14° CONGRESSO NAZIONALE SINut

SINut
Società Italiana di Nutraceutica

12-14 settembre 2024
Bologna

BRAIN LONGEVITY: I RIMEDI VENGONO DAL MARE

Giovanni Scapagnini

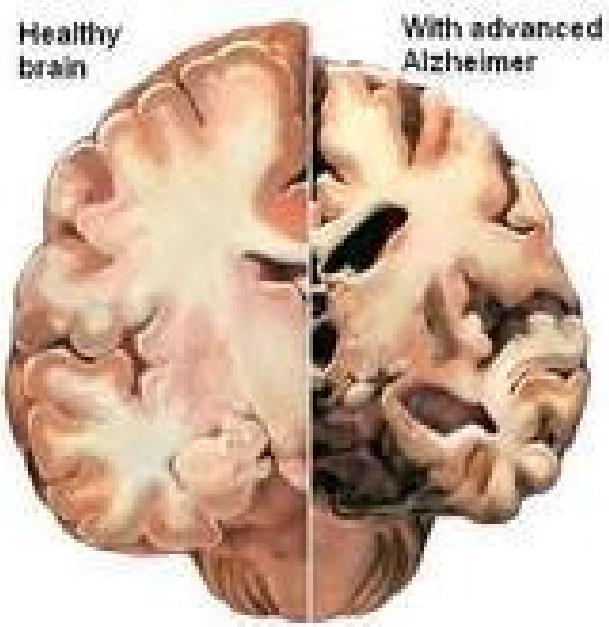
Dipartimento di Medicina e Scienze della Salute
«V. Tiberio», Università degli Studi del Molise

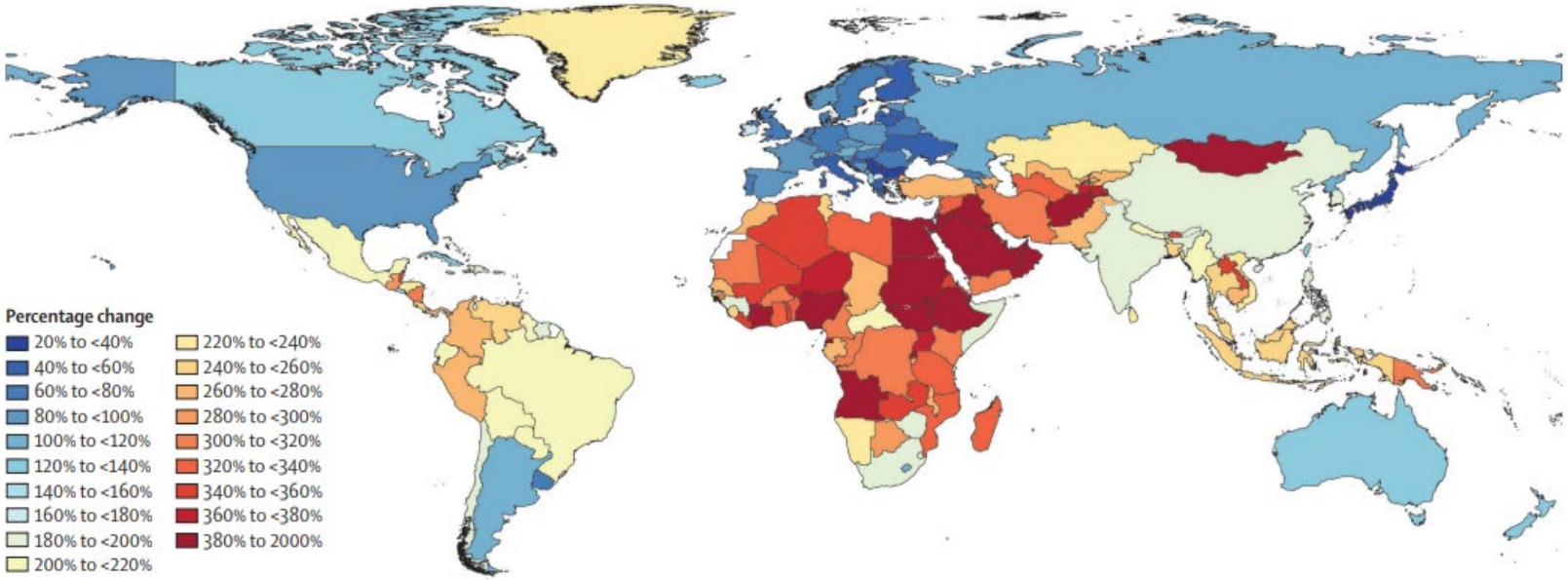
www.thelancet.com/public-health Vol 7 February 2022

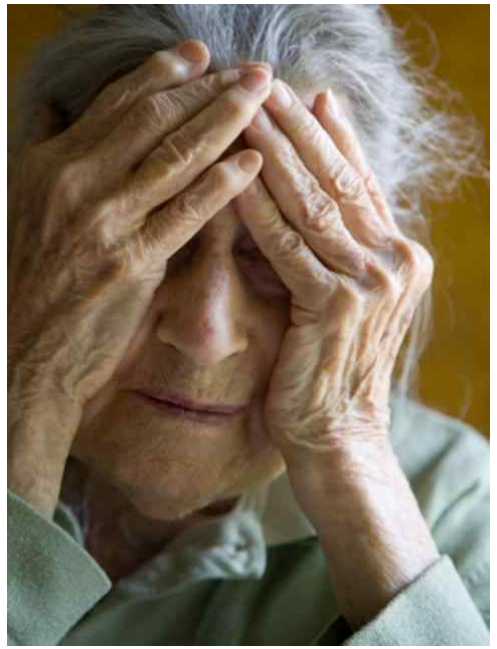
Estimation of the global prevalence of dementia in 2019 and forecasted prevalence in 2050: an analysis for the Global Burden of Disease Study 2019

GBD 2019 Dementia Forecasting Collaborators*

The number of people with dementia would increase from 57·4 (95% uncertainty interval 50·4–65·1) million cases globally in 2019 to 152·8 (130·8–175·9) million cases in 2050





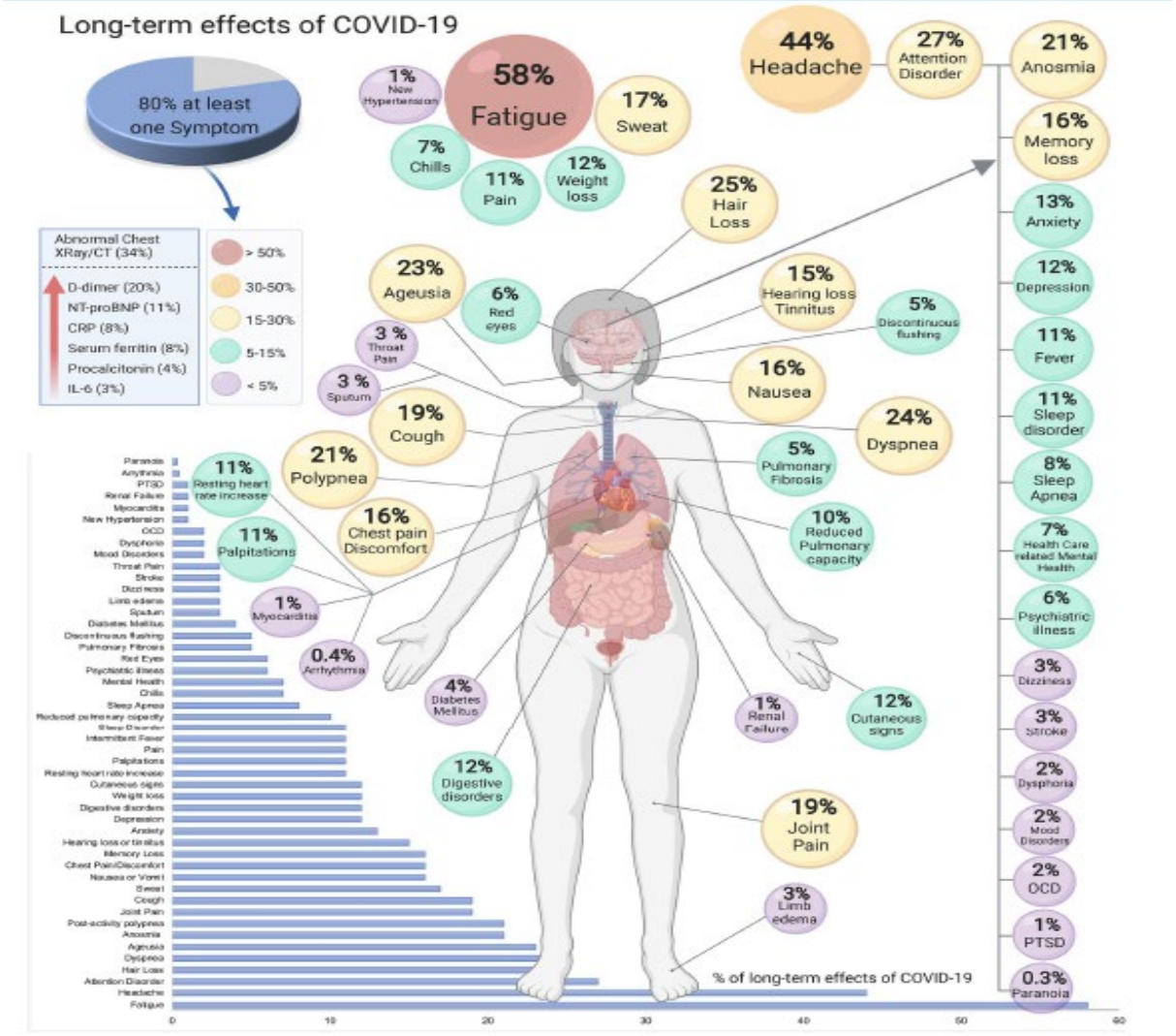


Scientific Reports | (2021) 11:16144

More than 50 long-term effects of COVID-19: a systematic review and meta-analysis

Sandra Lopez-Leon[1], Talia Wegman-Ostrosky[2], Carol Perelman[3], Rosalinda Sepulveda[4], Paulina A. Rebolledo[5,6], Angelica Cuapio[7] & Sonia Villapol[8,9]✉

Studies included in review
(n = 15) 55
Total Persons n= 47,910
Long-Term COVID19 effects

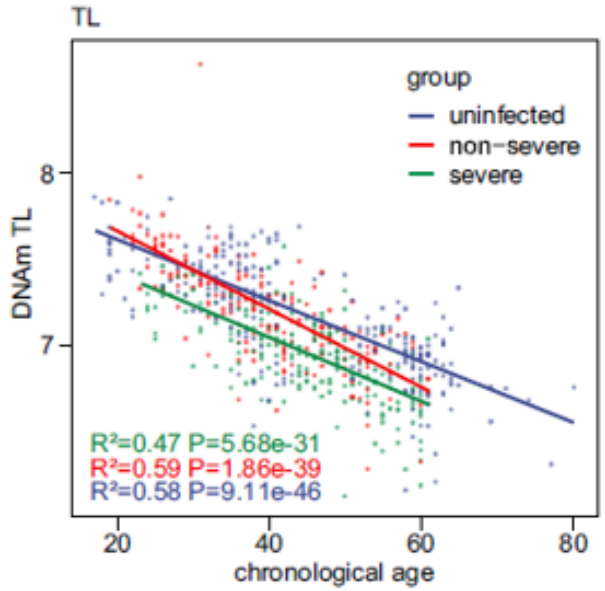


nature COMMUNICATIONS

Accelerated biological aging in COVID-19 patients

(2022) 13:2135

Xue Cao[1,2,3], Wenjuan Li[4], Ting Wang[5], Dongzhi Ran[6,7], Veronica Davalos[8], Laura Planas-Serra[9,10], Aurora Pujol[9,10,11], Manel Esteller[8,11,12,13], Xiaolin Wang[2] & Huichuan Yu[2,3]✉



Assessment of DNA methylation-based telomere length estimator in patient cohorts

Accelerated epigenetic aging is associated with the risk of SARS-CoV-2 infection and developing severe COVID-19. In addition, the accumulation of epigenetic aging from COVID-19 may contribute to the post-COVID-19 syndrome among survivors.

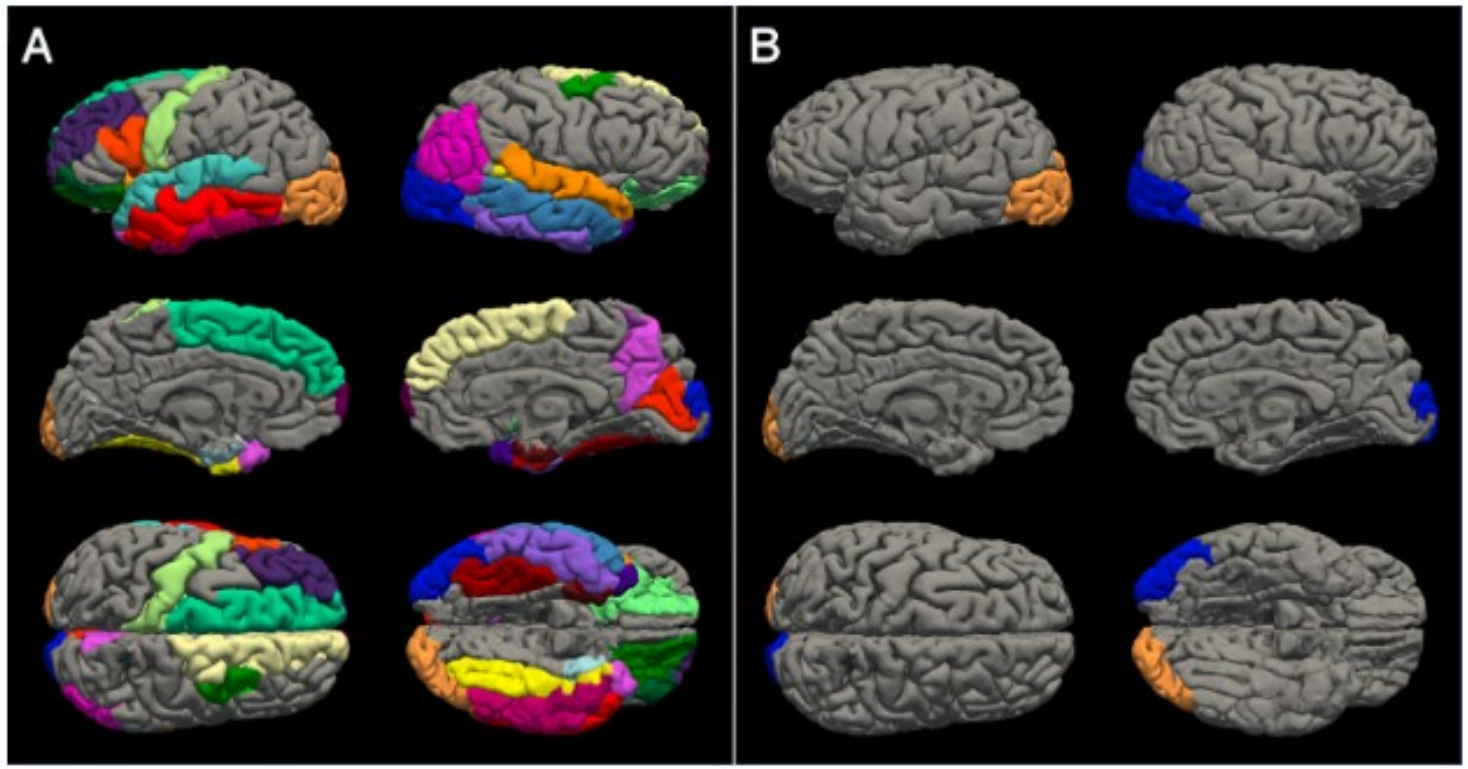
PNAS RESEARCH ARTICLE | NEUROSCIENCE OPEN ACCESS

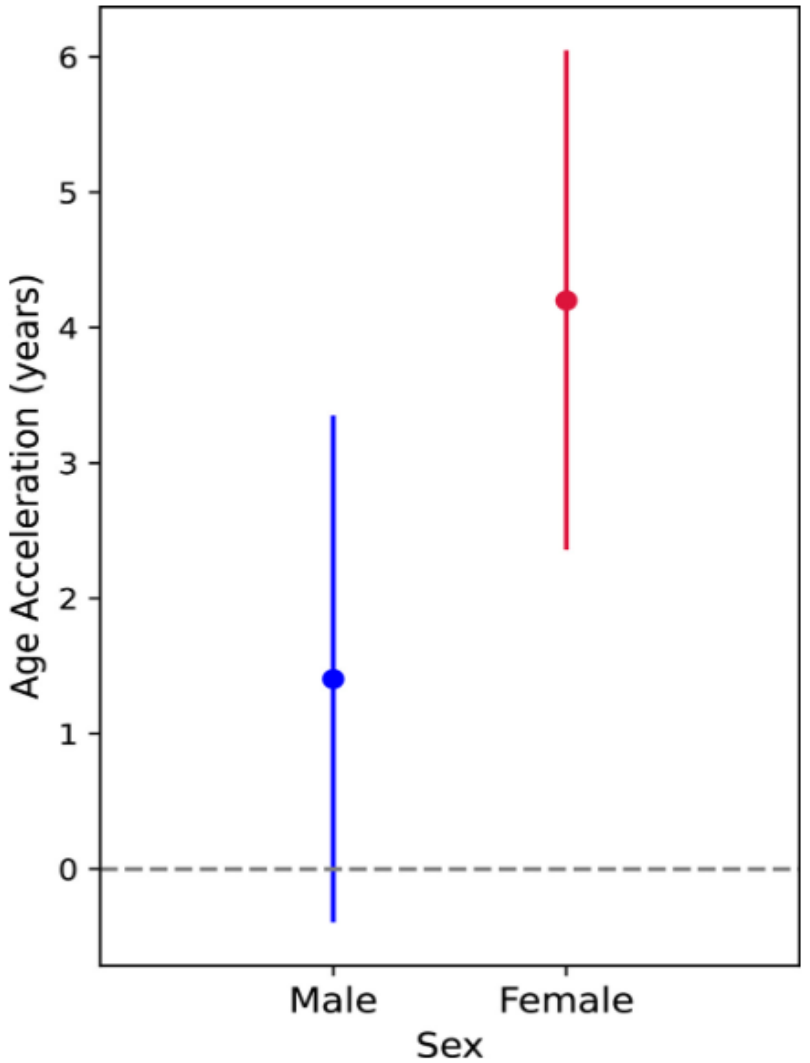
COVID-19 lockdown effects on adolescent brain structure suggest accelerated maturation that is more pronounced in females than in males

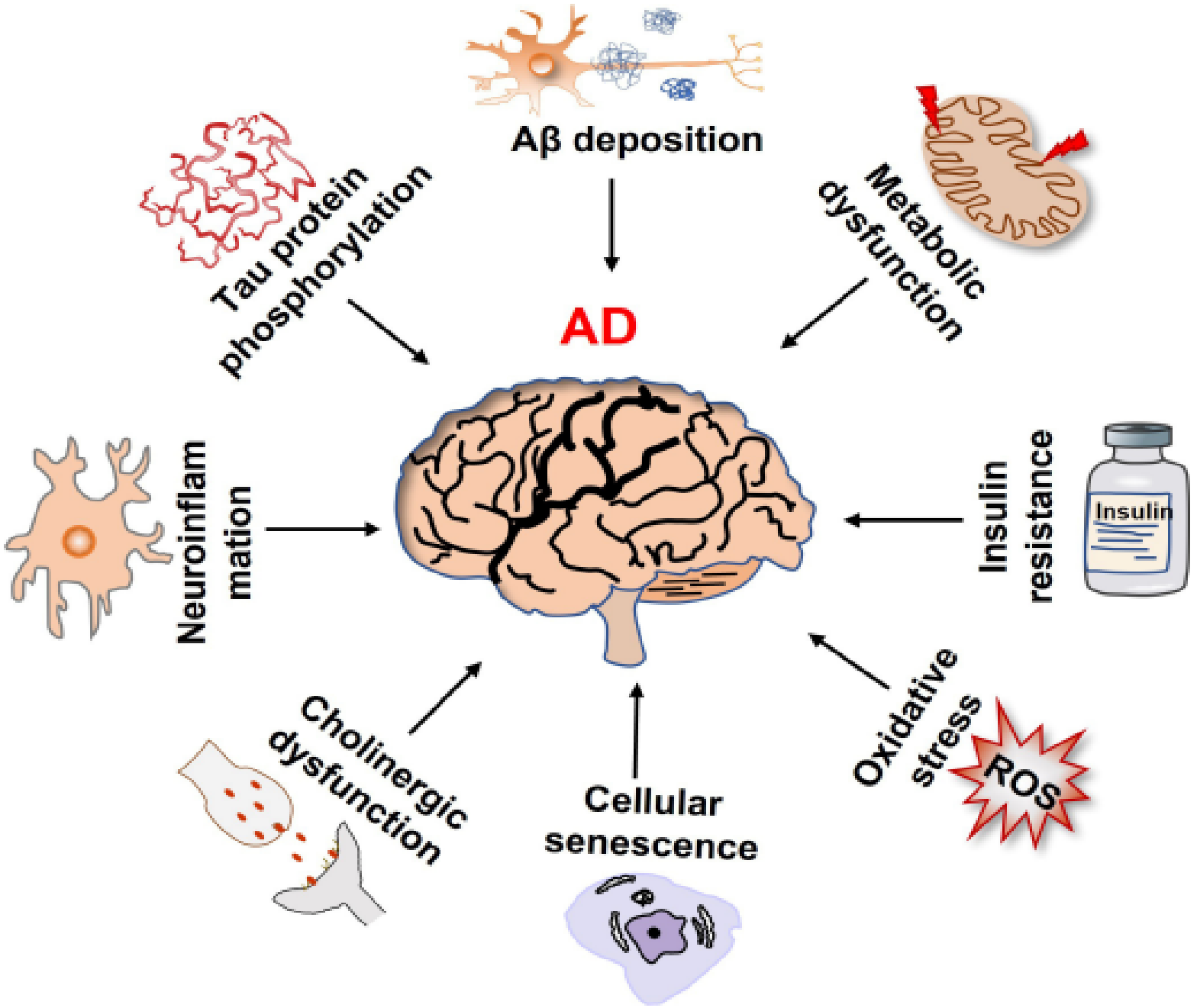
Neva M. Corrigan [a,b], Ariel Rokem [b,c,d], and Patricia K. Kuhl [a,e,1]

Contributed by Patricia K. Kuhl; received February 27, 2024; accepted July 26, 2024; reviewed by Russell T. Shinohara and Leah H. Somerville

September 9, 2024 | 121 (38) e2403200121

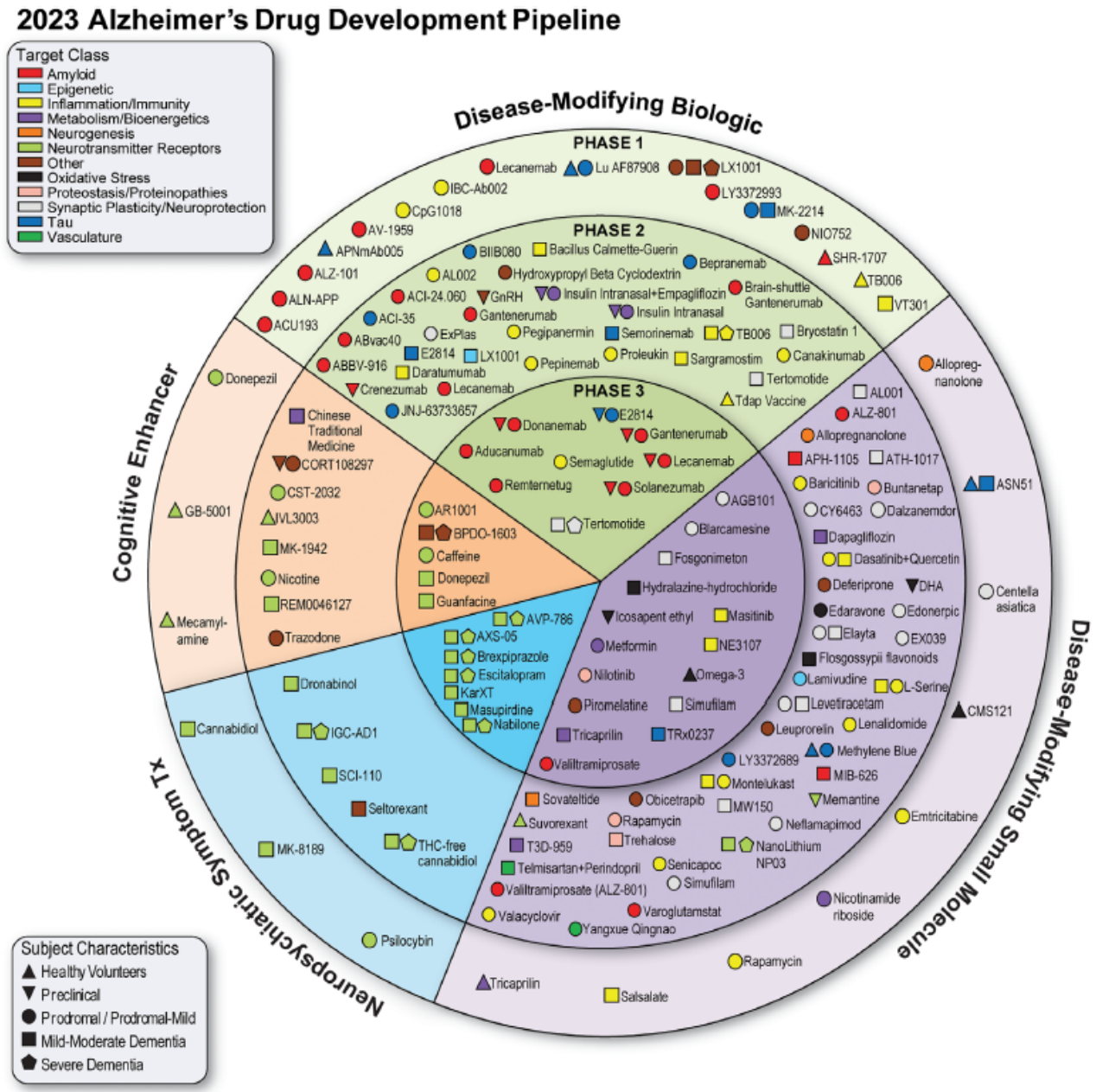


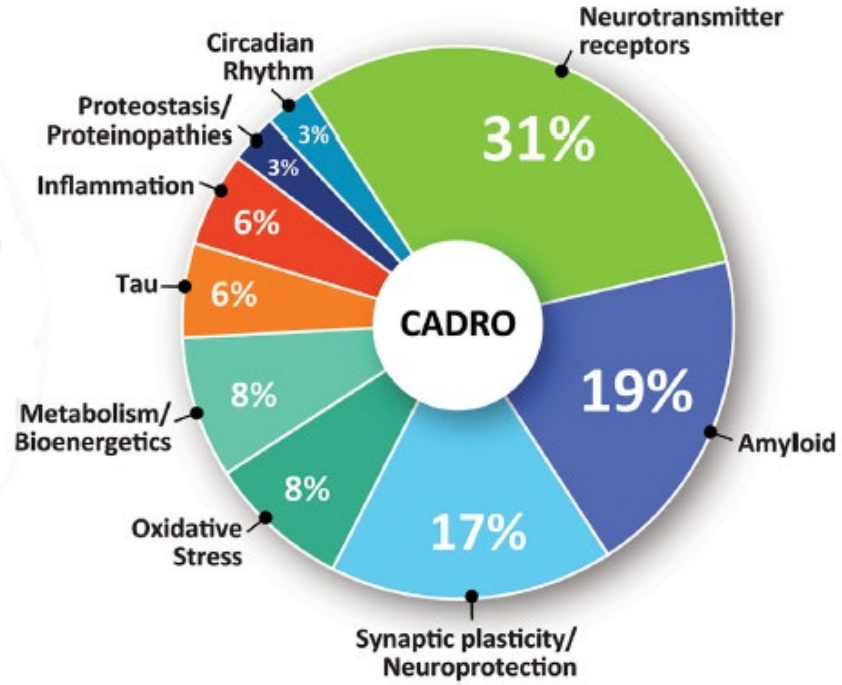


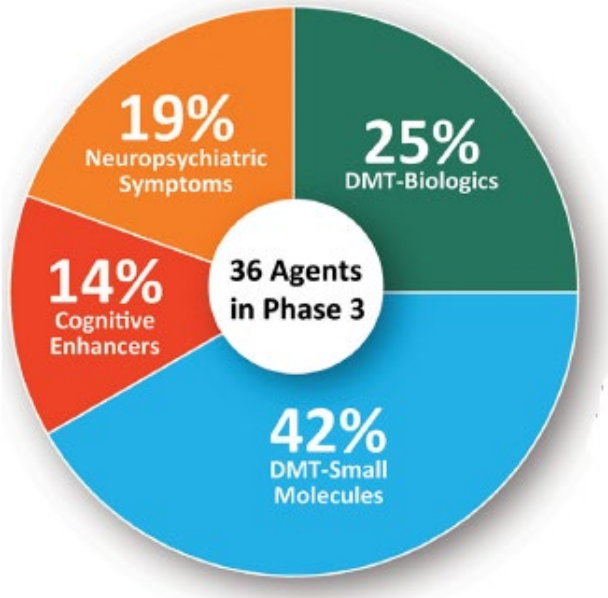

Aβ deposition
Tau protein phosphorylation
Metabolic dysfunction
AD
Neuroinflam mation
Insulin resistance
Insulin
Cholinergic dysfunction
Cellular senescence
Oxidative stress
ROS

Alzheimer's Dement. 2023;9:e12385.

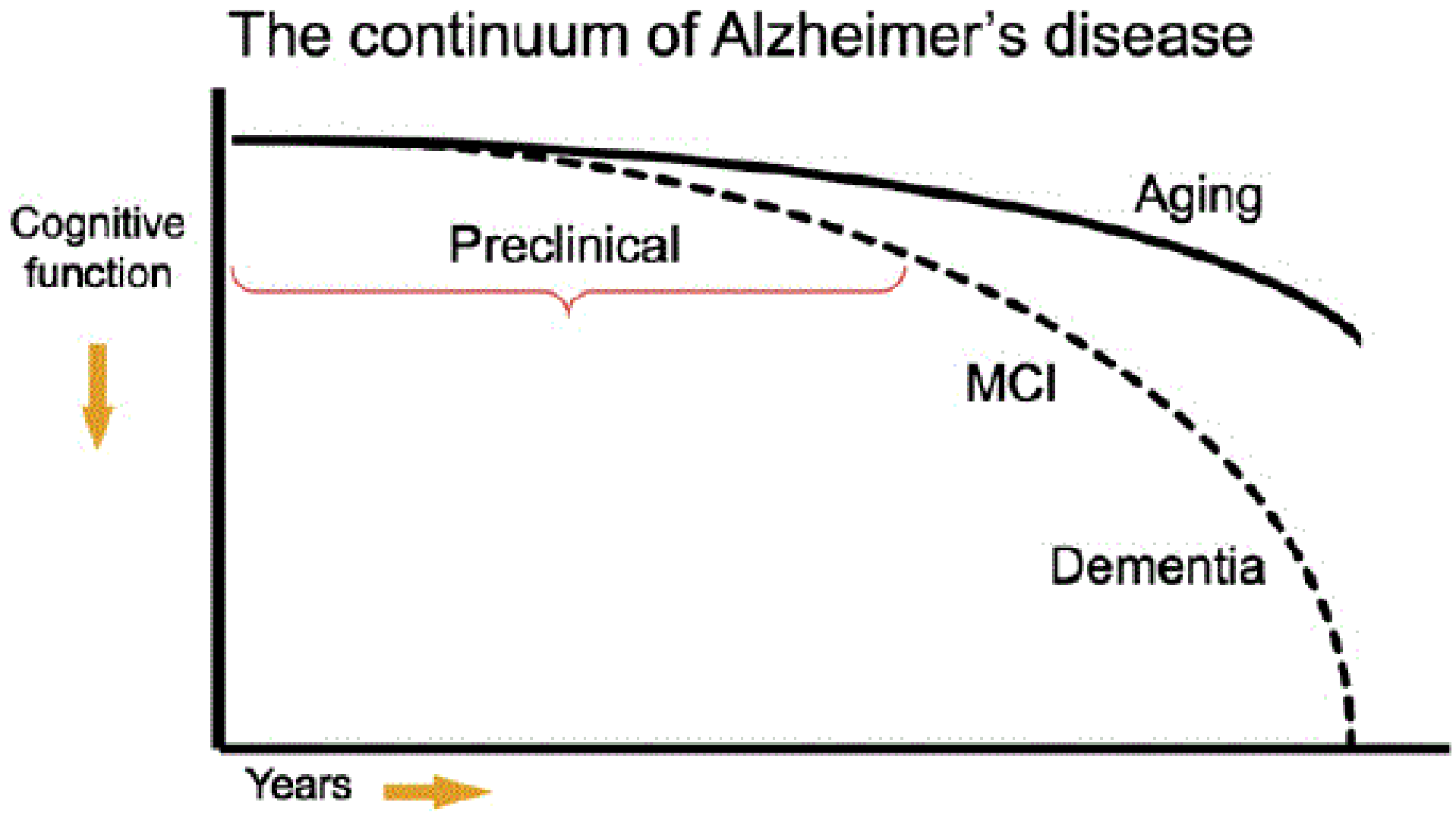
Alzheimer's disease drug development pipeline: 2023







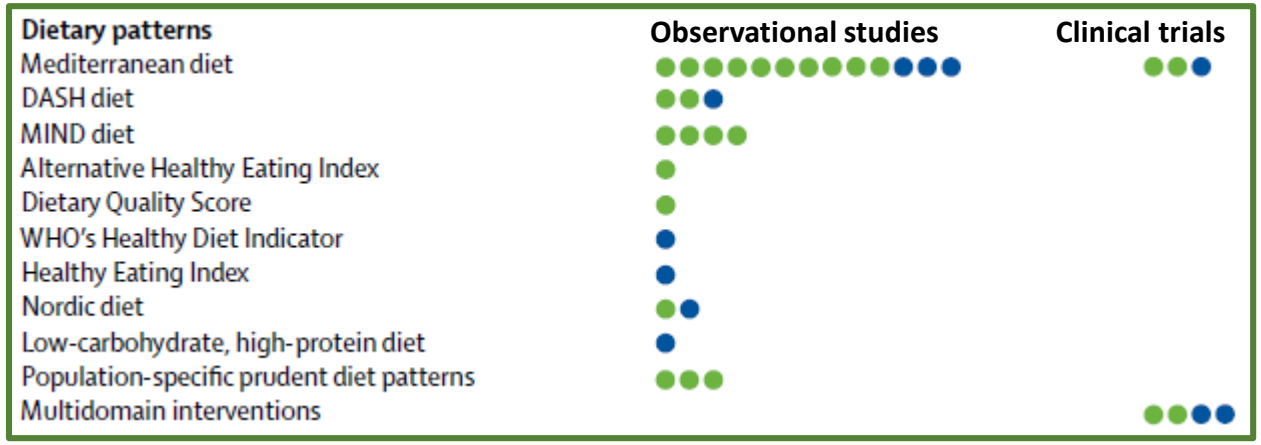
Toward defining the preclinical stages of Alzheimer's disease:
Recommendations from the National Institute on Aging and the Alzheimer's Association workgroup



Nutrition and prevention of cognitive impairment

Lancet Neurol 2018; 17: 1006–15

Nikolaos Scarmeas, Costas A Anastasiou, Mary Yannakoulia



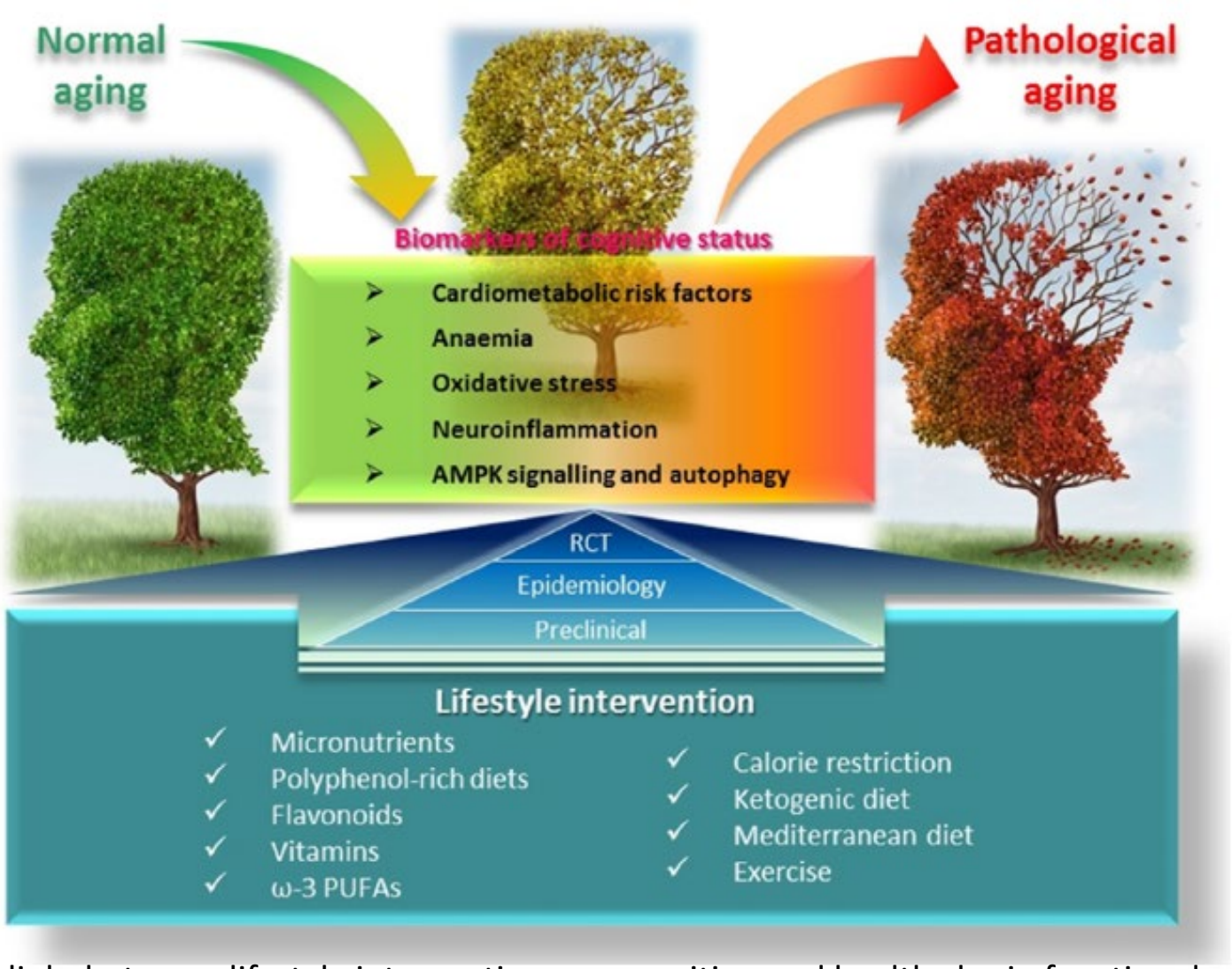
Antioxidants	
Vitamin C[14]	Fruits (berries, citrus fruits, kiwis, lychees, and papayas), vegetables (Brussels sprouts, cauliflowers, cabbages, sweet peppers, and tomatoes), and herbs and spices (parsley, sorrel, and chives)
Vitamin E[15]	Vegetable oils and fat spreads from vegetable oils, nuts and seeds, some fatty fish (eg, sardines, salmon, herring, swordfish, and trout), egg yolk, and wholegrain cereals
Carotenes[16]	Yellow or orange vegetables (sweet potatoes, carrots, and pumpkins), dark leafy vegetables (spinach, broccoli, and endives), and yellow or orange fruits (apricots, peaches, mangoes, and melons)
Flavonoids[17]	Fruits (mainly citrus fruits, bananas, and berries), vegetables (parsley and onions), tea (black and brewed)
Vitamin D[18]	Fish (especially fatty fish) and fish liver, full-fat dairy products (or fortified low-fat ones), egg yolk, meat and meat products, and offal (particularly liver)
n-3 fatty acids[19]	Fish (for eicosapentaenoic acid and docosahexaenoic acid) and some vegetable oils and nuts (eg, linseeds, rapeseed oil, and walnuts for α-linolenic acid)

Nutrients related to cognitive function

Ageing Research Reviews

Nutrition for the ageing brain: Towards evidence for an optimal diet

Vauzour D, et al. 2016



Overview of links between lifestyle interventions on cognition and healthy brain function during ageing.

EMBO reports

EMBO reports VOL 13 | NO 3 | 2012

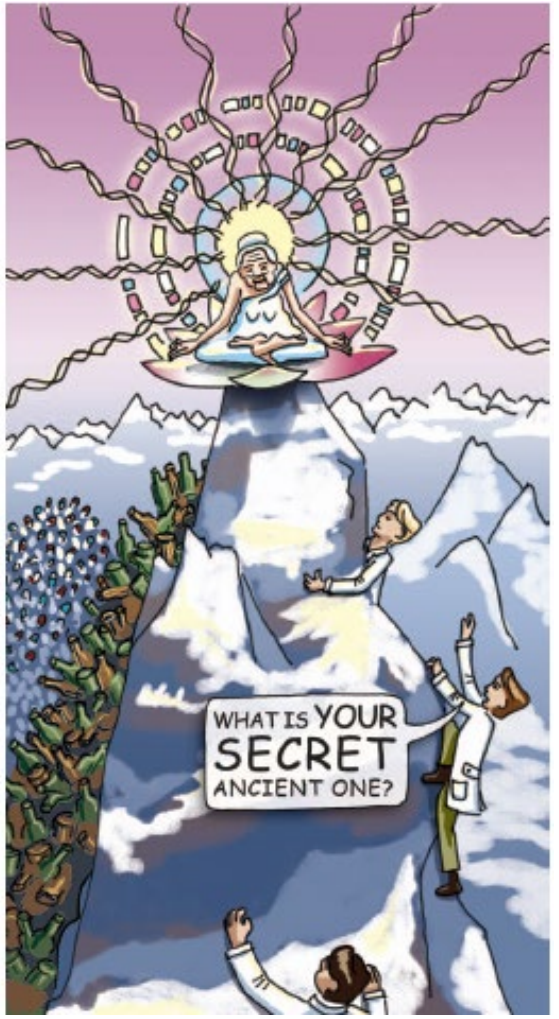
science & society

‘Positive biology’ as a new paradigm for the medical sciences

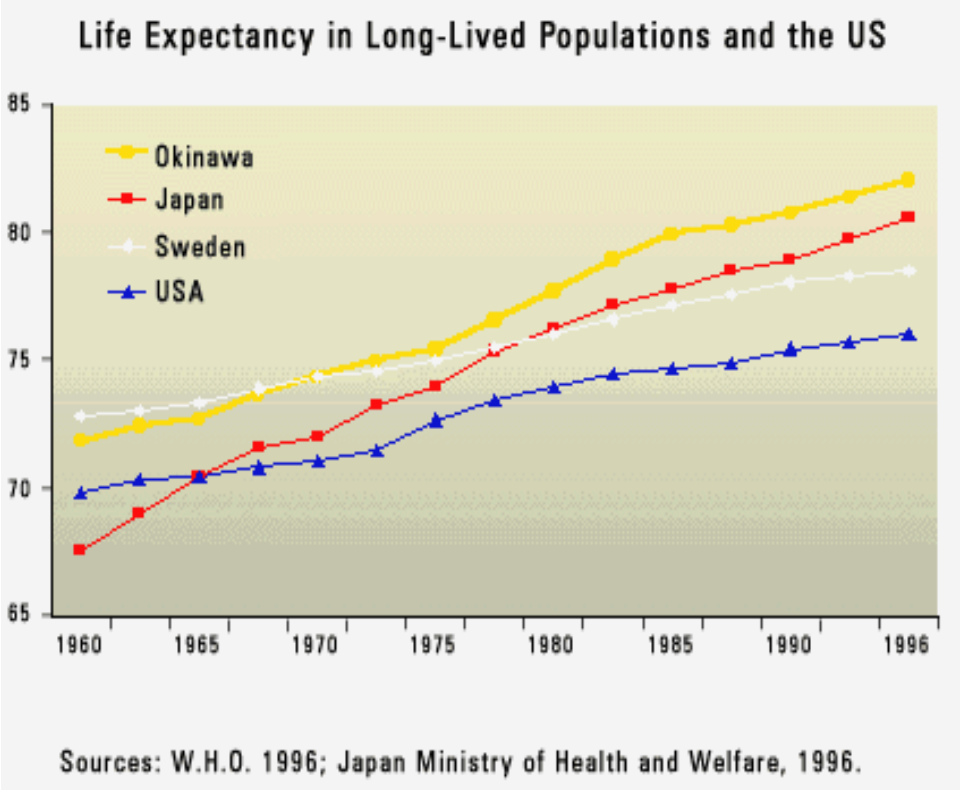
Focusing on people who live long, happy, healthy lives might hold the key to improving human well-being

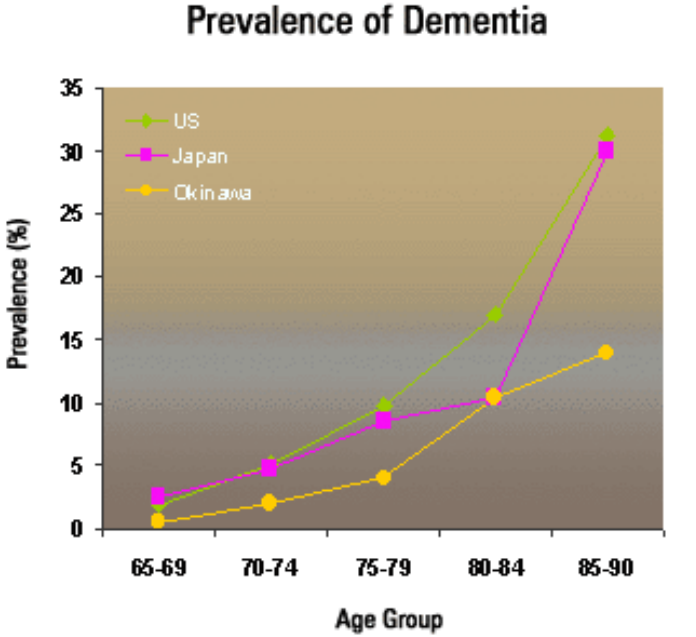
Colin Farrelly

> **Eliminating all types of cancer would increase life expectancy in the USA by approximately only three years**



BLUE ZONES – GEOGRAPHY OF LONGEVITY



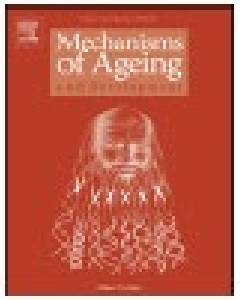


Sources: Yamada, M., et al. J Am Geriatr Soc 1999;47:189-95.
Kokmen, E., et al. Mayo Clin Proc 1996;71:275-82. Ogura, C., et al.
Internatl J Epidemiol 1995;24:373-80.

Mechanisms of Ageing and Development 136-137 (2014) 148–162

Healthy aging diets other than the Mediterranean: A focus on the Okinawan diet

Donald Craig Willcox [a,b,c,*], Giovanni Scapagnini [d], Bradley J. Willcox [b,c]



Key Features of Traditional Okinawa Diet

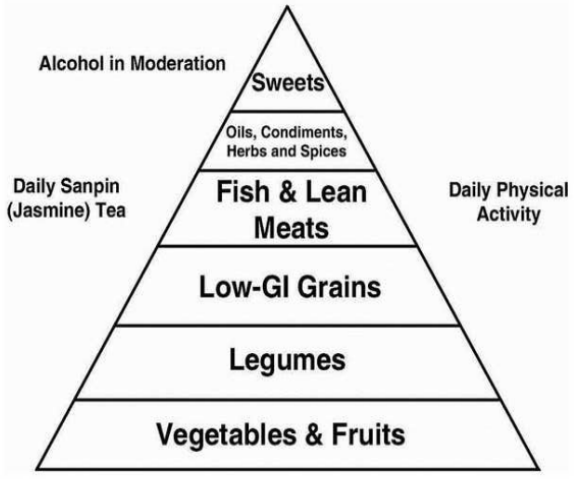
1) Low Caloric Density (plant-based, low fat, moderate protein from soy, fish, lean meats)

2) High Nutrient Density (Vitamins A,C, E, potassium, magnesium, folate, and healthy oils)

3) Phyto-nutrient Rich (polyphenols, carotenoids mostly from green leafy, yellow root vegetables and seaweed)

4) Low in Glycemic Load (high quality carbohydrates from staple sweet potato)

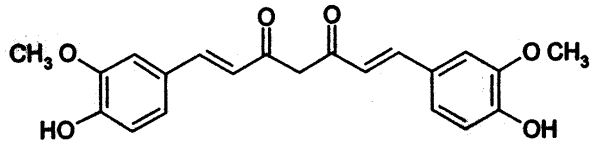
5) Anti-inflammatory (CR, polyphenols, omega 3 fatty acids)



Traditional Okinawan diet food pyramid

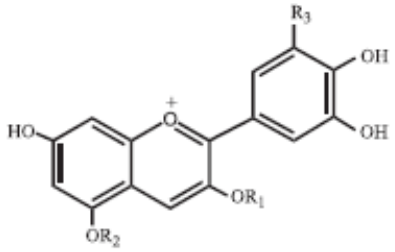
Healthy aging diets other than the Mediterranean: A focus on the Okinawan diet.
Willcox DC, Scapagnini G, Willcox BJ. Mech Ageing Dev. 2014 Jan 21.

Turmeric
Curcuma longa



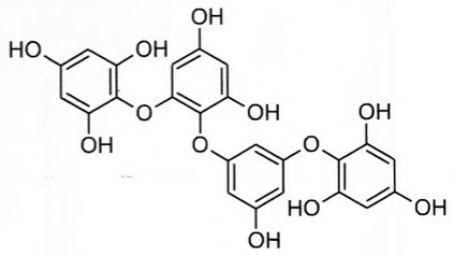
Curcumin

Ipomea batatas
cultivar Ayamurasaki



Anthocyanin

Wakame
Undaria pinnatifida

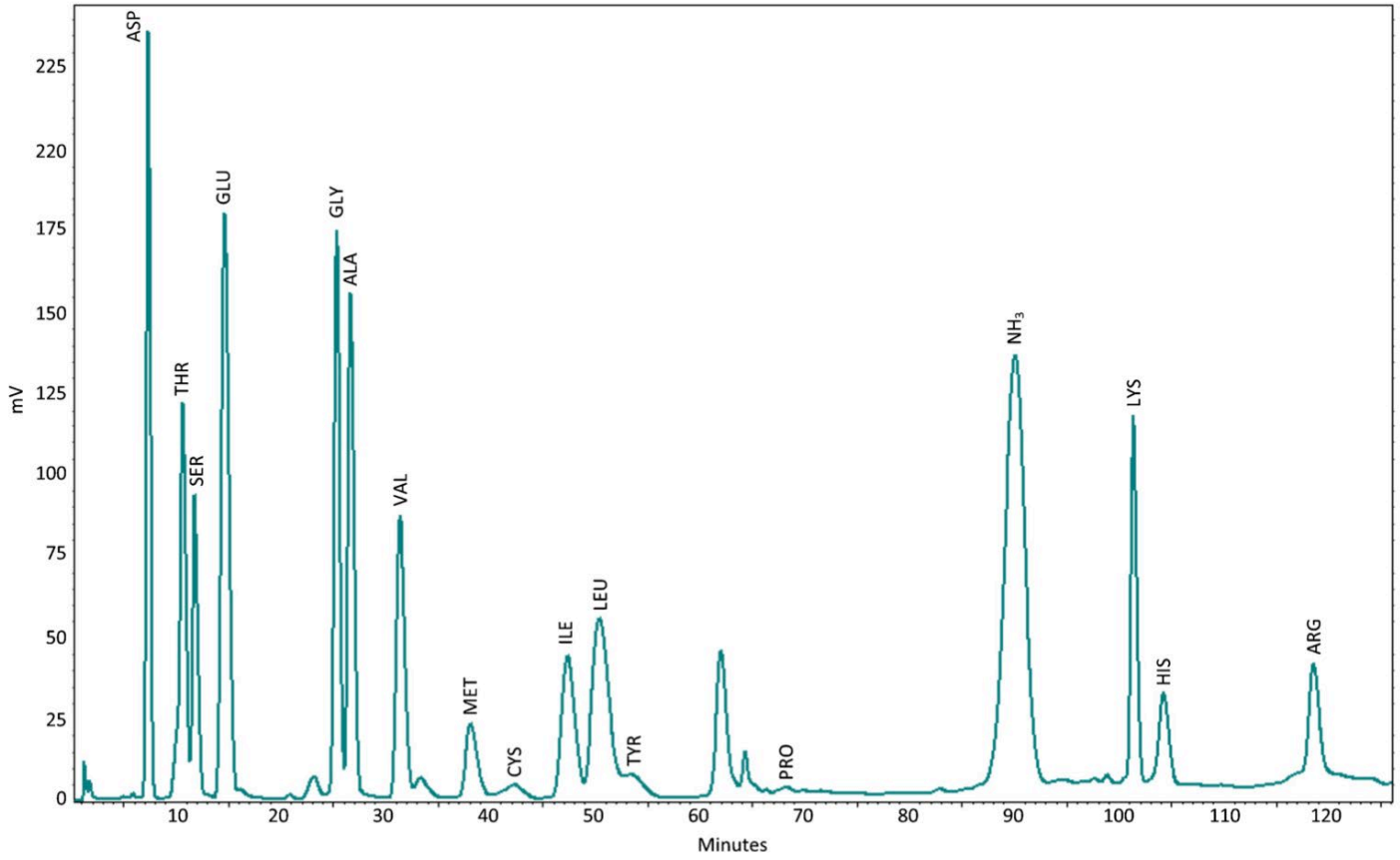


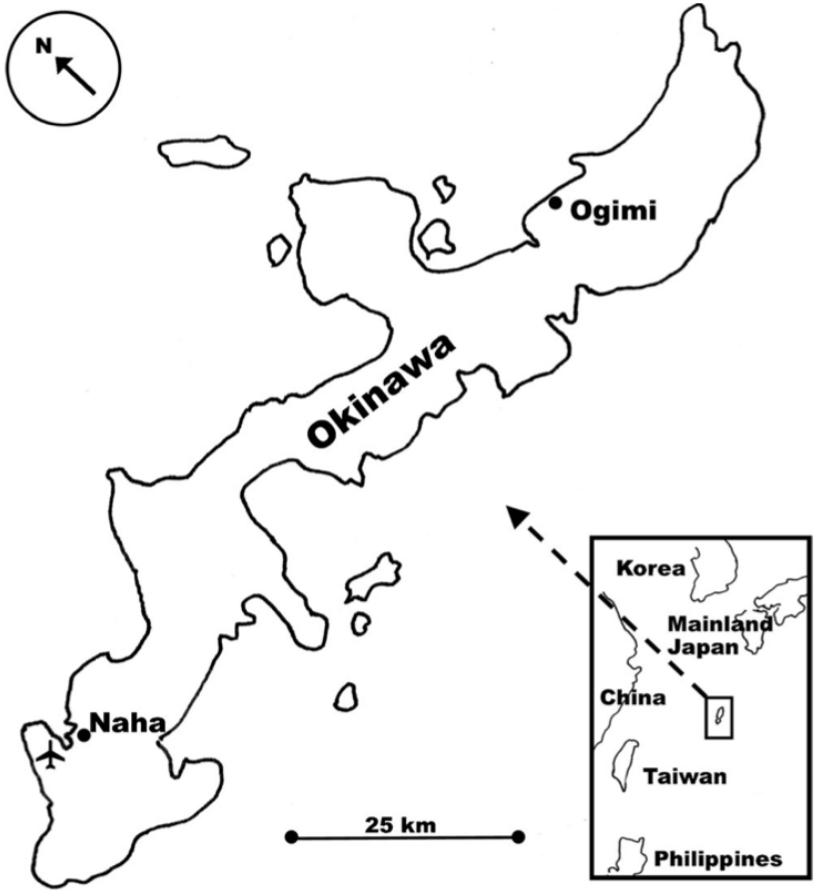
Phlorotannin

Curr Nutr Rep (2017) 6:24–31
DOI 10.1007/s13668-017-0191-0

Traditional Food Items in Ogimi, Okinawa: L-Serine Content and the Potential for Neuroprotection

Paul Alan Cox[1] · **James S. Metcalf**[1]






BEUCHAT

Breeding techniques

Land farming

Mariculture

Integrated aquaculture system

Extraction techniques

- Microwave-assisted extraction (MAE)
- Ultrasound-assisted extraction (UAE)
- Supercritical fluid extraction (SFE)
- Pressurized solvent extraction (PSE)
- Enzyme-assisted extraction (EAE)

Applications

Foods

Fodder

Medicines

Chemical

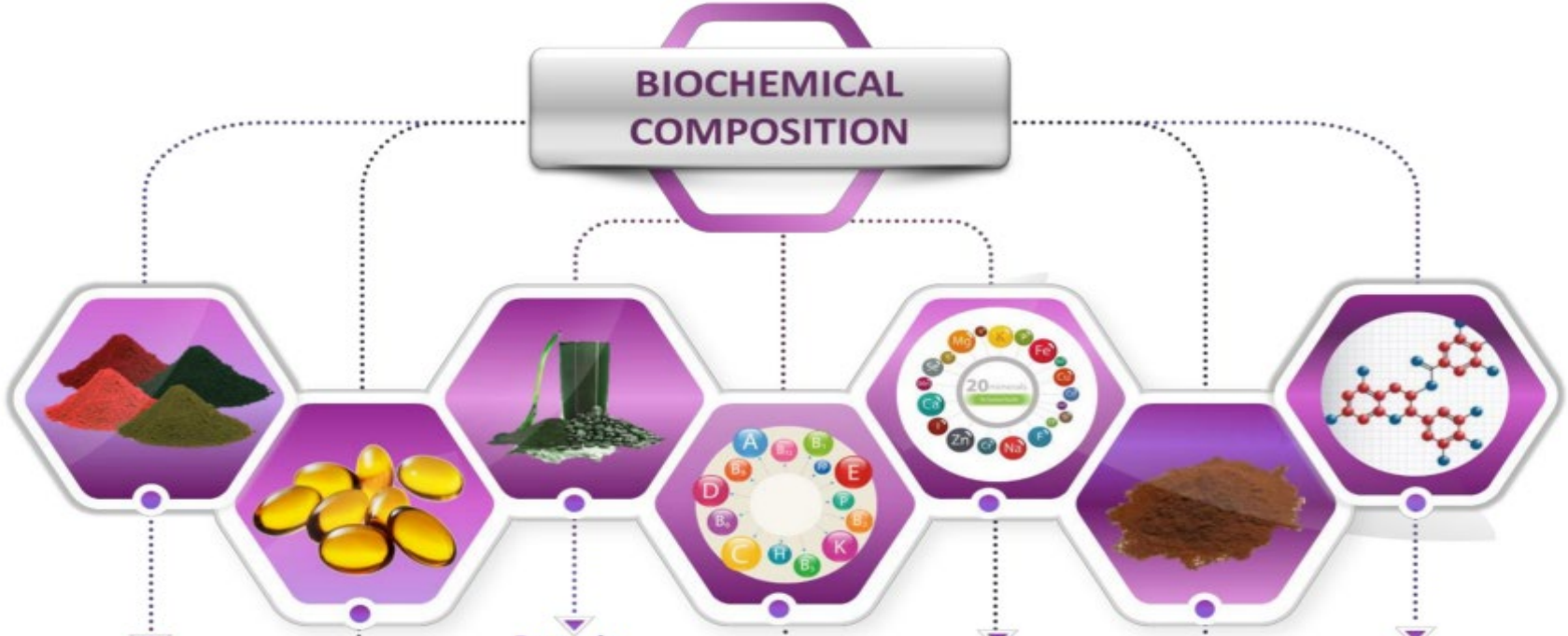
Energy sources

Building materials

The *Epic of Gilgamesh*
Written in Mesopotamia 2000 BC

"King Gilgamesh, you wish to live forever. There is a plant that grows under the sea. This seaweed will restore your health and strength. It contains the secret of eternal youth"

Bioactive compounds from marine seaweeds

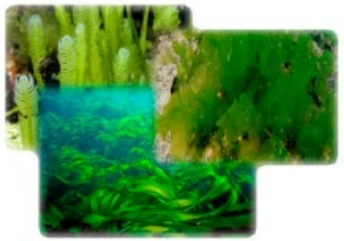


Carrageenans

Agars

Fucoidans

Alginates



Ulvans

Xylans

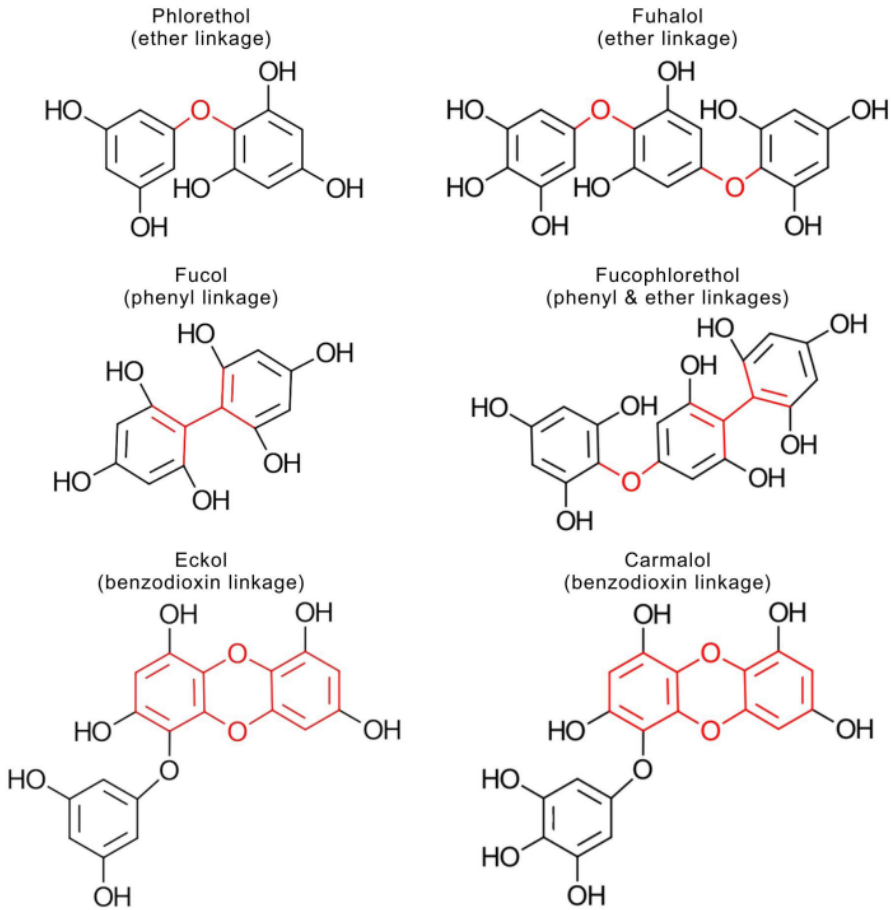
Galactans

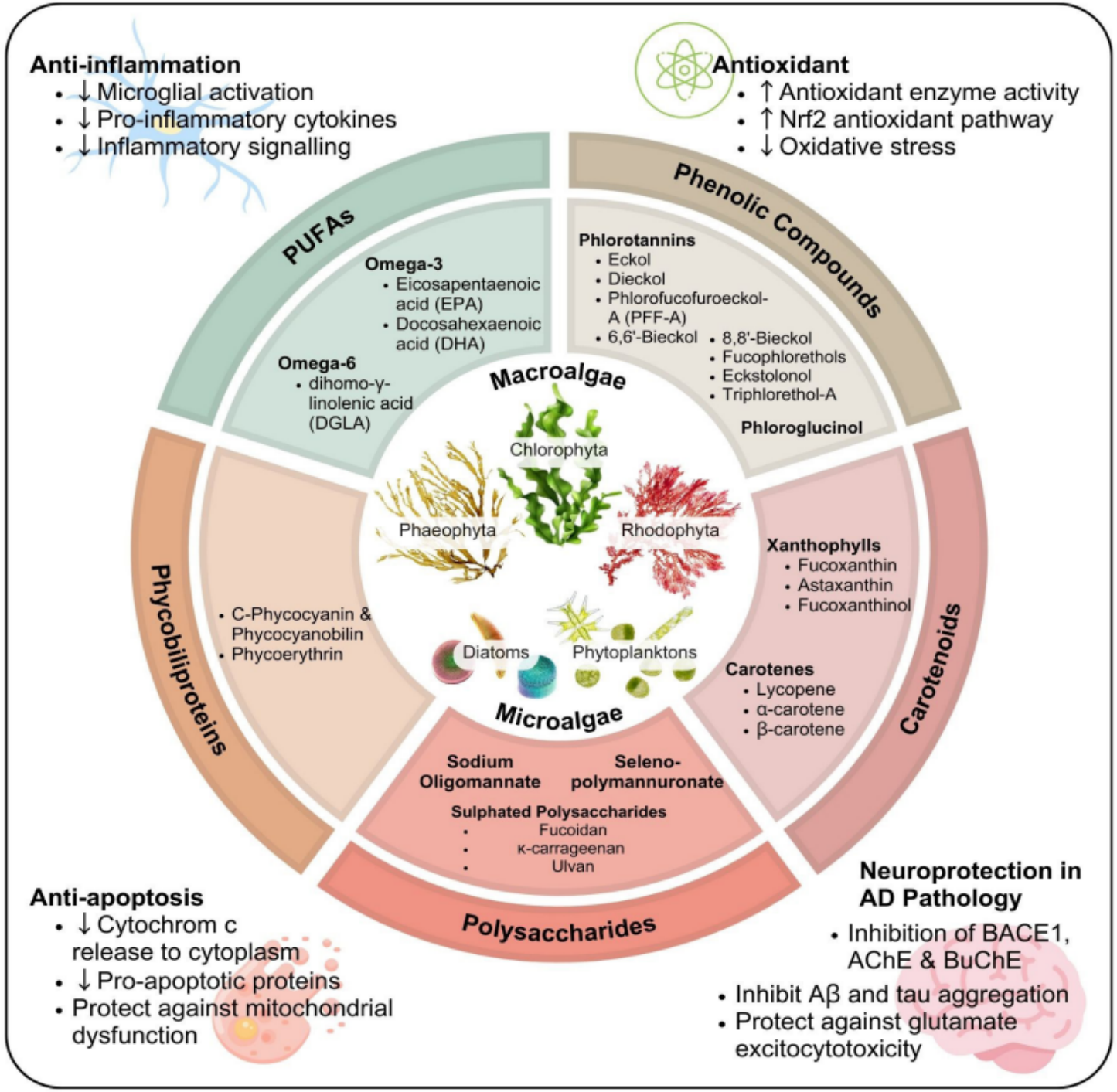
YALE JOURNAL OF BIOLOGY AND MEDICINE 97 (2024), pp.205-224. doi: 10.59249/JNKB9714

REVIEW

YALE JOURNAL OF BIOLOGY AND MEDICINE
YJBM

Natural Bioactive Compounds from Macroalgae and Microalgae for the Treatment of Alzheimer's Disease: A Review



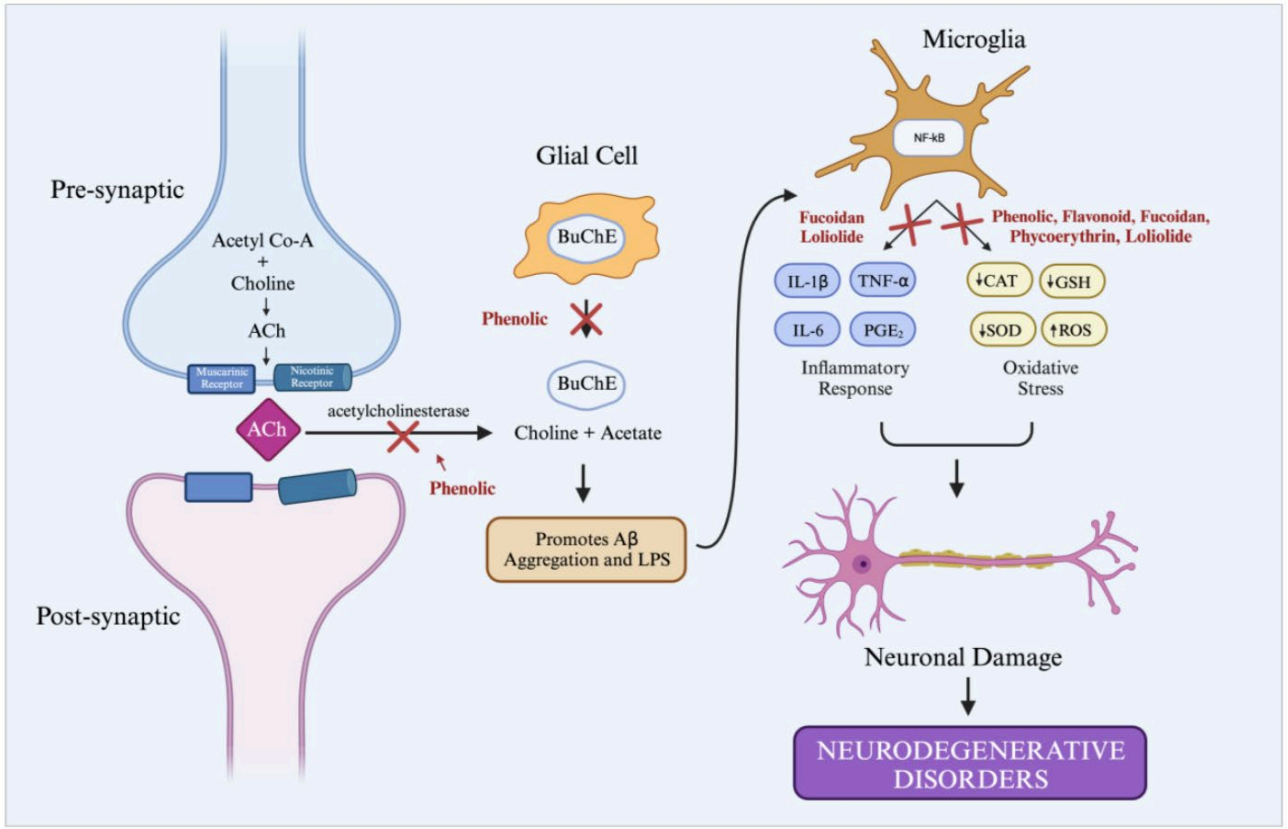


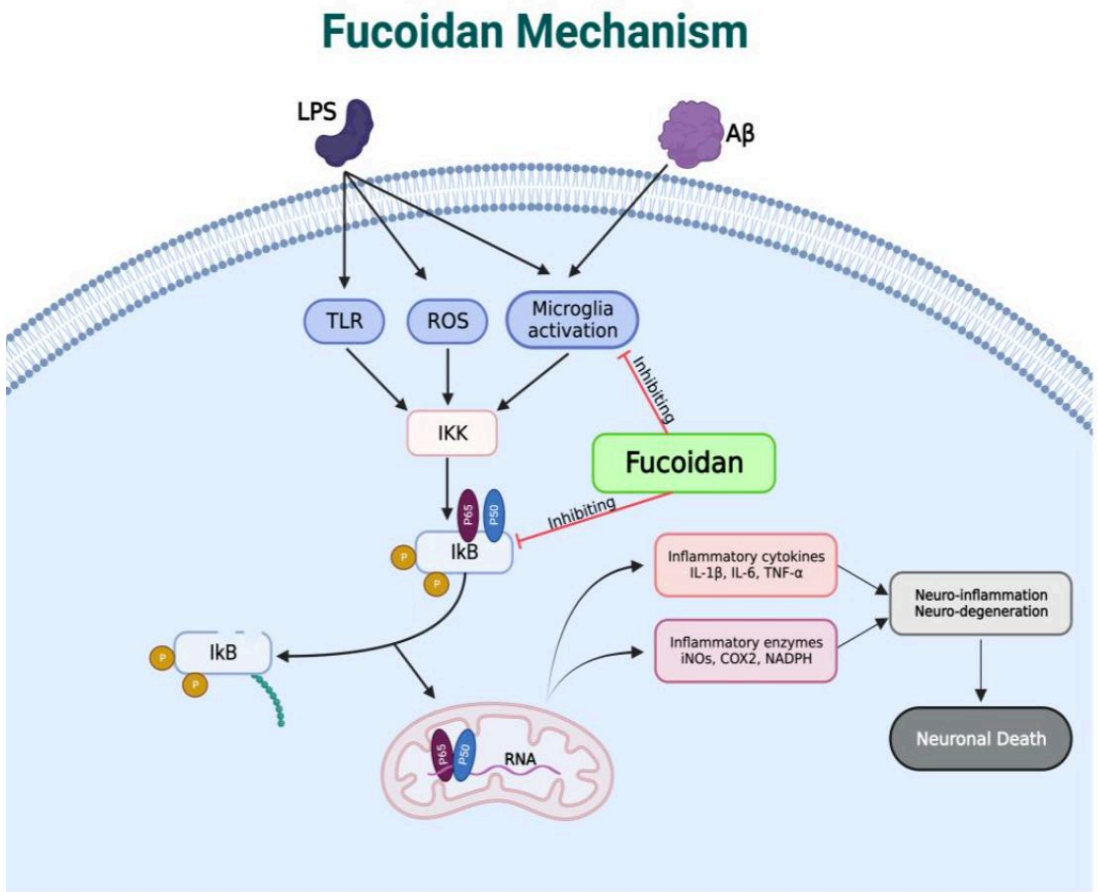
brain sciences

MDPI

Review

Potential Application of Marine Algae and Their Bioactive Metabolites in Brain Disease Treatment: Pharmacognosy and Pharmacology Insights for Therapeutic Advances

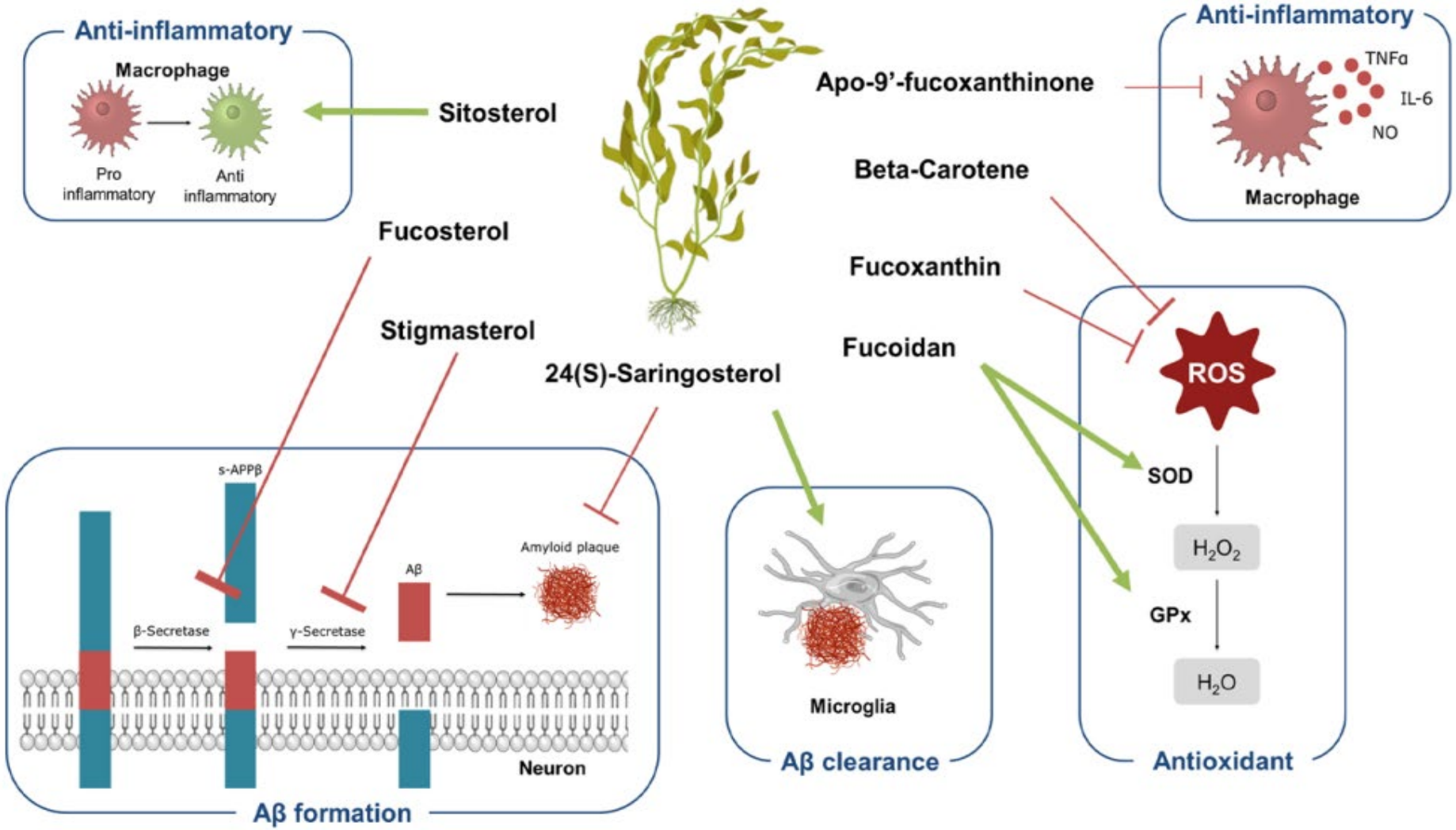




Edible seaweed-derived constituents: an undisclosed source of neuroprotective compounds

NEURAL REGENERATION RESEARCH, 2020

Melissa Schepers[1, 2, #], Nikita Martens[3, #], Assia Tiane[1, 2], Kenneth Vanbrabant[1, 4], Hong-Bing Liu[5], Dieter Lütjohann[4], Monique Mulder[3, #], Tim Vanmierlo[1, 2, *, #]

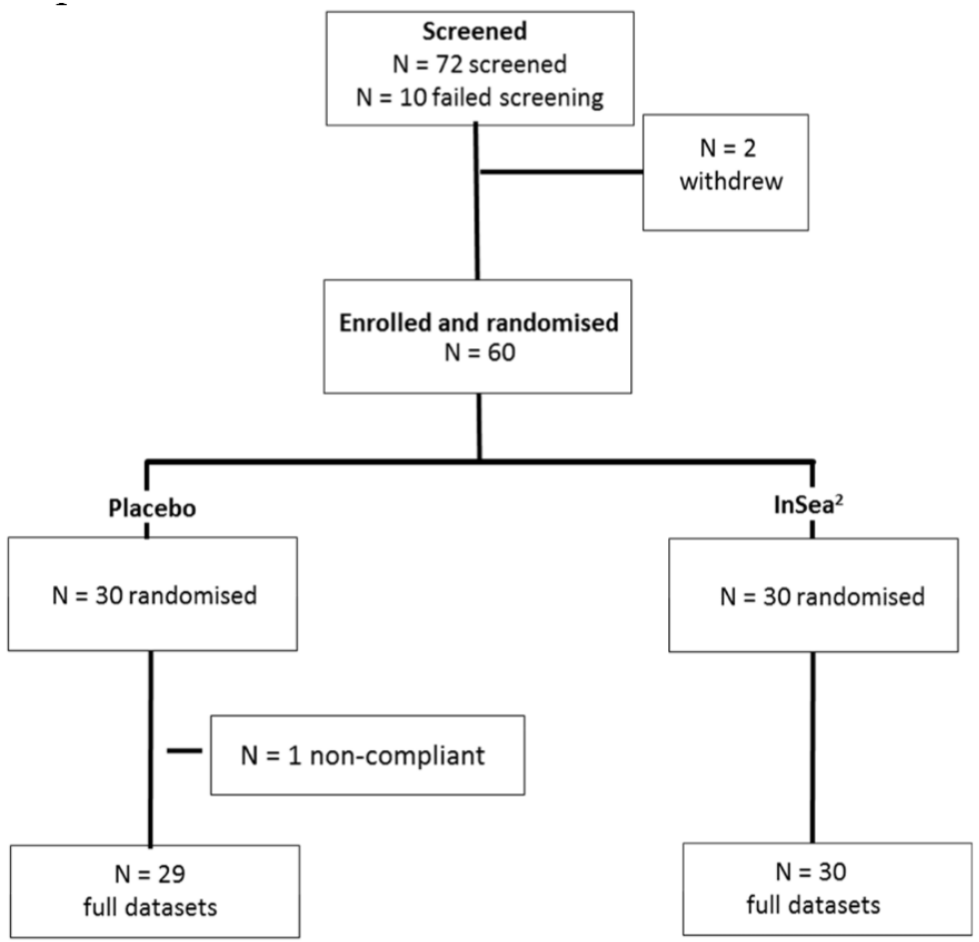


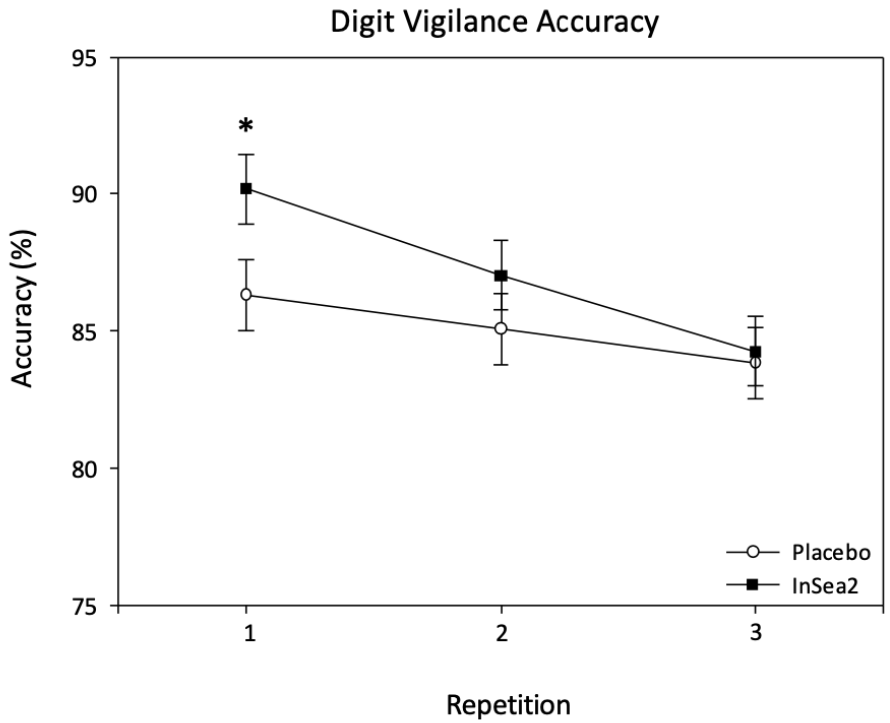
nutrients

MDPI

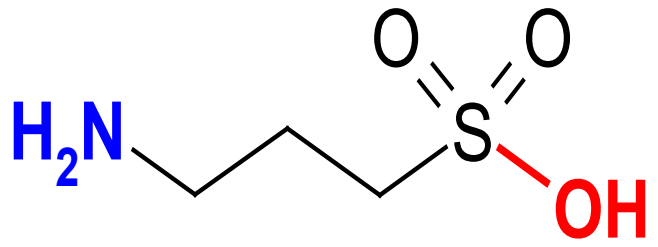
Article

Acute Post-Prandial Cognitive Effects of Brown Seaweed Extract in Humans





Aging Clinical and Experimental Research



- Homotaurine (Tramiprosate)

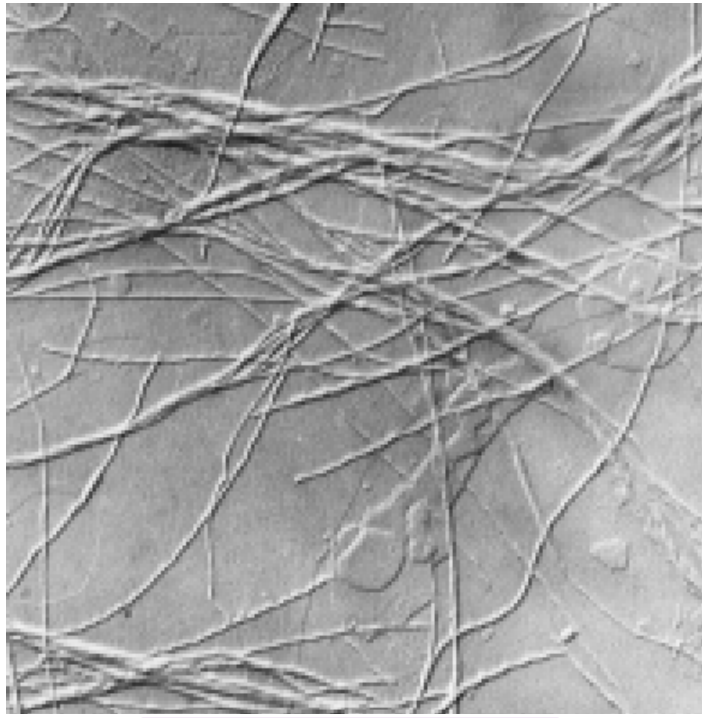
REVIEW ARTICLE

The potential protective effect of tramiprosate (homotaurine) against Alzheimer's disease: a review

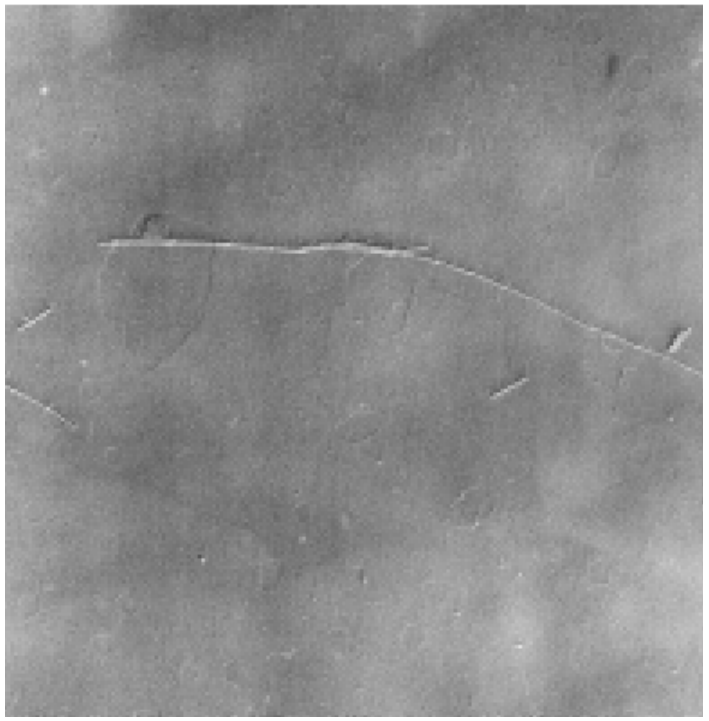
Carlo Caltagirone[1], Luigi Ferrannini[2], Niccolò Marchionni[3], Giuseppe Nappi[4], Giovanni Scapagnini[5] and Marco Trabucchi[6]

[1]Chair of Neurology, University of Roma Tor Vergata, and Scientific Director, IRCSS Santa Lucia Foundation, Rome, [2]Department of Mental Health and Addictions - ASL 3 Genoa, and President of the Italian Psychiatry Association, [3]Division of Geriatric Cardiology and Medicine, University of Florence, Azienda Ospedaliero-Universitaria Careggi, Florence, [4]Scientific Director, IRCCS "C. Mondino National Neurological Institute", Pavia, and Chair of Neurology, University "La Sapienza", Rome, [5]Department of Health Sciences, Faculty of Medicine and Surgery, University of Molise, Campobasso, [6]Geriatric Research Group, Brescia, Italy

Homotaurine Inhibits Formation of Toxic Amyloid Fibrils *in vitro*



Amyloid Aβ



Amyloid Aβ + homotaurine

24-hour incubation

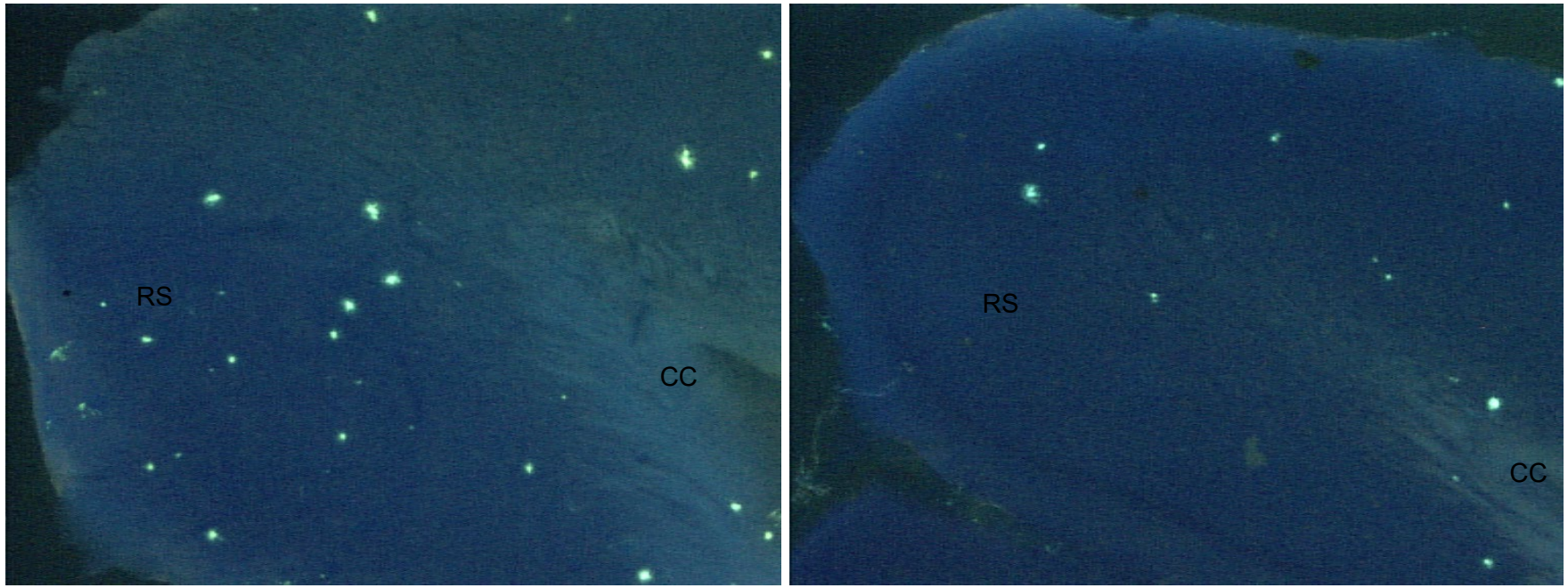
Aisen PS. Presented at: 9th International Geneva/Springfield Symposium on Advances in Alzheimer Therapy. April 2006.

Homotaurine Reduces Amyloid Deposition in hAPP Transgenic Mouse Brain

Control (untreated)

Homotaurine (100mg/kg/day)

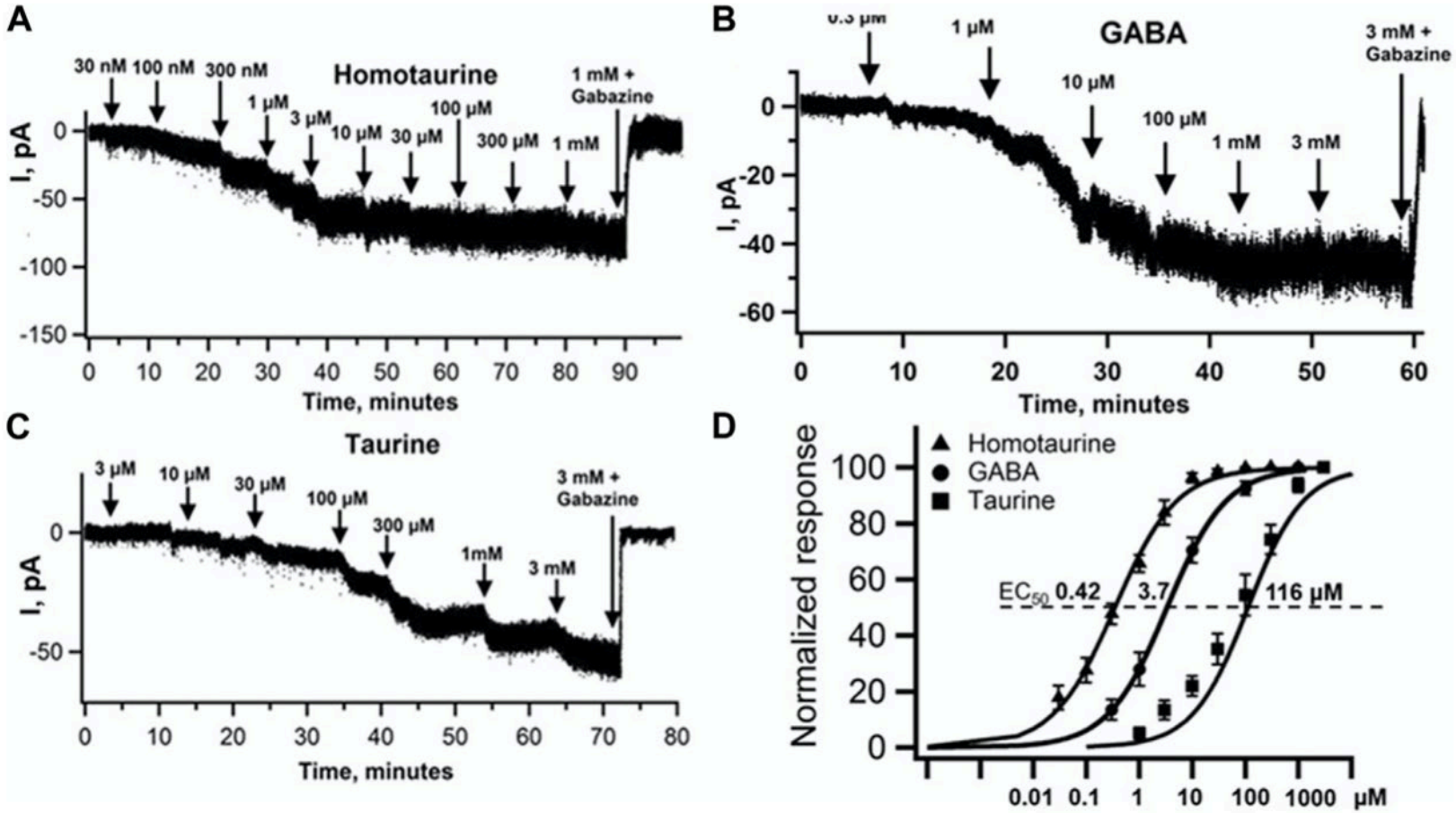
(8 weeks of treatment)



Gervais F et al. Neurobiol Aging 2007; 28(4):537-47.

$GABA_A$ receptors as plausible molecular targets and mediators for taurine and homotaurine actions

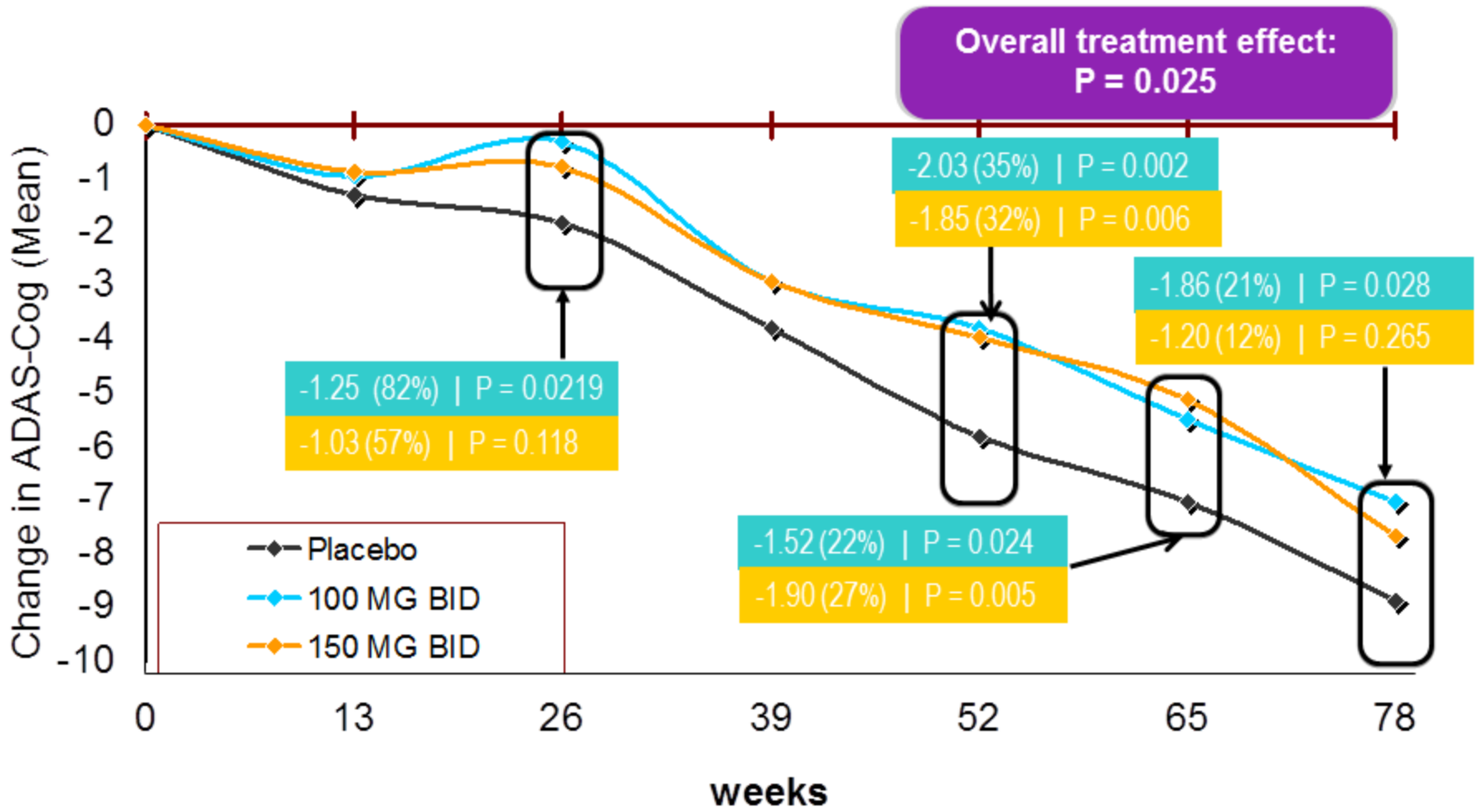
Pratap Meera [1], Mikko Uusi-Oukari [2], Gerald S. Lipshutz [3,4,5,6]* and Martin Wallner [3]*



16 Clinical Trials Involving > 2,000 Subjects

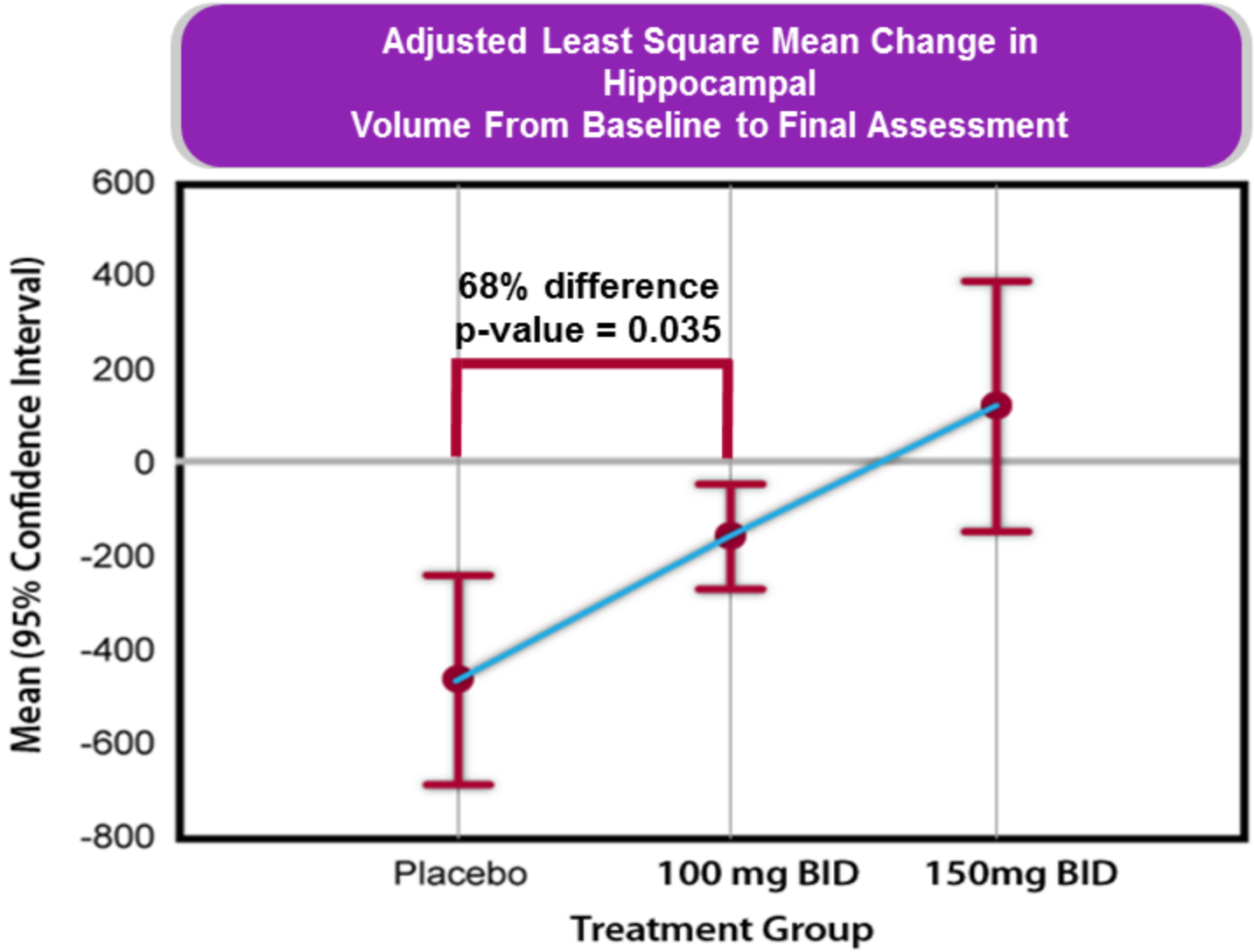
Studies	N	Population	Duration	Endpoints
10 Phase I	288	Healthy	7-10 days	Safety/PK
Phase II	58	AD	3 months	Cognitive function, Amyloid Aβ CSF level
Phase II Open-label extension	42	AD	41 months	Cognitive function
Phase II	24	Cerebral Amyloid Angiopathy	3 months	Neurological function, cognitive function
Phase III North America	1,052	AD	18 months	Cognitive function, brain volume
Phase III North America Open-label extension	738	AD	12 months	Cognitive function
Phase III Europe	975	AD	18 months	Cognitive function, brain volume

Homotaurine Reduces Cognitive Decline Significantly in AD Patients - ApoE4+



Adjusted by Mixed Effects Repeated Measures Model

Homotaurine Preserved Brain Volume by 68% vs. Control in AD Patients



Adjusted by Mixed Effects Model

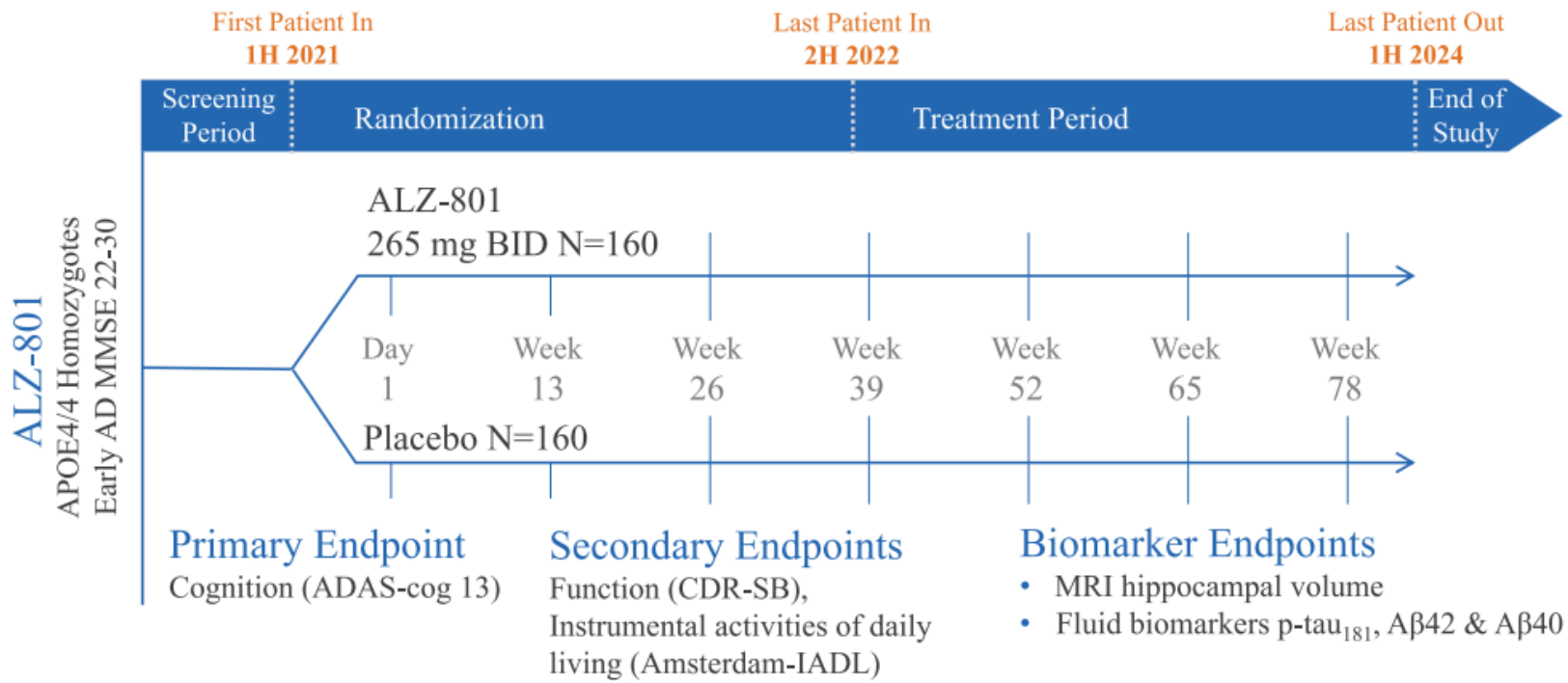
Received: 26 March 2024 | Revised: 24 June 2024 | Accepted: 18 July 2024

DOI: 10.1002/trc2.12498

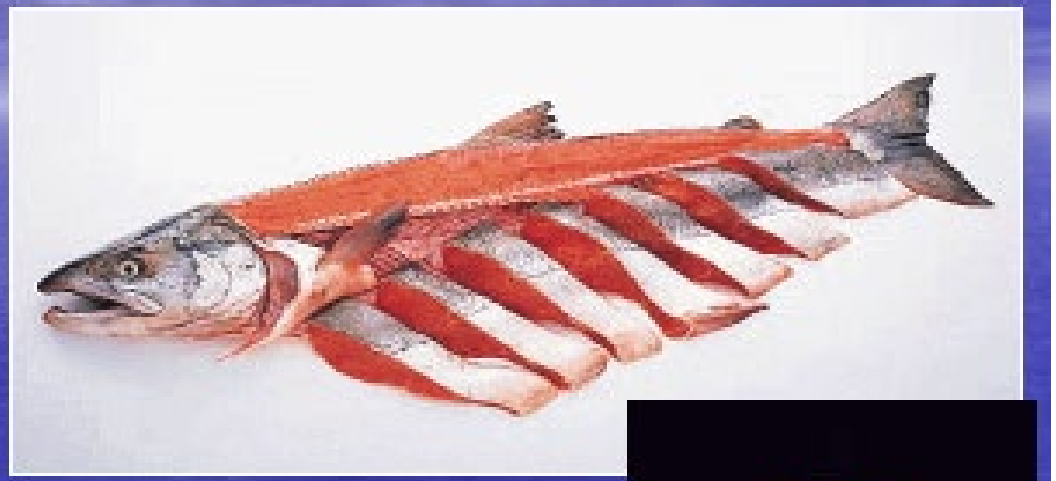
Alzheimer's & Dementia
Translational Research & Clinical Interventions

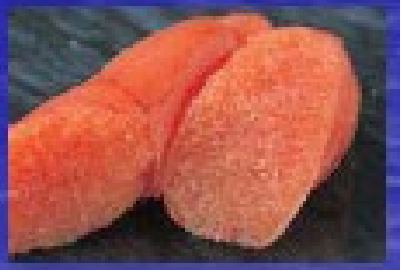
RESEARCH ARTICLE

APOLLOE4 Phase 3 study of oral ALZ-801/valiltramiprosate in *APOE* ε4/ε4 homozygotes with early Alzheimer's disease: Trial design and baseline characteristics

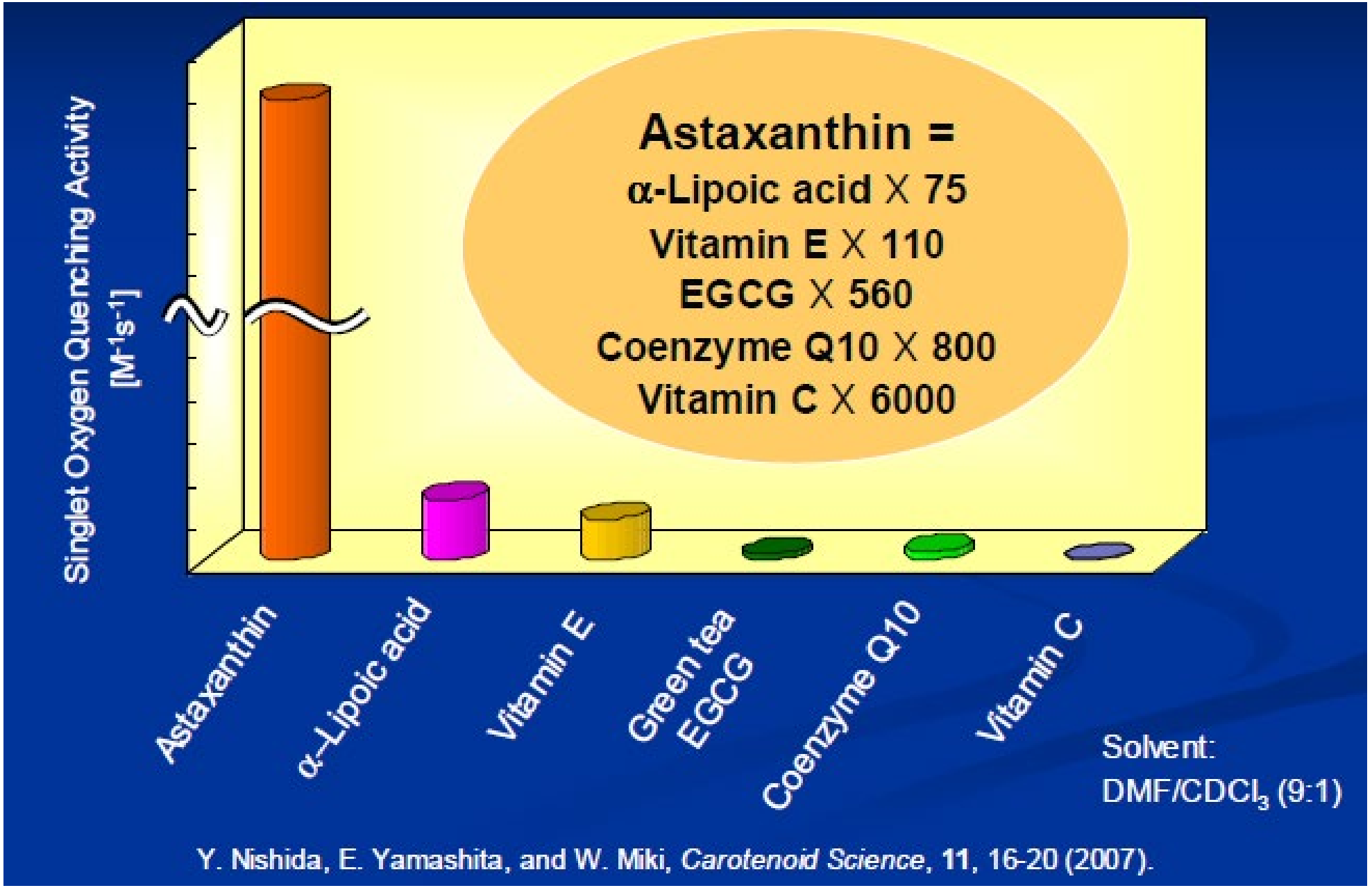


This Red Color is Astaxanthin





Astaxanthin the Most Powerful Natural Antioxidant



Y. Nishida, E. Yamashita, and W. Miki, *Carotenoid Science*, **11**, 16-20 (2007).

nutrients

MDPI

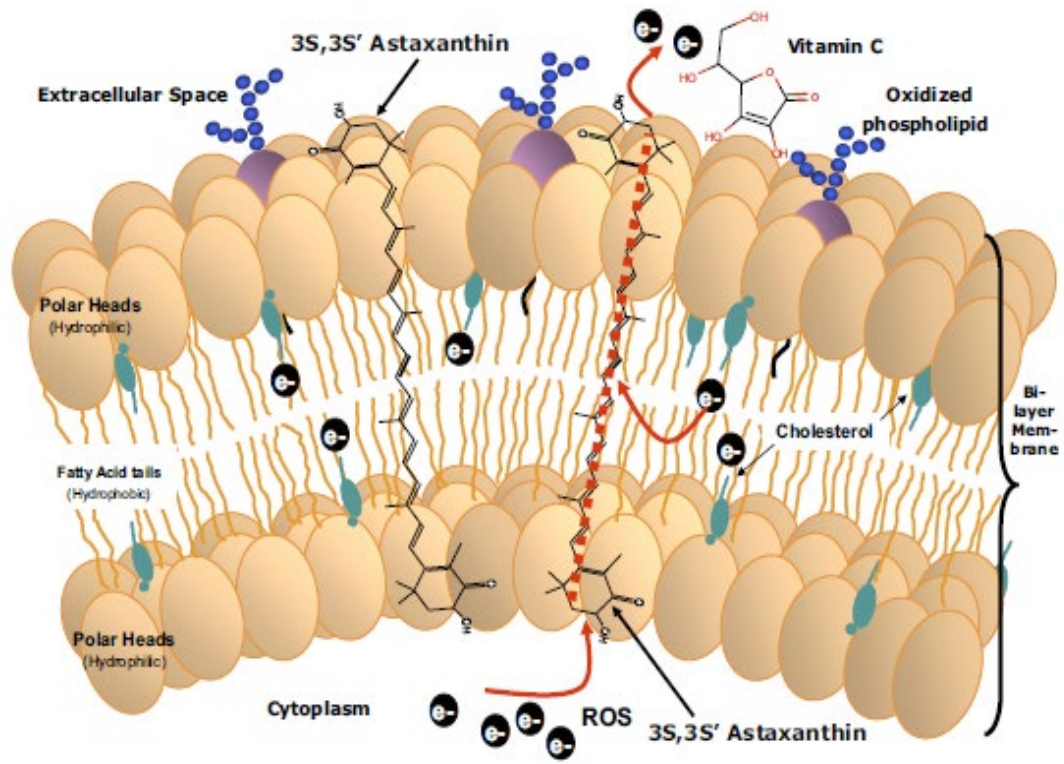
Review

Astaxanthin in Skin Health, Repair, and Disease: A Comprehensive Review

Sergio Davinelli [1,*], Michael E. Nielsen [2] and Giovanni Scapagnini [1]

Table 1. Summary of human intervention studies on skin and astaxanthin.

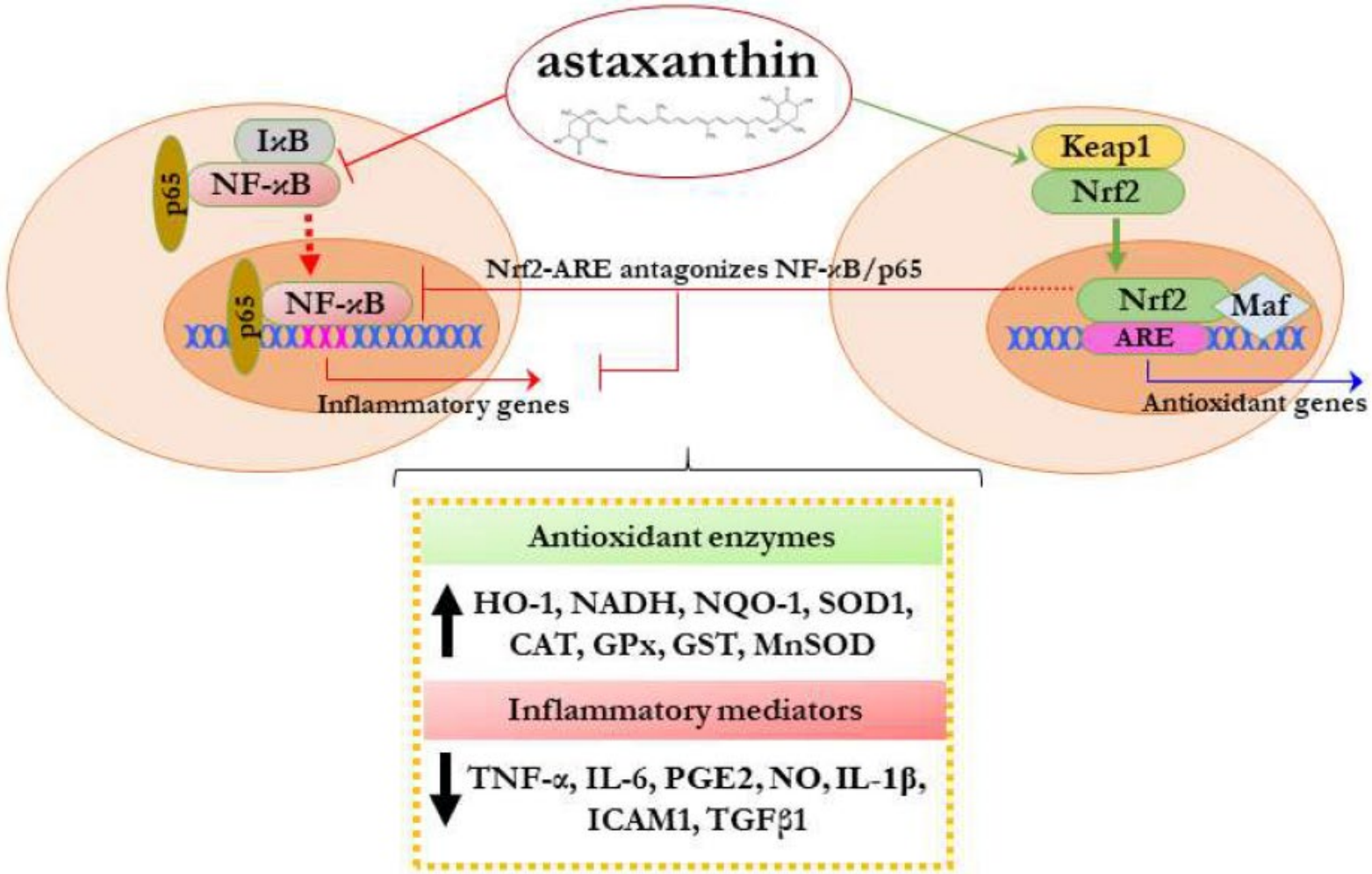
Intervention	Study Design	Control	Population (*n*)	Duration	Outcomes	Dosage	Author, Year
Administration of ASX capsules	Randomized double-blind, controlled study	Placebo	Healthy female subjects (14/diet group)	8 weeks	↓ DNA damage biomarkers; ↑ of NK cells, T cells, B cells, and IL-6	2 or 8 mg	Park, 2010
Administration of ASX capsules	Monitoring of oxidative stress and skin aging	None	31 middle-aged volunteers	4 weeks	↓ MDA; ↓ RSSC	4 mg	Chalyk, 2017
Administration of ASX capsules	Randomized, double-blind, parallel-group, placebo-controlled	Placebo	65 healthy female subjects	16 weeks	↓ Wrinkle parameters; ↓ IL-α	6 or 12 mg	Tominaga, 2017
Administration of ASX cream	Pilot study	None	3 healthy female subjects	2 weeks	↓ Wrinkle parameters	0.7 mg/g of ASX cream	Seki, 2001
Topical application of ASX	Pilot study	None	3 healthy male subjects	N/S	↓ erythema	N/S	Yamashita, 1995
Administration of ASX capsules	Randomized, single-blind, placebo-controlled	Placebo	49 healthy female subjects	6 weeks	↓ Wrinkle parameters	2 mg	Yamashita, 2006
Oral and topical treatment with ASX	N/S	N/S	28 healthy female subjects	8 weeks	↓ Wrinkle parameters	6 mg	Tominaga, 2009
Two oral forms (ASX capsules; tablets collagen)	Randomized, double-blind placebo-controlled	Placebo	44 healthy female volunteers	12 weeks	↑ viscoelastic parameters; ↓ TEWL; ↑ procollagen type I; ↓ MMP-1 and MMP-12	2 mg	Yoon, 2014
Capsules of ASX combined with topical application of ASX	Open-label noncontrolled	None	30 healthy female subjects	8 weeks	↓ wrinkles; ↓ age spot size; ↑ elasticity; ↑ skin texture	6 mg and 2 mL (78.9 μM solution)	Tominaga, 2012
Administration of ASX capsules	Randomized double-blind controlled	Placebo	36 healthy male subjects	6 weeks	↓ wrinkles; ↑ elasticity; ↓ TEWL; ↑ moisture content; ↓ sebum oil	6 mg	Tominaga, 2012



Astaxanthin as a Modulator of Nrf2, NF-κB, and Their Crosstalk: Molecular Mechanisms and Possible Clinical Applications

Molecules **2022**, *27*, 502.

Sergio Davinelli [1,*], Luciano Saso [2], Floriana D'Angeli [3], Vittorio Calabrese [3], Mariano Intrieri [1] and Giovanni Scapagnini [1]

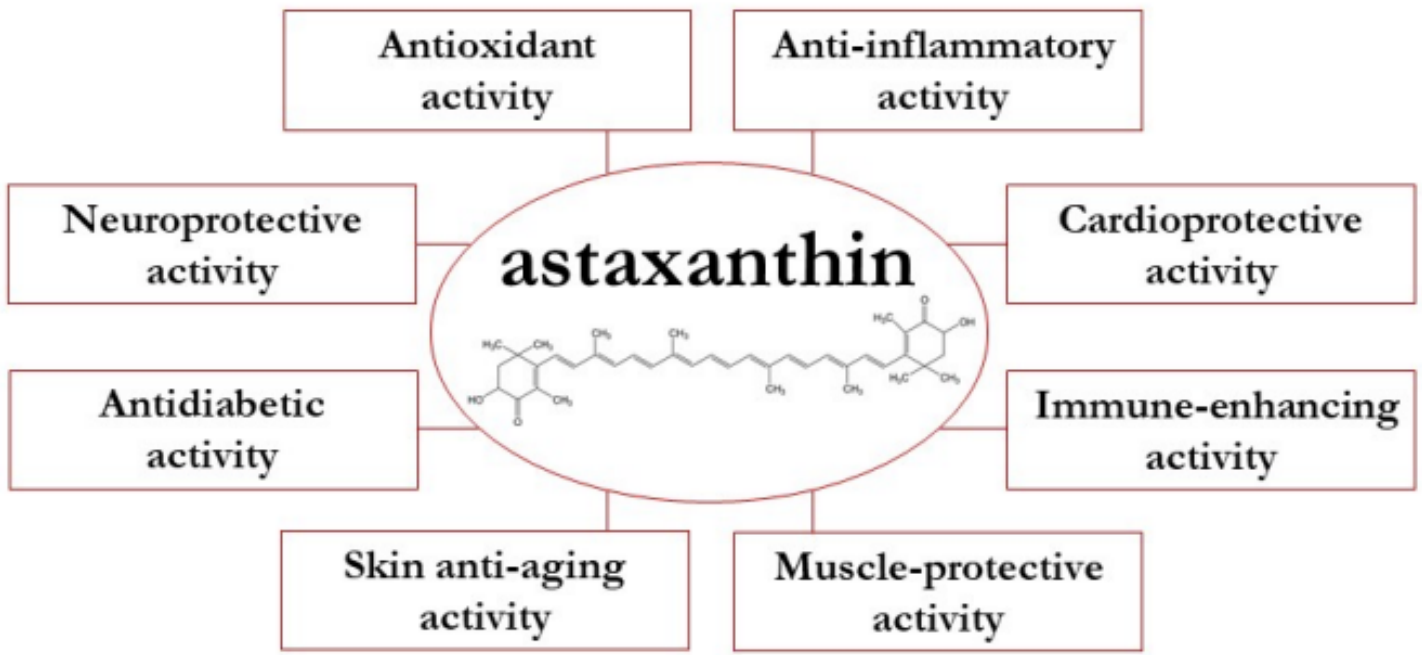


molecules *Molecules* **2022**, *27*, 502. https://doi.org/10.3390/molecules27020502 MDPI

Review

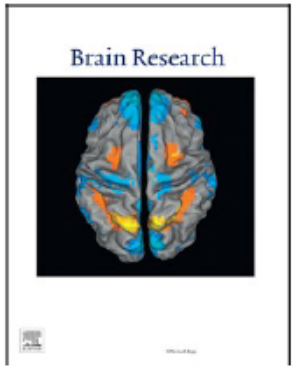
Astaxanthin as a Modulator of Nrf2, NF-κB, and Their Crosstalk: Molecular Mechanisms and Possible Clinical Applications

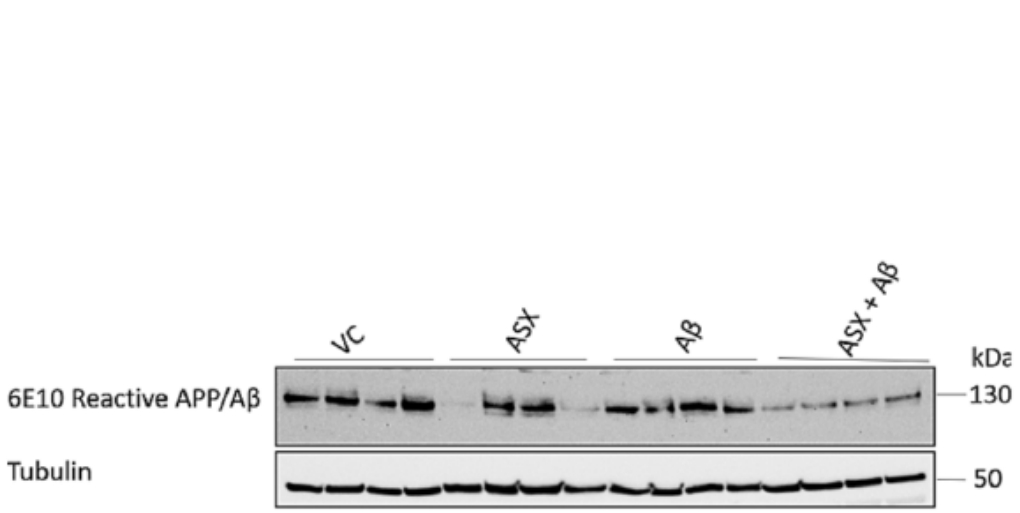
Sergio Davinelli [1,*], Luciano Saso [2], Floriana D'Angeli [3], Vittorio Calabrese [3], Mariano Intrieri [1] and Giovanni Scapagnini [1]

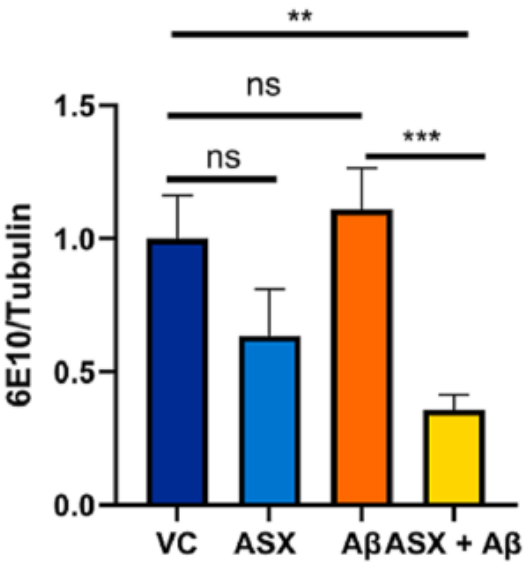


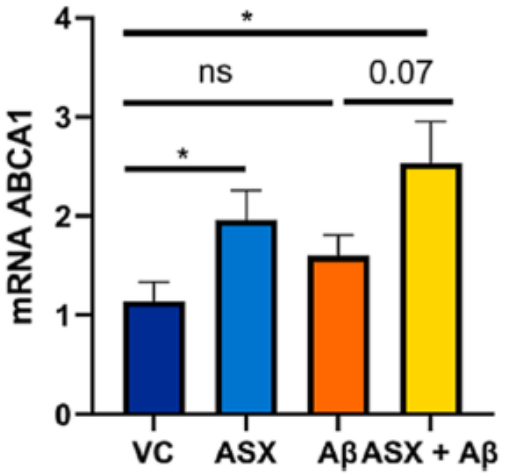
Brain Research 1819 (2023) 148518

Astaxanthin enhances autophagy, amyloid beta clearance and exerts anti-inflammatory effects in *in vitro* models of Alzheimer's disease-related blood brain barrier dysfunction and inflammation







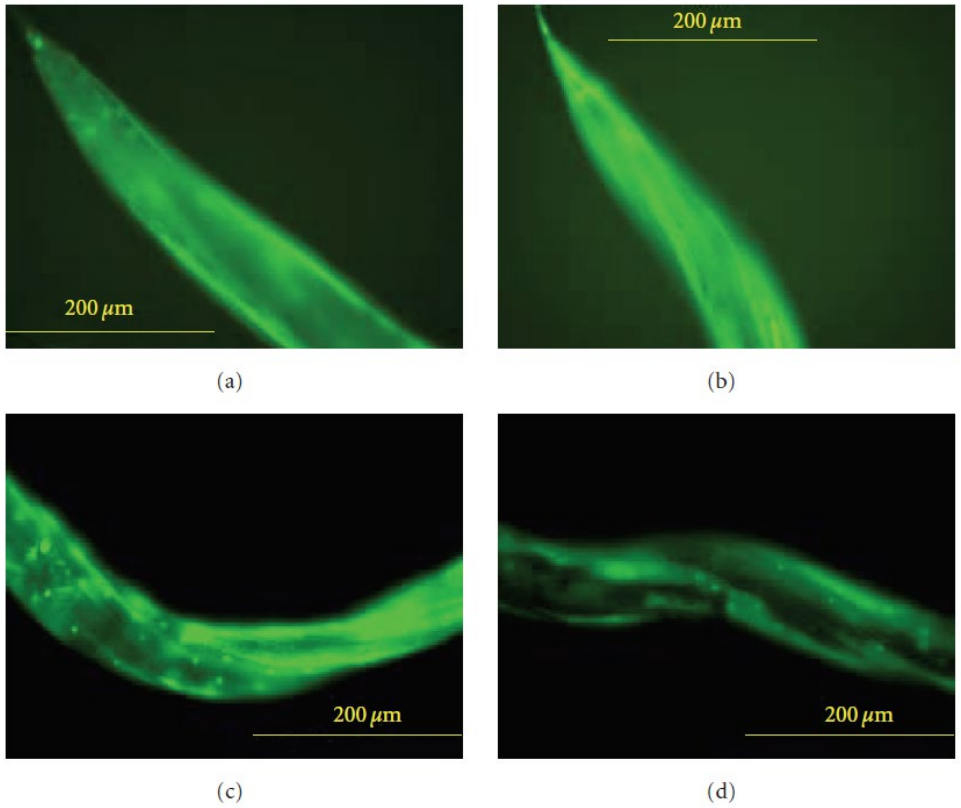


ASX reduces protein expression of APP/Aβ as well as increases expression of genes involved in Aβ clearance in Aβ-treated pBCECs.

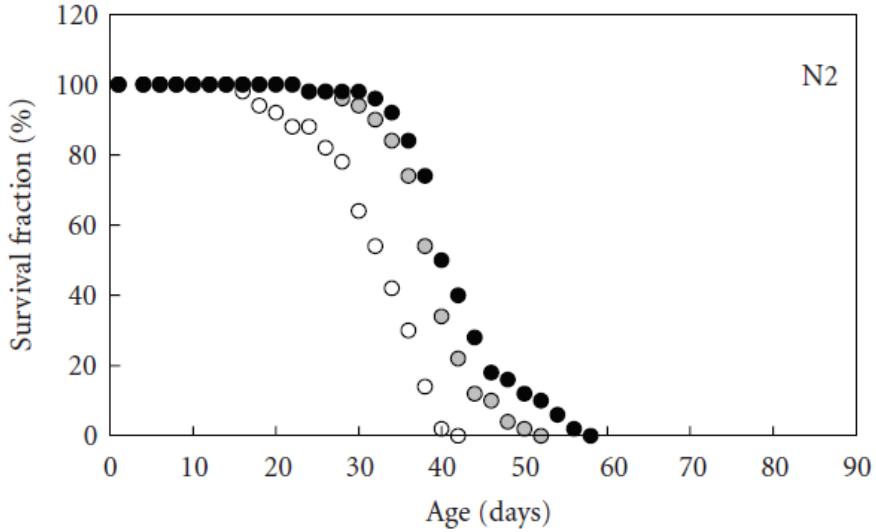
Oxidative Medicine and Cellular Longevity 2011

Supplemental Cellular Protection by a Carotenoid Extends Lifespan via Ins/IGF-1 Signaling in *Caenorhabditis elegans*

Koumei Yazaki, Chinatsu Yoshikoshi, Satoru Oshiro, and Sumino Yanase



Localization of DAF-16/FOXO : GFP

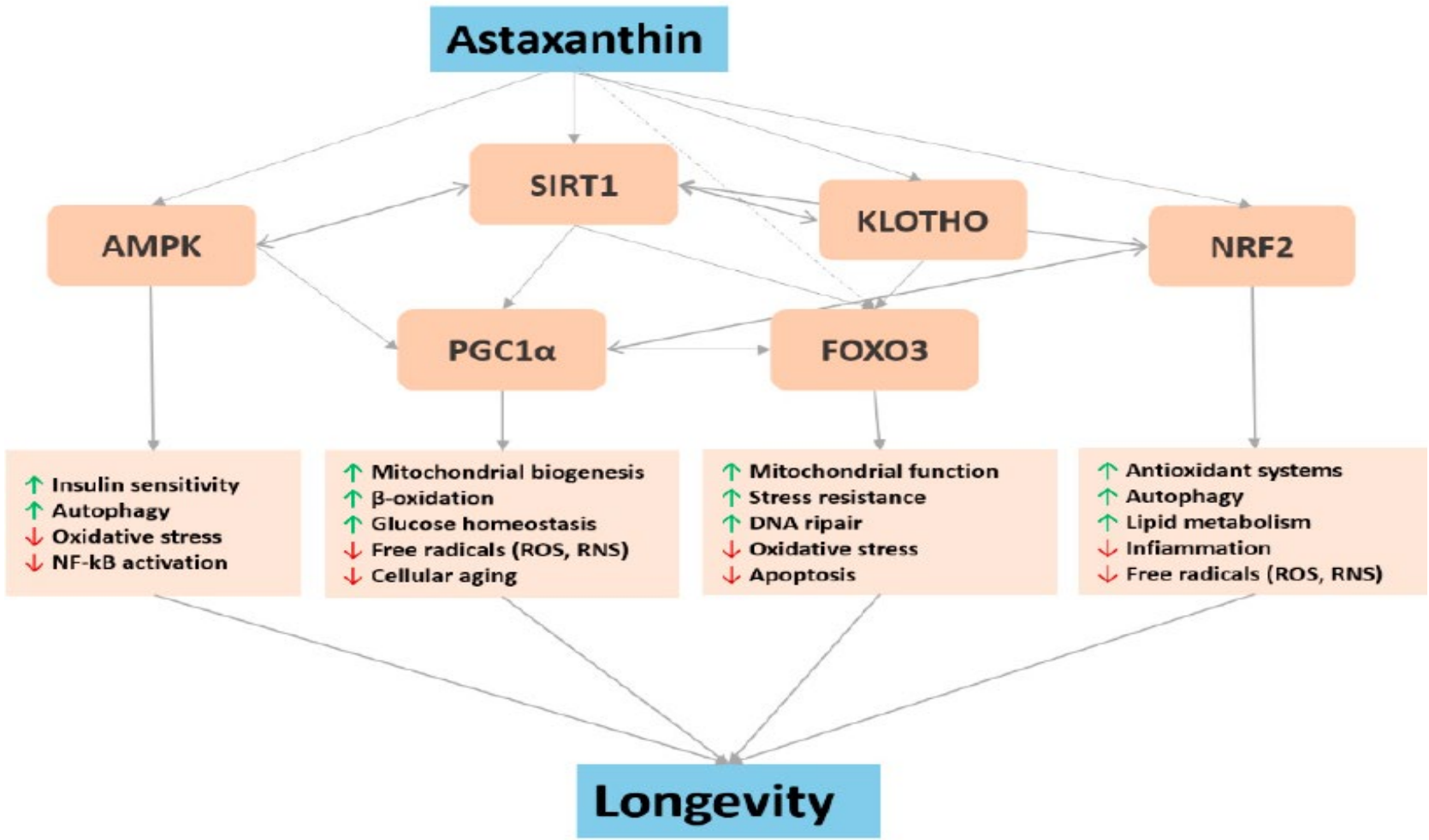


AX-containing NGM plates for measurement of lifespan in nematode

Astaxanthin as a Putative Geroprotector: Molecular Basis and Focus on Brain Aging

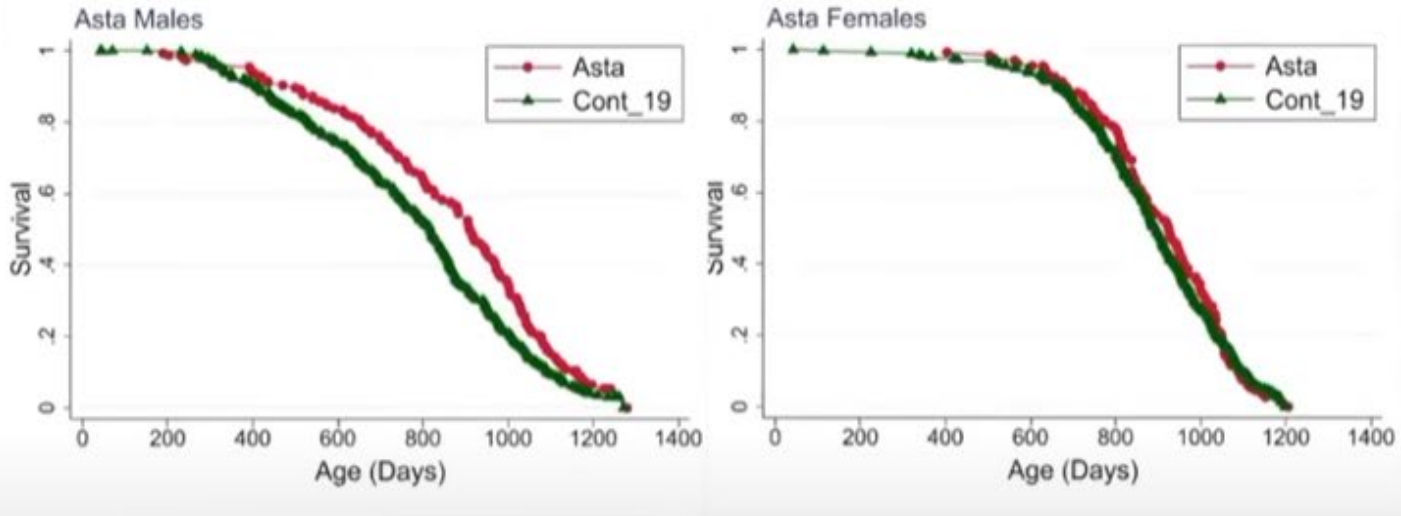
Mar. Drugs 2020, *18*, 351

Vincenzo Sorrenti [1,2,*], Sergio Davinelli [3], Giovanni Scapagnini [3], Bradley J. Willcox [4,5], Richard C. Allsopp [6] and Donald C. Willcox [4,5,7]



C2019: Astaxanthin

"Anti-oxidant" – Brad Willcox and Richard Allsopp
OTC for human use



12% increase in median
p = 0.003

3% increase in median
p = 0.6

Healthy Longevity

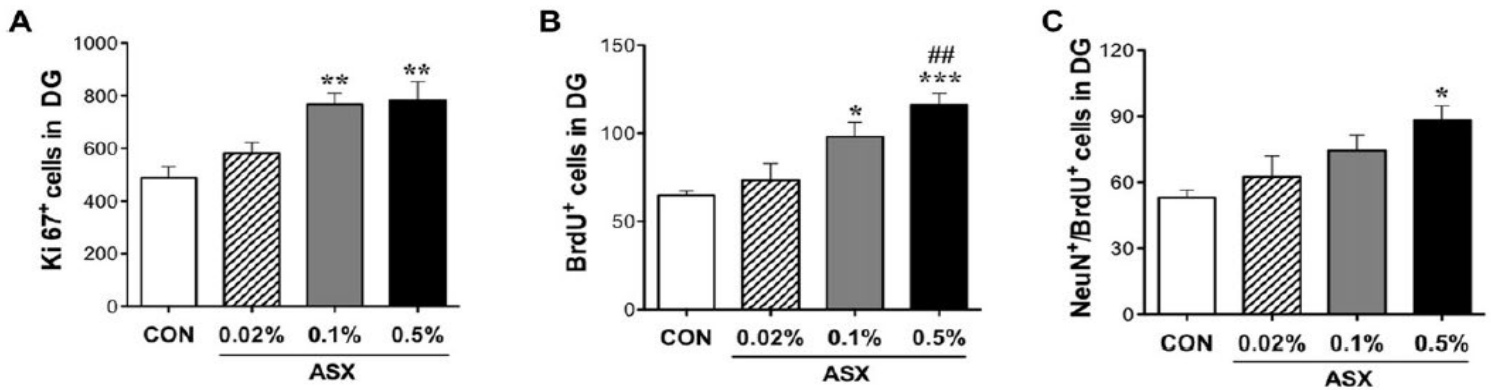
NUS National University of Singapore | Yong Loo Lin School of Medicine

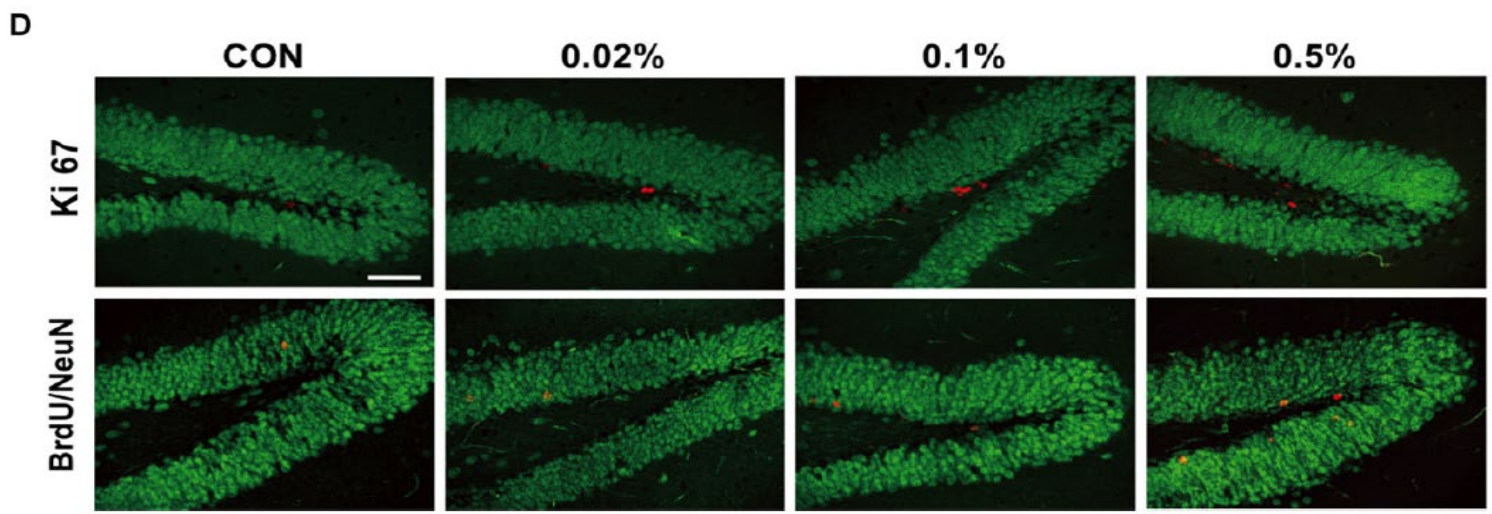
Mol. Nutr. Food Res. 2016, *60*, 589–599

RESEARCH ARTICLE

Astaxanthin supplementation enhances adult hippocampal neurogenesis and spatial memory in mice

Jang Soo Yook[1], Masahiro Okamoto[1], Randeep Rakwal[2], Junko Shibato[1], Min Chul Lee[1,3], Takashi Matsui[1], Hyukki Chang[4], Joon Yong Cho[5] and Hideaki Soya[1]





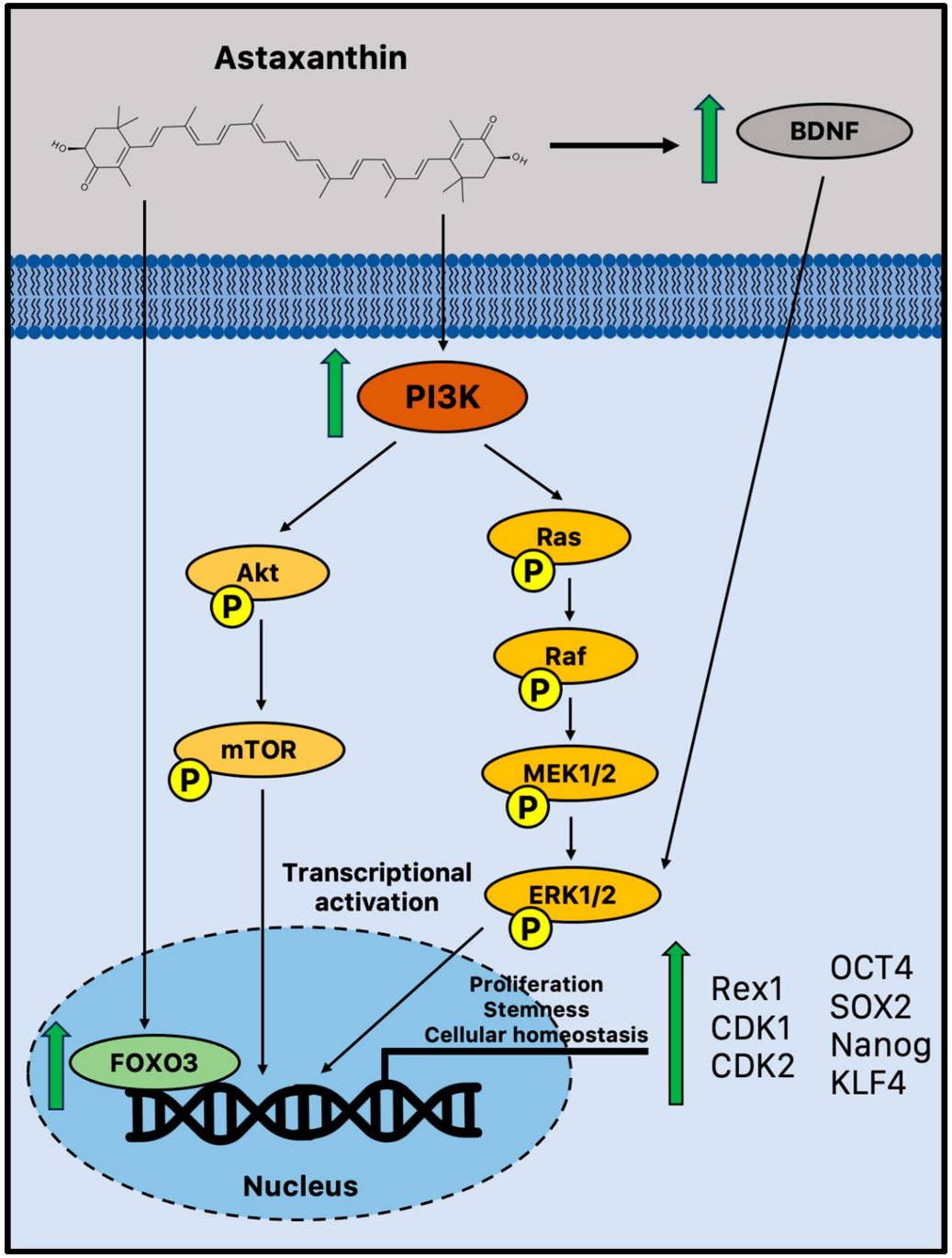
marine drugs

Mar. Drugs **2023**, *21*, 643

Dietary Astaxanthin: A Promising Antioxidant and Anti-Inflammatory Agent for Brain Aging and Adult Neurogenesis

Alessandro Medoro [1], Sergio Davinelli [1], Luigi Milella [2], Bradley J. Willcox [3,4], Richard C. Allsopp [3,5], Giovanni Scapagnini [1,*] and Donald Craig Willcox [3,4,6]

The unique chemical structure of astaxanthin enables it to cross the blood–brain barrier and easily reach the brain, where it may positively influence adult neurogenesis. Astaxanthin can affect molecular pathways involved in the homeostasis, through the activation of FOXO3-related genetic pathways, growth, and regeneration of adult brain neurons, enhancing cell proliferation and the potency of stem cells in neural progenitor cells.



antioxidants

Antioxidants 2021, 10, 223.

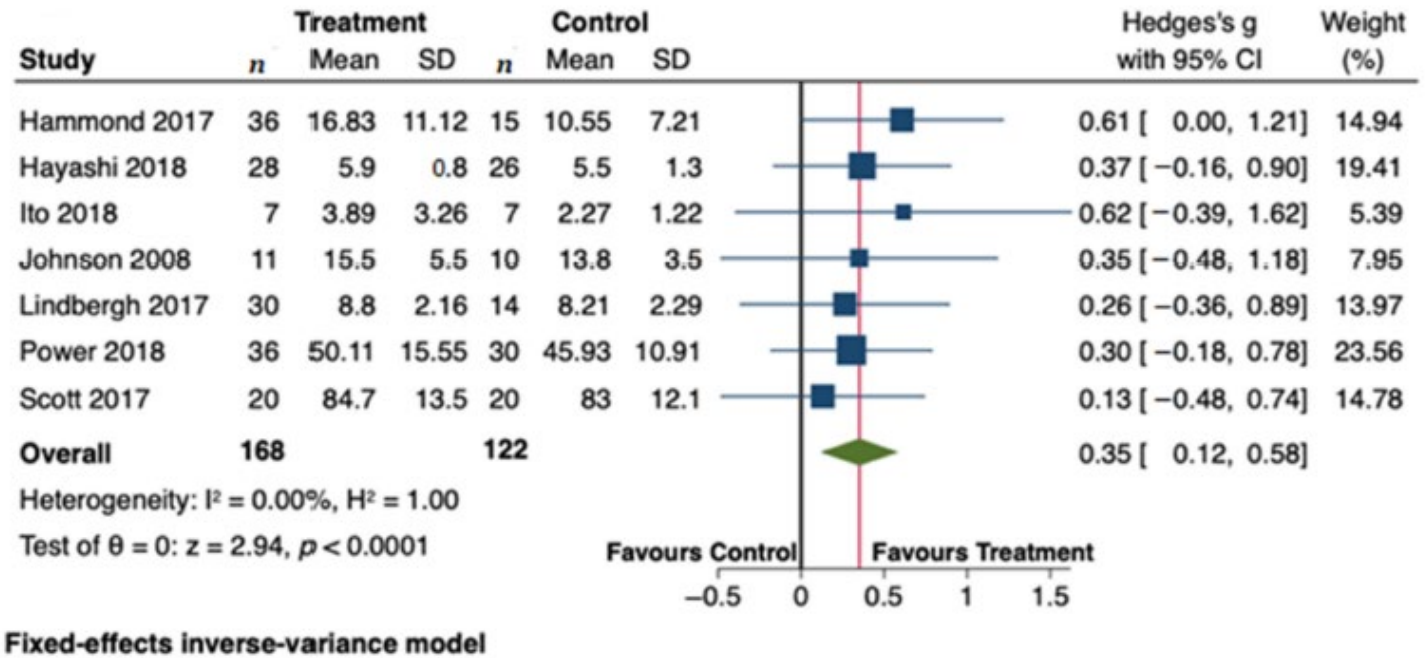
MDPI

Review

Carotenoids and Cognitive Outcomes: A Meta-Analysis of Randomized Intervention Trials

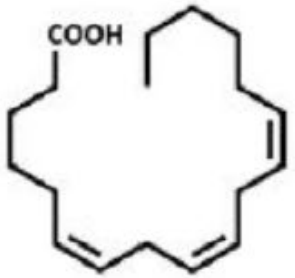
Sergio Davinelli [1,*], Sawan Ali [1], Vincenzo Solfrizzi [2], Giovanni Scapagnini [1] and Graziamaria Corbi [1]

In conclusion, these results highlight the potential role of carotenoids in the protection of mental functions even in subjects without cognitive impairment.

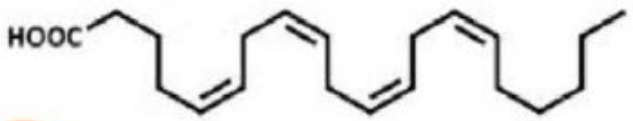


OMEGA 6

linoleic acid
LA

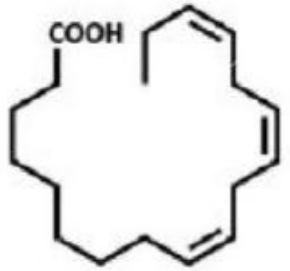


gamma linolenic acid
GLA

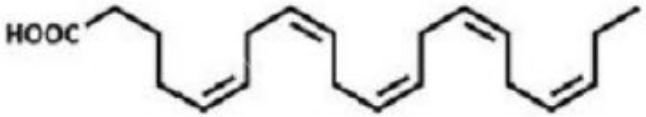


arachidonic acid
AA

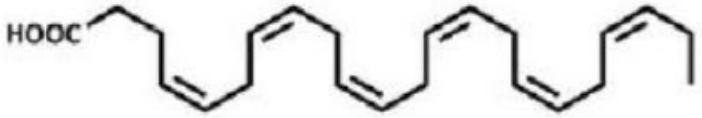
OMEGA 3



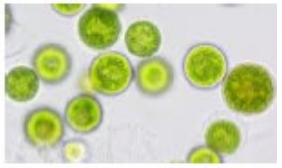
alpha linolenic acid
ALA



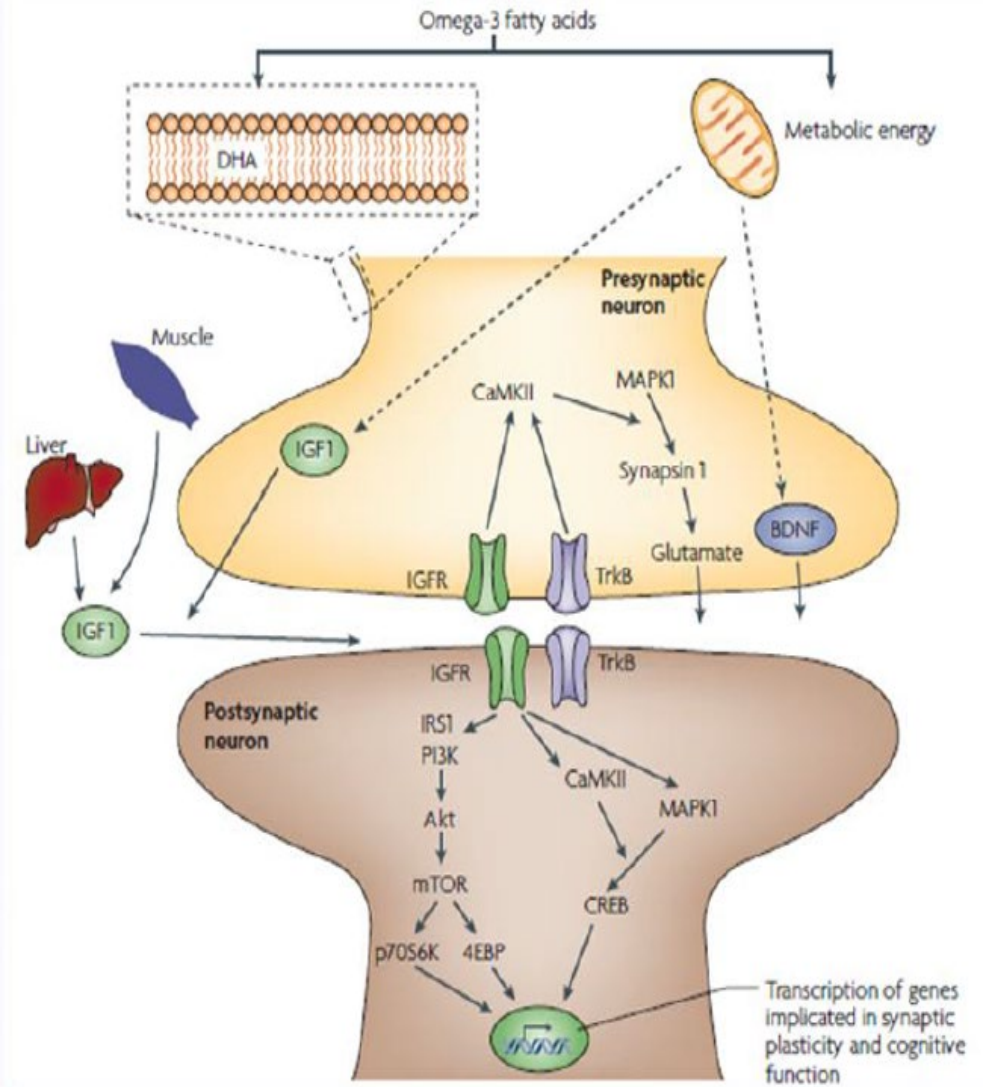
eicosapentaenoic acid
EPA



docosahexanoic acid
DHA

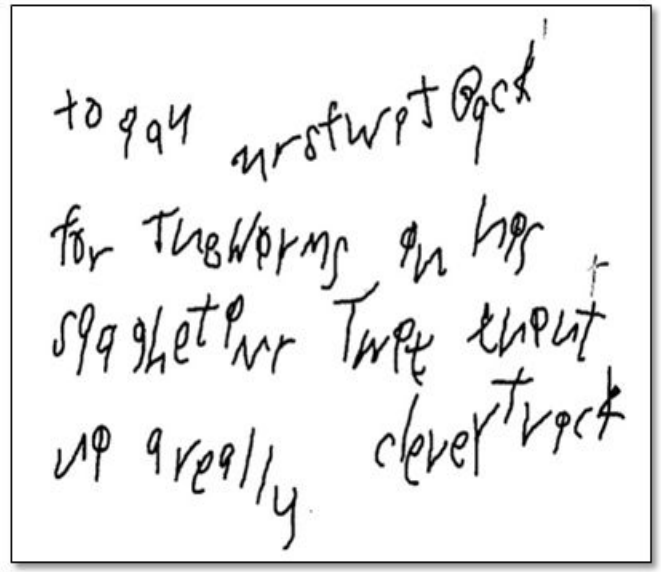


Dietary omega-3 fatty acids can affect synaptic plasticity and cognition.



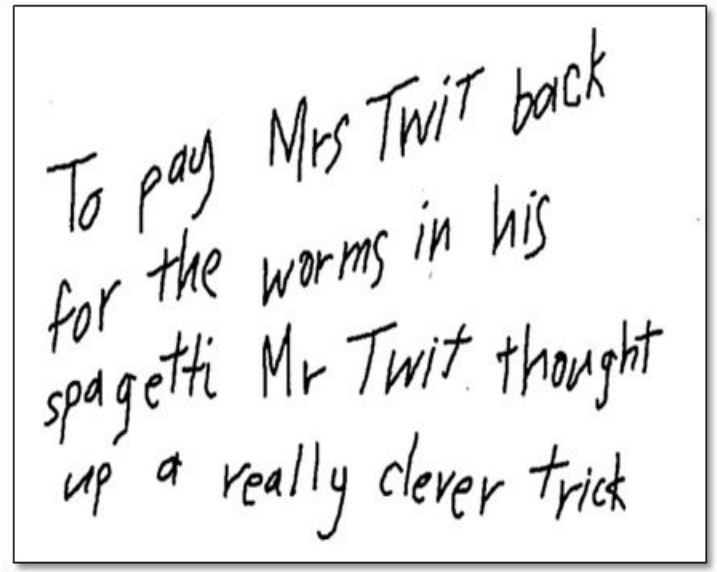
Performance & Learning

BEFORE



A six year old child's handwriting on a Junk Food diet.

AFTER



Six year old child's handwriting after one month of *change in diet.

First published:13 April 2020

alzheimer's association | Alzheimer's & Dementia®
THE JOURNAL OF THE ALZHEIMER'S ASSOCIATION

Adherence to a Mediterranean diet and cognitive function in the Age-Related Eye Disease Studies 1 & 2

Tiarnán D. Keenan, Elvira Agrón, Julie A. Mares, Traci E. Clemons, Freekje van Asten, Anand Swaroop, Emily Y. Chew ✉, for the AREDS and AREDS2 Research Groups

7,756 participants enrolled in two randomized trials of nutritional supplements for age-related macular degeneration: Age-Related Eye Disease Study (AREDS) and AREDS2.

Closer Mediterranean diet adherence was associated with lower risk of cognitive impairment but not slower decline in cognitive function.

Fish intake was associated with higher cognitive function. In AREDS2, rate of cognitive decline over 5 to 10 years was not significantly different by a MED but was significantly slower (P = .019) with higher fish intake.

Published in final edited form as:

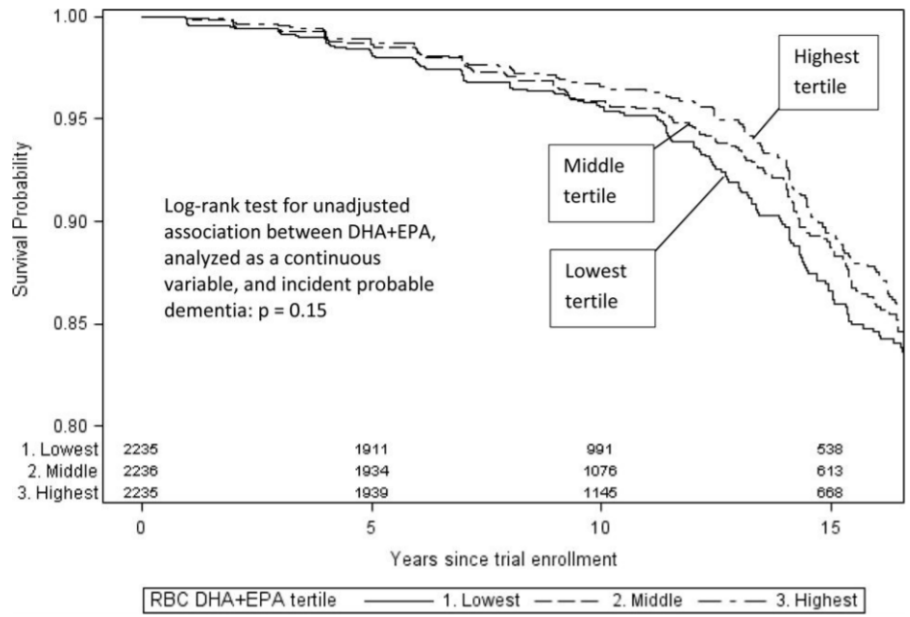
Prostaglandins Leukot Essent Fatty Acids. 2017 June ; 121: 68–75. doi:10.1016/j.plefa.2017.06.006.

Erythrocyte omega-3 fatty acids are inversely associated with incident dementia: Secondary analyses of longitudinal data from the Women's Health Initiative Memory Study (WHIMS)

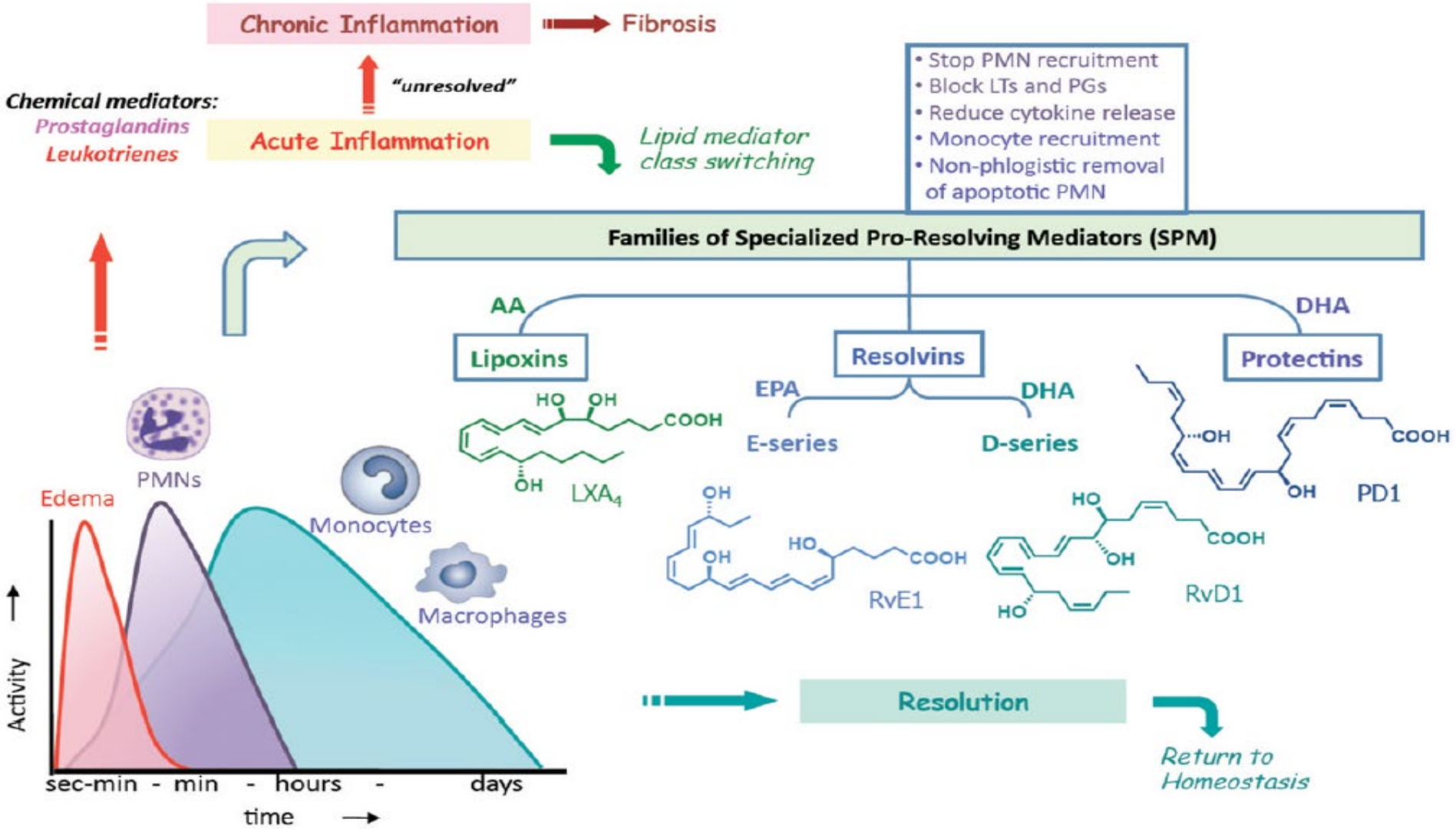
Eric M. Ammann, PhD[a], **James V. Pottala, PhD**[b], **Jennifer G. Robinson, MD MPH**[a,c], **Mark A. Espeland, PhD**[d], and **William S. Harris, PhD**[b,e,*]

Highlights

- We examined the association between erythrocyte EPA+DHA and risk for incident dementia in 6706 women in the USA.
- After about 10 years of follow-up and after appropriate adjustments, we found a significant, 8% decreased risk for probable dementia associated with a 1-SD increase in EPA+DHA.
- This large study confirms previous research suggesting that higher EPA+DHA levels may be protective against dementia.



Inflammatory response and resolution time course: Roles of pro-resolving lipid mediators.

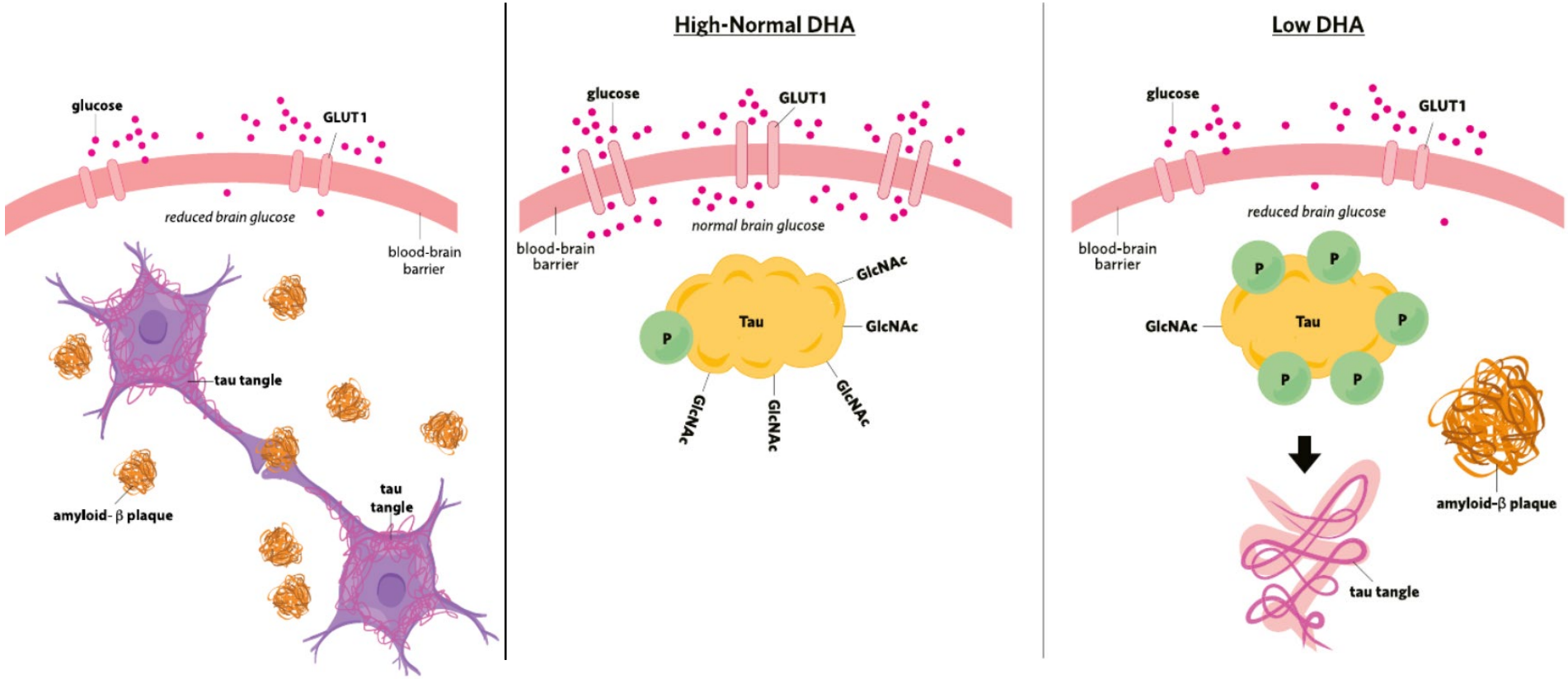


Serhan and Petasis Chem Rev. 2011

The FASEB Journal 2019

Role of phosphatidylcholine-DHA in preventing APOE4-associated Alzheimer's disease

Rhonda P. Patrick[1]



AD is associated with decreased GLUT1 transporters and glucose uptake, tau tangles inside of neurons, and amyloid-b plaques in the extracellular space between neurons.

DHA regulates brain glucose uptake, which prevents amyloid-b plaque and tau tangle formation

Low DHA concentrations in the brain reduce GLUT1 transporter expression, which leads to increased tau phosphorylation and promotes amyloid-b plaque formation.

EBioMedicine 59 (2020) 102883

Contents lists available at ScienceDirect

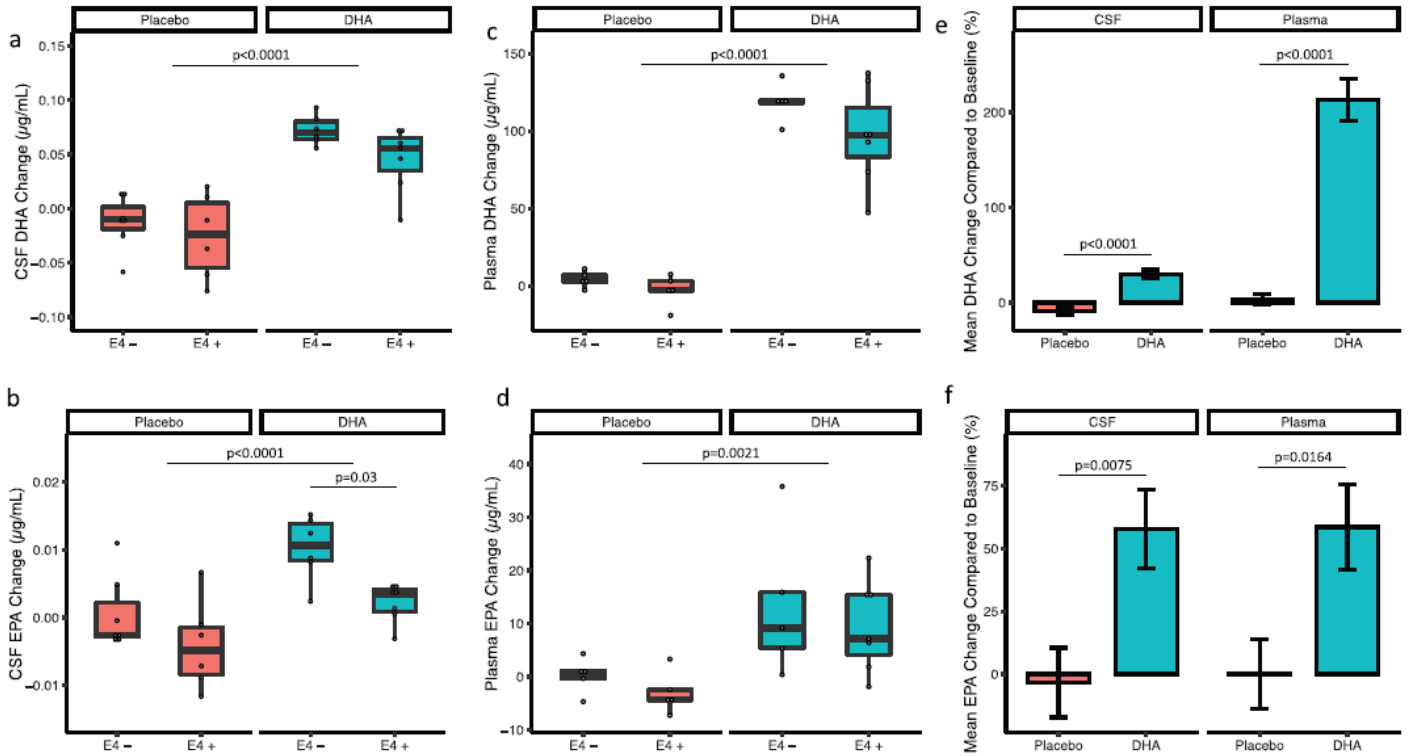
EBioMedicine

journal homepage: www.elsevier.com/locate/ebiom

Research paper

Brain delivery of supplemental docosahexaenoic acid (DHA): A randomized placebo-controlled clinical trial

Isabella C. Arellanes[a,1], Nicholas Choe[a,1], Victoria Solomon[a,1], Xulei He[a], Brian Kavin[a], Ashley E. Martinez[a], Naoko Kono[b], David P. Buennagel[c], Nalini Hazra[d], Giselle Kim[d], Lina M. D'Orazio[e], Carol McCleary[e], Abhay Sagare[f], Berislav V. Zlokovic[f], Howard N. Hodis[a,b], Wendy J. Mack[b], Helena C. Chui[e], Michael G. Harrington[c,e], Meredith N. Braskie[d], Lon S. Schneider[e,g], Hussein N. Yassine[a,e,*]



Added value of this study

In this placebo-controlled trial, cognitively unimpaired adults were provided with a vitamin B complex and randomized to 2 gs per day of DHA supplementation or placebo over 6 months. A modest increase in cerebrospinal fluid (CSF) DHA levels was observed following supplementation, with *APOE4* carriers having a lower increase than non-carriers.

Implications of all the available evidence

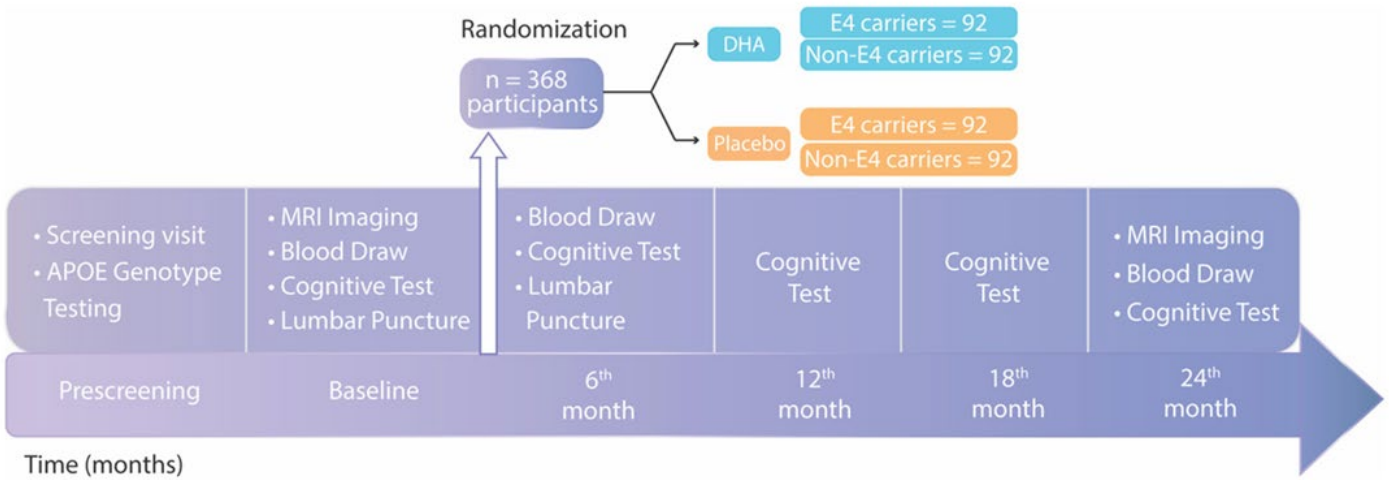
Dementia prevention trials that use omega-3 doses of equal or less than 1 g per day may have reduced brain effects, and especially for *APOE4* carriers.

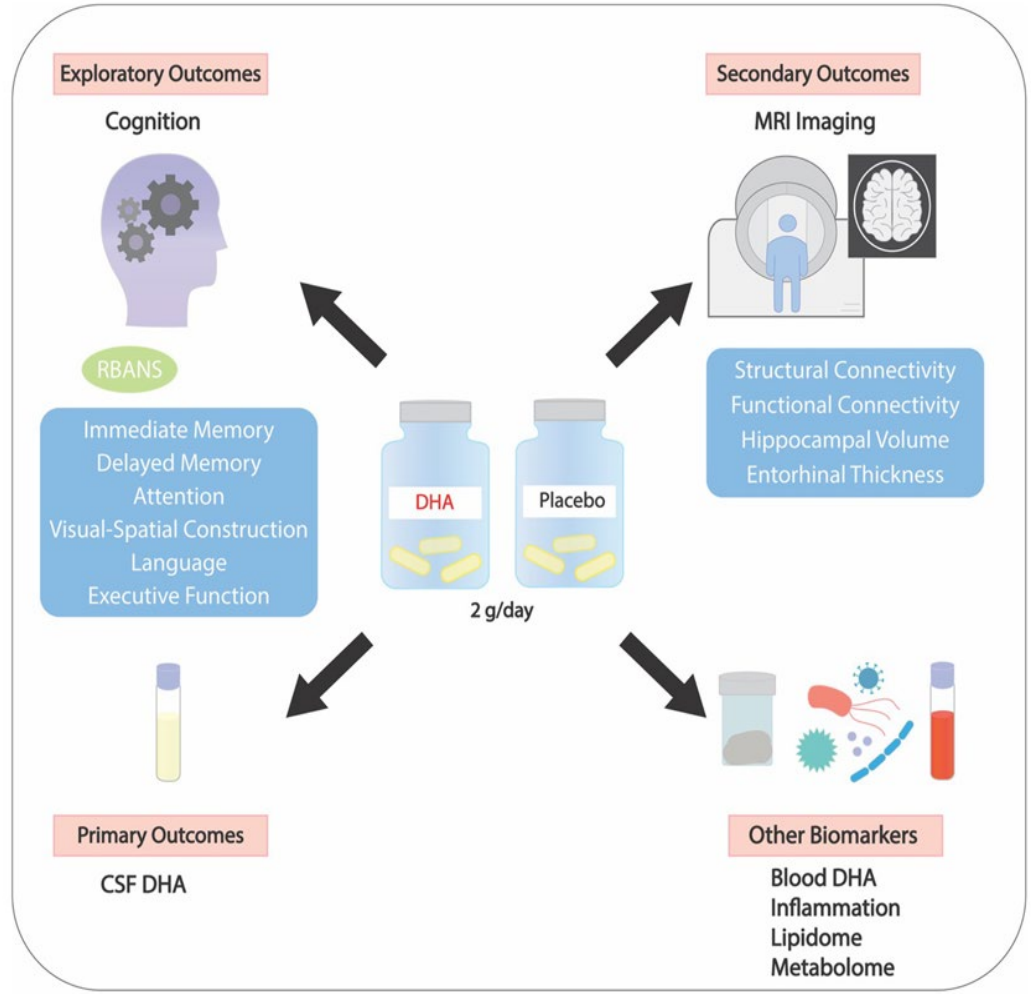
J Prev Alz Dis 2023;4(10):810-820
Published online June 19, 2023, http://dx.doi.org/10.14283/jpad.2023.77

Original Research

Baseline Findings of PreventE4: A Double-Blind Placebo Controlled Clinical Trial Testing High Dose DHA in APOE4 Carriers before the Onset of Dementia

H.N. Yassine[1,2], I.C. Arellanes[1], A. Mazmanian[1], L. De La Cruz[1], J. Martinez[1], L. Contreras[1], N. Kono[3], B.S. Liu[1], D. Badie[1], M.A. Bantugan[1], A. Grindon[1], T. Urich[1], L. D'Orazio[2], B.A. Emmanuel[2], H.C. Chui[2], W.J. Mack[3], M.G. Harrington[2], M.N. Braskie[4], L.S. Schneider[5]





LO-MAPT STUDY

Making dementia a priority:
changing perceptions, practice and policy.

Clinicaltrials.gov identifier	NCT03691519

Study Design

Study Type : Interventional (Clinical Trial)
Actual Enrollment : 774 participants
Allocation: Randomized

1. Study Information	
Name of the study	Prevention of cognitive decline in older adults with low Dha/Epa index in red blood cells
Study sponsor	University Hospital, Toulouse
Disease	At risk of developing Alzheimer's disease
Phase	Phase III

2. Information about the drug that will be tested in the study	
Name of drug	Omega-3
Administration	Three capsules taken orally per day


FRANCESCO CINELLI
GIOVANNI SCAPAGNINI
L'EDEN SOMMERSO
VIAGGIO NELLA SCIENZA DELLE ALGHE: ALIMENTAZIONE, LONGEVITÀ E SOSTENIBILITÀ
MONDADORI