
The Wahls Protocol® Seminar

Combating Neurodegeneration

A4M September 2020

Terry Wahls, MD, IFM

Clinical Professor of Medicine

Depts. Internal Medicine/ Neurology

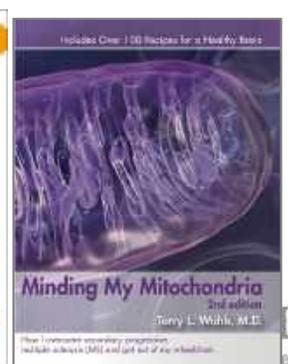
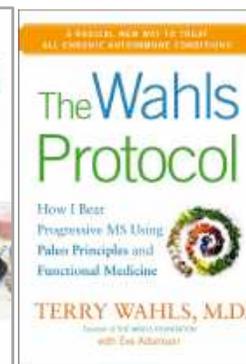
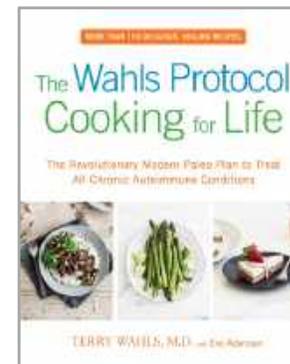
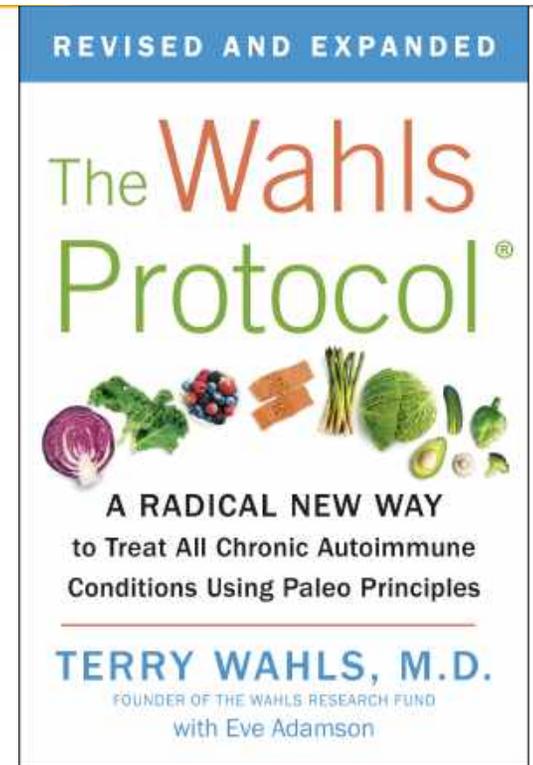
University of Iowa

info@wahlsinstitute.com

Disclosures

Books

- Grant Funding –
 - National MS Society
- Trademarks
 - Wahls™ Diet Plans,
 - Wahls Protocol®
- Financial relationships with Penguin Random House Inc.; Integrative Medicine for Mental Health; Institute for Health and Healing; Suttler Pacific, BioCeuticals; NCURA; MCG Health Inc.; Genova Diagnostics, Metagenics, Nutritional Therapy Association,
- Equity interest
 - Dr. Terry Wahls LLC
 - The Wahls Institute PLC
 - FBB Biomed
 - www.terrywahls.com



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Abstract

- In this session, underlying root causes for neurodegeneration will be reviewed. Dietary and lifestyle interventions, updates from her clinical research, clinical practice and Dr. Wahls' healing journey will be reviewed. Strategies to enhance patient success with adopting dietary and lifestyle interventions will also be discussed.

Objectives – after completing this session the participants should be able to

- Name at least four mechanisms by which environmental factors contribute to accelerated aging and neurodegenerative disease processes.
- Name specific food and lifestyle interventions that can stabilize and or reverse neuroinflammatory and neurodegenerative disease processes.
- Introduce three resilience factors into their patient conversations that contribute to improved success rates in adopting and sustaining health behaviour changes.

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- How do you respond when patients ask to stop Disease Modifying Drug Treatment?

Rebound Relapses After Ceasing Another Disease-Modifying Treatment in Patients With Multiple Sclerosis

- Interrupting treatments that have been working predictably causes rebound relapses.
- Patients must have **12-36 months good response to diet/lifestyle Tx before even attempting to gradually reduce the drug therapy.**

R Voskuhl. Rebound Relapses After Ceasing Another Disease-Modifying Treatment in Patients With Multiple Sclerosis: Are There Lessons to Be Learned? JAMA Neurol. 2016 May 2. doi: 10.1001/jamaneurol.2016.0934.

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Personalized Lifestyle Medicine: Relevance for Nutrition and Lifestyle Recommendations

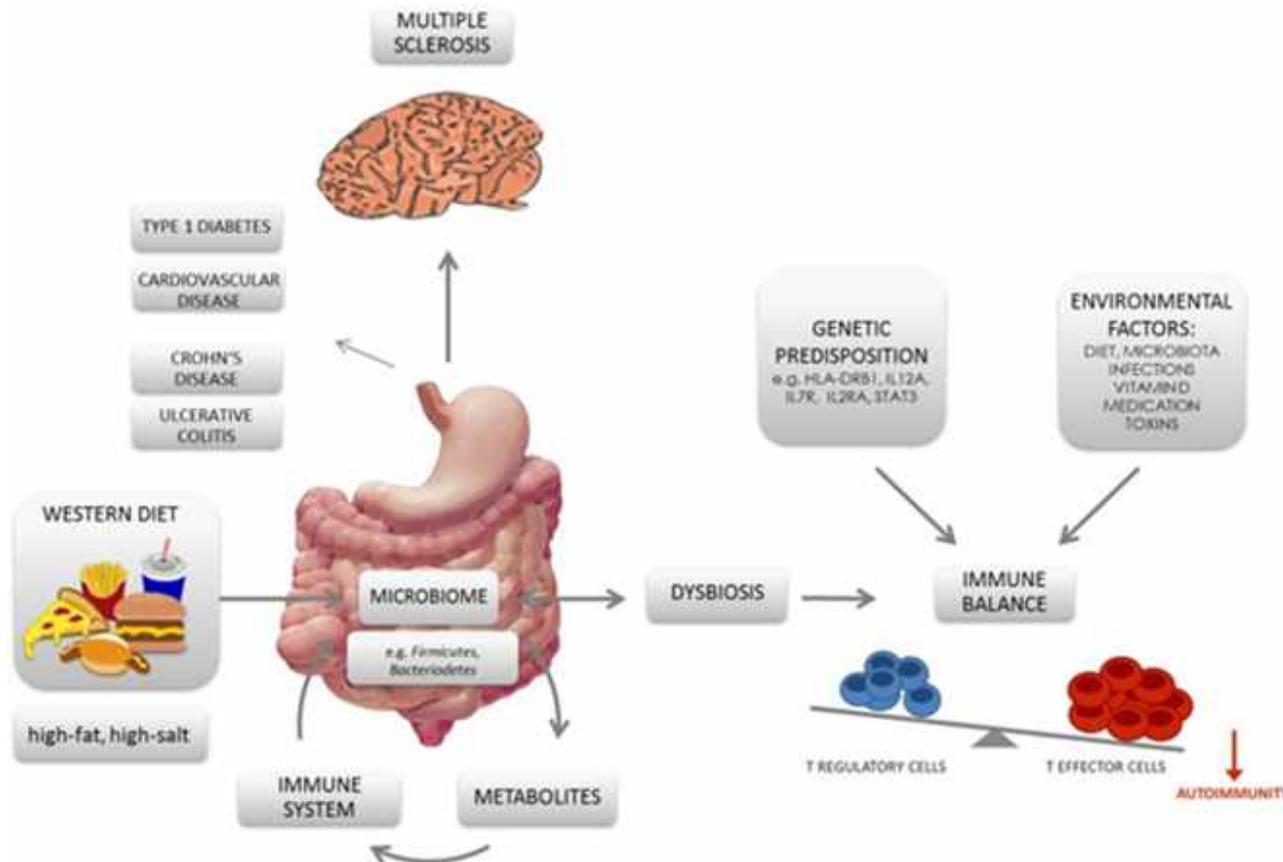


[ScientificWorldJournal. 2013; 2013: 129841.](https://www.scientificworldjournal.com/2013/2013/129841)

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Mis-Match Diseases

- Neurodegeneration increasing
- Genes are relatively stable
- Foodstuffs are very different
- Activity levels sharply declined

Environmental factors in autoimmune diseases and their role in multiple sclerosis.

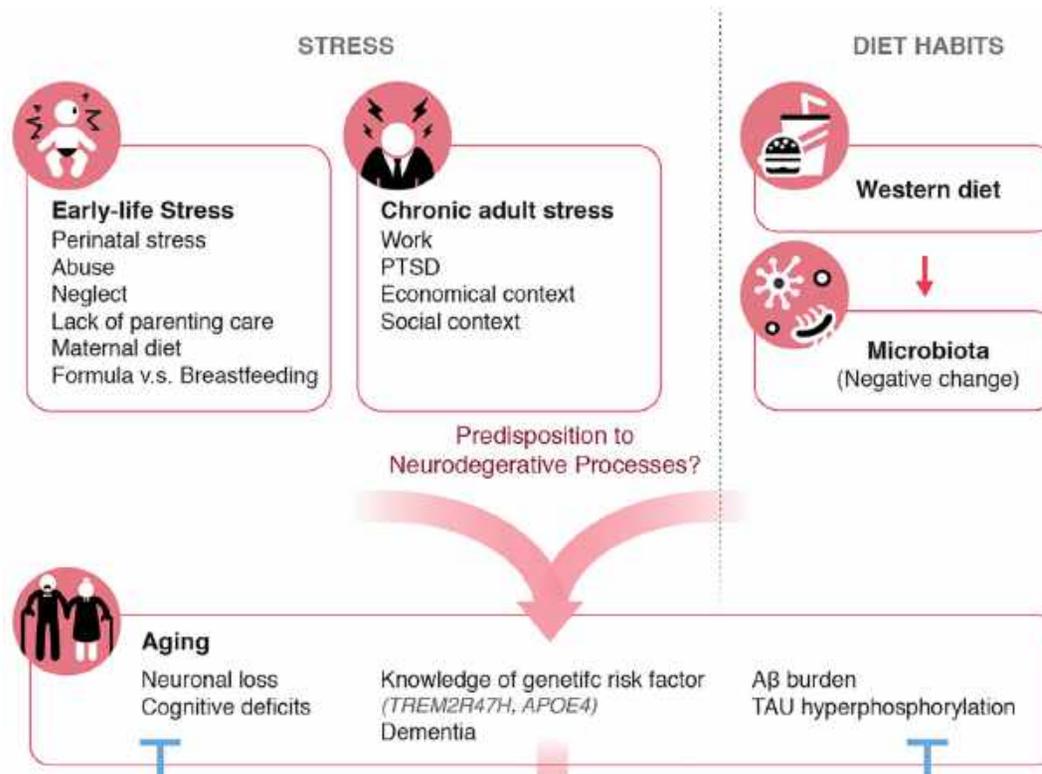


[Cell Mol Life Sci. 2016; 73\(24\): 4611–4622.](#)

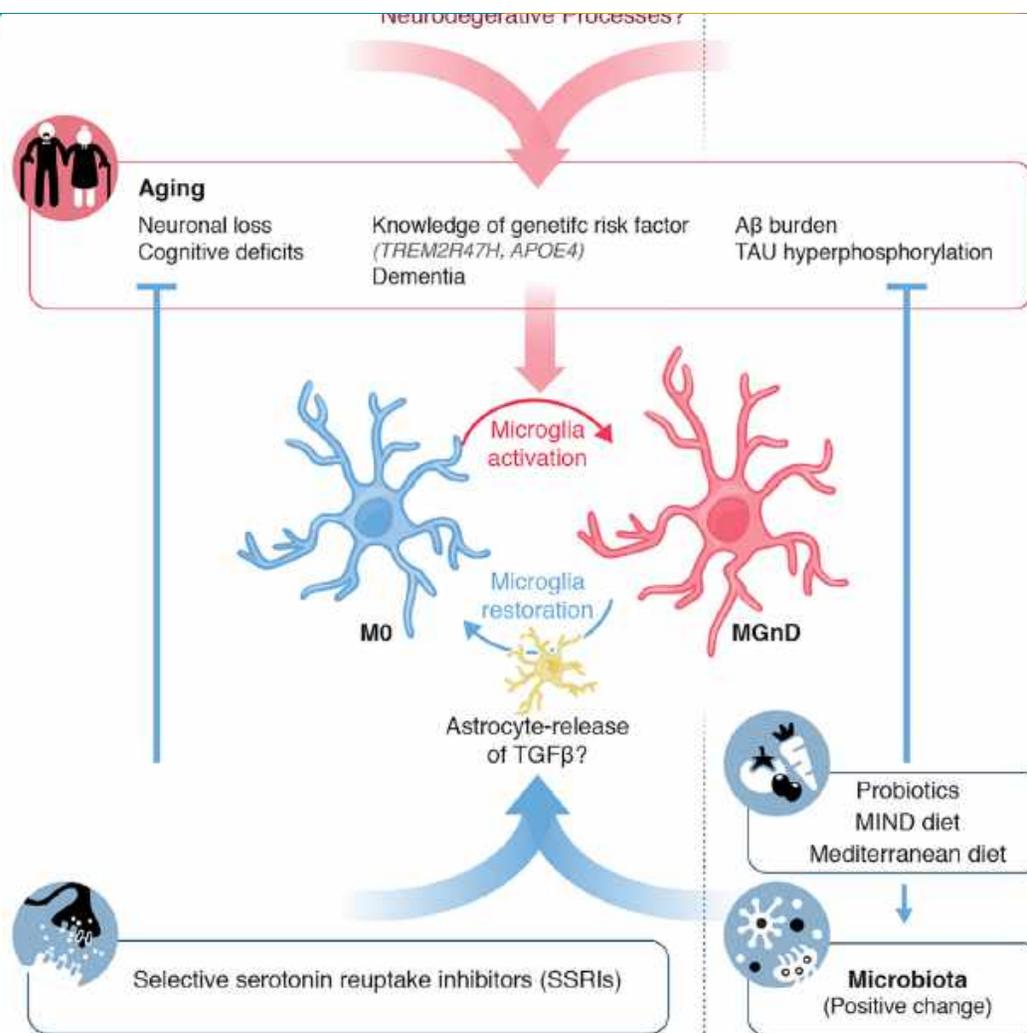
Causes of Neuroinflammation/ Neurodegeneration

- Microglia
- Blood brain barrier
- Intestinal permeability

Microglia, Lifestyle Stress, and Neurodegeneration



1. Microglia, Lifestyle Stress, and Neurodegeneration. [Immunity](#). Author manuscript; available in PMC 2020 May 18.



1. Microglia, Lifestyle Stress, and Neurodegeneration. [Immunity](#). Author manuscript; available in PMC 2020 May 18.

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Traumatic Brain Injury

TBI is associated with:

- Acute changes in **intestinal permeability**
- Increases permeability in the **blood brain barrier (BBB)**
- Increased **oxidative stress, inflammation, microglia activation**
- Continued and progressive **neurobehavioral symptoms**
- Risk for **hormonal compromise**

1. Kharrazian D. Traumatic Brain Injury and the Effect on the Brain-Gut Axis. Altern Ther Health Med. 2015 Aug;21 Suppl 3:28-32.

Blood Brain/ Intestinal Barriers

- Zonulin, IL-17, LPS increase permeability of intestine and the blood brain barrier
- Zonulin levels are associated with 1 year disease progression in MS
- Zonulin dysregulates tight junctions

1. IFN- γ , IL-17A, or Zonulin Rapidly Increase the Permeability of the Blood-Brain and Small Intestinal Epithelial Barriers: Relevance for Neuro-Inflammatory Diseases. *Biochem Biophys Res Commun.* 2018 Dec 9;507(1-4):274-279. doi: 10.1016/j.bbrc.2018.11.021. Epub 2018 Nov 16.
2. All Disease Begins in the (Leaky) Gut: Role of Zonulin-Mediated Gut Permeability in the Pathogenesis of Some Chronic Inflammatory Diseases. *F100Res.* 2020 Jan 31;9:F1000 Faculty Rev-69. doi: 10.12688/f1000research.20510.1. eCollection 2020.
3. Biomarkers of Intestinal Barrier Function in Multiple Sclerosis Are Associated With Disease Activity. *Mult scler.* 2019 Jul 18;1352458519863133. doi: 10.1177/1352458519863133.

Increased Intestinal Permeability

- Extreme exercise
- NSAIDs, ASA, PPI
- Emulsifiers/ surfactant (processed foods)
- Alcohol
- High fat diet/ bile acids

1. Role for diet in normal gut barrier function: developing guidance within the framework of food-labeling regulations. [m J Physiol Gastrointest Liver Physiol](#). 2019 Jul 1; 317(1): G17–G39.

Increased Intestinal Permeability

- Smoking
- Age
- Obesity
- Medications

1. Role for diet in normal gut barrier function: developing guidance within the framework of food-labeling regulations. [m J Physiol Gastrointest Liver Physiol](#). 2019 Jul 1; 317(1): G17–G39.

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Improving Gut Barrier

- Zinc
- Vitamin A
- EFAs
- Glutathione, NAC, glutamine
- SCFAs
- Dietary Fiber

1. Role for diet in normal gut barrier function: developing guidance within the framework of food-labeling regulations. [m J Physiol Gastrointest Liver Physiol](#). 2019 Jul 1; 317(1): G17–G39.
2. Effects of Omega-3 Fatty Acids on Immune Cells. [Int J Mol Sci](#). 2019 Oct; 20(20): 5028.

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Barrier Restoration

- Remove offending agents
 - Alcohol
 - NSAIDs
 - Steroids
 - Gluten, casein & other offending food proteins

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Barrier Restoration

- Address dysbiosis
- Bacteria, yeast dysbiosis higher in patients with chronic depression
- Lower carbohydrate diet, low glycemic index
- Anti-fungal herbals/ medications may be required

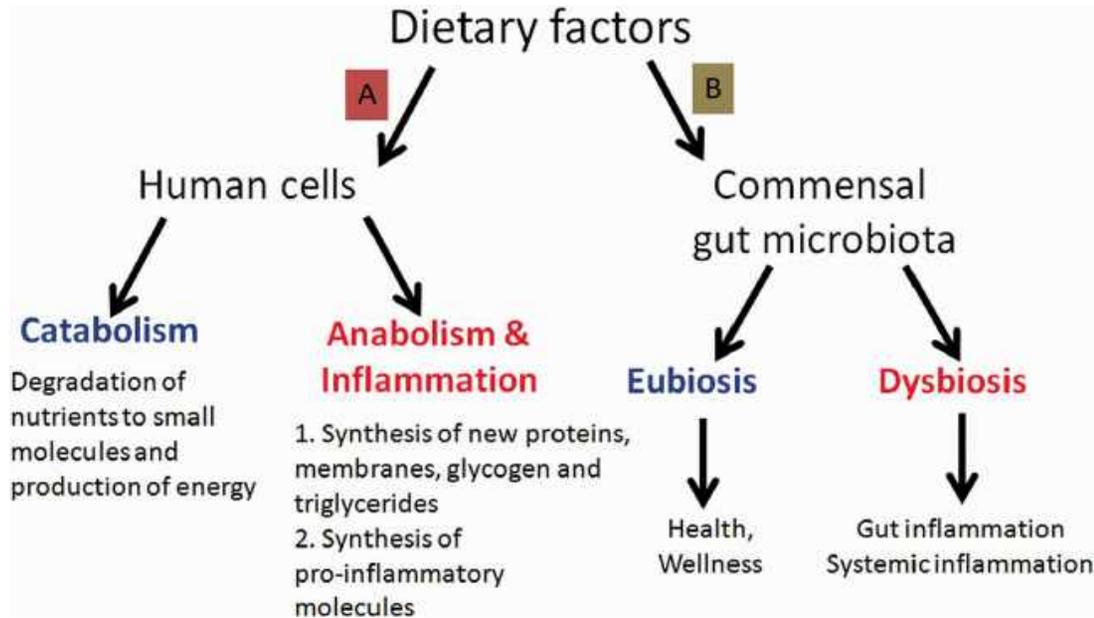
1. Altered Gut Bacterial-Fungal Interkingdom Networks in Patients With Current Depressive Episode. *Brain Behav.* 2020 Jun 12;e016777. doi: 10.1002/brb3.1677. Online ahead of print.
2. Alzheimer's Disease Might Depend on Enabling Pathogens Which Do Not Necessarily Cross the Blood-Brain Barrier. *Medical Hypotheses.* 2019 Apr;125:129-136. doi: 10.1016/j.mehy.2019.02.044. Epub 2019 Feb 21.

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Barrier Restoration

- Butyrate
- Endocannabinoid agonists
- Probiotics, prebiotics, fiber
- Digestive enzymes, bile, stomach acid
- Bone broth, cod liver oil, EFAs, glutamine
- Stress reduction/lifestyle

1. Targeting Zonulin and Intestinal Epithelial Barrier Function to Prevent Onset of Arthritis. Nature Commun 2020 Apr 24;11(1):1995. oi: 10.1038/s41467-020-15831-7.

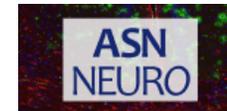
Nutrition Facts in Multiple Sclerosis



The two routes by which diet can influence our health:
(A) the metabolism of our cells and (B) the population of our gut microbiota.

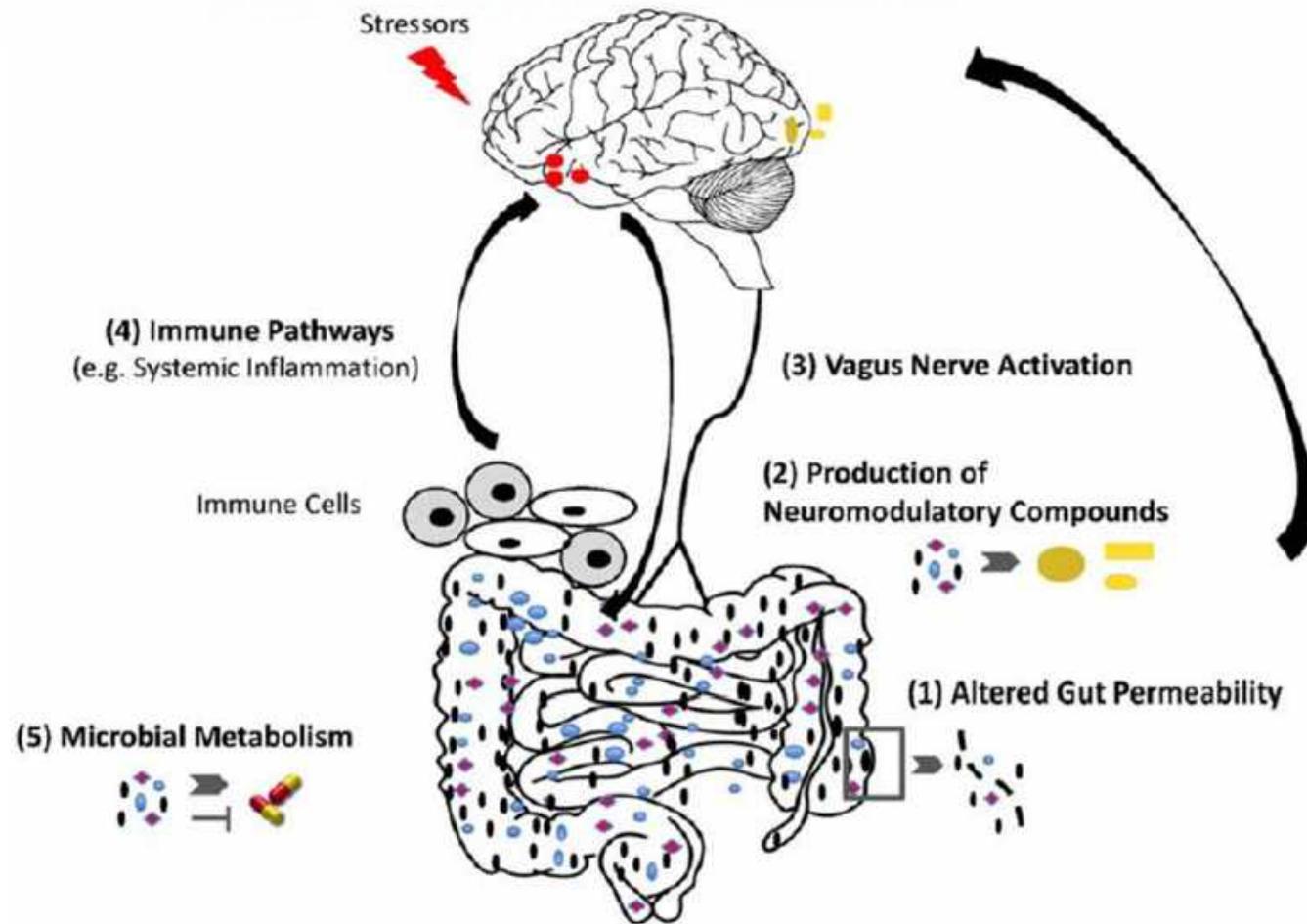
Paolo Riccio, and Rocco Rossano ASN Neuro
2015;7:1759091414568185

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Neuromicrobiology: How Microbes Influence the Brain

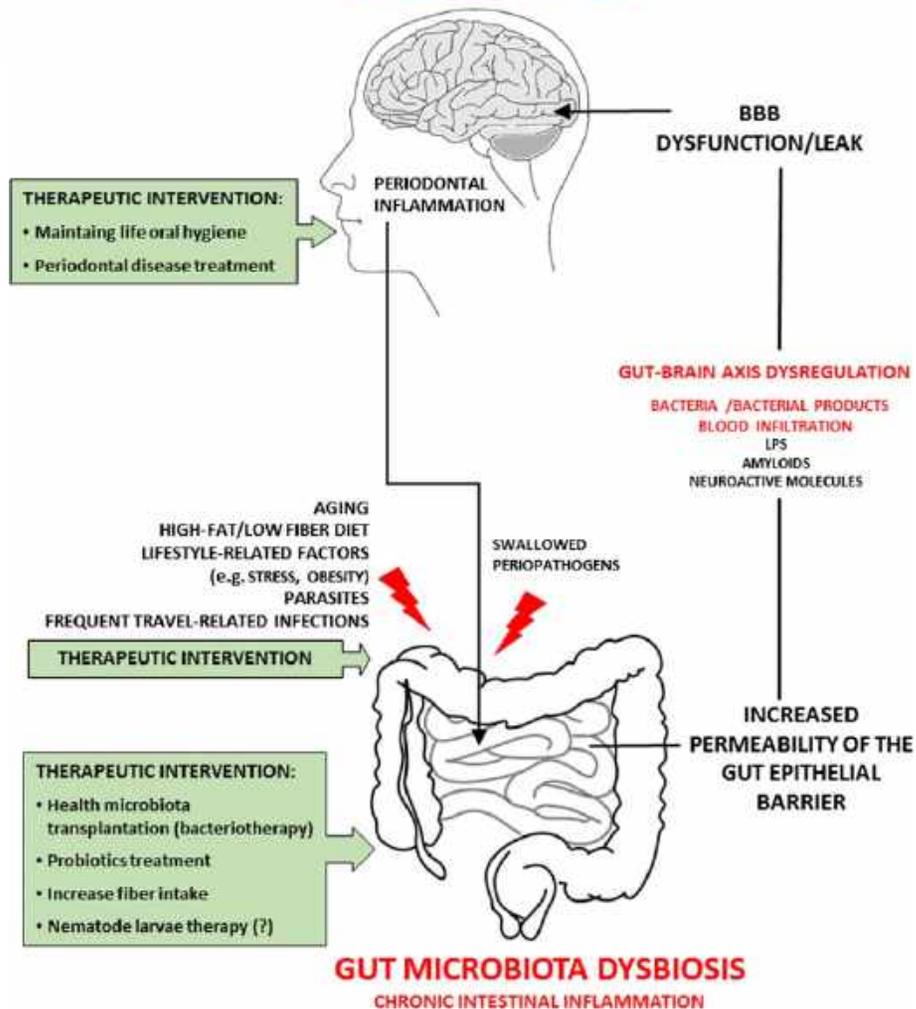
- Gut microbes involved and possibly contributing to
 - Autism spectrum disorders,
 - Alzheimer's disease,
 - Parkinson's disease,
 - Depression, and anxiety disorder.



The gut microbiome in human neurological disease: A review. *Ann Neurol.* 2017 Mar;81(3):369-382. doi: 10.1002/ana.24901.

ALZHEIMER'S DISEASE

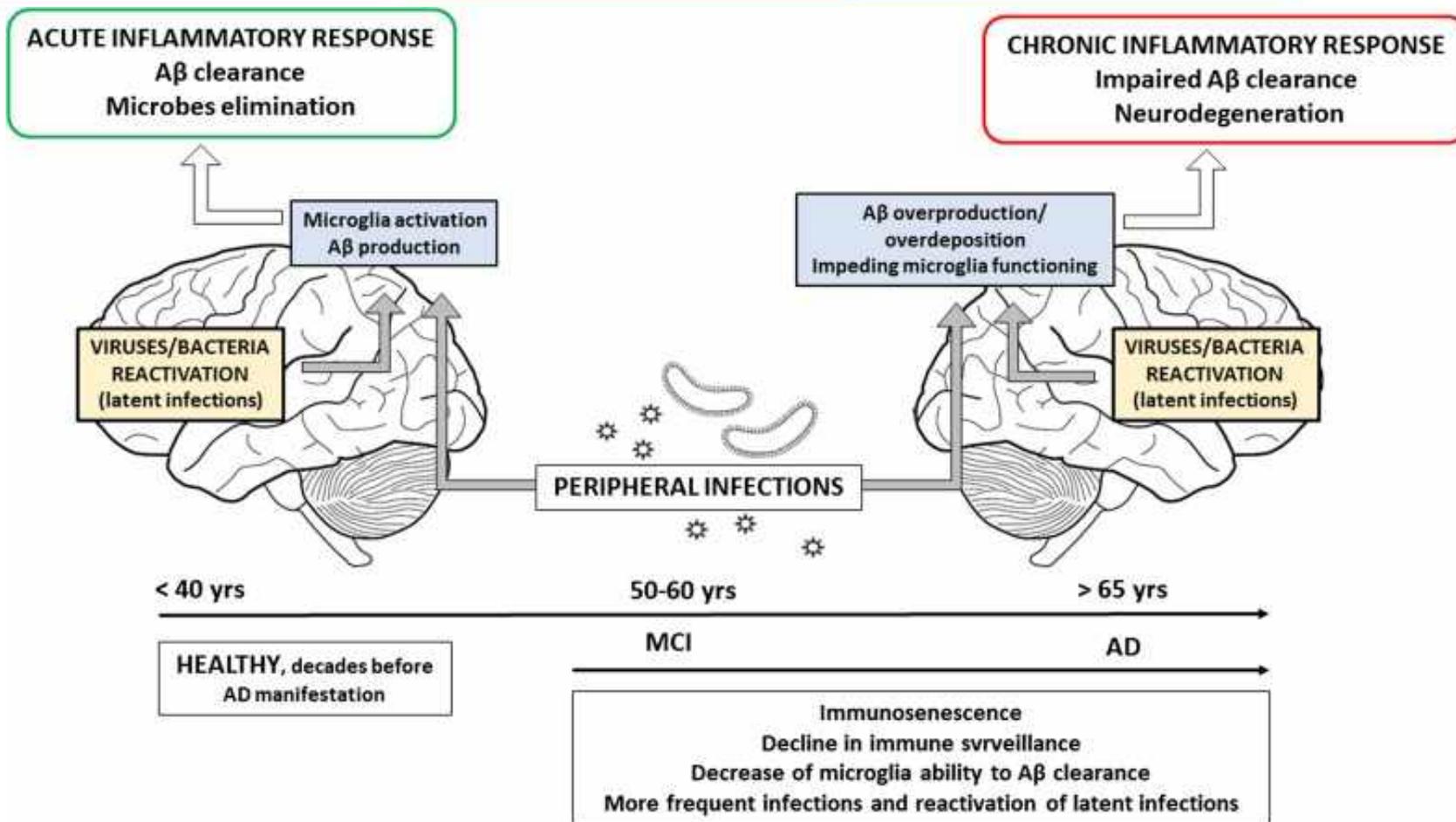
CHRONIC NEUROINFLAMMATION



Diet and Alzheimer's

Pathogenic bacteria and their products [LPS, amyloids] may induce increased permeability of intestine epithelial barrier and blood-brain barrier dysfunction/leak that may induce/support chronic inflammatory reactions in the brain.

The Gut Microbiome Alterations and Inflammation-Driven Pathogenesis of Alzheimer's Disease-a Critical Review. Mol Neurobiol. 019 Mar;56(3):1841-1851.
doi: 10.1007/s12035-018-1188-4. Epub 2018 Jun 23.



The Gut Microbiome Alterations and Inflammation-Driven Pathogenesis of Alzheimer's Disease-a Critical Review. Mol Neurobiol. 019 Mar;56(3):1841-1851. doi: 10.1007/s12035-018-1188-4. Epub 2018 Jun 23.

Diet and Parkinson's and LPS Bacteria

LPS-containing bacteria:

Are pro-inflammatory

Disrupt intestinal barrier integrity

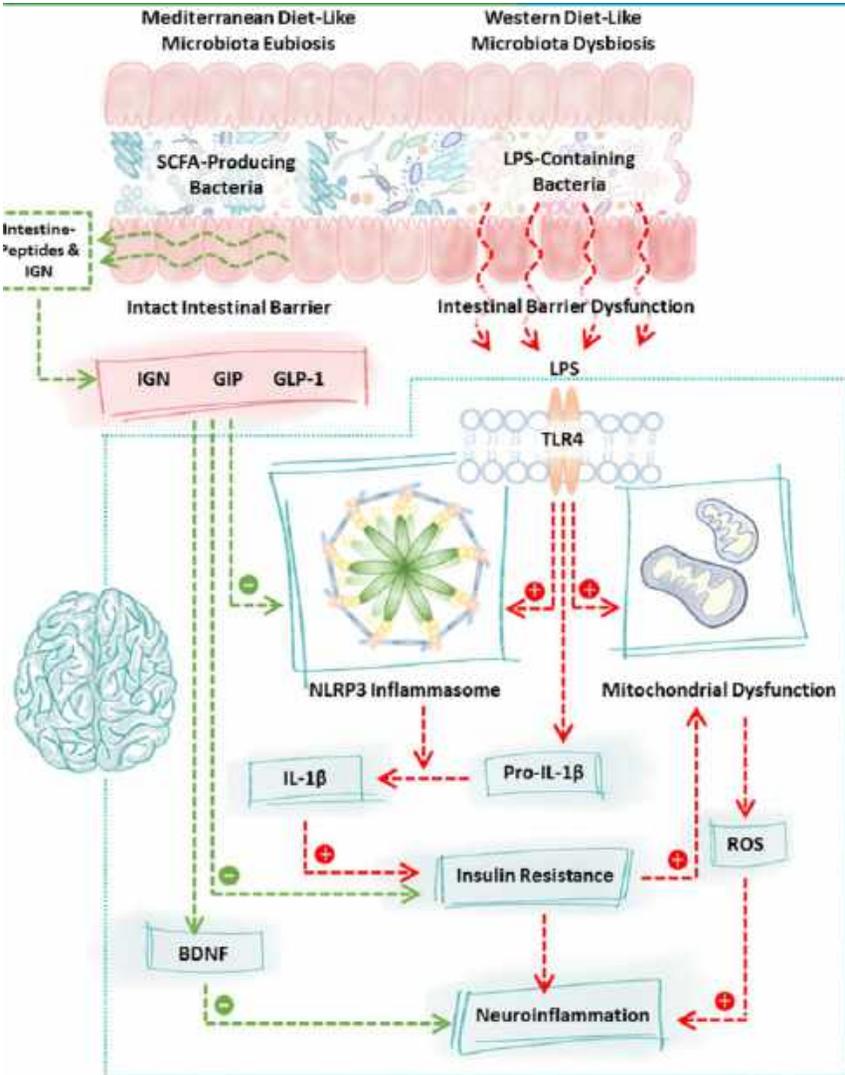
Bind to TLR4

Stimulates NLRP3 inflammasome activation

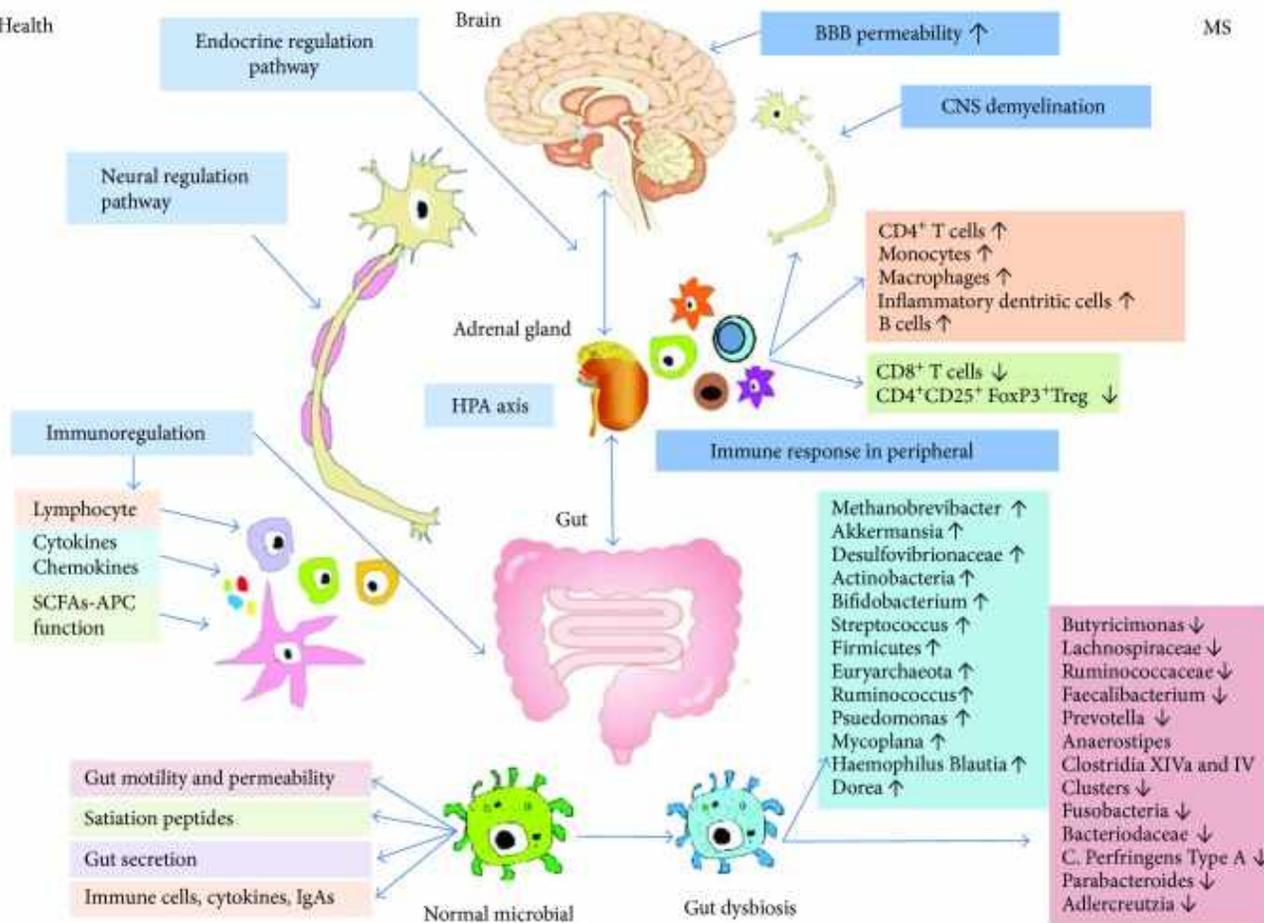
Disrupt mitochondrial function

Worsen insulin resistance

Culminating in neuroinflammation and neurodegeneration.



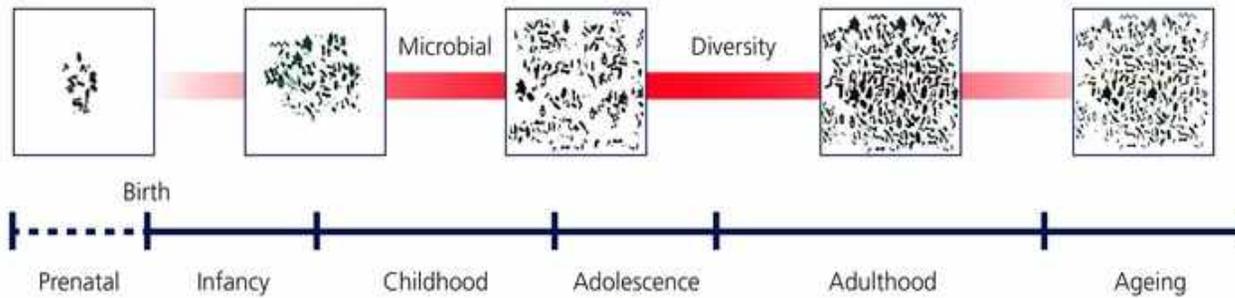
1. Diet in Parkinson's Disease: Critical Role for the Microbiome. Front Neurol. 2019; 10: 1245.



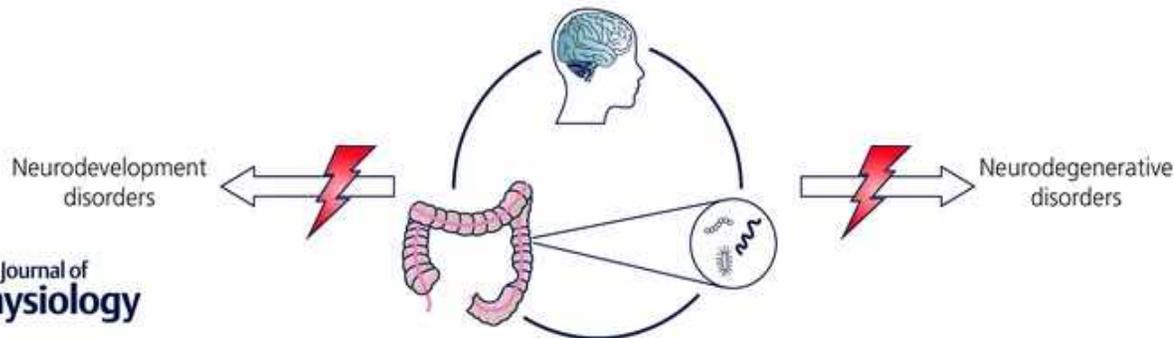
Diet and MS

The gut microbiota can affect neural pathways, the endocrine pathway-HPA axis, and the immunoregulating pathway (via lymphocyte, cytokines, chemokines, and antigens presenting effect of SCFAs).

1. Gut Microbiota in Multiple Sclerosis and Experimental Autoimmune Encephalomyelitis: Current Applications and Future Perspectives. *Mediators Inflamm.* 2018 Apr 2;2018:8168717. doi: 10.1155/2018/8168717.



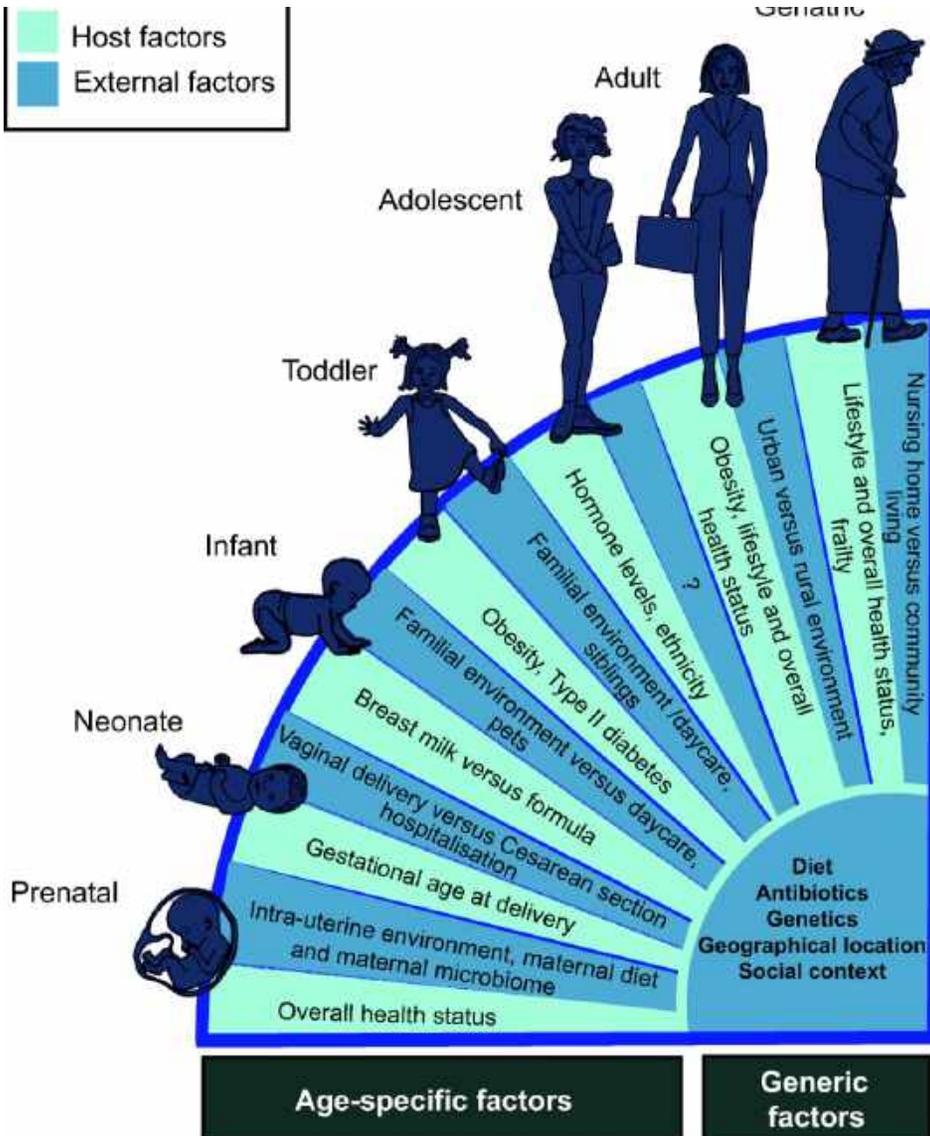
The microbiota dynamically changes across the lifespan, establishing its relationship with the host at critical windows during infancy, adolescence and ageing. At these time windows, there is an increased vulnerability to external insults, which may result in enhanced susceptibility to brain disorders.



The Journal of **Physiology**

Gut instincts: microbiota as a key regulator of brain development, ageing and neurodegeneration

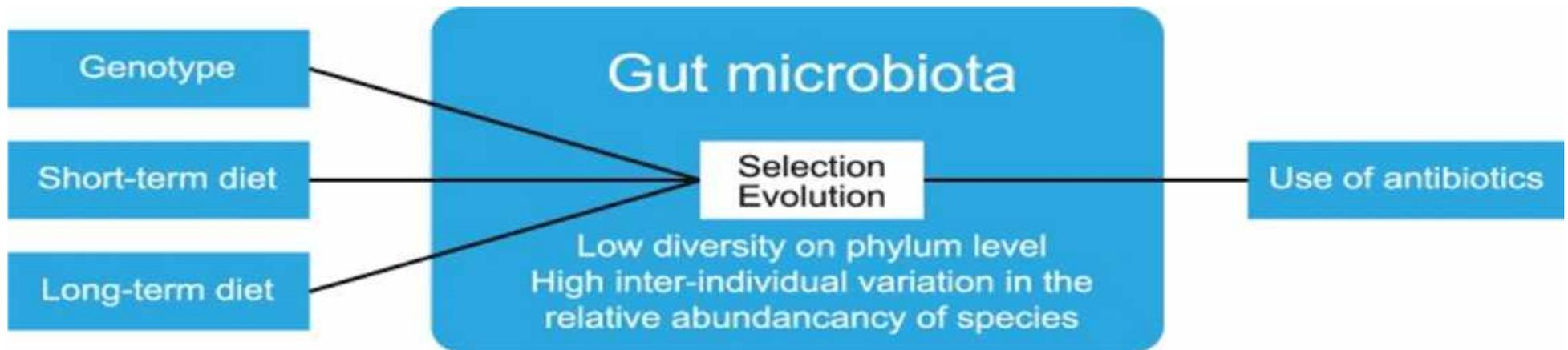
[J Physiol](#). 2017 Jan 15; 595(2): 489–503.



The human gut microbiome in health: establishment and resilience of microbiota over a lifetime

Environmental Microbiology, Volume: 18, Issue: 7,
 Pages: 2103-2116, First published: 05 April 2016, DOI:
 (10.1111/1462-2920.13318)

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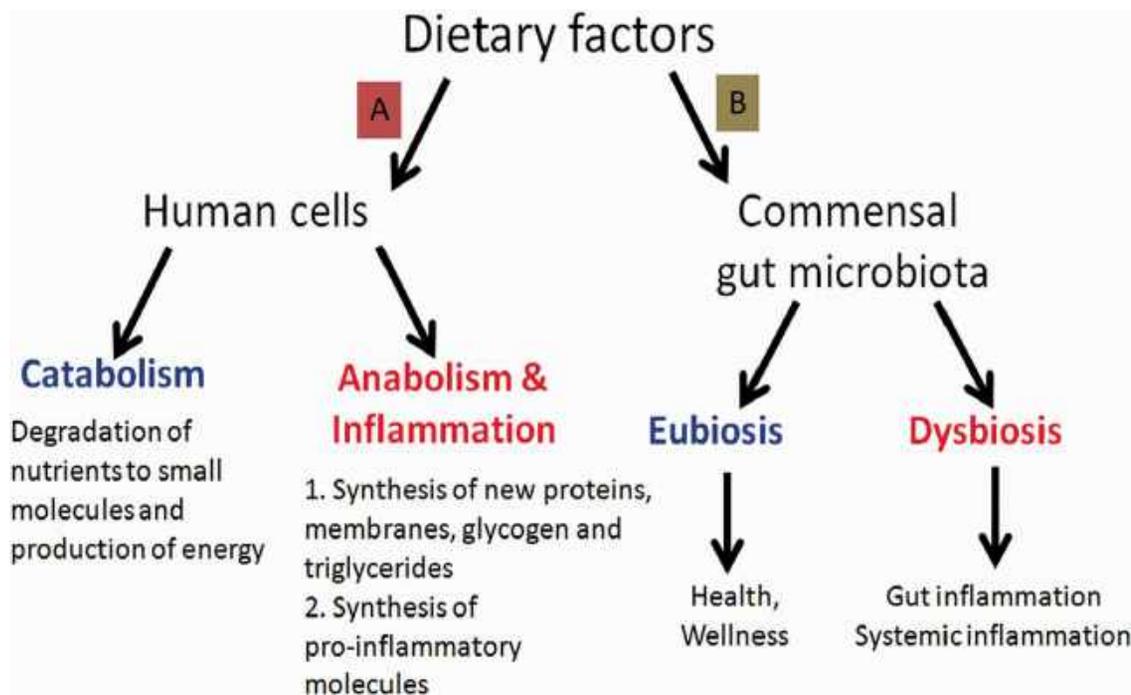


The composition of gut microbiota is influenced by multiple factors, such as diet and host genotype. Within the gut, ecological processes such as selection and evolution take place. The use of antibiotics reduces the numbers and diversity of gut microbiota.

[van den Hoogen WJ](#)¹, [Laman JD](#)², [t Hart BA](#)^{2,3}. Modulation of Multiple Sclerosis and Its Animal Model Experimental Autoimmune Encephalomyelitis by Food and Gut Microbiota. [Front Immunol. 2017; 8: 1081.](#)

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Nutrition Facts in Multiple Sclerosis



The two routes by which diet can influence our health:
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Paolo Riccio, and Rocco Rossano ASN Neuro
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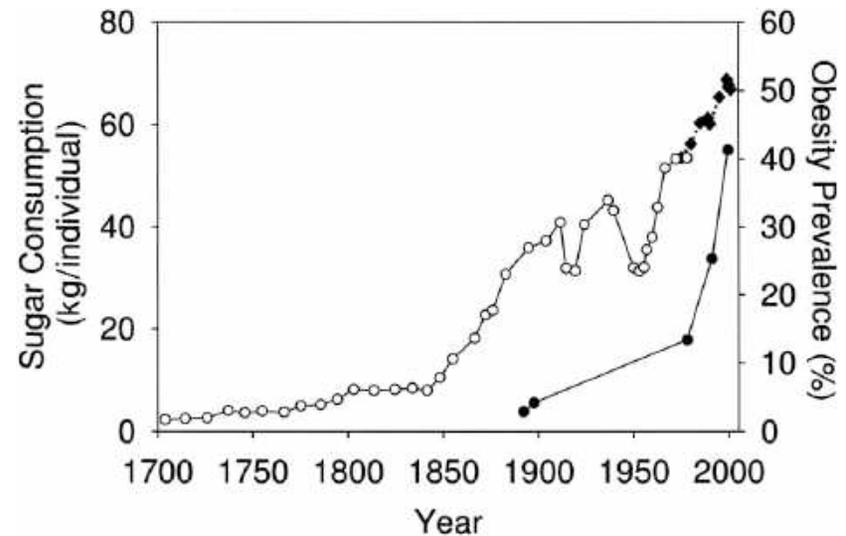
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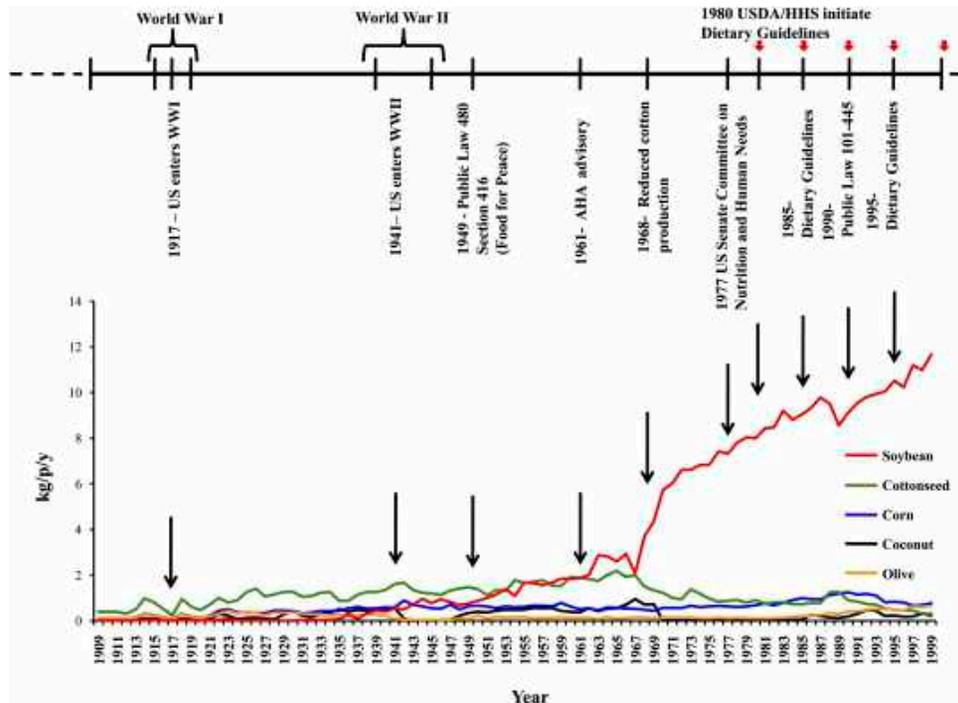
Potential Role of Sugar (Fructose) in the Epidemic of Hypertension, Obesity and the Metabolic Syndrome, Diabetes, Kidney Disease, and Cardiovascular Disease

Sugar intake per capita in the United Kingdom from 1700 to 1978 (30, 31; ○) and in the United States from 1975 to 2000 (32; ◆) is compared with obesity rates in the United States in non-Hispanic white men aged 60–69 y (17; •).



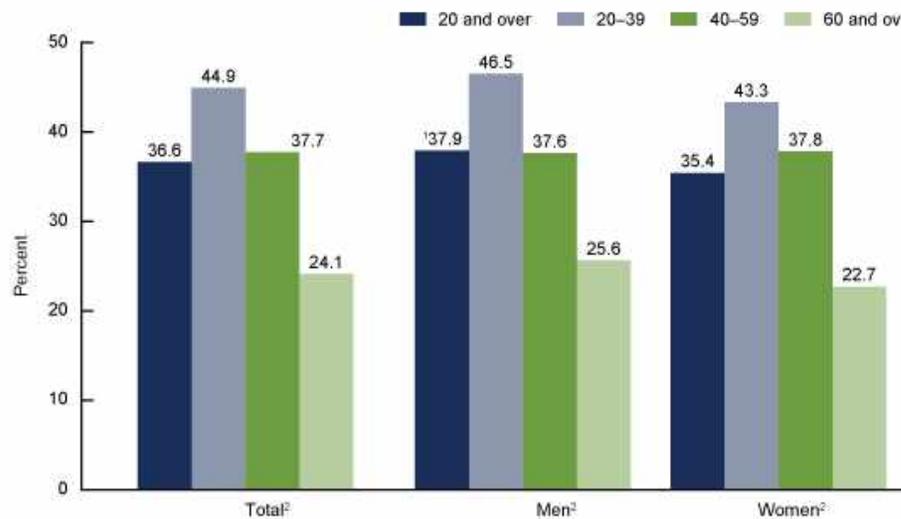
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Changes in consumption of omega-3 and omega-6 fatty acids in the United States during the 20th century.



[Am J Clin Nutr.](#) 2011 May;93(5):950-62

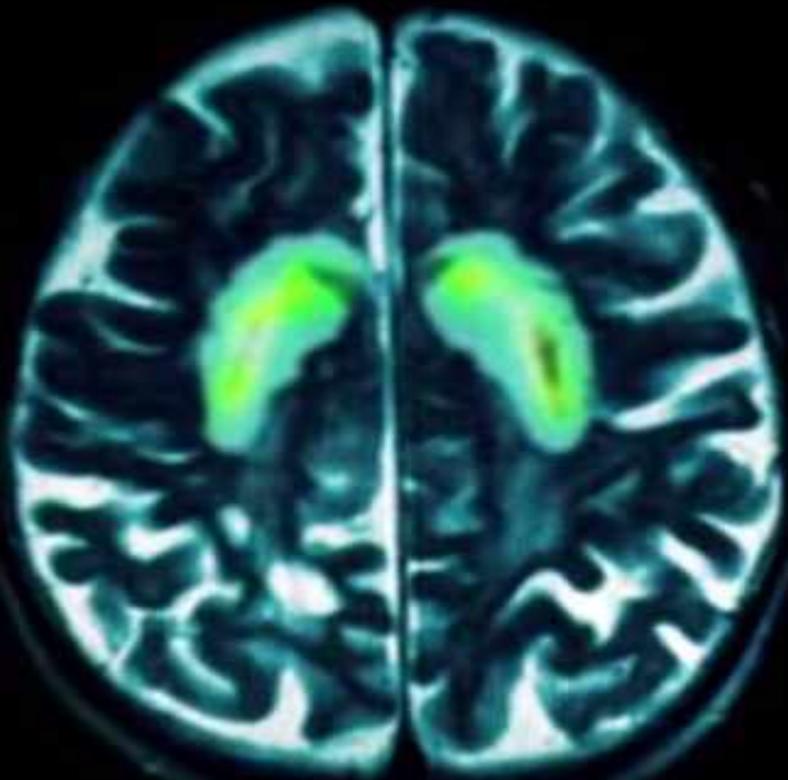
Fast Food Consumption Among Adults in the United States, 2013–2016



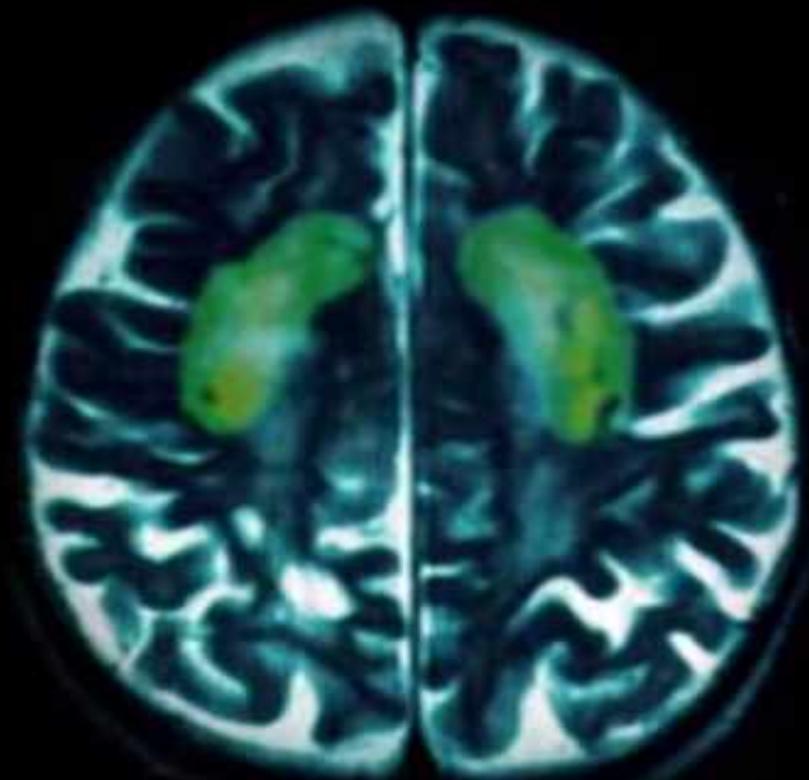
- 37% of Americans are eating fast food on a given day

- By Age
 - 20–39 - 45%,
 - 40–59- 38%
 - >60 -24%

<https://www.cdc.gov/nchs/products/databriefs/db322.htm>



SUGAR



COCAINE

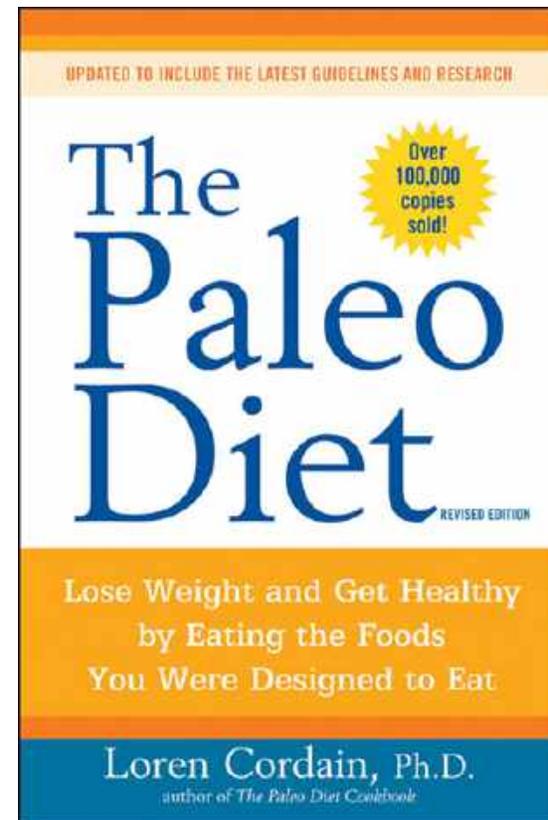


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Fish oil, creatine and co-enzyme Q 10

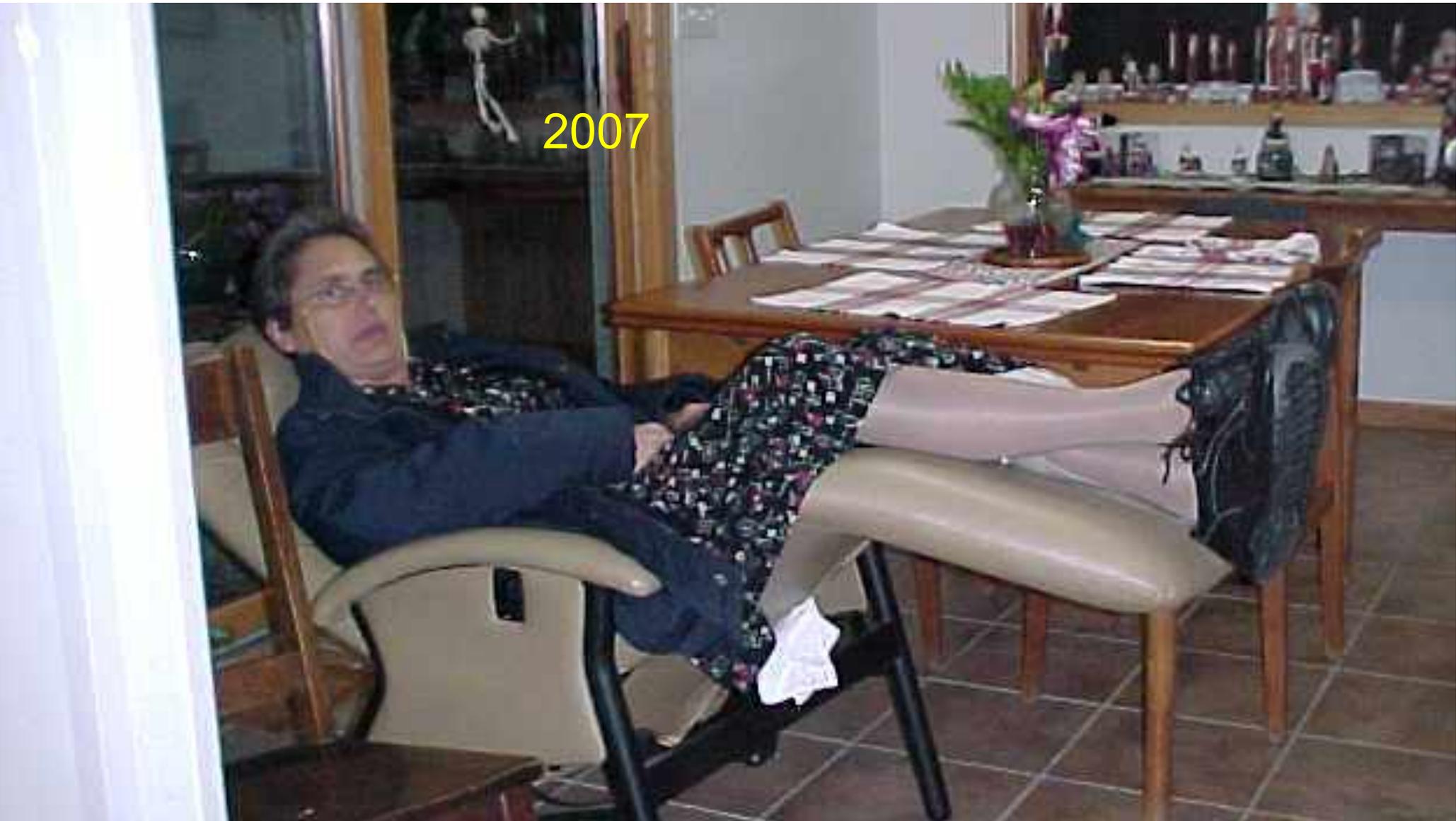


Ann Neurol. 2003;53 Suppl 3:S39-47
Neurobiol Dis. 2005 Apr;18(3):618-27.

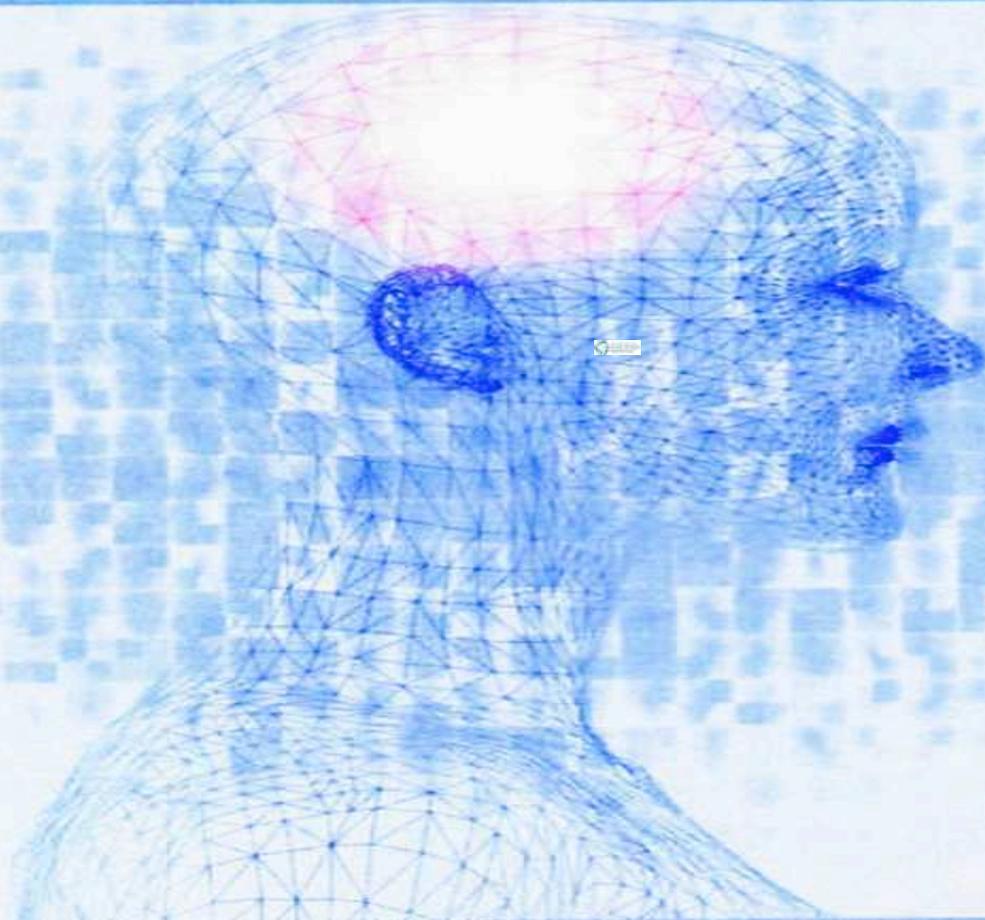


Terry Wahls MD
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2007



Neuroprotection: A Functional Medicine Approach for Common And Uncommon Neurologic Syndromes







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Open Access

Case report

Neuromuscular electrical stimulation and dietary interventions to reduce oxidative stress in a secondary progressive multiple sclerosis patient leads to marked gains in function: a case report

David Reese^{1,2}, ET Shivapour³, Terry L Wahls^{4,5,6*}, Shauna D Dudley-Javoroski² and Richard Shields²

Address: ¹Performance Therapies, PC, Ridgeway Drive, Coralville, Iowa, USA

²Department of Physical Therapy, University of Iowa Carver College of Medicine, Iowa City, Iowa, 52246, USA

³Department of Neurology, University of Iowa Carver College of Medicine, 200 Hawkins Drive, Iowa City, Iowa, 52246, USA

⁴Veterans Administration (VA), Iowa City VA Medical Center, 601 Highway 6 West, Iowa City, Iowa, 52246, USA

⁵Center for Research in the Implementation of Innovative Strategies in Practice (CRIISP) VA HSR&D Center of Excellence, Iowa City VA Medical Center, 601 Highway 6 West, Iowa City, Iowa, 52246, USA

⁶Division of General Medicine, Department of Internal Medicine, University of Iowa Carver College of Medicine, 200 Hawkins Drive, Iowa City, Iowa, 52246, USA

Email: DR - D.Reese@penther.com; ETS - et-shivapour@uiowa.edu; TLW* - Terry.Wahls@va.gov; SDDJ - shauna-dudley@uiowa.edu; RS - richard-shields@uiowa.edu

* Corresponding author

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Cases Journal 2009, 2:7601 doi:10.4076/1757-1626-2-7601

This article is available from: <http://casesjournal.com/casesjournal/article/view/7601>

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Abstract

“After 8 months of neuromuscular electrical stimulation (6 months of nutritional intervention) the patient's function had improved sufficiently that she **no longer used a scooter or cane and rode her bicycle routinely 8 miles, including hills.**”

Terry Wahls MD
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The Wahls Protocol[®] Seminar Safety and Feasibility Study

Trial record 5 of 5 for: terry wahls

[← Previous Study](#) | [Return to List](#) | [Next Study](#)

Nutrition, Neuromuscular Electrical Stimulation (NMES) and Secondary Progressive Multiple Sclerosis (SPMS)



The safety and scientific validity of this study is the responsibility of the study sponsor and investigators. Listing a study does not mean it has been evaluated by the U.S. Federal Government. Read our [disclaimer](#) for details.

ClinicalTrials.gov Identifier: NCT01381354

Recruitment Status ⓘ : Completed

First Posted ⓘ : June 27, 2011

Last Update Posted ⓘ : June 26, 2018

Sponsor:

University of Iowa

Collaborators:

Direct MS Canada

DJO Incorporated

Pinnacle Inc.

TZ Press, LLC

Information provided by (Responsible Party):

Terry L. Wahls, University of Iowa

[Study Details](#)

[Tabular View](#)

[No Results Posted](#)

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[How to Read a Study Record](#)

Study Description

Go to

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My Breakthrough

2011

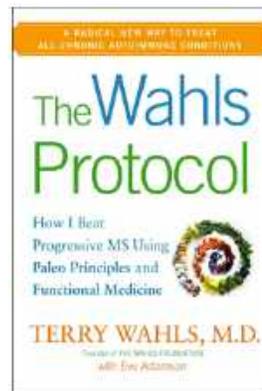


The Wahls Protocol® Seminar My Breakthrough



2011

2014



Multimodal Intervention Improves Fatigue and Quality of Life in Subjects With Progressive Multiple Sclerosis: A Pilot Study



Grass-fed Meats,
Organ Meats, and Wild Fish

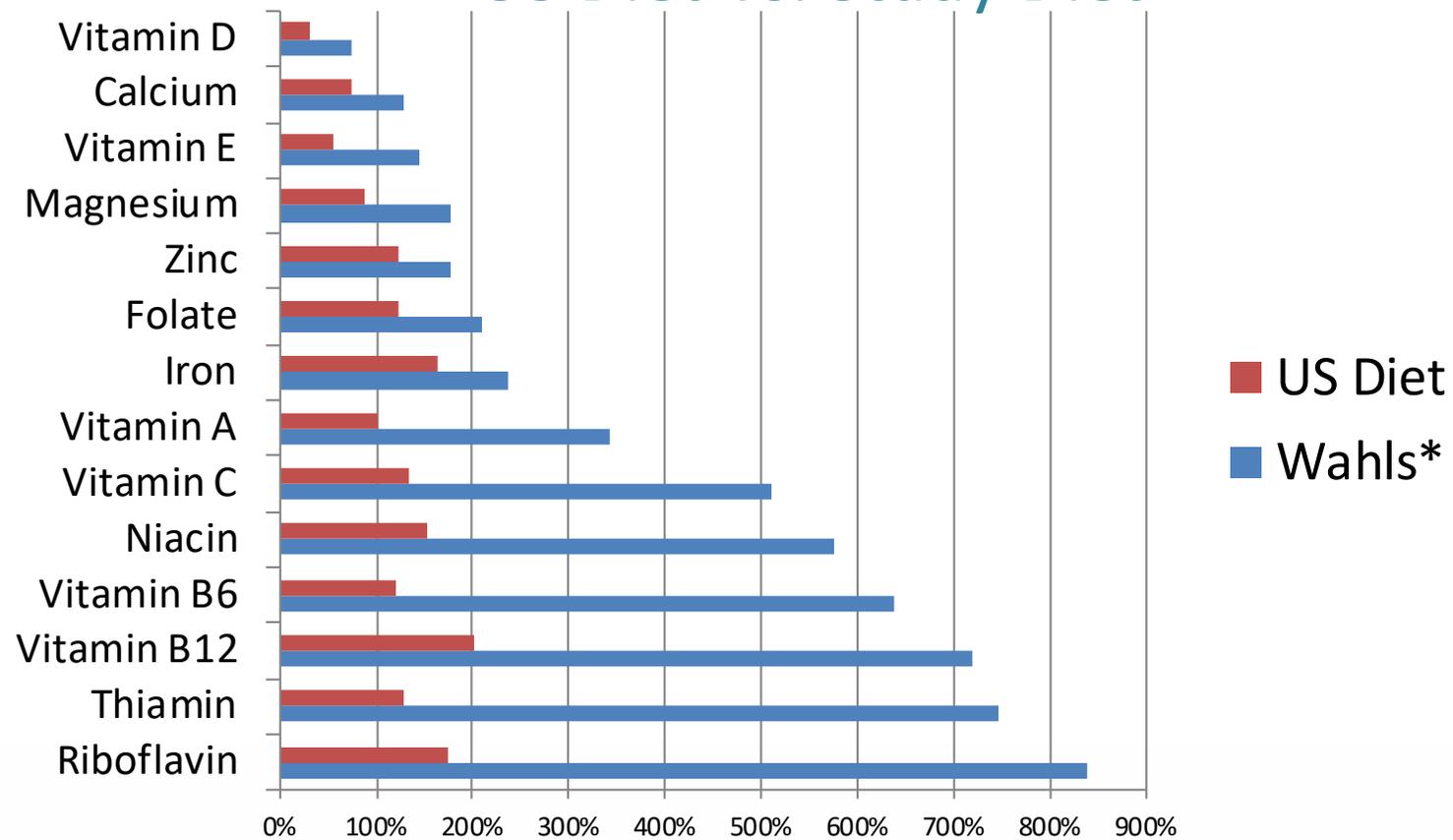


Meditation



Food	Instruction	Servings
Green leafy vegetables	Recommended*	3 cups cooked/6 cups raw=3srvg
Sulfur-rich vegetables	Recommended*	3 cups raw or cooked= 3srvg
Intensely colored fruits or vegetables	Recommended*	3 cups raw or cooked =3 srvg
Omega-3 oils	Encouraged	2 tablespoons
Animal protein	Encouraged	4 ounces or more
Gluten-containing grain	Excluded	
Dairy	Excluded	
Eggs	Excluded	

The Wahls Protocol[®] Nutritional Adequacy (%RDA) US Diet Vs. Study Diet



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Leafy Greens

- Vitamin K1 metabolized to K2-mk7 in gut
- K2 important in
 - Myelin production
 - Calcium influx into bones and teeth
- Carotenoids, magnesium, folate



1. Age- and brain region-specific effects of dietary vitamin K on myelin sulfatides. *Nutr Biochem.* 2010 Nov;21(11):1083-8.
2. Vitamin K and sphingolipid metabolism: evidence to date. *Nutr Rev.* 2005 Apr;63(4):111-21.
3. Bourre JM. Effects of nutrients (in food) on the structure and function of the nervous system: update on dietary requirements for brain. Part 1: micronutrients. *J Nutr Health Aging.* 2006 Sep-Oct;10(5):377-85.
4. Bourre JM. Effects of nutrients (in food) on the structure and function of the nervous system: update on dietary requirements for brain. Part 2 : macronutrients. *J Nutr Health Aging.* 2006 Sep-Oct;10(5):386-99.

Why deeply pigmented?



Pigments (especially **blue/purple/black**) is associated with improved cognitive performance and neuroprotection

1. Medicinal Effect of Nutraceutical Fruits for the Cognition and Brain Health. Scientifica (Cairo).2016;2016:3109254.
2. Berry antioxidants: small fruits providing large benefits. J Sci Food Agric.2014 Mar 30;94(5):825-33
3. Dietary and plant polyphenols exert neuroprotective effects and improve cognitive function in cerebral ischemia. Recent Pat Food Nutr Ag. 2013 Aug;5(2):128-43.
4. The impact of fruit flavonoids on memory and cognition. Br J Nutr.2010 Oct;104 Suppl 3:S40-7. d
5. Grape juice, berries, and walnuts affect brain aging and behavior. J Nutr. 2009 Sep;139(9):1813S-7S.
6. Fruit polyphenolics and brain aging: nutritional interventions targeting age-related neuronal and behavioral deficits. Ann N Y Acad Sci.2002 Apr;959:128-32.
7. Reversing the deleterious effects of aging on neuronal communication and behavior: beneficial properties of fruit polyphenolic compounds. Am J Clin Nutr.2005 Jan;81(1 Suppl):313S-316S.

Why Brassica and Allium?

- Improve detoxification
- Increase glutathione production
- Increase GABA production
- Enhance Neuroprotection
- Improve endothelial function



1. Neuroprotective Effect of Brassica oleracea Sprouts Crude Juice in a Cellular Model of Alzheimer's Disease. Med Cell Longev.2015;2015:781938
2. Learning and memory promoting effects of crude garlic extract. Indian J Exp Biol.2013 Dec;51(12):1094-100.
3. Enhancement of the neuroprotective activity of Hericium erinaceus mycelium co-cultivated with Allium sativum extract. Arch Physiol Biochem.2015 Feb;121(1):19-25

Why Stress Mushrooms?

- Increase nerve growth factors
- Increase re-myelination
- Activate natural killer cells
- Prime innate and adaptive immunity



1. Mori K, Obara Y, Hirota M, Azumi Y, Kinugasa S, Inatomi S, Nakahata N. Nerve growth factor-inducing activity of *Herichium erinaceus* in 1321N1 human astrocytoma cells. *Biol Pharm Bull.* 2008 Sep;31(9):1727-32.
2. Lee DH, Kim HW. Innate immunity induced by fungal β -glucans via dectin-1 signaling pathway. *Int J Med Mushrooms.* 2014;16(1):1-16.
3. Akramiene D, Kondrotas A, Didziapetriene J, Kevelaitis E Effects of beta-glucans on the immune system. *Medicina (Kaunas).*2007;43(8):597-606.
4. Lai PL, Naidu M, Sabaratnam V, Wong K, Davi P, Kuppusamy UR, Abdullah N, Malek SN. Neurotrophic properties of the Lion's mane medicinal mushroom, *Herichium erinaceus* (Higher Basidiomycetes) from Malaysia *Int J Med Mushrooms.*2013;15(6):539-54.
5. Phan CW, David P, Naidu M, Wong KH, Sabaratnam V. Therapeutic potential of culinary-medicinal mushrooms for the management of neurodegenerative diseases: diversity, metabolite, and mechanism. *Crit Rev Biotechnol.*2015;35(3):355-68.

Multimodal Intervention Improves Fatigue and Quality of Life in Subjects With Progressive Multiple Sclerosis: A Pilot Study

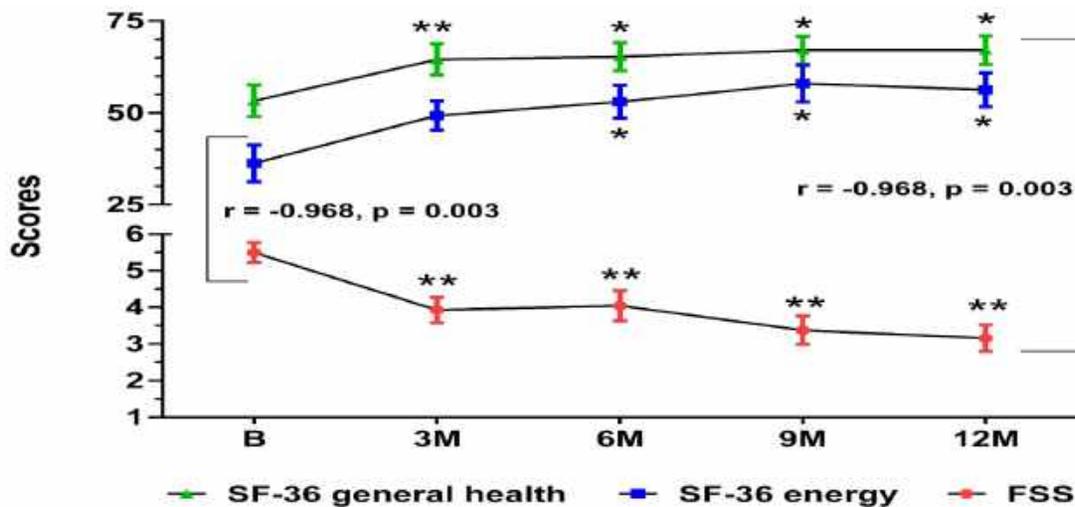
- N=20, single arm, feasibility study, 12 M
- Significant improvements obtained for
Fatigue Severity Scale
Performance Scale
SF 36 Energy and General Health



Degener Neurol Neuromuscul Dis. 2015;5:19-35. doi: 10.2147/DNND.S76523. Epub 2015 Feb 27

Multimodal Intervention Improves Fatigue and Quality of Life in Subjects With Progressive Multiple Sclerosis: A Pilot Study

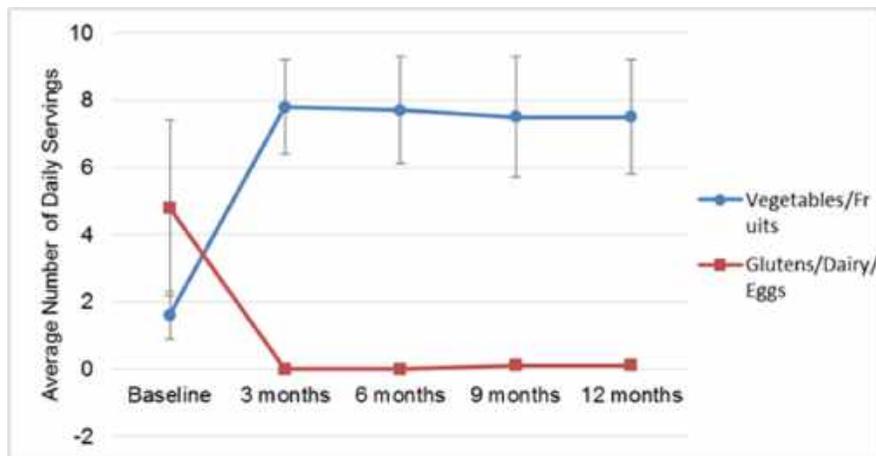
*p < 0.05



Degener Neurol Neuromuscul Dis. 2015;5:19-35. doi: 10.2147/DNND.S76523. Epub 2015 Feb 27

A Multimodal, Nonpharmacologic Intervention Improves Mood and Cognitive Function in People With Multiple Sclerosis

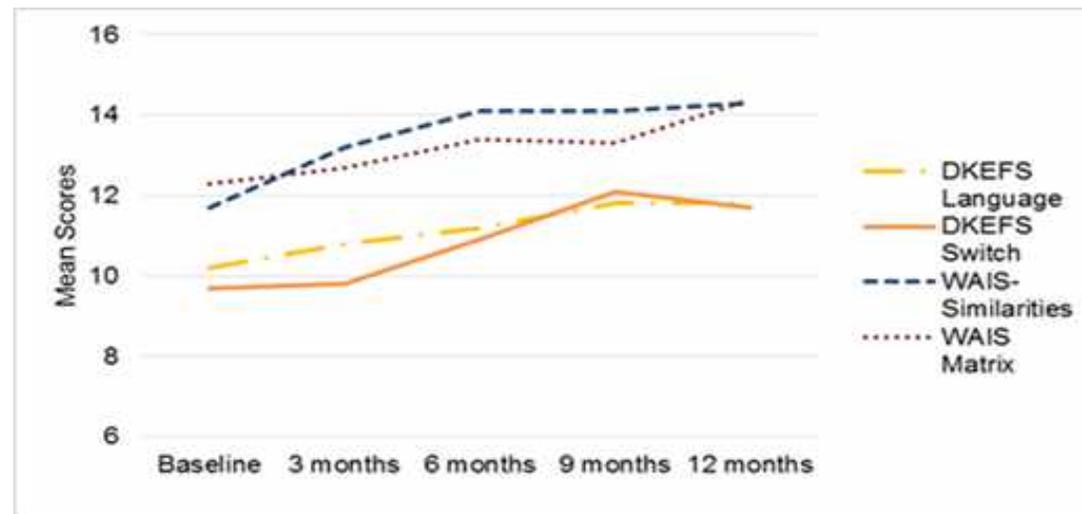
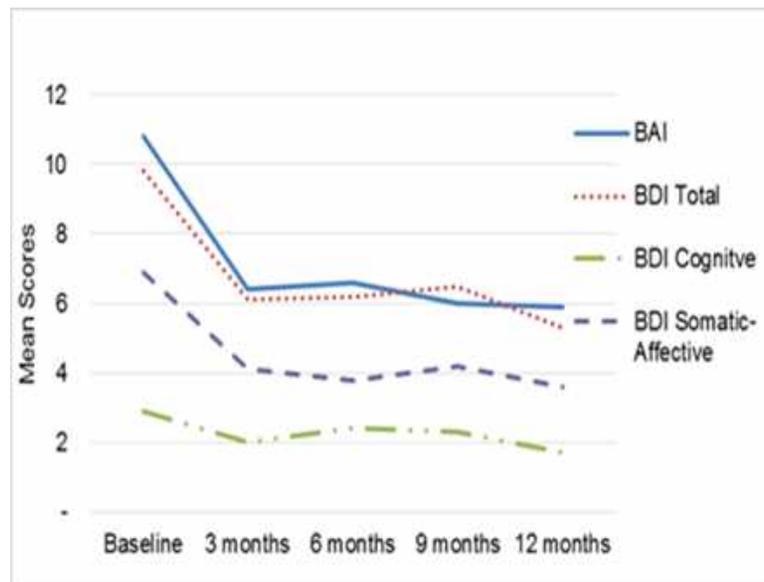
Average daily servings of the study diet recommended (vegetables/fruits) and excluded (gluten/dairy/eggs) foods $p < 0.01$ difference from baseline to 12 months



J Am Coll Nutr Mar-Apr 2017;36(3):150-168. doi: 10.1080/07315724.2016.1255160.

Terry Wahls MD
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A Multimodal, Nonpharmacologic Intervention Improves Mood and Cognitive Function in People With Multiple Sclerosis

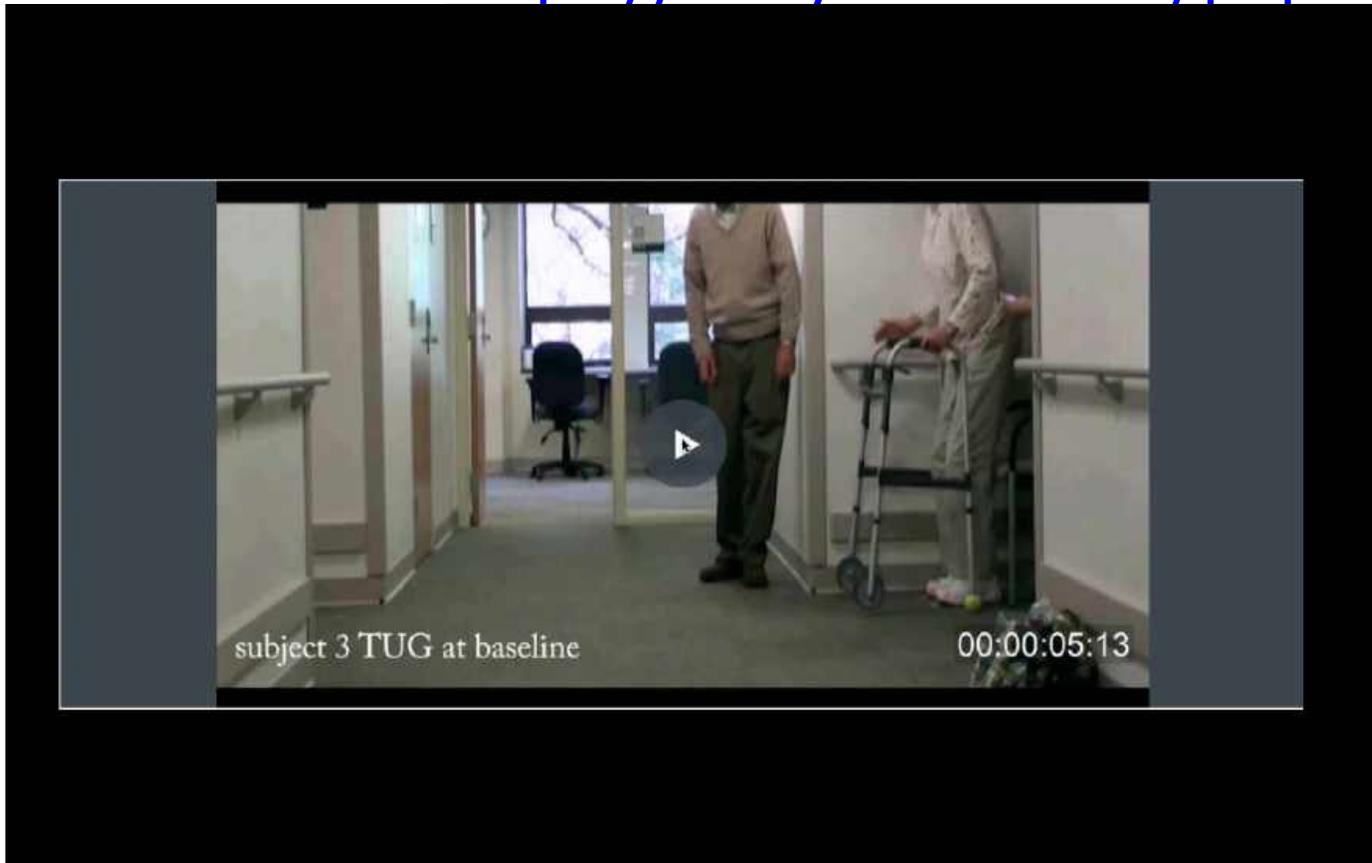


Mood and Cognition Improved

J Am Coll Nutr Mar-Apr 2017;36(3):150-168. doi: 10.1080/07315724.2016.1255160.

Copies of papers and video

<https://terrywahls.com/papers/>



[Degenerative Neurological and Neuromuscular Disease](#) | [Dovepress](#)
Journal Pre-proof

[ORIGINAL RESEARCH](#)

Effects of a multimodal intervention on gait and balance of subjects with progressive multiple sclerosis: a prospective longitudinal pilot study

Saira Bhat^{1*}
 Warren G. Darling²
 Emily C. Winter³
 Kacie A. Winter⁴
 E. Torajk Shivapour⁵
 H. Bridget Zimmerman⁶
 Terry L. Wahls^{1,7}

¹Department of Internal Medicine, University of Iowa, Iowa City, IA, USA
²Department of Internal Medicine, University of Iowa, Iowa City, IA, USA
³Department of Internal Medicine, University of Iowa, Iowa City, IA, USA
⁴Department of Internal Medicine, University of Iowa, Iowa City, IA, USA
⁵Department of Internal Medicine, University of Iowa, Iowa City, IA, USA
⁶Department of Internal Medicine, University of Iowa, Iowa City, IA, USA
⁷Department of Internal Medicine, University of Iowa, Iowa City, IA, USA

Purpose: To investigate the effects of a multimodal intervention including a modified Fitts test, nutritional supplements, stretching, strengthening exercises, with electrical stimulation of trunk and lower limb muscles, meditation and massage on walking performance and balance of subjects with progressive multiple sclerosis (MS).
Methods and results: Twenty subjects with mean (standard deviation) age of 51.7 (6.4) years and Expanded Disability Status Scale score of 4.2 (1) participated in a 12-month study. Assessments were completed at baseline, 3, 6, 9, and 12 months.
Results: The entire cohort did not show significant changes in any of the assessments over 12 months except higher speed of walking toward the 10-foot mark during total up-and-go (TUG) test and stride length compared with baseline (mean change 7.4 cm/s [95% confidence interval (CI), 0.3, 13.2], p=0.001). Walking step duration revealed that 30% subjects (n=6/20) showed decrease in TUG time from baseline to at least 1 of 4 time points, post-intervention and were considered as responders (TUG-Res), the remaining 10 subjects were considered as nonresponders (TUG-NRes). Over 12 months, TUG-Res showed decreased mean TUG time by 31% (95% CI, -32% to -27%), increased median Berg Balance Scale score (42 to 47), 30% increase in mean total 25-foot walk speed (0.20% considered clinically significant) and increased speed of walk toward 10-foot mark during TUG by 11.6 cm/s (95% CI, -10.23 to 33.03) associated with increases in step length and decrease in step duration. TUG-NRes showed deterioration in walking ability over 12 months. Comparison of TUG-Res and TUG-NRes showed no significant differences in additional to intervention but better stride duration and longer step length at baseline for TUG-Res than for TUG-NRes (p=0.001).
Conclusion: A multimodal lifestyle intervention may improve walking performance and balance in subjects with progressive MS who have mild-to-moderate gait impairment, while non-responders with severe gait impairment may not respond to this intervention. Future trials should assess effects of this intervention in subjects with MS during early stages of the disease.
Keywords: multiple sclerosis, Fitts test, exercise, neuromuscular electrical stimulation, gait, balance

Introduction
 Over 90% of persons with multiple sclerosis (MS) experience walking impairment, which is a major contributor to disability. Within 15 years of onset of MS, ~50% of MS subjects need some form of walking assistance and 10% become restricted to wheelchair. A recent study reported that mobility impairment in MS is a large burden to society as it leads to decreased work productivity, early departure from the work force, and decreased health-related quality of life.¹

Correspondence: Terry L. Wahls, Department of Internal Medicine, University of Iowa, 200 Hawkins Drive, Iowa City, IA 52242, USA. Tel: 319-335-3442; Email: terrywahls@iowa.edu

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Effects of a multimodal intervention on gait and balance of subjects with progressive multiple sclerosis: a prospective longitudinal pilot study, [Degenerative Neurological and Neuromuscular Disease](#) 2015, 5:91-92

The Wahls Protocol[®] Seminar

GF Diet Neuroprotective In MS Patients



- 72 patients with RRMS
- Randomized, followed 4.5 years
- GF diet versus usual diet
- EDSS 1.5 vs 2.1 (p<0.001)
- MRI GF had fewer patients with enhancing lesions 28% vs 67% (p< 0.001)
- Annual relapse rate was lower but not significantly different (0.4 vs. 0.6)

1. A randomized clinical trial comparing efficacy of a gluten-free diet versus regular diet in a series of relapsing-remitting multiple sclerosis patients. Int J Neurol Neurother. 2014; 1:1

2016 Started 4th clinical trial Funded by NMSS



National
Multiple Sclerosis
Society

Wahls et al. *Trials* (2016) 17:209
http://dx.doi.org/10.1186/s13063-016-2060-z

Trials

STUDY PROTOCOL

Open Access



Dietary approaches to treat MS-related fatigue: comparing the modified Paleolithic (Wahls Elimination) and low saturated fat (Swank) diets on perceived fatigue in persons with relapsing-remitting multiple sclerosis: study protocol for a randomized controlled trial

Terry Wahls^{1*}, Maria D. Scott², Zaidoon Akhrami³, Linda Rubenstein⁴, Warren Doring⁵, Lucas Carr⁶, Karen Smith⁷, Catherine A. Charard⁸, Nicholas LaRocca⁹ and Linda Srinetelau¹

Abstract

Background: Fatigue is one of the most disabling symptoms of multiple sclerosis (MS) and contributes to diminished quality of life. Although currently available interventions have had limited success in relieving MS-related fatigue, clinically significant reductions in perceived fatigue severity have been reported in a multimodal intervention pilot study that included a Paleolithic diet in addition to stress reduction, exercise, and electrical muscle stimulation. An optimal dietary approach to reducing MS-related fatigue has not been identified. To establish the specific effects of diet on MS symptoms, this study focuses on diet only instead of the previously tested multimodal intervention by comparing the effectiveness of two dietary patterns for the treatment of MS-related fatigue. The purpose of this study is to determine the impact of a modified Paleolithic and low saturated fat diet on perceived fatigue (primary outcome), cognitive and motor symptoms, and quality of life in persons with relapsing-remitting multiple sclerosis (RRMS).

Methods/Design: This 36-week randomized clinical trial consists of three 12-week periods during which assessments of perceived fatigue, quality of life, motor and cognitive function, physical activity and sleep, diet quality, and social support for eating will be collected. The three 12-week periods will consist of the following:

1. Observation: Participants continue eating their usual diet.
2. Intervention: Participants will be randomized to a modified Paleolithic or low saturated fat diet for the intervention period. Participants will receive support from a registered dietitian (RD) through in-person coaching, telephone calls, and emails.
3. Follow-up: Participants will continue the study diet for an additional 12 weeks with minimal RD support to assess the ability of the participants to sustain the study diet on their own.

(Continued on next page)

National MS Society and University of Iowa Launch \$1 Million Clinical Trial to Test Dietary Approaches to Treating Fatigue in MS

August 24, 2016

Summary

- ▶ The National MS Society has just committed over \$1 million to support a clinical trial led by Dr. Terry Wahls to compare the ability of two popular diets to treat multiple sclerosis-related fatigue.
- ▶ The award helps advance the Society's Wellness research goals to help people know what they can do today to feel their best, and whether lifestyle interventions can impact the course of MS.
- ▶ This financial commitment is the latest in the Society's relentless research efforts to move us closer to a world free of MS, and part of a projected investment of \$50 million in 2016 alone to support more than 380 new and ongoing studies around the world.
- ▶ This trial is recruiting participants with relapsing-remitting MS who experience fatigue, and who live within a 500-mile radius of Iowa City, IA. See below for details about participating and [Frequently Asked Questions](#) about the study.

* Correspondence: terry.wahls@uiowa.edu

¹University of Iowa, Iowa City, Iowa, USA
Full list of author information is available at the end of the article



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Memory and Aging Cohort and Diet

- Memory and Aging Project assesses diet impact on neurodegenerative delay - Observational study
- Assessments for memory, motor function, dietary intake
- FFQ to create diet scores for MIND Diet, Mediterranean-Dietary Approach to Systolic Hypertension (DASH), Mediterranean, DASH diets

1. MIND diet associated with reduced incidence of Alzheimer's disease. [Alzheimers Dement.](#) 2015 Sep;11(9):1007-14.
2. MIND diet slows cognitive decline with aging. [Alzheimers Dement.](#) 2015 Sep;11(9):1015-22.
3. MIND Diet Associated with Reduced Incidence and Delayed Progression of Parkinsonism in Old Age. [J Nutr Health Aging.](#) 2018;22(10):1211-1215.

Memory and Aging Cohort and Diet

- Cognition, N=906 followed 4.7 years
 - MIND less cognitive decline (MIND only)
- AD, N=923 followed 4.5 years –
 - MIND less Alzheimer's (more potent than DASH, Mediterranean)
- PD, N=706 followed 4.6 years –
 - MIND, Mediterranean less Parkinson's (DASH no effect)

1. MIND diet associated with reduced incidence of Alzheimer's disease. [Alzheimers Dement.](#) 2015 Sep;11(9):1007-14.
2. MIND diet slows cognitive decline with aging. [Alzheimers Dement.](#) 2015 Sep;11(9):1015-22.
3. MIND Diet Associated with Reduced Incidence and Delayed Progression of ParkinsonismA in Old Age. [J Nutr Health Aging.](#) 2018;22(10):1211-1215.

DASH ^a		MedDiet ^b		MIND	
DASH components	Max Score	Mediterranean Diet components	Max Score	MIND components	Max Score
Total Grains $\geq 7/d$	1	Nonrefined Grains $>4/d$	5	Whole Grains $\geq 3/d$	1
Vegetables $\geq 4/d$	1	Vegetables $>4/d$	5	Green Leafy $\geq 6/wk$	1
		Potatoes $>2/d$	5	Other Vegetables $\geq 1/d$	1
Fruits $\geq 4/d$	1	Fruits $>3/d$	5	Berries $\geq 2/wk$	1
Dairy $\geq 2/d$	1	Full-fat Dairy $\leq 10/wk$	5		
Meat, poultry & fish $\leq 2/d$	1	Red meat $\leq 1/wk$	5	Red Meats and products $<4/wk$	1
		Fish $>6/wk$	5	Fish $\geq 1/wk$	1
		Poultry $\leq 3/wk$	5	Poultry $\geq 2/wk$	1
Nuts, seeds & legumes $\geq 4/wk$	1	Legumes, nuts & beans $>6/wk$	5	Beans $>3/wk$	1
				Nuts $\geq 5/wk$	1
				Fast/fried food $<1/wk$	1
Total Fat $\leq 27\%$ of kcal	1				
Saturated Fat $\leq 6\%$ of kcal	1				
		Olive oil $\geq 1/d$	5	Olive Oil primary oil	1
				Butter, margarine $<1T/d$	1
				Cheese $<1/wk$	1
Sweets $\leq 5/wk$	1			Pastries, sweets $<5/wk$	1
Sodium $\leq 2400mg/d$	1				

- DASH
- MedDiet
- MIND

DASH ^a		MedDiet ^b		MIND	
DASH components	Max Score	Mediterranean Diet components	Max Score	MIND components	Max Score
Total Grains $\geq 7/d$	1	Nonrefined Grains $>4/d$	5	Whole Grains $\geq 3/d$	1
Vegetables $\geq 4/d$	1	Vegetables $>4/d$	5	Green Leafy $\geq 6/wk$	1
		Potatoes $>2/d$	5	Other Vegetables $\geq 1/d$	1
Fruits $\geq 4/d$	1	Fruits $>3/d$	5	Berries $\geq 2/wk$	1
Dairy $\geq 2/d$	1	Full-fat Dairy $\leq 10/wk$	5		
Meat, poultry & fish $\leq 2/d$	1	Red meat $\leq 1/wk$	5	Red Meats and products $<4/wk$	1
		Fish $>6/wk$	5	Fish $\geq 1/wk$	1
		Poultry $\leq 3/wk$	5	Poultry $\geq 2/wk$	1
Nuts, seeds & legumes $\geq 4/wk$	1	Legumes, nuts & beans $>6/wk$	5	Beans $>3/wk$	1
				Nuts $\geq 5/wk$	1
				Fast/fried food $<1/wk$	1
Total Fat $\leq 27%$ of kcal	1				
Saturated Fat $\leq 6%$ of kcal	1				
		Olive oil $\geq 1/d$	5	Olive Oil primary oil	1
				Butter, margarine $<1T/d$	1
				Cheese $<1/wk$	1
Sweets $\leq 5/wk$	1			Pastries, sweets $<5/wk$	1
Sodium $\leq 2400mg/d$	1				

- DASH
- MedDiet
- MIND
- Wahls™ Diet

Systematic review diet and AD biomarkers (tau and beta-amyloid)

- Meta-analysis of 15 studies met the inclusion criteria
- 13 studies found a significant relationship
- Revealed a small but significant effect of diet on AD biomarkers ($\beta = 0.11$ [95% CI 0.04-0.17], $p = 0.002$).

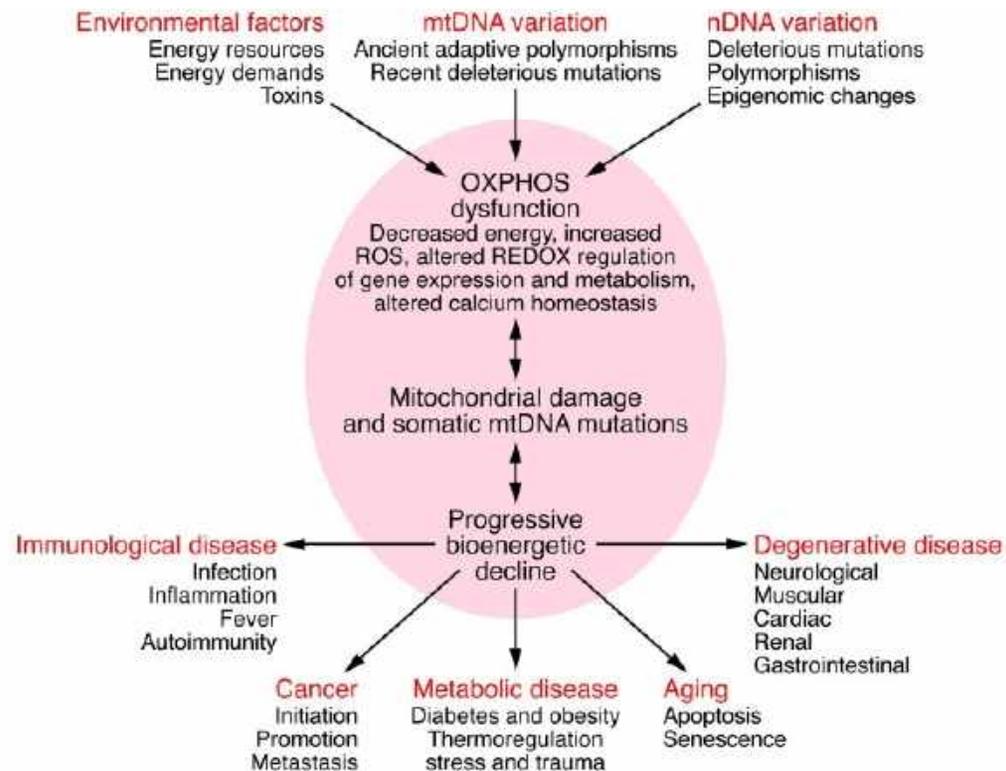
Diet and biomarkers of Alzheimer's disease: a systematic review and meta-analysis.
[Neurobiol Aging](#). 2019 Apr;76:45-52. doi: 10.1016/j.neurobiolaging.2018.12.008. Epub 2018 Dec 27.

Systemic review diet and AD biomarkers (tau and beta-amyloid)

- ↑ AD biomarker burden (4 studies)
 - High glycemic load
- ↓ AD biomarker burden (6 studies)
 - Mediterranean or "AD-protective" dietary pattern

The Wahls Protocol[®] Seminar

A mitochondrial bioenergetic etiology of disease





The Wahls Protocol[®] Seminar

Mitochondrial Support

Stop poisoning

- Heavy metals
- Pesticides
- Oxidized fats
- Chronic viral infections

Support

- B vitamins
- Lipoic acid/ carnitine
- Creatine
- Co-Q 10
- Minerals (esp. Mg, Zn)
- EFA's
- Antioxidants

1. Biochemical deficits and cognitive decline in brain aging: Intervention by dietary supplements. 2019 Jan; 95:70-80 doi: 10.1016/j.jchemneu.2018.04.002. Epub 2018 Apr 17.

The Wahls Protocol® Seminar

Mitochondrial Adaptation

- Mitochondrial Fuel sources
 - Carbohydrates (glucose)
 - Protein (amino acids)
 - Fat (ketone bodies)
- Endurance exercise/ Absence of food
 - Few carbohydrates
 - Protein if successful hunting
 - Stored fat

The Wahls Protocol® Seminar

Mitochondrial Adaptation

- It allows for survival during brief periods of natural starvation.
- Hepatic stores of glycogen ↓ to 0 within 12-24 hours.
- Most approach ketosis during the normal sleep cycle.

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Ketones

- Produced as by-products when fats (fatty acids) are broken down for energy in the liver and kidney.
- Inhibit the release of insulin and stress hormones.
- Blood sugar becomes more stable and hunger is calmed.
- Anxiety decreases.



Ketogenic Eating and Fasting Patterns

The Wahls Protocol® Seminar

Ketones = “Superfuel”

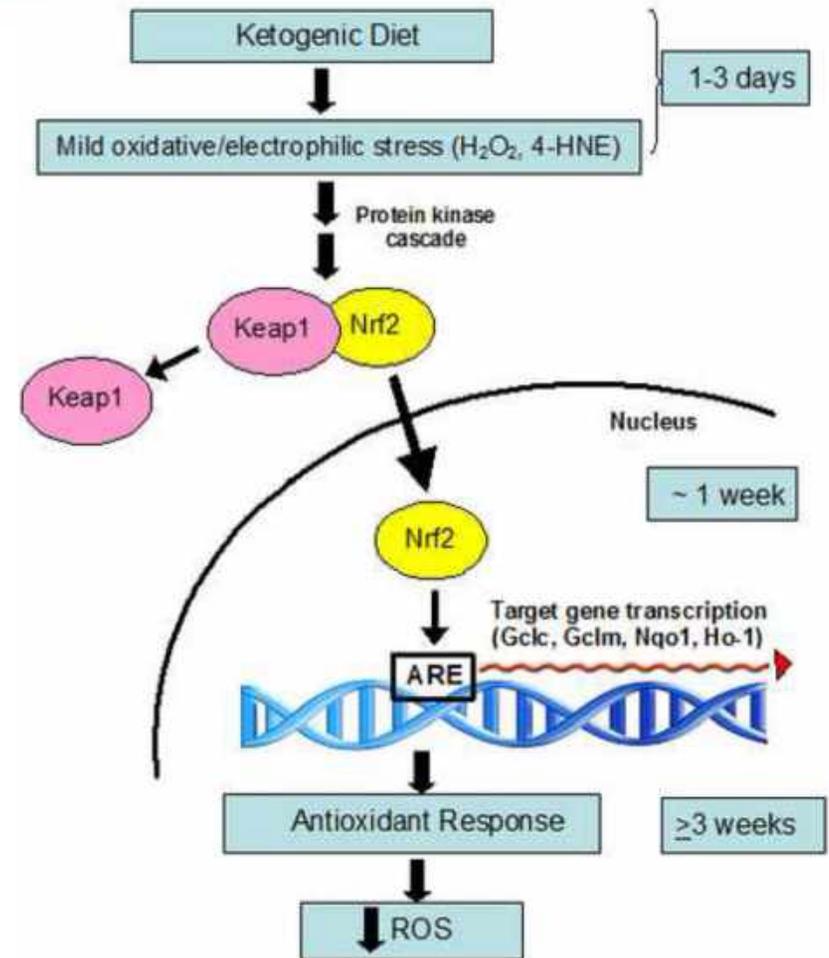


- β -hydroxybutyrate, the principal “ketone,” is not just a fuel, but a “superfuel,” more efficiently producing ATP energy than glucose or fatty acid.
- Without this adaptation, *H. sapiens* could not have evolved such a large brain.

Cahill GF Jr, Veech RL. Ketoacids? Good medicine? Trans Am Clin Climatol Assoc. 2003;114:149-61; discussion 162-3

The Wahls Protocol[®] Seminar

- Proposed temporal schematic of Nrf2 activation by the ketogenic diet.



- Milder JB, Patel M. Modulation of oxidative stress and mitochondrial function by the ketogenic diet. *Epilepsy Research*. 2012;100(3):295-303. doi:10.1016/j.epilepsyres.2011.09.021. Used with permission.

The Wahls Protocol® Seminar

Effects of Ketogenic Diet

- Reduces inflammation (NFκB)
- Enhances mitochondrial biogenesis
- Enhances ATP production
- Reduces ROS production
- Increases insulin sensitivity
- Increases leptin sensitivity

Branco AF, et al. Ketogenic diets: from cancer to mitochondrial diseases and beyond. Eur J Clin Invest. 2016 Mar;46(3):285-98. doi: 10.1111/eci.12591.

<p>Longevity</p>	<p>Preclinical studies on male mice show that <i>KD reduced midlife mortality</i></p>	<p>Newman JC et al. <i>Cell Metabolism</i> 2017; 26:547-57 Roberts MN et al. <i>Cell Metabolism</i> 2017; 26:539-46</p>
<p>Mental clarity</p>	<p>Preclinical studies on male rodents show that <i>KD improves learning and memory outcomes in models of neurodegenerative diseases</i></p>	<p>Kashiwaya Y et al. <i>Neurobiology of Aging</i> 2012; 1-10 Reger M et al. <i>Neurobiology of Aging</i> 2004; 25:311-14 Kim DY et al. <i>PLoS ONE</i> 2012; 7(5):e35476 Zhao W et al. <i>PLoS ONE</i> 2012; 7(11):49191</p>
<p>Cognition</p>	<p>KD research has historically focused on <i>neurological disorders</i> whereas cognitive outcomes in healthy subjects have been <i>anecdotally</i> reported</p>	<p>Kashiwaya Y et al. <i>Neurobiology of Aging</i> 2012; 1-10 Reger M et al. <i>Neurobiology of Aging</i> 2004; 25:311-14 Kim DY et al. <i>PLoS ONE</i>, 2012; 7(5):e35476 Zhao W et al. <i>PLoS ONE</i> 2012; 7(11):49191</p>
<p>Mood</p>	<p>Preclinical studies have shown <i>anxiolytic effects</i> associated with KD whereas few case reports have been published showing benefits in humans</p>	<p>Ari C et al. <i>Frontiers in Molecular Neuroscience</i> 2016; 9:137 El-Mallakh RS & Paskitti ME <i>Medical Hypothesis</i> 2001; 57(6):724-26 Bostock ECS et al. <i>Frontiers in Psychology</i> 2017; 8:43</p>

Modified Mediterranean-ketogenic diet vs. American Heart Association Diet

- N= 20
- Cerebrospinal fluid Alzheimer's biomarkers, neuroimaging measures, peripheral metabolism, and cognition in older adults at risk for Alzheimer's.

Modified ketogenic diet is associated with improved cerebrospinal fluid biomarker profile, cerebral perfusion, and cerebral ketone body uptake in older adults at risk for Alzheimer's disease: a pilot study. [eurobiol Aging](#). 2019 Sep 26. pii: S0197-4580(19)30336-7.

Modified Mediterranean-ketogenic diet MMKD vs. American Heart Association Diet

- MMKD was associated with increased cerebrospinal fluid A β 42 and decreased tau.
- There was increased cerebral perfusion and increased cerebral ketone body uptake (^{11}C -acetoacetate PET, in subsample) following MMKD.

Modified ketogenic diet is associated with improved cerebrospinal fluid biomarker profile, cerebral perfusion, and cerebral ketone body uptake in older adults at risk for Alzheimer's disease: a pilot study. [eurobiol Aging](#). 2019 Sep 26. pii: S0197-4580(19)30336-7.

Modified Mediterranean-ketogenic diet MMKD vs. American Heart Association Diet

- Memory performance improved after both diets, which may be due to practice effects.
- A ketogenic intervention targeted toward adults at risk for Alzheimer's may prove beneficial in the prevention of cognitive decline.

Modified ketogenic diet is associated with improved cerebrospinal fluid biomarker profile, cerebral perfusion, and cerebral ketone body uptake in older adults at risk for Alzheimer's disease: a pilot study. [eurobiol Aging](#). 2019 Sep 26. pii: S0197-4580(19)30336-7.

Low-fat Versus Ketogenic Diet in Parkinson's Disease: A Pilot Randomized Controlled Trial

N-47, 38 completed the study

Both groups significantly decreased their MDS-UPDRS scores, but the ketogenic group decreased more in Part 1 (-4.58 ± 2.17 points, representing a 41% improvement in baseline Part 1 scores) compared to the low-fat group (-0.99 ± 3.63 points,

Journal of Alzheimer's Disease & Parkinsonism
Case Report Open Access

Reversal of Cognitive Decline: 100 Patients

Dale E Brickman¹, Kenneth Martin¹, David Justicia¹, Miki Okano¹, Wei Youngberg², Sharon Hunsain Cobert³, Anne Stefan⁴, Ronald L Brown⁵, Seth Cooper⁶, Craig Tassaf⁷, Adam Hollaway⁸, Michael Kogut⁹, David Rajagopal¹⁰, Edwin Anwar¹¹, Amylou Ansel¹², Nathaniel Bergman¹³, Carol Diamond¹⁴, Jean Lawrence¹⁵, Rene Moore-Raaij¹⁶, Patricia Henry¹⁷ and Mary Bross¹⁸

¹Department of Molecular and Medical Pharmacology, David Geffen School of Medicine, University of California, Los Angeles, Los Angeles, CA, USA
²Waverley, Sydney, Australia
³Youngberg Liberty Medicine Clinic, Tennessee, GA, USA
⁴Wynston Health, Austin, TX, USA
⁵Kronos Healthcare Institute, Durham, NC, USA
⁶West Health, Hollywood, FL, USA
⁷Integrative Functional Medicine, San Rafael, CA, USA
⁸KUW Center for Integrative Medicine, George Washington University, Washington, DC, USA
⁹Chiropractic Medical Institute, Jacksonville, NC, USA
¹⁰Department of Neurology, University of California, Los Angeles, Los Angeles, CA, USA
¹¹Neuro Institute, Los Angeles, CA, USA
¹²Center for Parkinson Medicine, Cleveland Clinic, Cleveland, OH, USA
¹³Mount Sinai Hospital, New York, NY, USA
¹⁴Lamarque Health and Wellness, Toronto, ON, USA
¹⁵Brain and Behavior Clinic, Boulder, CO, USA

Abstract
The first examples of reversal of cognitive decline in Alzheimer's disease and the pre-Alzheimer's disease conditions MCI (Mild Cognitive Impairment) and SCI (Subjective Cognitive Impairment) have recently been published. These two publications described a total of 19 patients showing sustained subjective and objective improvement in cognition, using a comprehensive, precision medicine approach that involves determining the potential contributors to the cognitive decline (e.g., dysfunction of the innate immune system by pathogens or microbial permeability, reduction in trophic or neuronal support, specific toxin exposure, or other contributors), using a computer-based algorithm to determine subtype and then addressing each contributor using a personalized, targeted, multi-factorial approach dubbed ReCODE for reversal of cognitive decline.
An obvious criticism of the initial studies is the small number of patients reported. Therefore, we report here 100 patients, treated by several different physicians, with documented improvement in cognition, in some cases with documentation of improvement in electrophysiology or imaging, as well. This additional report provides further support for a randomized, controlled clinical trial of the protocol and the overall approach.

Keywords: Alzheimer's, Mild cognitive impairment, Precision medicine, ReCODE, Precision medicine, Amyloid precursor protein, Synaptic plasticity, Synaptotagmin.

Introduction
Alzheimer's disease is now the third leading cause of death in the United States [1-4], and the development of effective treatment and prevention is a major healthcare goal. However, clinical trials of drug candidates for Alzheimer's disease treatment have been almost uniformly unsuccessful. There may be several reasons for such repeated failure: (1) given the long pre-symptomatic period, treatment is typically initiated late in the pathophysiological process; (2) what is referred to as Alzheimer's disease is a heterogeneous group of related diseases [1,2,5,7] in which APP, the amyloid precursor protein, functions as a molecular switch due to its activity as an integrator dependent receptor [8-10] in the presence of sufficient support from trophic signaling. APP is cleaved at the alpha site, leading to the production of two synaptotoxic peptides, Aβ40 and Aβ42. In contrast, in the absence of sufficient support from trophic signaling, APP is cleaved at the beta, gamma, and epsilon sites, leading to the production of four synaptotoxic peptides, sAPPβ, Aβ, IsAPP, and C99. In this model, inflammation exerts an anti-trophic effect on APP signaling, at least in part via the NF-κB (nuclear factor-κB light chain enhancer of B cells) inducible of IκBα (inhibitor of κBα) (inhibitor of NF-κB) and gamma-secretase activity. Similarly, toxins such as divalent metals (e.g., mercury) also exert an anti-trophic effect on APP signaling, since these

2018 Aug;33(8):1306-1314. doi: 10.1002/mds.27390. Epub 2018 Aug 11.

Low-fat Versus Ketogenic Diet in Parkinson's Disease: A Pilot Randomized Controlled Trial

N-47, 38 completed the study

Representing an 11% improvement) ($P < 0.001$), with the largest between-group decreases observed for urinary problems, pain and other sensations, fatigue, daytime sleepiness, and cognitive impairment.

2018 Aug;33(8):1306-1314. doi: 10.1002/mds.27390. Epub 2018 Aug 11.



The image shows a page from the Journal of Alzheimer's Disease & Parkinsonism. The article title is "Reversal of Cognitive Decline: 100 Patients". The authors listed are Dale E. Brackman, Kenneth Martin, David Justicia, Miki Okano, Wei Youngberg, Sharon Hunsain Cobart, Anne Stefan, Ronald L. Brown, Seth Cooper, Craig Tassaf, Ann Hollaway, Michael Kogut, David Rapoport, Edwin Assouf, Amylou Assouf, Nathaniel Bergman, Carol Diamond, Jean Lawrence, Rene Moore-Raaij, Patricia Henry, and Mary Broad. The abstract discusses the reversal of cognitive decline in Alzheimer's disease and pre-Alzheimer's disease conditions (MCI and SCI) using a personalized, targeted, multi-factorial approach called ReCODE. It mentions that 19 patients showed sustained subjective and objective improvement in cognition, and that the authors report here on 100 patients, tracked by several different physicians, with documented improvement in cognition, in some cases with documentation of improvement in electrophysiology of imaging, as well. The abstract also notes that this additional report provides further support for a randomized, controlled clinical trial of the protocol and the overall approach.

Abstract

The first examples of reversal of cognitive decline in Alzheimer's disease and the pre-Alzheimer's disease conditions MCI (Mild Cognitive Impairment) and SCI (Subjective Cognitive Impairment) have recently been published. These two publications described a total of 19 patients showing sustained subjective and objective improvement in cognition, using a comprehensive, precision medicine approach that involves determining the potential contributors to the cognitive decline (e.g., reduction of the acute immune system by pathogen or microbial permeability, reduction in toxins or hormonal support, specific toxin exposure, or other contributors), using a computer-based algorithm to determine subtype and then addressing each contributor using a personalized, targeted, multi-factorial approach called ReCODE for reversal of cognitive decline.

An obvious criticism of the initial studies is the small number of patients reported. Therefore, we report here 100 patients, tracked by several different physicians, with documented improvement in cognition, in some cases with documentation of improvement in electrophysiology or imaging, as well. This additional report provides further support for a randomized, controlled clinical trial of the protocol and the overall approach.

Keywords: Alzheimer's; Mild cognitive impairment; Precision medicine; ReCODE; Precision medicine; Amyloid precursor protein; Synaptic; Synaptic; Synaptic.

Introduction

Alzheimer's disease is now the third leading cause of death in the United States [1-4], and the development of effective treatment and prevention is a major healthcare goal. However, clinical trials of drug candidates for Alzheimer's disease treatment have been almost uniformly unsuccessful. There may be several reasons for such repeated failure: (1) given the long pre-symptomatic period, treatment is typically initiated late in the pathophysiological process; (2) what is referred to as Alzheimer's disease is a multi-factorial process, not a single disease; (3) the disease is a complex process in which APP, the amyloid precursor protein, functions as a molecule which due to its activity as an integrator dependent receptor [8-10] in the presence of sufficient support from trophic signaling, APP is cleaved at the alpha site, leading to the production of two synaptotoxic peptides, Aβ42 and Aβ43. In contrast, in the absence of sufficient support from trophic signaling, APP is cleaved at the beta, gamma, and epsilon sites, leading to the production of four synaptotoxic peptides, sAPPβ, Aβ, sAPPα, and C99. In this model, inflammation exerts an anti-trophic effect on APP signaling, at least in part via the NF-κB (nuclear factor-κB) light chain enhancer of B cells) inducible of IκBα (inhibitor of κB kinase) and gamma-secretase activity; similarly, toxins such as divalent metals (e.g., mercury) also exert an anti-trophic effect on APP signaling, since these

Coconut Oil Enriched Mediterranean Diet

- **N=44**
- Coconut oil enriched Mediterranean diet for 21 days and a control group.
- 7 Minute Screen, which analyses temporal orientation, visuospatial and visuoconstructive abilities, and semantic and episodic memory.

Improvement of Main Cognitive Functions in Patients with Alzheimer's Disease after Treatment with Coconut Oil Enriched Mediterranean Diet: A Pilot Study. [J Alzheimers Dis.](#) 2018;65(2):577-587.

Coconut Oil Enriched Mediterranean Diet

- **RESULTS:**
- After intervention with coconut oil, improvements in episodic, temporal orientation, and semantic memory were observed, and it seems that the positive effect is more evident in women with mild-moderate state.

Improvement of Main Cognitive Functions in Patients with Alzheimer's Disease after Treatment with Coconut Oil Enriched Mediterranean Diet: A Pilot Study. [J Alzheimers Dis.](#) 2018;65(2):577-587.



A Modified MCT-Based Ketogenic Diet Increases Plasma β -Hydroxybutyrate but Has Less Effect on Fatigue and Quality of Life in People With Multiple Sclerosis Compared to a Modified Paleolithic Diet: A Waitlist-Controlled, Randomized Pilot Study

- N= 15; randomized, wait list control MCT ketogenic diet, modified paleo diet
- MCT ketogenic diet group achieved ketosis, improved insulin sensitivity
- Paleo diet had greater clinically significant improvements in fatigue, quality of life than the MCT ketogenic diet

J Am Coll Nutr 2020 Mar 26;1-13. doi: 10.1080/07315724.2020.1734988.

Pilot study of a ketogenic diet in relapsing-remitting MS

N=20, single arm, open label

- **Results** No subject experienced worsening disease on diet.
- Nineteen subjects (95%) adhered to KD^{MAD} for 3 months and 15 (75%) adhered for 6 months.
- Fatigue ($p = 0.002$) and depression scores ($p = 0.003$) were improved. Serologic leptin was significantly lower at 3 months ($p < 0.0001$) on diet.



<https://nn.neurology.org/content/6/4/e565>



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Ketogenic Diet Are Suitable for Diabetes

- LCD /KD can be effective in obesity and/or type 2 diabetes.
- LCD / KD should be tailored to individual needs
- Patients should be followed for an extended period of time.
- The use of those diets in patients with type 1 diabetes is still controversial and their long-term safety is still unproven.

What are the potential problems
with ketogenic eating?

Risks of Nutritional Ketosis Over Time

- Nutritional depletion
- Excessive weight loss
- Potential decreased bone density
- Body perceives insufficient nutrition for reproduction

1. The effect of the ketogenic diet on the developing skeleton. [Epilepsy Res.](#) 2017 Oct;136:62-66



The Wahls Protocol® Seminar Risks of Ketogenic Diets Pregnancy/ Hormones

- Shifts in sex hormones - not a good time to reproduce
- A ketogenic diet during gestation results in alterations in embryonic organ growth. Such alterations may be associated with organ dysfunction and potentially behavioral changes in postnatal life.
- Salt wasting, lower BP, lower appetite, weight loss

1. Effects of severe dietary restriction on male reproductive hormones. [J Clin Endocrinol Metab.](#) 1986 Feb;62(2):288-92.

2. Effects of a ketogenic diet during pregnancy on embryonic growth in the mouse. [BMC Pregnancy Childbirth.](#) 2013 May 8;13:109

Many Popular Ketogenic Diets

- Dairy based
- Stress eggs
- Have a 25 gram carb limit
- Can be inflammatory as a result
- Have less resistant starch
- Shifting microbiome



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Gluten and Casein and Opioids

- Gluten can be degraded into several morphine-like substances, named gluten exorphins.
 - Milk proteins are particularly strong allergens similar to gluten and may also trigger reactions if gluten sensitive.
1. The opioid effects of gluten exorphins: asymptomatic celiac disease. [J Health Popul Nutr.](#) 2015 Nov 24;33:24.
 2. Opioid receptor ligands derived from food proteins. [Curr Pharm Des.](#) 2003;9(16):1331-44.
 3. β -casomorphin-7 alters μ -opioid receptor and dipeptidyl peptidase IV genes expression in children with atopic dermatitis. [Peptides.](#) 2014 Dec;62:144-9.

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Risks of Dairy (casein)

- Butyrophilin – molecular mimicry -myelin oligodendrocyte glycoprotein (MOG)
- A1 casein metabolized to beta-casomorphin7 which is similar to morphine
- A1 casein associated with more gut and cognitive symptoms
- Casein cross reacts with gluten and associated with higher rates of MS and schizophrenia

1. Tolerance induction by molecular mimicry: prevention and suppression of experimental autoimmune encephalomyelitis with the milk protein butyrophilin. [Int Immunol.](#) 2004 Mar;16(3):489-99.
2. Systematic Review of the Gastrointestinal Effects of A1 Compared with A2 β -Casein. [Adv Nutr.](#) 2017 Sep 15;8(5):739-748
3. Influence of candidate polymorphisms on the dipeptidyl peptidase IV and μ -opioid receptor genes expression in aspect of the β -casomorphin-7 modulation functions in autism. [Peptides.](#) 2015 Mar;65:6-11. doi: 10.1016/j.peptides.2014.11.012
4. Effects of milk containing only A2 beta casein versus milk containing both A1 and A2 beta casein proteins on gastrointestinal physiology, symptoms of discomfort, and cognitive behavior of people with self-reported intolerance to traditional cows' milk. [Nutr J.](#) 2016 Apr 2;15:35.
5. The brain-gut axis dysfunctions and hypersensitivity to food antigens in the etiopathogenesis of schizophrenia. [Psychiatr Pol.](#) 2016;50(4):747-760.

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Risks of Eggs

- Pros - Grass fed - DHA, **choline**, biotin, lutein, Vitamins A, D, K2, and B3, B6, B9, B12 (eat organ meat if NOT eating eggs)
- Cons
 - Eggs are most common food allergen in IBD >70%
 - 60% IBD patients have IgG Ab to eggs
 - 13% seasonal allergies have IgG Ab to eggs
 - Wheat, milk, eggs are common food triggers to Eosinophilic Esophagitis

1. The utility of food antigen test in the diagnosis of Crohn's disease and remission maintenance after exclusive enteral nutrition. [Clin Res Hepatol Gastroenterol](#). 2017 Oct 25. pii: S2210-7401(17)30211-5
2. Prevalence of IgG-mediated food intolerance among patients with allergic symptoms [Ann Saudi Med](#). 2016 Nov-Dec;36(6):386-390..
3. Cracking the egg: An insight into egg hypersensitivity. [Mol Immunol](#). 2015 Aug;66(2):375-83. doi: 10.1016/j.molimm.2015.04.016. [Med J Malaysia](#). 2017 Aug;72(4):215-220.
4. Food allergy and allergic rhinitis in 435 asian patients - A descriptive review.
5. Allergy tests do not predict food triggers in adult patients with eosinophilic oesophagitis. A comprehensive prospective study using five modalities. [Aliment Pharmacol Ther](#). 2016 Aug;44(3):223-33.
6. Serological investigation of food specific immunoglobulin G antibodies in patients with inflammatory bowel diseases.

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	Dairy based	MCT based
Fat	90%	60 to 70%
Carbohydrate	5% 25 grams	15-20% 50 to 80 grams
Protein	5%	15- 20%

What Are the Risks of Coconut Oil

- Elevated lipids
 - Total cholesterol
 - Triglycerides
- Increased endotoxemia (LPS)

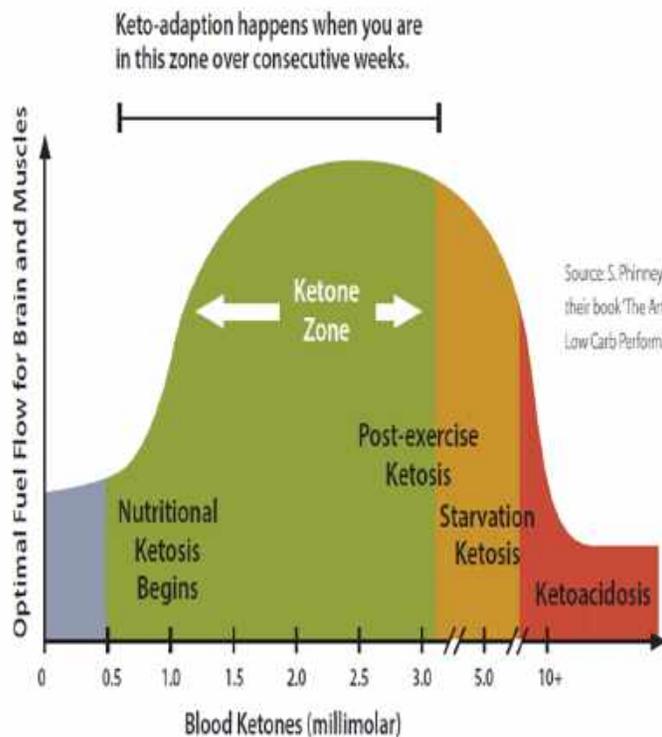
1. Postprandial serum endotoxin in healthy humans is modulated by dietary fat in a randomized, controlled, cross-over study. [Lipids Health Dis.](#) 2016 Nov 5;15(1):186.
2. [Dietary oil composition differentially modulates intestinal endotoxin transport and postprandial endotoxemia.](#) *Nutr Metab (Lond)*. 2013 Jan 10;10(1):6. doi: 10.1186/1743-7075-10-6.



The Wahls Protocol[®] Seminar Measuring Ketones

- **Breath**: measures **acetone**
- **Urine**: measures urinary excretion of **acetoacetate** - although this is the easiest and most common test, it may provide **false negative** results following keto-adaptation
- **Blood**: finger stick /serum measuring circulating β HB levels - **most accurate**

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➤ Optimal Levels of Ketosis:

- Overnight fasting: 0.2-0.5mM
- Nutritional Ketosis (KD): 0.5-3.0mM

➤ Dangerous Levels:

- Ketoacidosis: >10mM

Adapted from: Volek JS & Phinney SD et al. *The Art and Science of Low Carbohydrate Performance* 2012.



Clinical Choices

Monitor Lipids, Response

- Coconut oil/MCT or Olive oil ketogenic (check lipids)
- If Olive Oil – it will be harder to get into ketosis
- If using Olive Oil – I also have patients add fasting



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Other Options to Consider

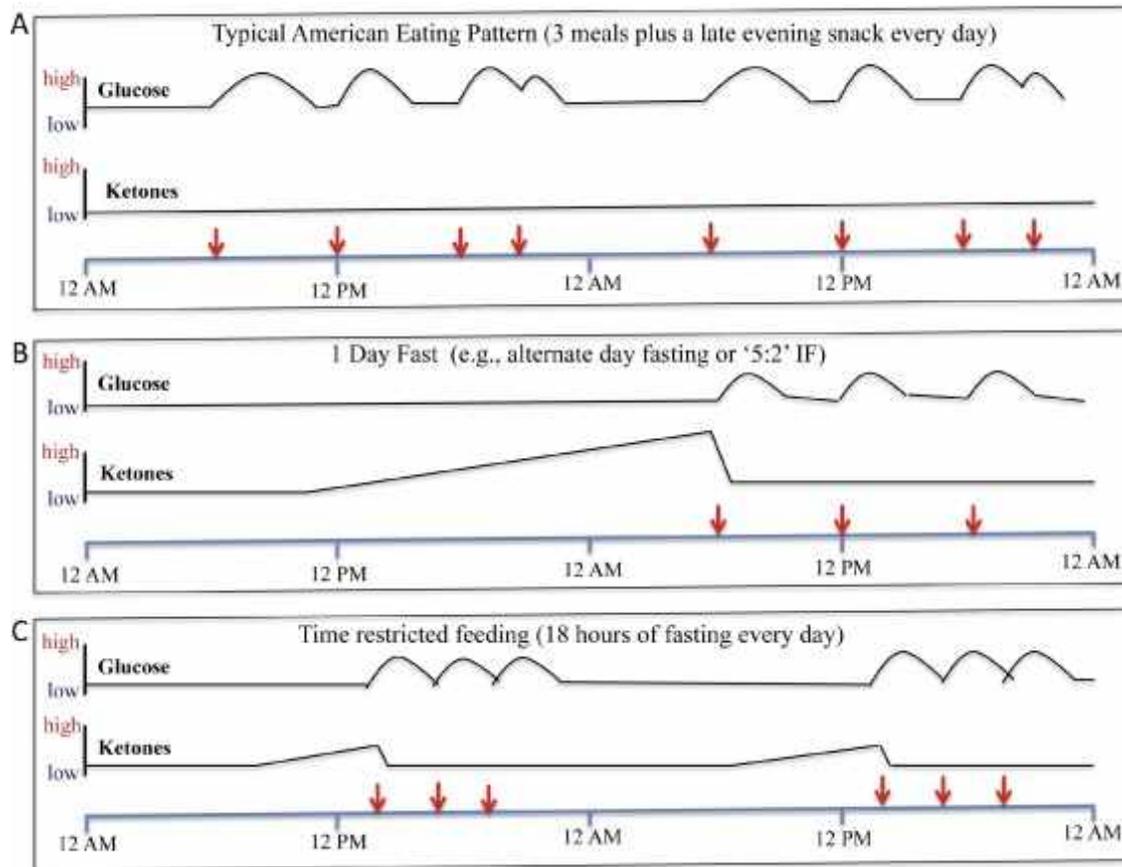
Low Glycemic Index Neuroprotective

- **Low-glycemic-index treatment: a liberalized ketogenic diet for treatment of intractable epilepsy.** Neurology. 2005 Dec 13;65(11):1810-2.
- **Dietary glycemic load and glycemic index and risk of cerebrovascular disease in the EPICOR cohort** PLoS One. 2013 May 23;8(5):e62625. doi: 10.1371/journal.pone.0062625. Print 2013.

The Wahls Protocol® Seminar
CR, IF, & Longevity

“[Caloric Restriction] increases the lifespan in a wide array of organisms including humans...these restrictions not only have a direct effect on metabolism but also are capable of regulation gene expression...the amount and quality of nutrients in the diet influence longevity by modifying the epigenetic pattern.”

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IF eg 60% energy restriction on 2 days per week or every other day

PF eg 5 -7day diet of 250-1100 kcal/day

TRF - limiting the daily period of food intake to 8h or less

With Their Current Dietary Pattern

- **Intermittent Fasting:**
 - 16-18 hour fast weekly or monthly
 - 24 hour fast monthly
 - 12+ hour fast every daily
 - 5:2 food plan

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Intermittent Fasting Time Restricted Eating

- 12 hours from dinner to breakfast every day
- 16 hours from dinner to lunch 1-2x week or month
- 24 hour fast weekly or monthly

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- **Caloric Restriction:**
 - 20-30% less BMR
 - or about 600 cal/day

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“....switching from eating 3 full meals per day to one moderate size meal every other day (500-600 calories 2d/wk)”

- Increased insulin sensitivity
- Increased BDNF
- Increased mobilization of fatty acids
- Elevated B-hydroxybutyrate

Mattson M, Allison D, Fontana L et al. Meal frequency and timing in health and disease. Proceedings of the National Academy of Sciences. 2014;111(47):16647-16653. doi:10.1073/pnas.1413965111.

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CR: 20-30% Reduction

- **MALES:** Average calories consumed per day for males (assuming moderate activity) is generally 2000– 2400 calories, so a **20–30% reduction of calories would be a range of approximately 1400– 1800 calories per day.**

CR: 20-30% Reduction

- **FEMALES:** Average calories consumed per day for females (assuming moderate activity) is generally 1400–1800 calories, so a **20–30% reduction of calories would be a range of approximately 1000–1400 calories per day.**

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CR 600 Cals

600 calorie menu plan

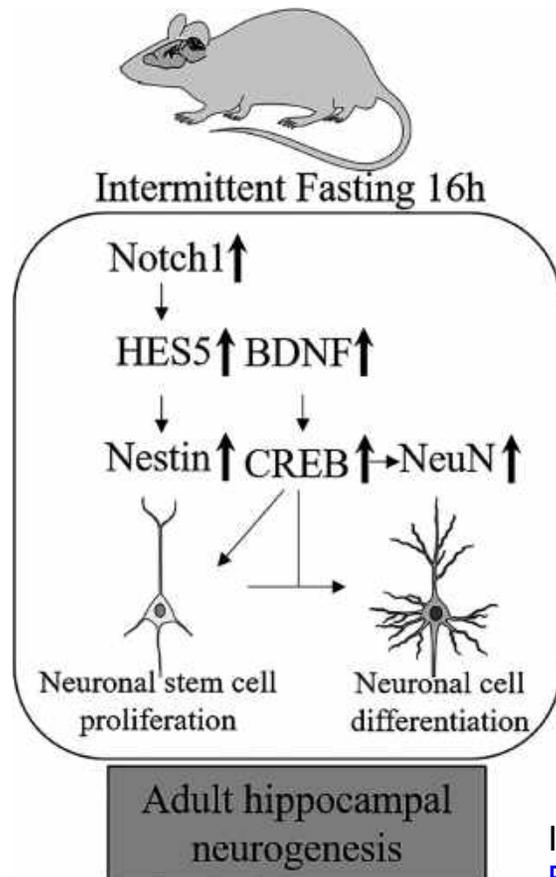
Breakfast: spinach omelet (two eggs) with 1 cup spinach cooked in coconut oil, plus a small handful of pumpkin seeds or walnuts and ½ cup blueberries

Lunch: grass-fed beef or buffalo burger or an organic turkey burger with 2 cups of salad greens (or a mixture of kale and greens) plus 2 cups of raw veggies, tossed with olive oil and your favorite vinegar, and a roasted seaweed snack

Dinner: wild salmon with 1 cup cooked broccoli and salad of 1 ½ cups greens, ½ cup cherry tomatoes, ½ cup thinly sliced red cabbage, handful of almonds, and ¼ avocado, tossed with olive oil and balsamic vinegar

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Intermittent Fasting



- Hippocampal neurogenesis increased
- 16 hour fasting superior
- Increased BDNF

Intermittent fasting increases adult hippocampal neurogenesis.
[Brain Behav.](#) 2019 Dec 5:e01444. doi: 10.1002/brb3.1444.

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Intermittent Metabolic Switching, Neuroplasticity and Brain Health

- Individuals whose brains and bodies functioned well in a fasted state were successful in acquiring food, enabling their survival and reproduction.
- With fasting and extended exercise, liver glycogen stores are depleted and ketones are produced from adipose-cell-derived fatty acids.
- Molecular adaptations of neural networks in the brain that enhance their functionality and bolster their resistance to stress, injury and disease.

Intermittent metabolic switching, neuroplasticity and brain health. [Nat Rev Neurosci](#). 2018 Feb;19(2):63-80. doi: 10.1038/nrn.2017.156. Epub 2018 Jan 11.

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Fasting Mimicking Diet

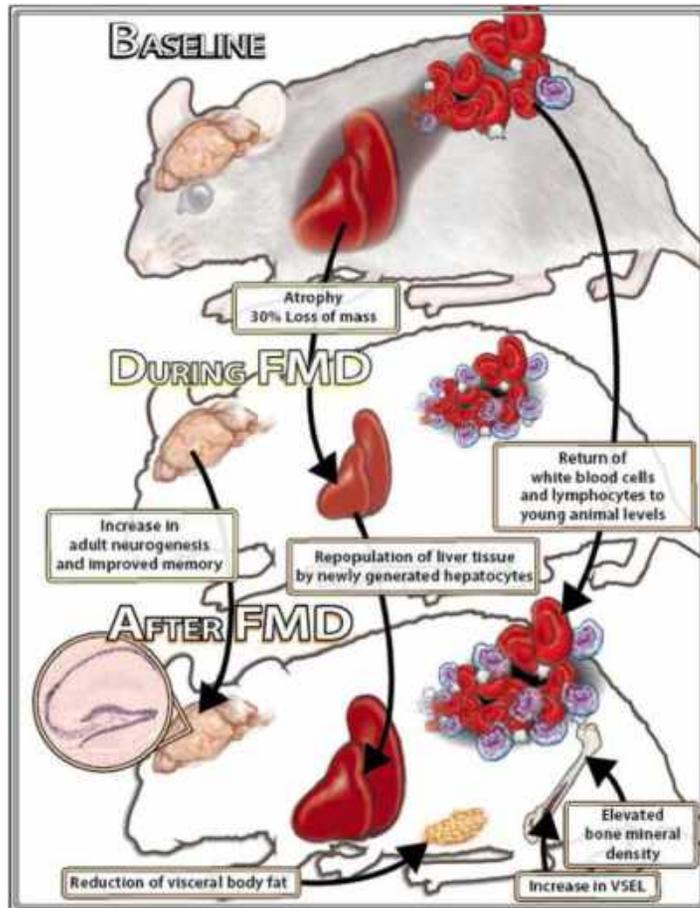
- N= 100 healthy adults, cross over
- 5 days/month for 3 months (FMD)
- Control diet 3 months
- FMD reduced weight, trunk, total fat, B/P, IGF-1
- FBS, Trigs, low-density LDL, CRP more benefit in at risk participants



Wei M, Brandhorst S, Shelehchi M, et al. Fasting-mimicking diet and markers/risk factors for aging, diabetes, cancer, and cardiovascular disease. *Science Translational Medicine*. 2017;9(377).

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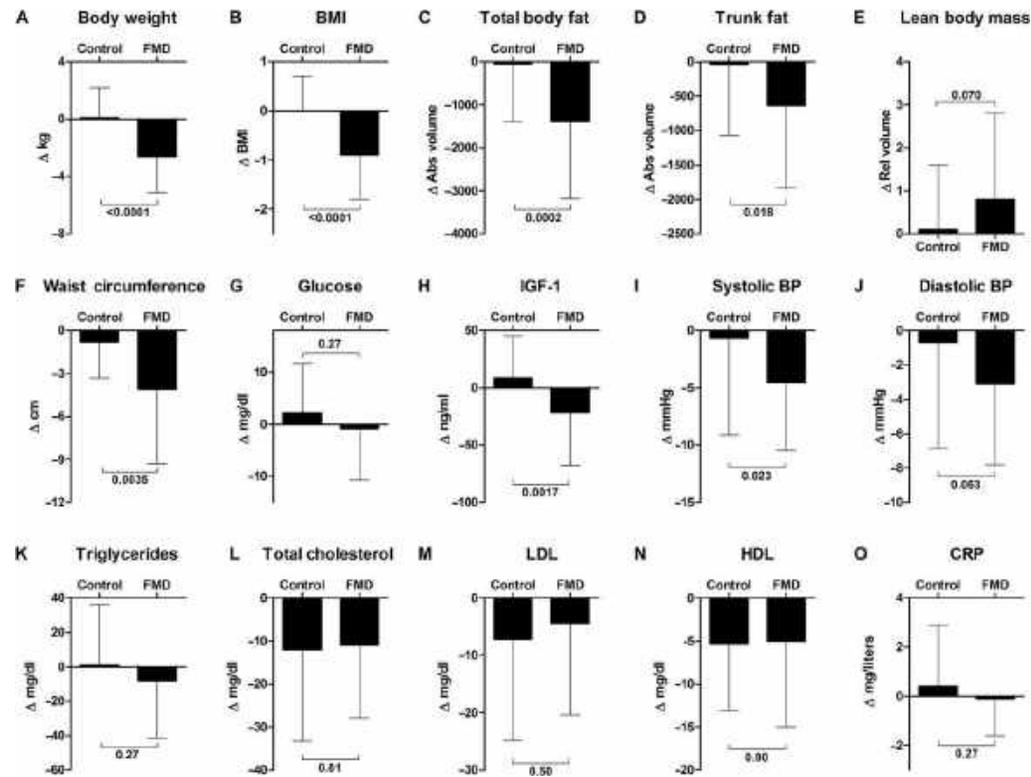
Fasting Mimicking Diet



Fasting-mimicking diet and markers/risk factors for aging, diabetes, cancer, and cardiovascular disease. [Sci Transl Med.](#) 2017 Feb 15;9(377).

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Fasting-mimicking diet and aging, DM, CA, CAD



Fasting-mimicking diet and markers/risk factors for aging, diabetes, cancer, and cardiovascular disease Fasting-mimicking diet and markers/risk factors for aging, diabetes, cancer, and cardiovascular disease
[Sci Transl Med.](#) 2017 Feb 15;9(377). pii: eaai8700.



Reduced: glucose, insulin, leptin, total cholesterol, CRP, TNF α , IL-6, markers of oxidative stress, IGF-1

Increased: 3OHB, adiponectin



Decreased resting heart rate
Increased heart rate variability
Decreased blood pressure

Increased insulin sensitivity
Ketone body production

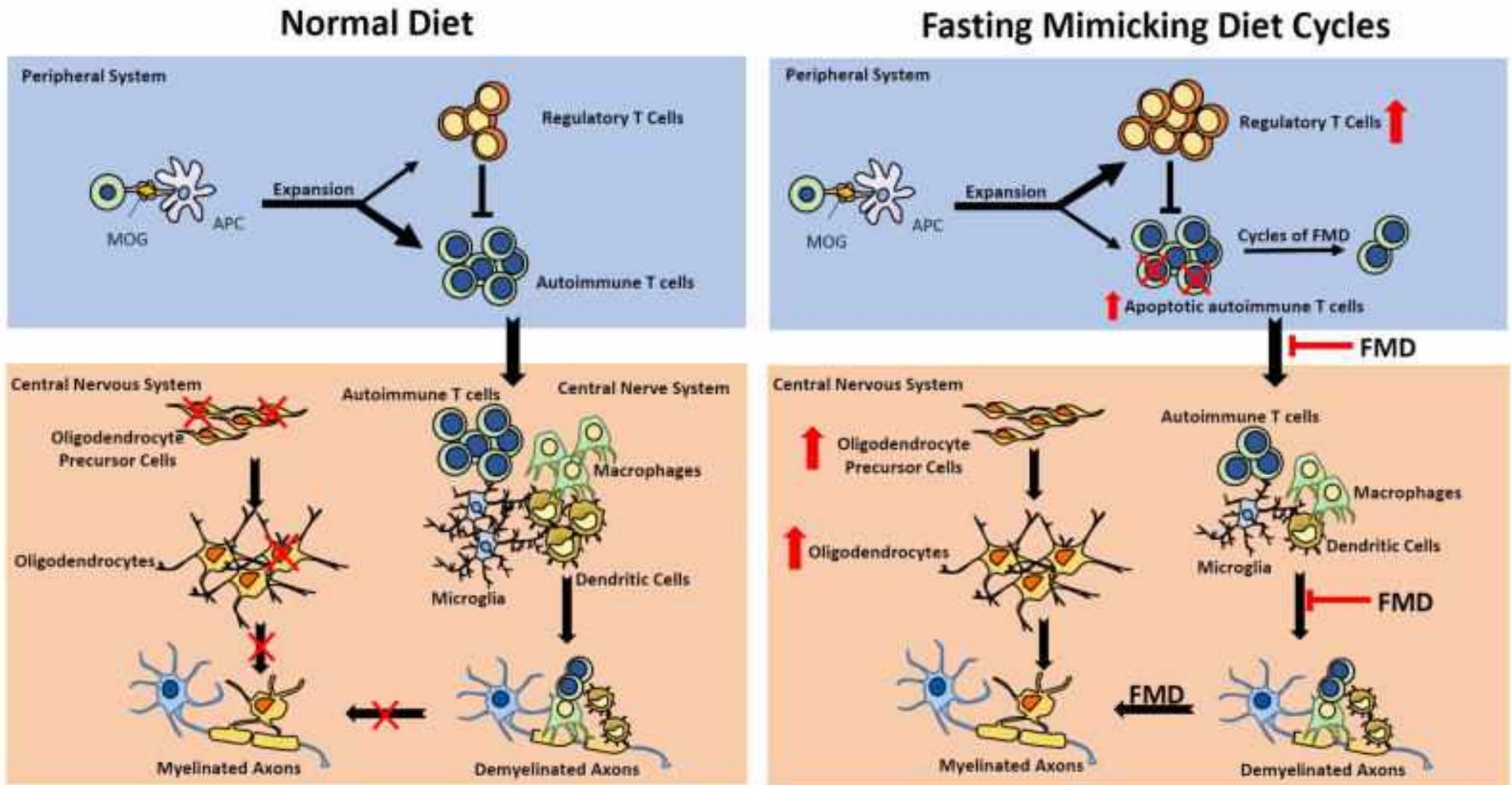


Increased insulin sensitivity
Enhanced autophagy

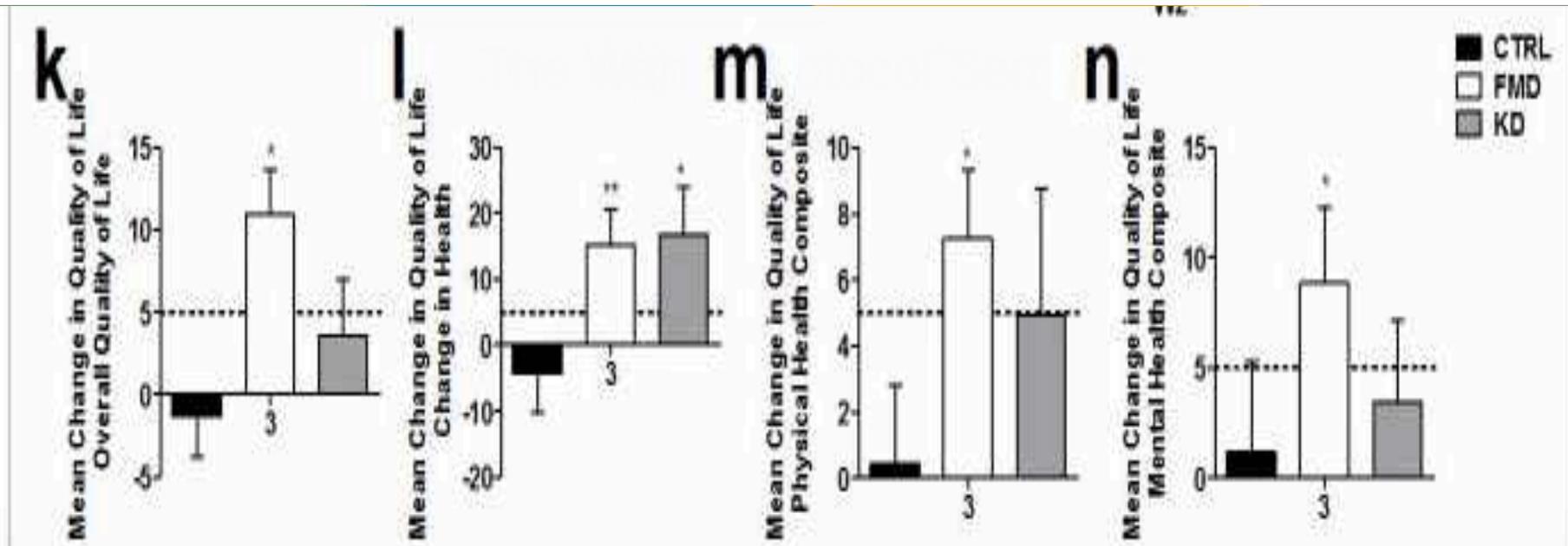


Fatty acid mobilization
Reduced inflammation

Impact of intermittent fasting on health and disease processes.
[Ageing Res Rev.](#) 2017 Oct;39:46-58



A Diet Mimicking Fasting Promotes Regeneration and Reduces Autoimmunity and Multiple Sclerosis Symptoms. Cell Rep. 2016 Jun 7; 15(10): 2136–2146.



Change at 3 month of (k) overall quality of life, (l) change in health, (m) physical health composite, and (n) mental health composite. The dotted line represents a threshold that is thought to be clinically important

FMD in Mouse Model of PD

- Fasting 3 days followed by 4 days of refeeding for three 1-week cycles
- (BDNF) increased in PD mice
- Neuroinflammation decreased
- Microbiome changed

Neuroprotection of Fasting Mimicking Diet on MPTP-Induced Parkinson's Disease Mice via Gut Microbiota and Metabolites
[Neurotherapeutics](#). 2019 Jul;16(3):741-760

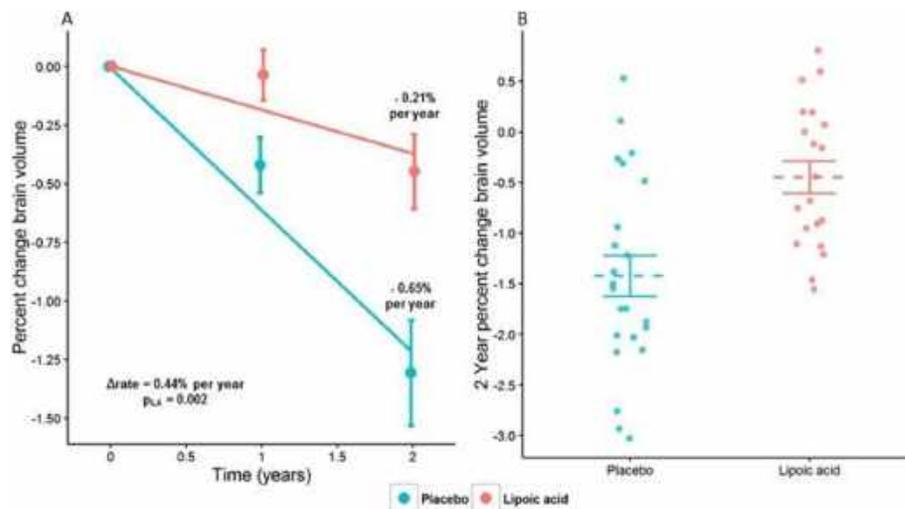
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Remyelination Research

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Lipoic Acid

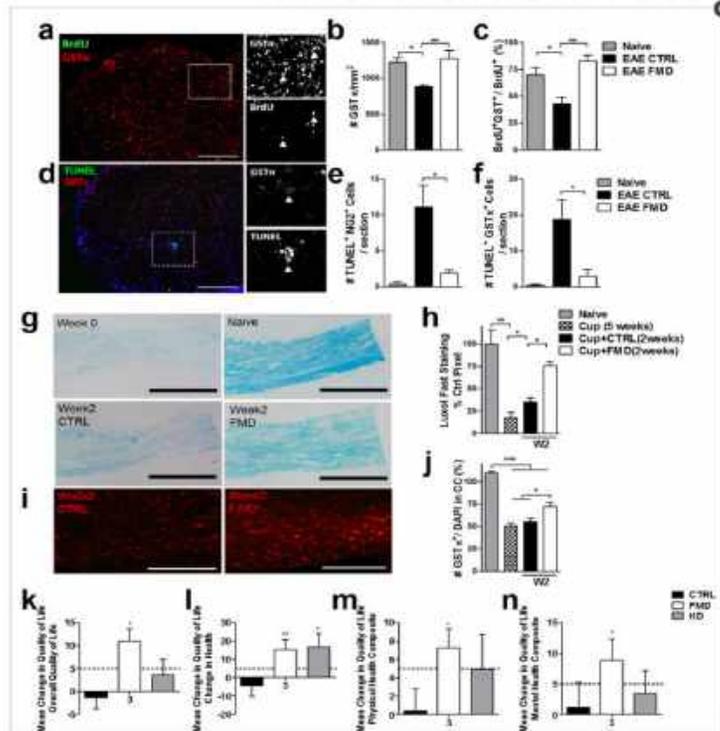
Slower Rates of Brain Volume Loss



N=51 SPMS
Annualized
Brain loss
-0.21% vs
-0.65%

Lipoic acid in secondary progressive MS: A randomized controlled pilot trial. [Neurol Neuroimmunol Neuroinflamm.](#) 2017 Jun 28;4(5):e374.

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Cell Rep. 2016 Jun 7; 15(10): 2136–2146.

Remyelination
Fasting Mimicking
Diet -Reduces loss of
oligodendrocyte
precursor cells and
oligodendrocytes and
enhances
remyelination

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Choline -Remyelination

- CDP-choline effectively enhanced myelin regeneration and reversed motor coordination deficits **[oligodendrocyte precursor cells]**
- Dose 500 mg to 1 gram bid
- *Upstream approach—Phosphatidylcholine (PC) 1-4 tbs / day blend with water to make liposomes*
- Eggs, organ meats

1. Skripuletz T, Manzel A, Gropengießer K, Schäfer N, et al. Pivotal role of citocholine metabolites in remyelination. [Brain](#) 2015 Feb;138(Pt 2):398-413
2. Minocycline plus N-acetylcysteine protect oligodendrocytes when first dosed 12 hours after closed head injury in mice. [Neurosci Lett](#). 2018 Aug 24;682:16-20. doi: 10.1016/j.neulet.2018.06.010. Epub 2018 Jun 6.



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Cholesterol Remyelination

- Supplemented cholesterol directly supports oligodendrocyte precursor proliferation and differentiation, and repair.
- This leads to attenuated axon damage, enhanced remyelination and improved motor learning.
- Remarkably, in experimental autoimmune encephalomyelitis, cholesterol supplementation does not exacerbate disease expression.

Dietary cholesterol promotes repair of demyelinated lesions in the adult brain. [Nat Commun](#). 2017 Jan 24;8:14241. doi: 10.1038/ncomms14241.



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Lithium Remyelination

- Lithium promoted motor neuron outgrowth and enhanced remyelination.
- An analysis of myelin-associated genes impacted by lithium.
- Efficient remyelination led to an earlier functional recovery.
- (Rat model peripheral nerve)

Lithium accelerates functional motor recovery by improving remyelination of regenerating axons following ventral root avulsion and reimplantation. [Neuroscience](#). 2016 Aug 4;329:213-25. doi: 10.1016/j.neuroscience.2016.05.010. Epub 2016 May 13



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Melatonin Remyelination

- Melatonin decreased neurological disability scores and enhanced remyelination.
- Reduced inflammation by reducing pro-inflammatory cytokines (IL-1 β and TNF- α)
- Increased anti-inflammatory cytokines (IL-4 and IL-10).
- (Mouse model)
- AM UV light/ PM UV blocking

Melatonin Therapy Modulates Cerebral Metabolism and Enhances Remyelination by Increasing PDK4 in a Mouse Model of Multiple Sclerosis [Front Pharmacol.](#) 2019 Feb 28;10:147. doi: 10.3389/fphar.2019.00147. eCollection 2019.

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Resveratrol - remyelination

- Resveratrol effectively enhanced motor coordination and balance, reversed cuprizone-induced demyelination, improved mitochondrial function, alleviated oxidative stress, and inhibited NF-κB signaling
- (Mouse study)
- Grapes, blueberries, cranberries, vegetable skins, cocoa

Resveratrol Promotes Remyelination in Cuprizone Model of Multiple Sclerosis: Biochemical and Histological Study. [Mol Neurobiol.](#) 2017 Jul;54(5):3219-3229. doi: 10.1007/s12035-016-9891-5. Epub 2016 Apr 11.

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Curcumin - remyelination

- The curcumin treatment increased expression myelin sheath thickness and, correspondingly, increased motor and sensitive nerve conduction velocity.
- (Mouse study)
- Turmeric/ curries

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Glycyrrhizic Acid - remyelination

- During the chronic stage when myelin and axon damage has already occurred, GA induced oligodendrocyte progenitor cell (OPC) differentiation into mature oligodendrocytes, thus effectively accelerating remyelination
- (Mouse study)
- Licorice

Glycyrrhizic acid promotes neural repair by directly driving functional remyelination. [Food Funct.](#) 2020 Jan 29;11(1):992-1005. doi: 10.1039/c9fo01459d.



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Quercetin - remyelination

- Quercetin treatment decreased the extent of demyelination areas and increased the remyelination
- Optic nerve repair
- (Mouse study)
- Onions, apples, cherries, citrus, greens

Quercetin improves myelin repair of optic chiasm in lyolecithin-induced focal demyelination model. [Biomed Pharmacother.](#) 2018 May;101:485-493. doi: 10.1016/j.biopha.2018.02.125. Epub 2018 Mar 22.

Terry Wahls MD
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Remyelination - Ursolic Acid

- Using multiple in vivo and in vitro strategies ursolic acid (UA), directly promotes oligodendrocyte maturation and CNS myelin repair
- Oral treatment with UA significantly decreased disease severity and CNS inflammation and demyelination
- (Mouse study)
- Red apple skins, basil, peppermint, lavender, oregano, dried plums

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Vitamin K2mk4 - remyelination

- Promotes Oligodendrogenesis and Myelination in the Adult Central Nervous System.
- (Mouse study)
- Greens / liver / ghee, Emu oil

1. Gas6 Promotes Oligodendrogenesis and Myelination in the Adult Central Nervous System and After Lysolecithin-Induced Demyelination. *ASN Neuro*. 2016 Sep 14;8(5). pii: 1759091416668430
2. Vitamin K enhances the production of brain sulfatides during remyelination. [PLoS One](#). 2018 Aug 27;13(8):e0203057. doi: 10.1371/journal.pone.0203057. eCollection 2018.

Minocycline + NAC

- MINO plus NAC synergistically protected resident oligodendrocytes and decreased the number of oligodendrocyte precursor cells.
- Calmed microglia (inflammation)
- (Rat study of TBI)

Minocycline plus N-acetylcysteine induces remyelination, synergistically protects oligodendrocytes and modifies neuroinflammation in a rat model of mild traumatic brain injury. [J Cereb Blood Flow Metab.](#) 2018 Aug;38(8):1312-1326. doi: 10.1177/0271678X17718106. Epub 2017 Jul 7.

Thymoquinone-Remyelination

- Black Cumin seed (**Thymoquinone**)
- 7.5 MG/KG Rat study
- Neuroprotective; Remyelination
- 1 tsp black seed oil =48 mg thymoquinone

1. Nigella sativa ameliorates inflammation and demyelination in the experimental autoimmune encephalomyelitis-induced Wistar rats. [Int J Clin Exp Pathol.](#) 2015 Jun 1;8(6):6269-86. eCollection 2015.
2. The effect of Nigella sativa oil against experimental allergic encephalomyelitis via nitric oxide and other oxidative stress parameters. [Cell Mol Biol \(Noisy-le-grand\).](#) 2005 Sep 5;51(3):337-42.
3. Amelioration of chronic relapsing experimental autoimmune encephalomyelitis (cr-eae) using thymoquinone - biomed 2009. [Biomed Sci Instrum.](#) 2009;45:274-9.
4. Thymoquinone: An edible redox-active quinone for the pharmacotherapy of neurodegenerative conditions and glial brain tumors. A short review. [Biomed Pharmacother.](#) 2016 Oct;83:635-640.
5. Thymoquinone: an emerging natural drug with a wide range of medical applications [Biomed Pharmacother.](#) 2016 Oct;83:635-640. Thymosin beta4 promotes oligodendrogenesis in the demyelinating central nervous system. [Neurobiol Dis.](#) 2016 Apr;88:85-95. doi: 10.1016/j.nbd.2016.01.010. Epub 2016 Jan 12.



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Thymosin Remyelination

- Thymosin alpha 1
- Thymosin beta 4
- Peptides – produced by Thymus are associated with myelin repair in animal models of myelin repair

1. Thymosins in multiple sclerosis and its experimental models: moving from basic to clinical application. [Mult Scler Relat Disord](#). 2019 Jan;27:52-60. doi: 10.1016/j.msard.2018.09.035. Epub 2018 Oct 2
2. Thymosin beta4 Promotes Oligodendrogenesis in the Demyelinating Central Nervous System. 2016 Apr;88:85-95. doi: 10.1016/j.nbd.2016.01.010. Epub 2016 Jan 12.

The Wahls Protocol[®] Seminar
Tobacco and Toxins

Smoking and Air Pollution

- Increases risk of
 - Alzheimer's
 - Multiple Sclerosis
 - Parkinson's



1. Smoking and Cerebral Oxidative Stress and Air Pollution: A Dreadful Equation with Particulate Matter Involved and One More Powerful Reason Not to Smoke Anything! Journal of Alzheimer's Disease, vol. 54, no. 1, pp. 109-112, 2016
2. Exposure to particulate matter air pollution and risk of multiple sclerosis in two large cohorts of US nurses. 2017 Dec;109:64-72. doi: 10.1016/j.envint.2017.07.013. Epub 2017 Sep 20.
3. Air pollution, a rising environmental risk factor for cognition, neuroinflammation and neurodegeneration: The clinical impact on children and beyond. 2016 Jan;172(1):69-80. doi: 10.1016/j.neurol.2015.10.008. Epub 2015 Dec 21

Pesticides and Neurodegeneration

- **PD, AD and ALS Risk Factors: Pesticides**
(e.g. paraquat, maneb, dieldrin, pyrethroids, organophosphates, glyphosate)
- These pesticides share **common features**:
 - Induce oxidative stress
 - Induce mitochondrial dysfunction
 - Cause neuronal cell death

1. Baltazar MT, Dinis-Oliveira RJ, de Lourdes Bastos M et al. Tsatsakis AM, Duarte JA, Carvalho F. Pesticides exposure as etiological factors of Parkinson's disease and other neurodegenerative diseases--a mechanistic approach. *Toxicol Lett.* 2014 Oct 15;230(2):85-103. doi: 10.1016/j.toxlet.2014.01.039.
2. Samel S, Seneff S, Glyphosate, pathways to modern diseases III: Manganese, neurological diseases, and associated pathologies. *Surg Neurol .Int.* 2015 Mar 24;6:45.

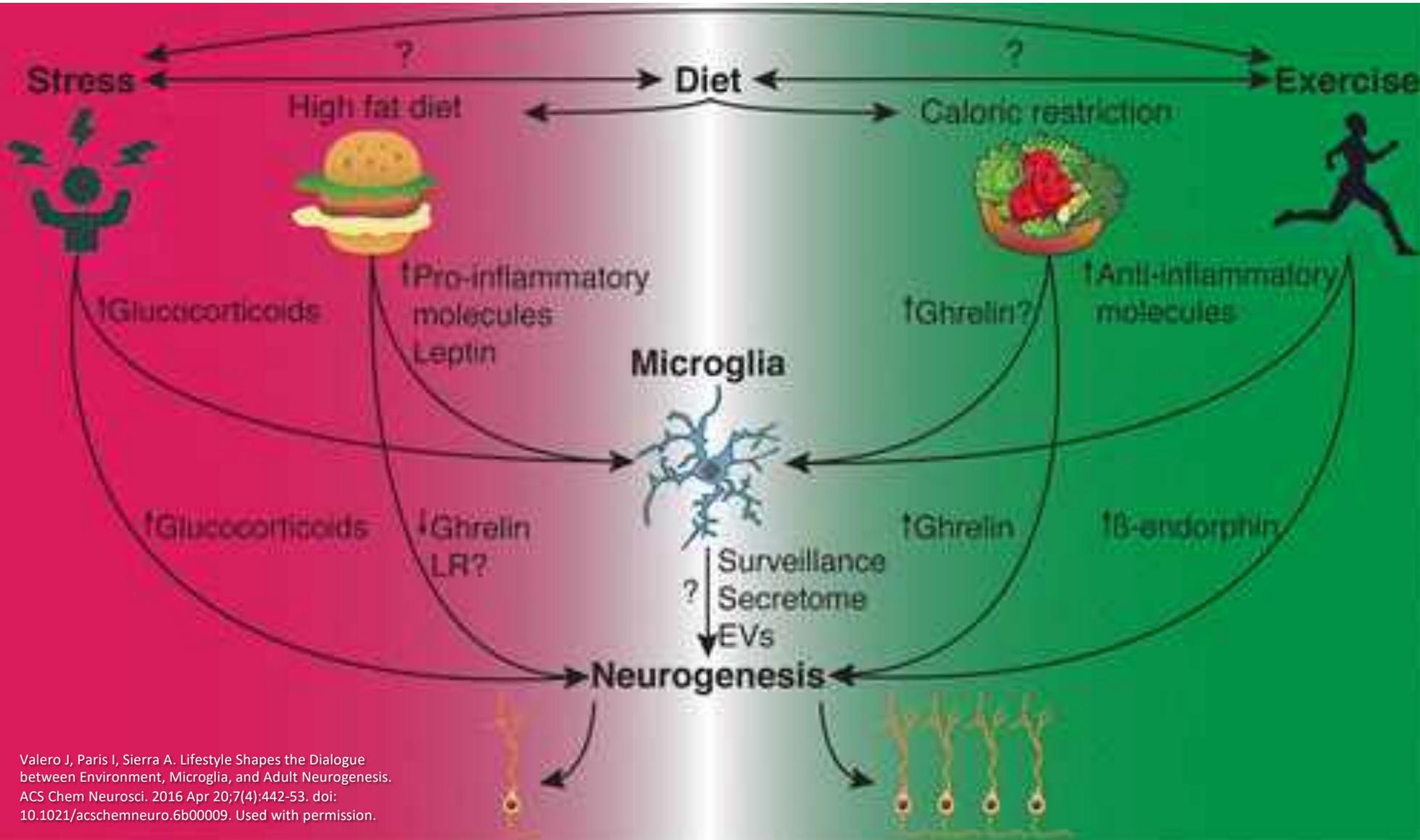
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Metals associated with neurodegeneration

Parkinson's, Alzheimer's and Huntington's disease

- Cd
- Cu
- Pb
- Mn
- Fe
- Methyl-Hg

1. Zhang Z, Miah M, Culbreth M, Aschner M. Autophagy in Neurodegenerative Diseases and Metal Neurotoxicity. *Neurochem Res.* 2016 Feb;41(1-2):409-22.



Valero J, Paris I, Sierra A. Lifestyle Shapes the Dialogue between Environment, Microglia, and Adult Neurogenesis. ACS Chem Neurosci. 2016 Apr 20;7(4):442-53. doi: 10.1021/acchemneuro.6b00009. Used with permission.

The Wahls Protocol® Seminar
Exercise Improves

- Cognition and Quality of Life
- Reduces Inflammation/Calms Microglia
 - Alzheimer's
 - Parkinson's
 - Multiple Sclerosis

1. Exercise Intervention Associated with Cognitive Improvement in Alzheimer's Disease. *Neural Plast.*. 2018 Mar 11;2018:9234195. doi: 10.1155/2018/9234105. eCollection 2018.
2. Exercise and Parkinson's disease. *Int Rev Neurobiol.* 2019;147:45-74. doi: 10.1016/bs.irm.2019.06.003. Epub 2019 Jun 20.
3. Exercise in patients with multiple sclerosis. *Lancet Neurol.* 2017 Oct;16(10):848-856. doi: 10.1016/S1474-4422(17)30281-8.
4. Exercise and Neuroinflammation in Health and Disease. *Int Neurourol J.* 2019 Nov;23(Suppl 2):S82-92. doi: 10.5213/inj.1938214.107. Epub 2019 Nov 30.

Restore Hormone Balance

- ↑ LH/sex-steroid-hormones ratio drives
↑TNF- α , amyloid- β
- **Goal:** correct to age-appropriate ratios/levels
- **Tx:**
 - Stress reduction, sleep
 - Diet, exercise (strength / HIIT), lifestyle
 - Nutraceuticals

The Wahls Protocol® Seminar

Restore Hormone Balance

- Restore cortisol, thyroid, sex hormones, insulin, IGF, leptin, NGF, BDNF
- Learn more from hormone modules

Hormesis

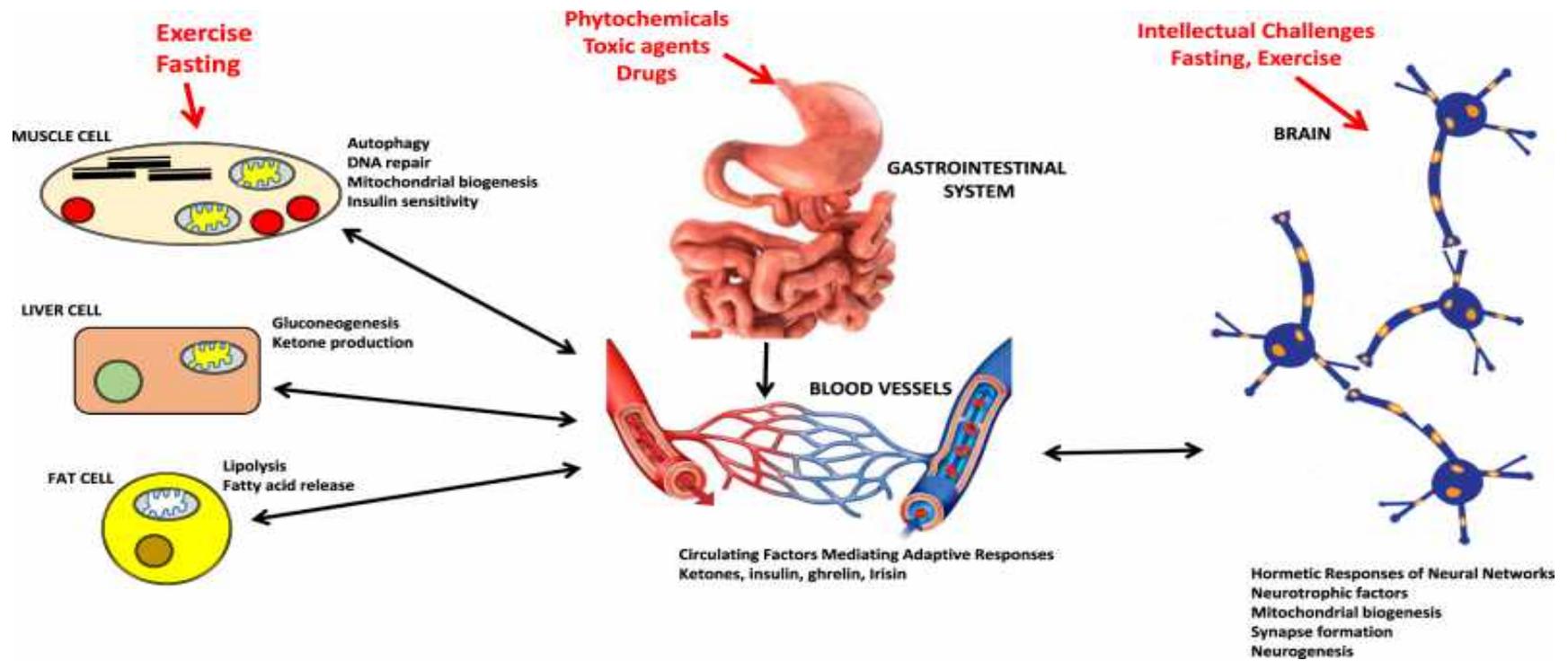
- Originally observed in toxicology
- High dose fatal
- Low dose may be beneficial
- Could this be used clinically?

The Wahls Protocol® Seminar

- Mild intermittent cellular stress with sufficient time for cellular recovery and repair may improve cellular adaptation

The Wahls Protocol[®] Seminar

Hormesis



How does hormesis impact biology, toxicology, and medicine? [NPJ Aging Mech Dis. 2017; 3: 13.](#)

Add Intermittent Mild To Moderate Stress Followed By Recovery Period

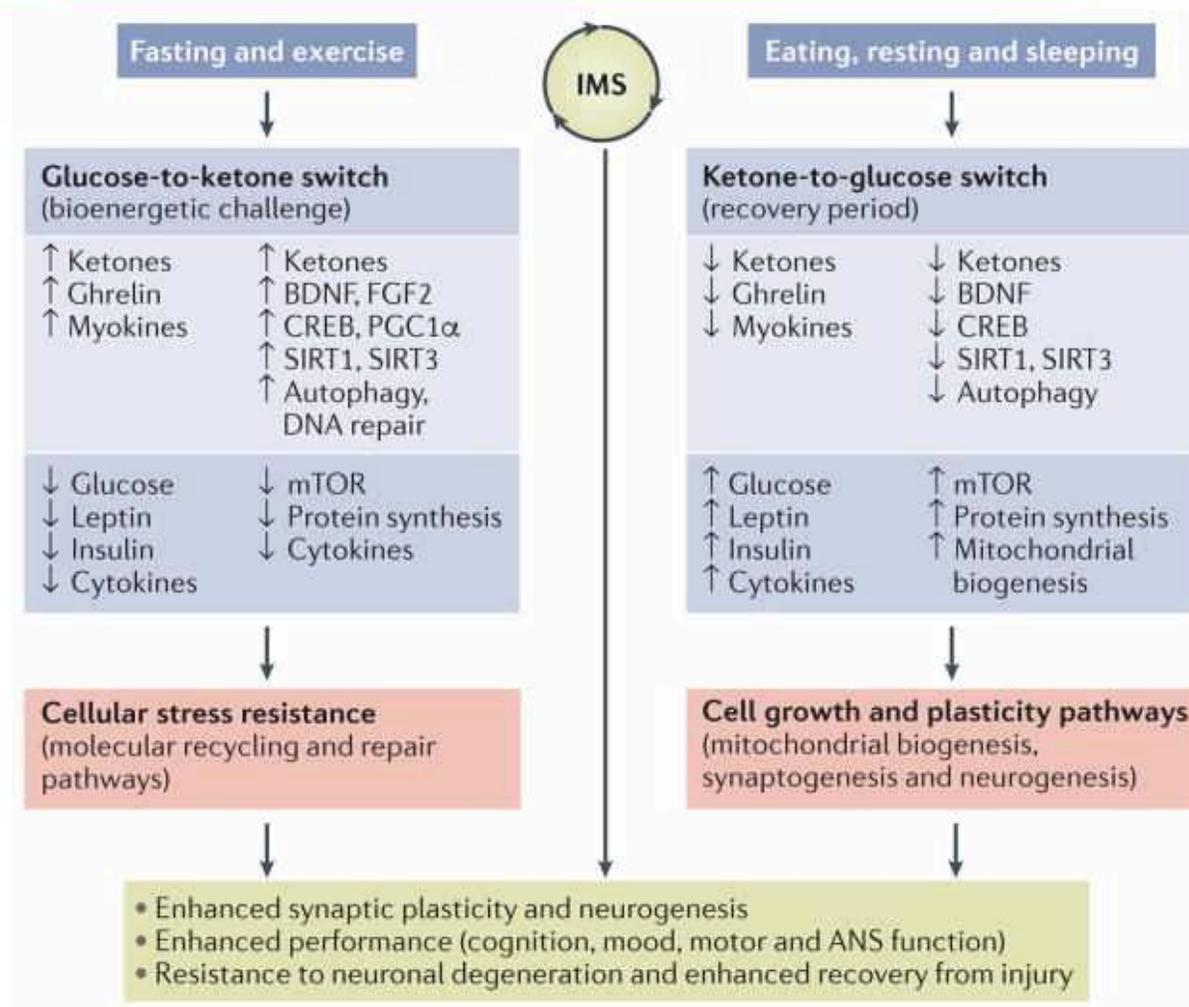
- Temperature
 - Hot
 - Cold
- Exercise
 - Harder/ easier workout
 - Interval training / recovery period
- Cognitive Training
 - New motor skills
 - Dancing
 - Language



The Wahls Protocol® Seminar

- Metabolic switching, repeating cycles of a metabolic challenge that induces ketosis (fasting and/or exercise) followed by a recovery period (eating, resting and sleeping), may optimize brain function and resilience.
- Impacts multiple signalling pathways that promote neuroplasticity, resistance to brain injury and disease.

Intermittent metabolic switching, neuroplasticity and brain health. [Nat Rev Neurosci](#). 2018 Feb;19(2):63-80. doi: 10.1038/nrn.2017.156. Epub 2018 Jan 11.



Intermittent metabolic switching, neuroplasticity and brain health. [Nat Rev Neurosci.](https://doi.org/10.1038/nrn.2017.156) 2018 Feb;19(2):63-80. doi: 10.1038/nrn.2017.156. Epub 2018 Jan 11.

The Wahls Protocol® Seminar

Traumatic Brain Injury Clinic

- Interdisciplinary -Speech Path, SW, Psychiatry, PM&R, Primary Care, Neuro-psychology
- 20 minutes with patient
- No labs
- Seen every 6 months
- Blast exposure and current neuropsychiatric symptoms

The Wahls Protocol® Seminar

Traumatic Brain Injury Clinic

- 32 y/o WM deployed X 3
- Multiple IEDs, dazed 2007 x2
- 1 LOC brief, dazed for hours 2008
- Issues – HA, poor memory, hypervigilant, can't get along, fatigue, back pain, ↑ 80lbs, nightmares, marriage failing, flunking out

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Traumatic Brain Injury Clinic

- Vaccines 30+ in 1 day prior to deployment
- Burn pits intermittent '05, daily in '07
- Diarrhea with Tx '07
- FHx autoimmunity in cousin (*IBD)
- PMH back surgery, PTSD
- Exam 250 lbs, weak gluteals

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Traumatic Brain Injury Clinic

- Energy drinks – many
- Poor sleep
- No friends, marriage failing
- No stress-reducing practices
- No exercise
- Lots of sugar, white flour
- No vegetables, or fruit

The Wahls Protocol® Seminar

Traumatic Brain Injury Clinic

- Education
- Lifestyle and diet key to healing his brain
- Building Blocks for Better Brain
 - ‘Starving for key building blocks’
 - [Unrecognized gluten/ casein sensitivity]
- Weight gain possibly tied to toxin body burden
- Stress, sleep, exercise

The Wahls Protocol® Seminar

Traumatic Brain Injury Clinic

- Intervention
- Modified Paleo diet
 - (9 cups – Greens, sulfur, color)
 - Organ meat
- Cut out energy drinks / caffeine
- Walking
- Stress reducing activity of choice
 - Epsom salts soak

The Wahls Protocol® Seminar

Traumatic Brain Injury Clinic

- Outcome
- 1 year ↓ 45 lbs, ↓ HA, marriage ended
- 2 years - fully compliant on the diet, back in school, getting As
- 2016 – back to pre-deployment weight, graduated with honors, married, thriving

The Wahls Protocol® Seminar
Therapeutic Lifestyle Clinic

- Established 2013
- Group classes
- Intro one-hour class
 - Decline, RD only, group classes**
- Half day intake group class
- 2 hrs with MD
 - Patients complete their own timeline / matrix
- 2 hrs with RD
 - Cooking demo, sample food, re-imagine meals

The Wahls Protocol® Seminar
Therapeutic Lifestyle Clinic

- Labs
- CBC,
- Creatinine,
- hs-CRP,
- Lipids,
- 25-OH Vitamin D,
- Homocysteine, B12, folate,
- glucose, a1c, insulin

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Therapeutic Lifestyle Clinic

- Referred from Pain clinic
- Progressive Neuropathic Pain
- Neuromas
- Contemplating Suicide

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Therapeutic Lifestyle Clinic

- 55 y/o WM S/p BKA (military), nerve stimulators not controlling pain any more, multiple ER visits, continual electrical pain
- PMH hx of substance abuse, depression, obesity, hyperlipidemia, HTN, asthma, constipation,
- Supportive wife
- MSQ score 64

Therapeutic Lifestyle Clinic

- FH brain, heart and autoimmune issues
- 20 + antibiotics as a child and young adult
- Pesticides (farm)
- Solvent exposure (work)
- Frequent steroid use (asthma)
- Very poor sleep (pain)
- No exercise (pain)
- Comfort food = ↑ Sugar, white flour, no vegetables
- Sober 22 years with AA

Therapeutic Lifestyle Clinic

- Homocysteine 11;
- Vit. D 24
- Trig:HDL cholesterol 4;
- A1c: 5.8
- Modified paleo/ low glycemic index
- Methyl-B12, methyl-folate, B-complex
- 2 grams cod liver oil
- Vitamin D
- Support group Q 6 weeks with MD + RD

Therapeutic Lifestyle Clinic

- 6 months later
- Reports 100% GF, DF, Sugar free
- Using smoothies “to get the 9 cups in”
- Swimming 3x week
- Pain much more manageable
- Sleep is good
- Mood much better
- Family life even better
- MSQ 11



The Wahls Protocol[®] Seminar

Response to Loss

- Denial
- Anger
- Bargaining
- Depression
- Acceptance

Kubler-Ross, E. On Death and Dying. 1973. doi: 10.4324/9780203010495



The Wahls Protocol[®] Seminar

After Acceptance

- Give all the control to medical team
- Learned Helplessness
- Depression
- Despair
- Worsening Disability
- Rage and violence

Smallheer BA, Vollman M, Dietrich MS. Learned Helplessness and Depressive Symptoms Following Myocardial Infarction. *Clin Nurs Res*. 2018;27(5):597-616. doi:10.1177/1054773816689752.

Kubera M, Obuchowicz E, Goehler L, Brzeszcz J, Maes M. In animal models, psychosocial stress-induced (neuro)inflammation, apoptosis and reduced neurogenesis are associated to the onset of depression. *Prog Neuropsychopharmacol Biol Psychiatry*. 2011;35(3):744-759. doi:10.1016/j.pnpbp.2010.08.026



The Wahls Protocol® Seminar

After Acceptance

- Higher Internal Locus of Control =
- Improved immune function

- Improved Natural Killer Cell, T and B lymphocyte function in those with higher internal locus of control

Reynaert C, Janne P, Bosly A, et al. From health locus of control to immune control: internal locus of control has a buffering effect on natural killer cell activity decrease in major depression. *Acta Psychiatr Scand.* 1995;92(4):294-300. doi:10.1111/j.1600-0447.1995.tb09585.x



The Wahls Protocol[®] Seminar Response to Loss

Learned helpless

- Despair
- Relentless decline
- Worsening disability

Learning and Adaptation

- Personal accountability
- Changing behaviors
- Diet quality
- Health behaviors
- Improving quality of life

The Wahls Protocol[®] Seminar

Response to Loss

Learned helplessness

- Despair
- Relentless decline
- Worsening disability

Learning and Adaptation

- Personal accountability
- Changing behaviors
- Diet quality
- Health behaviors
- Improving quality of life

Which are your patients doing?

Improving Diet Quality

- One of the most impactful strategies
- Reduces obesity, diabetes, heart disease, cancer risk
- Reduces microglial activation
- More favorable microbiome
- Improves Insulin Sensitivity
- First recommendation for all chronic health issues



ADHERENCE TO LONG-TERM THERAPIES: EVIDENCE FOR ACTION
https://www.who.int/chp/knowledge/publications/adherence_report/en/



Changing Dietary Patterns Is Hard

- WHO 25% patients begin dietary change recommended by physicians
- Standard American Diet ↑ risk obesity, high blood pressure, diabetes, heart disease

ADHERENCE TO LONG-TERM THERAPIES: EVIDENCE FOR ACTION

https://www.who.int/chp/knowledge/publications/adherence_report/en/

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Changing Dietary Patterns Is Hard

- Sugar, gluten, dairy processed foods are addictive
- Motivational interviewing and health coach
- People need a reason to do the work and get through the withdrawal from the excluded foods

ADHERENCE TO LONG-TERM THERAPIES: EVIDENCE FOR ACTION
https://www.who.int/chp/knowledge/publications/adherence_report/en/

Self Care: Improving Health Behaviors

- Diet quality
- Physical exercise
- Stress management
- Toxin avoidance
- Improving your chance of success





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Emotional Resilience

- Small clans 10 to 30 individuals
- Crave social contact
- Prolonged breast feeding
- Oxytocin – parental bonding deep
- Loneliness very inflammatory

Changing Habits Is Hard

- It is really hard to change habits
- When was the last time you changed a habit
- Chat How did you do it



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Why It Is Hard...

- Brains are wired for pleasure
- Immediate > future
- Fear of loss > current benefit
- Habits are automatic



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Our Biology:

- We crave salt, sugar, fat, sex
- Pleasure
- Comfort
- Inactivity





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Food Addiction Is **REAL**

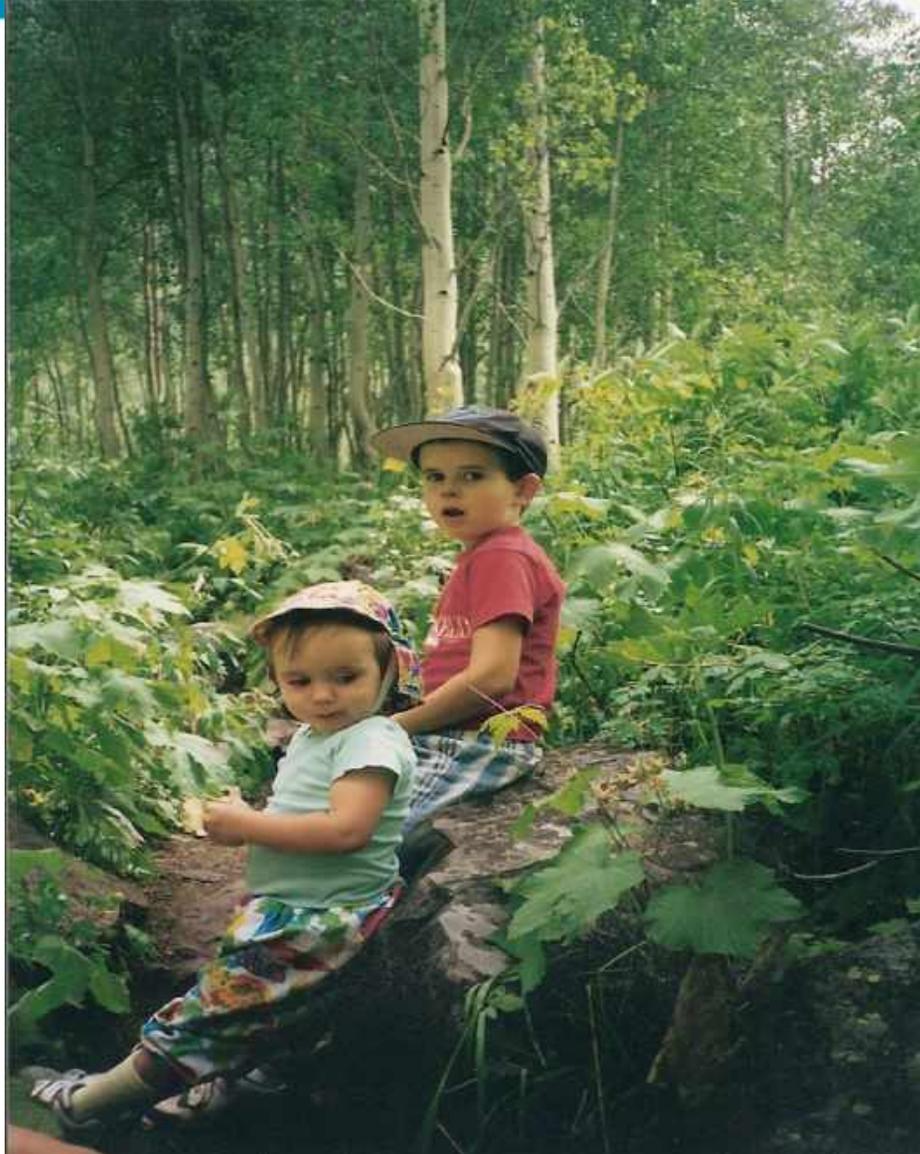
- Big food created addicting products
- Withdrawal symptoms often occur
- How do we change our diet/ lifestyle

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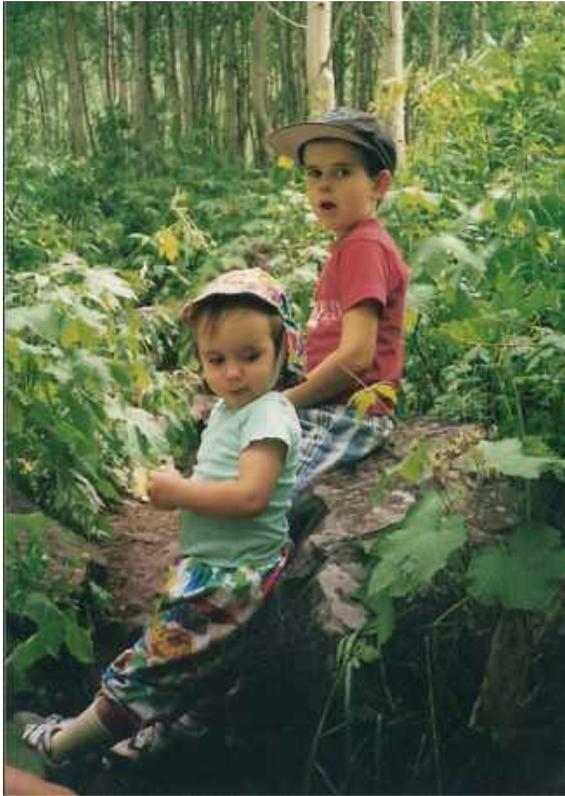
Choices Define Our Character

- What do you care so much about that you would run into a burning building to save what is inside
- What speaks to your character

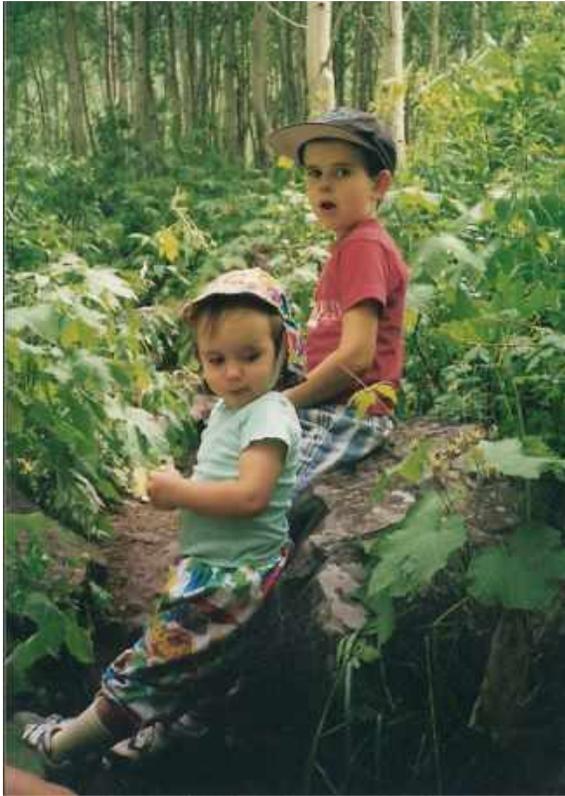




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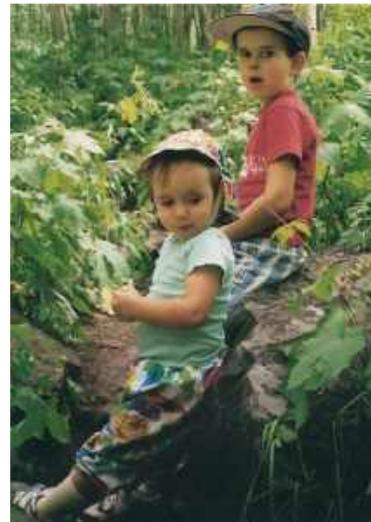


What was I modeling for them?

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What Is Your Why?

- We have a choice to make...



Your Personal Mission

- Chat
 - What is your mission
 - What/Who do you care so much about that you would you run into a burning building to save it?



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Gratitude Journal

Expressing gratitude reduces inflammation and stress hormone levels.

What are the gifts in your life/ circumstances?



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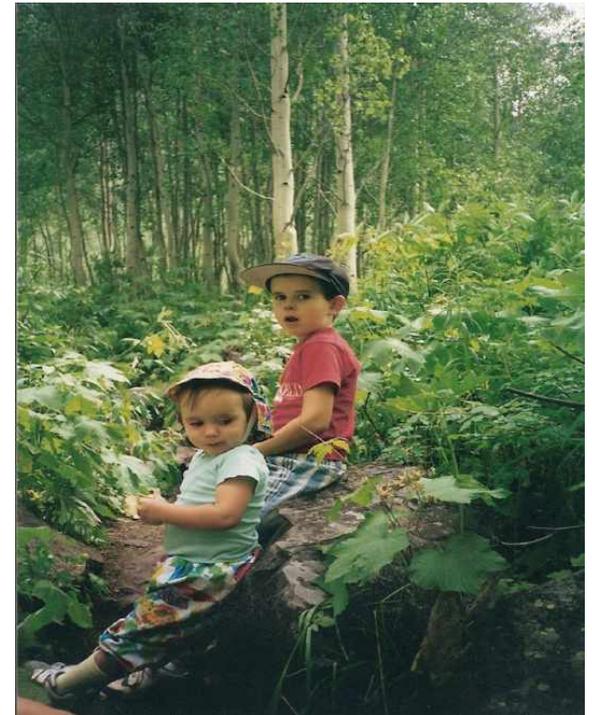
What Is Your WHY

- What do you care so much about that you would run into a burning building to save what is inside
- What speaks to your character



Changing Dietary Patterns Is Hard

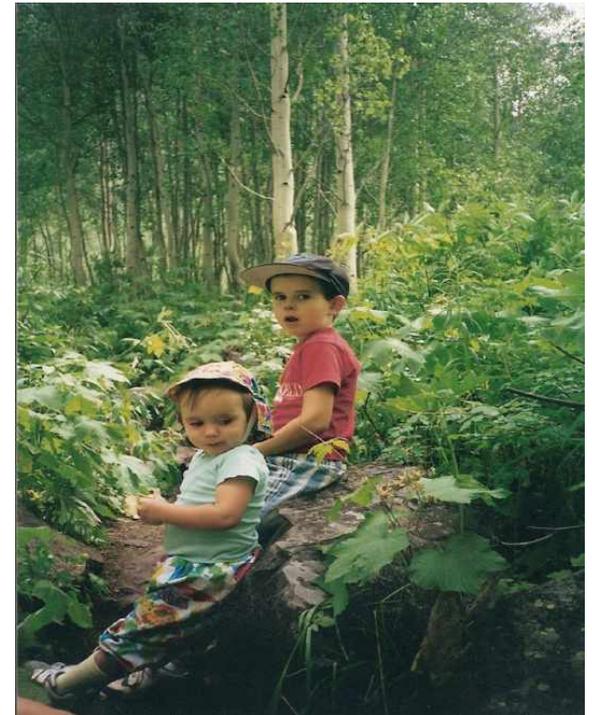
- Acknowledge food addictions
- Personal Mission Statement
- What do you want your health for?
- Is there someone (something) your care for deeply for that you would go in to a burning building to save?



ADHERENCE TO LONG-TERM THERAPIES: EVIDENCE FOR ACTION
https://www.who.int/chp/knowledge/publications/adherence_report/en/

Changing Dietary Patterns Is Hard

- Develop a mutually agreed upon dietary plan
- Family intervention
- Remove the excluded foods from the eating environment
- Treat the addiction
 - AA model
 - Peer support



ADHERENCE TO LONG-TERM THERAPIES: EVIDENCE FOR ACTION

https://www.who.int/chp/knowledge/publications/adherence_report/en/



The Wahls Protocol® Seminar

Martin Seligman: The Pursuit of Happiness

- Studied happiness using Confucius, Mencius and Aristotle with modern psychological theories
- Seligman's conclusion is that **happiness has three dimensions that can be cultivated.**

Seligman M. The Pursuit of Happiness. Martin Seligman on Psychology. *Pursuit-of-happiness.org*. 2018. Available at: <http://www.pursuit-of-happiness.org/history-of-happiness/martin-seligman-psychology/>. Accessed May 21, 2018.

Positive Psychology

Finding Joy and Meaning

- Pleasant life – e.g. enjoying nature, companionship, good tea
- Chat – how to enjoy the pleasant life in the face of disability

Positive Psychology

Finding Joy and Meaning

- Good life – e.g. achieved through discovering our unique virtues and strengths, and employing them creatively to enhance our lives
- Chat – how do you enjoy the good life in the face of disability

Positive Psychology

Finding Joy and Meaning

- Meaningful life – e.g. achieved by employing our unique strengths for a purpose greater than ourselves and giving back
- Chat – how do you enjoy the meaningful life in the face of disability



Diet Summary

- Standard American Diet associated with poorer outcomes
- *Improve diet quality*
- *Reduce/ eliminate sugar/processed foods*
- *Address constipation, heal the gut, removed offending items*
- *Find a dietary pattern that can be sustained*
- Several dietary patterns to consider
- Modified Paleo (Wahls), Mediterranean, MIND, Ketogenic



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Recommended Dietary Patterns

- Gluten free, casein free, low glycemic index
- Trial no eggs (eat liver/ or liver/ choline supplements)
- GF Mediterranean, Modified Paleo (Wahls), Ketogenic Eating
- Stress
 - Low glycemic index
 - Greens, sulfur, color
 - Omega 3 and omega 6 fats
 - Fermented foods



Diet Summary

- My approach depending on diagnosis/ patient interest
- Modified Paleo recommended; ketogenic
- OR GF vegetarian/ GF Mediterranean/ TRF
 - Greens, sulfur, color
 - Protein (meat/ or GF grains, + legumes
 - Essential Fatty acids
 - Organic strongly encouraged



Basic Monitoring

- Lipids, a1c, glucose, insulin
- Homocysteine, folate, B12, vitamin D,
- APOE status
- More advanced
 - EPA/ AA ratio
 - Food sensitivity
 - Toxin body burden
 - Hormones



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Add To Current Dietary Patterns

- Time Restricted Feeding
- Intermittent Fasting,
- Fasting Mimicking Diet/ Calorie Restriction
- Stress
 - Reducing/ limiting added sugar/ processed foods
 - Increasing greens, sulfur, color
 - Omega 3 and omega 6 fats
 - Fermented foods



The Wahls Protocol[®] Seminar If Ketogenic Dietary Pattern

- Ketogenic -
 - Medical team to monitor clinically (lipids, glucose, BP)
 - Ketones – blood (not urine) monitoring
- Contraindications
 - Low BMI (<19.5)
 - Wanting to get pregnant/ pregnancy
 - Thyroid / infection

IF Ketogenic Eating

Monitor Lipids, Response

- Monitor fasting lipids
 - Total cholesterol, HDL, LDL, Triglycerides
- Coconut/ MCT oil makes more ketones
 - 50 to 80 grams carbs
- Olive Oil makes fewer ketones
 - 25 grams carbs
 - Or add IF, TRF, or PF



Add Intermittent Mild To Moderate Stress Followed By Recovery Period

- Temperature (cold/heat)
- Exercise
- Cognitive Training
- Fasting /metabolic switching

Next Study

Therapeutic diet/lifestyle vs usual care

- Quasi experimental
- Patients within 1 year of Dx with RRMS or CIS
- Intervention -Offered and declined DMTs
- Control - Usual care treated by neurologist with MS expertise

The Wahls Protocol® Seminar

- **Primary outcome –**
- Quality of life MSQoL54
- Must live within lower 48 states
- No in person visits
- Neurologist must approve participation
- Control – usual care with DMTs
- Intervention Wahls™ diet, meditation, exercise
- Contact MSDietStudy@healthcare.uiowa.edu

Videos and papers at <https://terrywahls.com/papers/>



Effects of a multimodal intervention on gait and balance of subjects with progressive multiple sclerosis: a prospective longitudinal pilot study, [Degenerative Neurological and Neuromuscular Disease](#) 2015, 5:91-92

REVISED AND EXPANDED

The Wahls Protocol[®]



A RADICAL NEW WAY
to Treat All Chronic Autoimmune
Conditions Using Paleo Principles

TERRY WAHLS, M.D.
FOUNDER OF THE WAHLS RESEARCH FUND
with Eve Adamson

Access to the papers and GAIT video is
at terrywahls.com/papers



- Research referral
- MSDietStudy@healthcare.uiowa.edu
- Consult
- info@wahlsinstitute.com
- Terry-wahls@uiowa.edu

MORE THAN 100 DELICIOUS HEALING RECIPES

The Wahls Protocol Cooking for Life

The Revolutionary Modern Paleo Plan to Treat
All Chronic Autoimmune Conditions



TERRY WAHLS, M.D. with Eve Adamson

A RADICAL NEW WAY TO TREAT
ALL CHRONIC AUTOIMMUNE CONDITIONS

The Wahls Protocol

How I Beat
Progressive MS Using
Paleo Principles and
Functional Medicine



TERRY WAHLS, M.D.
FOUNDER OF THE WAHLS FOUNDATION
with Eve Adamson

Reversal of Cognitive Decline 100 Patients

In the current set of 100 patients, for those evaluated by MoCA, MMSE, or SLUMS pre- and post-treatment (72 of the 100), there was a **mean improvement of 4.9 points**, with a standard deviation of 2.6 and a range of 1-12.



Bredesen DE, Sharlin K, Jenkins D, et al. Reversal of Cognitive Decline: 100 Patients. Journal of Alzheimer's Disease & Parkinsonism. 2018;08(05).

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Reversal of Cognitive Decline 100 Patients

Since the natural history is one of decline, the improvements that were documented must be considered as additional to the prevention of decline that would otherwise have occurred.

Journal of Alzheimer's Disease & Parkinsonism
Case Report | Open Access

Reversal of Cognitive Decline: 100 Patients

Dale E. Bredesen¹, Sharlin K. Jenkins², David Jenkins³, Miki Okamoto⁴, Wei Youngberg⁵, Sharon Hunsman-Cohen⁶, Anne Stefanik⁷, Ronald L. Brown⁸, Seth Cooper⁹, Craig Tassaf¹⁰, Adam Hollaway¹¹, Michael Kogut¹², David Rapoport¹³, Edwin Aronik¹⁴, Amylose Anand¹⁵, Nathaniel Bergman¹⁶, Carol Diamond¹⁷, Jean Lawrence¹⁸, Rene Moore-Raaij¹⁹, Patricia Henry²⁰, and Mary Brause²¹

¹Department of Molecular and Medical Pharmacology, David Geffen School of Medicine, University of California, Los Angeles, Los Angeles, CA, USA
²UCLA Health and Neurology/Functional Medicine, Oxnard, CA, USA
³Wentworth, Sydney, Australia
⁴Youngberg Lifestyle Medicine Clinic, Temecula, CA, USA
⁵Windsor Health, Austin, TX, USA
⁶Kaiser Permanente Inland Empire, Claremont, CA, USA
⁷West Health, Hollywood, FL, USA
⁸Integrative Functional Medicine, San Rafael, CA, USA
⁹KUW Center for Integrative Medicine, George Washington University, Washington, DC, USA
¹⁰Chiropractic Medical Institute, Jacksonville, NC, USA
¹¹Department of Neurology, University of California, Los Angeles, Los Angeles, CA, USA
¹²Medical Institute, Los Angeles, CA, USA
¹³Center for Functional Medicine, Cleveland Clinic, Cleveland, OH, USA
¹⁴Mount Sinai Hospital, New York, NY, USA
¹⁵Lumina Health and Wellness, Toronto, ON, USA
¹⁶Brain and Behavior Clinic, Boulder, CO, USA

Abstract
The first examples of reversal of cognitive decline in Alzheimer's disease and the pre-Alzheimer's disease conditions MCI (Mild Cognitive Impairment) and SCI (Subjective Cognitive Impairment) have recently been published. These two publications described a total of 19 patients showing sustained subjective and objective improvement in cognition, using a comprehensive, precision medicine approach that involves determining the potential contributors to the cognitive decline (e.g., reduction of the acute immune system by pathogen or microbial permeability, reduction in toxins or hormonal support, specific toxin exposure, or other contributors), using a computer-based algorithm to determine subtype and then addressing each contributor using a personalized, targeted, multi-factorial approach called ReCODE for reversal of cognitive decline.
An obvious criticism of the initial studies is the small number of patients reported. Therefore, we report here 100 patients, treated by several different physicians, with documented improvement in cognition, in some cases with documentation of improvement in electrophysiology or imaging, as well. This additional report provides further support for a randomized, controlled clinical trial of the protocol and the overall approach.

Keywords: Alzheimer's; Mild cognitive impairment; Precision medicine; ReCODE; Precision medicine; Amyloid precursor protein; Synaptic; Synaptotagmin.

Introduction
Alzheimer's disease is now the third leading cause of death in the United States [1-4], and the development of effective treatment and prevention is a major healthcare goal. However, clinical trials of drug candidates for Alzheimer's disease treatment have been almost uniformly unsuccessful. There may be several reasons for such repeated failure: (1) given the long pre-symptomatic period, treatment is typically initiated late in the pathophysiological process; (2) what is referred to as the amyloid cascade hypothesis [5,6] is a linear model of disease [1,2,5,7] in which APP (the amyloid precursor protein, function as a molecule which due to its activity as an integrator dependent receptor [8-10] in the presence of sufficient support from trophic signaling, APP is cleaved at the alpha site, leading to the production of two synaptotoxic peptides, Aβ42 and Aβ40. In contrast, in the absence of sufficient support from trophic signaling, APP is cleaved at the beta, gamma, and epsilon sites, leading to the production of four synaptotoxic peptides, sAPPβ, Aβ, IsAPP, and C99. In this model, inflammation exerts an anti-trophic effect on APP signaling, at least in part via the NF-κB (nuclear factor-κB light chain enhancer of B cells) inducible of IκBα (inhibitor of κB kinase) and gamma-secretase activity. Similarly, toxins such as divalent metals (e.g., mercury) also exert an anti-trophic effect on APP signaling, since these

Bredesen DE, Sharlin K, Jenkins D, et al. Reversal of Cognitive Decline: 100 Patients. Journal of Alzheimer's Disease & Parkinsonism. 2018;08(05).

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The Wahls Protocol[®] Seminar

Interventions- Sleep/ Stress/ Relationships

Goal	Approach
Support sleep	Melatonin 0.5 to 5 mg, full spectrum lighting
Ensure nocturnal oxygenation	Exclude or treat sleep apnea
Reduce stress	Personalized—yoga, meditation, music, etc. Gardening, fishing, hunting, Epsom salts
Improve relationships	Create social connections

The Wahls Protocol® Seminar

Interventions- Exercise and Movement

Goal	Approach
Exercise	Strength training, balance training, High intensity interval training, PT or OT referral, consider adding NMES=Electrical stimulation of muscles DO NOT over train

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Nutrition/ Structure

Goal	Approach
Optimize diet: minimize simple CHO, minimize inflammation. Fasting insulin <7; HgbA1c <5.5	Modified paleo, ketogenic, low grain, eat 6 to 9 cups vegetables/ day, push fiber to poop 2 snakes day
Provide synaptic structural components	CDP choline. DHA, Phosphatidylcholine, organ meats, cod liver oil

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Microbiome

Goal	Approach
GI health	Repair if needed; prebiotics and probiotics; target 2-3 poop snakes per day, address food sensitivities
Infections, dysbiosis	Check for mold, water damaged buildings, infections, Lyme etc. Floss teeth, add mushrooms, vitamin D, Vitamin A (organ meat), vitamin K2

The Wahls Protocol[®] Seminar

Mitochondria

Goal	Approach
Enhance autophagy, ketogenesis	Fast 12 hr + each night, including 3 hr prior to bedtime, longer fasts
Optimize mitochondrial function	Organ meats 2-3 X week
Optimize antioxidants	6 to 9 cups vegetables (Greens, sulfur, color)/D; nuts+ seeds

The Wahls Protocol[®] Seminar

Toxins

Goal	Approach
Optimize Zn: Cu ratio	Depends on values obtained
Exclude heavy metal toxicity	Evaluate Hg, Pb, Cd, Mn, As address if indicated
↑bacterial biotransformation	↑ fiber to 2-3 soft BM day
Correct nutrient mineral lacks	Nutrient minerals, stomach acid, sea salt, soaks in Epsom salts, sodium bicarbonate

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Hormones/ growth factors

Goal	Approach
Optimize hormone balance	Optimize fT3, fT4, E2, T, progesterone, pregnenolone, cortisol.
TW optimize progenitor (stem cells)	TW – Diet, exercise, sleep, stress, social bonding, fasting, CDP choline, PC, DHA
Increase NGF	Lion's mane mushrooms Or ALCAR (acetyl-L-carnitine)
Brain stimulation	Posit or related neurocognitive software, TW –juggling, do not over train

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Other Interventions

Goal	Approach
Serum B12 >500 TW – prefer top quartile of ref. range	Me-B12 TW organ meat 2 to 3 X week
h.s. CRP <1.0	Anti-inflammatory diet; curcumin; DHA/EPA; optimize hygiene (floss teeth, coconut oil + essential oils to brush teeth, oil pulling) TW – 6 to 9 cups vegetables / day
Homocysteine <7	Me-B12, MTHF, P5P; TMG if necessary
25OH-D3 = 50-100ng/ml	Vitamins D3, K2

The Wahls Protocol® Seminar

Other Interventions

Goal	Approach
Reduction of A-beta	Curcumin, Ashwagandha
Increase focus	Pantothenic acid
Cognitive enhancement	Bacopa monniera, Mg threonate

REVISED AND EXPANDED

The Wahls Protocol[®]



A RADICAL NEW WAY
to Treat All Chronic Autoimmune
Conditions Using Paleo Principles

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Access to the papers and GAIT video is
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- Research referral
- MSDietStudy@healthcare.uiowa.edu
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