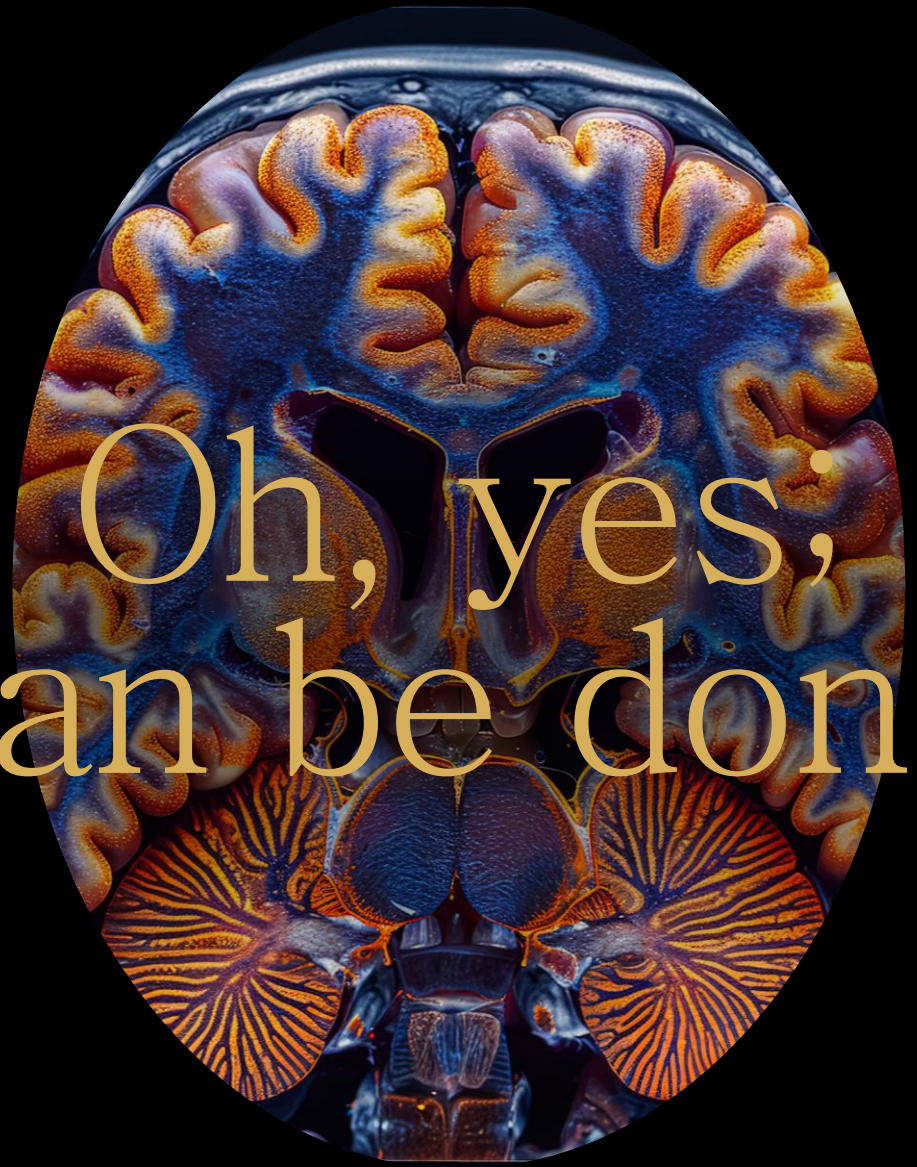
OUTSMARTING ALZHEIMER'S

REBECCA ROENTSCH MONTRONE, BS – WONDROUS ROOTS

Preventing & Stopping the Progression



Oh, yes;
it can be done…

THE SCIENCE EXITS

But preventing & CURING disease isn't PROFITABLE

DON’T WAIT

DON’T WALK

“Walking to end Alzheimer’s” only feeds the money machine…

…of the medical-industrial complex

What is the "medical-industrial complex?"

The medical-industrial complex (MIC) refers to ***the health industry****, which is composed of* ***the multibillion-dollar congeries of enterprises*** *including doctors, hospitals, nursing homes, insurance companies, drug manufacturers, hospital supply and equipment companies, real estate and construction businesses, health systems consulting and accounting firms, and banks. The concept conveys the idea that an important (if not the primary) function of the health care system in the United States is business (****that is, to make profits****) with two other secondary functions, research and education.* Source

Profiting off grief…

Profiting by creating disease…

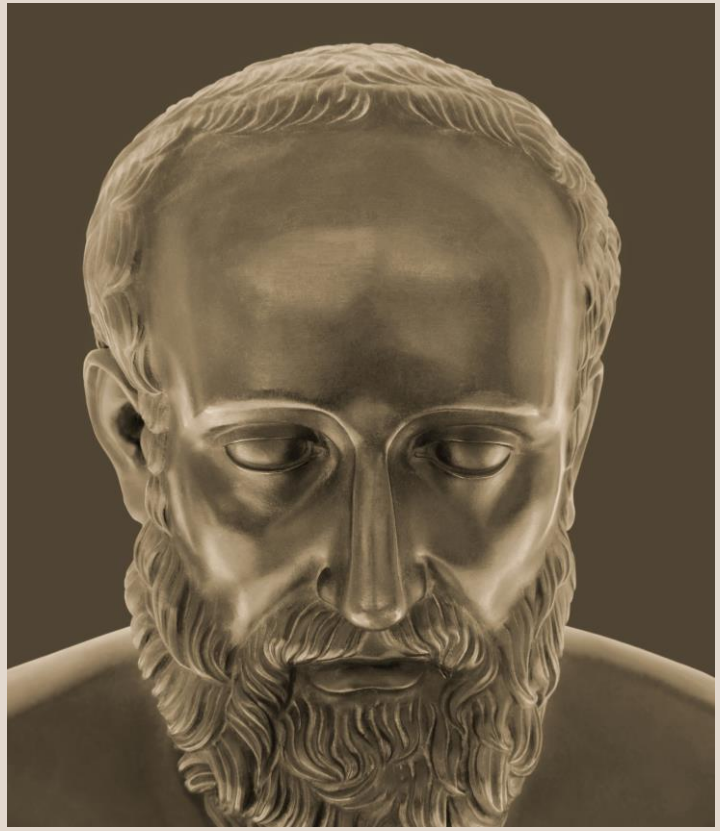
Then further profiting by treating created diseases.

Funneling dollars from the unsuspecting…

But for all
the money spent,
where are the…

CURES?

It's Official! Curing Patients Is Bad for Business



“First, do no harm.”

— Milton Packer describes the end-result of profit-dominated drug development

*“The potential to deliver 'one shot cures' is one of the most attractive aspects of gene therapy, genetically-engineered cell therapy and gene editing. However, such treatments offer a very different outlook with regard to **recurring revenue** versus chronic therapies…. While this proposition carries tremendous value for patients and society, it could represent a challenge for genome medicine developers looking for **sustained cash flow**.”*

“Is curing patients a sustainable business model?” Goldman Sachs analysts ask

For a real-world example, they pointed to Gilead Sciences, which markets treatments for hepatitis C that have cure rates exceeding 90 percent.

In 2015, the company’s hepatitis C treatment sales peaked at $12.5 billion. But as more people were cured and there were fewer infected individuals to spread the disease, sales began to languish. Goldman Sachs analysts estimate that the treatments will bring in less than $4 billion this year (2018).

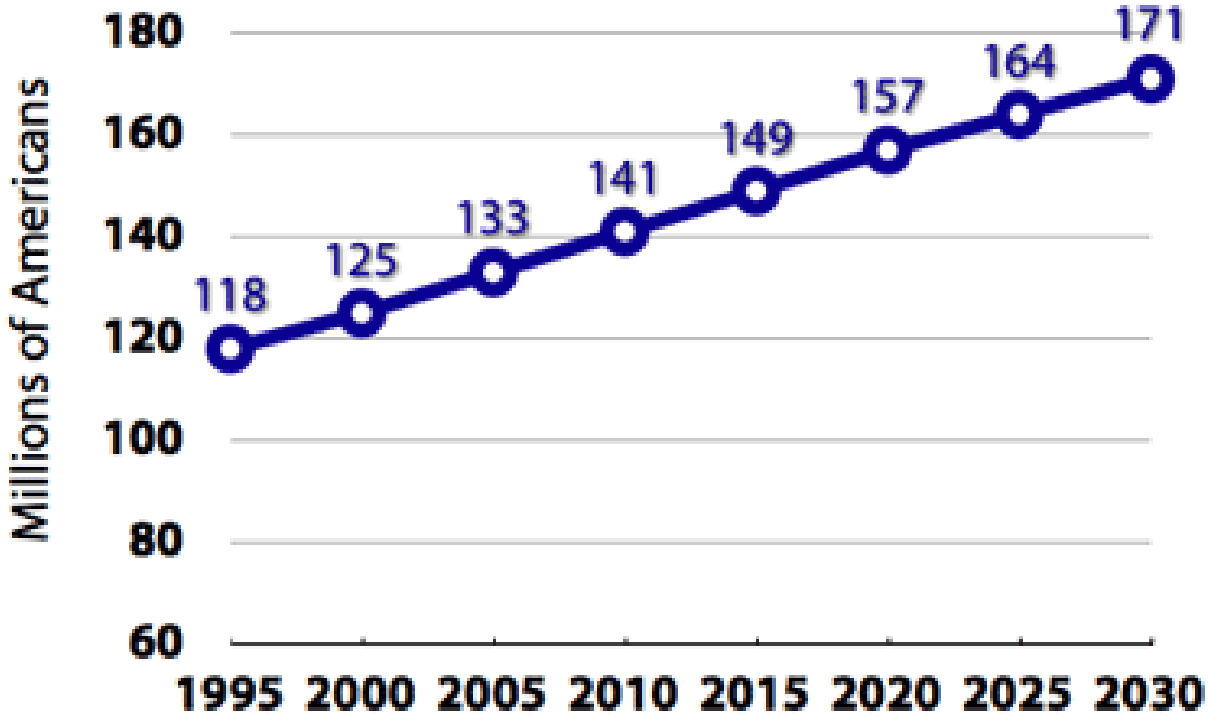
Here’s a question…

If the current paradigm is working, why is chronic disease of every kind on the increase?

Does that make sense to you?

It doesn’t to me, either.

Prevalence of Chronic Disease in the U.S.

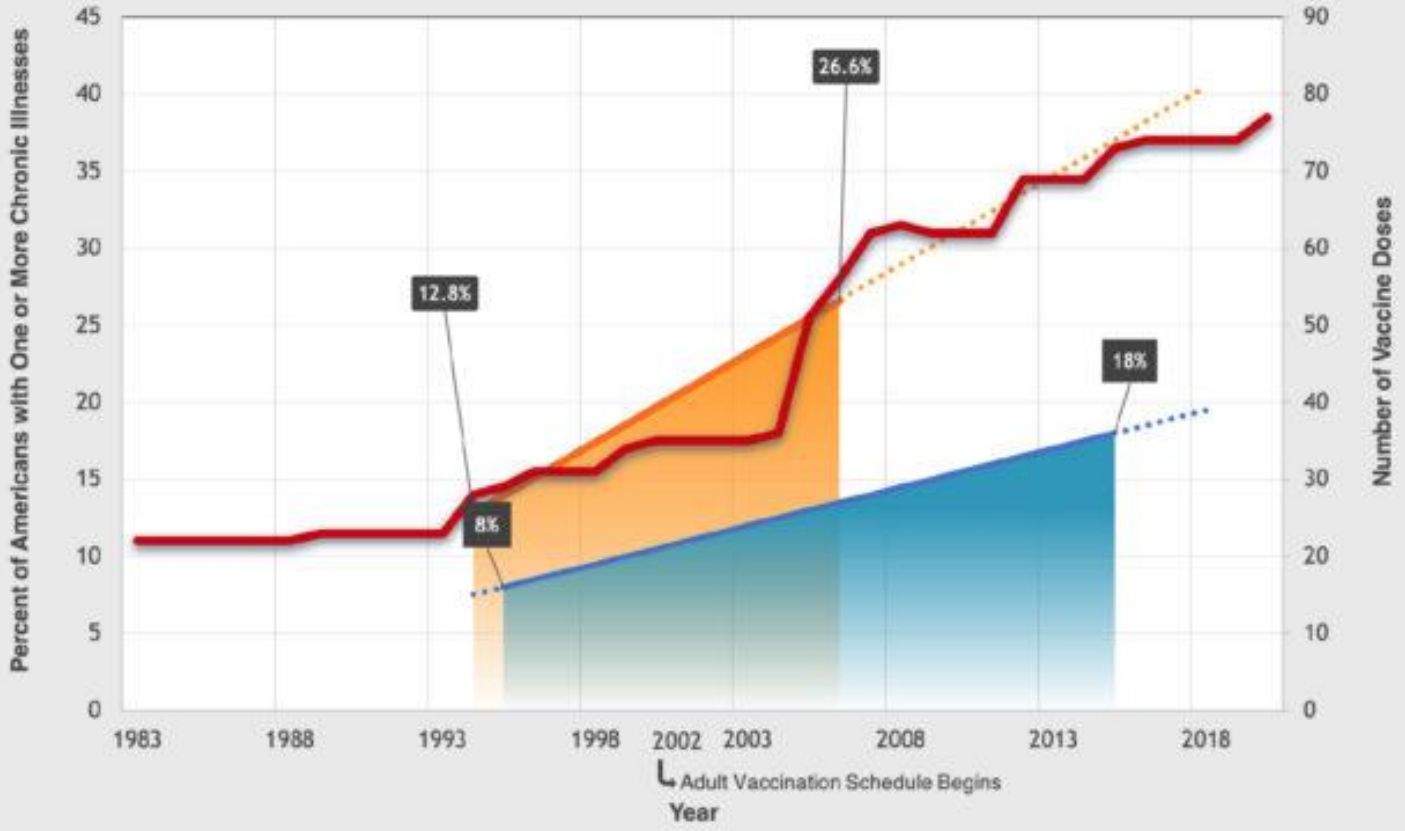


Source: Wu, Shin-Yi *et al*. 2000. Projection of Chronic Illness Prevalence and Cost Inflation. RAND Corporation.

Rebecca Roentsch Montrone, BS - Wondrous Roots

VACCINES ARE A REASONABLE SUSPECT IN AMERICA'S PANDEMIC OF CHRONIC DISEASES AND DISORDERS

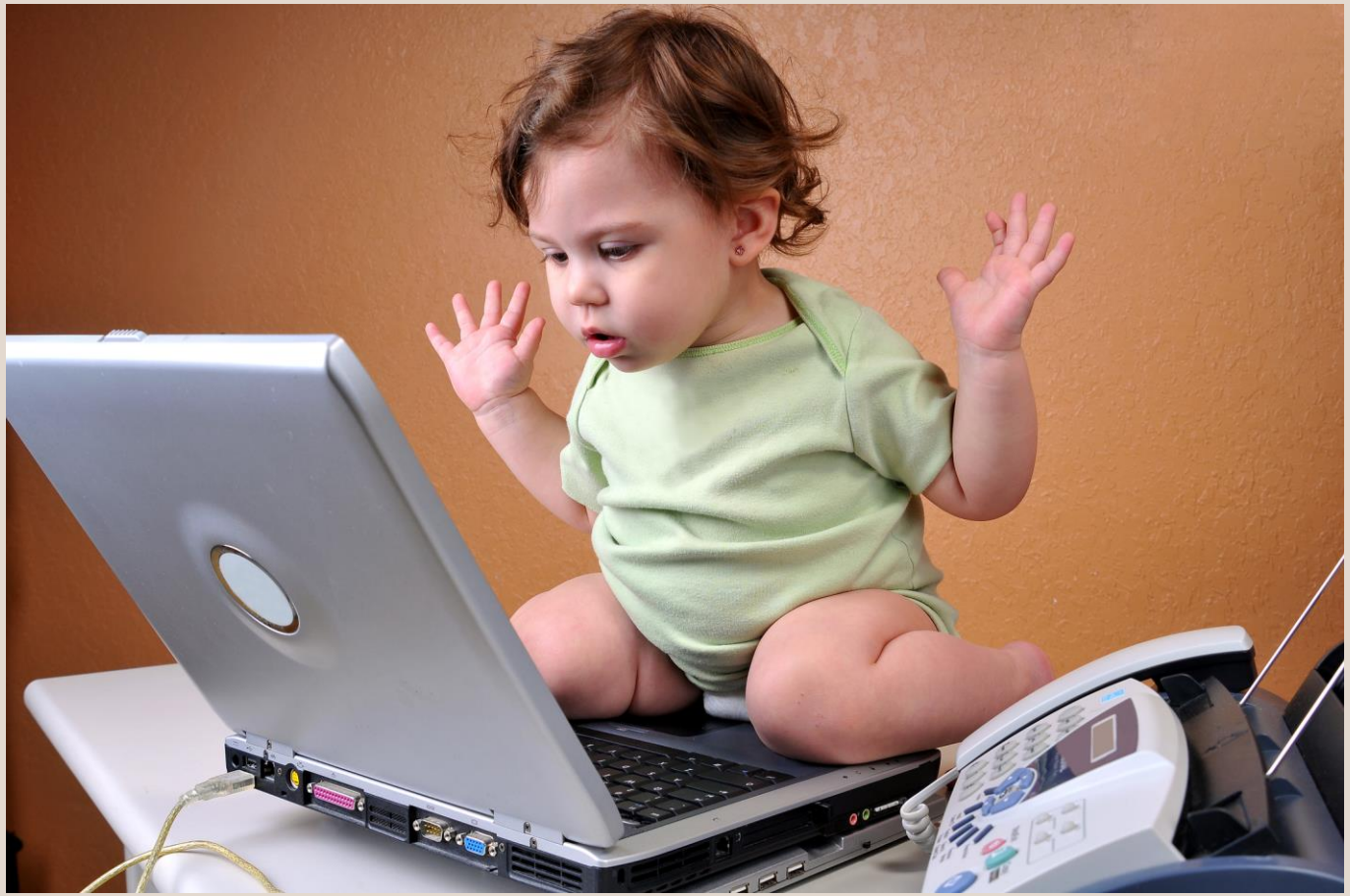
Increase in Chronic Disease Rates in the U.S. Population



Pearson Correlation Coefficient†		
This graph is here	1.0	Perfect Correlation
	0.99 – 0.90	Very High Correlation
	0.89 – 0.80	High Correlation
	0.79 – 0.60	Moderately High Correlation
	0.59 – 0.40	Moderate Correlation
	0.39 – 0.20	Low Correlation
	0.19 – 0.10	Negligible Correlation
	< 0.09	No Correlation

- Child Chronic Illnesses*
- Adult Chronic Illnesses**
- # of CDC Recommended Childhood Vaccine Doses

Look at that graph? What happened in 1993, I wonder…



1993

The Institute of Medicine publishes **"The Children's Vaccine Initiative: Achieving the Vision."** Later, following the events of September 11, 2001, the Institute of Medicine again called for the creation of **a national vaccine authority** "to advance the development, production, and procurement of new and improved vaccines of limited commercial potential but of global public health need." *1993*

The National Immunization Program (NIP) was created as a separate program reporting directly to the Office of the Director at CDC. NIP was established to provide federal leadership and services to all local and state public health departments involved in immunization activities (e.g., **disease surveillance for vaccine-preventable diseases, and development of vaccine information management systems**). *1993*

The costs of the influenza vaccine and its administration become a covered benefit under Medicare Part B. *May 1, 1993*

Conjugated *Haemophilus influenzae* type b vaccines (ActHIB by Connaught/Mérieux and OmniHib by SmithKline Beecham) are licensed. *March 1993*

A combined *Haemophilus influenzae* type b vaccine and whole-cell DTP vaccine (Tetramune by Lederle/Praxis) was licensed. *March 1993*

The development **of immunization registries was promoted at the national level**. A national health goal for 2010 was subsequently established to **increase participation in population-based immunization registries to 95 percent**. *1993*

The Vaccines for Children Program was established after the passage of the Omnibus Budget Reconciliation Act of 1993. Federally purchased vaccines under this program are made available to children from birth through 18 years old who meet one of the following requirements: Medicaid-enrolled, without health insurance, and American Indian or Alaskan native. Also, children with health insurance that does not cover the costs of immunization are eligible to receive vaccines at a federally qualified health center or a rural health clinic. All ACIP-recommended vaccines receive funding, which includes new vaccines, new vaccine combinations, and revised recommendations for vaccine use. *1993*

Looking Back, Looking Forward: Cancer and Vaccines

Cancer is the leading disease-related cause of death in American children, and the rise in childhood cancers has occurred alongside dramatic expansion of the childhood vaccine schedule.

Vaccine history illustrates that the presence of adventitious agents and contaminants in viral vaccines has been a recurrent problem, including monkey virus in polio vaccines and pig viruses in rotavirus vaccines—these unwanted and unanticipated contaminants may be linked to cancer risks.

Vaccine manufacturers are interested in using continuous cell lines (which can reproduce indefinitely) for viral vaccines, including cell lines from human tumors and cell lines that cause tumors in lab animals.

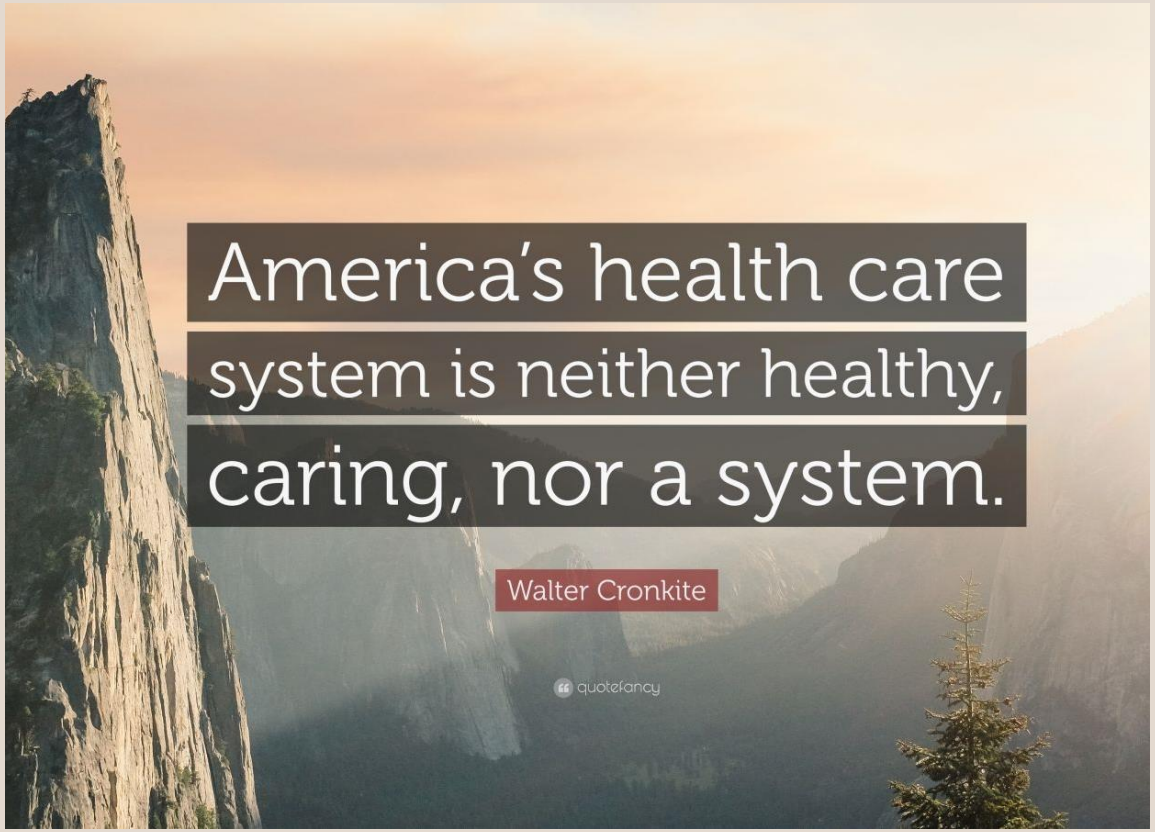
- Although the Food and Drug Administration (FDA) did not previously allow tumor-derived or tumor-causing cell lines to be used in vaccines—due to concerns about their potential for transmitting diseases, including cancer—the FDA now says that these cell lines are “optimal” for growing some viruses.
- If tumor-derived and tumor-causing cell lines come into widespread use in viral vaccines, could potential “worst-case scenarios” unfold that include further increases in childhood cancer?

Many people might be shocked to learn that cancer is the leading disease-related cause of death in American children. Over the past several decades, there have been significant increases in various types of childhood cancers, including leukemia and non-Hodgkin’s lymphoma. The rise in childhood cancers has played out in tandem with other worrisome child health trends, including escalating rates of autism spectrum disorder (ASD) and other neurodevelopmental disorders.

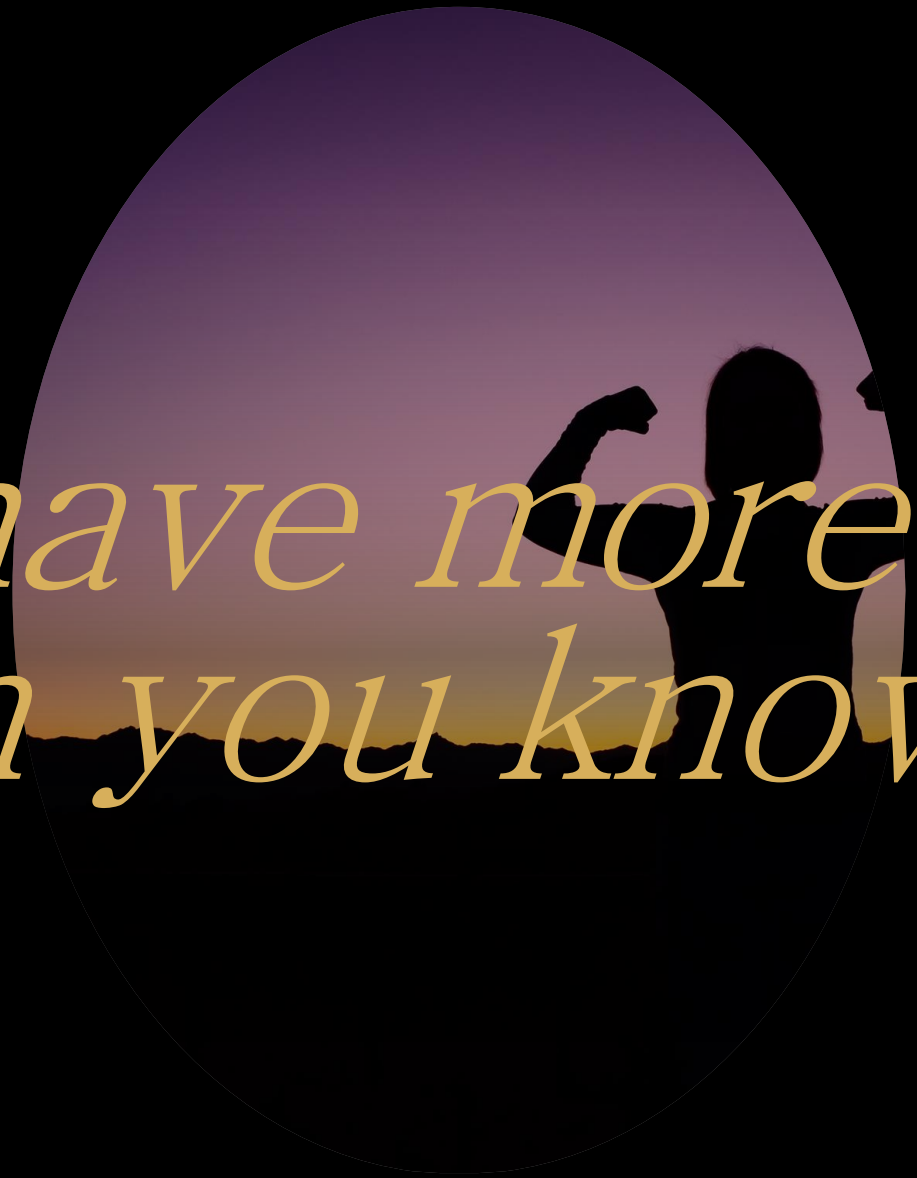
But whatever you do, DON’T get the flu!

What's wrong with this picture?

“Looking for *health* in all the wrong places…”



Don’t wait… turn in here!



“You have more power than you know…”

Let’s learn!

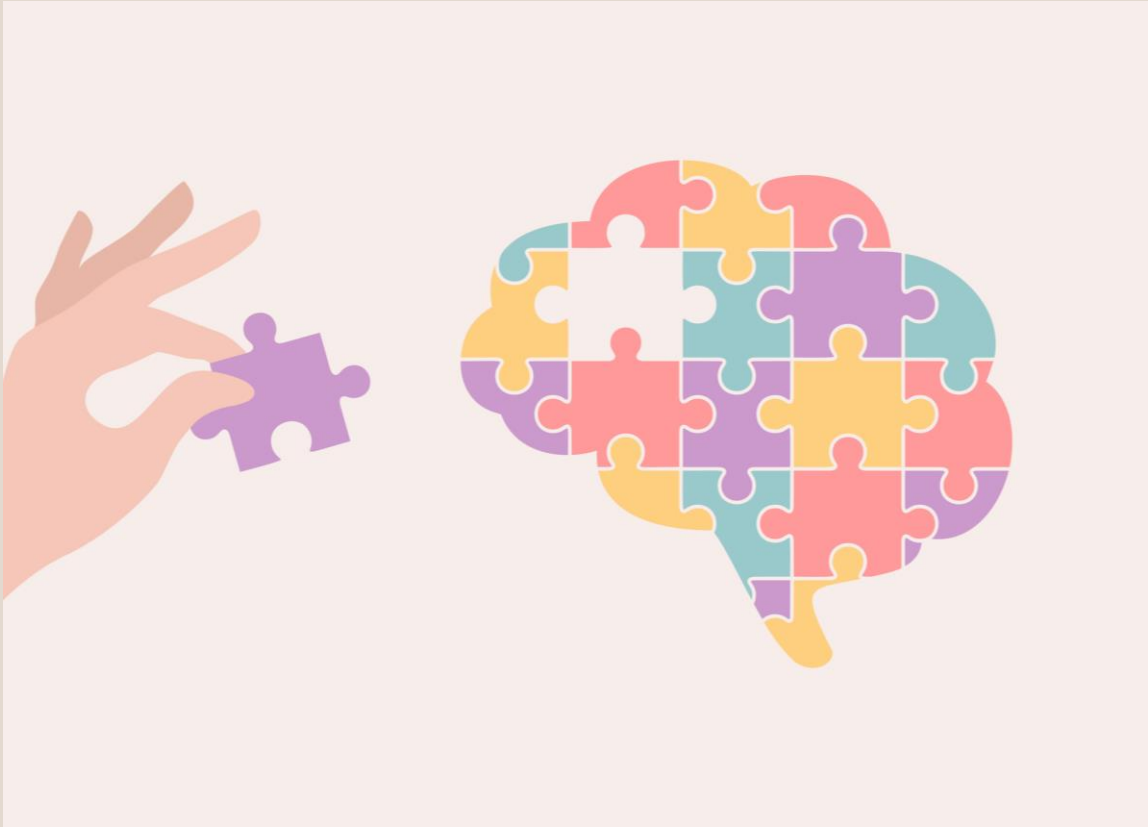
ALZHEIMER'S DISEASE

Here we go!

And those of you who know me are going to find all my favorite friends in the slap–it–silly approach!

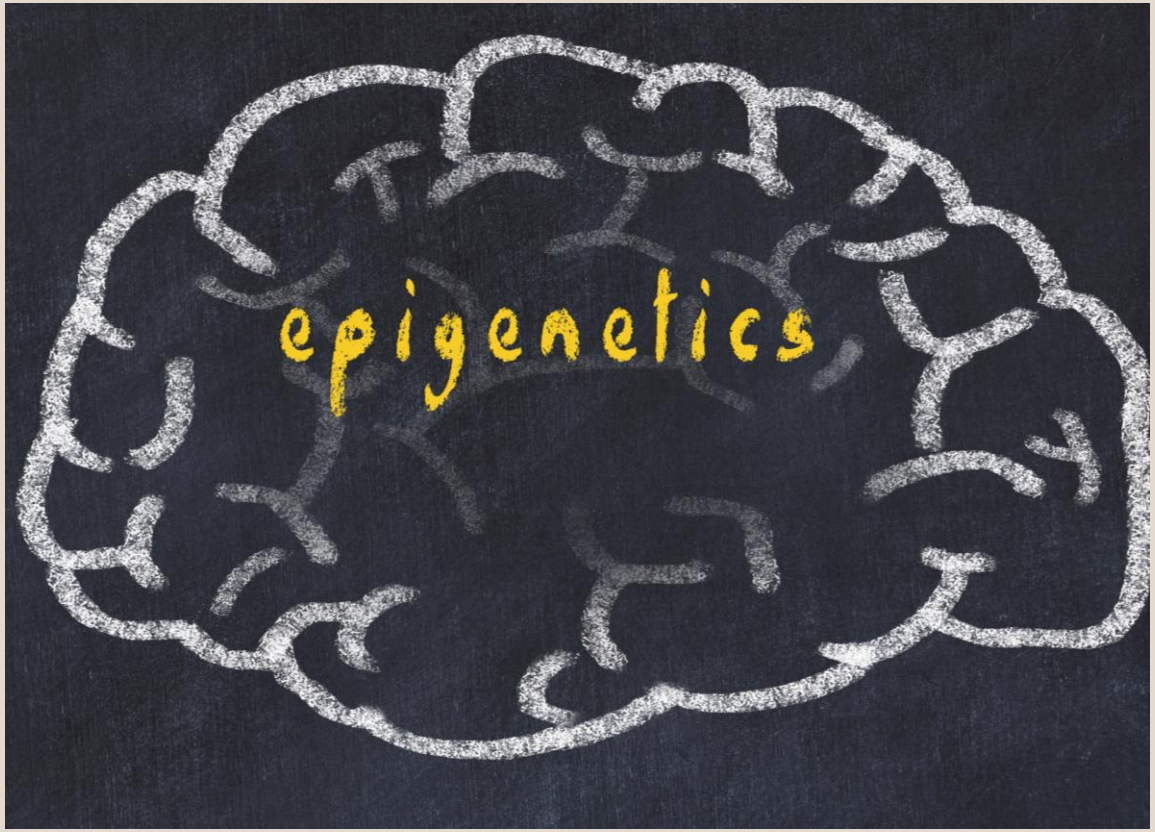
First, what goes missing?

- Alzheimer's disease happens over a long period of time.
- Understanding the genetic, hormonal, mitochondrial, and other pieces, as well as aggravating toxic exposures that feed degenerative processes, is critical.
- If we know what pieces go missing, we can take measures to keep them from going missing and/or replenish them as they do.



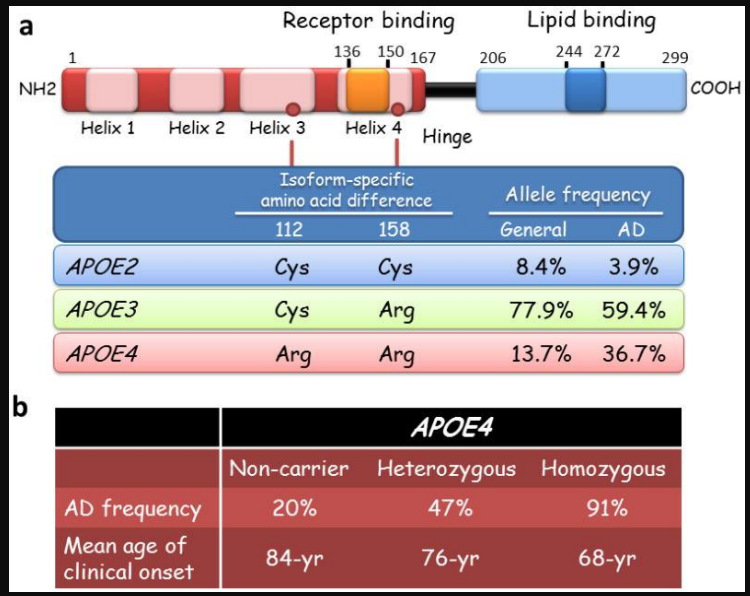
Genetic Defects & Epigenetics

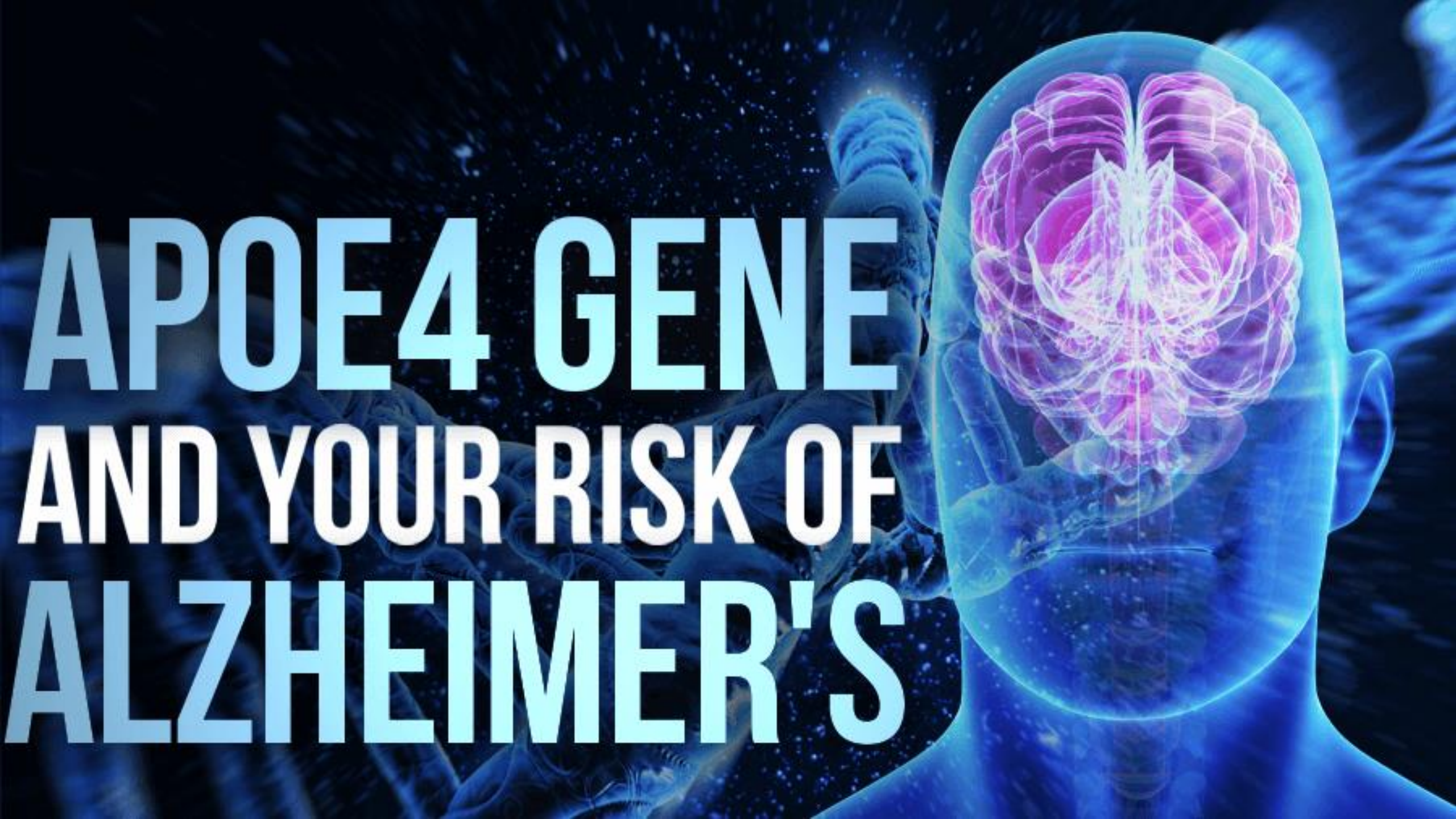
- Most genetic defects are not deterministic. The exciting science of epigenetics tells us that we can alter the expression of our genes or go in another way and overcome the deficits they produce.
- Do you know what your genes aren't doing for you?
- Go in and do it another way.



Problem genes

- Apolipoprotein E4
- MTHFR A1298C
- Possibly influential
  - ABCA7
  - CLU
  - CR1
  - PICALM
  - PLD3
  - TREM2
  - SORL1



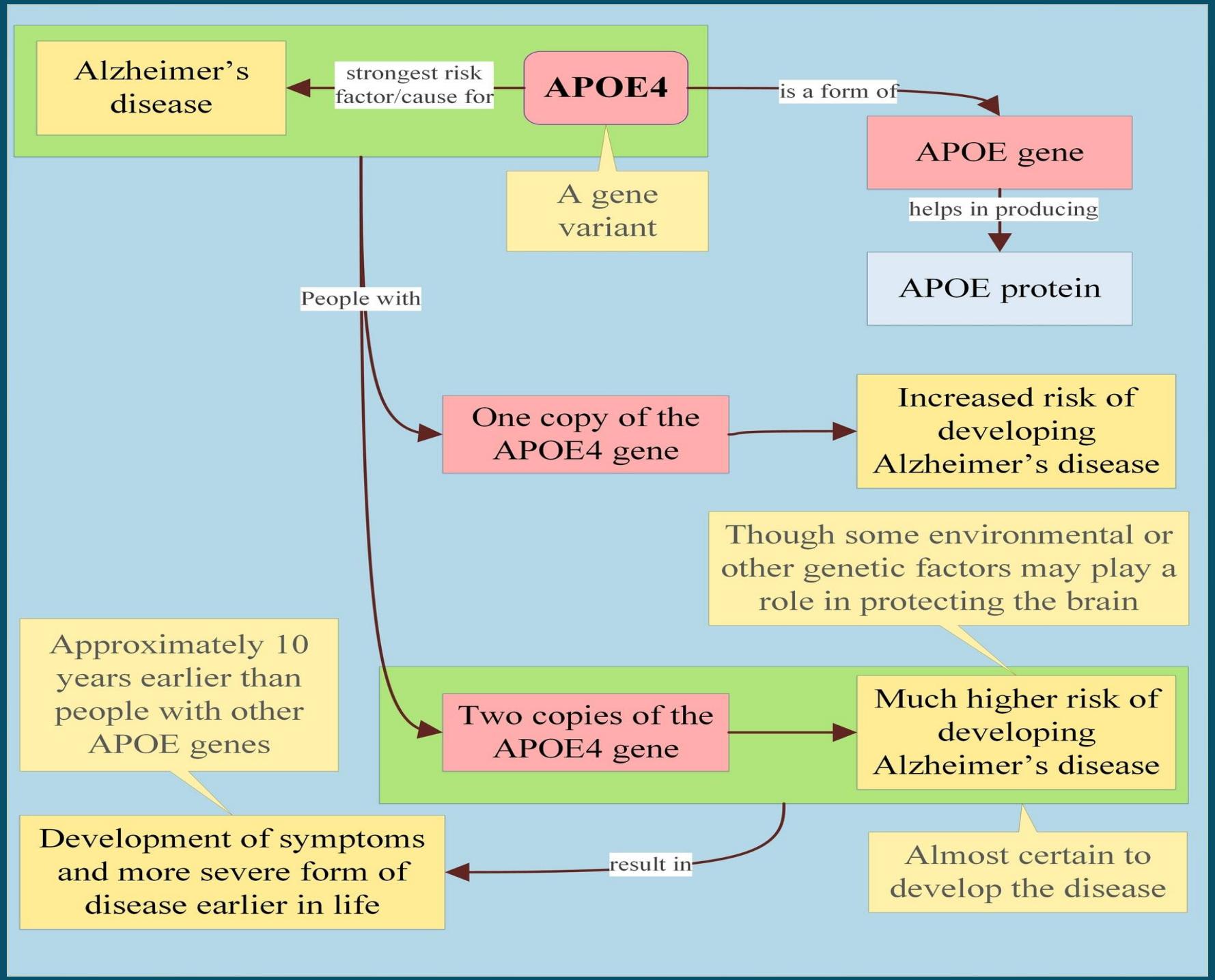

APOE4 GENE
AND YOUR RISK OF
ALZHEIMER'S

3 apolipoprotein E gene varieties

APOE e2. This is the least common. It reduces the risk of Alzheimer’s.

APOE e3. This most common gene doesn't seem to affect the risk of Alzheimer’s.

APOE e4. This gene is a little more common. It increases the risk of Alzheimer's. And it's linked to getting a worse form of the disease


Alzheimer's disease
strongest risk factor/cause for
APOE4
is a form of
APOE gene
A gene variant
helps in producing
APOE protein
People with
One copy of the APOE4 gene
Increased risk of developing Alzheimer's disease
Though some environmental or other genetic factors may play a role in protecting the brain
Approximately 10 years earlier than people with other APOE genes
Two copies of the APOE4 gene
Much higher risk of developing Alzheimer's disease
Development of symptoms and more severe form of disease earlier in life
result in
Almost certain to develop the disease

APOE4 & Alzheimer's

- ApoE4: an emerging therapeutic target for Alzheimer's disease
- Apolipoprotein E and Alzheimer's Disease: Findings, Hypotheses, and Potential Mechanisms
- Apolipoprotein E4 targets mitochondria and the mitochondria–associated membrane complex in neuropathology, including Alzheimer's disease
- An exhausted-like microglial population accumulates in aged and APOE4 genotype Alzheimer's brains
- Age, APOE and sex: Triad of risk of Alzheimer's disease
- Roles of ApoE4 on the Pathogenesis in Alzheimer's Disease and the Potential Therapeutic Approaches
- Independent and Correlated Role of Apolipoprotein E ε4 Genotype and Herpes Simplex Virus Type 1 in Alzheimer's Disease

WAIT! WHAT?

Although we've known about the APOE4 link for 4 decades…

Here, from a review as recent as **2019**!

"Conclusion: *ApoE4 is a promising AD therapeutic target that remains understudied. Recent studies are now paving the way for effective apoE4–directed AD treatment approaches."*

“…remains understudied?”

“Now paving the way?”

You’ve got to be kidding me!

What about all that money raised *“walking to end Alzheimer’s?”*

Where do the funds from *"Walk to End Alzheimer's"* go?

"The funds raised through Walk to End Alzheimer's advance the efforts of the Alzheimer's Association. With your help, we are able to deliver ***information and education*** *to millions of individuals, caregivers and medical professionals who face dementia every day, provide care and support across the country, advocate for the needs and rights of people facing Alzheimer's, and advance research seeking methods of prevention, treatment and ultimately, a cure."*

AND YET…

…it's been *40 years* since we've known about the significance of the APOE genotype, and we're just now *"paving the way!"*

In 1993, APOE genotype was found to strongly modulate risk for Alzheimer disease (AD)

Apolipoprotein E (ApoE) is of great interest due to its role as a cholesterol/lipid transporter in the central nervous system (CNS) and as the most influential genetic risk factor for Alzheimer disease (AD). Work over **the last four decades** has given us important insights into the structure of ApoE and how this might impact the neuropathology and pathogenesis of AD. In this review, we highlight the history and progress in the structural and molecular understanding of ApoE and discuss how these studies on ApoE have illuminated the physiology of ApoE, receptor binding, and interaction with amyloid-β (Aβ). We also identify **future areas of study needed** to advance our understanding of how ApoE influences neurodegeneration.

Source

And we'll see more of this…

As we move on through this presentation, many studies will be cited regarding known, promising targets of focus when it comes to Alzheimer's disease.

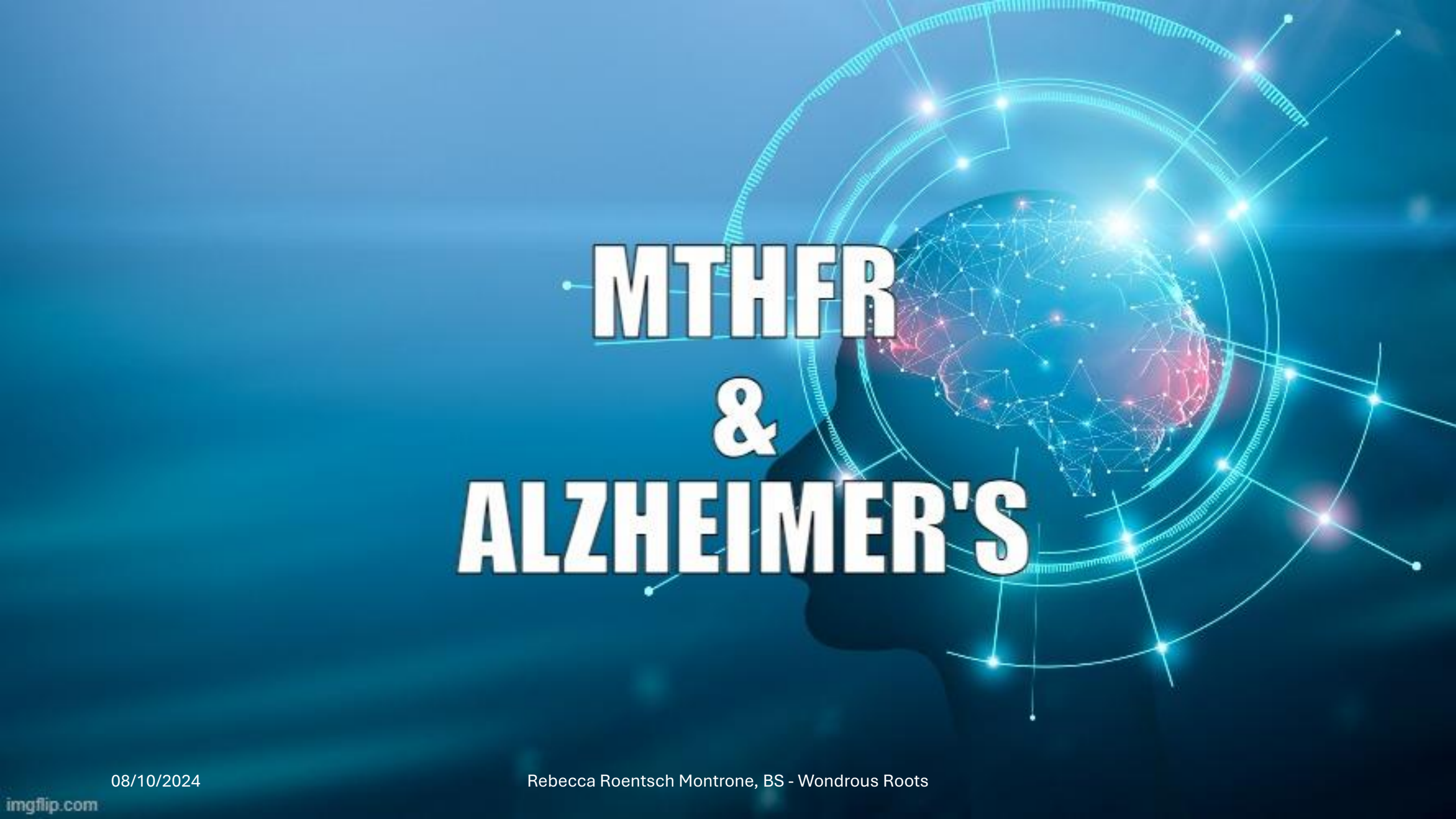
I think you will be flabbergasted when you note how so much solid research has **never** seen the light of day when it comes to actually doing anything *at all* about Alzheimer's disease!

What ***ARE*** we waiting for?

The good news? *We do not have to wait!*

OOPS – back to genes!

I can get carried away…



Association of methylenetetrahydrofolate reductase polymorphisms with susceptibility to Alzheimer's disease

Abstract

Background: Genetic risk factors play an important role in the pathogenesis of Alzheimer's disease (AD). In this case-control study, we examined the C677T and A1298C polymorphisms in the methylenetetrahydrofolate reductase (MTHFR) gene and their correlation with this pathology.

Objective: To verify the association between MTHFR C677T and A1298C polymorphisms and Alzheimer's disease.

Method: This work was conducted as a case–control study. Cases consisted of thirty-eight patients and 100 individuals without dementia constituted the control group. Genotyping of MTHFR polymorphisms was performed on patients and controls.

Result: Genetic analyses did not indicate a significant association between the MTHFR C677T mutation and AD (C/T: 63.15% versus 39%, $p = 0.087$). However, the genotype prevalence of the missense variant MTHFR A1298C was significantly different between patients and controls (A/C: 55% versus 7%, $p < 10^{-3}$). Our data suggest an association between the MTHFR A1298C mutation and AD; however, the MTHFR C677T mutation did not contribute to susceptibility for AD.

Conclusion: The **MTHFR A1298C** polymorphism is a possible risk factor for Alzheimer's disease.

Genetic effect of MTHFR C677T, A1298C, and A1793G polymorphisms on the age at onset, plasma homocysteine, and white matter lesions in Alzheimer's disease in the Chinese population

- Background: Three polymorphisms in the Methylenetetrahydrofolate reductase (MTHFR) gene (C677T, A1298C, and A1793G) were reported associated with AD. However, their genotype distributions and associations with age at onset (AAO), homocysteine, and white matter lesions (WML) were unclear in the Chinese AD population.
- Method: We determined the presence of C677T, A1298C, and A1793G polymorphisms in the MTHFR gene using Sanger sequencing in a Chinese cohort comprising 721 AD patients (318 early-onset AD patients (EOAD) and 403 late-onset AD patients (LOAD)) and 365 elderly controls. Additionally, the homocysteine level and WML were evaluated in 121 AD patients.
- Results: The frequency of allele T of C677T polymorphism was significantly higher in AD patients than in controls ($P = 0.040$), while no statistical difference was observed in A1298C and A1793G ($P > 0.05$). Besides, genotype distributions of C677T and A1298C polymorphisms statistically varied between AD patients and controls ($P = 0.021$, $P = 0.012$). Moreover, the AAO was significantly lower in CT/TT (C677T) genotypes carriers ($P = 0.042$) and higher in AC/CC (A1298C) and AG/GG (A1793G) genotypes carriers ($P = 0.034$, $P = 0.009$) in patients with LOAD. We also found that patients with CT/TT (C677T) genotypes were prone to present an increased homocysteine level ($P = 0.036$) and higher Fazekas score ($P = 0.024$). In comparison, patients with AG/GG genotypes (A1793G) had a significantly lower Fazekas score ($P = 0.013$).
- Conclusions: The genotype distributions of C677T and A1298C polymorphisms are associated with AD in the Chinese population. Moreover, AD patients with C677T polymorphism are prone to present an earlier onset, higher homocysteine level, and more severe WML.

There is data that disagrees…

Lack of association between MTHFR A1298C variant and Alzheimer's disease: evidence from a systematic review and cumulative meta-analysis

Conclusion This meta-analysis indicated that MTHFR A1298C polymorphism might not be related to genetic susceptibility of AD in the general population based on existing studies. Additional studies with large sample sizes, gene-gene, and gene-environment interactions are necessary to provide a reliable assessment of the association between MTHFR A1298C polymorphism and AD risk.

Other genes that may influence…

- ABCA7. This gene seems to be linked to a greater risk of Alzheimer's disease. Researchers suspect that it may have something to do with the gene's role in how the body uses cholesterol.
- CLU. This gene helps the brain clear the protein called amyloid-beta. Research suggests that an imbalance in the making and clearing of amyloid-beta is key to getting Alzheimer's disease.
- CR1. Not enough of the protein this gene makes might cause chronic swelling and irritation, called inflammation, in the brain. Inflammation is another possible factor in getting Alzheimer's disease.
- PICALM. This gene is linked to how brain nerve cells, called neurons, talk to each other. How they talk to each other is important for them to work well and to form memories.
- PLD3. Scientists don't know much about the role of PLD3 in the brain. But it's recently been linked to a significantly increased risk of Alzheimer's disease.
- TREM2. This gene affects how the brain responds to swelling and irritation, called inflammation. Rare changes in this gene are lined to an increased risk of Alzheimer's disease.
- SORL1. Some forms of SORL1 on chromosome 11 appear to be linked to Alzheimer's disease.

How do the genes influence?

Knowing this is key
to modifying their expression
or putting back what's missing
another way:

EPIGENETICS!


HOW?

First, find out what's missing. What isn't happening as it should be happening?

MITOCHONDRIA

Mitochondrial alterations in AD

“Morphometric analysis showed that mitochondria are significantly reduced in Alzheimer's disease. The relationship between the site and extent of mitochondrial abnormalities and the synaptic alterations suggests an intimate and early association between these features in Alzheimer's disease.” Source

“Mitochondrial bioenergetic deficit precedes Alzheimer's pathology in female mouse model of Alzheimer's disease.”

“Mitochondrial dysfunction provides a plausible mechanistic rationale for the hypometabolism in brain that precedes AD diagnosis and suggests therapeutic targets for prevention of AD.” Source

Defects in Mitochondrial Dynamics and Metabolomic Signatures of Evolving Energetic Stress in Mouse Models of Familial Alzheimer's Disease

Conclusions: Mutation-specific alterations in mitochondrial dynamics, morphology and function in FAD mice occurred **prior to the onset of memory and neurological phenotype and before* the formation of amyloid deposits.** Metabolomic signatures of mitochondrial stress and altered energy metabolism indicated alterations in nucleotide, Krebs cycle, energy transfer, carbohydrate, neurotransmitter, and amino acid metabolic pathways. Mitochondrial dysfunction, therefore, is an underlying event in AD progression, and FAD mouse models provide valuable tools to study early molecular mechanisms implicated in AD

*My note: here is where preventions strategies come in – *BEFORE*

Alzheimer's disease via enhanced calcium signaling caused by the decrease of endoplasmic reticulum–mitochondrial distance

"The **mitochondrial Ca overload** can lead to increased generation of reactive oxygen species, inducing the opening of the mitochondrial permeability transition pore and ultimately causing neuronal apoptotic and necrotic cell death. The resultant death of neurons which are responsible for memory and cognition would contribute to the pathogenesis of AD. Therefore, we propose that the reduction in the distance between ER and mitochondria may be implicated in AD pathology by enhanced Ca signaling, which provides a more complete picture of the Ca hypothesis of AD."

Note the calcium regulation piece…

Okay, class: *“What nutrient regulates calcium homeostasis?”*

Magnesium in Alzheimer’s disease

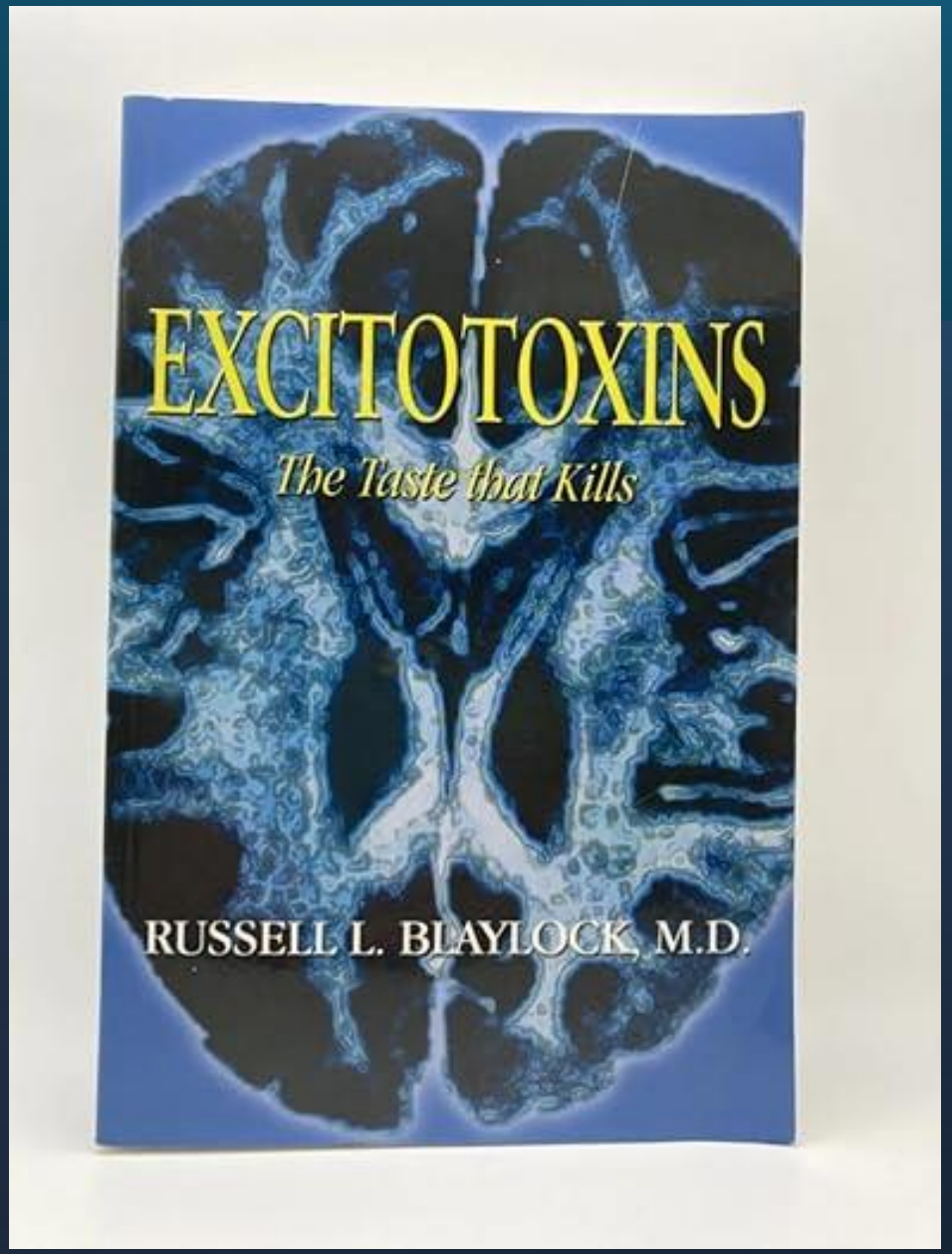
Magnesium (Mg) affects many biochemical mechanisms vital for neuronal properties and synaptic plasticity, including the response of N-methyl D-aspartate (NMDA) receptors to excitatory amino acids, stability and viscosity of the cell membrane, and **antagonism of calcium**. Mg levels were found to be decreased in various tissues of AD patients and negatively correlated with clinical deterioration. Moreover, Mg was demonstrated to modulate the trafficking and processing of amyloid-β precursor protein, which plays a central role in the pathogenesis of AD. Here, we review in vitro and in vivo data that indicated a role for magnesium in many biological and clinical aspects of AD.

And what popular “sweet” exitotoxin also causes calcium homeostasis dysfunction?

Aspartame: Decades of science point to serious health risks

And it isn’t just the destruction of brain cells due to this pathway:

- People drinking diet soda daily were almost three times as likely to develop stroke and dementia as those who consumed it weekly or less. This included a higher risk of ischemic stroke, where blood vessels in the brain become obstructed, and Alzheimer’s disease dementia, the most common form of dementia, reported a 2017 study in Stroke.
- “Daily Consumption of Sodas, Fruit Juices and Artificially Sweetened Sodas Affect Brain,” video of neurologist Matthew Pase, Boston University School of Medicine (4.20.2017)
- “Study links diet soda to higher risk of stroke, dementia,” by Fred Barbash, Washington Post (4.21.2017)
- In the body, the methyl ester in aspartame metabolizes into methanol and then it may be converted to formaldehyde, which has been linked to Alzheimer’s disease. A two-part study published in 2014 in the Journal of Alzheimer’s Disease linked chronic methanol exposure to memory loss and Alzheimer’s Disease symptoms in mice and monkeys.

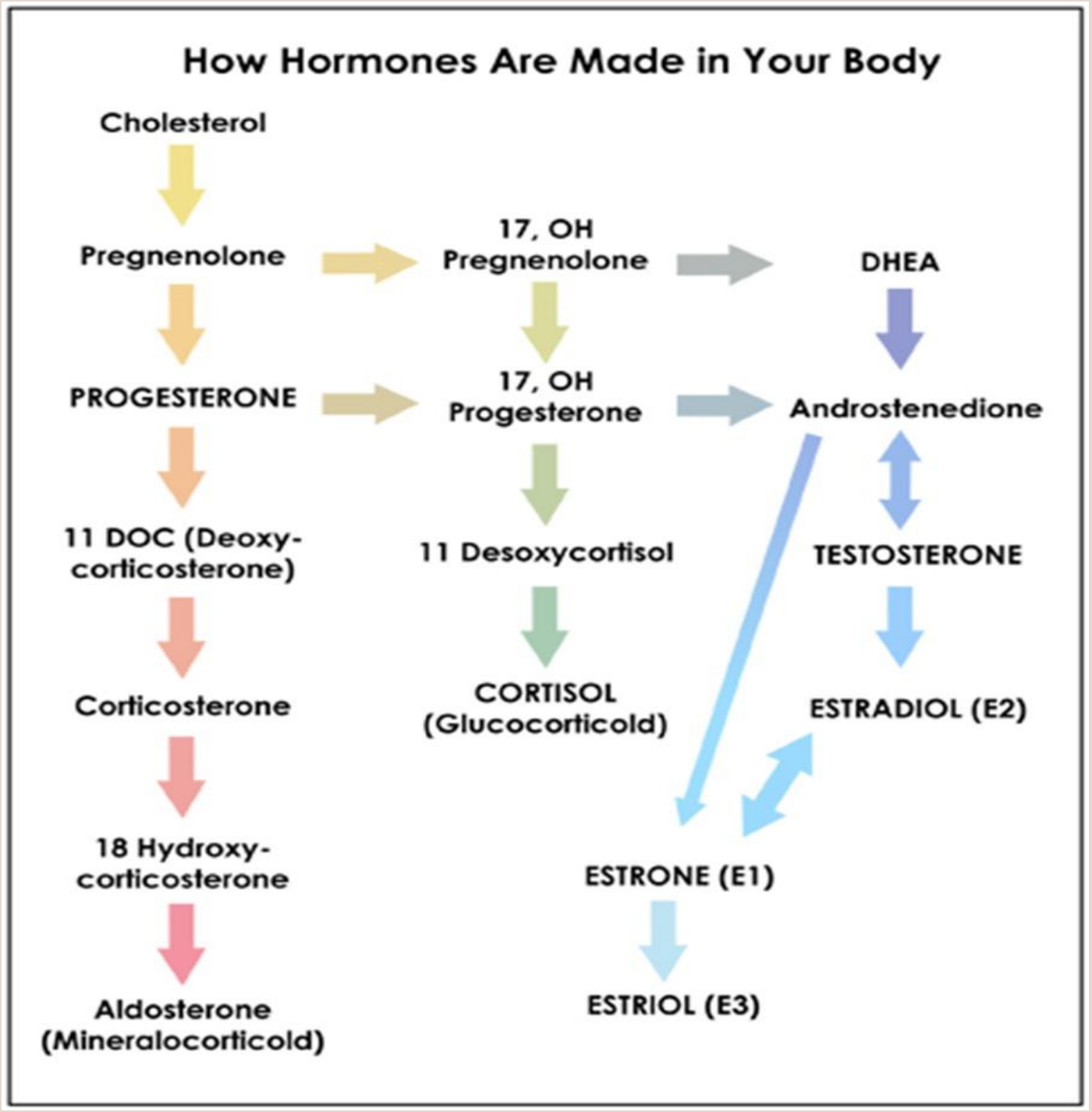

EXCITOTOXINS
The Taste that Kills
RUSSELL L. BLAYLOCK, M.D.

OUTSMARTING ALZHEIMER'S

REBECCA ROENTSCH MONTRONE, BS - WONDROUS ROOTS

PART 2

HORMONES


How Hormones Are Made in Your Body
Cholesterol
Pregnenolone
17, OH Pregnenolone
DHEA
PROGESTERONE
17, OH Progesterone
Androstenedione
11 DOC (Deoxy-corticosterone)
11 Desoxycortisol
TESTOSTERONE
Corticosterone
CORTISOL (Glucocorticold)
ESTRADIOL (E2)
18 Hydroxy-corticosterone
ESTRONE (E1)
Aldosterone (Mineralocorticold)
ESTRIOL (E3)

Let’s start with…

Cholesterol

A very misunderstood fella!

Cholesterol – back to APOE

"Neurons have ApoE receptors, which suggests that ApoE plays a role in the delivery and clearance of fatty acids, cholesterol, and phospholipids to and from the brain.

Delivery and recycling of cholesterol in the brain is critical because **the brain contains 25 percent of the body's total cholesterol**—used as an antioxidant, electrical insulator and key structural component of plasma membranes.

ApoE4 is associated with **reduced LDL uptake** and all the consequences that would result from an inability to deliver cholesterol and fatty acids to target cells.[6] **Cholesterol is an essential contributor to structure and function in the brain, and any interruption in its supply would have extreme consequences for cognitive function."**

The cholesterol problem in AD

Not enough getting into the brain, so blood levels might be on the high side because of that.

Note the LDL – the so-called “BAD” cholesterol, is the form of cholesterol the brain utilizes!

When your doctor prescribed a statin drug for you, did he or she happen to mention, that in the brain, cholesterol is used as:

- An antioxidant
- An electrical insulator
- A key component of plasma membranes

Nutrition and Alzheimer's disease: the detrimental role of a high carbohydrate diet

In this paper, we highlight how an excess of dietary carbohydrates, particularly fructose, alongside a relative deficiency in dietary fats and cholesterol, may lead to the development of Alzheimer's disease. A first step in the pathophysiology of the disease is represented by **advanced glycation end-products** in crucial plasma proteins concerned with fat, cholesterol, and oxygen transport. This leads **to cholesterol deficiency in neurons, which significantly impairs their ability to function.** Over time, a cascade response leads to impaired glutamate signaling, increased oxidative damage, mitochondrial and lysosomal dysfunction, increased risk to microbial infection, and, ultimately, apoptosis. Other neurodegenerative diseases share many properties with Alzheimer's disease and may also be due in large part to this same underlying cause.

Did I see the word…

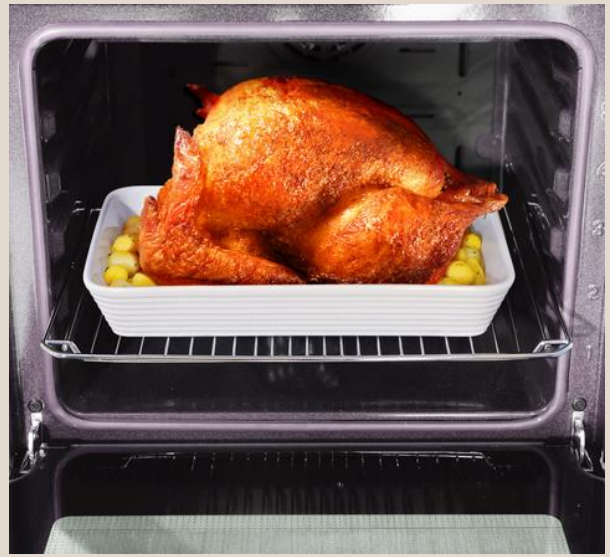
“Glycation?”

Glycation and AGEs

I've talked about glycation and advanced glycation end products (AGEs) before! **Glycation is the binding of sugar to protein.** Think of how the skin of a turkey or chicken turns brown, sticky, and sweet while roasting in the oven. This is a perfect picture of glycation.

Glycation is a process busy at work in those with diabetes, as the chronically high levels of glucose coursing through the bloodstream interact with.

- The nerves – resulting in diabetic neuropathy
- The kidneys – resulting in diabetic nephropathy
- The eyes – resulting in diabetic retinopathy



And some have called Alzheimer's…

Diabetes of the brain!

Medium-chain-triglycerides & diabetes

Dietary Medium-Chain Triglyceride Decanoate Affects Glucose Homeostasis Through GPR84-Mediated GLP-1 Secretion in Mice

Dietary triglycerides are an important energy source; however, their excess intake causes metabolic diseases such as obesity and type 2 diabetes. **Medium-chain triglycerides (MCTs)** as triglyceride forms of medium-chain fatty acids (MCFAs) are applied to meet the energy demands of athletes, the elderly, and people with stunted growth, because MCFAs are efficiently converted into energy for immediate utilization by the organs and do not accumulate as fat.

Conclusions: Dietary MCT (C10:0/decanoate) intake efficiently may protect against obesity and improve insulin resistance via GLP-1 secretion.

PS: Traditionally, **coconut** and **palm-kernel oils** are used as a good sources of **decanoic acid**. Source

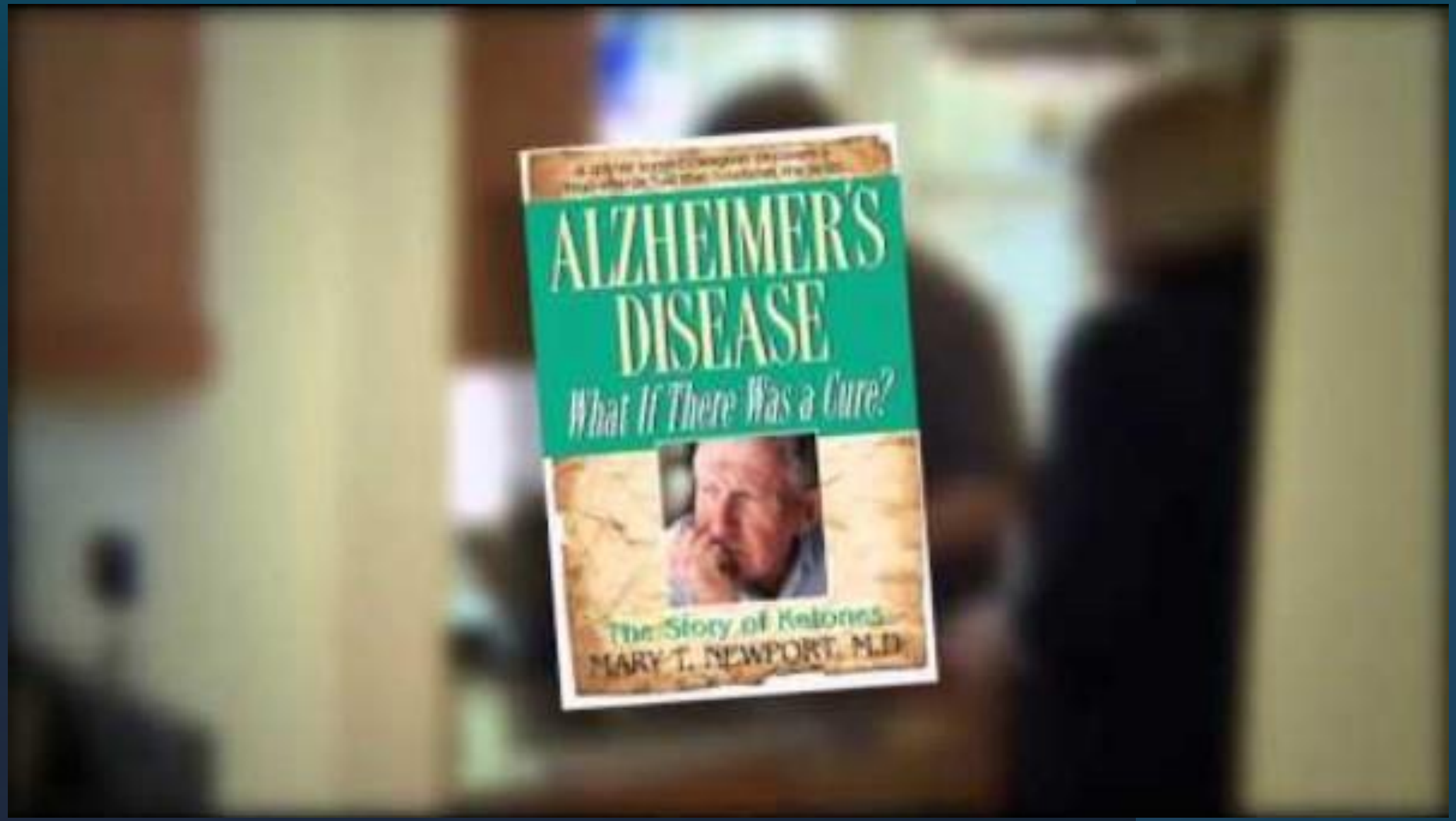
Use of medium chain triglyceride (MCT) oil in subjects with Alzheimer's disease

- Introduction Cerebral glucose and insulin metabolism is impaired in Alzheimer's disease (AD). Ketones provide alternative energy. Will medium chain triglyceride (MCT) oil, a nutritional source of ketones, impact cognition in AD?
- Methods This was a 6-month randomized, double-blind, placebo-controlled, crossover study, with 6-month open-label extension in probable AD subjects, on stable medications. MCT dose was 42 g/day, or maximum tolerated. Cognition was assessed with Mini-Mental State Examination (MMSE), Montreal Cognitive Assessment (MoCA), and Cognigram®.
- Discussion
- This is the longest duration MCT AD study to date. **Eighty percent had stabilization or improvement in cognition, and better response with 9-month continual MCT oil.**

"EIGHTY PERCENT"??????

Coconut oil as a therapeutic treatment for alzheimer's disease: a review

The principal biochemical hallmarks behind the pathogenesis of AD are the development of extracellular amyloid β plaques and the accumulation of intracellular neurofibrillary tangles. Occurrence of Cardiovascular diseases (CVD) with elevated LDL levels, hypertension, Type 2 diabetes, obesity, and insulin resistance are some key risk factors that are responsible for the increasing prevalence and incidence of AD. There is sufficient evidence to prove that MCTs in coconut oil are metabolized and absorbed in such a way that retards the severity of these physiological risk factors. Besides, coconut oil is endowed with many polyphenolic compounds that are serving as antioxidants by combating oxidative stress and inflammation, which in turn downregulates the etiology of AD. But depending on the different processing conditions applied in extraction techniques of coconut oil, variations in antioxidant capacity can take place. Even though there are inadequacies in peer-reviewed large cohort clinical data for the long run, this article reviews that coconut oil, its constituents, and metabolism have positive findings on the potentiality to treat AD as a nutritional supplement.


ALZHEIMER'S
DISEASE
What If There Was a Cure?
The Story of Ketones
MARY T. NEWPORT, M.D.

Question:

Has anyone you know with Alzheimer's disease been advised by his or her doctor to use MCT oil in the daily diet as a treatment for Alzheimer's Disease?

Answer: "NO"

Question:

Has anyone you know with Alzheimer's disease been advised by his or her doctor to use <u>any</u> natural substance, dietary approach – anything but prescriptions – to treat the Alzheimer's disease?

Answer: "NO"

Back to hormones & the brain!

The neurosteroid allopregnanolone is reduced in prefrontal cortex in Alzheimer's disease

Conclusions: Subjects with AD demonstrate significant reductions in PFC(prefrontal cortex) allopregnanolone levels, a finding that may be relevant to neuropathological disease stage severity. Neurosteroids may have utility as candidate biomarkers in AD

Pregnenolone derivatives for the treatment of Alzheimer's disease: synthesis, and in vitro inhibition of amyloid β1–42 peptide aggregation, acetylcholinesterase and carbonic anhydrase-II†

"The amyloid state, which is a specific conformation of proteins, offers valuable information about both functional protein structures and the pathological assemblies associated with various diseases. One of the major hallmarks of Alzheimer's disease includes primarily the extracellular build-up of a peptide known as amyloid-β, which has a sequence consisting of 39 to 42 amino acid residues, and the formation of intracellular neurofibrillary tangles mostly consisting of hyperphosphorylated tau protein. Drugs that are expected to reduce Aβ production, prevent Aβ aggregation, and promote Aβ clearance are promising approaches for treating AD.

Pregnenolone-based derivatives have been synthesized to inhibit the protofibril formation in order to reduce $A\beta_{1-42}$ production and prevent its aggregation."

The neurosteroid pregnenolone promotes degradation of key proteins in the innate immune signaling to suppress inflammation

"Pregnenolone is a steroid hormone precursor that is synthesized in various steroidogenic tissues, in the brain, and in lymphocytes. In addition to serving as the precursor for other steroid hormones, pregnenolone exerts its own effect as an anti-inflammatory molecule to maintain immune homeostasis in various inflammatory conditions. Pregnenolone and its metabolic derivatives have been shown to have beneficial effects in the brain, including enhancing memory and learning, reversing depressive disorders, and modulating cognitive functions. **A decreased level of pregnenolone has been observed in neuroinflammatory diseases, which emphasizes its role in neuroprotection and neuro-regeneration.**"

DHEA-S plasma levels and incidence of Alzheimer's disease

Background: Cross-sectional studies controlling for age and gender reported a relationship between Alzheimer's disease and low dehydroepiandrosterone sulphate (DHEA-S) plasma levels. Prospective data with sufficient control for confounding factors are lacking.

Conclusions: This population-based prospective study supports the role of DHEA-S as a risk factor for Alzheimer's disease.

Neuroprotective effects of dehydroepiandrosterone (DHEA) in rat model of Alzheimer's disease

“The current study was undertaken to elucidate a possible neuroprotective role of dehydroepiandrosterone (DHEA) against the development of Alzheimer's disease in experimental rat model.”

“Significant amelioration in all investigated parameters was detected as a result of treatment of Al-intoxicated ovariectomized rats with DHEA. These results were confirmed by histological examination of brain sections. **These results clearly indicate a neuroprotective effect of DHEA against Alzheimer's disease.**”

Effects of progesterone on glucose uptake in neurons of Alzheimer's disease animals and cell models

Aims: Alzheimer's disease (AD) is closely related to abnormal glucose metabolism in the central nervous system. Progesterone has been shown to have obvious neuroprotective effects in the pathogenesis of AD, but the specific mechanism has not been fully elucidated. Therefore, the purpose of this study was to investigate the effect of progesterone on the glucose metabolism of neurons in amyloid precursor protein (APP)/presenilin 1 (PS1) mice and Aβ-induced AD cell model.

Significance: These results confirm that progesterone significantly improves the glucose metabolism of neurons. One of the mechanisms of this effect is that progesterone upregulates protein expression of GLUT3 and GLUT4 through pathways PGRMC1/CREB/GLUT3 and PGRMC1/PPARɣ/GLUT4.

Serotonin

Serotonin: A New Hope in Alzheimer's Disease?

Alzheimer's disease (AD) is the most common form of dementia affecting 35 million individuals worldwide. Current AD treatments provide only brief symptomatic relief. It is therefore urgent to replace this symptomatic approach with a curative one. Increasing serotonin signaling as well as developing molecules that enhance serotonin concentration in the synaptic cleft have been debated as possible therapeutic strategies to slow the progression of AD. In this Viewpoint, we discuss exciting new insights regarding the modulation of serotonin signaling for AD prevention and therapy.

Depression in patients with mild cognitive impairment increases the risk of developing dementia of Alzheimer type: a prospective cohort study

Conclusions: We conclude that patients with mild cognitive impairment and depression are at more than twice the risk of developing dementia of Alzheimer type as those without depression. Patients with a poor response to antidepressants are at an especially increased risk of developing dementia.

The role of serotonin within the microbiota-gut-brain axis in the development of Alzheimer's disease: A narrative review

- Highlights
- •Serotonin (5-HT) alterations are implicated in Alzheimer's disease (AD) development.
- •SSRI and 5-HT receptor a(nta)gonists might attenuate AD neuropathology and symptoms.
- •Gut microbiota form a viable target in AD for inducing profound 5-HT brain changes.
- •Pre-/probiotics, diet and fecal microbiota transplants are promising approaches.
- •A shift from animal to human trials in prodromal up to mild AD is a prerequisite.

Mitochondrial Interaction with Serotonin in Neurobiology and Its Implication in Alzheimer's Disease

Abstract. Alzheimer's disease (AD) is a lethal neurodegenerative disorder characterized by severe brain pathologies and progressive cognitive decline. While the exact cause of this disease remains unknown, emerging evidence suggests that dysregulation of neurotransmitters contributes to the development of AD pathology and symptoms. **Serotonin, a critical neurotransmitter in the brain, plays a pivotal role in regulating various brain processes and is implicated in neurological and psychiatric disorders, including AD.** Recent studies have shed light on the interplay between mitochondrial function and serotonin regulation in brain physiology. **In AD, there is a deficiency of serotonin, along with impairments in mitochondrial function, particularly in serotoninergic neurons.** Additionally, altered activity of mitochondrial enzymes, such as **monoamine oxidase**, may contribute to serotonin dysregulation in AD. Understanding the intricate relationship between mitochondria and serotonin provides valuable insights into the underlying mechanisms of AD and identifies potential therapeutic targets to restore serotonin homeostasis and alleviate AD symptoms. This review summarizes the recent advancements in unraveling the connection between brain mitochondria and serotonin, emphasizing their significance in AD pathogenesis and underscoring the importance of further research in this area. Elucidating the role of mitochondria in serotonin dysfunction will promote the development of therapeutic strategies for the treatment and prevention of this neurodegenerative disorder.

Supplementing with 5-HTP

This is easy to do. I was able to immediately arrest my PMDD – premenstrual dysphoric disorder – an OCD form of PMS and a forerunner of Alzheimer's disease – using 5-HTP. If you suffer from serotonin deficiency syndrome in any way, you need to take care of it, or it will lead to further problems down the road. Premenstrual dysphoria disorder: It's biology, not a behavior choice – Harvard Health

5-HTP vs. Prozac - the serotonin deficiency syndrome

Women with Premenstrual Dysphoria Lack the Seemingly Normal Premenstrual Right-Sided Relative Dominance of 5-HTP-Derived Serotonergic Activity in the Dorsolateral Prefrontal Cortices - A Possible Cause of Disabling Mood Symptoms

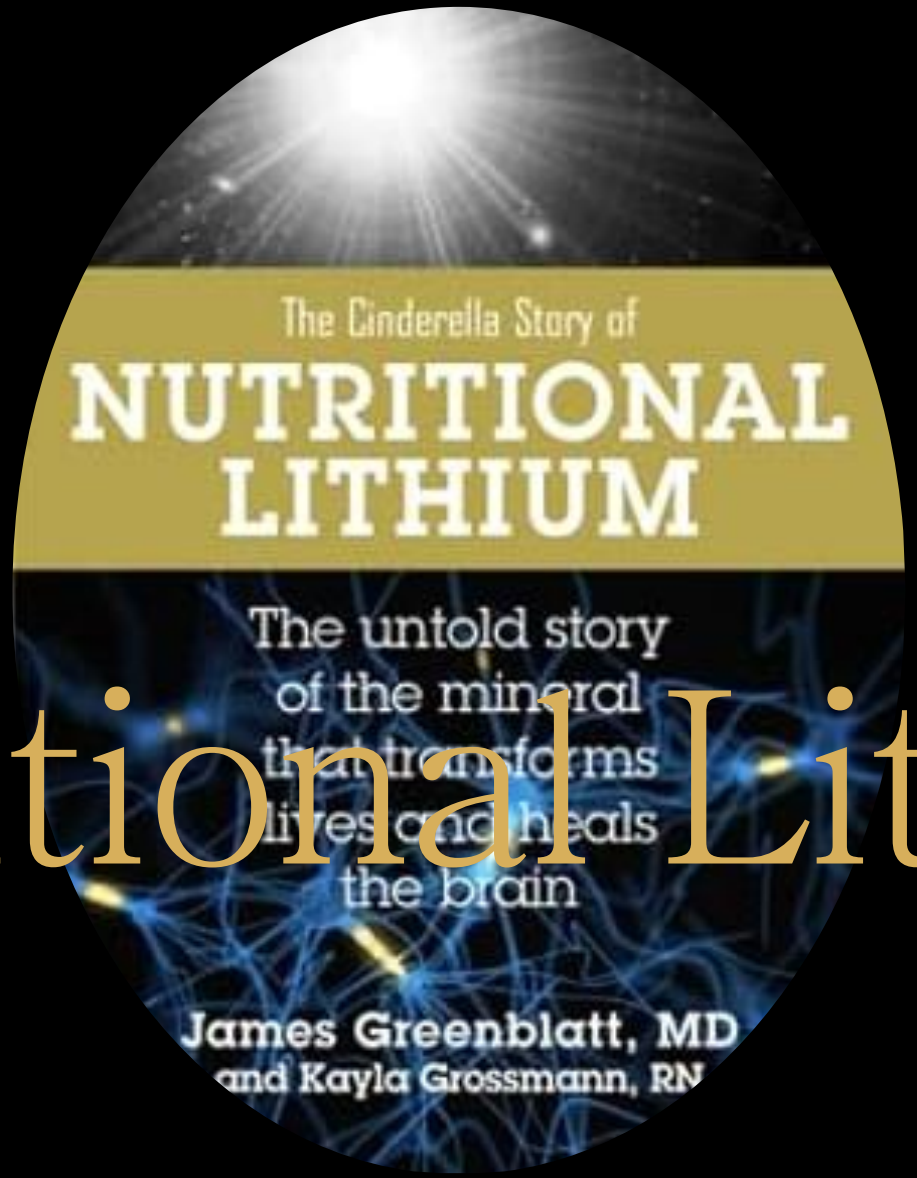
MTHFR Gene & PMDD: Unlocking the Connection

“I wish you were my daughter…”

OUTSMARTING ALZHEIMER'S

REBECCA ROENTSCH MONTRONE, BS - WONDROUS ROOTS

PART 3



Nutritional Lithium

Lithium microdose could stop Alzheimer's from advancing

- In 2017, *Medical News Today* reported on a study that proposed that the mood stabilizer lithium might help stave off dementia.
- The study found that people exposed to drinking water with higher concentrations of lithium were **17% less likely to develop dementia** than people whose water contained barely any lithium.
- Since then, other epidemiological, preclinical, and clinical studies have suggested that a microdose of lithium can reduce the risk of Alzheimer's by influencing key pathological mechanisms at play in the neurodegenerative condition.

Reducing the progression of Alzheimer's disease in Down syndrome patients with micro-dose lithium

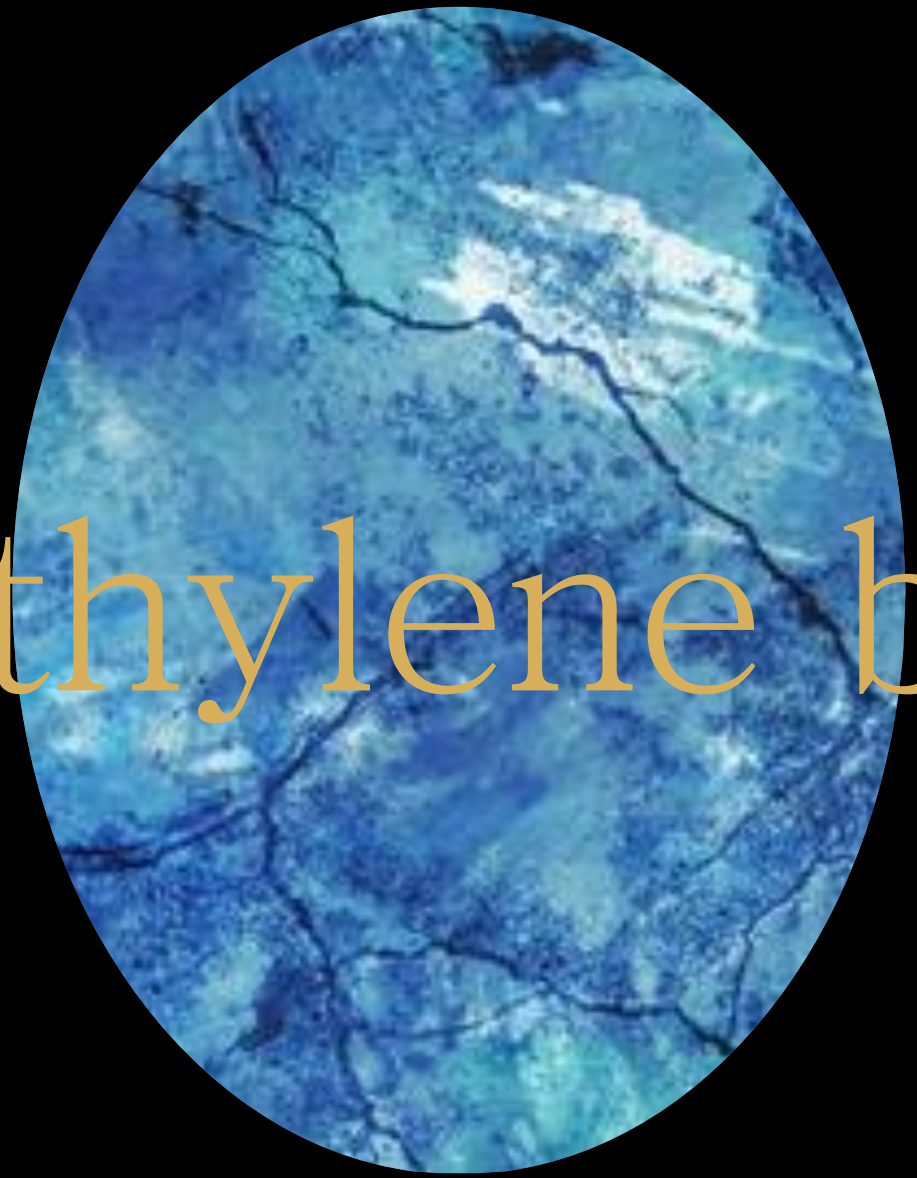
There is growing consensus in the literature that lithium salts, well-established as efficacious in the treatment of select affective disorders, may also provide neuroprotection from the development and progression of AD by targeting multiple processes implicated in the disease. T

"micro-dose" lithium (300 micrograms daily in one study) demonstrated **stabilization of cognitive decline in AD patients with mild cognitive impairment.** With encouraging data suggesting that lithium confers a clinically significant benefit in AD by impeding accumulation of the aberrant proteins central to the putative pathogenesis, **it follows to reason that a population with a genetic predisposition rooted in this disease mechanism may benefit from it.**

Lithium as a Nutrient

In high doses, lithium acts as a drug, accompanied by potentially serious and debilitating side effects. In low doses, lithium acts as a nutrient required for B12 and folate transport and uptake, neuromodulation, and the function of many biochemical processes in both humans and animals. Studies since the 1970s have shown the ability of lithium to stimulate the proliferation of stem cells. Recent studies have described its ability to up-regulate neurotrophins such as brain-derived neurotrophic factor (BDNF) and nerve-growth factor (NGF), which are important in neuronal function, plasticity, and repair. With its newly described antioxidant and anti-inflammatory activity along with powerful neuroprotective effects, low-dose lithium therapy has largely unrealized potential to prevent or treat a wide-range of neurological disorders such as traumatic brain injury (TBI), **Alzheimer's disease**, Parkinson's disease, amyotrophic lateral sclerosis (ALS), chronic pain, mercury toxicity, depression/anxiety, alcoholism, and drug addiction.

Methylene blue



Methylene Blue - Nootropics Expert

Methylene Blue resists Alzheimer's Disease

Alzheimer's disease and other forms of dementia are associated with a buildup of the protein Tau. Clinical trials show that Methylene Blue inhibits Tau formation. And is under consideration as a treatment for Alzheimer's.[xi] Methylene Blue has an inhibitory action on the cGMP pathway, and affects other molecular events closely related to the progression of Alzheimer's. Methylene Blue boosts neuron resistance to the formation of amyloid plaques and neurofibrillary tangles. And helps repair impairments in mitochondrial function and cellular metabolism. Research also shows that cholinergic, serotonergic and glutamatergic systems all play important roles in the development of Alzheimer's and other cognitive disorders. Methylene Blue provides beneficial effects in mediating these pathways.[xii] This is particularly significant because most existing treatments for Alzheimer's can only prevent the disease before it is diagnosed. But Methylene Blue shows promise in delaying the effects of Alzheimer's and dementia after it is diagnosed.

Exploring Methylene Blue and Its Derivatives in Alzheimer's Treatment: A Comprehensive Review of Randomized Control Trials

The literature review includes randomized clinical trials investigating MB's potential benefits in treating AD. The findings of the studies indicate that the administration of MB has demonstrated enhancements in cognitive function, reductions in the accumulation of plaques containing beta-amyloid, improvements in memory and cognitive function in animal subjects, and possesses antioxidant properties that can mitigate oxidative stress and inflammation within the brain. This review evaluates the modern and latest research on the application of MB for treating AD.

Methylene Blue Reduces Aβ Levels and Rescues Early Cognitive Deficit by Increasing Proteasome Activity

"Here, we report that chronic dietary MB treatment reduces Aβ levels and improves learning and memory deficits in the 3xTg-AD mice. The mechanisms underlying the effects of MB on Aβ pathology appears to be mediated by an increase in Aβ clearance as we show that MB increases the chymotrypsin- and trypsin-like activities of the proteasome in the brain. To our knowledge, this is the first report showing that MB increases proteasome function and ameliorates AD-like pathology *in vivo*. Overall, the data presented here support the use of MB for the treatment of AD and offer a possible mechanism of action."

FYI- this was published in 2011 – yet no one in medical practice is using methylene blue in their patients with Alzheimer's disease! Walk till you drop; it won't benefit anyone you know in your lifetime.

Methylene blue and Alzheimer's disease

“The relationship between methylene blue (MB) and Alzheimer's disease (AD) has recently attracted increasing scientific attention since it has been suggested that MB may slow down the progression of this disease. In fact, MB, in addition to its well characterized inhibitory actions on the cGMP pathway, affects numerous cellular and molecular events closely related to the progression of AD. Currently, MB has been shown to attenuate the formations of amyloid plaques and neurofibrillary tangles, and to partially repair impairments in mitochondrial function and cellular metabolism. Furthermore, various neurotransmitter systems (cholinergic, serotonergic and glutamatergic), believed to play important roles in the pathogenesis of AD and other cognitive disorders, are also influenced by MB. Recent studies suggest that the combination of diverse actions of MB on these cellular functions is likely to mediate potential beneficial effects of MB. This has lead to attempts to develop novel MB-based treatment modalities for AD. In this review article, actions of MB on neurotransmitter systems and multiple cellular and molecular targets are summarized with regard to their relevance to AD.”

And this was published in 2009; what are we waiting for?

New study shows a minimum dose of hydromethylthionine could slow cognitive decline and brain atrophy in mild-to-moderate Alzheimer's disease

And THIS in 2019!

ABERDEEN, Scotland and Singapore, 26 November, 2019 – In a paper published in today's online issue of the Journal of Alzheimer's Disease, TauRx has reported unexpected results of a pharmacokinetic analysis of the relationship between treatment dose, blood levels and pharmacological activity of the drug hydromethylthionine on the brain in over 1,000 patients with mild-to-moderate Alzheimer's disease. These results showed that, even at the lowest dose of hydromethylthionine previously tested in two Phase 3 global clinical trials (8 mg/day), the drug produced concentration-dependent effects on cognitive decline and brain atrophy.

Breaking down into key points

- The dose of methylene blue in this study was very low; just 8–16 mg daily
- The efficacy when used alone – without typical Alzheimer's drugs – demonstrated an 85% arrest of disease progression
- When combined with Alzheimer's disease medications, the efficacy was reduced by half
- Hydromethylthionine is a stable reduced form of methylthioninium, which is better absorbed than methylene blue and has been tested in clinical trials in mild–to–moderate Alzheimer's disease.
- My comment: still, using methylene blue, stick with the lower dose, since the lower dose is what does its beautiful work in the electron transport chain.

How Methylene Blue's Antioxidants Can Slow Cognitive Decline

In a 2021 study entitled "The Potentials of Methylene Blue as an Anti-Aging Drug," the authors found that **mitochondrial dysfunction** is observed in systematic aging that affects many tissues, including the brain and skin, which can lead to increased oxidative stress. [2] **The brain has, by far, one of the highest concentrations of mitochondria, considered the "powerhouse" of the cells.** Methylene Blue normalizes compromised mitochondrial function in the brain, which can improve brain cell energy production. This can result in improved memory retention. [3]

How to take…

Methylene blue – amazing for so many protections when it comes to our health. And it is the lower dose that does “the trick.”

Take your weight in lb, divide by 2 to convert to kilograms, and take 0.5 mg/kg daily, divided into two doses.

Contraindicated if you have a G6PD enzyme deficiency. Though this is a common deficiency, it occurs primarily in men of Asian, Middle-Eastern, or African descent. You can easily be tested for this.

Proteolytic enzymes

Serrapeptase &
Nattokinase

What are serrapeptase & nattokinase?

Serrapeptase is a proteolytic enzyme, meaning it breaks down proteins into smaller components called amino acids. Along with its anti-inflammatory properties, it offers a host of other health benefits. Nattokinase is a natural enzyme in natto, a Japanese soy-based food, that can dissolve blood clots, lower blood pressure, and improve sinus and gut health.

Serrapeptase and nattokinase intervention for relieving Alzheimer's disease pathophysiology in rat model

Oral administration of SP or NK in a rat model of AD daily for 45 days resulted in ***a significant decrease*** in brain AchE activity, TGF-β, Fas and IL-6 levels. Also, the treatment with these enzymes produced ***significant increase*** in BDNF and IGF-1 levels when compared with the untreated AD-induced rats. Moreover, both SP and NK could markedly increase the expression levels of ADAM9 and ADAM10 genes in the brain tissue of the treated rats. These findings were well confirmed by the histological examination of the brain tissue of the treated rats. *The present results support our hypothesis that the oral administration of proteolytic enzymes, SP and/or NK, would have an effective role in modulating certain factors characterizing AD. Thus, these enzymes may have a therapeutic application in the treatment of AD. – 2013*

Easy to do!


Doctor's BEST
Science-Based Nutrition™
Dietary Supplement
Best
120,000 SPUs
High Potency
Serrapeptase
120,000 SERRATIOPEPTIDASE UNITS PER VEGGIE CAP
90 Veggie Caps
Vegan


Doctor's BEST
Science-Based Nutrition™
Nattokinase
2,000 FUs
90 Veggie Caps
Vegan

Glutathione & Alzeimer's

The “Glutathione Girl” strikes again!

The emerging role of glutathione in Alzheimer's disease

Abstract With millions of older individuals presently suffering from Alzheimer's disease (AD) worldwide, AD is an unduly common form of dementia that exacts a heavy toll on affected individuals and their families. One of the emerging causative factors associated with AD pathology is oxidative stress. This AD-related increase in oxidative stress has been attributed to decreased levels of the brain antioxidant, glutathione (GSH). In this article, we review the role of GSH in AD from a pathological as well as a diagnostic point of view. We recapitulate the literature that has assessed the role of GSH in AD onset and progression. We discuss the various methodologies through which alterations in GSH levels might be monitored and highlight the yet uncharted potential of assaying GSH levels in vivo with magnetic resonance spectroscopy in AD therapeutics and prognostics. Finally, the present manuscript integrates findings from various studies to elucidate the possible molecular mechanisms through which disruptions in GSH homeostasis may contribute to AD pathology.

Elevation of glutathione as a therapeutic strategy in Alzheimer disease

Abstract Oxidative stress has been associated with the onset and progression of mild cognitive impairment (MCI) and Alzheimer disease (AD). AD and MCI brain and plasma display extensive oxidative stress as indexed by protein oxidation, lipid peroxidation, free radical formation, DNA oxidation, and decreased antioxidants. The most abundant endogenous antioxidant, glutathione, plays a significant role in combating oxidative stress. The ratio of oxidized to reduced glutathione is utilized as a measure of intensity of oxidative stress. Antioxidants have long been considered as an approach to slow down AD progression. In this review, we focus on the elevation on glutathione through N-acetyl-cysteine (NAC) and ɣ-glutamylcysteine ethyl ester (GCEE) as a potential therapeutic approach for Alzheimer disease. This article is part of a Special Issue entitled: Antioxidants and Antioxidant Treatment in Disease.

Beta-amyloidolysis and glutathione in Alzheimer's disease (note interaction glutathione/proteolytic activity)

Abstract In this review, we hypothesized the importance of the interaction between the brain glutathione (GSH) system, the proteolytic tissue plasminogen activator (t-PA)/plasminogen/ plasmin system, regulated by plasminogen activator inhibitor (PAI-1), and neuroserpin in the pathogenesis of Alzheimer's disease. The histopathological characteristic hallmark that gives personality to the diagnosis of Alzheimer's disease is the accumulation of neurofibroid tangles located intracellularly in the brain, such as the protein tau and extracellular senile plaques made primarily of amyloidal substance. These formations of complex etiology are intimately related to GSH, brain protective antioxidants, and the proteolytic system, in which t-PA plays a key role. There is scientific evidence that suggests a relationship between aging, a number of neurodegenerative disorders, and the excessive production of reactive oxygen species and accompanying decreased brain proteolysis. The plasminogen system in the brain is an essential proteolytic mechanism that effectively degrades amyloid peptides ("betaamyloidolysis") through action of the plasmin, and this physiologic process may be considered to be a means of prevention of neurodegenerative disorders. In parallel to the decrease in GSH levels seen in aging, there is also a decrease in plasmin brain activity and a progressive decrease of t-PA activity, caused by a decrease in the expression of the t-PA together with an increase of the PAI-1 levels, which rise to an increment in the production of amyloid peptides and a lesser clearance of them. Better knowledge of the GSH mechanism and cerebral proteolysis will allow us to hypothesize about therapeutic practices.

Melatonin & Alzheimer's

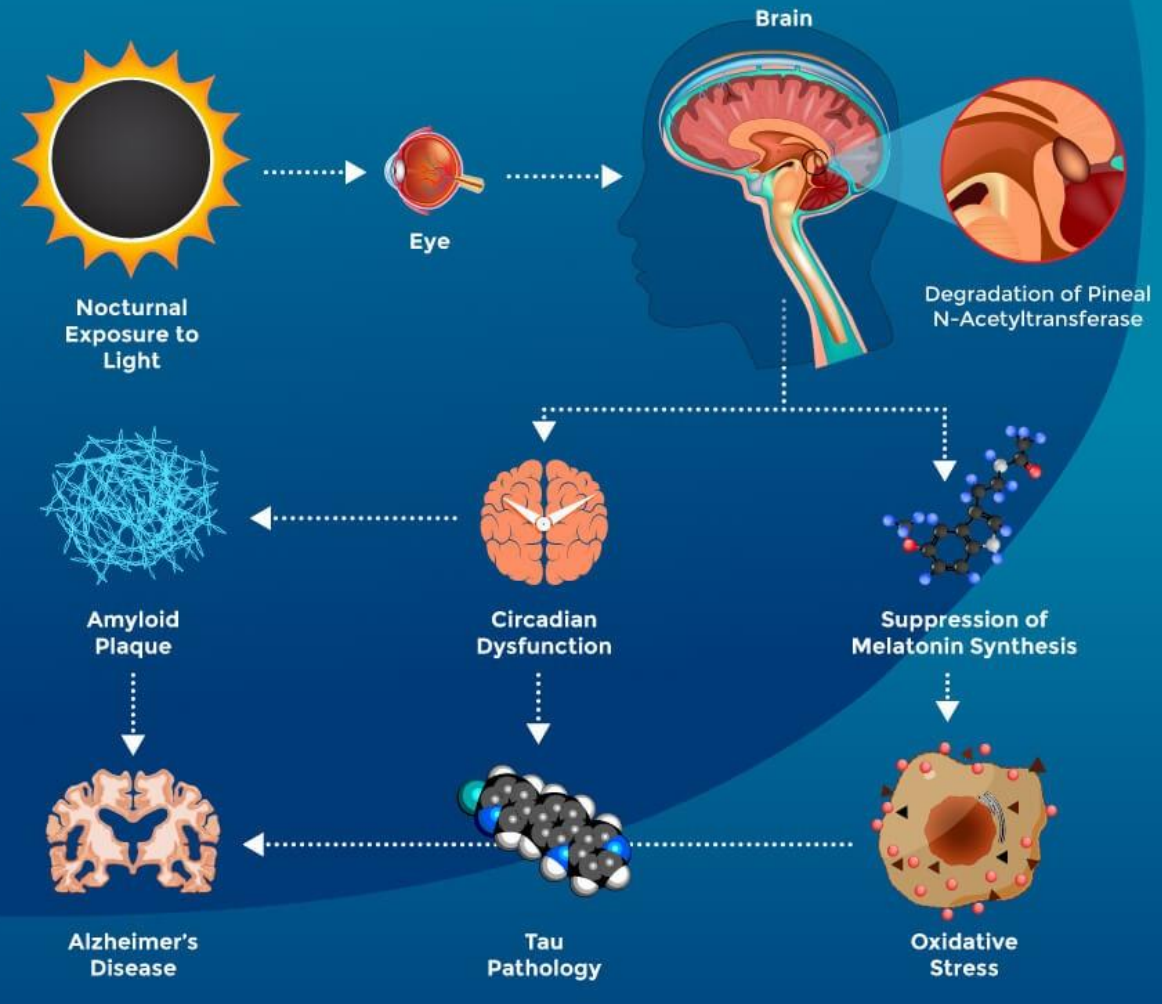
Melatonin & Alzheimer's Disease

Melatonin secretion decreases in Alzheimer´s disease (AD) and this decrease has been postulated as responsible for the circadian disorganization, decrease in sleep efficiency and impaired cognitive function seen in those patients.

Clinical Aspects of Melatonin Intervention in Alzheimer's Disease Progression

Circadian Rhythm Disruption, Melatonin Suppression and Alzheimer's Disease

One of the hallmarks of Alzheimer's is the reduction in melatonin synthesis and the disruption of circadian rhythm activity. With insufficient melatonin production, the brain cannot handle the oxidative stress levels and inflammation and the brain cells develop dysfunctional proteins called amyloid plaque and Tau protein pathology.



Prophylactic melatonin significantly reduces Alzheimer's neuropathology and associated cognitive deficits independent of antioxidant pathways in AβPPswe/PS1 mice

Conclusions: These findings demonstrate that prophylactic MEL (melatonin) ***significantly reduces AD neuropathology and associated cognitive deficits*** in a manner that is independent of antioxidant pathways. Future identification of direct molecular targets for MEL action in the brain should open new vistas for development of better AD therapeutics

Melatonin in Alzheimer's disease and other neurodegenerative disorders

"The ability of melatonin and its kynuramine metabolites to interact directly with the electron transport chain by increasing the electron flow and reducing electron leakage are unique features by which melatonin is able to increase the survival of neurons under enhanced oxidative stress. Moreover, anti-fibrillogenic actions have been demonstrated in vitro, also in the presence of pro-fibrillogenic apoE4 or apoE3, and in vivo, in a transgenic mouse model. Amyloid-β toxicity is antagonized by melatonin and one of its kynuramine metabolites."

So, again, think:

- electron transport chain repair (methylene blue)
- anti-fibrillogenic actions (serrapeptase/nattokinase/glutathione)

Melatonin Therapy in Patients with Alzheimer's Disease

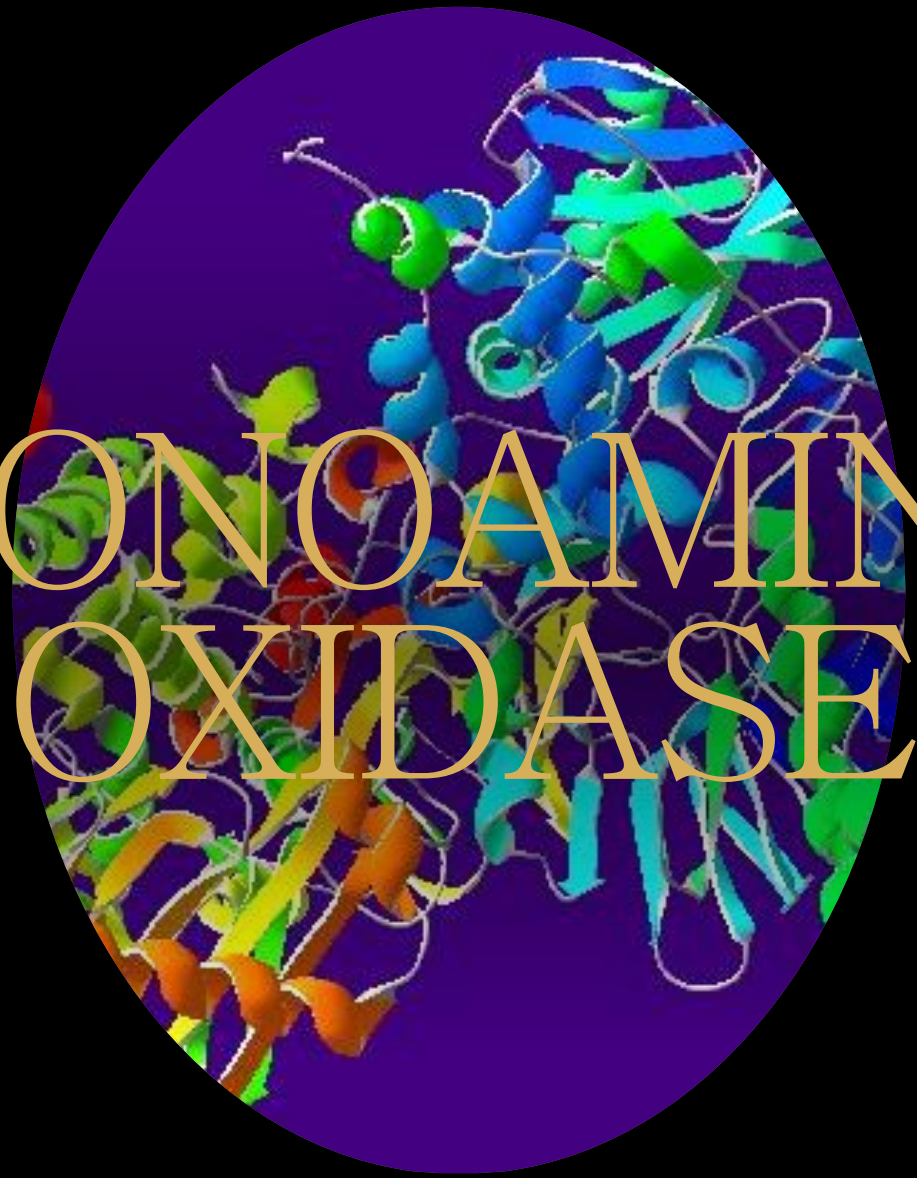
Abstract: Alzheimer's disease (AD) is a major health problem and a growing recognition exists that efforts to prevent it must be undertaken by both governmental and non-governmental organizations. In this context, the pineal product, melatonin, has a promising significance because of its chronobiotic/cytoprotective properties potentially useful for a number of aspects of AD. One of the features of advancing age is the gradual decrease in circulating melatonin levels. A limited number of therapeutic trials have indicated that melatonin has a therapeutic value as a neuroprotective drug in the treatment of AD and minimal cognitive impairment (which may evolve to AD). Both in vitro and in vivo, melatonin prevented the neurodegeneration seen in experimental models of AD. For these effects to occur, doses of melatonin about two orders of magnitude higher than those required to affect sleep and circadian rhythmicity are needed. More recently, attention has been focused on the development of potent melatonin analogs with prolonged effects, which were employed in clinical trials in sleep-disturbed or depressed patients in doses considerably higher than those employed for melatonin. In view that the relative potencies of the analogs are higher than that of the natural compound, clinical trials employing melatonin in the range of 50–100 mg/day are urgently needed to assess its therapeutic validity in neurodegenerative disorders such as AD.

This paper is from 10 years ago – 2014! Of what use is it? Who is benefitting?

How many people have died of Alzheimer's disease in the last 10 years? How many people were diagnosed with Alzheimer's disease in the last ten years?

How many of them or their family members were told anything at all about the possible help of melatonin – or any of the things we are talking about here – by their physicians or the Alzheimer's Association?

MONOAMINE OXIDASE



Exploring the Role of Monoamine Oxidase Activity in Aging and Alzheimer's Disease

Monoamine oxidases (MAOs) are a family of flavin adenine dinucleotide–dependent enzymes that have a crucial role in the metabolism of neurotransmitters of the central nervous system. Impaired function of MAOs is associated with copious brain diseases. The alteration of monoamine metabolism is a characteristics feature of aging. MAO plays a crucial role in the pathogenesis of Alzheimer's disease (AD), a progressive neurodegenerative disorder associated with an excessive accumulation of amyloid-beta (Aβ) peptide and neurofibrillary tangles (NFTs). Activated MAO plays a critical role in the development of amyloid plaques from Aβ as well as the formation of the NFTs. In the brain, MAO mediated metabolism of monoamines is the foremost source of reactive oxygen species formation. The elevated level of MAO-B expression in astroglia has been reported in the AD brains adjacent to amyloid plaques. Increased MAO-B activity in the cortical and hippocampal regions is associated with AD. This review describes the pathogenic mechanism of MAOs in aging as well as the development and propagation of Alzheimer's pathology.

Procaine – Gerovital GH3

"The MAO B inhibitory action of procaine was reported following pharmacodynamics studies, and GH3 was included in the category of reversible and competitive inhibitors [112, 113]."

Procaine – GH3 – lipid metabolism

Remember the problem with cholesterol/lipid metabolism in Alzheimer's disease associated with the APOE4 genetic mutation?

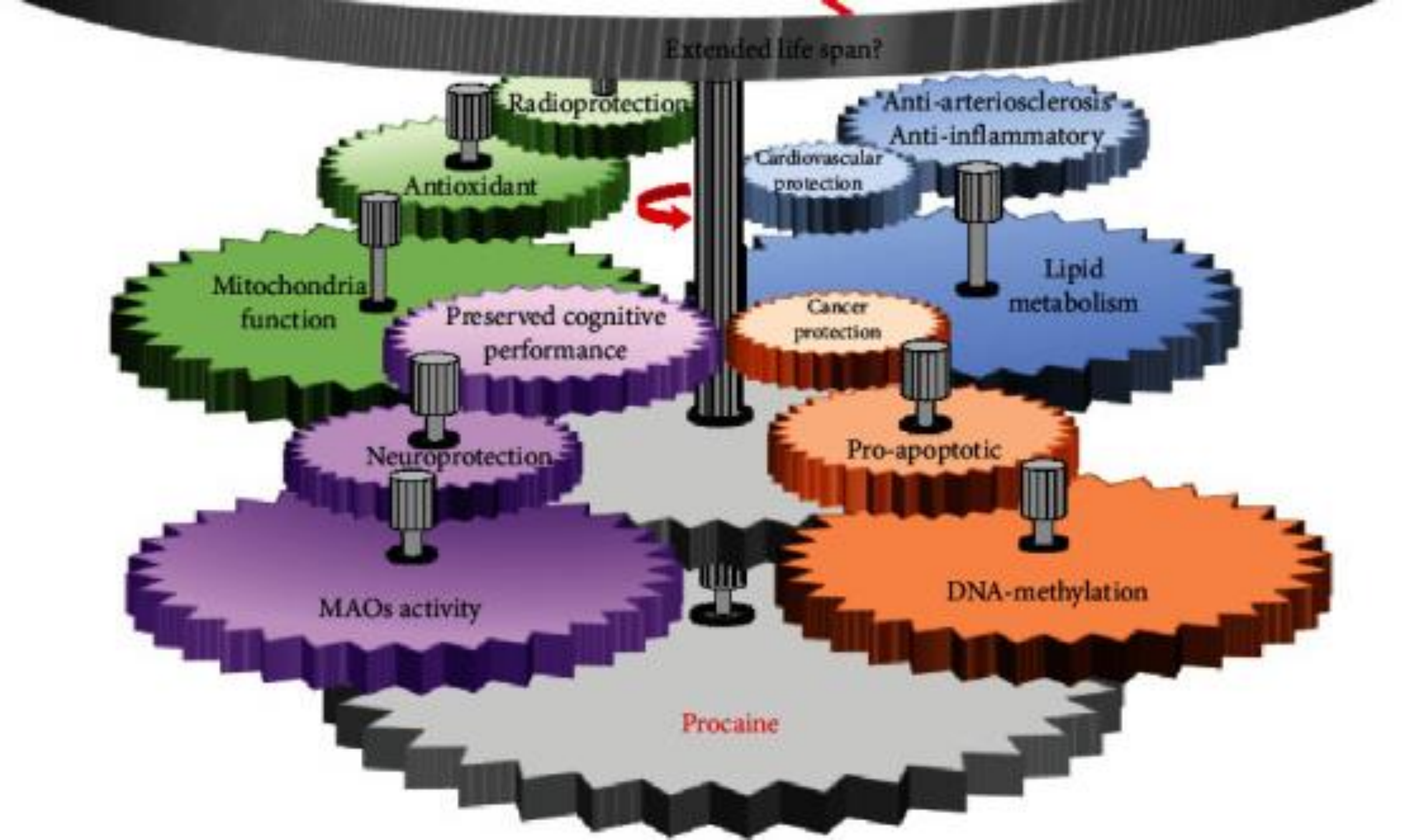
"These results lead to a complex pharmacological profile of procaine, which includes **the modulation of cholesterol metabolism at all levels**, from **genetic control** of sterol biosynthesis to its esterification in plasma and tissues, with potential clinical applications in the treatment of hypercholesterolemia. Moreover, elevated glucocorticoid levels are associated with many pathologies, including age-related depression, hypertension, Alzheimer's disease (AD), or acquired immunodeficiency syndrome, cortisol biosynthesis reducing agents being a possible useful complementary therapy for all these conditions."

Procaine–The Controversial Geroprotector Candidate: New Insights Regarding Its Molecular and Cellular Effects

Procaine – Gerovital GH3

Are the terms starting to sound more and more familiar?

Besides its antioxidant, cytoprotective, anti-inflammatory, and antiatherogenic effects, at cellular and molecular levels, procaine has multiple targets, supporting a large number of potential "geroprotective" effects [30, 31]. Older and more recent data revealed that procaine and its metabolites modulate several biochemical and cellular processes like mitochondrial structure and function [32–34], cholesterol biosynthesis [35], monoamine oxidase (MAO) activity [36, 37], and DNA methylation [38–41].


Extended life span?
Radioprotection
Antioxidant
Anti-arteriosclerosis
Anti-inflammatory
Cardiovascular protection
Mitochondria function
Preserved cognitive performance
Lipid metabolism
Cancer protection
Neuroprotection
Pro-apoptotic
MAOs activity
DNA-methylation
Procaine

B VITAMINS


vitamin B1
vitamin
vitamin B3
vitamin B5
vitamin B6
vitamin B7
B9
vitamin

The preventive efficacy of vitamin B supplements on the cognitive decline of elderly adults: a systematic review and meta-analysis

Background The irreversibility of cognitive impairment of Alzheimer's disease (AD) prompts that preventing or delaying the onset of AD should be a public health priority. Vitamin B supplements can lower the serum homocysteine (Hcy) level, but whether it can prevent cognitive decline or not remains unclear. We aimed to evaluate the preventive efficacy of vitamin B supplements on the cognitive decline of elderly adults.

Conclusions Vitamin B supplements might delay or maintain the cognitive decline of elderly adults. We can recommend that the vitamin B supplements should be considered as a preventive medication to MCI patients or elderly adults without cognitive impairment. More well-designed RCTs with large sample sizes were required to clarify the preventive efficacy in the future.

Cerebral deficiency of vitamin B5 (d-pantothenic acid; pantothenate) as a potentially-reversible cause of neurodegeneration and dementia in sporadic Alzheimer's disease (2020)

Alzheimer's disease (AD) is the most common cause of age-related neurodegeneration and dementia, and there are no available treatments with proven disease-modifying actions. It is therefore appropriate to study hitherto-unknown aspects of brain structure/function in AD to seek alternative disease-related mechanisms that might be targeted by new therapeutic interventions with disease-modifying actions. During hypothesis-generating metabolomic studies of brain, we identified apparent differences in levels of vitamin B5 between AD cases and controls. We therefore developed a method based on gas chromatography-mass spectrometry by which we quantitated vitamin B5 concentrations in seven brain regions from nine AD cases and nine controls. We found that widespread, severe cerebral deficiency of vitamin B5 occurs in AD. This deficiency was worse in those regions known to undergo severe damage, including the hippocampus, entorhinal cortex, and middle temporal gyrus. Vitamin B5 is the obligate precursor of CoA/acetyl-CoA (acetyl-coenzyme A), which plays myriad key roles in the metabolism of all organs, including the brain. In brain, acetyl-CoA is the obligate precursor of the neurotransmitter acetylcholine, and the complex fatty-acyl groups that mediate the essential insulator role of myelin, both processes being defective in AD; moreover, the large cerebral vitamin B5 concentrations co-localize almost entirely to white matter. Vitamin B5 is well tolerated when administered orally to humans and other mammals. We conclude that cerebral vitamin B5 deficiency may well cause neurodegeneration and dementia in AD, which might be preventable or even reversible in its early stages, by treatment with suitable oral doses of vitamin B5.

The Association Between Folate and Alzheimer's Disease: A Systematic Review and Meta-Analysis

Alzheimer's disease (AD) is the most common type of neurodegenerative disease leading to dementia in the elderly. Increasing evidence indicates that folate plays an important role in the pathogenesis of AD. To investigate the role of folate deficiency/possible deficiency in the risk of AD and the beneficial effect of sufficient folate intake on the prevention of AD, a systematic review and meta-analysis were performed. The Web of Science, PubMed, CENTRAL, EBSCO, CNKI, CQVIP, and Wanfang databases were searched. The analysis of cross-sectional studies showed that the standardized mean difference (SMD) was −0.60 (95% confidence interval (CI): −0.65, −0.55), indicating that plasma/serum folate level is lower in AD patients than that in controls. Moreover, the combined odds ratio (OR) of case-control studies was 0.96 (95% CI: 0.93, 0.99), while the combined ORs were 0.86 (95% CI: 0.46, 1.26) and 1.94 (95% CI: 1.02, 2.86) in populations with normal levels of folate (≥13.5 nmol/L) and folate deficiency/possible deficiency (<13.5 nmol/L), respectively. In addition, the risk ratio (RR) of the cohort studies was 1.88 (95% CI: 1.20, 2.57) in populations with folate deficiency/possible deficiency. **Furthermore, when the intake of folate was equal to or higher than the recommended daily allowance, the combined RR and hazard ratio (HR) were 0.44 (95% CI: 0.18, 0.71) and 0.76 (95% CI: 0.52, 0.99), respectively. These results indicate that folate deficiency/possible deficiency increases the risk for AD, while sufficient intake of folate is a protective factor against AD.**

Mechanistic Link between Vitamin B12 and Alzheimer's Disease

Abstract: Alzheimer's disease (AD) is the most common form of dementia in the elderly population, affecting over 55 million people worldwide. Histopathological hallmarks of this multifactorial disease are an increased plaque burden and tangles in the brains of affected individuals. Several lines of evidence indicate that B12 hypovitaminosis is linked to AD. In this review, the biochemical pathways involved in AD that are affected by vitamin B12, focusing on APP processing, Aβ fibrillization, Aβinduced oxidative damage as well as tau hyperphosphorylation and tau aggregation, are summarized. Besides the mechanistic link, an overview of clinical studies utilizing vitamin B supplementation are given, and a potential link between diseases and medication resulting in a reduced vitamin B12 level and AD are discussed. Besides the disease-mediated B12 hypovitaminosis, the reduction in vitamin B12 levels caused by an increasing change in dietary preferences has been gaining in relevance. In particular, vegetarian and vegan diets are associated with vitamin B12 deficiency, and therefore might have potential implications for AD. In conclusion, our review emphasizes the important role of vitamin B12 in AD, which is particularly important, as even in industrialized countries a large proportion of the population might not be sufficiently supplied with vitamin B12.

Riboflavin in Neurological Diseases: A Narrative Review

Riboflavin is classified as one of the water-soluble B vitamins. It is part of the functional group of flavin mononucleotide (FMN) and flavin adenine dinucleotide (FAD) cofactors and is required for numerous flavoprotein-catalysed reactions**. Riboflavin has important antioxidant properties, essential for correct cell functioning. It is required for the conversion of oxidised glutathione to the reduced form and for the mitochondrial respiratory chain as complexes I and II contain flavoprotein reductases and electron transferring flavoproteins**. Riboflavin deficiency has been demonstrated to impair the oxidative state of the body, especially in relation to lipid peroxidation status, in both animal and human studies. In the nervous system, riboflavin is essential for the synthesis of myelin and its deficiency can determine the disruption of myelin lamellae. The inherited condition of restricted riboflavin absorption and utilisation, reported in about 10–15% of world population, warrants further investigation in relation to its association with the main neurodegenerative diseases. Several successful trials testing riboflavin for migraine prevention were performed, and this drug is currently classified as a Level B medication for migraine according to the American Academy of Neurology evidence-based rating, with evidence supporting its efficacy.

Therapeutic riboflavin administration has been tried in other neurological diseases, including stroke, multiple sclerosis, Friedreich's ataxia and Parkinson's disease. Unfortunately, the design of these clinical trials was not uniform, not allowing to accurately assess the real effects of this molecule on the disease course. In this review we analyse the properties of riboflavin and its possible effects on the pathogenesis of different neurological diseases, and we will review the current indications of this vitamin as a therapeutic intervention in neurology.

Dietary Intake of Riboflavin and Unsaturated Fatty Acid Can Improve the Multi-Domain Cognitive Function in Middle-Aged and Elderly Populations: A 2-Year Prospective Cohort Study

Objective This study was aimed to explore the effects of dietary nutrients on cognitive function among the middle-aged and elderly populations.

Results Dietary riboflavin was protective for global cognitive function (β = 1.31, 95% CI: 0.26, 2.35) and the verbal memory domain (β = 0.37, 95% CI: 0.02, 0.71). Unsaturated fatty acid (USFA) played a protective role in global cognitive function (β = 1.15, 95% CI: 0.16, 2.14). The protective effects of riboflavin and USFA on cognitive function were consistent and reliable when different confounders were adjusted during sensitivity analyses. During the follow-up, neuropsychological measure scores revealed a reduced decline in the high-riboflavin group (d-MoCA, $P = 0.025$; d-AVLT-IR, $P = 0.001$; d-DST-B, $P = 0.004$; and d-composite score, $P = 0.004$) and the high-USFA group (d-AVLT-IR, $P = 0.007$; d-LMT, $P = 0.032$; d-DST-B, $P = 0.002$; and d-composite score, $P = 0.008$).

Conclusion Higher intake of riboflavin and USFA can improve multi-dimensional cognitive functioning in middle-aged and elderly people. These findings were consistent in different models of sensitivity analyses.

Biomedical aspects of pyridoxal 5'-phosphate availability – (B6)

The biologically active form of vitamin B6, pyridoxal 5'-phosphate (PLP), is a cofactor in over 160 enzyme activities involved in a number of metabolic pathways, including neurotransmitter synthesis and degradation. In humans, PLP is recycled from food and from degraded PLP-dependent enzymes in a salvage pathway requiring the action of pyridoxal kinase, pyridoxine 5'-phosphate oxidase and phosphatases. Once pyridoxal 5'-phosphate is made, it is targeted to the dozens different apoenzymes that need it as a cofactor. The regulation of the salvage pathway and the mechanism of addition of PLP to the apoenzymes are poorly understood and represent a very challenging research field. Severe neurological disorders, such as convulsions and epileptic encephalopathy, result from a reduced availability of pyridoxal 5'-phosphate in the cell, due to inborn errors in the enzymes of the salvage pathway or other metabolisms and to interactions of drugs with PLP or pyridoxal kinase. **Multifactorial neurological pathologies, such as autism, schizophrenia, Alzheimer's disease, Parkinson's disease and epilepsy have also been correlated to inadequate intracellular levels of PLP.**


DANGER

Routine Vaccinations, Metals…

An Alzheimer’s Risk?

Aluminum and Alzheimer's disease: after a century of controversy, is there a plausible link?

Research, however, reveals that: 1) very small amounts of Al are needed to produce neurotoxicity and this criterion is satisfied through dietary Al intake, 2) Al sequesters different transport mechanisms to actively traverse brain barriers, 3) incremental acquisition of small amounts of Al over a lifetime favors its selective accumulation in brain tissues, and 4) since 1911, experimental evidence has repeatedly demonstrated that chronic Al intoxication reproduces neuropathological hallmarks of AD. AD.

Misconceptions about Al bioavailability may have misled scientists regarding the significance of Al in the pathogenesis of AD. The hypothesis that Al significantly contributes to AD is built upon very solid experimental evidence and should not be dismissed. Immediate steps should be taken to lessen human exposure to Al, which may be the single most aggravating and avoidable factor related to AD.

Aluminum vaccine adjuvants: are they safe?

Aluminum is an experimentally demonstrated neurotoxin and the most commonly used vaccine adjuvant. Despite almost 90 years of widespread use of aluminum adjuvants, medical science's understanding about their mechanisms of action is still remarkably poor. There is also a concerning scarcity of data on toxicology and pharmacokinetics of these compounds. In spite of this, the notion that aluminum in vaccines is safe appears to be widely accepted. Experimental research, however, clearly shows that aluminum adjuvants have a potential to induce serious immunological disorders in humans. In particular, aluminum in adjuvant form carries a risk for autoimmunity, long-term brain inflammation and associated neurological complications and may thus have profound and widespread adverse health consequences. **In our opinion, the possibility that vaccine benefits may have been overrated and the risk of potential adverse effects underestimated, has not been rigorously evaluated in the medical and scientific community. We hope that the present paper will provide a framework for a much needed and long overdue assessment of this highly contentious medical issue.**

Mercury and Alzheimer's disease: a look at the links and evidence

Mercury's effect on Alzheimer's disease hallmarks formation, extracellular senile plaques and intracellular neurofibrillary tangles, has been widely studied. This review demonstrates the involvement of mercury, in its different forms, in the pathway of amyloid beta deposition and tau tangles formation. It aims to understand the link between mercury exposure and Alzheimer's disease so that, in the future, prevention strategies can be applied to halt the progression of this disease.

Thimerosal-Derived Ethylmercury Is a Mitochondrial Toxin in Human Astrocytes: Possible Role of Fenton Chemistry in the Oxidation and Breakage of mtDNA

My comment: Thimerosal is the form of mercury present in routine vaccinations containing mercury; i.e., flu shot, pneumonia, etc. This is shocking info:

Thimerosal generates ethylmercury in aqueous solution and is widely used as preservative. We have investigated the toxicology of Thimerosal in normal human astrocytes, paying particular attention to mitochondrial function and the generation of specific oxidants. We find that ethylmercury not only inhibits mitochondrial respiration leading to a drop in the steady state membrane potential, but also concurrent with these phenomena increases the formation of superoxide, hydrogen peroxide, and Fenton/Haber-Weiss generated hydroxyl radical. These oxidants increase the levels of cellular aldehyde/ketones. Additionally, we find a five-fold increase in the levels of oxidant damaged mitochondrial DNA bases and increases in the levels of mtDNA nicks and blunt-ended breaks. Highly damaged mitochondria are characterized by having very low membrane potentials, increased superoxide/hydrogen peroxide production, and extensively damaged mtDNA and proteins. These mitochondria appear to have undergone a permeability transition, an observation supported by the five-fold increase in Caspase-3 activity observed after Thimerosal treatment.

Oral Health & Alzheimer's

Association of Alzheimer's disease and periodontitis - a systematic review and meta-analysis of evidence from observational studies

The relationship between periodontitis (or periodontal disease) with Alzheimer's disease has been reported by various primary sources in the past decade, but not with a solid secondary research statement. A systematic review and meta-analysis was conducted in accordance with the guidelines of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement and registered (Reference number: CRD42020185264) with PROSPERO (International prospective register for systematic reviews). A literature search was conducted on specific databases for suitable articles in English language. Out of 612 studies selected, 41 underwent full-text analysis; five studies were eligible for systematic review, and 3 for meta-analysis. Meta-analysis was performed with tests for sensitivity and statistical heterogeneity followed by calculation of summary effect measures in terms of odds ratio (OR) and 95% confidence interval (CI). **The results of this review showed a significant association between periodontitis and Alzheimer's disease in the meta-analysis** [OR 1.67 (1.21–2.32)].

Dietary Dangers

Alzheimer's risk from food & beverages

Dietary Sugar Intake Associated with a Higher Risk of Dementia in Community-Dwelling Older Adults

Results: 118 participants developed dementia during 7.3 ± 3.8 years of follow-up. Those in the highest quintile of total sugar intake were twice as likely to develop dementia than those in the lowest quintile (Q5 versus Q1:HR=2.10 (95%CI: 1.05, 4.19) when adjusted for age, sex, education, *APOE ε4* allele, calories from sources other than sugar, physical activity, and diet score. Higher percent calories from sugar were positively associated with dementia risk (β=0.042, p = 0.0009). In exploratory analyses, the highest versus lowest quintile of fructose and sucrose in the diet had higher dementia risk by 2.8 (95%CI: 1.38, 5.67) and 1.93 (95%CI: 1.05, 3.54) times, respectively.

Conclusions: A higher intake of total sugar or total calories from sugar is associated with increased dementia risk in older adults. Among simple sugars, fructose (e.g., sweetened beverages, snacks, packaged desserts) and sucrose (table sugar in juices, desserts, candies, and commercial cereals) are associated with higher dementia risk.

Insulin resistance from high-sugar diet may lead to brain decline

- **About 15% of people around the world have a neurodegenerative disease.**
- **A known risk factor for developing a neurodegenerative condition is obesity.**
- **Researchers from the Fred Hutch Cancer Center show evidence suggesting a high-sugar diet causes insulin resistance in the brain, reducing the brain's ability to remove neuronal debris, thus increasing neurodegeneration risk.**

Aspartame: Decades of science point to serious health risks

- **Stroke, dementia and Alzheimer's disease**
- People drinking diet soda daily were almost three times as likely to develop stroke and dementia as those who consumed it weekly or less. This included a higher risk of ischemic stroke, where blood vessels in the brain become obstructed, and Alzheimer's disease dementia, the most common form of dementia, reported a 2017 study in Stroke.
- "Daily Consumption of Sodas, Fruit Juices and Artificially Sweetened Sodas Affect Brain," video of neurologist Matthew Pase, Boston University School of Medicine (4.20.2017)
- "Study links diet soda to higher risk of stroke, dementia," by Fred Barbash, Washington Post (4.21.2017)
- In the body, the methyl ester in aspartame metabolizes into methanol and then it may be converted to formaldehyde, which has been linked to Alzheimer's disease. A two-part study published in 2014 in the Journal of Alzheimer's Disease linked chronic methanol exposure to memory loss and Alzheimer's Disease symptoms in mice and monkeys.
- "[M]ethanol-fed mice presented with partial AD-like symptoms … These findings add to a growing body of evidence that links formaldehyde to [Alzheimer's disease] pathology." (Part 1)
- "[M]ethanol feeding caused long-lasting and persistent pathological changes that were related to [Alzheimer's disease] … these findings support a growing body of evidence that links methanol and its metabolite formaldehyde to [Alzheimer's disease] pathology." (Part 2)

Pesticides & Alzheimer's

Pesticide exposure and risk of Alzheimer's disease: a systematic review and meta-analysis

Evidence suggests that lifelong cumulative exposure to pesticides may generate lasting toxic effects on the central nervous system and contribute to the development of Alzheimer's disease (AD). A number of reports indicate a potential association between long-term/low-dose pesticide exposure and AD, but the results are inconsistent. Therefore, we conducted a meta-analysis to clarify this association. Relevant studies were identified according to inclusion criteria. Summary odds ratios (ORs) were calculated using fixed-effects models. A total of seven studies were included in our meta-analysis. A positive association was observed between pesticide exposure and AD (OR = 1.34; 95% confidence interval [CI] = 1.08, 1.67; n = 7). The summary ORs with 95% CIs from the crude and adjusted effect size studies were 1.14 (95% CI = 0.94, 1.38; n = 7) and 1.37 (95% CI = 1.09, 1.71; n = 5), respectively. The sensitivity analyses of the present meta-analysis did not substantially modify the association between pesticide exposure and AD. Subgroup analyses revealed that high-quality studies tended to show significant relationships. **The present meta-analysis suggested a positive association between pesticide exposure and AD, confirming the hypothesis that pesticide exposure is a risk factor for AD. Further high-quality cohort and case-control studies are required to validate a causal relationship.**

OUTSMARTING ALZHEIMER'S

REBECCA ROENTSCH MONTRONE, BS – WONDROUS ROOTS

PART 4

FATTY ACIDS

Omega-3 & Alzheimer's

- Herring: 1.7 grams per 3 ounces.
- Wild salmon: 1.6 grams per 3 ounces.
- Bluefin tuna: 1.3 grams per 3 ounces.
- Mackerel: 1 gram per 3 ounces.
- Sardines: 0.9 grams per 3.75-ounce can.
- Anchovies: 0.9 grams per 2-ounce can.
- Lake trout: 0.8 grams per 3 ounces.
- Striped bass: 0.8 grams per 3 ounces.

The Relationship of Omega-3 Fatty Acids with Dementia and Cognitive Decline: Evidence from Prospective Cohort Studies of Supplementation, Dietary Intake, and Blood Markers

Longitudinal data were derived from 1135 participants without dementia (mean age = 73 y) in the Alzheimer's Disease Neuroimaging Initiative (ADNI) cohort to evaluate the associations of omega-3 fatty acid supplementation and blood biomarkers with incident AD during the 6-y follow-up. A meta-analysis of published cohort studies was further conducted to test the longitudinal relationships of dietary intake of omega-3 and its peripheral markers with all-cause dementia or cognitive decline.

Moderate-to-high levels of evidence indicated that elevated levels of plasma EPA (RR: 0.88, I^2 = 38.1%) and erythrocyte membrane DHA (RR: 0.94, I^2 = 0.4%) were associated with a lower risk of cognitive decline. Dietary intake or long-term supplementation of omega-3 fatty acids may help reduce risk of AD or cognitive decline.

The effects of omega-3, DHA, EPA, Souvenaid® in Alzheimer's disease: A systematic review and meta-analysis

Results

We identified 14 studies with 2766 subjects aligned with our criteria. Most publications described positive cognitive outcomes from supplements (58%). The most common adverse events reported were gastrointestinal symptoms. CDR scale showed reduced progression of cognitive decline (SMD = −0.4127, 95% CI: [−0.5926; −0.2327]), without subgroup differences between different dietary supplement interventions. ADCS-ADL, MMSE, ADAS-cog, adverse events, and ventricular volume did not demonstrate significant differences. However, Souvenaid® showed a significant negative effect (SMD = −0.3593, 95% CI: −0.5834 to −0.1352) in ventricular volumes.

Conclusions

The CDR scale showed reduced progression of cognitive decline among patients with n-3-PUFA supplemental interventions, with no differences between different n-3-PUFA supplements.

Omega-5 & Alzheimer's disease

- Pomegranate seed oil
- Coconut oil
- Full-fat grassfed beef & dairy products
- Moringa oil
- Salmon

The Effects of Pomegranate Seed Oil on Mild Cognitive Impairment

- **Background:** In recent years, there has been a growing interest, supported by many experimental and clinical studies, about the benefits of pomegranate in preventing various pathologic conditions, including brain neurodegeneration. The pomegranate seed oil (PSO) contains high levels of fatty acids that have antioxidant and anti-inflammatory properties.
- **Objective:** Due to the lack of clinical trials, the aim of the present study was to investigate the effects of PSO on cognition of people with mild cognitive impairment (MCI).
- **Methods:** Eighty people with the diagnosis of MCI were randomized forty to take 5 drops of PSO and follow the Mediterranean Diet (MeDi) and forty just followed MeDi. All were examined with an extensive neuropsychological assessment before and after one year of treatment.
- **Results:** The results showed that the participants who took the PSO had statistically significantly better global cognition ($p = 0.004$), verbal episodic memory ($p = 0.009$), and processing and executive functions ($p < 0.001$) in contrast with the participants who did not take it.
- **Conclusions:** In conclusion, the PSO can be beneficial for people with MCI as it is helpful for some important cognitive domains. As PSO is a natural product that does not burden the human body, it can be used by people with MCI and be a significant and promising part of holistic approaches for the prevention of dementia.

And… as a source of urolithin A!

Remember? Great for increasing muscular strength in the aging…

Pomegranate's Neuroprotective Effects against Alzheimer's Disease Are Mediated by Urolithins, Its Ellagitannin-Gut Microbial Derived Metabolites

Pomegranate shows neuroprotective effects against Alzheimer's disease (AD) in several reported animal studies. However, whether its constituent ellagitannins and/or their physiologically relevant gut microbiota-derived metabolites, namely, urolithins (6H-dibenzo[b,d]pyran-6-one derivatives), are the responsible bioactive constituents is unknown. Therefore, from a pomegranate extract (PE), previously reported by our group to have anti-AD effects in vivo, 21 constituents, which were primarily ellagitannins, were isolated and identified (by HPLC, NMR, and HRESIMS). In silico computational studies, used to predict blood-brain barrier permeability, revealed that none of the PE constituents, but the urolithins, fulfilled criteria required for penetration. Urolithins prevented β-amyloid fibrillation in vitro and methyl-urolithin B (3-methoxy-6H-dibenzo[b,d]pyran-6-one), but not PE or its predominant ellagitannins, had a protective effect in Caenorhabditis elegans post induction of amyloid β(1-42) induced neurotoxicity and paralysis. Therefore, urolithins are the possible brain absorbable compounds which contribute to pomegranate's anti-AD effects warranting further in vivo studies on these compounds.

Sulforaphane & Alzheimer's

Beneficial Effects of Sulforaphane Treatment in Alzheimer's Disease May Be Mediated through Reduced HDAC1/3 and Increased P75NTR Expression

In conclusion, this study demonstrates that sulforaphane can ameliorate neurobehavioral deficits and reduce the Aβ burden in Alzheimer's disease model mice, and the mechanism underlying these effects may be associated with up-regulation of p75 neurotrophin receptor mediated, apparently at least in part, via reducing the expression of histone deacetylase1 and 3.

Efficacy of sulforaphane in neurodegenerative diseases

Abstract: Sulforaphane (SFN) is a phytocompound belonging to the isothiocyanate family. Although it was also found in seeds and mature plants, SFN is mainly present in sprouts of many cruciferous vegetables, including cabbage, broccoli, cauliflower, and Brussels sprouts. SFN is produced by the conversion of glucoraphanin through the enzyme myrosinase, which leads to the formation of this isothiocyanate. SFN is especially characterized by antioxidant, anti-inflammatory, and anti-apoptotic properties, and for this reason, it aroused the interest of researchers. The aim of this review is to summarize the experimental studies present on Pubmed that report the efficacy of SFN in the treatment of neurodegenerative disease, including Alzheimer's disease (AD), Parkinson's disease (PD), and multiple sclerosis (MS). Therefore, thanks to its beneficial effects, SFN could be useful as a supplement to counteracting neurodegenerative diseases.

Mushrooms & Alzheimer's

The Potential of Mushrooms in Dementia and Alzheimer's Prevention: A Comprehensive Guide

- From the forest floor to the frontiers of neuroscience, an unlikely hero emerges in the battle against cognitive decline: the humble mushroom. As our understanding of brain health evolves, researchers are increasingly turning their attention to the potential of fungi in preventing and managing neurodegenerative disorders. This growing interest in mushrooms for cognitive health comes at a crucial time, as the prevalence of conditions like dementia and Alzheimer's disease continues to rise globally.
- Dementia, a broad term encompassing various cognitive impairments, affects millions of people worldwide. Alzheimer's disease, the most common form of dementia, accounts for 60-80% of cases. As our population ages, the number of individuals affected by these conditions is expected to increase dramatically, placing a significant burden on healthcare systems and families alike. In light of this looming crisis, scientists and medical professionals are exploring alternative strategies for prevention and treatment, with mushrooms emerging as a promising area of study.

Magnesium & Alzheimer's disease

Mg levels were found to be decreased in various tissues of AD patients and negatively correlated with clinical deterioration. Moreover, Mg was demonstrated to modulate the trafficking and processing of amyloid-β precursor protein, which plays a central role in the pathogenesis of AD. Here, we review in vitro and in vivo data that indicated a role for magnesium in many biological and clinical aspects of AD.

Magnesium-l-threonate: Breakthrough Brain Enhancer

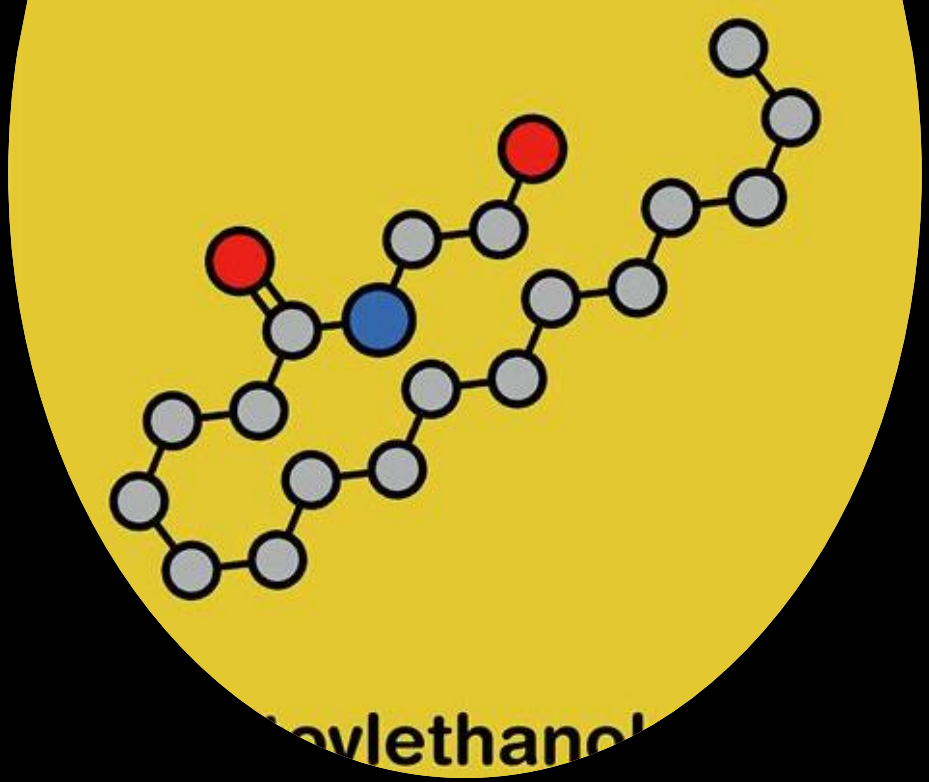
Here are the three known ways in which magnesium l–threonate works:

1. Magnesium l–threonate readily crosses the brain's protective filter, the blood–brain barrier, to get into the brain where it is needed.
2. Magnesium l–threonate has been shown to increase brain plasticity. Neuroplasticity (brain plasticity) is the brain's ability to change and grow and is fundamental for memory and learning to take place.
3. There's evidence that magnesium l–threonate can increase brain–derived neurotrophic factor (BDNF), a protein that stimulates the formation of new brain Illustration of the blood–brain barrier. cells.

Herbs & Alzheimer's

Introducing the Starts of Wondrous Roots Super Brain Blast herbal formula

Brahmi herb(Bacopa monnieri), >Gotu kola herb(Centella asiatica), Ginkgo leaf (Ginkgo biloba), Prickly Ash bark (Zanthoxylum (Xanthoxylum) americanum), Grape seed(Vitis vinifera), Bilberry fruit(Vaccinium myrtillus), Turmeric root(Curcumin longa), Frankincense resin(Boswellia carterii), Fo-Ti root(Polygonum multiflorum),Holy Basil leaf(Ocimum sanctum), Rhodiola root(Rhodiola rosea), Rosemary leaf(Rosmarinus officinalis), Lemon Balm leaf(Melissa officinalis), Ashwagandha root (Withania somnifera), Sage leaf(Salvia officinalis), Prickly Pear Cactus – Nopal– (Opuntia streptocantha), Lion's Mane mushroom (Hericium erinaceus) (Lion's mane not yet added to informational index).Grain alcohol 60%, spring water. Strength 1:5.



Palmitoylethanolamide (PEA)

Effects of Palmitoylethanolamide on Neurodegenerative Diseases: A Review from Rodents to Humans

Neurodegenerative diseases are widespread throughout the world, and although they are numerous and different, they share common patterns of conditions that result from progressive damage to the brain areas involved in mobility, muscle coordination and strength, mood, and cognition. The present review is aimed at illustrating in vitro and in vivo research, as well as human studies, using PEA treatment, alone or in combination with other compounds, in the presence of neurodegeneration. Namely, attention has been paid to the effects of PEA in counteracting neuroinflammatory conditions and in slowing down the progression of diseases, such as Alzheimer's disease, Parkinson's disease, Huntington's disease, Frontotemporal dementia, Amyotrophic Lateral Sclerosis, and Multiple Sclerosis. Literature research demonstrated the efficacy of PEA in addressing the damage typical of major neurodegenerative diseases.

Palmitoylethanolamide Protects Against the Amyloid-b25-35- Induced Learning and Memory Impairment in Mice, an Experimental Model of Alzheimer Disease

*According with the neuroprotective profile of PEA observed during behavioral studies, experimental molecular and biochemical markers induced by Ab25–35 injection, such as lipid peroxidation, protein nytrosylation, inducible nitric oxide synthase induction, and caspase3 activation, were reduced by PEA treatment. **These data disclose novel findings about the therapeutic potential of PEA, unrevealing a previously unknown therapeutic possibility to treat memory deficits associated with AD.***

Neuropsychopharmacology (2012) 37, 1784–1792; doi:10.1038/npp.2012.25; published online 14 March 2012

I'll be talking about PEA in more depth very soon…

In the meantime, check out my informational resource page:

PEA/Palmitoylethanolamide | Wondrous Roots

Thank you for joining me! Go back as often as you wish to review this tomb of vital information when it comes to protecting your brain and the brains of those you love.

The science exists. The propaganda also exists. So do your own research and run with the power being informed provides!

Wondrous Roots:
Wondrous Roots | Holistic Nutrition | Keene, NH, USA
Welcome to the Wondrous Roots Online Store! (shopwondrousroots.com)
603-439-2603
Rebecca@wondrousroots.org

"Don't just go with the flow; go with the KNOW!"