

ALZHEIMERS IS CAUSED BY YOUR IMMUNE CELLS TURNING AGAINST YOU- featuring mainly Microglial cells, that allow blood brain barrier to operate correctly and help neurogenesis, but can be transformed into toxic attackers of our brain and enter a decades-long destructive degenerative cycle by mitochondrial toxins like paraquat and long covid unless corrected.

https://youtu.be/2Az4a6CKI_4?si=FkCwHOvmnfJMGZUV Slide 3571

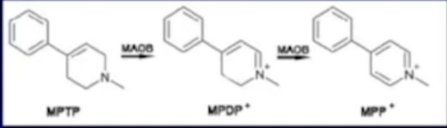
~When these cells change due to epigenetic environmental conditions like paraquat and long covid they can switch and transform the microglial cells into toxic attackers. Hurting brain neurogenesis and metabolism, and hurting the blood brain barrier And causing Alzheimer's disease.

~The reason **Act Rx** works on Alzheimer's so well is the microglia, once transformed to M1 enter a glycolytic cycle that uses 15 times more iron than normal, similar to cancer cells, that are both very prone to the peroxide moiety on the artemisia/ artemisinin molecule, creating violent ferroptosis reaction killing the cell selectively: **ferroptosis**, an iron- dependent form of cell death driven by lipid peroxidation. When excess intracellular ferrous iron (Fe^{2+}) reacts with hydrogen peroxide (H_2O_2), it triggers the **Fenton reaction**, producing highly toxic hydroxyl radicals (OH^-) that destroy cell membranes and cause ferroptosis.



Chronic Parkinsonism in Humans Due to a Product of Meperidine-Analog Synthesis

Chronic Parkinsonism in Humans Due to a Product of Meperidine-Analog Synthesis



MPTP MPDP⁺ MPP⁺

J. William Langston., et al., *Science*. February 25, 1983

Evidence of Active Nerve Cell Degeneration in the Substantia Nigra of Humans Years after 1-Methyl-4-Phenyl-1,2,3,6-Tetrahydropyridine Exposure

J. W. Langston, MD,* L. S. Forno, MD,† J. Tetrad, MD,* A. G. Reeves, MD,‡
J. A. Kaplan, MD,§ and D. Karlick, MD‡

This report provides the first detailed neuropathological study of 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridines (MPTP)-induced parkinsonism in humans. All 3 subjects self-administered the drug under the impression it was "synthetic heroin" and subsequently developed severe and unremitting parkinsonism, which was L-dopa responsive, at least in the earlier stages of illness. Survival times ranged from 3 to 16 years. Neuropathological examination revealed moderate to severe depletion of pigmented nerve cells in the substantia nigra in each case. Lewy bodies were not present. In Patients 1 and 2, there was gliosis and clustering of microglia around nerve cells. Patient 3 had a similar picture and also showed large amounts of extraneuronal melanin. These findings are indicative of active, ongoing nerve cell loss, suggesting that a time-limited insult to the nigrostriatal system can set in motion a self-perpetuating process of neurodegeneration. Although the mechanism by which this occurs is far from clear, the precedent set by the cases could have broad implications for human neurodegenerative disease.

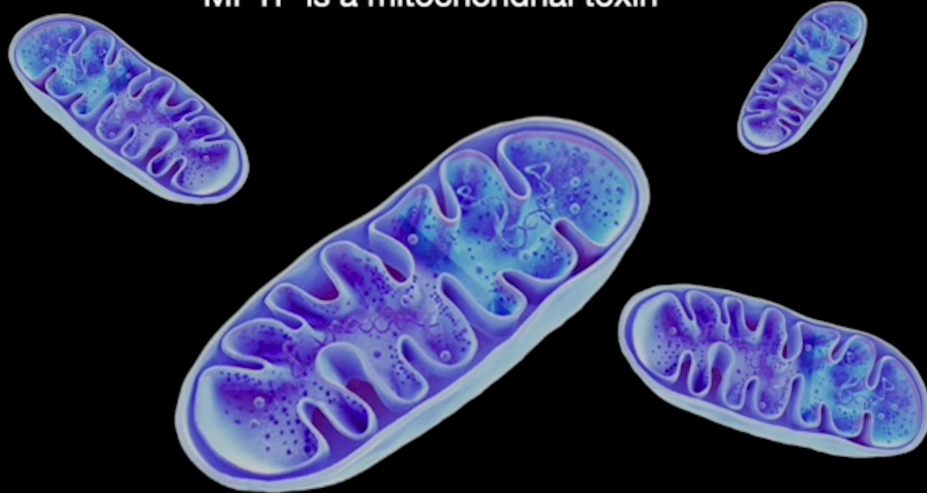
Langston JW, Forno LS, Tetrad J, Reeves AG, Kaplan JA, Karlick D. Evidence of active nerve cell degeneration in the substantia nigra of humans years after 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine exposure. *Ann Neurol* 1999;46:598-605

Evidence of Active Nerve Cell Degeneration in the Substantia Nigra of Humans Years after MPTP Exposure

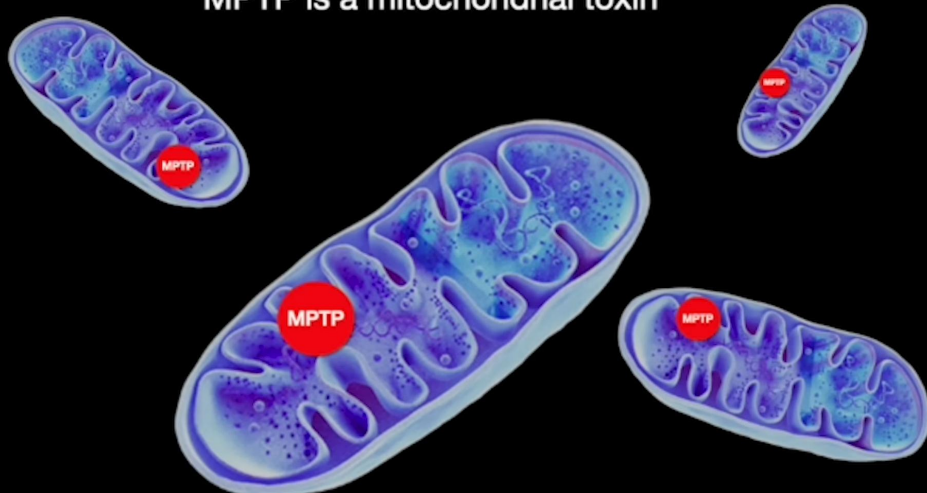
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Langston, J.W, et al., *Ann Neurol.* 1999;46:598–605

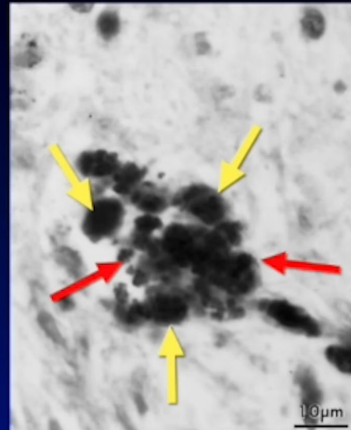
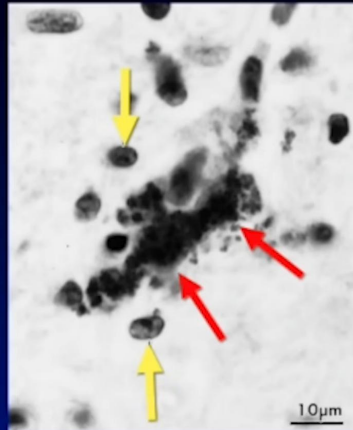
MPTP is a mitochondrial toxin



MPTP is a mitochondrial toxin



MPTP Affected dopamine producing cells in substantia nigra creating palsy.



Remnants of neurons and neuromelanin

Langston, J.W, et al., *Ann Neurol.* 1999;46:598-605

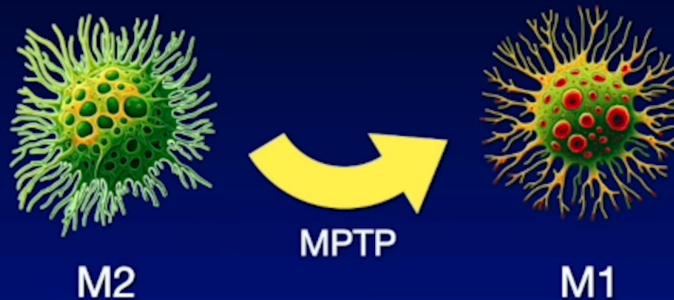
The melanin is digested away and M2 microglia shown are attacking the substantia nigra migration cells because their mitochondria was poisoned 3 years prior, and created an inflammation and immune response that is self-perpetuating and killed the patient at 42 from MPTP

Evidence of Active Nerve Cell Degeneration in the Substantia Nigra of Humans Years after MPTP Exposure

"A self-perpetuating inflammatory process represents another possible explanation for the neuropathological picture seen in these patients. In fact, as noted above, the inflammatory changes reported here are highly reminiscent of those seen in the active stages of Parkinson's disease. It is well established that microglial activation takes place in the substantia nigra in Parkinson's disease..."

Langston, J.W, et al., *Ann Neurol.* 1999;46:598-605

A self-perpetuating inflammatory process



Activated microglia destroying blood brain barrier

Shift from helping M2

To M1

Destroying brain cells

Make cytokines and shifts more M2 cells to M1

Long covid DOES THE SAME

PTSD

PARAQUAT- INCREASEs by 60% PARKINSON'S- which is a mitochondria poison, which causes inflammation, switching the phenotype of microglial M2 to the destructive M1.



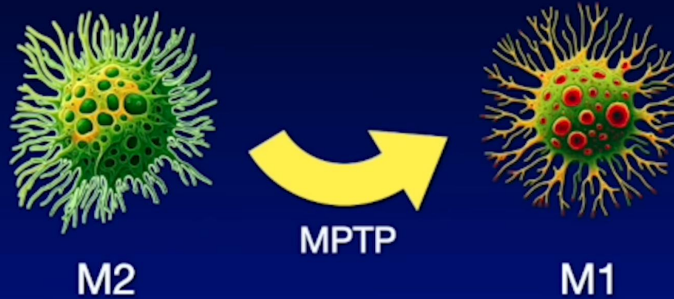
Paraquat is used in the lab to create Alzheimer's in animals. Meanwhile our use has increased dramatically (above chart) in the American agriculture today because pests are becoming immune to glyphosate.

Evidence of Active Nerve Cell Degeneration in the Substantia Nigra of Humans Years after MPTP Exposure

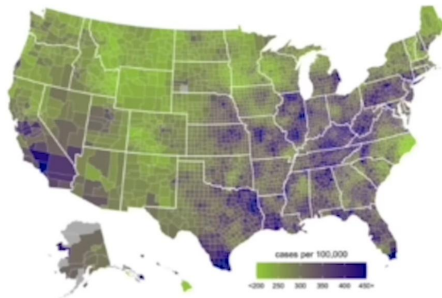
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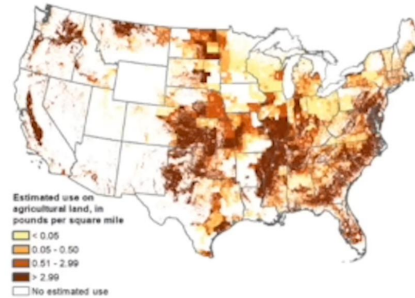
A self-perpetuating inflammatory process



Parkinson's prevalence



Agricultural paraquat usage



The incidence of Parkinson's matches the heavy use of paraquat shown above on left.

Cell Tissue Research, 2004

Cell Tissue Res (2004) 318: 225–241
DOI 10.1007/s00441-004-0937-z

REVIEW

Vladimir N. Uversky

Neurotoxicant-induced animal models of Parkinson's disease: understanding the role of rotenone, maneb and paraquat in neurodegeneration

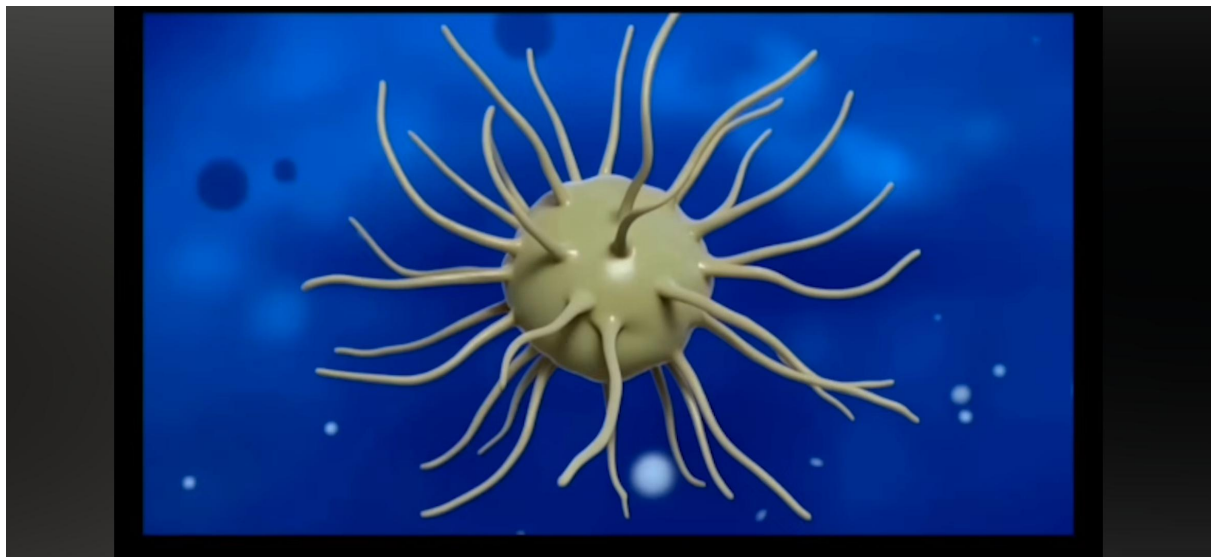
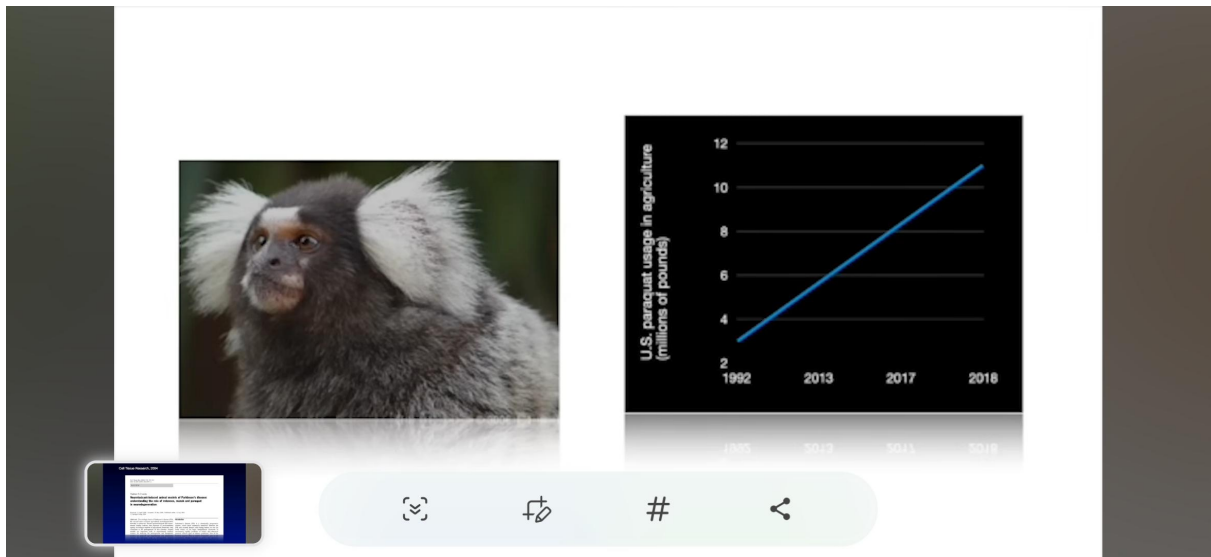
Received: 13 April 2004 / Accepted: 28 May 2004 / Published online: 16 July 2004
© Springer-Verlag 2004

Abstract The etiologic basis of Parkinson's disease (PD), the second most common age-related neurodegenerative disorder, is unknown. Recent epidemiological and experimental studies indicate that exposure to environmental agents, including a number of agricultural chemicals, may contribute to the pathogenesis of this disorder. Animal models are important tools in experimental medical science for studying the pathogenesis and therapeutic

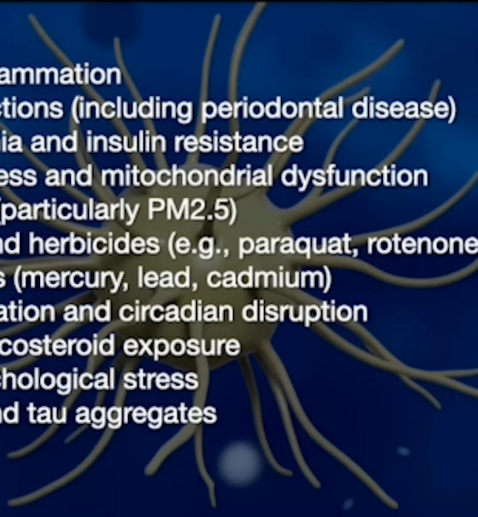
Introduction

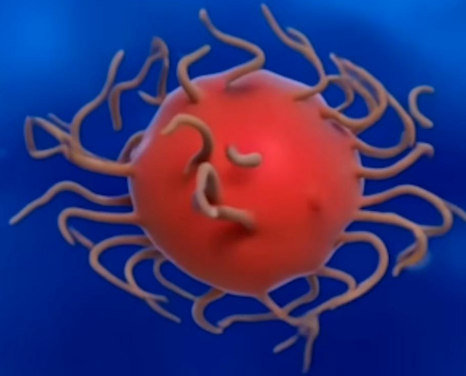
Parkinson's disease (PD) is a chronically progressive disease, which most commonly manifests between the fifth and seventh decade with resting tremor on one (or both) side(s) of the body, bradykinesia (slowness of movement), rigidity (stiffness of limbs), and abnormal postural reflexes (gait or balance problems). One of the

Thus, everything you've been told about Alzheimer's, that it's caused by sticky plaque building up in your brain, is missing the real story?



M2 microglial cell that is part of the body's immune system and nurtures neuron cells and growth and helps maintain blood brain barrier.

- 
- Systemic inflammation
 - Chronic infections (including periodontal disease)
 - Hyperglycemia and insulin resistance
 - Oxidative stress and mitochondrial dysfunction
 - Air pollution (particularly PM2.5)
 - Pesticides and herbicides (e.g., paraquat, rotenone, glyphosate)
 - Heavy metals (mercury, lead, cadmium)
 - Sleep deprivation and circadian disruption
 - Chronic corticosteroid exposure
 - Chronic psychological stress
 - Amyloid- β and tau aggregates



The M1 microglial cell is quite destructive once activated and changes from oxidative phosphorylation (the TCA cycle) to anaerobic glycolysis, just like cancer cells.

- 
- Neuroinflammation
 - Mitochondrial dysfunction
 - Increased ROS formation
 - Neuronal dysfunction
 - Synapse elimination
 - Blood-brain barrier destabilization
 - Activation of neighboring microglia
 - Decreased neurogenesis
 - Decreased phagocytosis
 - Increased amyloid- β and tau aggregates

- Systemic inflammation
- Chronic low-grade "inflammaging"
- Acute infections (viral, bacterial, fungal)
- Periodontal infection
- Endotoxin/LPS translocation
- Dysbiosis
- Increased intestinal permeability
- High glucose/hyperglycemia
- Insulin resistance
- Advanced glycation end products (AGEs)
- High-fructose intake
- Uric acid elevation
- Obesity/visceral adiposity
- Dyslipidemia/oxidized LDL
- Ceramides/lipotoxicity
- Mitochondrial dysfunction

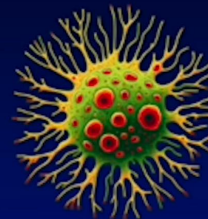
- Mycotoxins
- Air pollution PM2.5
- Diesel exhaust/ultrafine particles
- Ozone and NOx
- Cigarette smoke/secondhand smoke
- Microplastics/nanoplastics
- Endocrine-disrupting chemicals (phthalates, BPA)
- Glyphosate and other agrochemicals
- Chronic pain
- Hyperhomocysteinemia
- Ionizing radiation
- Persistent viral reservoirs (e.g., post-viral)
- Poor omega-3 status
- Excess omega-6 linoleic acid
- Alcohol misuse
- High salt intake

- Reactive oxygen species (oxidative stress)
- Reactive nitrogen species (nitrosative stress)
- Hypoxia/sleep apnea
- Sleep deprivation
- Circadian disruption/light at night
- Psychological/chronic stress
- Social isolation
- Sedentary behavior
- Traumatic brain injury/concussion
- Stroke/ischemia-reperfusion
- Blood-brain barrier breakdown
- Excitotoxicity/glutamate excess
- Amyloid- β oligomers
- Tau aggregates
- α -Synuclein aggregates
- Huntingtin fragments

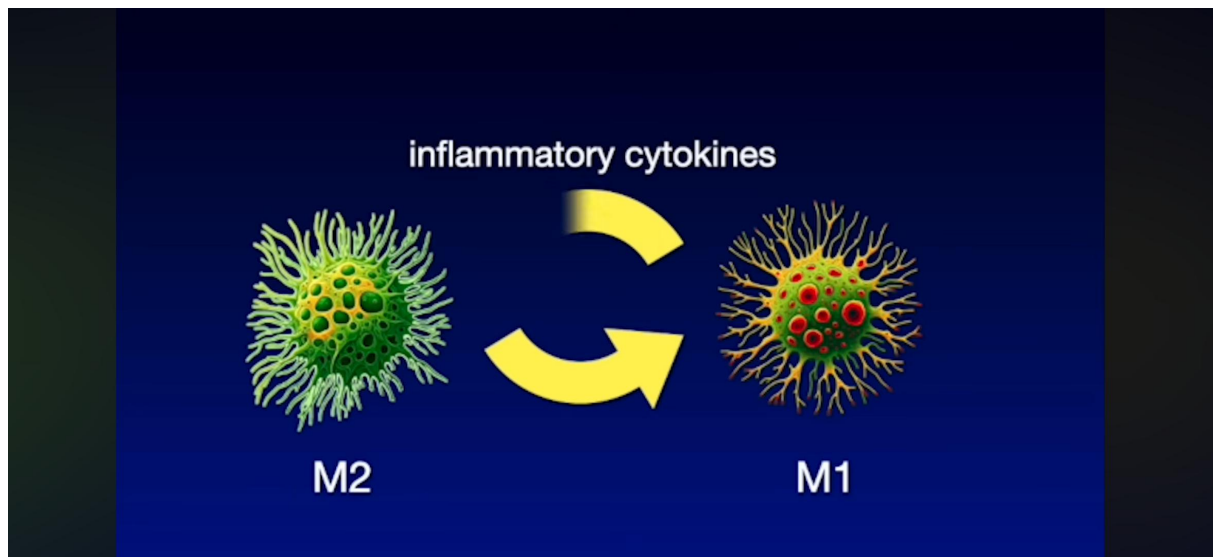
- Iron overload
- Copper/zinc dyshomeostasis
- Heavy metals (mercury, lead, cadmium, manganese)
- Pesticides (e.g., rotenone, organophosphates)
- Herbicides
- Industrial solvents/volatile organics
- Mycotoxins
- Air pollution PM2.5
- Diesel exhaust/ultrafine particles
- Ozone and NOx
- Cigarette smoke/secondhand smoke
- Microplastics/nanoplastics
- Endocrine-disrupting chemicals (phthalates, BPA)
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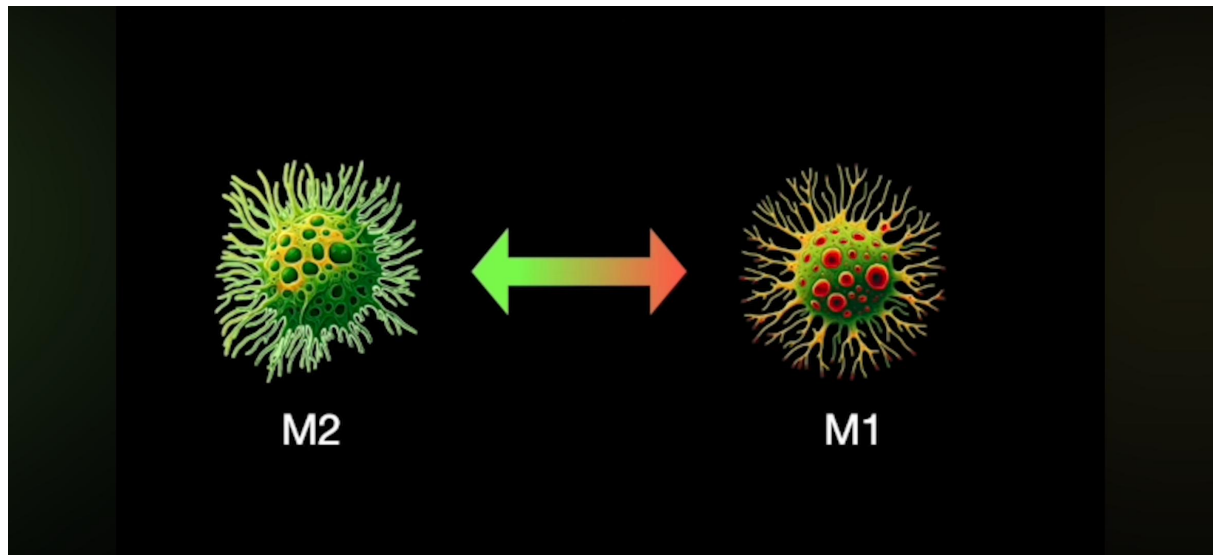
M2



M1

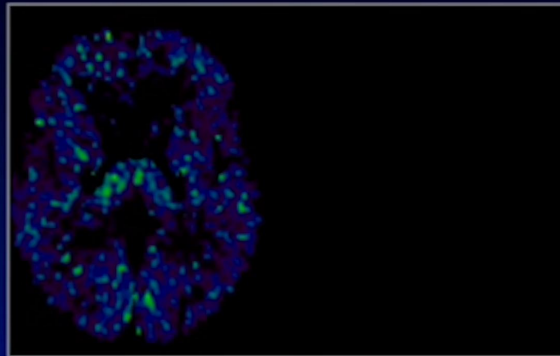


The M2 feedback loop is created by M1 cytokines being released and transforming M2 to M1 cells, and this pattern can turn into an endless feedback loop for many years and decades unless stopped.



Dr. David Perlmutter shows that the true driver of neurodegeneration isn't plaque at all. It's your own brain's immune cells turning against you.

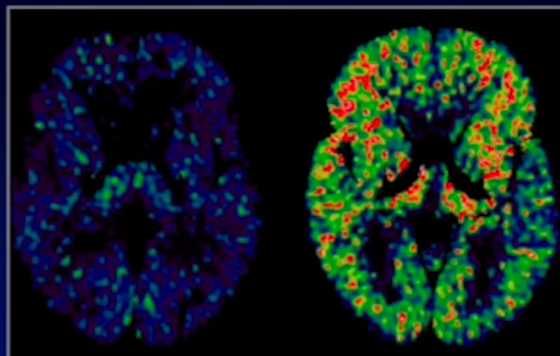
Pet TSPO imaging of activated microglia



Healthy control

Zimmer, E.R., et al., Journal of Neuroinflammation, W., et al., 2014 (11)

Pet TSPO imaging of activated microglia

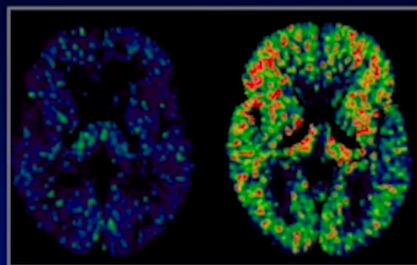


Healthy control

Alzheimer's disease

Zimmer, E.R., et al., Journal of Neuroinflammation, W., et al., 2014 (11)

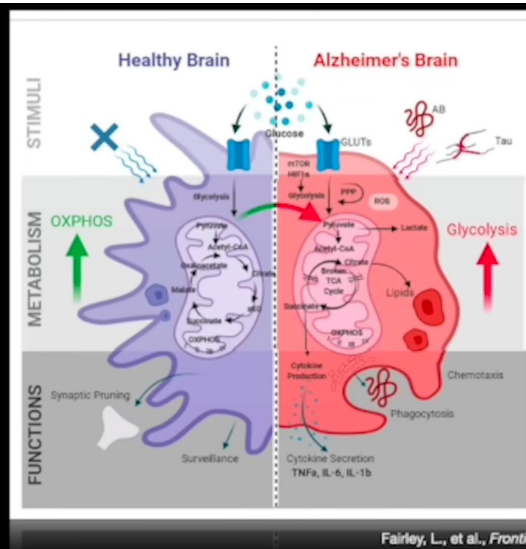
Diseases in Which TSPO Scans are Positive



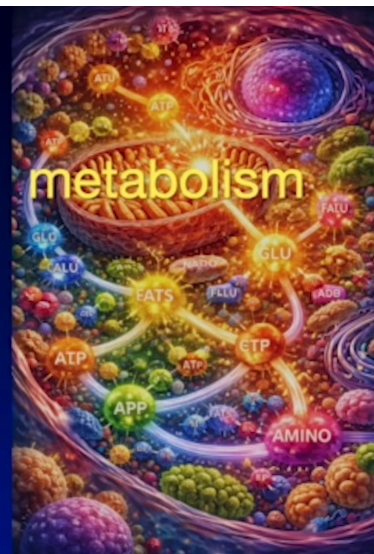
- Alzheimer's disease
- Mild cognitive impairment
- Parkinson's disease
- Multiple system atrophy (MSA)
- Progressive supranuclear palsy (PSP)
- Frontotemporal dementia
- Dementia with Lewy bodies
- Huntington's disease
- Amyotrophic lateral sclerosis (ALS)
- Multiple sclerosis
- Traumatic brain injury (acute and chronic)
- Ischemic stroke
- Epilepsy (including temporal lobe epilepsy)
- Long COVID
- Chronic Fatigue Syndrome
- Post-treatment Lyme disease syndrome
- Gulf War Illness
- Fibromyalgia
- Major depressive disorder

For decades the field blamed beta-amyloid protein for Alzheimer's. Perlmutter walks through a mechanism reshaping the science: the dysregulation of microglia, the immune cells that can either protect your brain or actively destroy it depending on how you live.

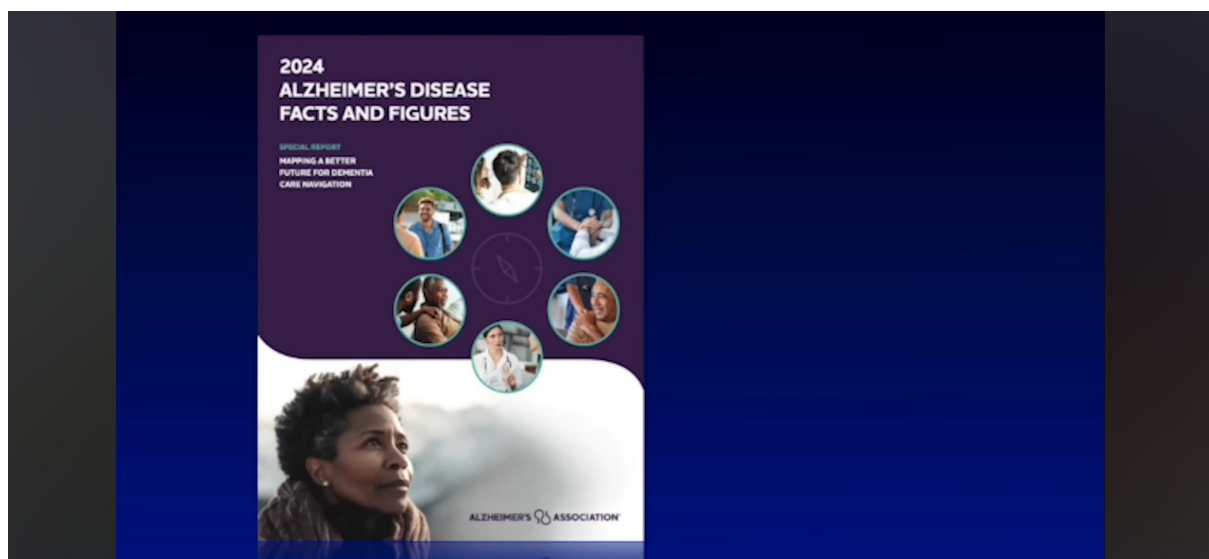
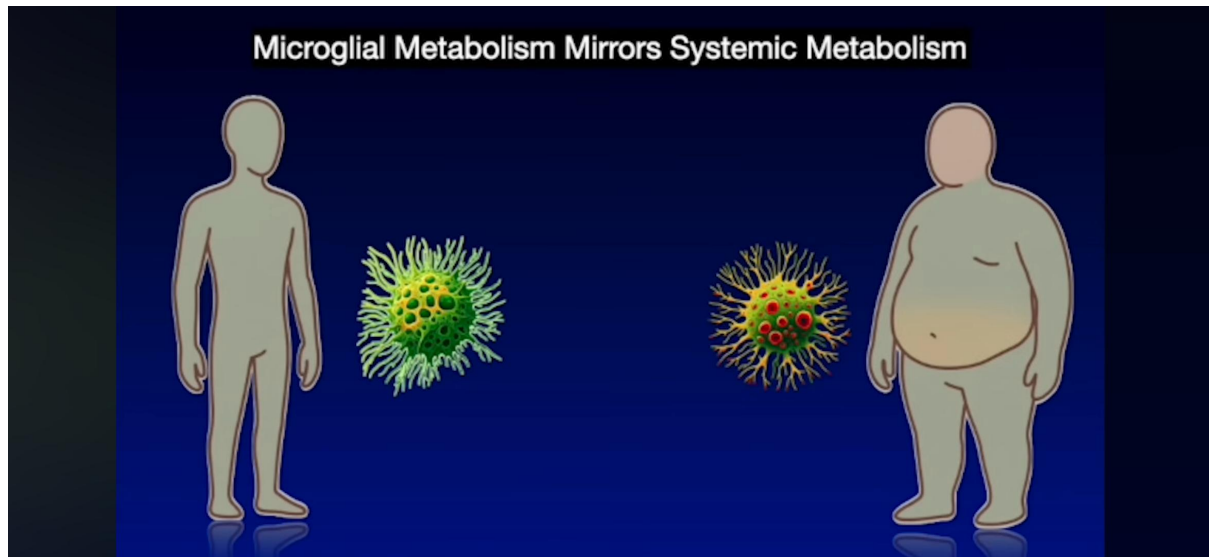
This transformation of microglial cells is what causes Alzheimer's and how pesticides and long covid cause a type of self attacking on immune system on the brain that builds up long after the initial incursion



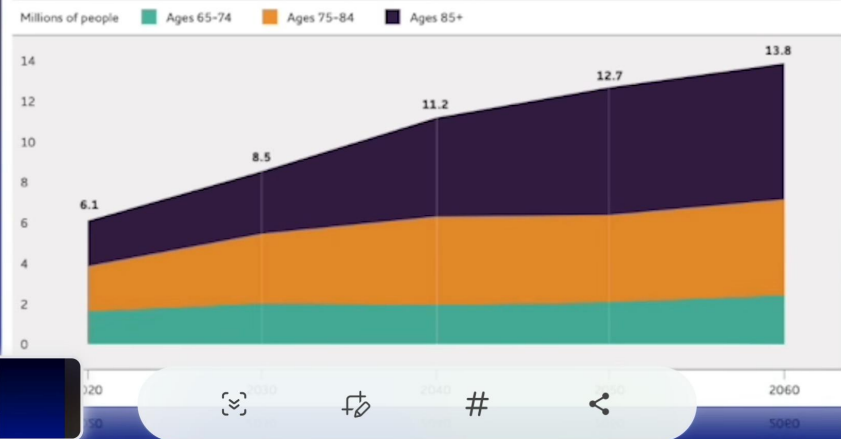
Immunometabolism



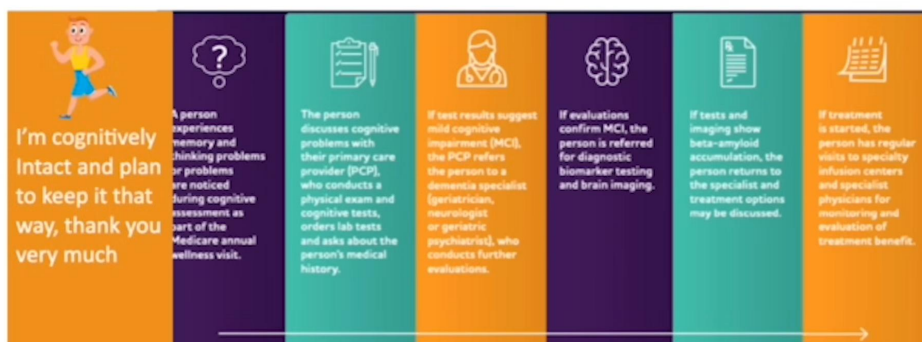
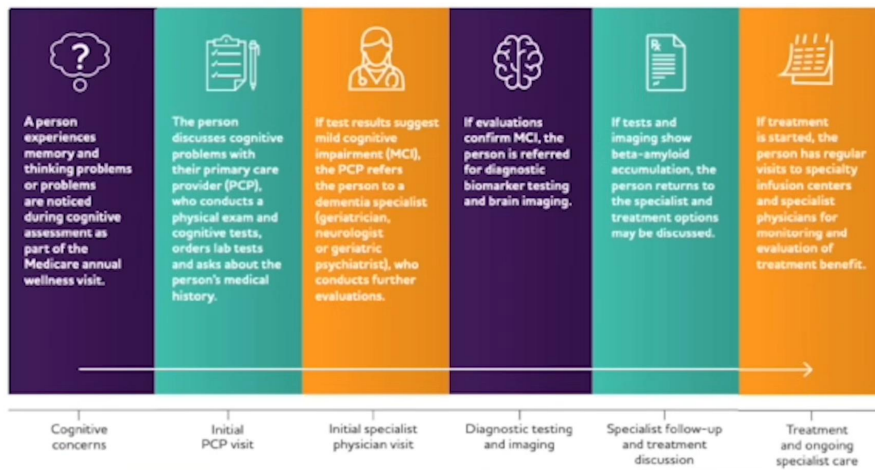
We dig into the chilling Parkinson's case where contaminated heroin froze patients like statues and revealed immune cells still attacking the brain decades later, why the same self-perpetuating inflammation shows up in CTE, long COVID, and PTSD, how your gut and blood sugar flip these cells into attack mode, the 14 metabolic risk factors that could prevent up to half of dementia cases, and the MIT-pioneered 40 Hz light and sound therapy that slowed cognitive decline and stabilized brain volume in human trials.



Projected Number of People Age 65 and Older (Total and by Age) in the U.S. Population with Alzheimer's Dementia, 2020 to 2060



Patient Journey from Awareness of Cognitive Issues to Care from a Physician Specialist and Treatment^{155, 159}

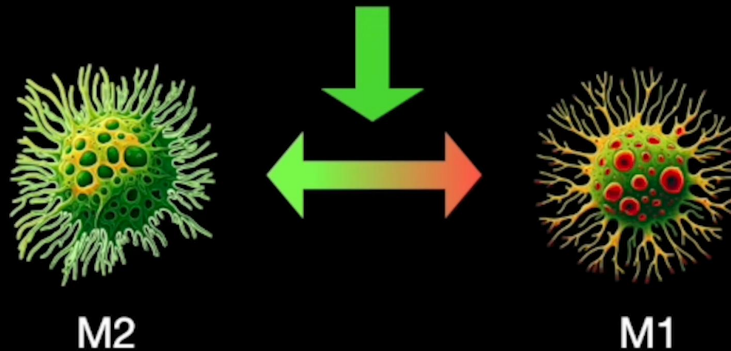


Metabolic Reprograming of Microglia in the Regulation of the Innate Inflammatory Response

- Microglia represent an intriguing target for the treatment of neurodegenerative diseases and **targeting their metabolism in order to change their immunological phenotype** could represent a promising future therapeutic approach.

Lauro, C., et al., *Frontiers in Immunology*. March, 2020

Can we intervene here?



Metabolic Reprograming of Microglia in the Regulation of the Innate Inflammatory Response

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Microglial Metabolism Mirrors Systemic Metabolism

Lauro, C., et al., *Frontiers in Immunology*. March, 2020

Reprogramming Microglia

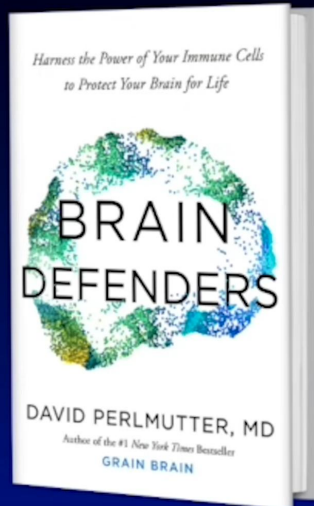


Reprogramming Microglia

Ketogenic diet
Exercise
Hyperbaric Oxygen Therapy
Nitric Oxide Upregulation
Urolithin-A
Fasting
GLP-1 Agonists
Evoked Gamma Oscillation
EEG biofeedback
Specialized Pro-resolving Mediators
TNF-alpha antibody
Improved Sleep

Reprogramming Microglia

Ketogenic diet	Fiber
Exercise	Polyphenols
Hyperbaric Oxygen Therapy	Akkermansia Mucinophilia
Nitric Oxide Upregulation	Allulose
Urolithin-A	SSRIs
Fasting	PGC-1 Activators
GLP-1 Agonists	CRISPR-based genetic tools
Evoked Gamma Oscillation	Metformin
EEG biofeedback	Weight loss
Specialized Pro-resolving Mediators	Lithium
TNF-alpha antibody	Transcranial Ultrasound
Improved Sleep	Lion's Mane



BRAIN DEFENDERS

Harness the Power of Your Immune Cells to Protect Your Brain for Life

"A science-based actionable blueprint to shift the brain from decline to repair."

— David A. Sinclair, PhD, author of *Lifespan*,
Professor of Genetics, Harvard Medical School

David Perlmutter, MD

August, 2026

BrainDefenders.com



Li-Huei Tsai, Ph.D.
Director, The Picower Institute for Learning and Memory,
Massachusetts Institute of Technology

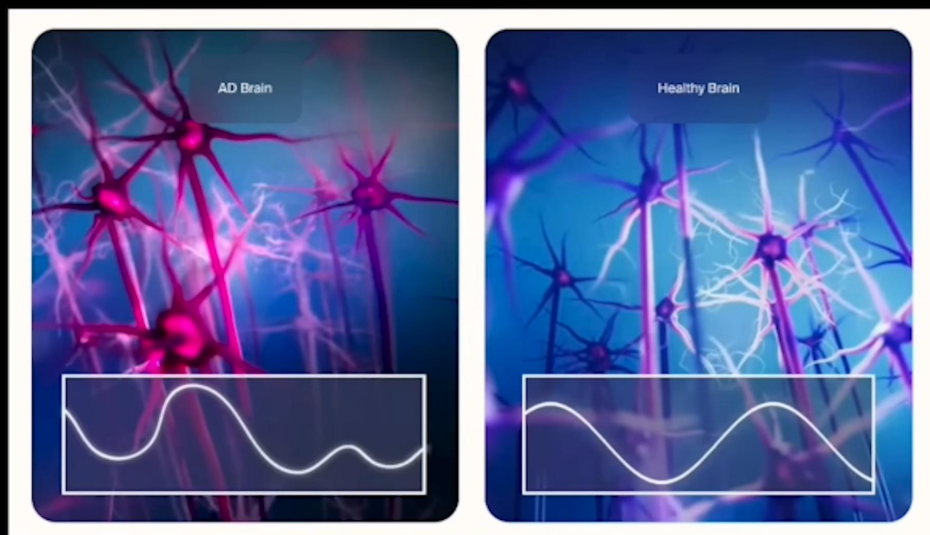
Gamma frequency entrainment attenuates amyloid load and modifies microglia

- Gamma entrainment refers to the modulation or **synchronization** of brain wave activity in the gamma frequency range (typically around 30-100 Hz), which is associated with various cognitive functions, such as attention, memory, and perception.

Iaccarino, H.F., et al. *Nature*. December, 2016

Changes or abnormalities in gamma entrainment are observed in multiple neurological disorders:

- Alzheimer's disease
- Schizophrenia
- Autism Spectrum Disorder
- Bipolar Disorder
- Epilepsy
- Parkinson's Disease
- Major Depressive Disorder



Gamma frequency entrainment attenuates amyloid load and modifies microglia

- Reduced gamma oscillations *before* plaque formation and cognitive decline in mouse model of Alzheimer's disease

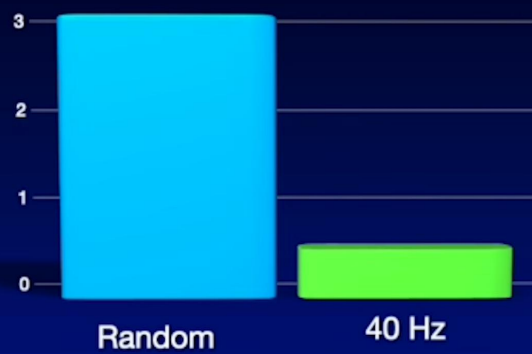
Gamma frequency entrainment attenuates amyloid load and modifies microglia

- Visual stimulation with 40 Hz flicker



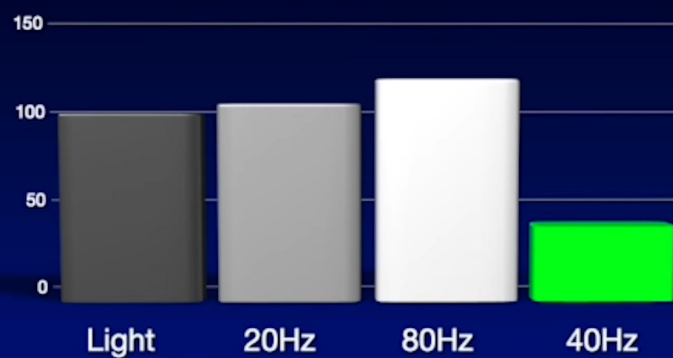
Iaccarino, H.F., et al. *Nature*. December, 2016

A β in hippocampus of AD mouse



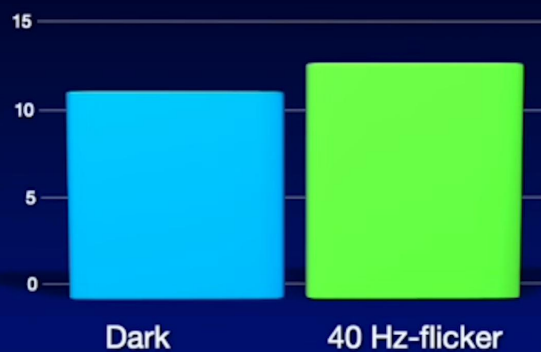
Iaccarino, H.F., et al. *Nature*. December, 2016

A β 1-40 in visual cortex of AD mouse



Iaccarino, H.F., et al. *Nature*. December, 2016

Microglial count (number per ROI)



Iaccarino, H.F., et al. *Nature*. December, 2016

Safety, tolerability, and efficacy estimate of evoked gamma oscillation in mild to moderate Alzheimer's disease

- Randomized, double blind, sham-controlled, 6 month trial
- 6-month, 76 participants, mild to moderate Alzheimer's
- MMSE scores between 14-26
- 2:1 intervention vs control (sham)
- EEG-verified gamma oscillation induced by auditory and visual stimulation, 1 hour daily

Hajós, M., et al. *Frontiers in Neurology*. March, 2024

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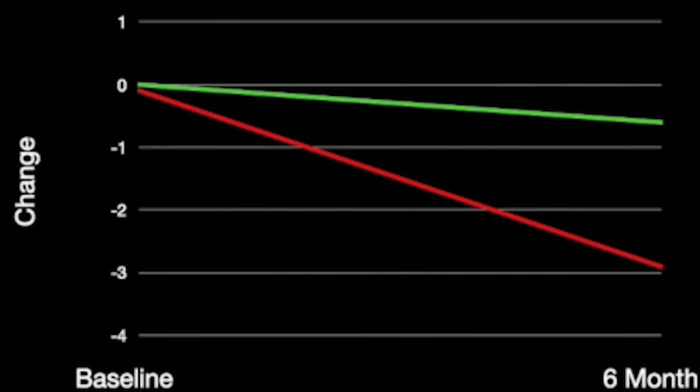
Hajós, M., et al. *Frontiers in Neurology*. March, 2024

Safety, tolerability, and efficacy estimate of evoked gamma oscillation in mild to moderate Alzheimer's disease



Hajós, M., et al. *Frontiers in Neurology*. March, 2024

Mini-Mental State Exam



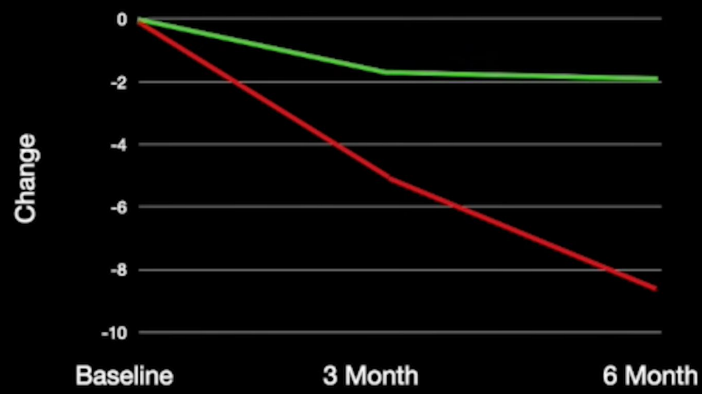
Hajós, M., et al. *Frontiers in Neurology*. March, 2024

Alzheimer's Disease Cooperative Study-ADL Scale



Hajós, M., et al. *Frontiers in Neurology*. March, 2024

Alzheimer's Disease Cooperative Study-ADL Scale

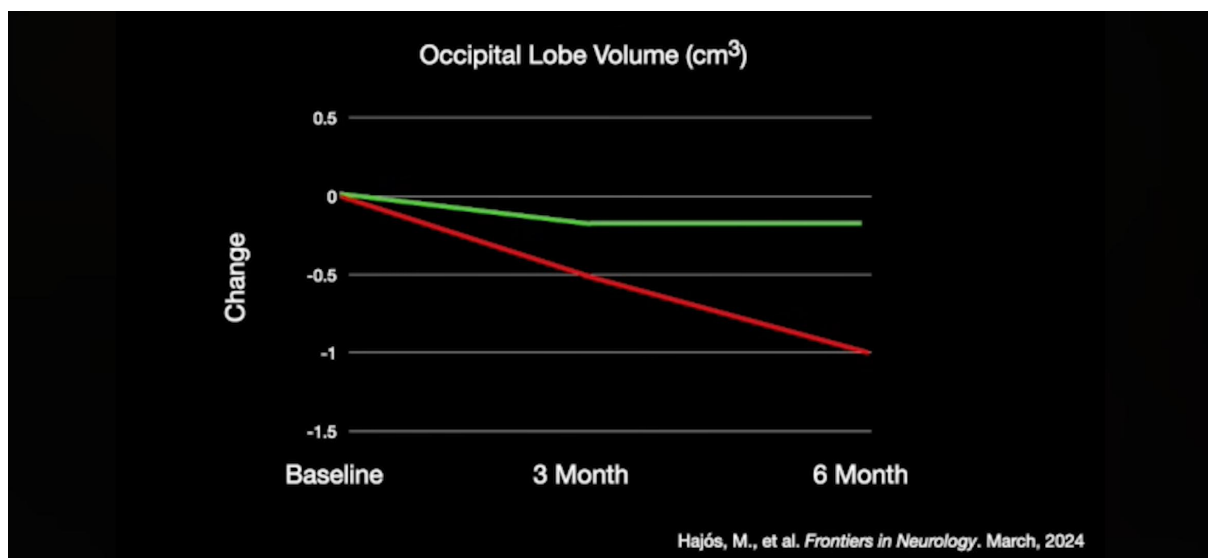
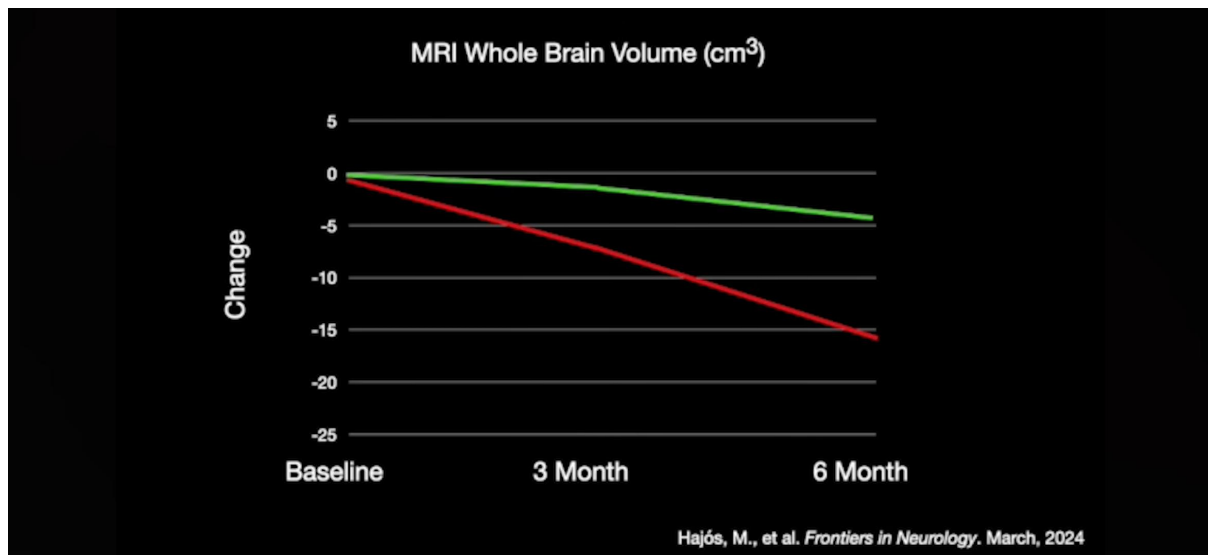


Hajós, M., et al. *Frontiers in Neurology*. March, 2024

MRI Whole Brain Volume (cm³)



Hajós, M., et al. *Frontiers in Neurology*. March, 2024



- ~The Plaque Theory of Parkinson's and Why It's Incomplete
- ~Meet the Microglia: Your Brain's Immune System
- ~Supportive vs. Threatening: The M1/M2 Switch
- ~Why This Underlies Nearly Every Neurodegenerative Disease
- ~The Frozen Patients: A Parkinson's Mystery at Stanford
- ~Contaminated Heroin and the MPTP Discovery
- ~How a Mitochondrial Toxin Destroys Dopamine Cells
- ~Microglia Still Attacking Decades Later
- ~The Self-Perpetuating Inflammatory Cycle
- ~The Same Pattern in CTE, Long COVID, and PTSD
- ~Paraquat, Pesticides, and Parkinson's Risk
- ~What Flips Your Cells Into Attack Mode
- ~Leaky Gut, the Microbiome, and Your Brain
- Imaging Threatening Cells in Living People
- ~Immunometabolism: Why Brain Cells Change Function
- ~14 Risk Factors That Could Prevent Half of Dementia
- ~The Breakthrough: Reprogramming Your Microglia
- ~Don't Wait for Symptoms: Intervene Early

~The Toolkit: Diet, Exercise, Fasting, Sleep, and More
~40 Hz Gamma Frequency: MIT's Pioneering Technology
~Light Flicker Studies and Beta-Amyloid Reduction
~Conclusion: You Are the Architect of Your Brain

Dr. David Perlmutter, MD is a board-certified neurologist and author: ***Brain Defenders:*** Harness the Power of Your Immune Cells to Protect Your Brain for Life (Avery / Penguin), focuses on microglia and is scheduled for publication in August 2026.
