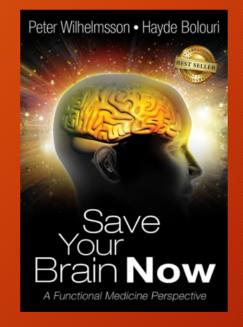


Dr. Bolouri Research Center, AB

Haydeh Bolouri (PhD) Neuroscientist October 2024 www.drbolouri.net

Your Dynamic Masterpiece, Your Brain!

The whole idea of the universe would have been a failure if it were not for the brain!



Scientific background

Molecular Cell Biology and Immunology, University of Gothenburg

Traumatic Brain Injury, University of Gothenburg

Medicine doctor in Neuroscience (post doctoral fellowship)

Educational & Confocal microscopy and stereology

Senior research in Dermato-Cosmetic Science









Research field

- Traumatic brain injuries (TBI & mTBI): Concussions in NFL
- Violence to the head: Blast overpressure (Swedish Armed forces)

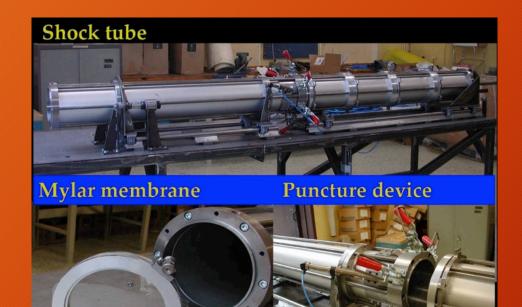
Traumatic Brain Injury (TBI)

CONCUSSIVE TBI, NFL



- Concussion in professional football: animal model of brain injury--part 15 Neurosurgery. 2009, Viano DC, Hamberger A, Bolouri H, Säljö A.
- Concussion in professional football: morphology of brain injuries in the NFL concussion model- Part 16. Neurosurgery. 2009. Hamberger A, Viano DC, Saljo A, Bolouri H.
- Animal model for sport-related concussion; ICP and cognitive function. Acta Neurol Scand. 2011, Oct 29. Bolouri H, Säljö A, Viano DC, Hamberger A.
- Evaluation of Three Animal Models for Concussion and Serious Brain Injury. Annals of Biomedical Engineering, 2011. Viano DC, Hamberger A, Bolouri H, Saljo A.

BLAST INDUCED TBI SWEDISH ARMED FORCES



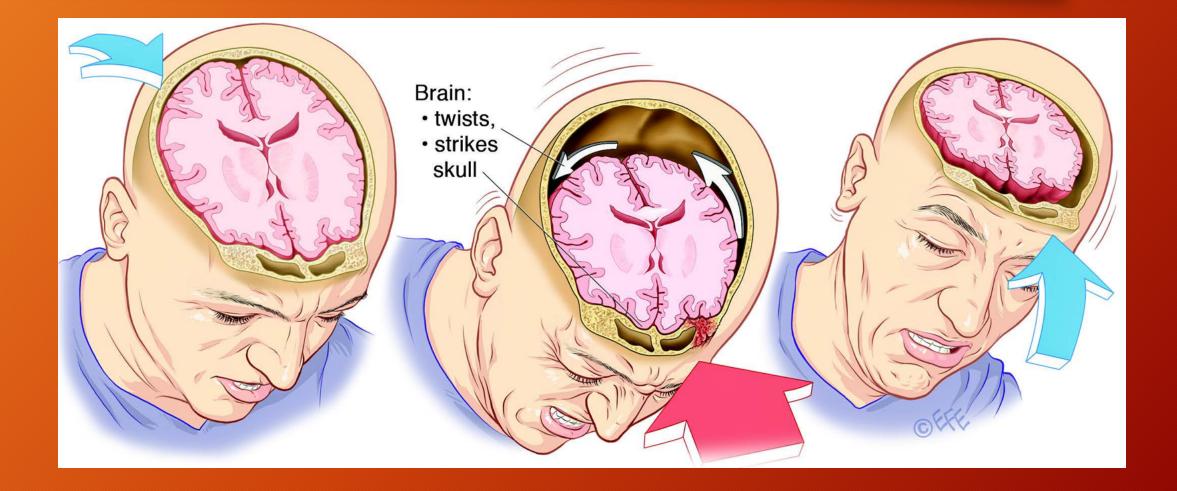
• Neuropathology and pressure in the pig brain resulting from low-impulse noise exposure. J Neurotrauma. 2008 Dec; 25(12):1397. Säljö A, Arrhén F, Bolouri H, Mayorga M, Hamberger A.

• Low-level blasts raise intracranial pressure and impair cognitive function in rats. J Neurotrauma. 2009. Säljö A, Svensson B, Mayorga M, Hamberger A, Bolouri H.

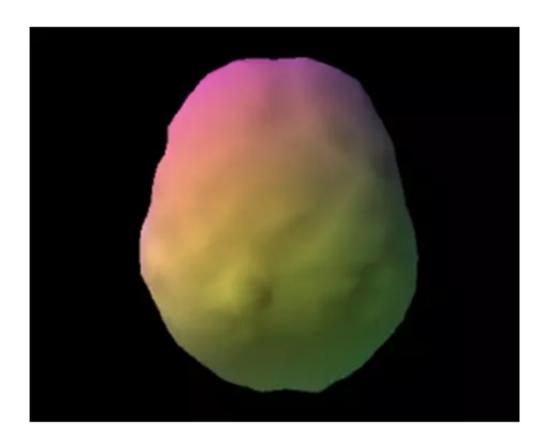
Low-level blast raises intracranial pressure and impairs cognitive function in rats. Säljö A, Bolouri H, Mayorga M, Svensson B, Hamberger A.J. Neurotrauma. 2010 Feb;27(2):383-9.

• Mechanisms and Pathophysiology of the low-level blast brain injury in animal models. Neuroimage, 2011. Epub 2010 May Säljö A, Mayorga M, Bolouri H, Svensson B, Hamberger A.

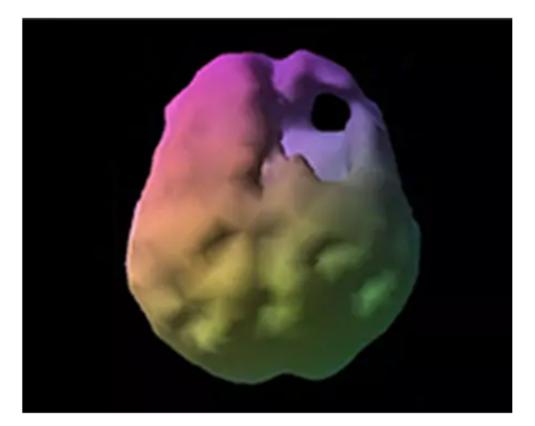
What is concussion?



Single-Photon-Emission-Computed-Tomography (SPECT)



Healthy Brain Scan



Concussion Brain Scan

Ann Neurol. 2013 Dec 13. doi: 10.1002/ana.24087. [Epub ahead of print]

Innate defence regulator peptide 1018 protects against perinatal brain injury.

Bolouri H, Sävman K, Wang W, Thomas A, Maurer N, Dullaghan E, Fjell CD, Ek CJ, Hagberg H, Hancock RE, Brown KL, Mallard C. Author information

Abstract

Objective: There is currently no pharmacological treatment that provides protection against brain injury in neonates. It is known that activation of an innate immune response is a key, contributing factor in perinatal brain injury, therefore, the neuroprotective therapeutic potential of innate defence regulator peptides (IDRs) was investigated. Methods: The anti-inflammatory effects of three IDRs was measured in LPSactivated murine microglia. IDRs were then assessed for their ability to

Radixin expression in microglia after cortical stroke lesion. Glia, 2013; DOI 10.1002/glia, 22473. Åsa Persson^{1*}, Ahmed Osman^{1*}, Hayde Bolouri², Carina Mallard², H. Georg Kuhn¹

Inflammatory-induced hibernation in the fetus: Priming of the fetal sheep metabolism correlates with developmental brain injury (Plos One, 2011, vol. 6, issue 12) Matthias Keller, David P. Enot, Mark Hodson4, Emeka I. Igwe, Hans-Peter Deigner, Justin Dean, Hayde Bolouri, Henrik Hagberg, Carina Mallard

Delayed cortical impairment following lipopolysaccharide exposure in fetal sheep. Ann Neurol. Dean JM, van de Looij Y, Sizonenko SV, Lodygensky GA, Lazeyras F, Bolouri H, Kjellmer I, Huppi PS, Hagberg H, Mallard C.

Brain Neurotrauma: Molecular, Neuropsychological, and Rehabilitation Aspects Taylor and Francis Publishers in collaboration with American researchers and American university of Beirut, 2014



46 Animal Models for Concussion Molecular and Cognitive Assessments—Relevance to Sport and Military Concussions

Hayde Bolouri and Henrik Zetterberg

CONTENTS

46.1	Introduction: Background and Definitions	643
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46.3	Animal Models of TBI	645
	46.3.1 Head Impacts	645

Peer reviewer:

- Journal of Neuroscience
- Brain Research
- Psychological and behavioural management

What is Functional medicine? Multimodal Approaches

As a catalyst in the transformation of healthcare, functional medicine treats root causes of disease and restores healthy function through a personalized patient experience.



Conventional medicine High level of scientific evidence	Functional medicine High level of scientific evidence
Best for emergency conditions	Best for chronic diseases
Symptom suppressant	Treatment of underlying causes
Drug oriented	Prevention
Diagnose-focused	Patient-centered

Functional medicine is a vital partner to conventional medicine.

One condition, many causes One cause, many conditions

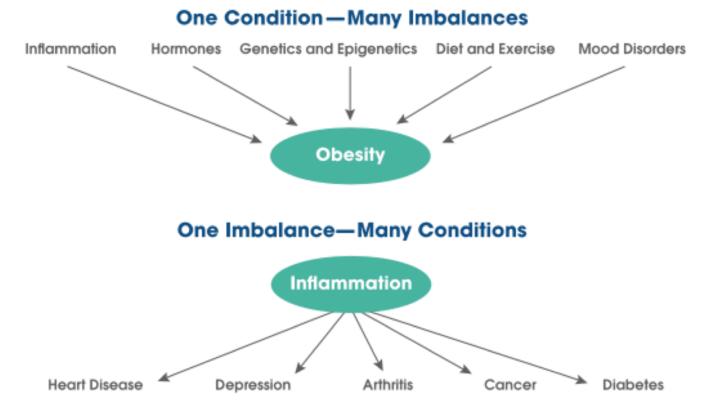


Figure 2. The relationship between Core Clinical Imbalances and Disease



Autoimmune diseases

- Autoimmunity in chronic health conditions!?
- The immune system attacks its own cells!?
- It is inherited!?

Inflammation "95.4% of factory- farmed beef and lamb contained residual antibiotics"

Food Sci Nutr. 2021 Nov; 9(11): 6152–6161.	PMCID: PMC8565197
Published online 2021 Sep 13. doi: <u>10.1002/fsn3.2568</u>	PMID: <u>34760246</u>
Antibiotic residues in cattle and sheep meat and human exposure assessm Xinjiang, China	nent in southern
Yu Zhang, ¹ Jianjiang Lu, ^{® 1} Yujun Yan, ^{® 1} Jinhua Liu, ¹ and Manli Wang ¹	
Author information Article notes Copyright and License information PMC Disclaimer	
Supplementary Materials	
Data Availability Statement	
Abstract	Go to:

fluoroquinolones, four tetracyclines, and five macrolides) were screened in 88 meat samples (cattle muscles

Don't we have a built in healing system?



By a Functional Medicine approach



Dermatology Case Reports

Case Report

Bolouri and Hajimirsadeghi, Dermatol Case Rep 2017,2:3

OMICS International

A Holistic Approach and Successful Treatment of Chronic Wound in Diabetes Mellitus by Platelet-Rich Plasma (PRP) Combined with Optimized Diet

Bolouri H* and Hajimirsadeghi A

Hagaklinik Research Institute, Specialist Polyclinic of Primary Health Care, Gothenburg, Sweden



(a) Wound area with (length × width) measurement of 35 × 25 mm² prior to the treatment in our clinic.
 (a-j) The patient underwent a total of 13 PRP treatments over 24 weeks starting on 27 February 2017.
 Figure 1: Step by step successful treatment of chronic wound in diabetes mellitus by platelet-rich plasma (PRP) combined with optimized diet.

Ref: A Holistic Approach and Successful Treatment of Chronic Wound in Diabetes Mellitus by Platelet-Rich Plasma (PRP) Combined with Optimized Diet (2017). Bolouri, H. and Hajimirsadeghi, Dermatol Case Rep. Vol. 2:3, p. 1-3.

IS DEMENTIA A NATURAL PART OF AGING?

Memory loss is not part of the aging process.

Studies have shown that 20% of individuals over the age of 100 show no signs of memory loss or brain disease.

Ref; Perls, T., "Dementia free centenarians," Exp Gerontol 2004; 39:1 587-93

Alzheimer's pathology can start in your 20s

We think of Alzheimer's as only affecting older people, but that is changing. Our fast-paced lifestyles, the widespread impact from COVID, and the increasing toxicity of our environment may be factors converging to create an astounding increase in early-onset dementia among younger people.

49

The average age of someone living with dementia is 49

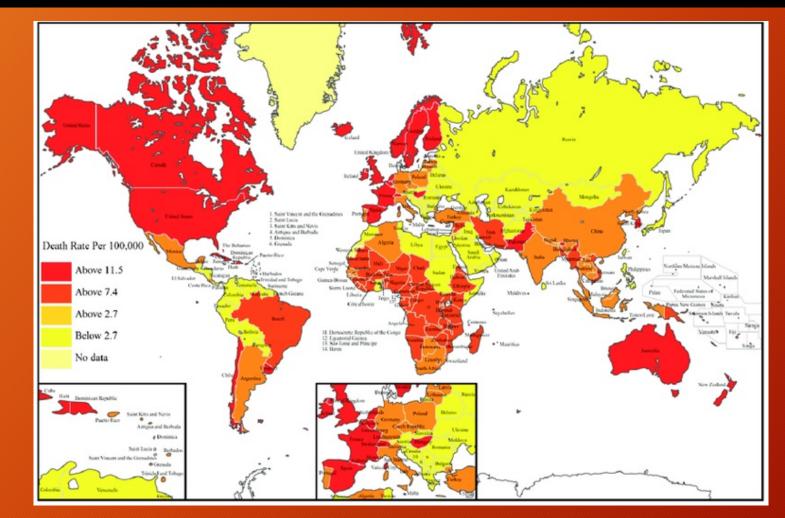
373%

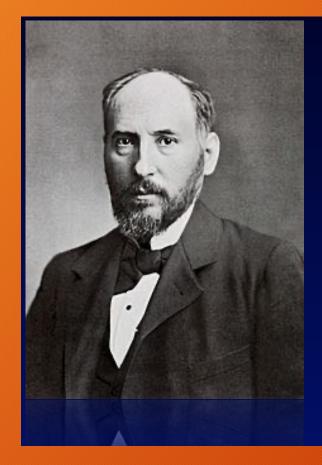
Increase in dementia among people aged 30 to 44 years old

7th

Alzheimer's is the 7th leading cause of death worldwide

GLOBAL ALZHEIMER'S PREVALENCE





"In the adult centers, the nerve paths are something fixed, and immutable: everything must die, nothing may be regenerated."

- Santiago Ramón y Cajal, Nobel laureate (1852-1934)

Neuroplasticity The brain is plastic



"Our study demonstrates that cell genesis occurs in human brains and that the human brain retains the potential for self-renewal throughout life."

- Dr. Peter Eriksson, 1998

Neuroplasticity

• A 44-year-old official missing 90 percent of his brain, lived normally......



https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(07)61127-1/fulltext

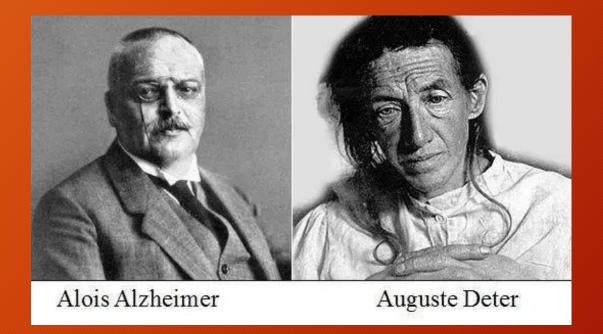
Statistics according to the Alzheimer's Association

- Over 55 millions diagnosed globally
- Every 3 secs someone develop AD worldwide
- Every 65 secs someone in the United States is diagnosed with AD
- By 2050, the total number diagnosed will grow to 14 millions

Your most powerful tools you have at your disposal: your life choices!

What is Alzheimer's?

In 1901, Alzheimer discovered build up amyloid plaque formation & fibrillary tangles in the brain



One of three AD patients is a woman

Higher risk of Alzheimer's than breast cancer.

Prevent ALZHEIMER'S!

Avoid?Prevent?Reverse?

WHO, March 2023

Dementia; several diseases that affect memory, thinking, and the ability to perform daily activities.

Things that increase the risk of developing dementia include:

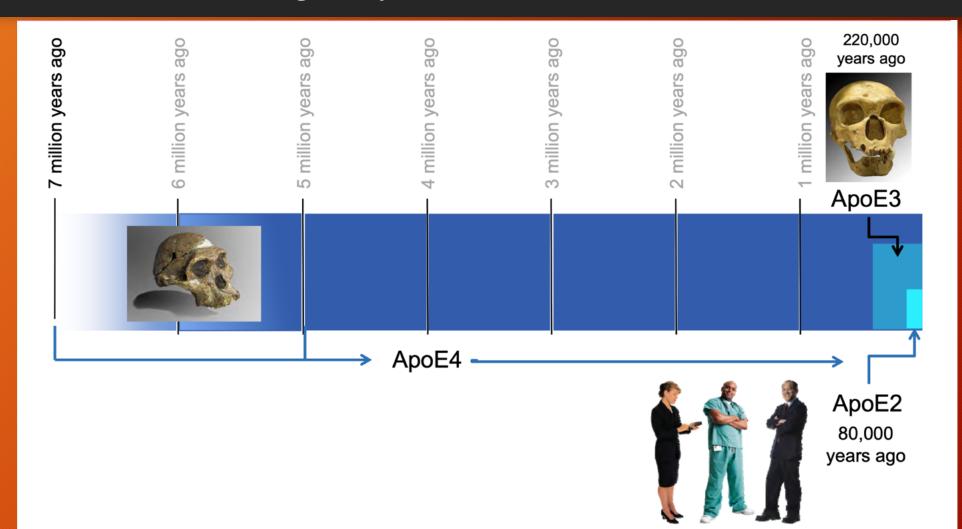
- age (more common in those 65 or older)
- high blood pressure (hypertension)
- high blood sugar (diabetes)
- being overweight or obese
- \circ smoking
- drinking too much alcohol
- being physically inactive
- being socially isolated
- o depression.

The most common form of dementia is Alzheimer by 60-70% of cases

Is it the ApoE4 gene that causes Alzheimer's?

APOE Status and Alzheimer's risk						
Genotype	E2/ E2	<mark>E2/</mark> E3	E2/ E4	E3/ E3	E3/ E4	E4/ E4
Disease risk	40% less likely	40% less likely	2.6 X more likely	Average risk	3.2 times more likely	14.9 times more likely

The chimp that killed the rhino Evolution, shortgevity, Alzheimer's and the God Gene



Remember, Your destiny is not written in your genes!

- Your genes
- Epigenetik
- Microbiome

What do we know about ApoE-4 gene?

The Tsimane of Bolivia; the majority have heavy Ascaris loads (70%).

ApoE4-negatives suffer age-related cognitive decline + heavy parasite load.
ApoE4-positives do not suffer age-related cognitive decline + parasite load.

However, those who are ApoE4+ actually do as well or slightly better cognitively if they have parasites.

This may be related to alterations in microbiome (cf. IBS).

Hypotheses behind Alzheimer's

Three well-known hypotheses so far:

- Beta amyloid plaque,
- Tau-protein tangles,
- Hypoglycemia (type II diabetes)

Everyone knows someone who is a cancer survivor,

no one knows an Alzheimer's survivor.

Alzheimer's Disease Therapeutic Landscape

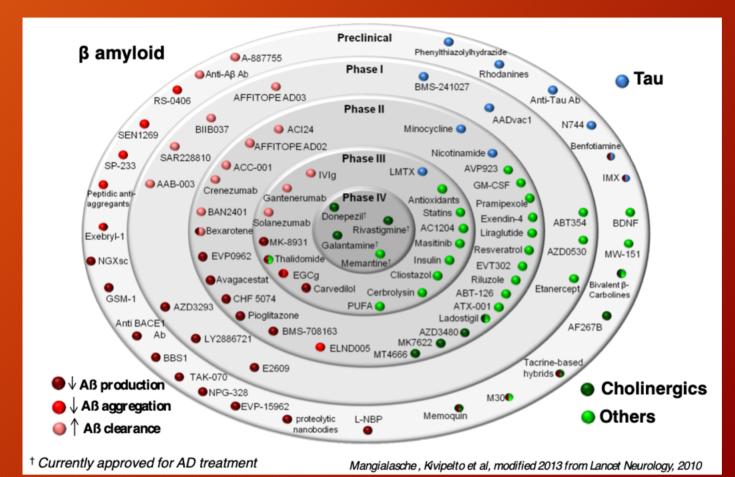
• Cognitive medicine - a new approach in health care science Cognitive medicine - an emerging field, Wallin et al. BMC Psychiatry (2018)

Demensdagen 2019

Aducanumab, the future drug inhibit beta amyloid?

Swedish research result showed the clearing of beta amyloid in the brain, presented in 2024.

Aducanumab, monoclonal antibody clears the blood 10-15 years storage of beta amyloid for one year.





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<u>nature</u> > <u>news</u> > article

NEWS 04 May 2023

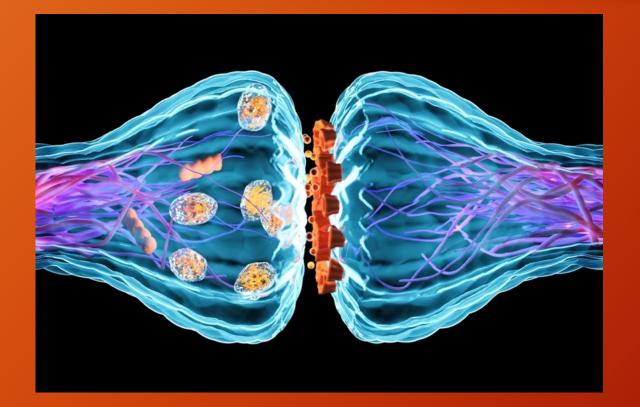
Alzheimer's drug donanemab: what promising trial means for treatments

Results suggest that the amyloid-targeting drug candidate slows cognitive decline in some people, but questions remain over its potential side effects.





Persistence of memory by kidney - brain connection at activated synapses



A synapse is a structure enabling a neuron to communicate with another neuron or effector cell by exchanging an electrical or chemical signal

The perfect Alzheimer's drug would

Reduce APP β -cleavage, reduce γ -cleavage, increase α -cleavage, reduce caspase-6 cleavage, reduce caspase-3 cleavage, prevent oligomerization, increase neprilysin, increase IDE, increase microglial clearance of $A\beta$, increase autophagy, increase BDNF, increase NGF, increase netrin-1, increase ADNP, reduce homocysteine, increase PP2A activity, reduce phospho-tau, increase phagocytosis index, increase insulin sensitivity, improve axoplasmic transport, enhance mitochondrial function and biogenesis, reduce oxidative damage and optimize ROS production, enhance cholinergic neurotransmission, increase synaptoblastic signaling, reduce synaptoclastic signaling, improve LTP, optimize estradiol, progesterone, E2:P ratio, free T3, free T4, TSH, pregnenolone, testosterone, cortisol, DHEA, and insulin, reduce inflammation, increase resolvins, enhance detoxification, improve vascularization, increase cAMP, increase glutathione, provide synaptic components, optimize all metals, increase GABA, increase vitamin D signaling, increase SirT1, reduce NFkB, increase telomere length, reduce glial scarring, enhance repair, etc.

Dale Bredesen 2014

Alzheimer's would be a rare condition



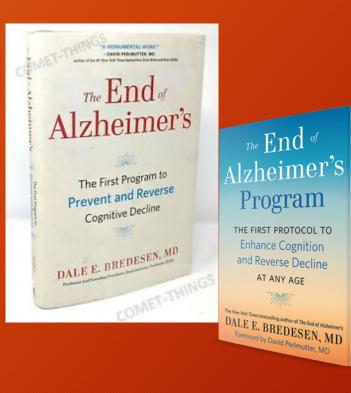


Reversal of Cognitive Decline: Evolution, Pathology, Physiology



DALE BREDESEN, MD

REVERSING COGNITIVE DECLINE: Advanced Clinical Training December 2017 Miami, FL



DALE E. BREDESEN, MD Restrict Press bestarting author of The End of Althonmers The First Survivors of Alzheimer's We How Patients Recovered

Treating Alzheimer's is analogous to repairing

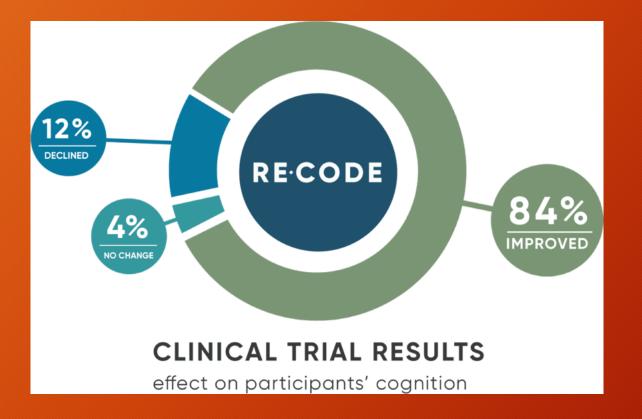
A roof with 36 holes...



RECODE, Bredesen's Cognoscopy

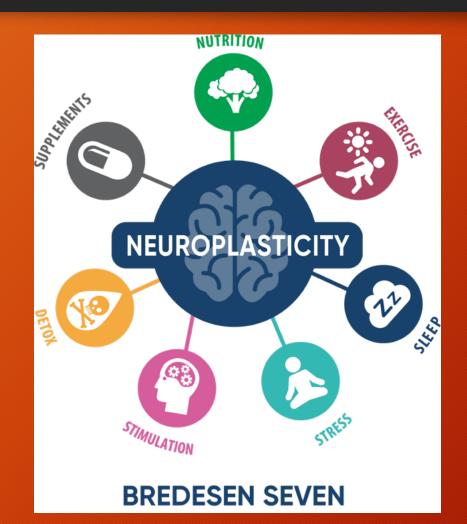
- Type 1: Inflammatory
- Type 2: Atrophic
- Type 1.5: Glycotoxic
- Type 3: Toxic,
- Type 4: Vascular
- Type 5: Traumatic brain injuries

Improvement of cognitive function up to 74% by RECODE



Observed Improvement in Cognition During a Personalized Lifestyle Intervention in People with Cognitive Decline. **2023**. Heather Sandison et al. Clinical Trial, J Alzheimers Dis. 94(3):993-1004.

Stop the ongoing neurodegenerative process & reverse cognitive decline by enhancing the neuroplasticity



Cognitive decline associated with Alzheimer's disease

can now be reversed, and improvement sustained, using a personalized programmatic approach that is targeted to the underlying pathophysiology.

INSULINRESISTENS

Root cause of all chronic diseases
Driving the aging processes faster
Leads cognitive dysfunctions

How to fight insulin resistance?

- Healthy gut linning to cure insulin resistance.
- Accelerat the autophagy cellulary.
- High diastolic blood pressure insulin resistance.
- An optimized ketogenic diet increases autophagy.
- An excellent marker: triglycerides / HDL <1.5

Aging process accelerates with insulin resistance

Most people spend every waking moment in a state of elevated insulin.

Heavy metals & Cognoscopy

 Review
 > Trends Pharmacol Sci. 2018 Dec;39(12):1049-1063. doi: 10.1016/j.tips.2018.10.001.

 Epub 2018 Oct 20.

Copper and Zinc Dysregulation in Alzheimer's Disease

Review > J Alzheimers Dis. 2020;76(4):1215-1242. doi: 10.3233/JAD-200282.

Heavy Metals Exposure and Alzheimer's Disease and Related Dementias

The breakdown of the blood-brain barrier (BBB) in neurodegenerative disease

- Type 2 diabetes increases the risk of Alzheimer's disease
- Lack of omega-3 fatty acids (EPA and DHA) in the brain
- High blood pressure increases, an important modifiable lifestyle factor
- Alcohol consumption, higher risk of breast cancer and general health conditions
- Lack of protein & muscle mass; strength training and activity
- High stress levels

Autophagy & intermittent fasting (IF)

- IF Starts autophagy through an optimized ketogenic diet.
- Most often, the proponents follow blindly without knowledge of the 34 fatty acids.
- They write about enormous successes such as weight loss.
- When restoring insulin resistance, Zn, Cr, Se levels need to be adjusted
- (The Journal of Nutritional Biochemistry, October 2021).
- Serious life-threatening deficiencies; low RBC Mg, Ca, Cu, D3 as well as the 34 fatty acids are at the core of healing everything from gut to brain but also Covid.

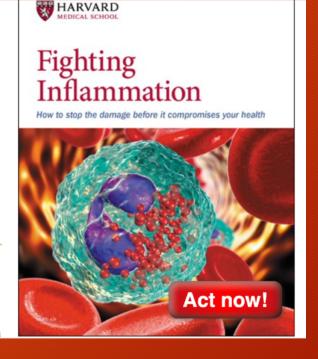
Low-grade chronic inflammation, silently simmers for years without our knowledge, can affect almost anyone and contribute to CVD, cancer, type 2 diabetes and other conditions.



Get started TODAY! Fight Health-Robbing Inflammation! with 7 Simple Steps

Science has proven that chronic, low-grade inflammation can turn into a silent killer that contributes to cardiovascular disease, cancer, type 2 diabetes and other conditions.

The fact that three out of five people around the world die from a



Shockingly, 3 out of 5 people around the world die from a disease that has been linked to inflammation.

The significance of diet and nutrition for the brain and genes!



Most of us today know more about how our car or iPhone works than our own bodies

- Japanese study; laughing can turn off genes involved in prostate cancer.
- The power of social connections to influence our immune system and gene expression.
- In each other's presence, the ECG and EEG of both are connected.

Vitamin D, Homocysteine, and Folate in Subcortical Vascular Dementia and Alzheimer Dementia

Moretti R, Caruso P, Dal Ben M, Conti C, Gazzin S, Tiribelli C.Front Aging Neurosci. 2017 May

The statistical models confirmed the association between lack of vitamin D & folate and high levels of homocysteine with dementia.

Can flavonoids help fend off forgetfulness?

September 17, 2021

By Heidi Godman, Executive Editor, Harvard Health Letter





The foundation of a healthy diet is a vibrant rainbow of fruits and vegetables, like rosy red strawberries, dark green spinach leaves, or sunny yellow peppers. Their colors often come from flavonoids, powerful plant chemicals (phytochemicals) that appear to contribute to many aspects of health. And now a large Harvard study published online in *Neurology* in July suggests that <u>flavonoids may also play a role in protecting</u>

Green coffee fruit extract is rich in polyphenols!

Decaffeinated coffee also contains about 75% of the antioxidants that increase the BDNF level in the plasma.



https://foodrevolution.org/blog/food-and-health/coffee-health/ https://www.psychologytoday.com/blog/your-brain-food/201105/why-decaf-coffee-is-just-healthy https://foodrevolution.org/blog/coffee-health/l

What are polyphenols?

MACRONUTRIENTS (carbohydrates, proteins and fats) MICRONUTRIENTS (vitamins and minerals).

 Polyphenols naturally found in plant-based food, such as fruits, vegetables, herbs, spices, tea, dark chocolate, and wine.

How does polyphenols affect the brain?

- Polyphenols are hardly absorbed in gut, but these are food for the microbiome in the intestine

- Their metabolites are transported to the brain through the blood!

Healthy integrity of the intestinal mucosa means a healthy BBB!

Green tea & anti-cancerogena effekt



Turmeric: More than 5 000 years popular in India

Related to their low prevalence of Alzheimer's in the world.



- https://foodrevolution.org/blog/food-and-health/prevent-reverse-alzheimers/
- https://www.ncbi.nlm.nih.gov/labs/pmc/articles/PMC2781139/
- http://www.worldlifeexpectancy.com/cause-of-death/alzheimers-dementia/by-country/ -
- https://pubmed.ncbi.nlm.nih.gov/19966973/
- http://www.ncbi.nlm.nih.gov/pubmed/24335167
- https://nutritionfacts.org/2015/02/05/why-pepper-boosts-turmeric-blood-levels/
- https://pubmed.ncbi.nlm.nih.gov/29065496/

Antocyaniner



- https://www.huffingtonpost.com/2012/04/26/cognitive-impairment-study- berries_n_1453557.html

- https://www.huffingtonpost.com/2012/04/26/cognitive-impairment-study-berries_n_1453557.html

- http://www.ncbi.nlm.nih.gov/pubmed/20047325

Omega 3 fatty acids

Flaxseed and chia seed both contain high omega 3 fatty acids while Flaxseed contains ALA in addition to high polyphenols and fiber.



https://www.webmd.com/diet/features/benefits-of-flaxseed

Ubiquinol, Co Q10 in case of statin usage

Accumulation of Beta amyloid & Tau protein increase in the brain by Statin

Green & cruciferous vegetables; broccoli, cabbage, kale, and Brussels sprouts

Nutrient dense that benefit brain health. According to research from Rush University in Chicago in 2015; cognitive functions improved in older people when they ate more greens.



http://www.sciencedaily.com/releases/2015/03/150330112227.htm

Resveratrol improves brain function in the elderly According to a study in the British Journal of Nutrition



https://www.organicfacts.net/health-benefits/fruit/health-benefits-of-grapes.html https://www.canceractive.com/cancer-active-page-link.aspx?n=1906 https://www.eurekalert.org/pub_releases/2017-02/ral-psh020317.php

Your BDNF-stimulating brain food

- Polyphenols and flavonoids: Blueberry, chocolate, green tea, coffee fruit extract, olive oil and black pepper
- Meditation
- Sleep
- Music
- Social relationships and interactions
- Psychedelic like CBD oil (without thc)
- Spend time under the sun

MEDICINAL MUSHROOMS

Supports the immune system, Anti-inflammatory, Strong antioxidants, Adaptogenic.

- Reishi; "immortality mushroom"
- Lion's mane; protects against anxiety and depression, cognitive impairment, depression, lengthens axons and dendrites, improves synaptic function
- Cordyceps; anti-cancer properties, increases energy levels and improves libido
- Maitake; regulates blood sugar, blood fats and cholesterol, strengthens the immune system
- Germini; high levels of B2, B3 and B5
- Shiitake; fights obesity, protects cardiovascular and immune systems

Referenser

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