

Vitamin D supplementation and incident dementia: Effects of sex, APOE, and baseline cognitive status Ghahremani M et al Alzheimer's & Dementia: Diagnosis, Assessment & Disease Monitoring, 2023



Neuroplasticity: The Brain That Changes Itself

- Time is of the essence with neuroplasticity
- Neurogenesis is the ability to create new neurons and connections between neurons throughout a lifetime
- Life should be an ongoing enrichment experience .
Novelty is key
- Continued practice is essential
- Devote the time to brain recovery
- Be Patient Neurogenesis takes time



Ways to Enhance Your Brain: Brain Games and More

- Read, learn a new language, music, meditation, social connections, gratitude practice, love and joy
- **BrainHQ \$14/ month**
- Luminosity \$9.95/ month
- Cogmed \$1500 for 5 weeks with a clinician
- Heart Math \$249 for the device



Think Faster
Focus Better
Remember More
@ Your Library



brainHQ
from Posit Science

A Demo and Evanced Solutions
exclusive for public libraries

Treats

- **Mosh bars** are GF/ no added sugar/12 grams/ protein and have 7 brain nutrients and superfoods including: lion's mane, ashwagandha, omega 3's, collagen, flaxseed, vitamin B12, and D3)
- **Coco-Via** –3 potential benefits of cocoa flavanols are enhanced circulation, improved cognitive function and Improvements to skin (decreased wrinkles and increased skin elasticity). CocoaVia contains 500mg of cocoa flavanols per serving.

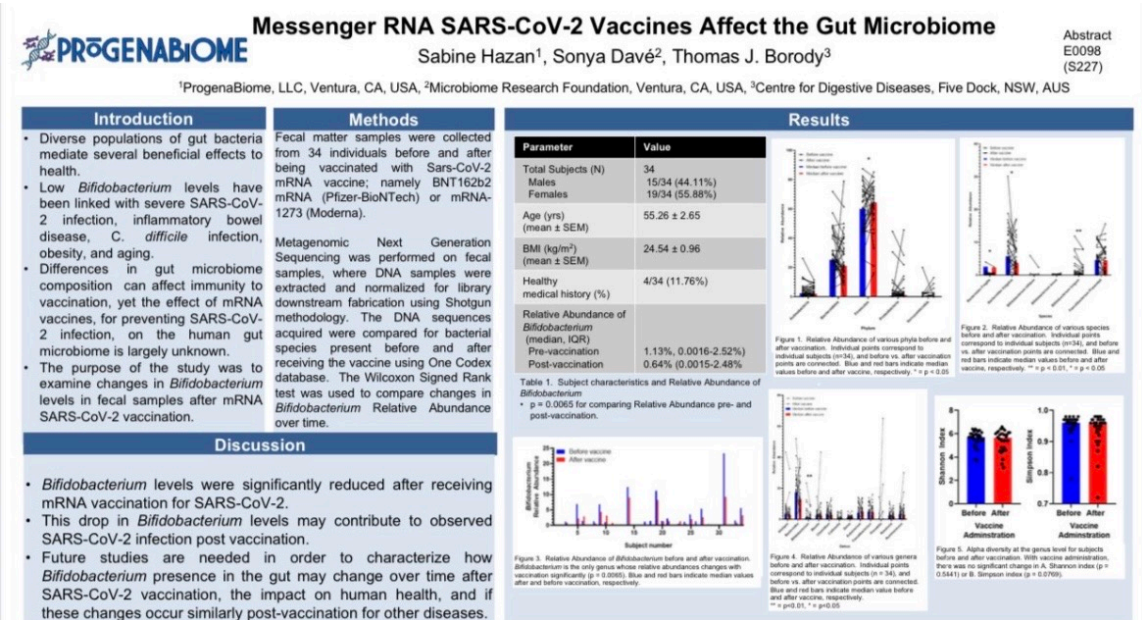
To explore the benefits of eating the right chocolate:

<https://www.suzannegazdamd.com/blog/listen-to-your-brain-and-go-ahead-and-eat-the-chocolate>



Heal the Gut

- Diet
- Rhizo health
- Probiotics and for some Prebiotics
- Address MCAS
- Oral Vitamin C or HD Vit C
- Bioflavonoids
- Butyrate



HBOT

- Increases telomere length and decreases immunosenescence
- Induces the release of stem cells and tissue growth factors & influences genetics
- Promotes tissue regeneration, neuro-genesis, increases angiogenesis, reduces inflammation & improves mitochondrial health
- Lowers amyloid and Improves CBF (Shapira 2021) In AD most do 60 one-hour sessions over 2-3 months
- In LC: 10 sessions of HBOT to 2.4 atmospheres over 12 days. Each treatment session last 105 minutes, consisting of three 30-minute exposures to 100% oxygen, interspersed with 5-minute air brakes (Robins T 2021)



Others

- **Amantadine** has been shown to interfere with the SARS COV 2 docking domain and has anti-inflammatory and dopaminergic effects/weakly blocks glutamate
- **Monteleukast:** 6-week treatment of young (4 months) and old (20 months) rats with montelukast, , reduced neuroinflammation, elevated hippocampal neurogenesis and improved learning and memory in old animals. (Aigner L et al)
- **Fluvoxamine** improves autophagy, reduces platelet aggregation and may promote neuroplasticity (Li W 2021)
- **L Carnosine** might help with loss of smell for the olfactory bulb is low in this Dose is 1000 mg tid
- **TUDCA** exerts its effects not only by regulating and inhibiting the apoptotic cascade, but also by reducing oxidative stress, protecting the mitochondria. Being studied in ALS (1 gram bid)
- **Ozone therapy** seems useful in controlling inflammation, stimulating immunity, has antiviral activity and may reduce microglial cell activation



Others

- **Ambroxol** may mitigate protein misfolding and is being studied in ALS and Lewy Body Dementia. Research published in 2020 showed the drug also lowered levels of alpha-synuclein in Parkinson's patients and potentially improved motor symptoms. (Dose 60-300mg tid in trial)
- **Aprepitant** is an antagonist of NK-1R and is a selective antagonist of the NK1 receptors of neurokinins, whose main natural ligand is substance P, which is capable by itself of inducing intense emesis. It may block the storm of cytokines that maintain the state of neuro-inflammation activated by substance P. Dose: 3 consecutive days at doses of 125 mg on day 1, and 80 mg on days 2 and 3 (Reno-Ajra 2022)
- **Ubrelvy and other CGRP inhibitors** : spike protein shares molecular mimicry with the CGRP receptors therefore may be stimulating these inflammatory/ pain pathways
- **Agmatine** attenuates the detrimental effects of activated microglia in CNS and reduces glutamate (a metabolite of L Arginine) Rescues insulin signaling in the brain



Others

- **Donepezil** inhibits acetylcholinesterase, produces angiogenesis and neurogenesis in the hippocampus by releasing insulin like GF 1
- **Memantine** and donepezil markedly increases BDNF levels (Meisner et al 2008) Memantine blocks the NMDA-receptor subtype of glutamate receptors preventing over-activation of glutamine receptors
- **Topiramate** increases nitric oxide and proton mediated CGRP secretion (Durham P 2006)
- **Minocycline** inhibits microglial activity, reduced gliosis, synaptic deficits and cognitive impairments at early pathological stages



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Dr Suzanne K Gazda

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