Functional Approach to Treating Neurodegenerative Disorders

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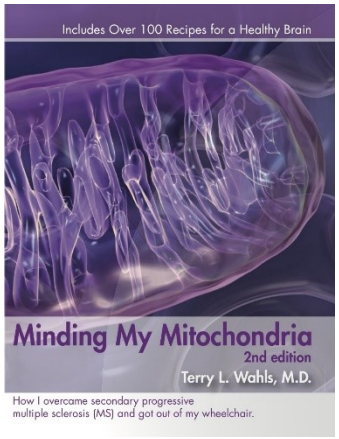
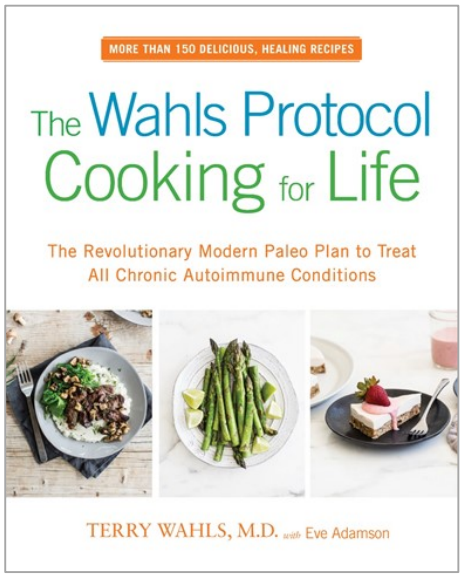
AARM
Association for the Advancement of Restorative Medicine

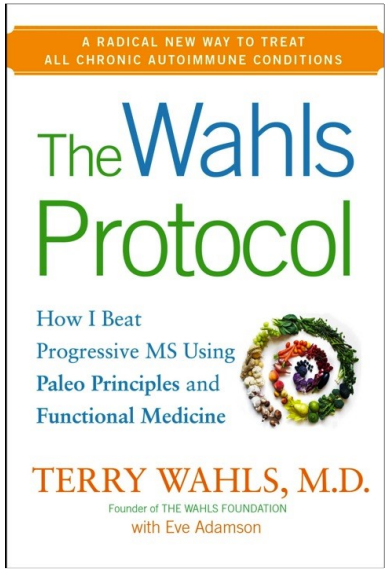
Disclosures

- Grant Funding –
  - National MS Society
- Trademarks – Wahls™, Wahls Paleo™ , Wahls Paleo Plus™ 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
- Equity interest
  - Dr. Terry Wahls LLC
  - The Wahls Institute PLC
  - www.terrywahls.com

Books







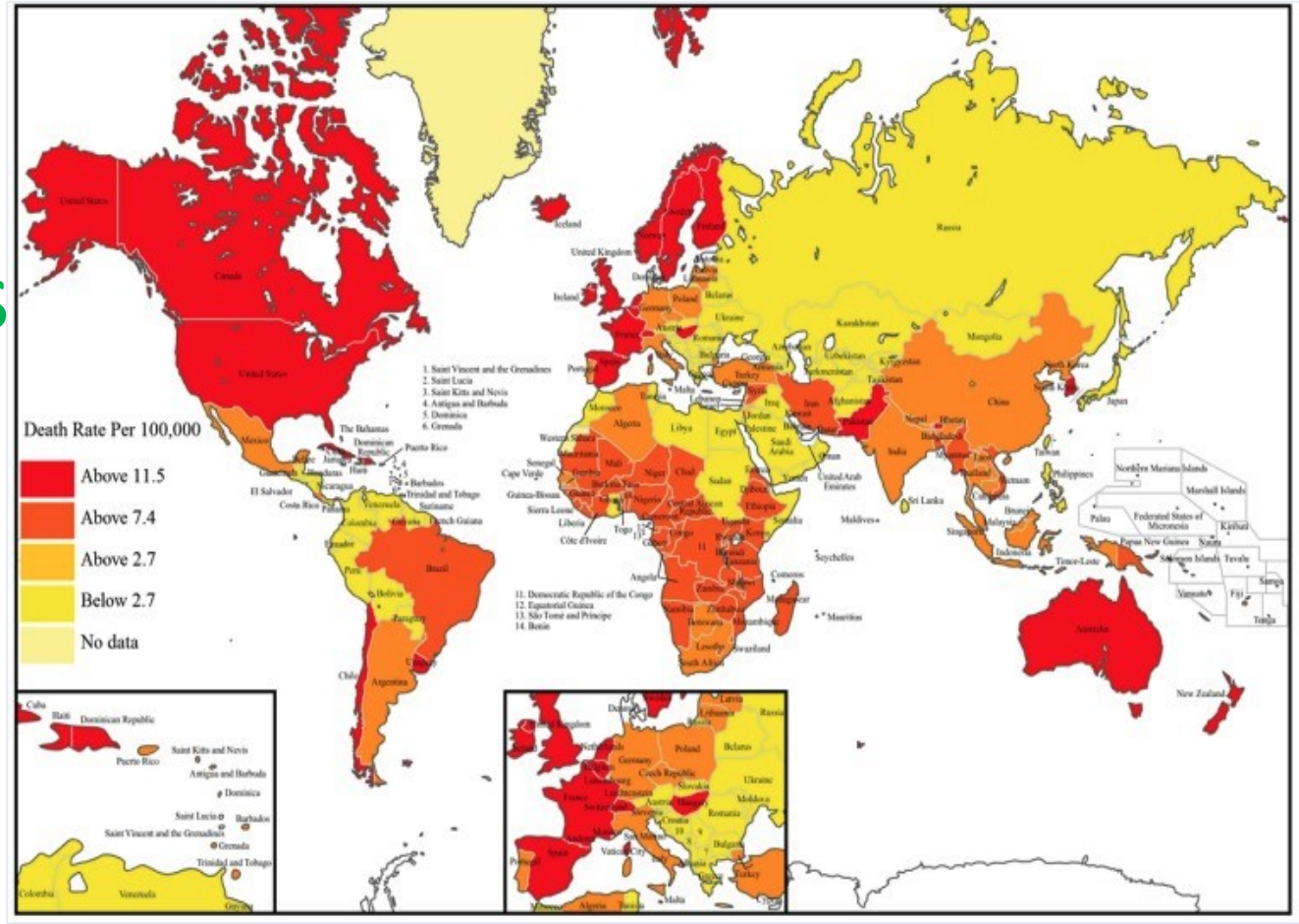
The Wahls Protocol®

Objectives

- Name one mechanisms by which dietary factors may contribute to neuroinflammation and neurodegenerative disease processes and potential worsening of symptoms.
- •Name at least at least three specific food groups that can help stabilize and or reverse neuroinflammation and neurodegenerative disease processes and related symptoms.
- Identify an effective and inexpensive test that clinicians and patient can use to monitor the microbiome.
- Name one mechanism by which a paleo diet may reduce symptoms in the setting of neuroinflammation and neurodegenerative disease processes


1 cup

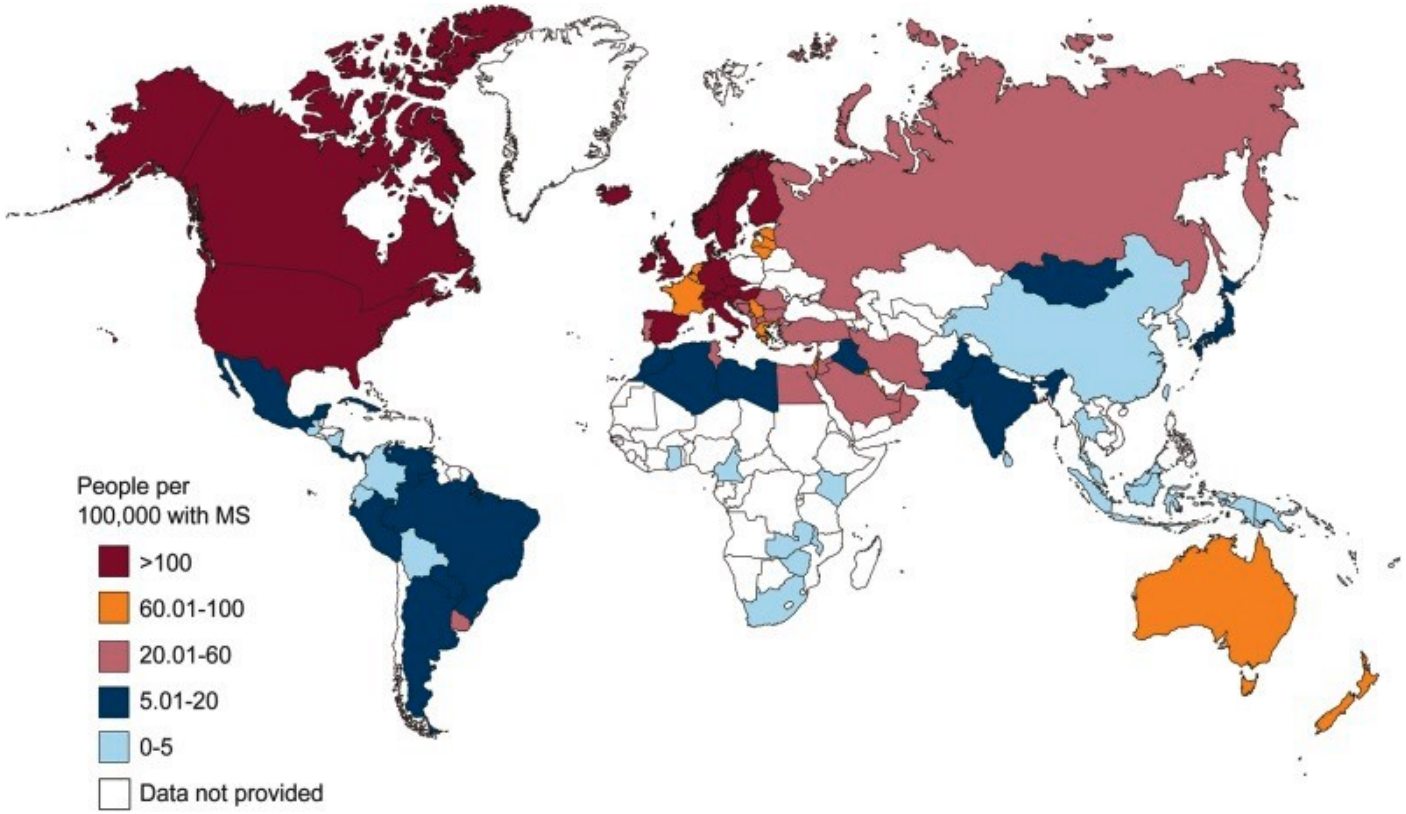
Global Alzheimer's Prevalence



World map illustrating the global distribution of deaths caused due to Alzheimer's Disease/ Dementia.
WHO 2011

Manivannan Y, Manivannan B, Beach TG, Halden RU. Role of Environmental Contaminants in the Etiology of Alzheimer's Disease: A Review. Current Alzheimer Research. 2015;12(2):116-146. doi:10.2174/1567205012666150204121719.

Global MS Prevalence



Browne P1, Chandraratna D, Angood C , et al. Atlas of Multiple Sclerosis 2013: A growing global problem with widespread inequity. Neurology. 2014 Sep 9;83(11):1022-4. doi: 10.1212/WNL.0000000000000768.

TBI & AD, PD, ALS, MS

TBI increases the Odds Ratio (OR)

- **AD by 2.32** (moderate) 4.51 (severe TBI)
- **PD 11.0** (pooled moderate & severe)
- **ALS 3.1** (TBI within 10 years of onset)
- **MS 1.97** (TBI within 6 years of onset)

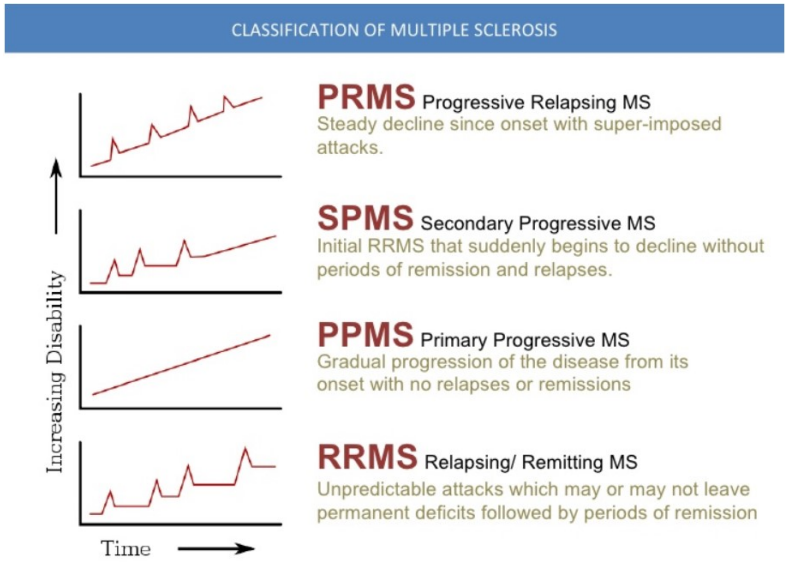
1. Plassman BL, Havlik RJ, Steffens DC, Helms MJ, Newman TN, Drosdick D, et al. Documented head injury in early adulthood and risk of Alzheimer's disease and other dementias. *Neurology.* 2000;55:1158–66.
2. Bower JH, Maraganore DM, Peterson BJ, McDonnell SK, Ahlskog JE, Rocca WA. Head trauma preceding PD: A case-control study. *Neurology*. 2003;60:1610–5.
3. Chen H, Richard M, Sandler DP, Umbach DM, Kamel F. Head injury and amyotrophic lateral sclerosis. *Am J Epidemiol.* 2007;166:810–6.
4. Kang JH, Lin HC. Increased risk of multiple sclerosis after traumatic brain injury: a nationwide population-based study. *J Neurotrauma.* 2012 Jan 1;29(1):90-5.

In 2000 I Became A Patient

- Left leg weakness
- Prior history visual dimming
- Lesions in spinal chord
- Abnormal CSF
- Diagnosis relapsing-remitting MS

How MS Progresses

- Optic Neuritis / clinically isolated syndrome, BUT 50% progress to MS
  - **10% benign**
  - **10% Primary Progressive MS** (PPMS)
  - **80%** diagnosed with **Relapsing–Remitting MS** (RRMS)



Progressive Relapsing Multiple Sclerosis | Health Life Media. http://healthlifemedia.com/healthy/progressive-relapsing-multiple-sclerosis/. Accessed May 15, 2018.

Cost of MS to Society/Individual

- **RRMS Annual cost of disease-modifying drugs**
  - $45,000 to $72,000/ year
  - Mean cost (Poland $41,400)
- **+ Annual MRI, labs, therapy, office visits**
- **Within 10 years of diagnosis**
  - 50% exit work force due to fatigue disability
  - 30% gait disability
  - Most convert to SPMS
  - **SPMS** – chemotherapy, progressive disability

Kolasa K. How much is the cost of multiple sclerosis--systematic literature review. *Przegl Epidemiol*. 2013;67(1):75-79, 157-160.

Cost of MS to Society/Individual

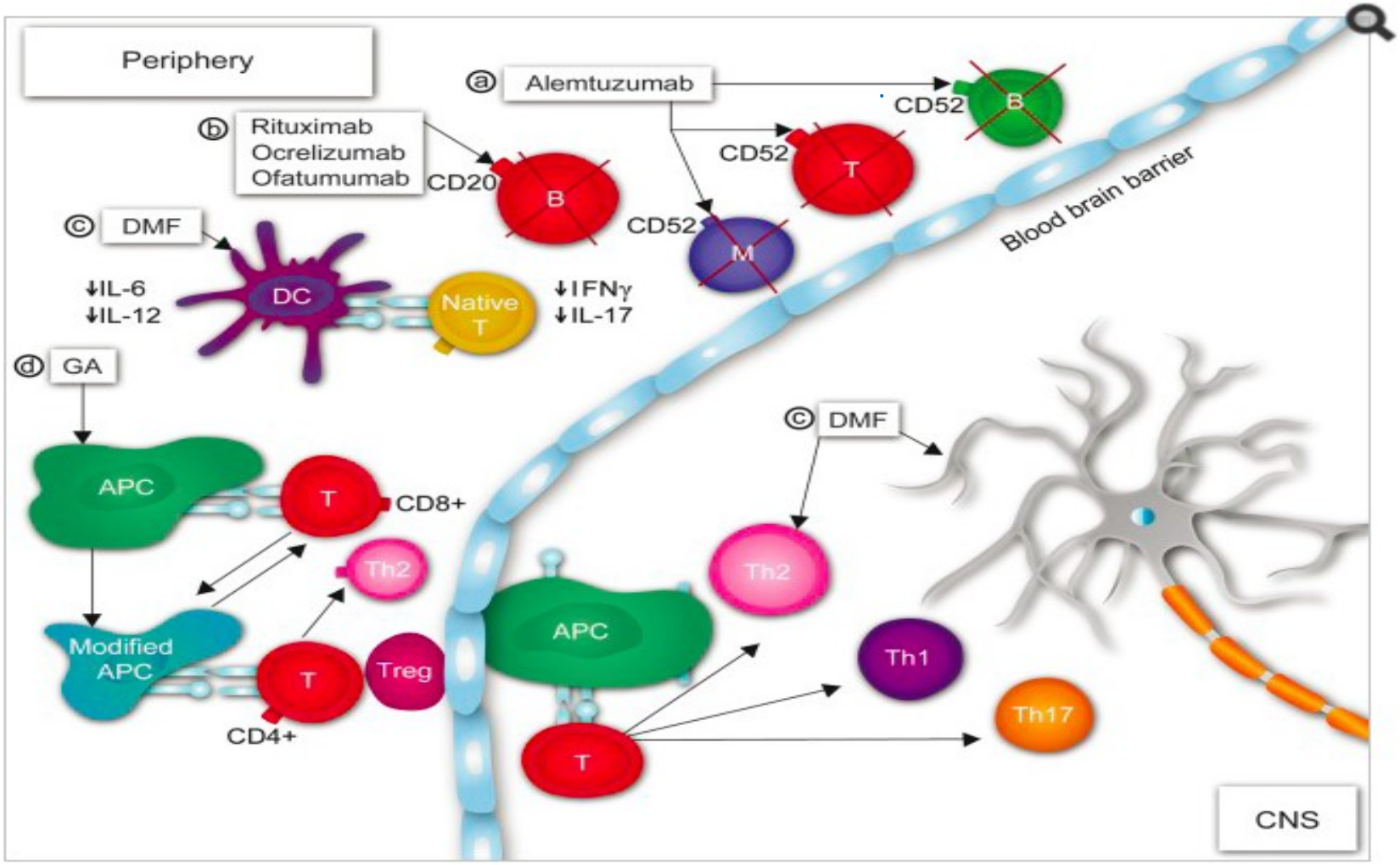
- **Lost of income** from person with MS
- Leading cause of **early disability**
- **Caregiving cost** from strangers
- Family **caregiver lost income**
- Early and lengthy **nursing home care**
- Leading diagnosis for those requesting **assisted suicide** from Dr. Kevorkian

The total lifetime cost per patient with MS is estimated to be $4.1 million

(in 2010 dollars)[2]

1. Naci H, Fleurence R, Birt J, Duhig A. Economic burden of multiple sclerosis: a systematic review of the literature. Pharmacoeconomics. 2010;28(5):363-79. doi: 10.2165/11532230-000000000-00000.
2. Economic Burden of Multiple Sclerosis and the Role of Managed Care Organizations in Multiple Sclerosis Management. AJMC. http://www.ajmc.com/journals/supplement/2016/cost-effectiveness-multiple-sclerosis/cost-effectiveness-multiple-sclerosis-economic-burden. Accessed May 15, 2018.

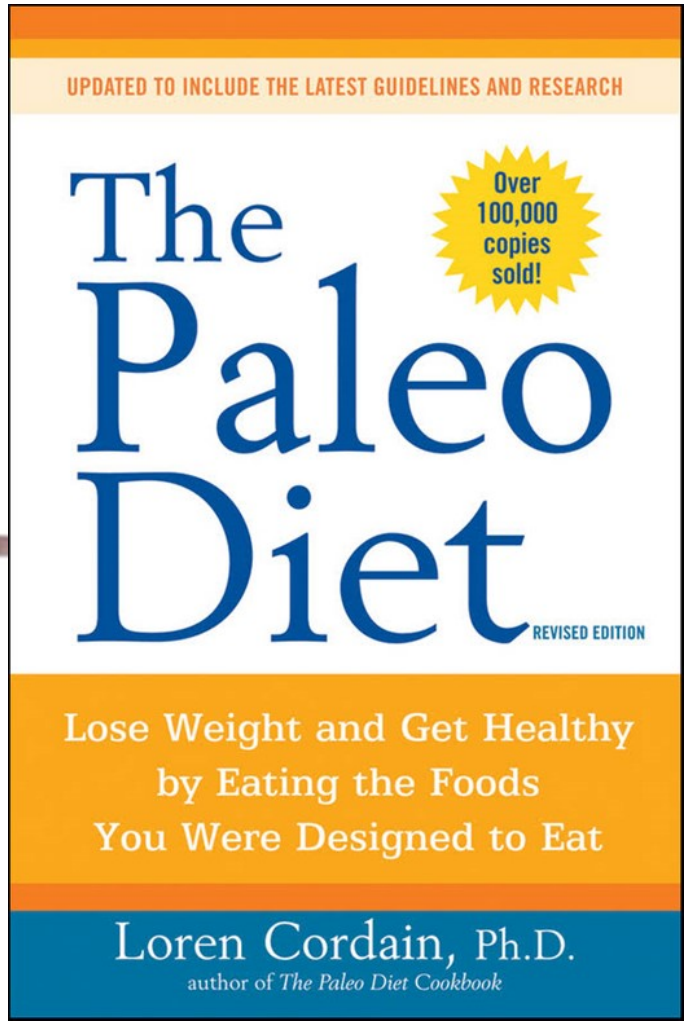
The Wahls Protocol®



Proposed mechanisms of action of highlighted multiple sclerosis therapies

Multiple sclerosis: Five new things. Neurol Clin Pract. 2013 Oct;3(5):404-412.

The Cleveland Clinic



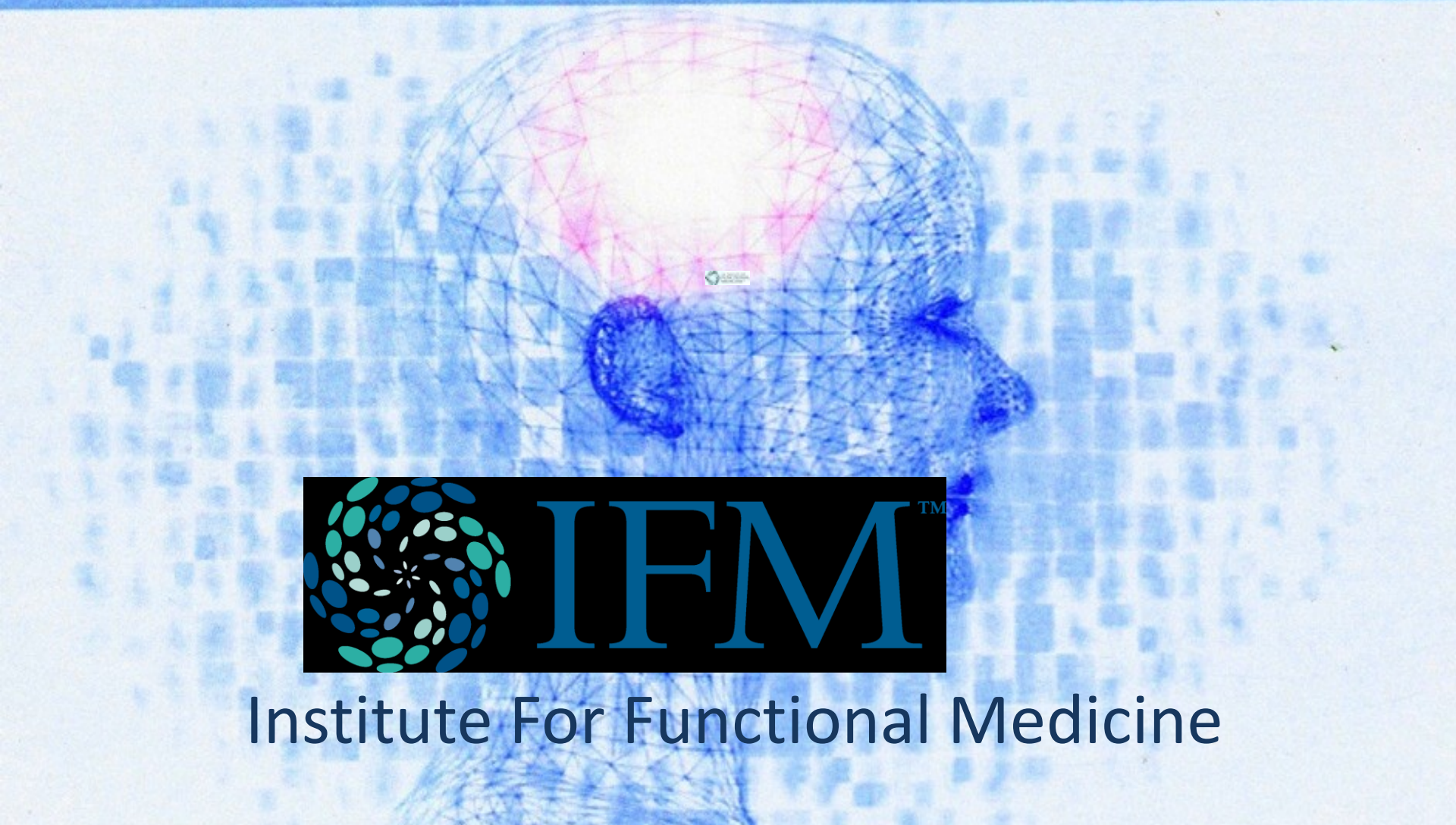
2002

The Wahls Protocol®

7 Years of Decline
NARCOMS QOL Survey

	11/23/05	6/2/06	11/28/06	5/5/07
MS Sx Overall	Worse	Worse	Worse	Worse
Fatigue	Mod	Severe	Total	Total

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

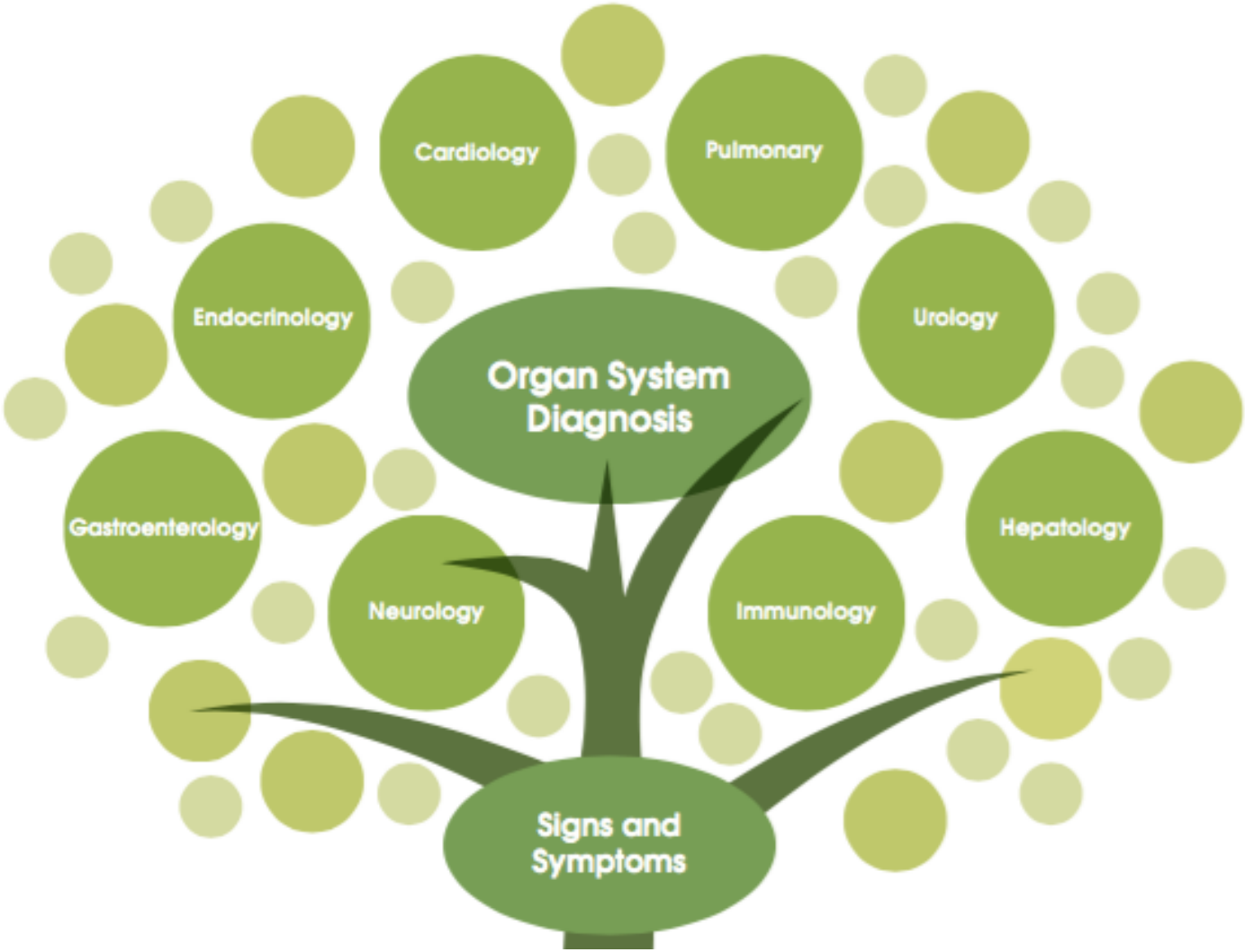


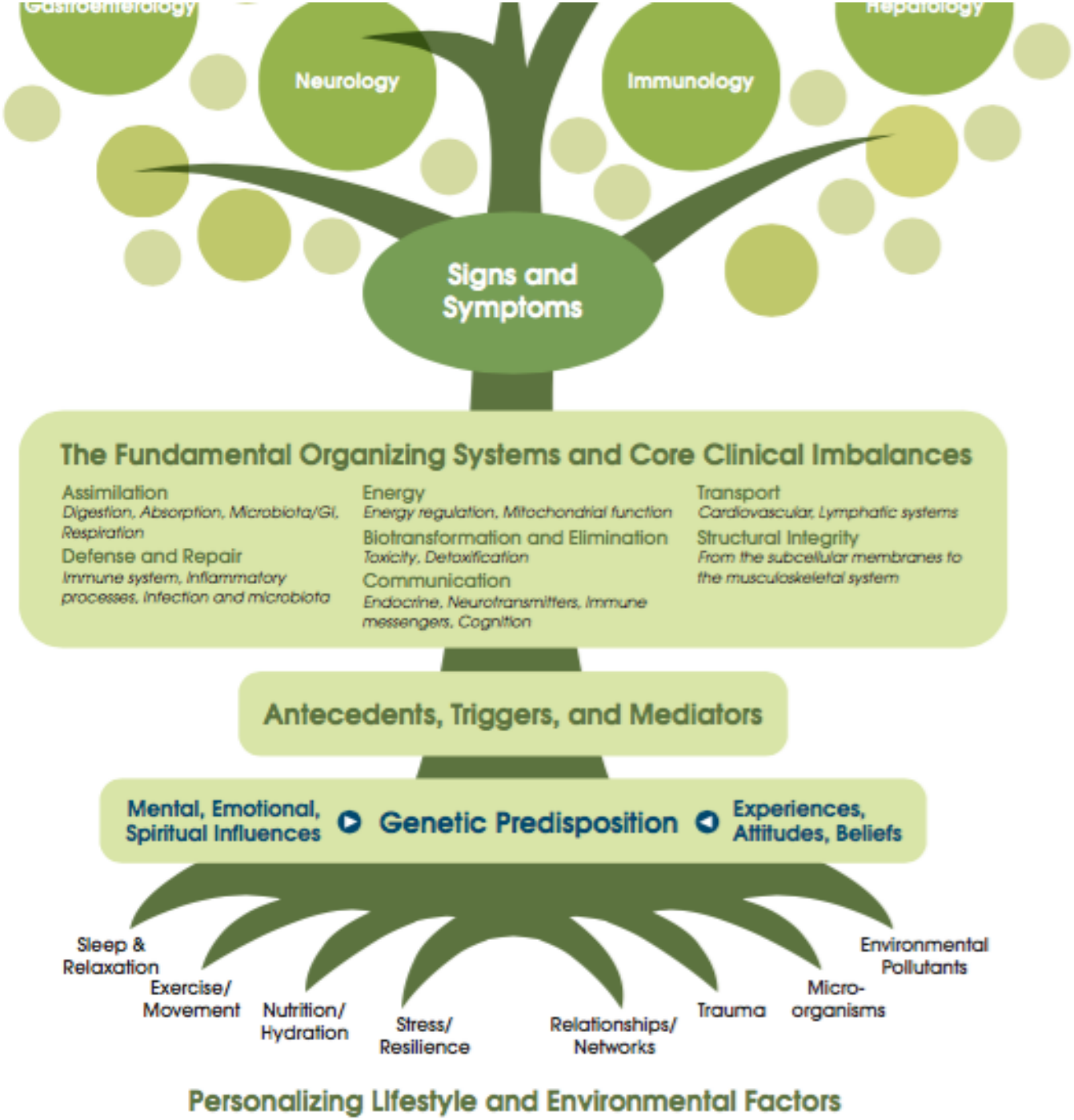
IFM™

Institute For Functional Medicine

THE INSTITUTE FOR FUNCTIONAL MEDICINE®

THE FUNCTIONAL MEDICINE TREE




Gastroenterology
Neurology
Immunology
Hepatology
Signs and Symptoms
The Fundamental Organizing Systems and Core Clinical Imbalances
Assimilation
Digestion, Absorption, Microbiota/GI, Respiration
Defense and Repair
Immune system, Inflammatory processes, Infection and microbiota
Energy
Energy regulation, Mitochondrial function
Biotransformation and Elimination
Toxicity, Detoxification
Communication
Endocrine, Neurotransmitters, Immune messengers, Cognition
Transport
Cardiovascular, Lymphatic systems
Structural Integrity
From the subcellular membranes to the musculoskeletal system
Antecedents, Triggers, and Mediators
Mental, Emotional, Spiritual Influences
Genetic Predisposition
Experiences, Attitudes, Beliefs
Sleep & Relaxation
Exercise/ Movement
Nutrition/ Hydration
Stress/ Resilience
Relationships/ Networks
Trauma
Micro-organisms
Environmental Pollutants
Personalizing Lifestyle and Environmental Factors

The Wahls Protocol®

Personalizing Lifestyle

The Wahls Protocol®

Terry Wahls MD

The Wahls Protocol®

CASES JOURNAL

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

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* 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

Reese D, Shivapour ET, Wahls TL, Dudley-Javoroski SD, Shields R. 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. *Cases Journal*. 2009;2(1):7601. doi:10.4076/1757-1626-2-7601

The Wahls Protocol®

Personalizing Lifestyle

Sleep Disturbances & MS

N=100

Both **depression and fatigue** are associated with poorer sleep in MS patients.

Restless legs also more frequent.

Table 1 Relationships between ESS and SID results in patients with MS and gender, disease-related variables and coexisting conditions

	ESS			SID		
	Mean	SD	*p*	Mean	SD	*p*
Gender						
Men ($n = 31$)	5.58	3.74	0.23	6.62	4.4	0.15
Women ($n = 69$)	7.74	5.04		8.13	5.26	
MS course						
RR-MS ($n = 79$)	5.99	3.93	0.42	7.81	5.17	0.52
SP/PP-MS ($n = 21$)	7.33	5.31		8.67	5.26	
Immunomodulating treatment						
Yes ($n = 34$)	6.09	4.08		6.24	4.29	**0.02**
No ($n = 66$)	6.62	4.37		8.89	5.38	
Coexisting diseases						
Yes ($n = 23$)	6.13	4.96	0.58	8.74	6.06	0.67
No ($n = 77$)	6.31	4.07		7.77	4.09	
Depression						
Yes ($n = 13$)	3.92	3.62	**0.01**	10.69	7.12	0.11
No ($n = 87$)	6.62	4.26		7.59	4.74	
Fatigue						
Yes (FSS > 3.5) ($n = 49$)	6.35	3.93	0.56	6.06	3.92	**0.0001**
No (FSS ≤ 3.5) ($n = 51$)	6.18	4.67		10.0	5.58	

ESS Epworth Sleepiness Scale, *FSS* Fatigue Severity Scale, *MS* multiple sclerosis, *PP-MS* primary progressive multiple sclerosis, *RR-MS* relapsing–remitting multiple sclerosis, *SD* standard deviation, *SID* sleep disturbances (the questionnaire score), *SP-MS* secondary progressive multiple sclerosis

Statistically significant level of $p < 0.05$ was highlighted with bold

Pokryszko-Dragan A, Bilińska M, Gruszka E, Biel Ł, Kamińska K, Konieczna K. Sleep disturbances in patients with multiple sclerosis. Neurol Sci. 2013 Aug;34(8):1291-6. doi: 10.1007/s10072-012-1229-0. Epub 2012 Oct 30.

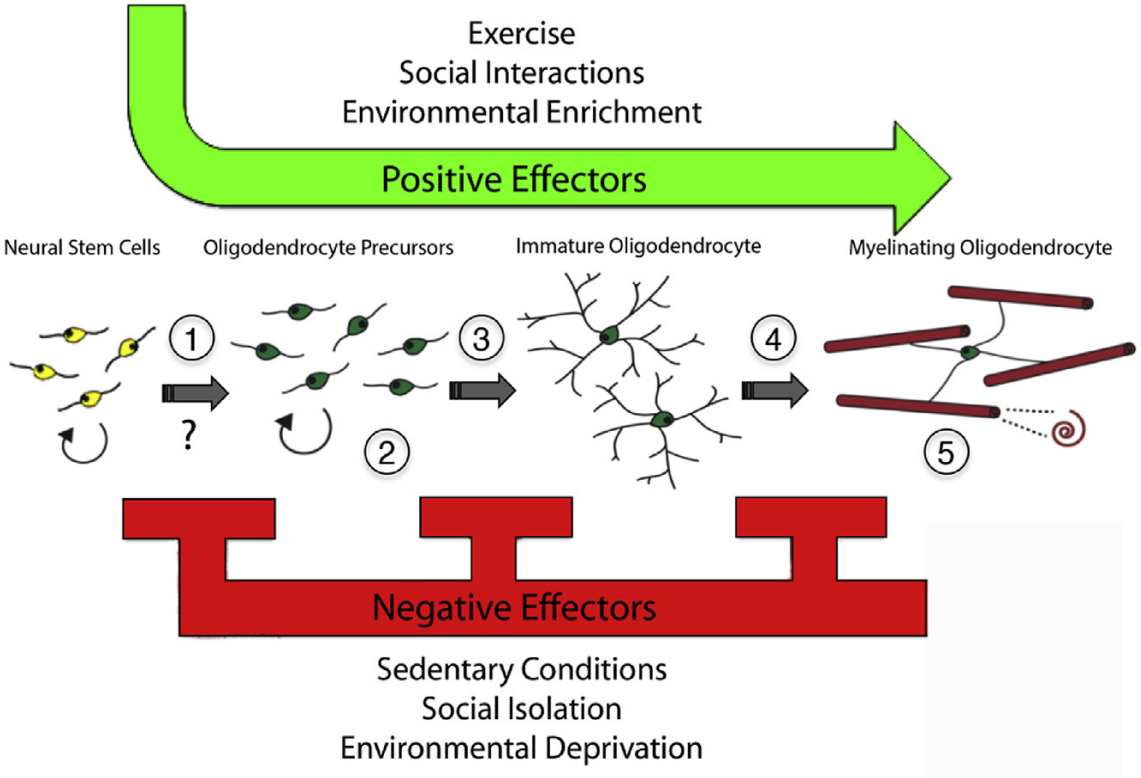
Stress

- ↑ Risk of Alzheimer's disease
- ↑ Risk of MS Relapse, relapse severity
- ↑ Freezing in Parkinson's and worsening PD gait
- ↑ Risk of CVD and Stroke
- **Tx:** Add stress reducing/relieving practices

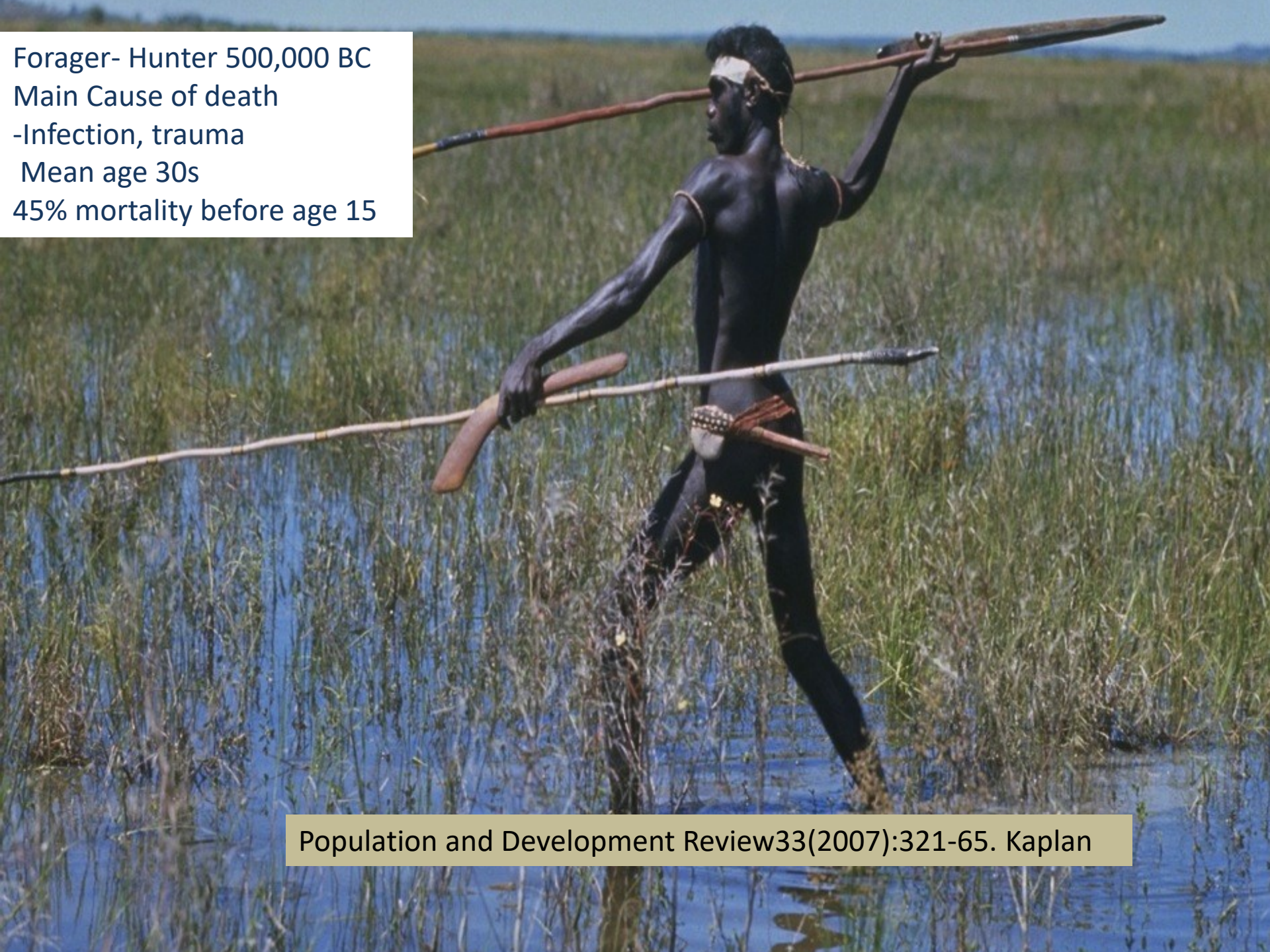
Stress References

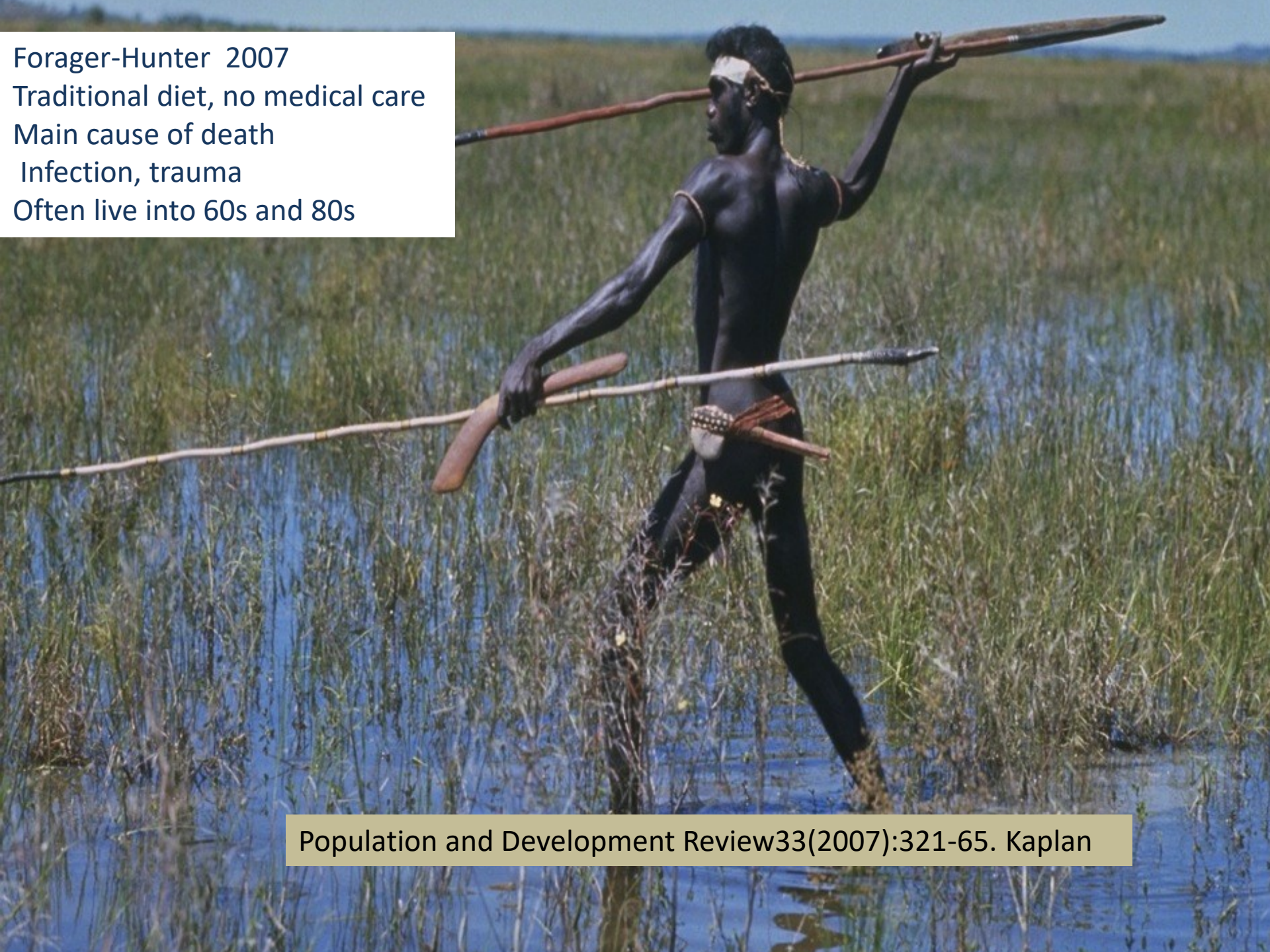
1. Burnes DP, Burnette D. Broadening the etiological discourse on Alzheimer's disease to include trauma and posttraumatic stress disorder as psychosocial risk factors. *J Aging Stud*.2013 Aug;27(3):218-24.
2. Starkstein S, Dragovic M, Brockman S, Wilson M, Bruno V, Merello M. The impact of emotional distress on motor blocks and festination in Parkinson's disease. *J Neuropsychiatry Clin Neurosci.*2015;27(2):121-6
3. Melief J, de Wit SJ, van Eden CG et al. HPA axis activity in multiple sclerosis correlates with disease severity, lesion type and gene expression in normal-appearing white matter. Acta Neuropathol. 2013 Aug;126(2):237-49. doi: 10.1007/s00401-013-1140-7.
4. Mitsonis CI, Zervas IM, Mitropoulos PA et al. The impact of stressful life events on risk of relapse in women with multiple sclerosis: a prospective study. Eur Psychiatry. 2008 Oct;23(7):497-504
5. Rozaski A, Blementhal JA, Kaplan J. Impact of psychological factors on the pathogenesis of cardiovascular disease and implications for therapy. Circulation 1999 (16):2192-217.

Exercise Influences Oligodendrocyte Precursor Cell Production and Maturation

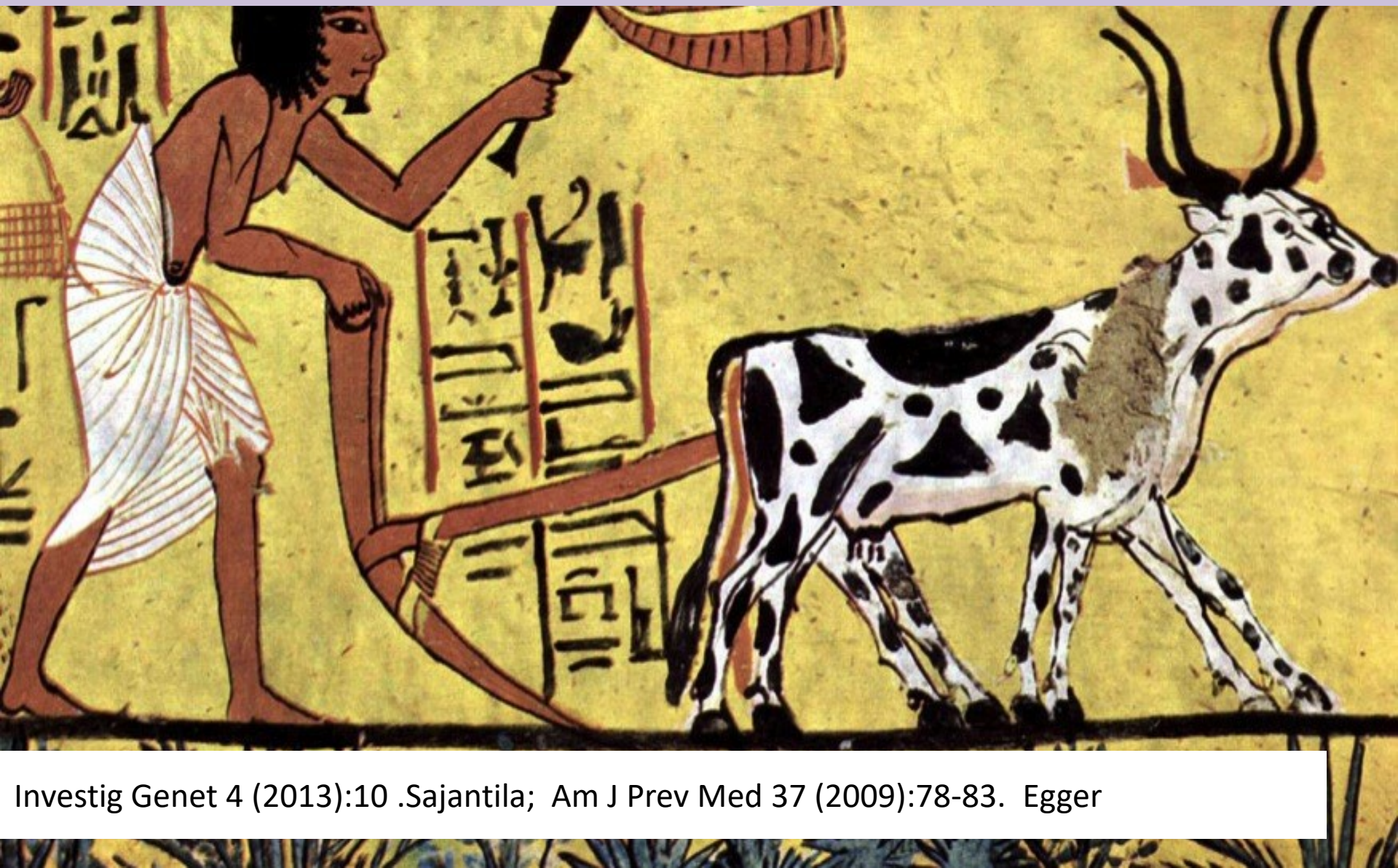


Tomlinson L, Leiton CV, Colognato H. Behavioral experiences as drivers of oligodendrocyte lineage dynamics and myelin plasticity. Neuropharmacology. 2015 Sep 28. pii: S0028-3908(15)30108-8. doi: 10.1016/j.neuropharm.2015.09.016.


Forager- Hunter 500,000 BC
Main Cause of death
-Infection, trauma
Mean age 30s
45% mortality before age 15
Population and Development Review33(2007):321-65. Kaplan


Forager-Hunter 2007
Traditional diet, no medical care
Main cause of death
Infection, trauma
Often live into 60s and 80s
Population and Development Review33(2007):321-65. Kaplan

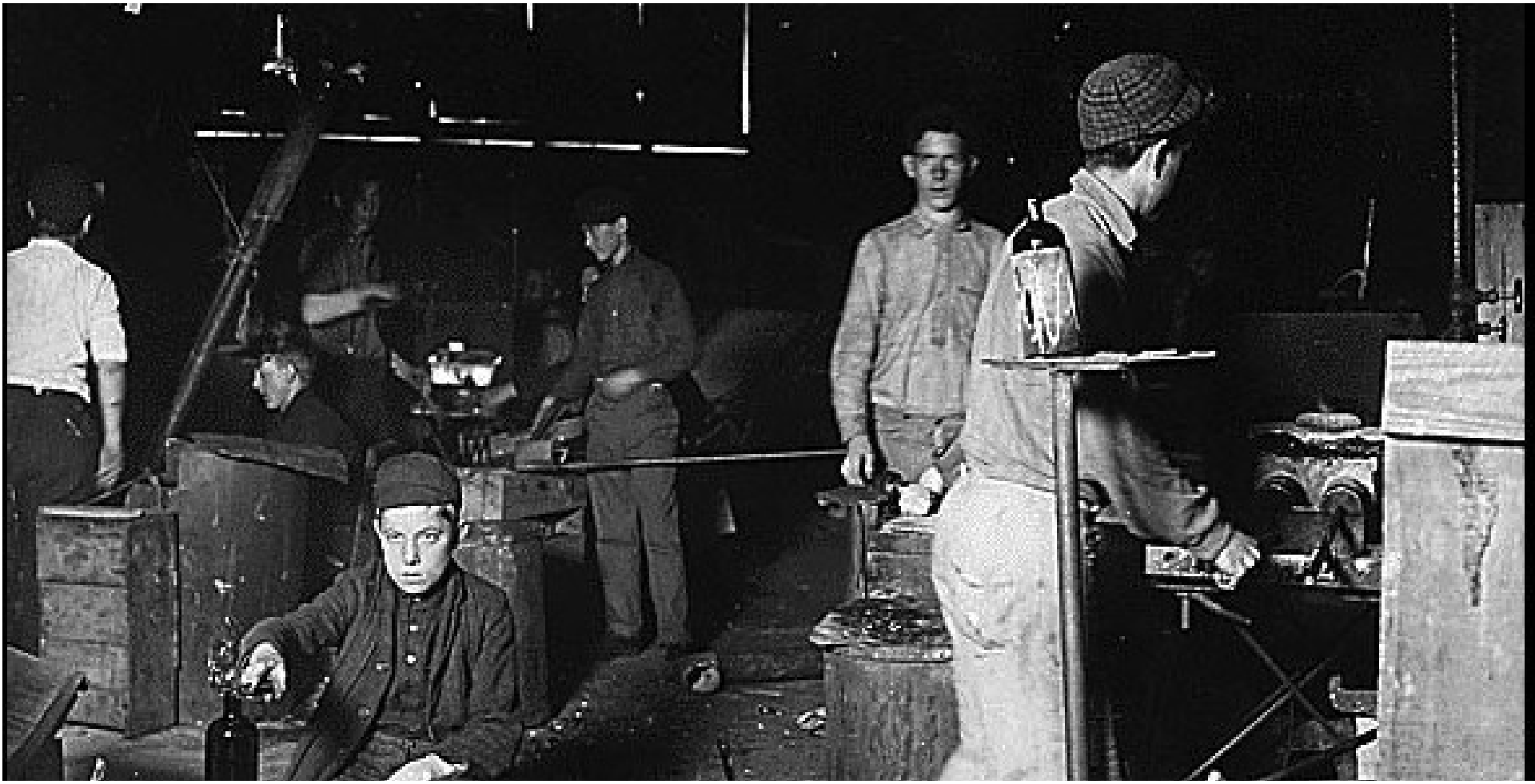
Forager-Hunter to Farmer -10,000 BC
↑ fertility, infection; ↓height



Investig Genet 4 (2013):10 .Sajantila; Am J Prev Med 37 (2009):78-83. Egger

Industrial Revolution 1800s

↑ sugar, white flour; ↓ breast feeding↑ obesity, CVD, DM



Investig Genet 4 (2013):10 .Sajantila; Am J Prev Med 37 (2009):78-83. Egger

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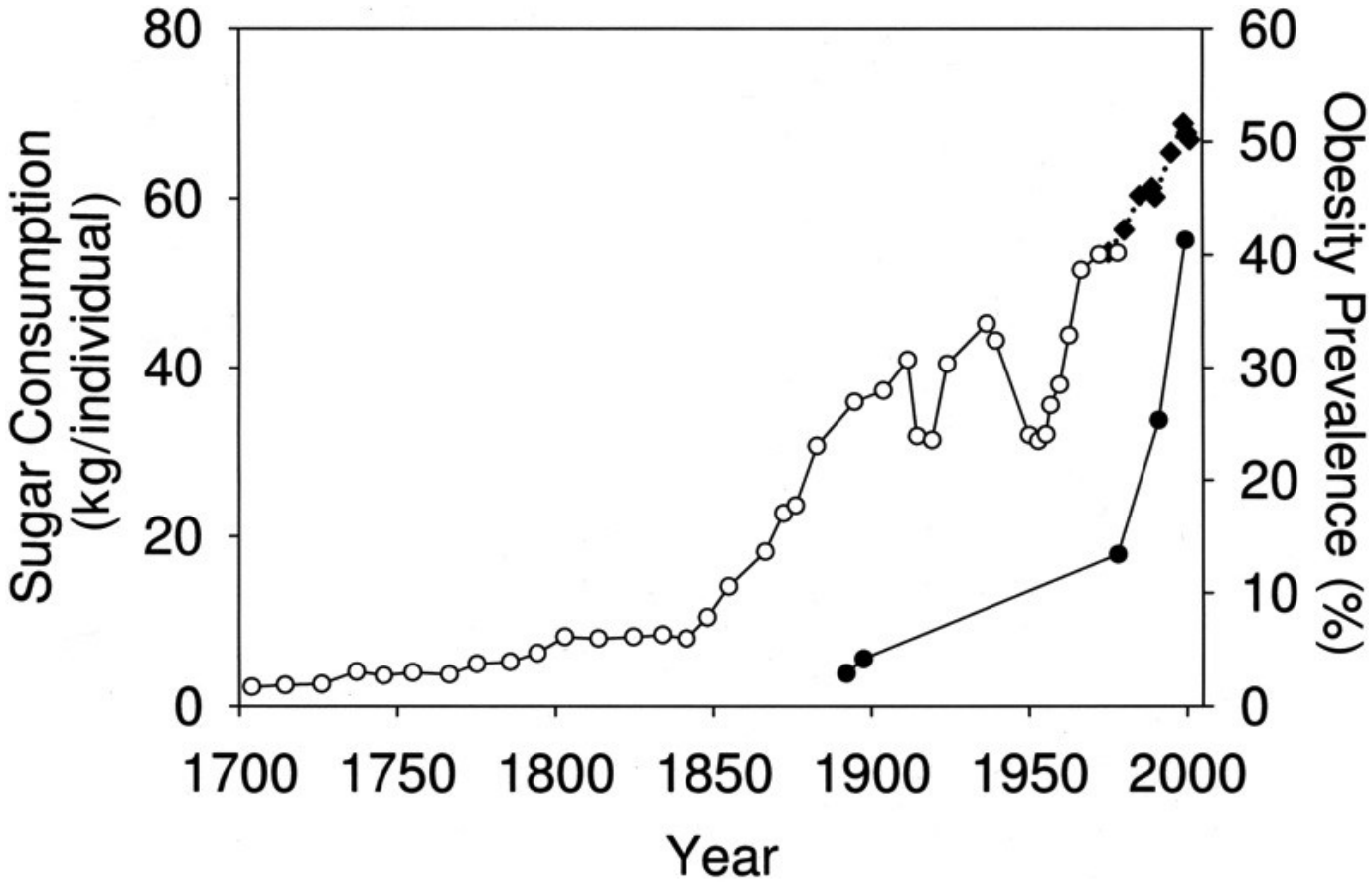
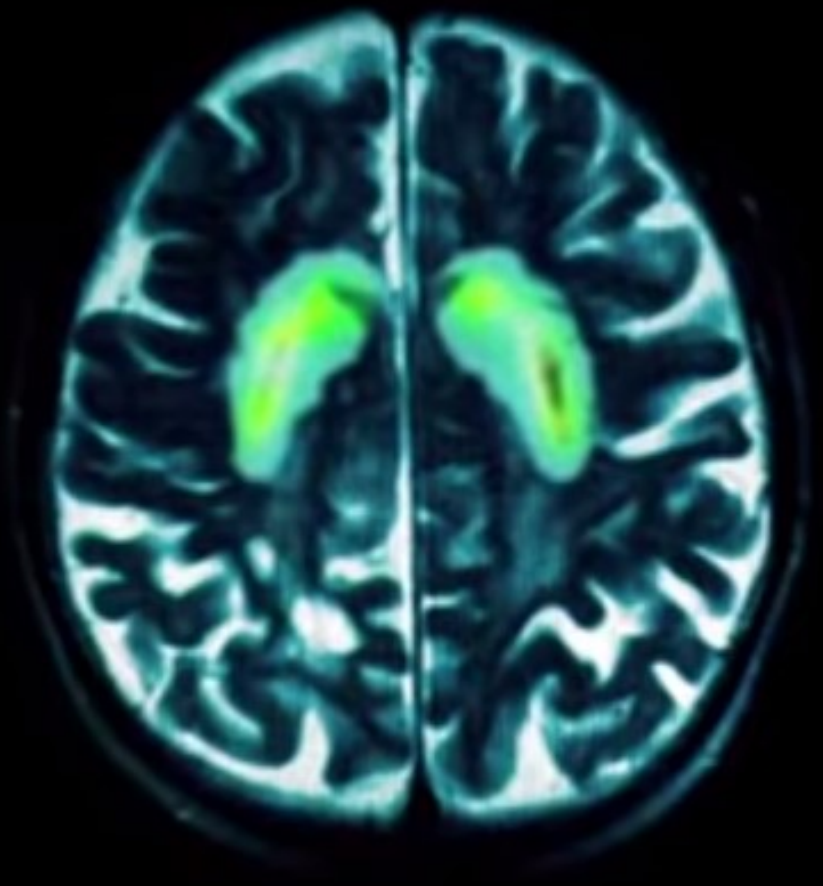
The American Journal of Clinical Nutrition

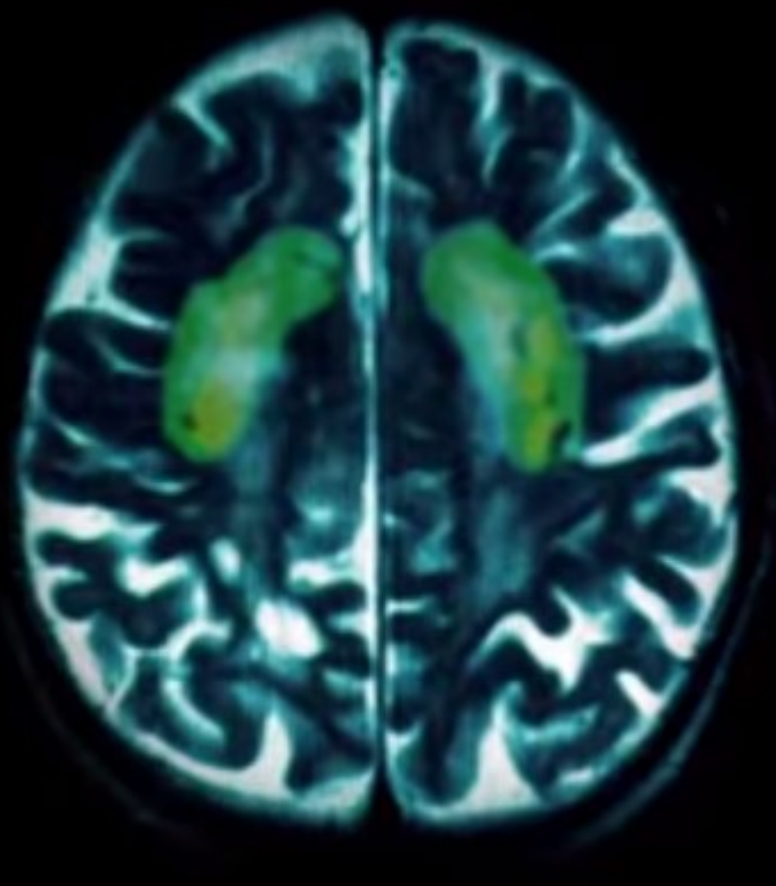
Sugar intake per capita in the United Kingdom from 1700 to 1978 (30, 31; ○) and in the United States from 1975 to 2000 (32; ♦) is compared with obesity rates in the United States in non-Hispanic white men aged 60–69 y (17; •).



Johnson R J et al. Am J Clin Nutr 2007;86:899-906



SUGAR



COCAINE

Diet Papers

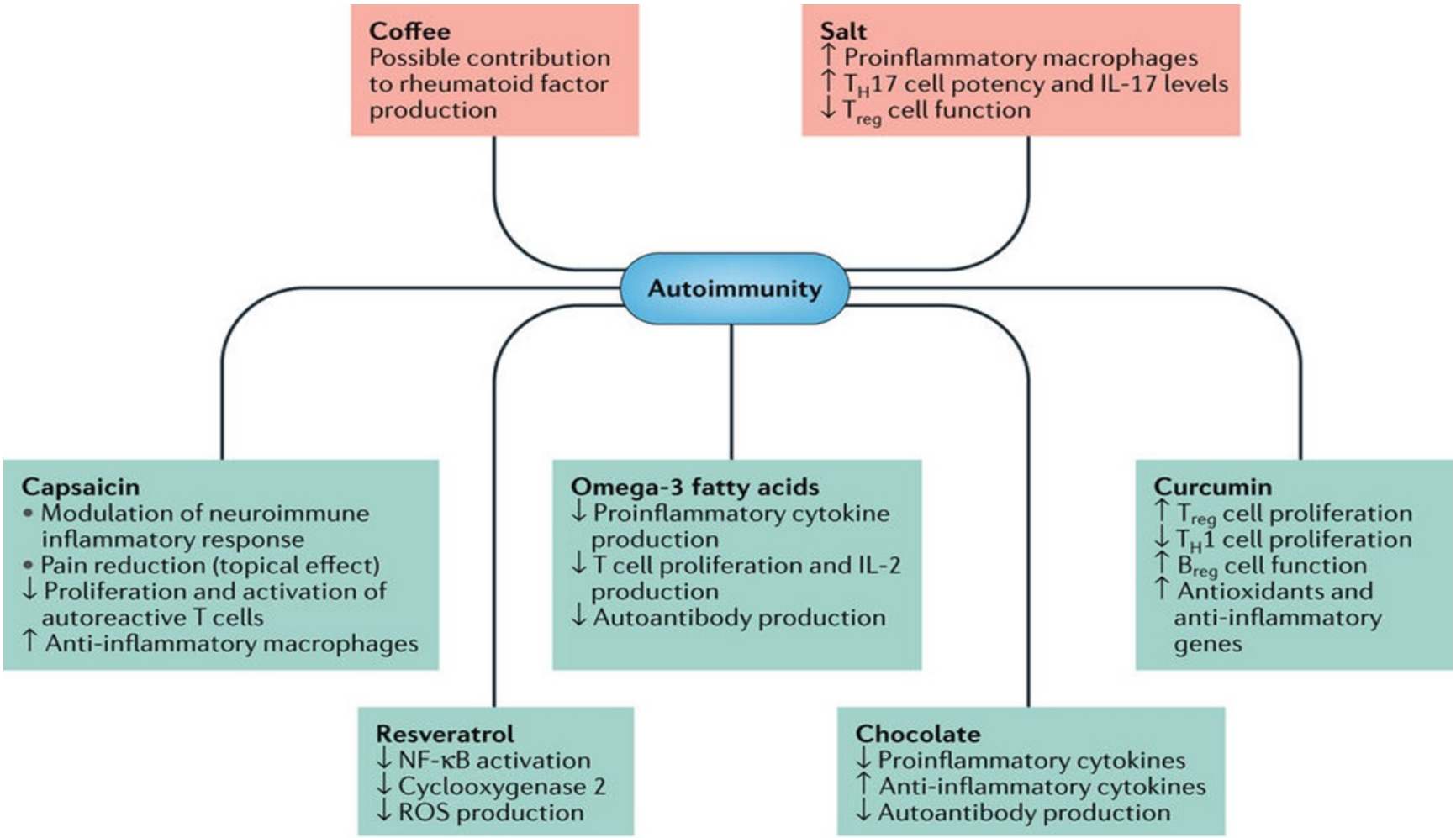
Autoimmune

- 1999 – 36
- 2002 -57
- 2008 – 78
- 2013 – 125
- 2016 – 150

Multiple Sclerosis

- 1999 – 9 papers (supplement)
- 2002 – 2 papers (supplement)
- 2008 – 26 papers
- 2013 - 48 papers
- 2016 -54 papers

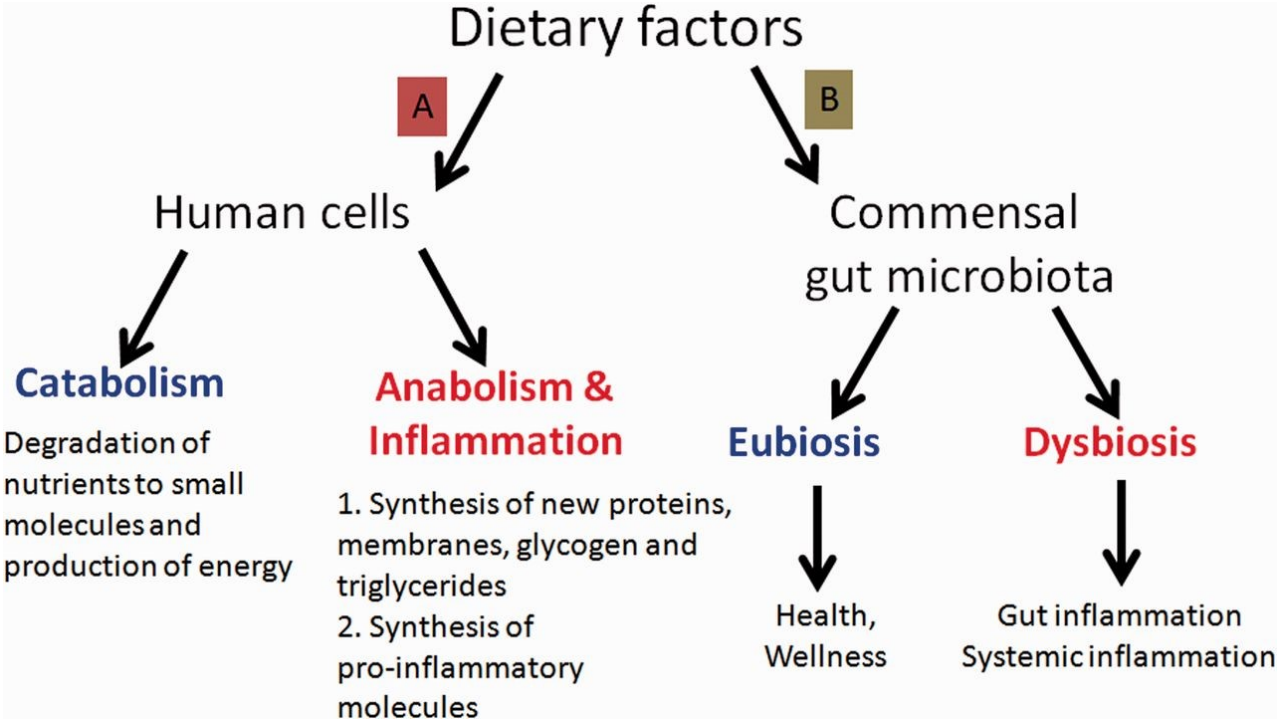
| Dietary factors associated with autoimmunity



Nature Reviews | Rheumatology

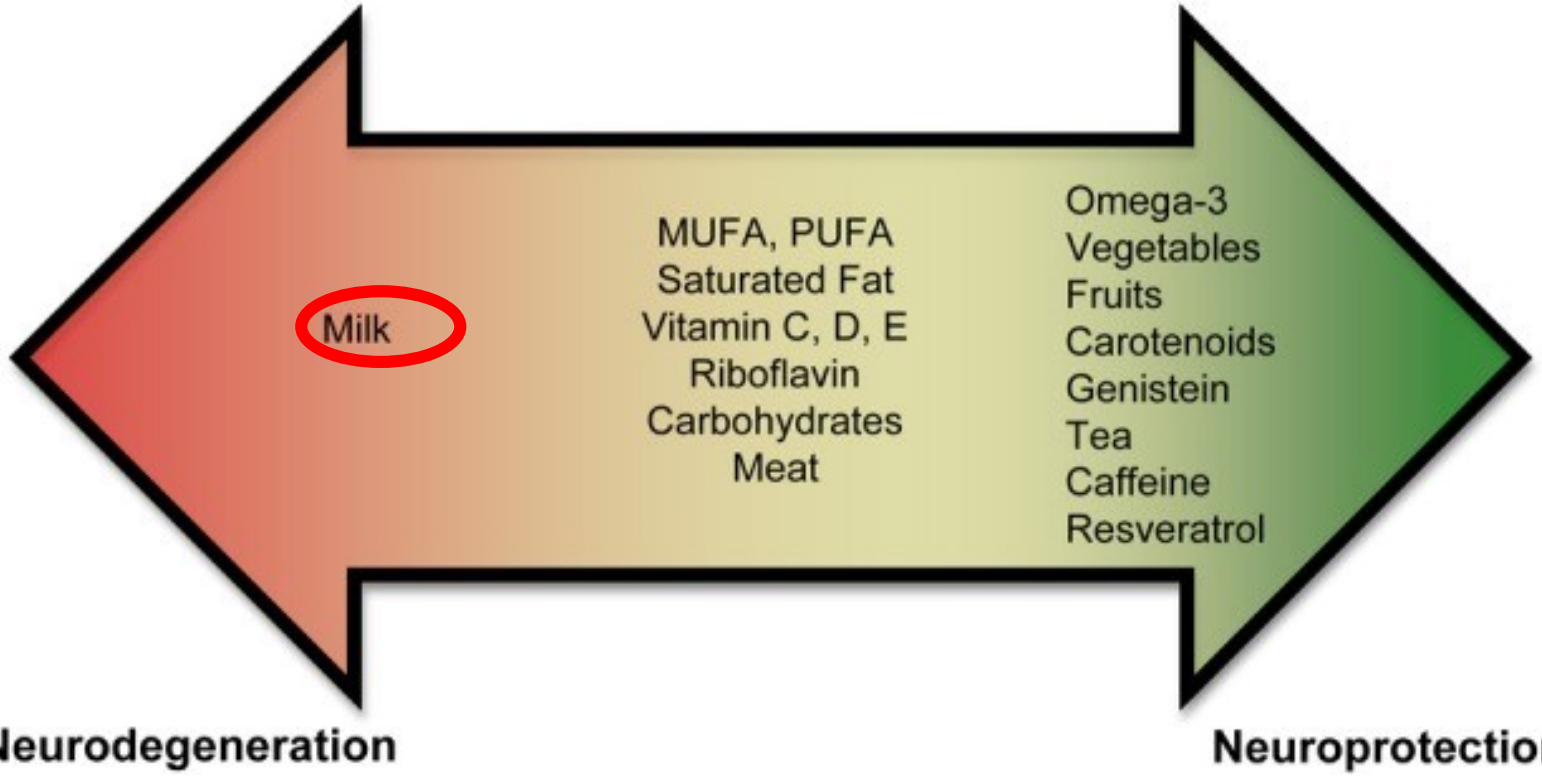
Nat Rev Rheumatol. 2017 Jun;13(6):348-358.

Figure 1. 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

Nutrition in Parkinson's Disease



Seidl SE, Santiago JA, Bilyk H, Potashkin JA. The emerging role of nutrition in Parkinson's disease. Front Aging Neurosci. 2014 Mar 7;6:36. doi: 10.3389/fnagi.2014.00036. eCollection 2014.

Gluten sensitivity: from gut to brain

Marios Hadjivassiliou, David S Sanders, Richard A Grünewald, Nicola Woodroofe, Sabrina Boscolo, Daniel Aeschlimann

010; 9: 318–30

s of Neurology
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vald DPhil) and
troenterology
ders MD), Royal
pital, Sheffield,
edical Research
heffield Hallam
, Sheffield, UK

Gluten sensitivity is a systemic autoimmune disease with diverse manifestations. This disorder is chara abnormal immunological responsiveness to ingested gluten in genetically susceptible individuals. Coeliac gluten-sensitive enteropathy, is only one aspect of a range of possible manifestations of gluten sensitivity neurological manifestations in patients with established coeliac disease have been reported since 1966, until 30 years later that, in some individuals, gluten sensitivity was shown to manifest solely with n dysfunction. Furthermore, the concept of extraintestinal presentations without enteropathy has only recen accepted. In this Personal View, we review the range of neurological manifestations of gluten sensitivity a recent advances in the diagnosis and understanding of the pathophysiological mechanisms underlying n dysfunction related to gluten sensitivity.

Gluten sensitivity is an abnormal immune response to gluten in genetically susceptible individuals and may manifest solely with neurological dysfunction. 90% of gluten sensitive individuals have no GI symptoms.

Lancet Neurol. 2010 Mar;9(3):318-30 Hadjivassiliou M

espondence to:
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rshire Hospital,
Road, Sheffield
S10 2JF, UK
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was transcribed to coeliac. The study of coeliac disease was renewed by Gee[2] in 1888. His lecture on the coeliac affection described the disease according to his observations while treating children with the disease. Although clinicians began to recognise and diagnose coeliac disease, its aetiology remained obscure until 1953 when Dicke and colleagues[3] reported "the presence in wheat, of a factor having a deleterious effect in cases of celiac disease". Because gastrointestinal symptoms were dominant in patients with coeliac disease, and

neurological dysfunction continued to be pu
The key findings from these reports were
(with and without myoclonus) and neuropath
most common manifestations; neurological
ations were usually reported in the context of
coeliac disease and were almost always at
malabsorption of vitamins; and the effects
restriction were inconsistent. A gluten-free d
always alleviate neurological dysfunction,
assessment of the effect of the gluten-free di
the main aim of these reports. None of t

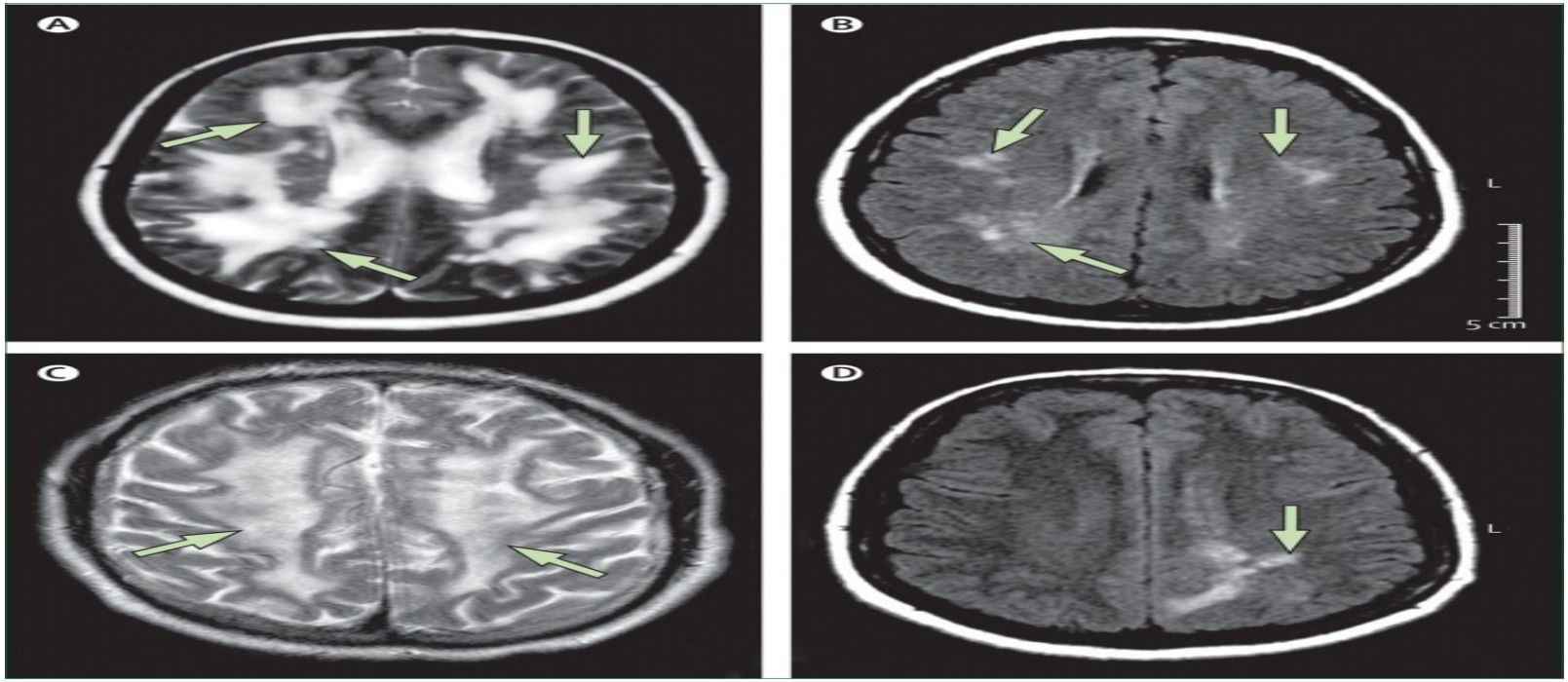


Figure 2 MRI in four patients with gluten encephalopathy The extent and variability of white matter abnormalities caused by gluten sensitivity can be seen in these four patients (A–D). A and C show diffuse white matter changes, whereas B and D show more f...

Marios Hadjivassiliou , David S Sanders , Richard A Grünewald , Nicola Woodroofe , Sabrina Boscolo , Daniel Aeschl...

Gluten sensitivity: from gut to brain

The Lancet Neurology Volume 9, Issue 3 2010 318 - 330

http://dx.doi.org/10.1016/S1474-4422(09)70290-X

Dairy & MS
Casein, Gluten & Schizophrenia

- Liquid cow milk (not cheese) and MS prevalence was highly correlated (rho = 0.836) across 27 countries and 29 populations.

- IgG to Casein and gluten were significantly ↑ in recent onset and non-recent onset schizophrenia compared to controls ($p \leq 0.00001$-0.004) .

1. Correlation between milk and dairy product consumption and multiple sclerosis prevalence: a worldwide study. Neuroepidemiology. 1992;11(4-6):304-12.
2. Severance EG, Alaedini A, Yang S, Halling M, Gressitt KL, Stallings CR, Origoni AE, Vaughan C, Khushalani S, Leweke FM, Dickerson FB, Yolken RH. Gastrointestinal inflammation and associated immune activation in schizophrenia Schizophr Res.2012 Jun;138(1):48-53.

Gluten and Casein and Opioids

- Gluten can be degraded into several morphine-like substances, named gluten exorphins.
- Milk proteins are particularly strong allergens and are additional source of bioactive peptides including β-casomorphin-7 and exerts its influence on nervous, digestive, and immune functions via the opioid receptor

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.

Dairy & MS
Casein, Gluten & Schizophrenia

1. Malosse D, Perron H, Sasco A, Seigneurin JM. Correlation between milk and dairy product consumption and multiple sclerosis prevalence: a worldwide study. Neuroepidemiology. 1992;11(4-6):304-12.
2. Severance EG, Alaedini A, Yang S, et al. Gastrointestinal inflammation and associated immune activation in schizophrenia. Schizophrenia research. 2012;138(1):48-53. doi:10.1016/j.schres.2012.02.025.
3. Pruimboom L, de Punder K. The opioid effects of gluten exorphins: asymptomatic celiac disease. Journal of Health, Population, and Nutrition. 2015;33:24. doi:10.1186/s41043-015-0032-y.
4. Teschemacher H. Opioid receptor ligands derived from food proteins. Curr Pharm Des. 2003;9(16):1331-44.
5. Fiedorowicz E, Kaczmarski M, Cieślińska A et al. β-casomorphin-7 alters μ-opioid receptor and dipeptidyl peptidase IV genes expression in children with atopic dermatitis. Peptides. 2014 Dec;62:144-9. doi: 10.1016/j.peptides.2014.09.020

MS and Gluten References

1. Gluten antibodies in patients with multiple sclerosis. Hum Nutr Appl Nutr. 1984 Apr;38(2):142-3.
2. Multiple sclerosis and gluten sensitivity. Clin Neurol Neurosurg. 2007 Oct;109(8):651-3.
3. Prevalence of celiac disease in multiple sclerosis. BMC Neurol. 2011 Mar 7;11:31.
4. Celiac disease with neurologic manifestations in children. Rev Med Chir Soc Med Nat Iasi. 2013 Jan-Mar;117(1):88-94.
5. Celiac disease with cerebral and peripheral nerve involvement mimicking multiple sclerosis. J Med Life. 2014 Sep 15;7(3):440-4. Epub 2014 Sep 25.
6. A case of multiple sclerosis and celiac disease. Case Rep Neurol Med. 2013;2013:576921.
7. Gluten-related disorders: gluten ataxia. Dig Dis. 2015;33(2):264-8.
8. Transglutaminase-6 is an autoantigen in progressive multiple sclerosis and is upregulated in reactive astrocytes. Mult Scler. 2016 Dec 1:1352458516684022.
9. The progression of coeliac disease: its neurological and psychiatric implications. Nutr Res Rev. 2017 Jun;30(1):25-35.

Risks of Eggs

- **Pros**
  - Grass fed - DHA, choline, biotin, lutein, Vitamins A, D, K2, and B3, B6, B9, B12
- **Cons**
  - Eggs are most common food allergen in IBD >70%
  - 60% allergy patients have IgG Ab to eggs
  - 13% seasonal allergies have IgG Ab to eggs
  - Wheat, milk, eggs are common food triggers to Eosinophilic Esophagitis

Risks of Eggs

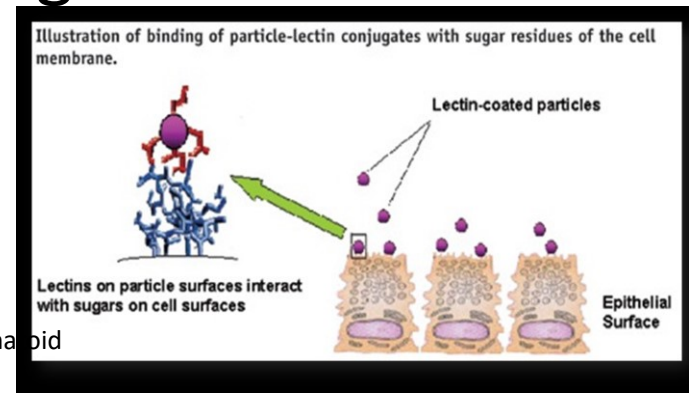
1. Wang G, Ren J, Li G, et al. The utility of food antigen test in the diagnosis of Crohn's disease and remission maintenance after exclusive enteral nutrition. Clin Res Hepatol Gastroenterol. 2018;42(2):145-152. doi:10.1016/j.clinre.2017.09.002
2. Shakoor Z, AlFaifi A, AlAmro B, AlTawil LN, AlOhaly RY. Prevalence of IgG-mediated food intolerance among patients with allergic symptoms. Ann Saudi Med. 2016 Nov-Dec;36(6):386-390.
3. Dhanapala P, De Silva C, Doran T, Suphioglu C. Cracking the egg: An insight into egg hypersensitivity. Mol Immunol. 2015 Aug;66(2):375-83. doi: 10.1016/j.molimm.2015.04.016.
4. Pang KA, Pang KP, Pang EB, Tan YN, Chan YH, Siow JK. Food allergy and allergic rhinitis in 435 asian patients - A descriptive review. Med J Malaysia. 2017 Aug;72(4):215-220.
5. Philpott H, Nandurkar S, Royce SG, Thien F, Gibson PR. 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. doi: 10.1111/apt.13676.
6. Cai C, Shen J, Zhao D, et al. Serological Investigation of Food Specific Immunoglobulin G Antibodies in Patients with Inflammatory Bowel Diseases. Boone DL, ed. PLoS ONE. 2014;9(11):e112154. doi:10.1371/journal.pone.0112154.

Lectins

- "By eliminating dietary elements, particularly lectins, which adversely influence both enterocyte and lymphocyte structure and function, it is proposed that the peripheral antigenic stimulus (both pathogenic and dietary) will be reduced and thereby result in a diminution of disease symptoms in certain patients with RA."

1. Cordain L, Toohey L, Smith MJ, Hickey MS. Modulation of immune function by dietary lectins in rheumatoid arthritis. *British Journal of Nutrition*. 2000;83(03):207-217.

- Lectins are **proteins found in plants and animals that bind sugars** (hemagglutinins)
- They can bind the glycoproteins on the intestinal lining leading to **barrier damage**
- Lectins are found in most foods but are especially high in grains (esp wheat), dairy, legumes, and nightshade vegetables
- Most traditional methods cooking these foods such as soaking, ferment-ing & cooking will decrease the lectin content.



1. Cordain L, Toohey L, Smith MJ, Hickey MS. Modulation of immune function by dietary lectins in rheumatoid arthritis. *British Journal of Nutrition*. 2000;83(03):207-217.
2. de Punder K, Pruimboom L. The dietary intake of wheat and other cereal grains and their role in inflammation. Nutrients. 2013 Mar 12;5(3):771-87.

Paleo Diet Benefits

- Reduced BP, BMI, central obesity
- Improved insulin sensitivity, HgbA1c
- Improved HDL Cholesterol, Triglycerides
- Improved endothelial function

1. Lindeberg, S., Jönsson, T., Granfeldt, Y. et al. Diabetologia (2007) 50: 1795. doi:10.1007/s00125-007-0716-y
2. Österdahl M, Kocturk T, Koochek A, Wändell PE. Effects of a short-term intervention with a paleolithic diet in healthy volunteers. European Journal of Clinical Nutrition. 2007;62(5):682–685. doi:10.1038/sj.ejcn.1602790.
3. Jönsson T, Granfeldt Y, Ahrén B, et al. Beneficial effects of a Paleolithic diet on cardiovascular risk factors in type 2 diabetes: a randomized cross-over pilot study. Cardiovascular Diabetology. 2009;8:35. doi:10.1186/1475-2840-8-35.
4. Frassetto LA, Schloetter M, Mietus-Synder M, Morris RC, Sebastian A. Metabolic and physiologic improvements from consuming a paleolithic, hunter-gatherer type diet. European Journal of Clinical Nutrition. 2009;63(8):947–955. doi:10.1038/ejcn.2009.4.
5. Halberg N, Henriksen M, Söderhamn N, et. al, Effect of intermittent fasting and refeeding on insulin action in healthy men. *J Appl Physiol* (1985). 2005 Dec;99(6):2128-36.
6. Ryberg M, Sandberg S, Mellberg C, et al. A Palaeolithic-type diet causes strong tissue-specific effects on ectopic fat deposition in obese postmenopausal women. Journal of Internal Medicine. 2013;274(1):67–76. doi:10.1111/joim.12048.
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8. Otten J, Stomby A, Waling M, et al. Benefits of a Paleolithic diet with and without supervised exercise on fat mass, insulin sensitivity, and glycemic control: A randomized controlled trial in individuals with type 2 diabetes. Diabetes/Metabolism Research and Reviews. January 2016. doi:10.1002/dmrr.2828.
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10. Spreadbury I. Comparison with ancestral diets suggests dense acellular carbohydrates promote an inflammatory microbiota, and may be the primary dietary cause of leptin resistance and obesity. Diabetes Metab Syndr Obes. 2012;5:175-89.
11. Eaton SB, Konner MJ, Cordain L. Diet-dependent acid load, Paleolithic nutrition, and evolutionary health promotion. Am J Clin Nutr. 2010;91:295-7. Andersson A, et al. Whole-grain foods do not affect insulin sensitivity or markers of lipid peroxidation and inflammation in healthy, moderately overweight subjects. J Nutr.2007 Jun;137(6):1401-7.
12. Tighe P, et al. Effect of increased consumption of whole - grain foods on blood pressure and other cardiovascular risk markers in healthy middle-aged persons: a randomized controlled trial. Am J Clin Nutr. 2010 Oct;92(4):733-40.
13. Brownlee IA, et al. Markers of cardiovascular risk are not changed by increased whole-grain intake: the WHOLEheart study, a randomised, controlled dietary intervention. Br J Nutr. 2010 Jul;104(1):125-34.
14. Masters RC, et al. Whole and refined grain intakes are related to inflammatory protein concentrations in human plasma. J Nutr. 2010 Mar;140(3):587-94.
15. Katcher HI, et al. The effects of a whole grain-enriched hypocaloric diet on cardiovascular disease risk factors in men and women with metabolic syndrome. Am J Clin Nutr. 2008 Jan;87(1):79-90.

Nutrient Triage

- Low micronutrient intake may accelerate the degenerative diseases of aging through allocation of scarce micronutrients by triage.
  - Zn, Mg, biotin, Vitamin K, D, A
  - Lipoic Acid, Acetyl carnitine

Low micronutrient intake may accelerate the degenerative diseases of aging through allocation of scarce micronutrients by triage.Proc Natl Acad Sci U S A. 2006 Nov 21;103(47):17589-94.

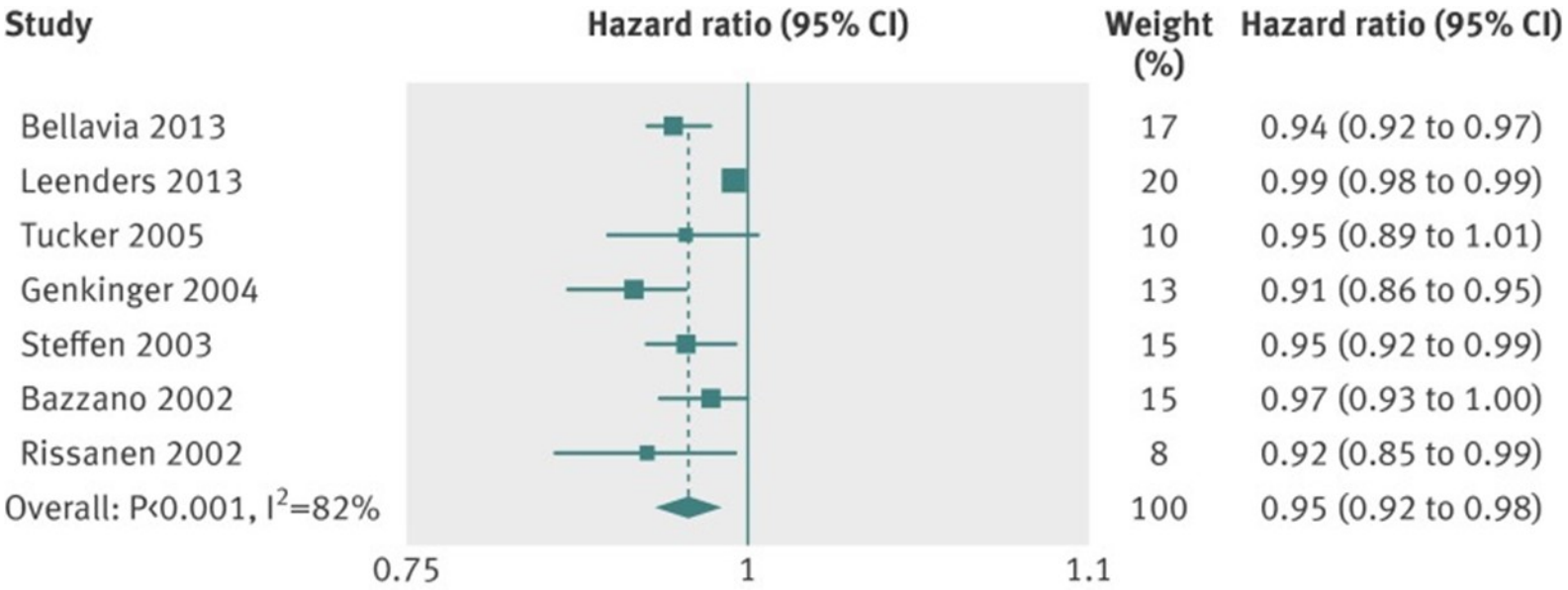
What to Eat?

Fruit and vegetable consumption and mortality from all causes, cardiovascular disease, and cancer: systematic review and dose-response meta-analysis of prospective cohort studies.

16 studies - 833,234 participants

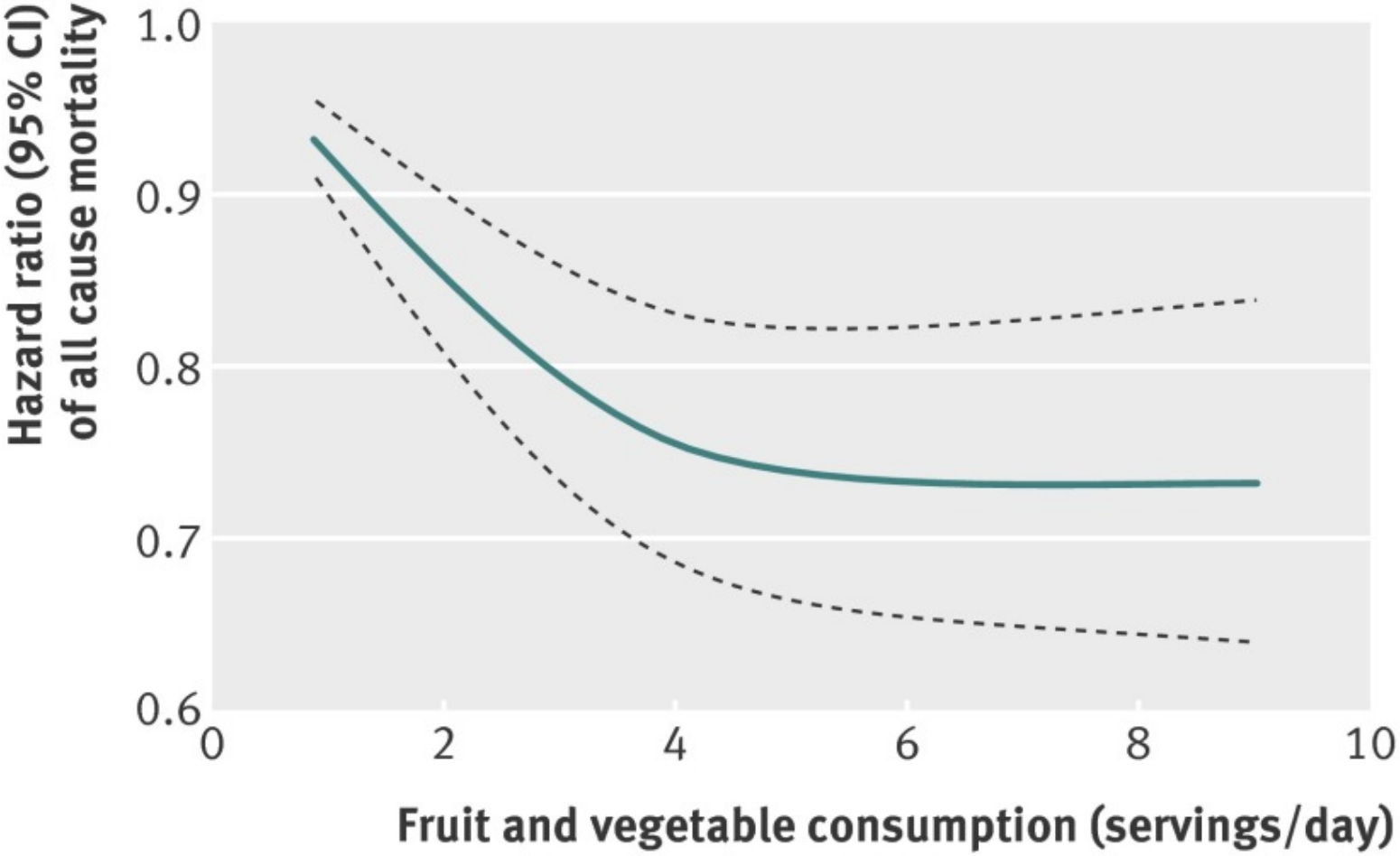
BMJ. 2014; 349: g4490

Risk of all cause mortality associated with servings/day of fruit and vegetables.



BMJ. 2014; 349: g4490

Dose-response relation between fruit and vegetable consumption and risk of all cause mortality



BMJ. 2014; 349: g4490.

Mediterranean diet adherence and risk of multiple sclerosis – Case control study

- N=70 RRMS 140 controls Interviews re diet
- Reduced risk of MS
  - Fruits (OR=0.28, 95% CI: 0.12-0.63, p-value: 0.002)
  - Vegetables (OR=0.23, 95% CI: 0.10-0.53, p-value: 0.001)

Mediterranean diet adherence and risk of multiple sclerosis: a case-control study. Asia Pac J Clin Nutr. 2016;25(2):377-84.

Mediterranean Diet

- High olive oil
- High vegetable/ polyphenol
- Whole grains
- Low red meat

Potential for diet to prevent and remediate cognitive deficits in neurological disorders. Nutr Rev. 2018 Mar 1;76(3):204-217.
The Role of Diet in Multiple Sclerosis: Mechanistic Connections and Current Evidence. Curr Nutr Rep. 2018 Aug 16.
Anti-inflammatory Activity of Extra Virgin Olive Oil Polyphenols: Which Role in the Prevention and Treatment of Immune-Mediated Inflammatory Diseases? Endocr Metab Immune Disord Drug Targets. 2018;18(1):36-50.

36 Key Micronutrients

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.
Part 2 Macronutriients

J Nutr Health Aging 2006;10(5):377-85.

Bowman **Nutrient biomarker patterns, cognitive function, and MRI measures of brain aging.** Neurology. 2012 Jan 24;78(4):241-9. Bowman

Nutrients

Vitamin A, retinol	Alpha carotene	Carnitine
Vitamin B_1 (thiamine)	Beta carotene	Lipoic acid
Vitamin B_2 (riboflavin)	Beta cryptoxanthin	Creatine
Vitamin B_3 (niacin)	Lutein	Cholesterol
Vitamin B_5 (Pantothenic acid)	Lycopene	Alpha-linolenic fatty acid (ALA)
Vitamin B_6 (pyridoxine)	Zeaxanthin	Eicosapentaenoic acid (EPA)
Vitamin B_9 (folic acid)	Iron	Docosahexaenoic acid (DHA)
Vitamin B_{12} (cobalamin)	Copper	Arachidonic acid (AA)
Vitamin C	Zinc	Gamma-linolenic faty acid (GLA)
Vitamin D	Iodine	Linoleic acid (LA)
Vitamin E	Magnesium	N Acetyl cysteine
Vitamin K	Selenium	Taurine

Sulfur Rich Foods

Why Brassica and Allium?

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

Brassica and Allium References

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 Emphasize Mushrooms?

- Increase nerve growth factors (NGF)
- *Hericium erinaceus* (Yamabushitake or **Lion's Mane**) stimulate the production of NGF (in vitro)
- Activate natural killer cells
- Prime innate and adaptive immunity

- Mori K, Obara Y, Hirota M, Azumi Y, Kinugasa S, Inatomi S, Nakahata N. Nerve growth factor-inducing activity of Hericium erinaceus in 1321N1 human astrocytoma cells. Biol Pharm Bull. 2008 Sep;31(9):1727-32.
- 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.
- Akramiene D, Kondrotas A, Didziapetriene J, Kevelaitis E Effects of beta-glucans on the immune system. Medicina (Kaunas).2007;43(8):597-606.
- Lai PL, Naidu M,Sabaratnam V,Wong K, DaviP, Kuppusamy UR, Abdullah N, Malek SN. Neurotrophic properties of the Lion's mane medicinal mushroom, Hericium erinaceus (Higher Basidiomycetes) from Malaysia Int J Med Mushrooms.2013;15(6):539-54.
- 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.

Leafy Greens

Why Greens?

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

Greens References

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.

Colored Foods

Why deeply pigmented?

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

Blueberries and Mild Cognitive Impairment (MCI)

- N = 47 with MCI, 68 y/o +, Blueberry powder vs. placebo, 16 weeks, equivalent of 1 cup berries
- "There was improvement in cognitive performance and brain function compared with placebo"

- N=94 62 to 80 y/o with memory complaints
- Fish oil + blueberries vs. fish oil + placebo, 24 weeks
- The blueberry-supplemented participants had a better sense of well-being, fewer memory mistakes and were less inefficient.

Krikorian R, Shidler MD, Nash TA, Kalt W, Vinqvist-Tymchuk MR, Shukitt-Hale B, Joseph JA. Blueberry supplementation improves memory in older adults. J Agric Food Chem.2010 Apr 14;58(7):3996-4000.
Funding for the studies was provided by the US Highbush Blueberry Council, the National Institute on Aging, and Wild Blueberries of North America. Dr. Krikorian has disclosed no relevant financial relationships.

Pigment & Blueberry References

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.

The Wahls Protocol®

3 Greens

3 Colored

3 Sulfur

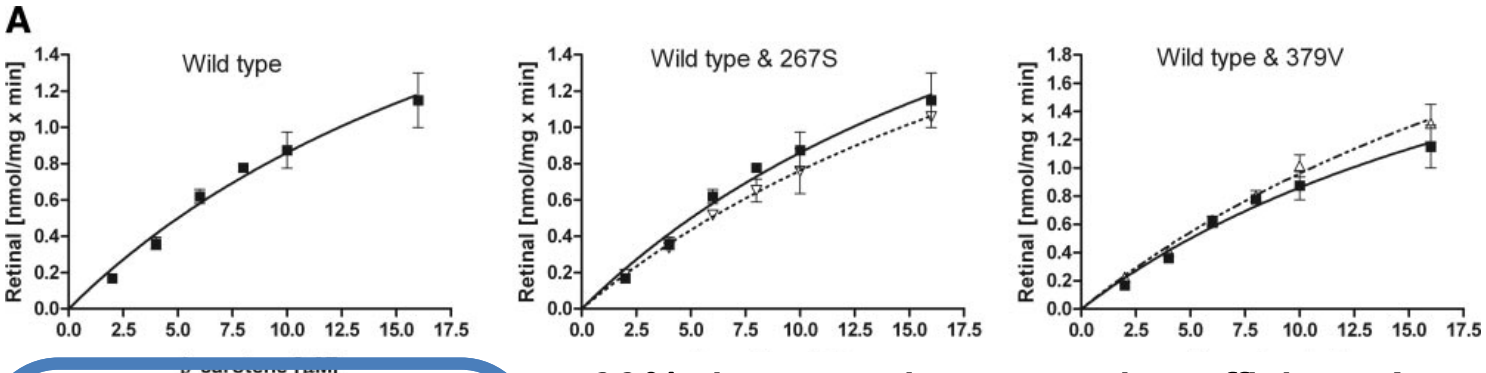
Why Organ Meat

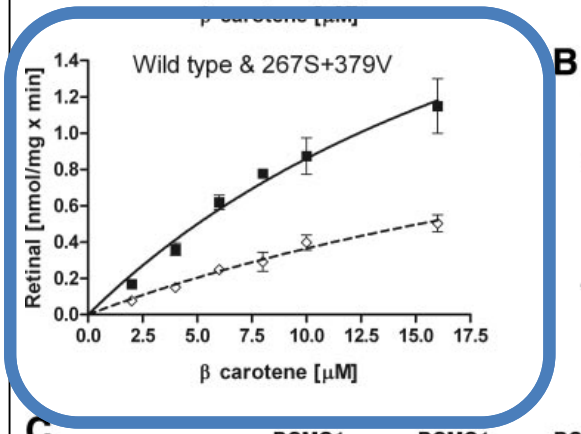
- Pre-industrial - 30% of all meat consumed was organ meat
- Excellent source of ubiquinone, minerals, essential fatty acids, fat and water soluble vitamins, especially
  - Vitamin K2-mk4
  - Retinol, Vitamin A

β-carotene Is Not Retinol (Vitamin A)

- β-Carotene is converted to vitamin A in the intestine by the enzyme β-carotene-15,15'-monoxygenase (BCMO1) to support vision, reproduction, immune function, and cell differentiation.
- Considerable variability in BCMO1 exists and can effect individual vitamin A status

Lobo GP Amengual J, Baus D, Shivdasani RA Genetics and diet regulate vitamin A production via the homeobox transcription factor ISX. J Biol Chem.2013 Mar 29;288(13):9017-27.





69% decrease in conversion efficiency!

B

BCMO1 variant	K_m [μM]	V_{max} [nmol·mg protein^{-1}· min^{-1}]
Wild type	18.3	2.3
267S	17.9	2.2
379V	12.3	2.0
267S+379V	19.5	1.0 *

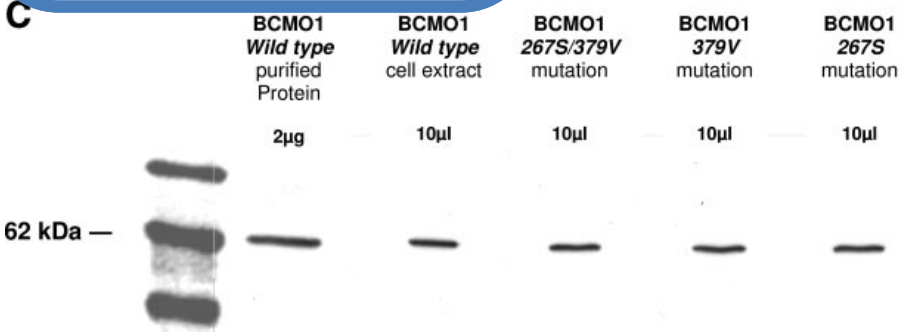


Figure 4. *In vitro* kinetic analysis of four recombinant human BCMO1 variants. *A*) Reaction velocity (nmol product formed/mg protein × min) as a function of substrate concentration (μM) is plotted for a 15 min reaction with 10.4 μg of recombinant BCMO1 and 2.5–16 μM β-carotene as substrate. Four BCMO1 variants are wild-type (■; R267/A379) and 3 mutants: 267S (▽), 379V (△), and 267S + 379V (◇). *B*) K_m and V_{max} values are averages of 6 independent experiments performed in triplicate, calculated based on the average substrate curve for each protein. *C*) Detection of BCMO1 variants by quantitative immunoblot analysis. Supernatant fluid from the cell lysate (used for enzymatic activity tests) was subjected to SDS-PAGE, and proteins were electrotransferred to membranes. BCMO1 variants were then detected by anti-His antibodies and ECL system, and were quantified using affinity purified wild-type BCMO1 protein. *$P < 0.001$ *vs.* wild type; independent sample *t* test.

Leung WC, Hessel S, Méplan C, Flint J, Oberhauser V, Tourniaire F, Hesketh JE, von Lintig J, Lietz G. Two common single nucleotide polymorphisms in the gene encoding beta-carotene 15,15'-monoxygenase alter beta-carotene metabolism in female volunteers. FASEB J. 2009 Apr;23(4):1041-53. doi: 10.1096/fj.08-121962. Epub 2008 Dec 22.

Grass-fed Meats, Organ Meats, and Wild Fish

EFAs Mediate Cognitive Function and Brain Biochemistry

- Fatty acids exert a controlling function in the modulation of neuronal membrane fluidity.
- **The critical factor in FA action and efficacy is not absolute level but rather the ratio between various groups of FA.**
- Best ratio **4:1** (ω-6 to ω-3)

1. Yehuda S, Rabinovitz S, Mostofsky DI. Essential fatty acids are mediators of brain biochemistry and cognitive functions. J Neurosci Res. 1999 Jun 15;56(6):565-70.
2. Yehuda S. Essential fatty acids may improve the neuronal membrane functions of the aging brain. 2013. http://www.nutri-facts.org/en_US/news/essential-fatty-acids-may-improve-the-neuronal-membrane-function.html. Accessed May 17, 2018.

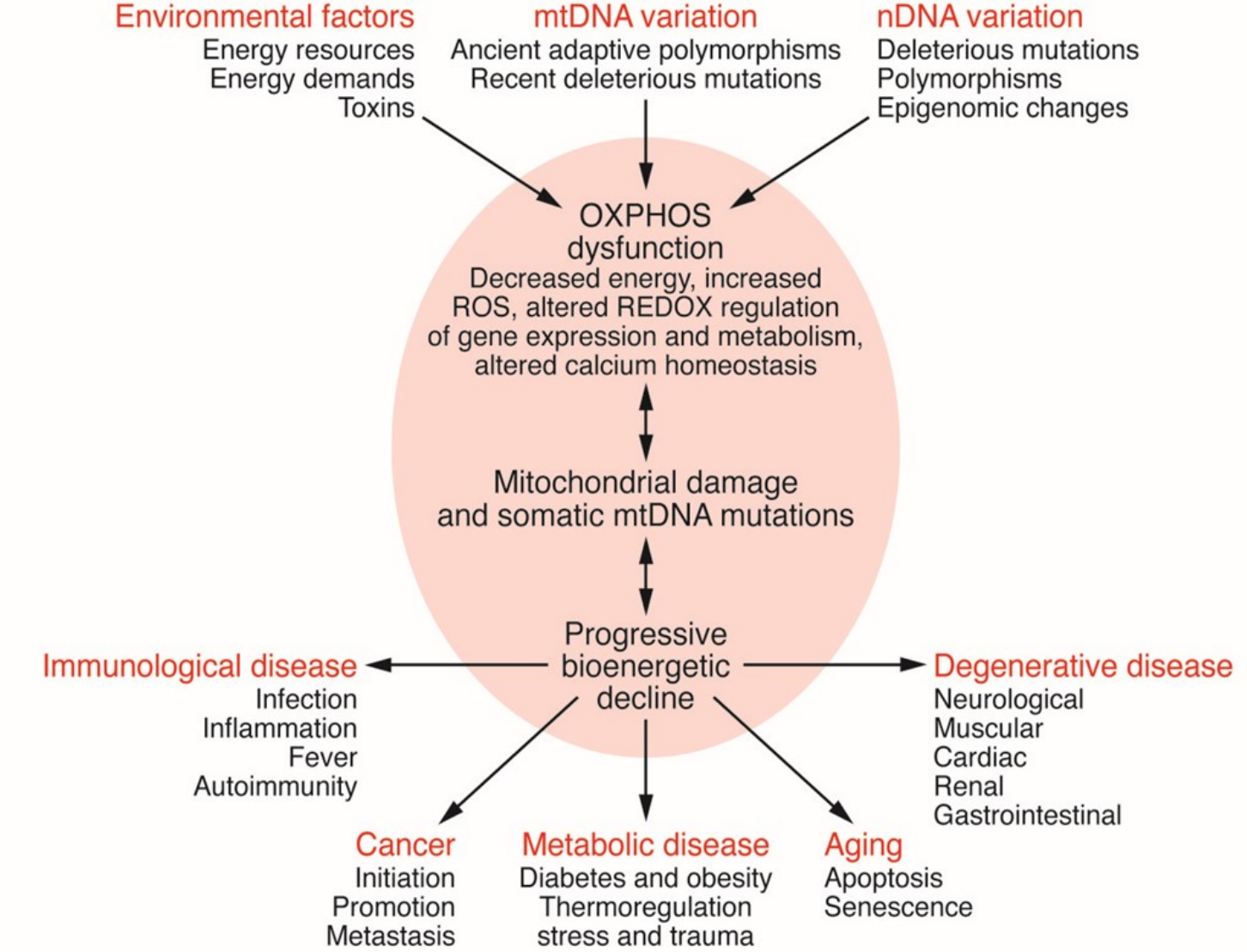
Fatty Acids: Key Concepts

- Need **both** ω-6 and ω-3 fats
- Mediators in the brain
- Ratio more important than total amount
- Critical to visual and pre-fontal cortex
- Levels at birth predict behaviors and cognition at age 10

Fatty Acid References

1. Yehuda S. Essential fatty acids may improve the neuronal membrane functions of the aging brain. 2013. http://www.nutri-facts.org/en_US/news/essential-fatty-acids-may-improve-the-neuronal-membrane-function.html.
2. Yehuda S, Rabinovitz S, Carasso RL, Mostofsky DI. Fatty acids and brain peptides. *Peptides.* 1998;19(2):407-19.
3. Yehuda S, Rabinovitz S, Mostofsky DI. Essential fatty acids are mediators of brain biochemistry and cognitive functions. *J Neurosci Res*. 1999 Jun 15;56(6):565-70.
4. Uauy R, Hoffman DR, Peirano P, Birch DG, Birch EE. Essential fatty acids in visual and brain development. Lipids. 2001 Sep;36(9):885-95.
5. Kohlboeck G, Glaser C, Tiesler C et al. LISAplus Study Group. Effect of fatty acid status in cord blood serum on children's behavioral difficulties at 10 y of age: results from the LISAplus Study. *Am J Clin Nutr.* 2011 Dec;94(6):1592-9. doi: 10.3945/ajcn.111.015800.
6. Bowman GL, Silbert LC, Howieson D, et al. Nutrient biomarker patterns, cognitive function, and MRI measures of brain aging. *Neurology*. 2012;78(4):241-249. doi:10.1212/WNL.0b013e3182436598.

The Wahls Protocol®



Wallace DC. A mitochondrial bioenergetic etiology of disease. J Clin Invest. 2013 Apr;123(4):1405-12.

Terry Wahls MD

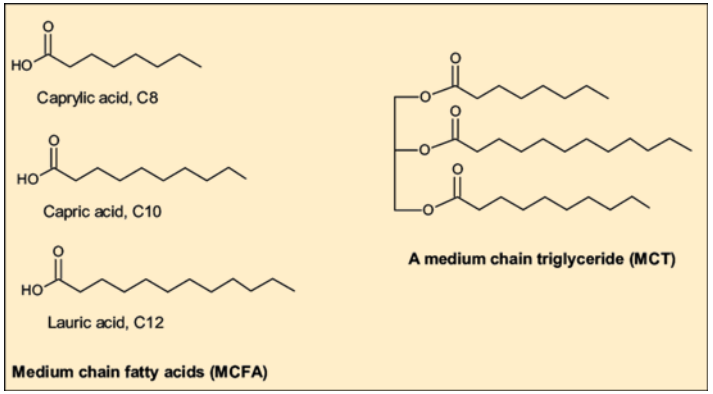
Nutritional Ketosis

- Mitochondria - can utilize glucose, amino acids or ketone bodies (fat) to generate ATP
- Different from Ketoacidosis
- Utilize **ketone bodies → ATP**
- Fasts, winter, drought, famine, war

- Increases # and efficiency of mitochondria
- Bypasses dysfunctional bioenergetics processes
- Increases nerve growth factors
- Sirt 1
- iNOS
- Many studies underway for neurological, psychiatric, metabolic syndrome, diabetes, cancer.

- **Dairy-based:** 90% fat, 25 grams CHO, Protein
  - Stresses dairy and eggs

- **MCT-based** MCT = medium chain triglycerides:
  - 60 to 70% fat, 50 to 80 grams CHO, Protein



Risks of Ketogenic Diets Pregnancy/ Hormones

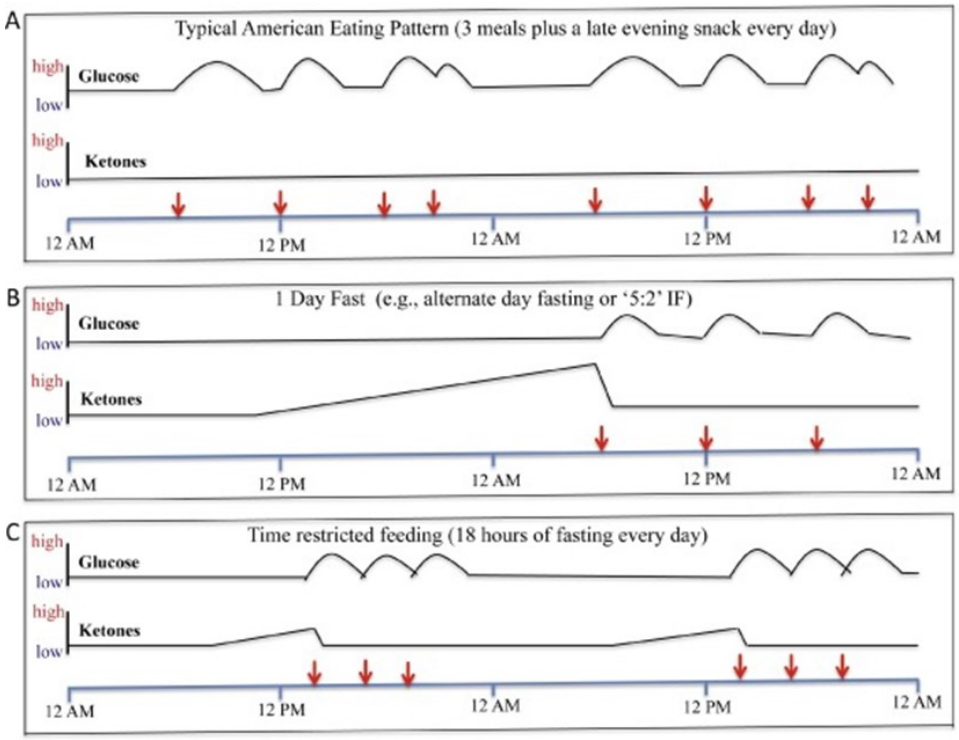
- Shifts in sex hormones - not a good time to reproduce
- A ketogenic diet during gestation results in alterations in embryonic organ growth. Such alterations may be associated with organ dysfunction and potentially behavioral changes in postnatal life.

Effects of severe dietary restriction on male reproductive hormones. J Clin Endocrinol Metab. 1986 Feb;62(2):288-92.
Effects of a ketogenic diet during pregnancy on embryonic growth in the mouse. BMC Pregnancy Childbirth. 2013 May 8;13:109

Other Options

- Calorie restriction (70% of required kcals)
- Restricted feeding (13 to 16 hr fast)
- Alternate day feeding (without increasing kcals on the days you eat)
- Periodic fasts (water only)
- Fasting Mimicking Diet

The Wahls Protocol®



- **IF** eg 60% energy restriction on 2 D/wk or QOD
- **PF** eg 5 -7 D at 250-1100 kcal
- **TRF** - limiting the daily period of food intake to 8h or less

- *IF=intermittent fast*
- *PF=periodic fast*
- *TFR=time restricted feeding*

Ketosis vs. Low Glycemic Index

- Arctic dwellers are NOT in ketosis and they still have a summer season
- Problems with long-term ketosis:
  - It is difficult to sustain
  - Increases risk for nutrient deficiencies, microbiome issues, hormone disruptions.
- Seasonal ketosis OR
- Low glycemic

1. Terry's Opinion and Experience
2. Pfeifer HH, Thiele EA. Low-glycemic-index treatment: a liberalized ketogenic diet for treatment of intractable epilepsy. *Neurology.* 2005 Dec 13;65(11):1810-2.
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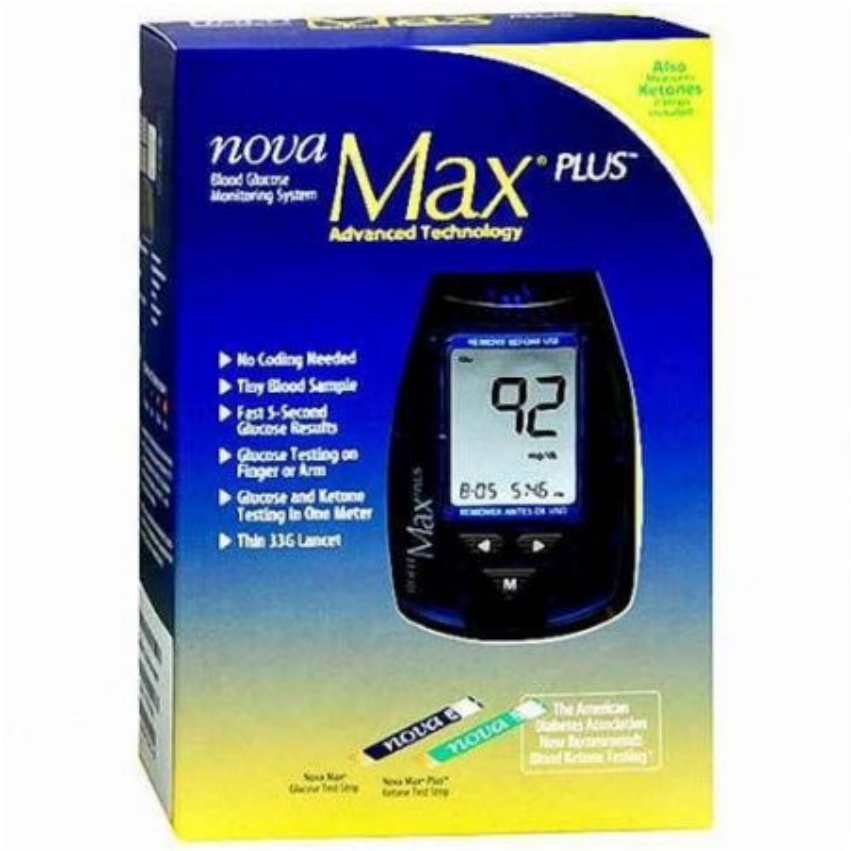
The Wahls Protocol® Seminar

Monitor Ketones



Ketosis References

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2. Murphy P, Likhodii S, Nylen K, Burnham WM. The antidepressant properties of the ketogenic diet. *Biol Psychiatry.* 2004 Dec 15;56(12):981-3.
3. Krikorian R, Shidler MD, Dangelo K, Couch SC, et al. Dietary ketosis enhances memory in mild cognitive impairment. *Neurobiol Aging*. 2012 Feb;33(2):425.e19-27.
4. Abdelwahab MG, Fenton KE, Preul MC, et al. The ketogenic diet is an effective adjuvant to radiation therapy for the treatment of malignant glioma. *PLoS One*. 2012;7(5):e36197.

Remyelination - Clemastine (Tavist) -

- First randomised controlled trial to document efficacy of a remyelinating drug for the treatment of chronic demyelinating injury in multiple sclerosis
- 5 mg bid 90 days
- But Tavist worsened fatigue severity
- Chronic use increases risk RLS, movement disorder

1. Clemastine fumarate as a remyelinating therapy for multiple sclerosis (ReBUILD): a randomised, controlled, double-blind, crossover trialDOI: http://dx.doi.org/10.1016/S0140-6736(17)32346-2
2. Clemastine Enhances Myelination in the Prefrontal Cortex and Rescues Behavioral Changes in Socially Isolated Mice. J Neurosci. 2016 Jan 20;36(3):957-62.
3. Clemastine rescues behavioral changes and enhances remyelination in the cuprizone mouse model of demyelination. Neurosci Bull. 2015 Oct;31(5):617-25
4. Clemastine Confers Neuroprotection and Induces an Anti-Inflammatory Phenotype in SOD1(G93A) Mouse Model of Amyotrophic Lateral Sclerosis. Mol Neurobiol. 2016 Jan;53(1):518-531.

Remyelination

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

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 amliorates 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.

Vitamin K2mk4 - remyelination

- Gas6 Promotes Oligodendrogenesis and Myelination in the Adult Central Nervous System and After Lysolecithin-Induced Demyelination. Mouse study
- Greens / liver / ghee
- Emu oil, vitamins K2mk4, K2mk7

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

The Swank Diet

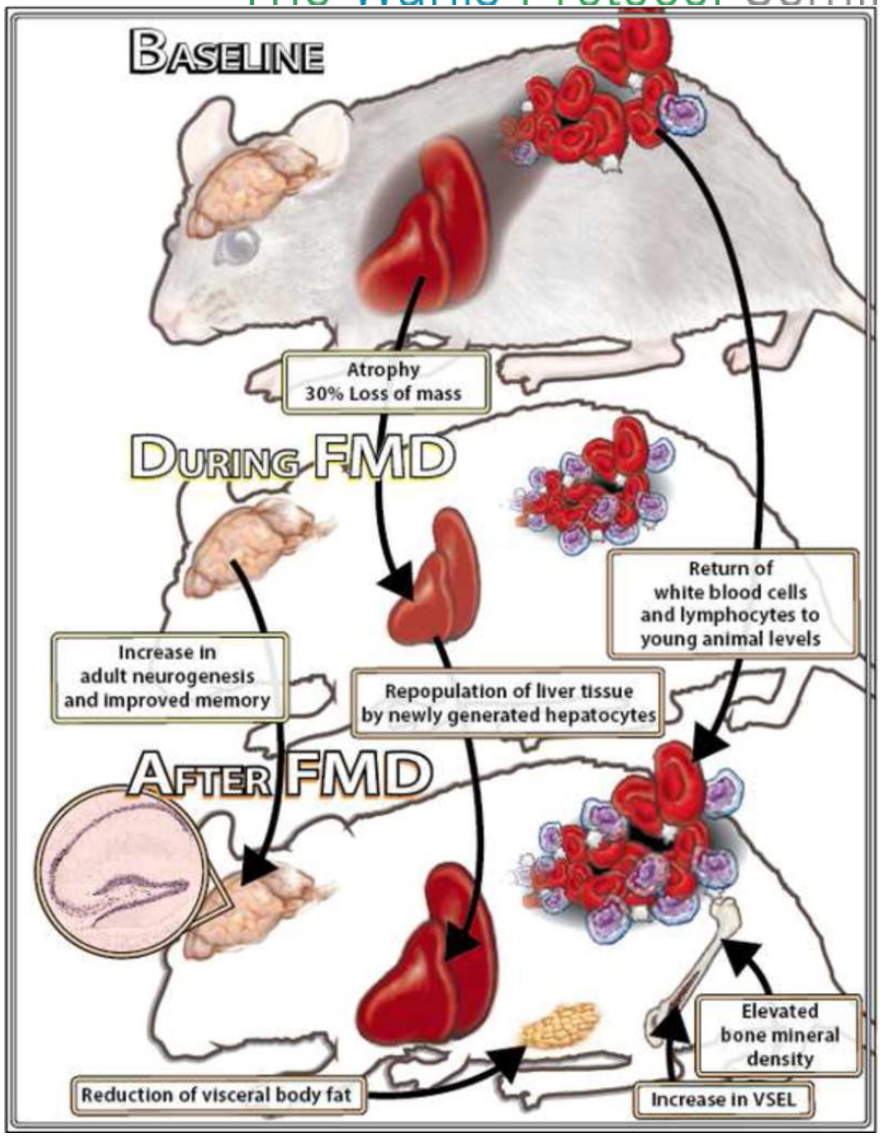
- N=144 followed 50 years
- < 15 grams saturated fat vs. > 20 grams
- Greatest benefit earlier in the disease course
- More likely to remain ambulatory

1. Review of MS patient survival on a Swank low saturated fat diet.
2. Nutrition. 2003 Feb;19(2):161-2. Review.
3. Effect of low saturated fat diet in early and late cases of multiple sclerosis.
4. Lancet. 1990 Jul 7;336(8706):37-9.
5. Multiple sclerosis: twenty years on low fat diet.
6. Arch Neurol. 1970 Nov;23(5):460-74.

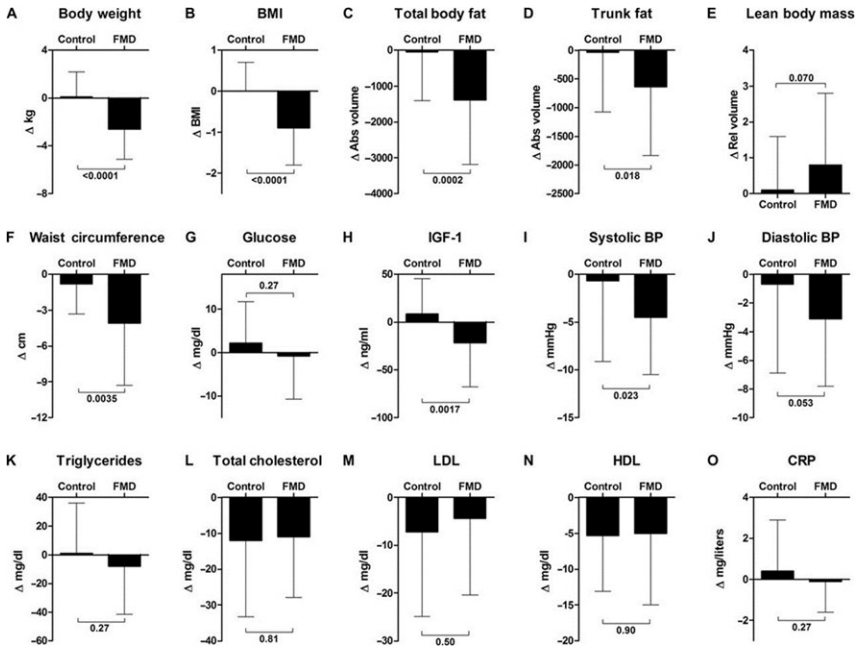
Low-fat, plant-based diet in multiple sclerosis: A randomized controlled trial

- This was a randomized-controlled, assessor-blinded, one-year long study
- N=61
- No change in EDSS, MRI
- Trend towards reduced FSS (fatigue)

Low-fat, plant-based diet in multiple sclerosis: A randomized controlled trial
Mult Scler Relat Disord. 2016 Sep;9:80-90.



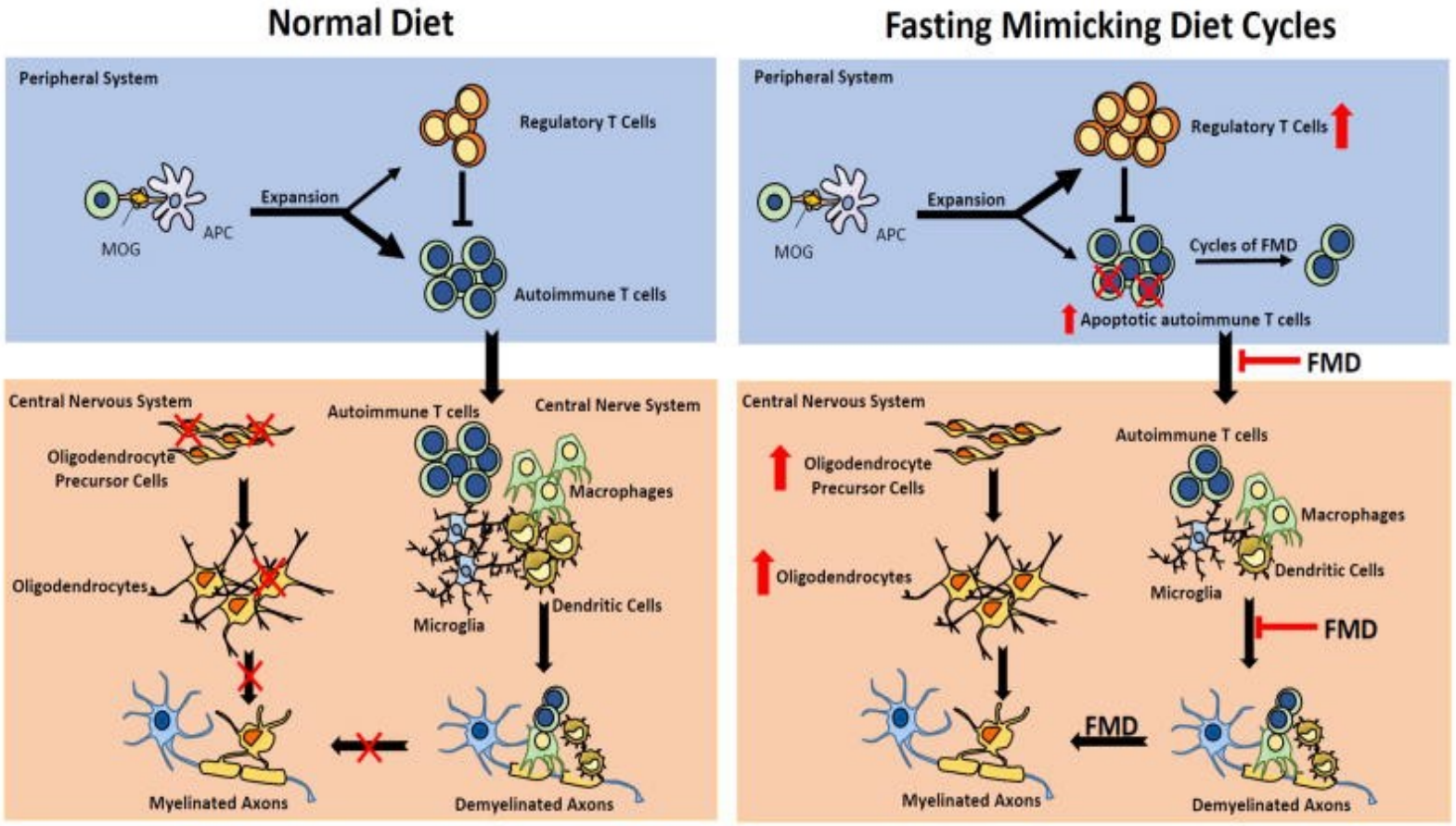
Fasting-mimicking diet and markers/risk factors for aging, diabetes, cancer, and cardiovascular disease.
Sci Transl Med. 2017 Feb 15;9(377).



- Fasting-mimicking diet and aging, diabetes, cancer, and cardiovascular disease

Wei M, Brandhorst S, Shelehchi M et al. Fasting-mimicking diet and markers/risk factors for aging, diabetes, cancer, and cardiovascular disease. Sci Transl Med. 2017 Feb 15;9(377).

A simplified model of FMD-mediated effects on glucocorticoid, immune suppression & oligodendrocyte regeneration and differentiation in MS

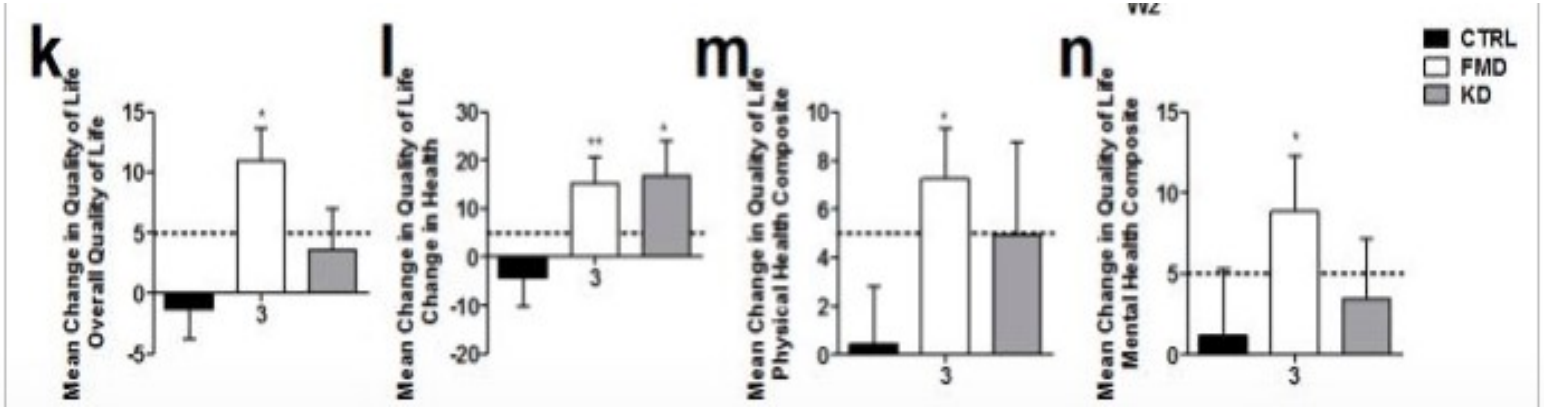


A Diet Mimicking Fasting Promotes Regeneration and Reduces Autoimmunity and Multiple Sclerosis Symptoms. Cell Rep. 2016 Jun 7; 15(10): 2136–2146.

N=60 6 month human clinical trial

- FMD 100 ml broth, 1 T flax oil tid, 200 – 350 Kcal, Plus enema as needed 7 days Mediterranean diet
- Ketogenic (KD) 160 gm fat m < 100 g Pro, < 50 g CHO
- Usual diet

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



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

Alzheimer's Disease

www.impactaging.com AGING, September 2014, Vol 6 N 9

Review

Reversal of cognitive decline: A novel therapeutic program

Dale E. Bredesen[1, 2]

[1] *Mary S. Easton Center for Alzheimer's Disease Research, Department of Neurology, University of California, Los Angeles, CA 90095;*
[2] *Buck Institute for Research on Aging, Novato, CA 94945.*

Key words: *Alzheimer's, dementia, mild cognitive impairment, neurobehavioral disorders, neuroinflammation, neurodegeneration, systems biology*
Received: *9/15/14; Accepted: 9/26/14; Published: 9/27/14*
Correspondence to: *Dale E. Bredesen, MD;* ***E-mail:*** *dbredesen@mednet.ucla.edu; dbredesen@buckinstitute.org*

Reversal of early and moderate dementia using functional medicine approach

Bredesen et al., J Alzheimers Dis Parkinsonism 2018, 8:5
DOI: 10.4172/2161-0460.1000450

Journal of
Alzheimer's Disease & Parkinsonism

Case Report Open Access

Reversal of Cognitive Decline: 100 Patients

Dale E Bredesen[1*], Kenneth Sharlin[2], David Jenkins[3], Miki Okuno[3], Wes Youngberg[4], Sharon Hausman Cohen[5], Anne Stefani[5], Ronald L Brown[6], Seth Conger[6], Craig Tanio[7], Ann Hathaway[8], Mikhail Kogan[9], David Hagedorn[10], Edwin Amos[11], Amylee Amos[12], Nathaniel Bergman[13], Carol Diamond[14], Jean Lawrence[15], Ilene Naomi Rusk[16], Patricia Henry[16] and Mary Braud[16]

[1]*Department of Molecular and Medical Pharmacology, David Geffen School of Medicine, University of California, Los Angeles, Los Angeles, CA, USA*
[2]*Sharlin Health and Neurology/Functional Medicine, Ozark, MO, USA*
[3]*NeuroHub, Sydney, Australia*
[4]*Youngberg Lifestyle Medicine Clinic, Temecula, CA, USA*
[5]*Resilient Health, Austin, TX, USA*
[6]*Carolina Healthspan Institute, Charlotte, NC, USA*
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[8]*Integrative Functional Medicine, San Rafael, CA, USA*
[9]*GW Center for Integrative Medicine, George Washington University, Washington, DC, USA*
[10]*Coastal Integrative Medicine, Jacksonville, NC, USA*
[11]*Department of Neurology, University of California, Los Angeles, Los Angeles, CA, USA*
[12]*Amos Institute, Los Angeles, CA, USA*
[13]*Center for Functional Medicine, Cleveland Clinic, Cleveland, OH, USA*
[14]*Mount Sinai Hospital, New York, NY, USA*
[15]*Lawrence Health and Wellness, Toccoa, GA, USA*
[16]*Brain 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

Bredesen et al., J Alzheimers Dis Parkinsonism 2018, 8:5 DOI: 10.4172/2161-0460.1000450

Table 1. Therapeutic System 1.0

Goal	Approach	Rationale and References
Optimize diet: minimize simple CHO, minimize inflammation.	Patients given choice of several low glycemic, low inflammatory, low grain diets.	Minimize inflammation, minimize insulin resistance.
Enhance autophagy, ketogenesis	Fast 12 hr each night, including 3 hr prior to bedtime.	Reduce insulin levels, reduce Aβ.
Reduce stress	Personalized—yoga or meditation or music, etc.	Reduction of cortisol, CRF, stress axis.
Optimize sleep	8 hr sleep per night; melatonin 0.5mg po qhs; Trp 500mg po 3x/wk if awakening. Exclude sleep apnea.	[36]
Exercise	30-60′ per day, 4-6 days/wk	[37, 38]
Brain stimulation	Posit or related	[39]
Homocysteine <7	Me-B12, MTHF, P5P; TMG if necessary	[40]
Serum B12 >500	Me-B12	[41]
CRP <1.0; A/G >1.5	Anti-inflammatory diet; curcumin; DHA/EPA; optimize hygiene	Critical role of inflammation in AD
Fasting insulin <7; HgbA1c <5.5	Diet as above	Type II diabetes-AD relationship
Hormone balance	Optimize fT3, fT4, E2, T, progesterone, pregnenolone, cortisol	[5, 42]
GI health	Repair if needed; prebiotics and probiotics	Avoid inflammation, autoimmunity
Reduction of A-beta	Curcumin, Ashwagandha	43-45
Cognitive enhancement	Bacopa monniera, MgT	[46, 47]
25OH-D3 = 50-100ng/ml	Vitamins D3, K2	[48]
Increase NGF	H. erinaceus or ALCAR	[49, 50]
Provide synaptic structural components	Citicoline, DHA	[51].
Optimize antioxidants	Mixed tocopherols and tocotrienols, Se, blueberries, NAC, ascorbate, α-lipoic acid	[52]
Optimize Zn:fCu ratio	Depends on values obtained	[53]
Ensure nocturnal oxygenation	Exclude or treat sleep apnea	[54]
Optimize mitochondrial function	CoQ or ubiquinol, α-lipoic acid, PQQ, NAC, ALCAR, Se, Zn, resveratrol, ascorbate, thiamine	[55]
Increase focus	Pantothenic acid	Acetylcholine synthesis requirement
Increase SirT1 function	Resveratrol	[32]
Exclude heavy metal toxicity	Evaluate Hg, Pb, Cd; chelate if indicated	CNS effects of heavy metals
MCT effects	Coconut oil or Axona	[56]

CHO, carbohydrates; Hg, mercury; Pb, lead; Cd, cadmium; MCT, medium chain triglycerides; PQQ, polyquinoline quinone; NAC, N-acetyl cysteine; CoQ, coenzyme Q; ALCAR, acetyl-L-carnitine; DHA, docosahexaenoic acid; MgT, magnesium threonate; fT3, free triiodothyronine; fT4, free thyroxine; E2, estradiol; T, testosterone; Me-B12, methylcobalamin; MTHF, methyltetrahydrofolate; P5P, pyridoxal-5-phosphate; TMG, trimethylglycine; Trp, tryptophan

DE Bredesen. Reversal of cognitive decline: A novel therapeutic program. Aging (Albany NY). 2014 Sep; 6(9): 707–717.

Window of opportunity for restoration

- Loss of trophic support – the brain downsizes
- Stops making new memories
- Subjective loss of mental clarity 10 years
- Mild cognitive impairment 2-3 years
- Early AD 1 year
- Late AD unlikely to recover

The Wahls Protocol® Seminar

Functional Approach to Treating Neurodegenerative Disorders Part 2

Dr. Terry Wahls, MD, IFMCP
University of Iowa
Departments of Internal Medicine and Neurology
Wahls Institute, P.L.C.
Dr. Terry Wahls LLC

Study Diet

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	

Stop processed foods, gluten, dairy, eggs

More Vegetables

3 Greens

3 Colored

3 Sulfur

- Fermented food
- Seaweed
- Nutritional yeast
- Algae

Spices – Superfoods

Neuroprotection by spice-derived nutraceuticals:

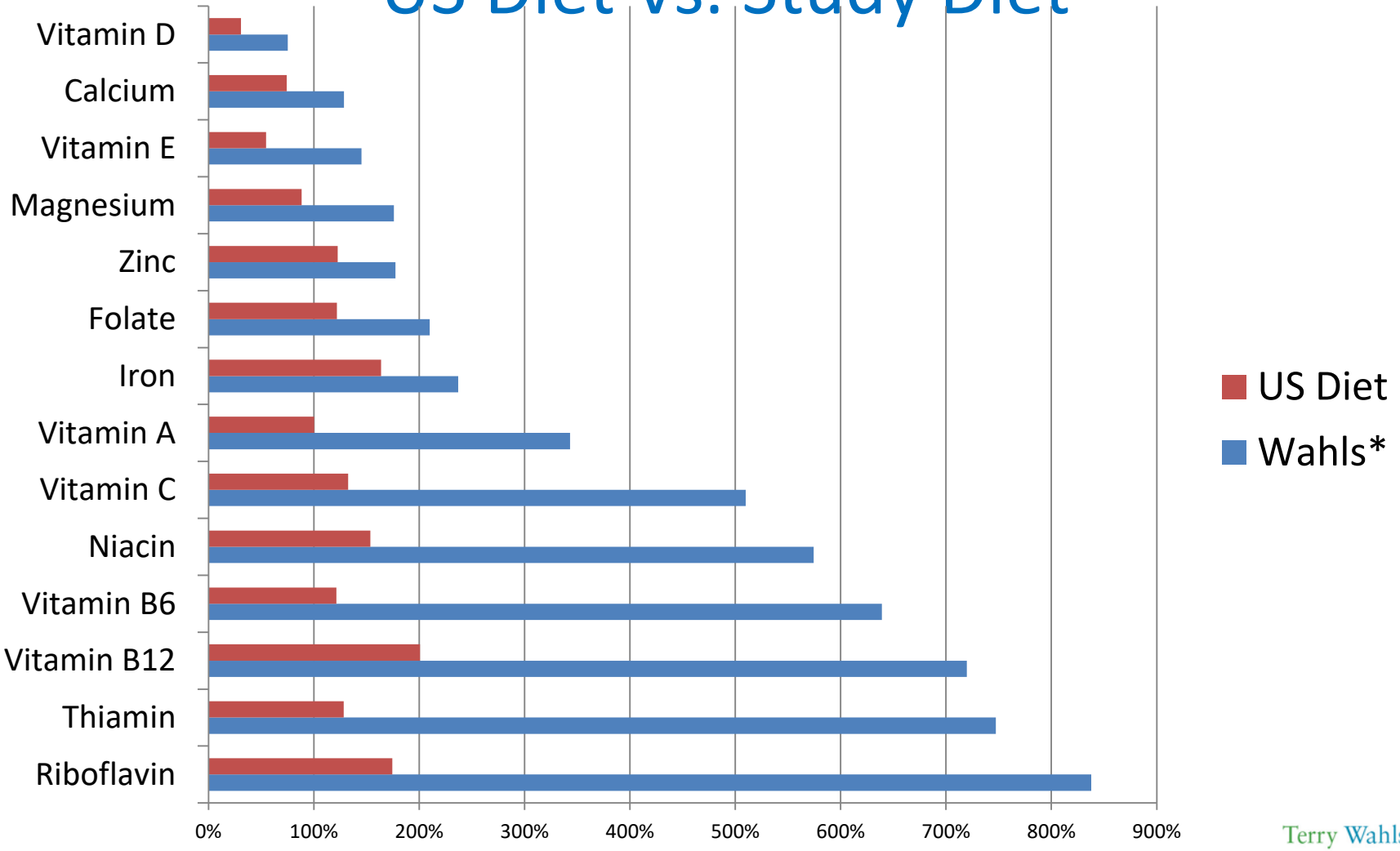
you are what you eat!

- Extensive research over the last 10 years has indicated that nutraceuticals derived from such spices as turmeric, red pepper, black pepper, licorice, clove, ginger, garlic, coriander, and cinnamon target inflammatory pathways, thereby may prevent neurodegenerative diseases.

Mol Neurobiol. 2011 Oct;44(2):142-59. doi: 10.1007/s12035-011-8168-2

The Wahls Protocol® Seminar

Nutritional Adequacy (%RDA)
US Diet Vs. Study Diet



Terry Wahls MD

Methyl B12, Methyl Folate, Vitamin D, Fish Oil

http://vitaminreviewsite.com/wp-content/uploads/2013/04/natural-Vitamins.jpg

The Wahls Protocol® Seminar

Meditation

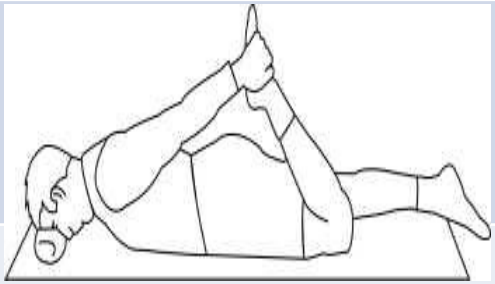
Terry Wahls MD

Stretching Exercises

Gastro-soleus

Hamstring

Quadriceps



Erector spinae

Electrical Stimulation of Muscles Builds Muscle Mass

Degenerative Neurological and Neuromuscular Disease

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ORIGINAL RESEARCH

Multimodal intervention improves fatigue and quality of life in subjects with progressive multiple sclerosis: a pilot study

This article was published in the following Dove Press journal:
Degenerative Neurological and Neuromuscular Disease
27 February 2015
Number of times this article has been viewed

Babita Bisht[1]
Warren G Darling[2]
E Torage Shivapour[3]
Susan K Lutgendorf[4–6]
Linda G Snetselaar[7]
Catherine A Chenard[1]
Terry L Wahls[1,8]

[1]Department of Internal Medicine, Carver College of Medicine, University of Iowa, [2]Department of Health and Human Physiology, College of Liberal Arts and Sciences, University of Iowa, [3]Department of Neurology, Carver College of Medicine, University of Iowa, [4]Department of Psychology, College of Liberal Arts and Sciences, University of Iowa, [5]Department of Obstetrics and Gynecology, Carver College of Medicine, University of Iowa, [6]Department of Urology, Carver College of Medicine, University of Iowa, [7]Department of Epidemiology, College of Public Health, University of Iowa, [8]Department of Internal Medicine, VA Medical Center, Iowa City, IA, USA

Background: Fatigue is a disabling symptom of multiple sclerosis (MS) and reduces quality of life. The aim of this study was to investigate the effects of a multimodal intervention, including a modified Paleolithic diet, nutritional supplements, stretching, strengthening exercises with electrical stimulation of trunk and lower limb muscles, and stress management on perceived fatigue and quality of life of persons with progressive MS.

Methods: Twenty subjects with progressive MS and average Expanded Disability Status Scale (EDSS) score of 6.2 (range: 3.5–8.0) participated in the 12-month phase of the study. Assessments were completed at baseline and at 3 months, 6 months, 9 months, and 12 months. Safety analyses were based on monthly side effects questionnaires and blood analyses at 1 month, 3 months, 6 months, 9 months, and 12 months.

Results: Subjects showed good adherence (assessed from subjects' daily logs) with this intervention and did not report any serious side effects. Fatigue Severity Scale (FSS) and Performance Scales-fatigue subscale scores decreased in 12 months ($P<0.0005$). Average FSS scores of eleven subjects showed clinically significant reduction (more than two points, high response) at 3 months, and this improvement was sustained until 12 months. Remaining subjects (n=9, low responders) either showed inconsistent or less than one point decrease in average FSS scores in the 12 months. Energy and general health scores of RAND 36-item Health Survey (Short Form-36) increased during the study ($P<0.05$). Decrease in FSS scores during the 12 months was associated with shorter disease duration ($r=0.511$, $P=0.011$), and lower baseline Patient Determined Disease Steps score ($r_s=0.563$, $P=0.005$) and EDSS scores ($r_s=0.501$, $P=0.012$). Compared to low responders, high responders had lower level of physical disability ($P<0.05$) and lower intake of gluten, dairy products, and eggs ($P=0.036$) at baseline. High responders undertook longer duration of massage and stretches per muscle ($P<0.05$) in 12 months.

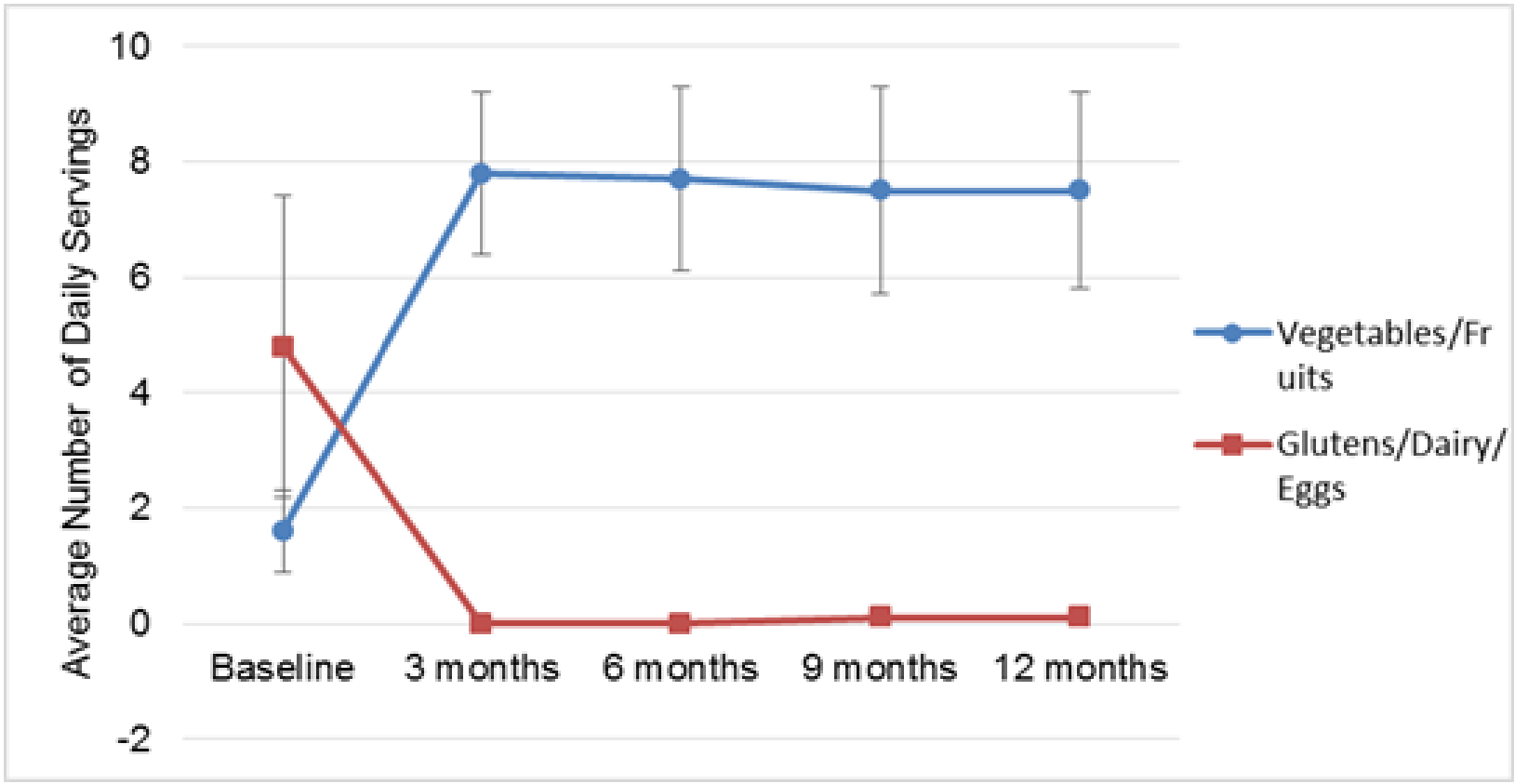
Conclusion: A multimodal intervention may reduce fatigue and improve quality of life of subjects with progressive MS. Larger randomized controlled trials with blinded raters are needed to prove efficacy of this intervention on MS-related fatigue.

Keywords: modified Paleolithic diet, exercise, neuromuscular electrical stimulation, stress management, lifestyle changes, vitamins, supplements

Subject Demographics

- 20 individuals (18 SPMS, 2 PPMS)
- Age: 51.7 (± 6.4) years
- Baseline EDSS: 6.2 (±1)
- Fatigue Severity Scale Score: 5.5 (± 1.2)

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



Degenerative Neurological and Neuromuscular Disease

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ORIGINAL RESEARCH

Multimodal intervention improves fatigue and quality of life in subjects with progressive multiple sclerosis: a pilot study

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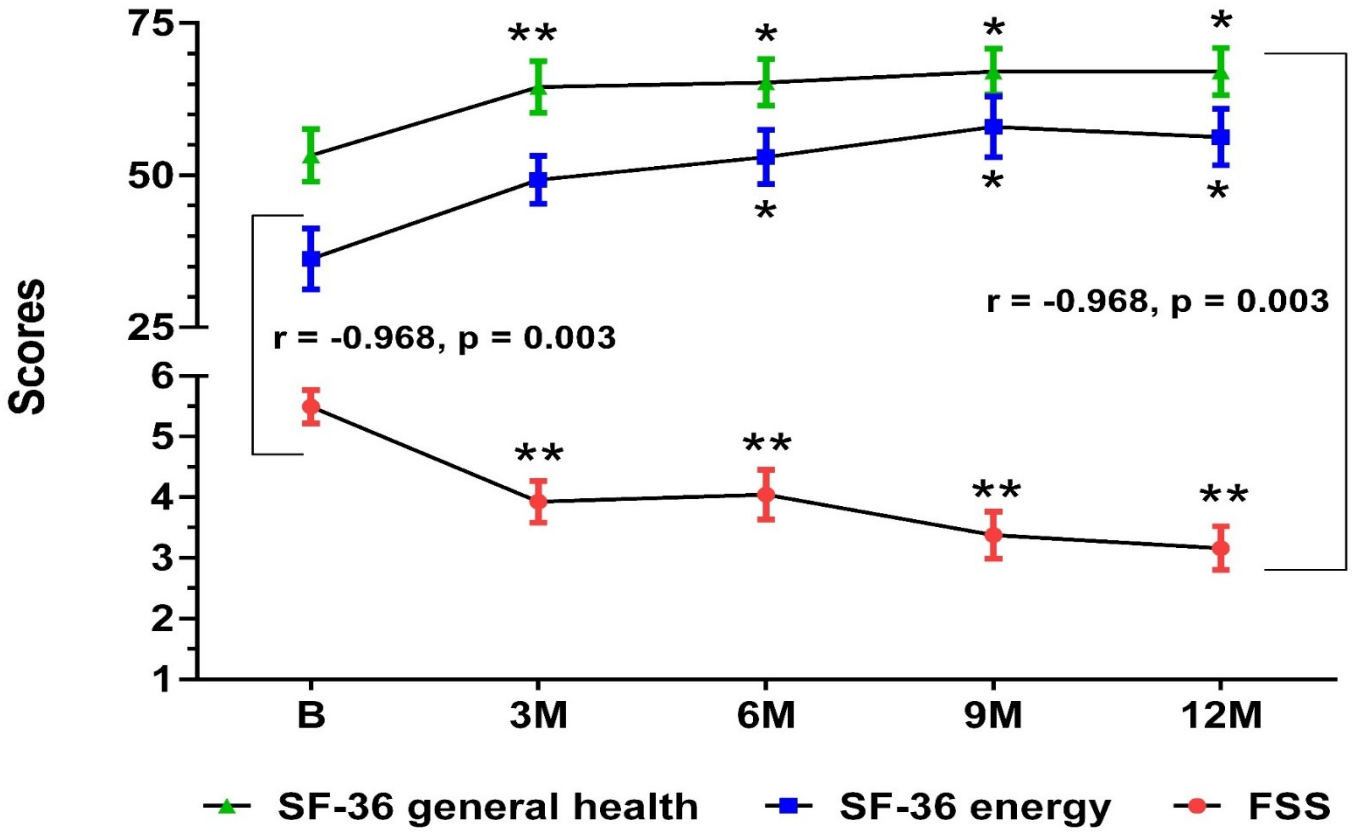
Side effect – Overweight and obese subjects lost weight and got to a healthy weight

Multimodal intervention improves quality of life



**p<0.0005

*p< 0.05

Mood and Cognition

JOURNAL OF THE AMERICAN COLLEGE OF NUTRITION
http://dx.doi.org/10.1080/07315724.2016.1255160

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OPEN ACCESS

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

Jennifer E. Lee, PhD, MA[a,b], Babita Bisht, PhD, BPT[c], Michael J. Hall, PhD[d,e], Linda M. Rubenstein, PhD, MS[f], Rebecca Louison, BS[a], Danielle T. Klein, BS[c], and Terry L. Wahls, MD[c,g]

[a]Department of Psychology, Mount Mercy University, Cedar Rapids, Iowa; [b]College of Nursing, The University of Iowa, Iowa City, Iowa; [c]Department of Internal Medicine, Carver College of Medicine, The University of Iowa, Iowa City, Iowa; [d]Department of Psychiatry, Iowa City VA Health Care System, Iowa City, Iowa; [e]Department of Psychiatry, Carver College of Medicine, University of Iowa, Iowa City, Iowa; [f]College of Public Health, The University of Iowa, Iowa City, Iowa; [g]Extended Care and Rehabilitation Service Line, Iowa City VA Health Care System, Iowa City, Iowa

ABSTRACT

Objective: The objective of this study was to examine whether participation in a 12-month multimodal intervention would improve mood and cognitive function in adults with progressive multiple sclerosis (MS).

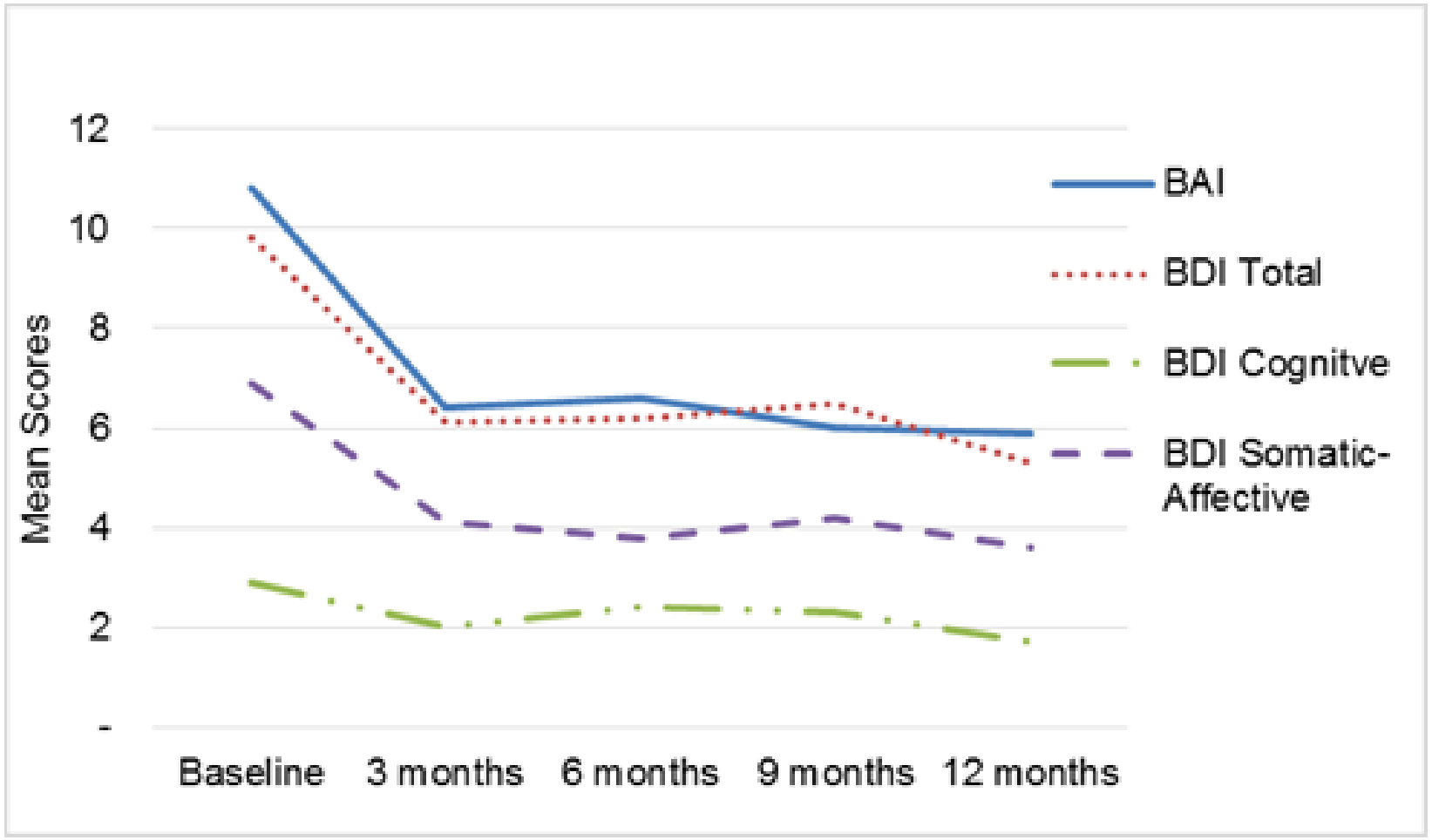
Methods: In this one-arm, open-label feasibility trial, participants were prescribed a home-based multimodal intervention, including (1) a modified Paleolithic diet; (2) an exercise program (stretching and

ARTICLE HISTORY
Received 27 July 2016
Accepted 27 October 2016

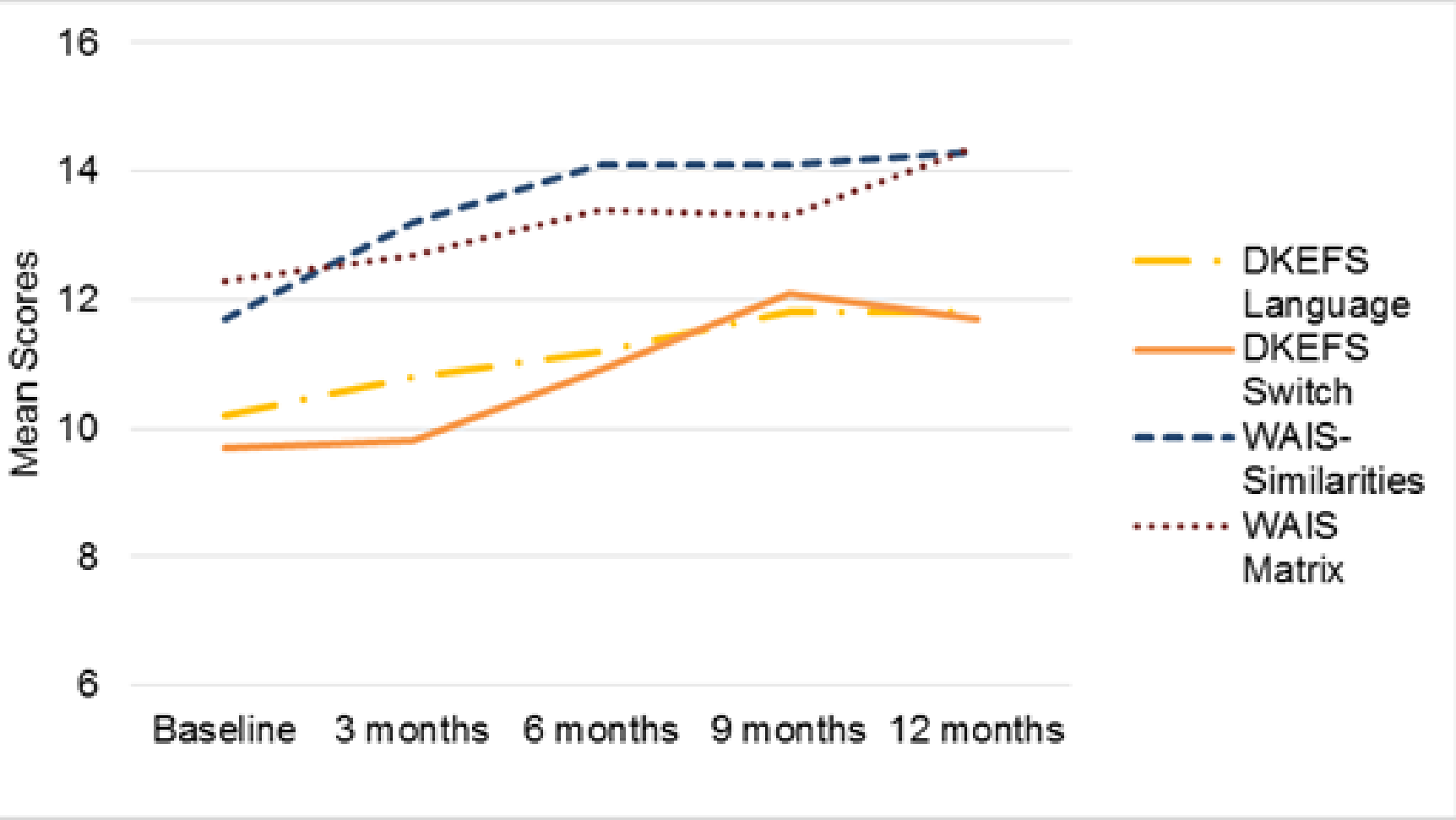
KEYWORDS
Multiple sclerosis; Wahl's Protocol; diet; exercise;

In the setting of progressive MS
Improved thinking ability and
reduced anxiety and reduced depression

Average scores on the mood measures at each study visit

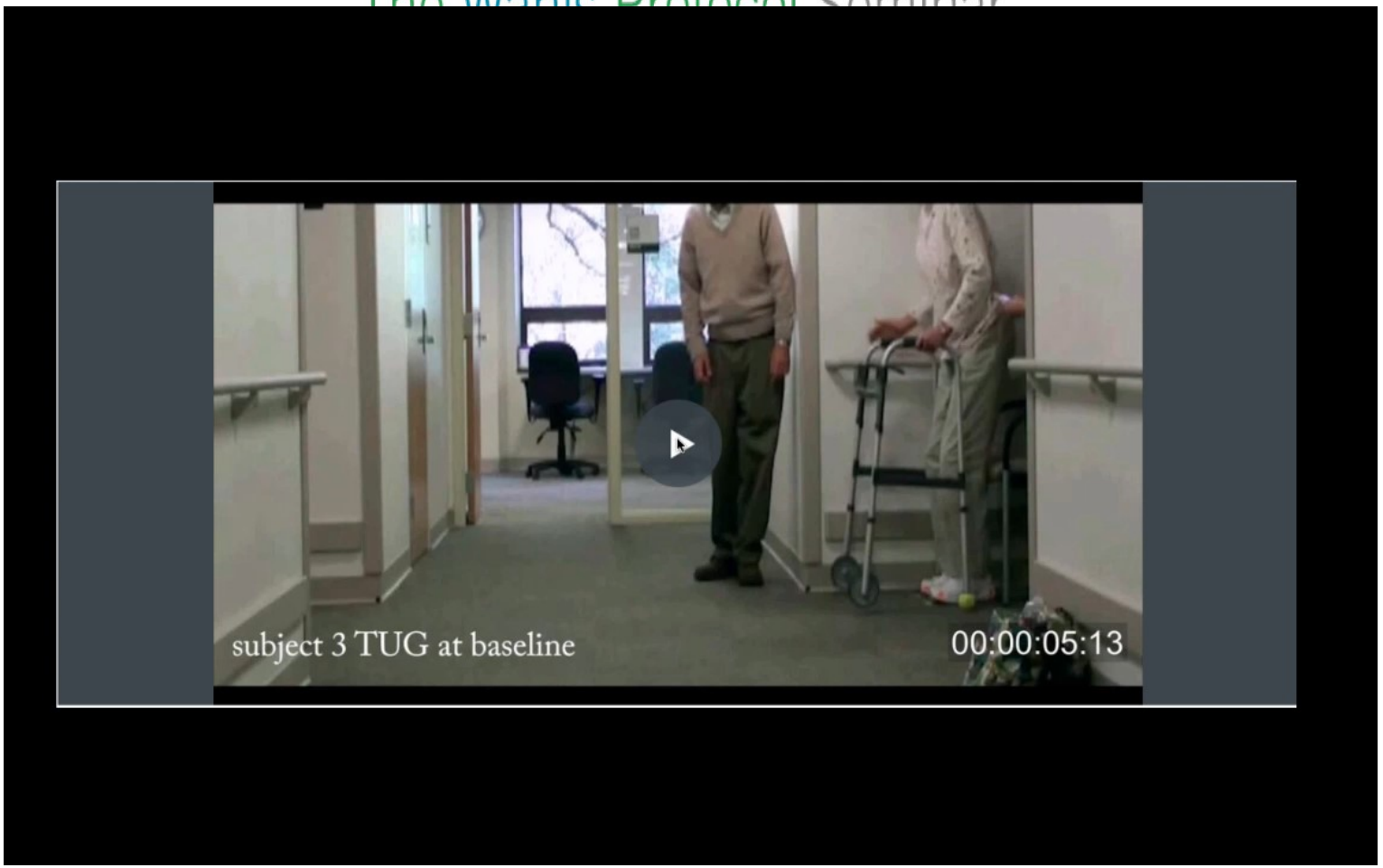


Average scores on the DKEFS and WAIS subscales at each study visit.



Associations Between Adherence and Outcomes P values

Variables 0 to 12 months	Mood BDA/ BDI	Cognition Verbal reasoning	Fatigue
Vegetables/ fruits	0.0001	<0.0001	<0.0001
Gluten, dairy, egg free	0.001	0.005	<0.0001



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

Relapsing Remitting MS

Degenerative Neurological and Neuromuscular Disease

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CLINICAL TRIAL REPORT

Randomized control trial evaluation of a modified Paleolithic dietary intervention in the treatment of relapsing-remitting multiple sclerosis: a pilot study

This article was published in the following Dove Press journal:
Degenerative Neurological and Neuromuscular Disease
4 January 2017
Number of times this article has been viewed

Amanda K Irish[1]
Constance M Erickson[1]

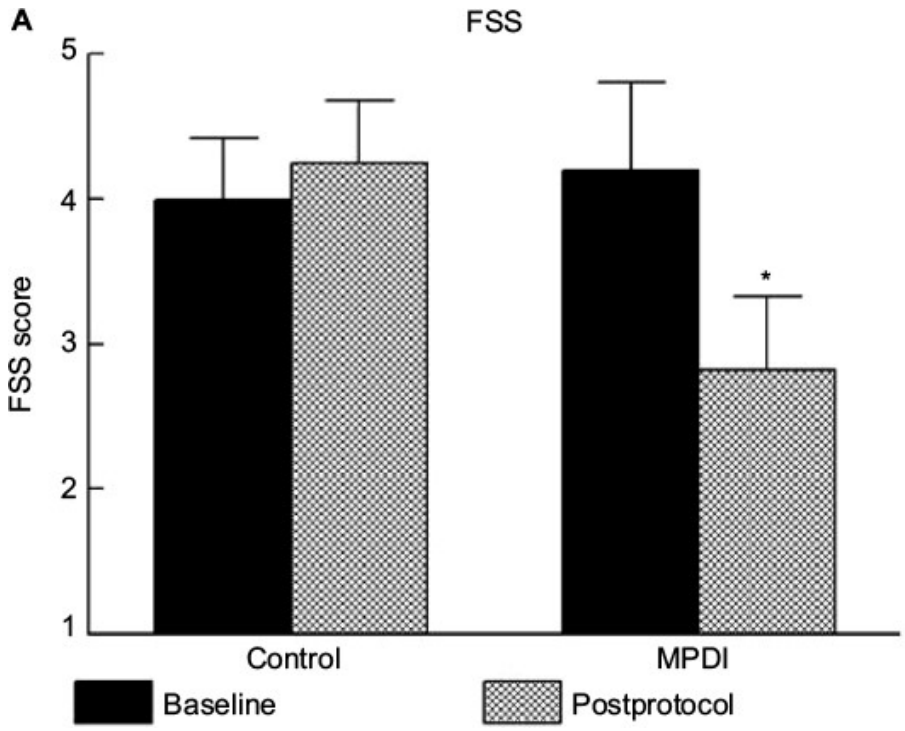
Background/objective: A Paleolithic diet may improve fatigue and quality of life in progressive multiple sclerosis (MS) patients, but past research has evaluated the effects of this dietary

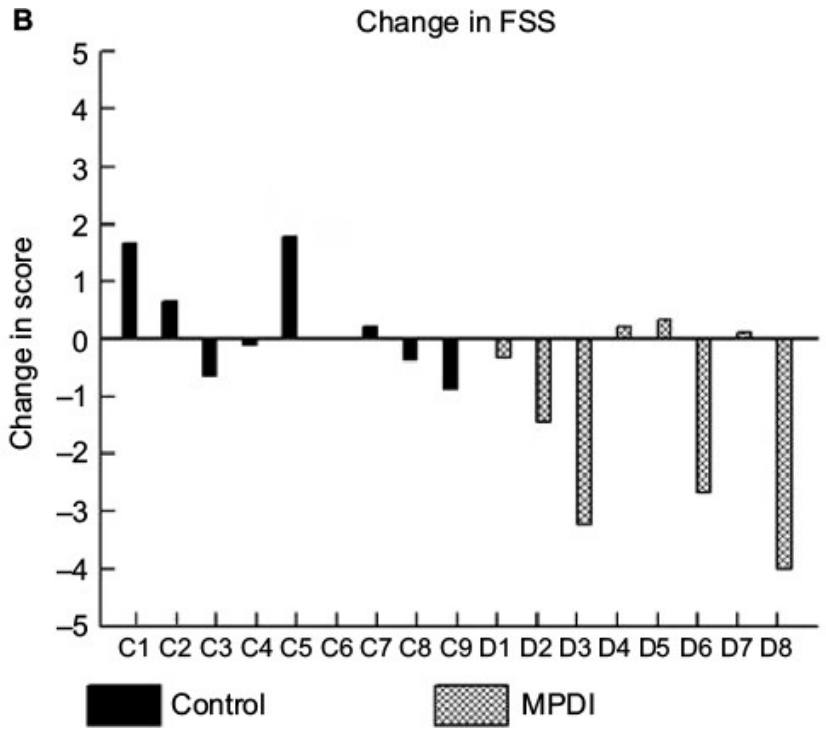
In the setting of relapsing-remitting MS
Reduction of fatigue and improved motor function

Physiology, College of Liberal Arts and Sciences, The University

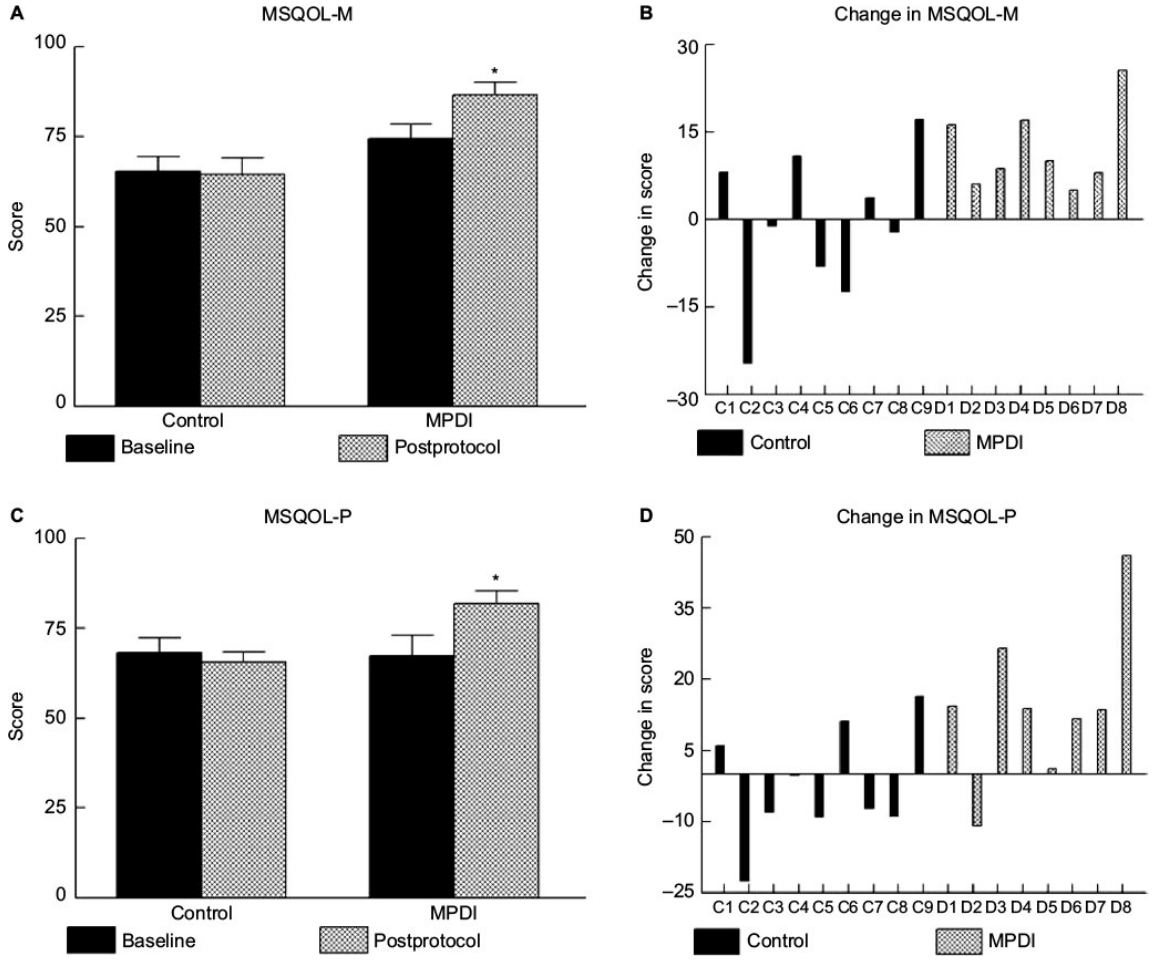
jects (one man) completed the control group and eight subjects (one man) completed the MPDI.
Results: Significant improvements were seen in Fatigue Severity Scale score and also in Mul-

Reduced Fatigue

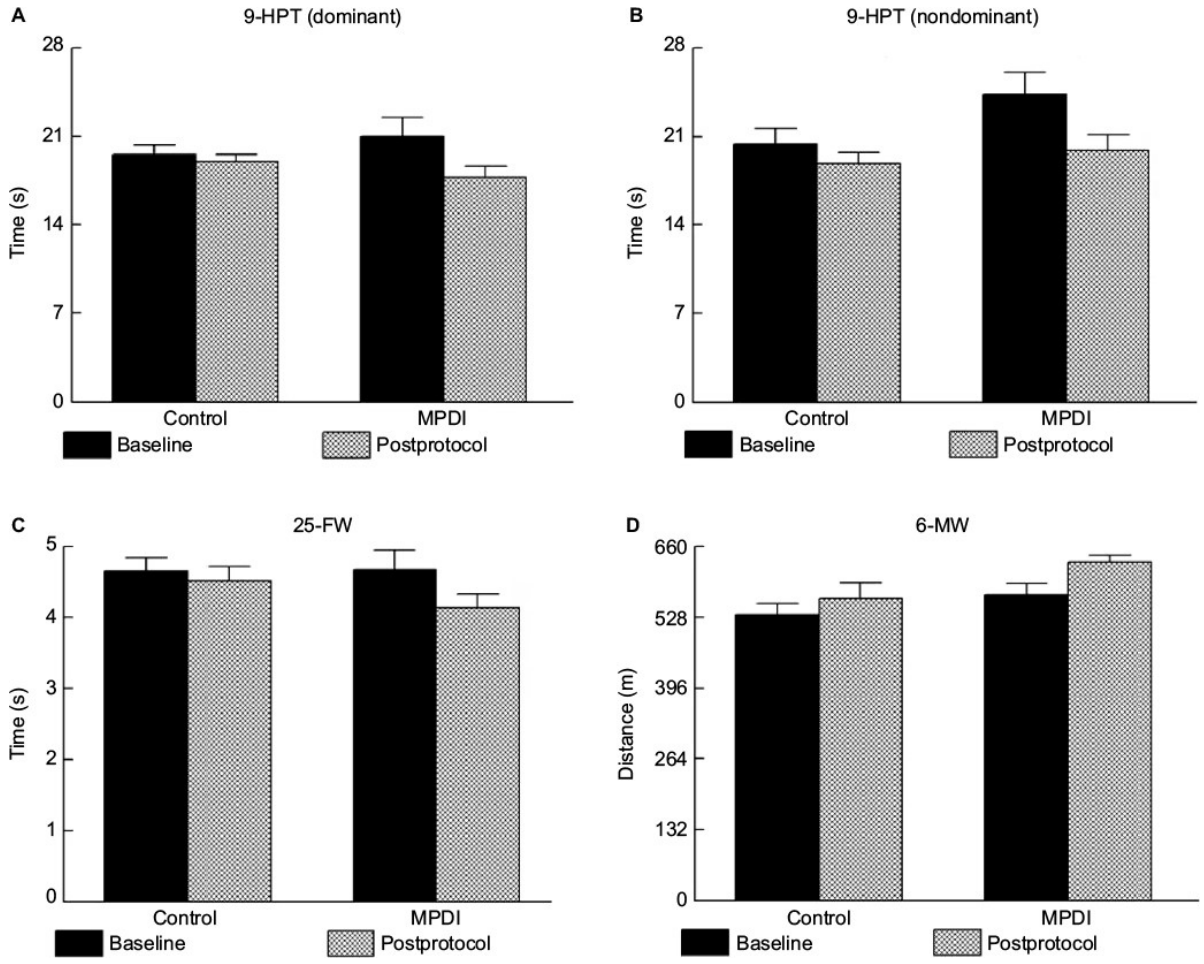




Improved Mental and Physical QoL

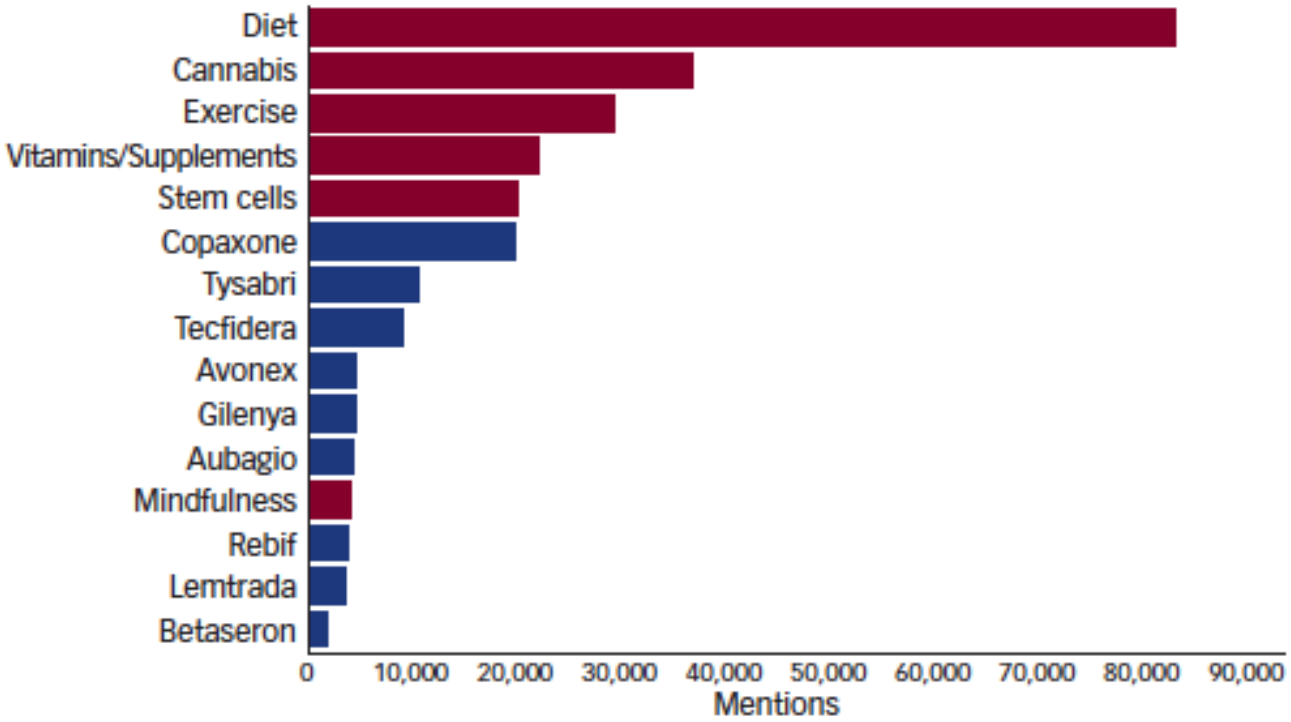


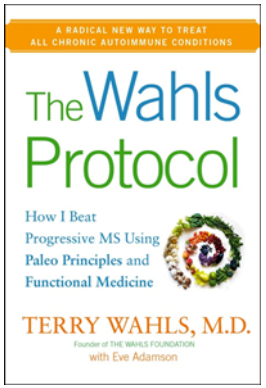
Improved Motor Function



National MS Society Responds to the Public

Figure 2: Alternative versus Traditional Treatment Topics Mentioned in Social Media (July 2014–June 2015)





Your Patients with Multiple Sclerosis have Set Wellness as a High Priority— And the National Multiple Sclerosis Society is Responding *US Neurology*, 2015;11(2):80–6

Table 1: Diets for Multiple Sclerosis at a Glance

Diet	Basic Guidelines	Restrictions	Possible Deficiencies	Evidence for Benefit in Multiple Sclerosis	Evidence for Benefit in Other Diseases
Paleolithic diet[44]	Emphasizes consumption of game meats (30–35 % of daily caloric intake) and plant foods (besides cereals), multiple daily servings of green, and sulfur-rich and intensely colored vegetables and fruits, with a high intake of PUFAs to target a ratio of saturated to unsaturated fats of 1.4:2.1	Processed food, domesticated meats, dairy, eggs	Folic acid, thiamine, vitamin B6, calcium and vitamin D, insufficient caloric intake	Single-observation study demonstrating possible improvement in fatigue in progressive MS patients (however diet was bundled with other interventions and there was no comparison group)[43]	Single study showed improvement in cardiovascular risk factors[45]
Mediterranean diet[46]	High intake of whole grains, vegetables, fruits, legumes, olive oil, and fish; a low intake of saturated fats (butter and other animal fats), red meat, poultry, and dairy products; and a regular but moderate intake of ethanol (mainly red wine)	No specific exclusions	None expected	None	Extensive evidence for a benefit on cardiovascular health, diabetes, and possibly on cancer risk[46–49]
McDougall diet[50]	High-carbohydrate, low-fat, low-sodium vegan diet with cereals, potatoes, and legumes as staples. Fruits and vegetables are allowed in any amount. Low-sodium intake and small amounts of sugar are recommended	Dairy, eggs, meat, poultry, fish, and all oils	Iron, vitamin B12, vitamin D, calcium, and ω3-fatty acids	None	One study showed improvement in cardiovascular risk factors with 1 week of the diet (did not look at long-term effects)[50]
Gluten-free diet[51]	Avoidance of all foods containing wheat, barley, and triticales or their derivatives	Foods containing wheat, barley, or triticales or their derivatives	None expected	None[52,53]	Treatment for celiac disease and non-celiac gluten sensitivity
Swank diet[54]	Low-fat diet that advocates reduction in the intake of saturated fats. Whole-grain cereals are recommended; daily intake	Processed food with saturated fats, high-fat dairy products, and red	None expected (possibly vitamin A, C, E, and folate)	Observational data from a single cohort of patients treated with this diet	None

http://www.nationalmssociety.org/NationalMSSociety/media/MSNationalFiles/Documents/Diet-and-Multiple-Sclerosis-Bhargava-06-26-15.pdf

- Peer reviewed diet papers since 1985
  - Paleo 180
  - Vegan 525
  - Atkins 1478
  - Vegetarian 3020
  - Mediterranean 4834
- 2014 Paleo the most frequent diet related google search
- 2017 US News and World Report Paleo diet ranked 38 of 38 diets reviewed due to lack of RCTs

My Assessment for Qualities of Evidence
Peer reviewed literature

Risks

- Risk of death
- Risk of side effects
- Monitoring required
- Cost
- Time

Benefits

- Physiologic sense
- All cause mortality and morbidity
- Health
- QoL, function, pain
- Potential to reduce need for prescription medication

- Higher quality diet (food), stress reduction, movement – are relatively safe with large favorable benefits for all cause mortality
- 3 month trial of a grain free, dairy free, sugar free vegetable rich (or gluten free vegetarian) diet is relatively safe with potential for many favorable benefits

Original Investigation

Rebound Syndrome in Patients With Multiple Sclerosis After Cessation of Fingolimod Treatment

Stacy Ellen Hatcher, BS; Emmanuelle Waubant, MD, PhD; Bardia Nourbakhsh, MD; Elizabeth Crabtree-Hartman, MD; Jennifer S. Graves, MD, PhD, MAS

Editorial

IMPORTANCE The appropriate sequencing of agents with strong immune system effects has become increasingly important. Transitions require careful balance between safety and protection against relapse. The cases presented herein highlight that rebound events after ceasing fingolimod treatment may happen even with short washout periods (4 weeks) and may perpetuate despite steroid treatment or the immediate use of fast-acting immune therapies, such as rituximab.

OBJECTIVE To describe rebound syndrome in patients with multiple sclerosis (MS) after cessation of fingolimod treatment.

DESIGN, SETTING, AND PARTICIPANTS Clinical and demographic data were extracted from electronic medical records from the University of California, San Francisco, Multiple Sclerosis Center from January 2014 to December 2015. Magnetic resonance images were reviewed by MS neurologists (J.S.G., E.W., B.N., and E.C.H.). Rebound syndrome was defined as new severe neurological symptoms after ceasing fingolimod treatment, with the development of

We conclude that discontinuation of fingolimod results in the return of disease activity, which then leads to severe exacerbations (i.e., rebounds) in a clinically significant proportion of patients.

Severe disease exacerbations in patients with multiple sclerosis after discontinuing fingolimod. Neurol Neurochir Pol. 2017 Mar - Apr;51(2):156-162.

Stopping DMTs

- N=721; 53% stop DMTs of which 57% resume
- N=70; middle age and clinically stable
- N=221; >45y/o, >4 years relapse, MRI stable
  N=1339; after a long period clinically stable no greater risk of relapse but disability may progress sooner off DMTs

1. Mult Scler Relat Disord. 2017 Feb;12:82-87. Discontinuation of disease modifying treatments in middle aged multiple sclerosis patients. First line drugs vs natalizumab.
2. Discontinuation of disease-modifying therapies in multiple sclerosis - Clinical outcome and prognostic factors.Mult Scler. 2017 Aug;23(9):1241-1248.
3. Discontinuing disease-modifying therapy in MS after a prolonged relapse-free period: a propensity score-matched study. J Neurol Neurosurg Psychiatry. 2016 Oct;87(10):1133-7.
4. Persistence to disease-modifying therapies for multiple sclerosis in a Canadian cohort. Patient Prefer Adherence. 2017 Jun 28;11:1093-1101

Abrupt Stopping of DMT Leads to Disease Flare

- Research data
  - >44 years old
  - > 3- 4 years no relapses, progression
  - No enhancing MRI lesions
  - Similar risk for relapse as those who continue on Drug DMTs
  - Increased risk of disability progression
  - Need therapeutic diet/lifestyle

- Stopping drug disease modifying therapy
  - Ongoing commitment to 100% compliance therapeutic diet/lifestyle forever
  - Mitochondrial support
  - Optimize vitamin D levels

- Dietary Approaches
  - Modified Paleo
  - Ketogenic
  - Fasting Mimicking Diet
  - Swank
  - McDougal
  - ? Mediterranean
- Remyelination
  - Omega 6:3 in 4 to1 ratio
  - Phosphatidylcholine
  - Black Cumin Seed oil
  - Vitamin K2
  - Fasting Mimicking Diet
  - ? Clemastine (Tavist)

Subject 3- Baseline and 12 Month Walk

SPMS TUG-127 sec.
FSS-5.6

SPMS TUG-41.8 sec.
FSS-4.4

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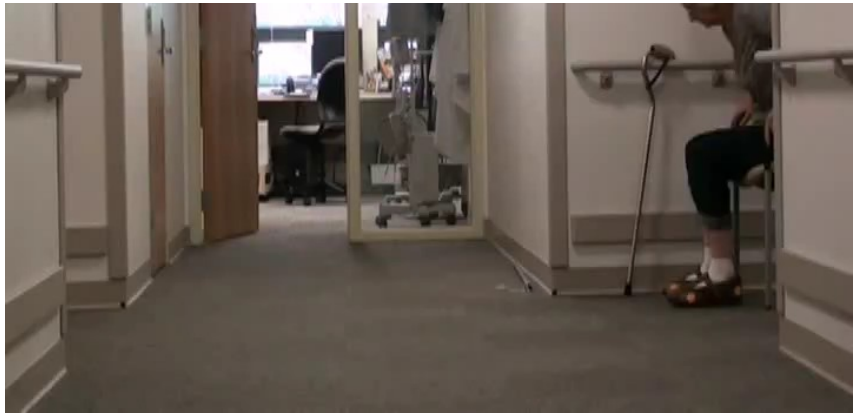
Subject 17- Baseline and 3 Month Walk

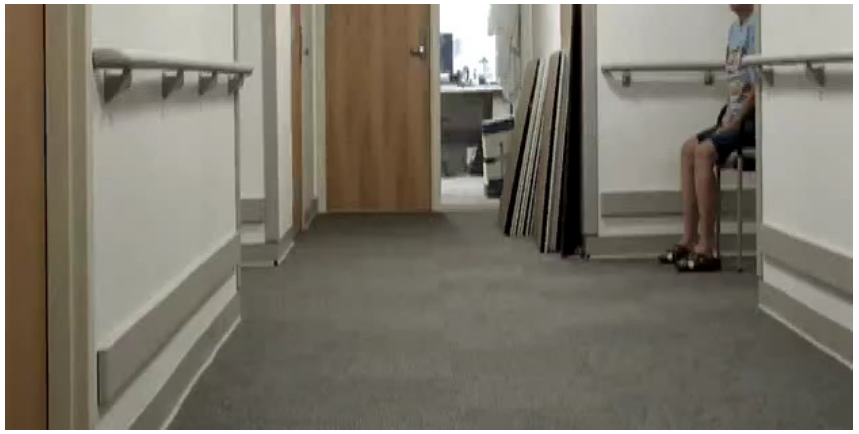
PPMS
TUG-21 sec.
FSS-6.7



PPMS
TUG- 15.3 sec. with one cane
17.6 sec. without cane
FSS-4.9

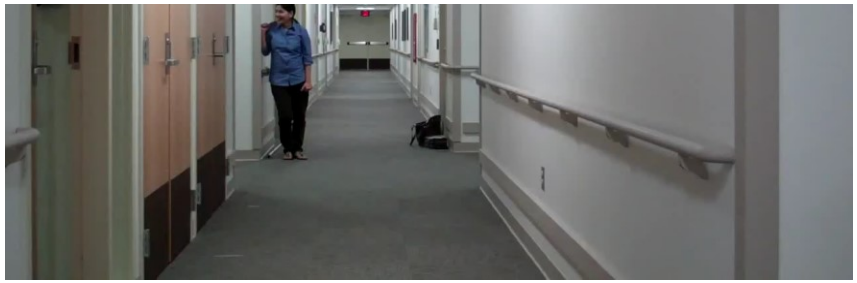
Subject 11- Baseline and 3 Month Walk

SPMS TUG-14.9 sec.
FSS-5.3



SPMS TUG- 8.6 sec.
FSS-1.4

Subject 11- 6 months



"Between stimulus and response, there is a space. In that space lies our freedom and power to choose our response. In our response lies our growth and freedom."

—Viktor Frankl

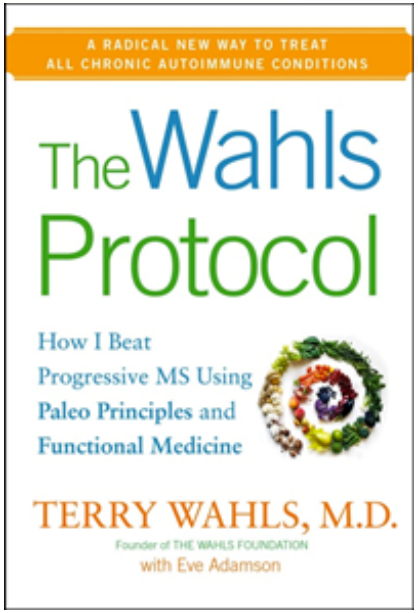
Terry Wahls MD

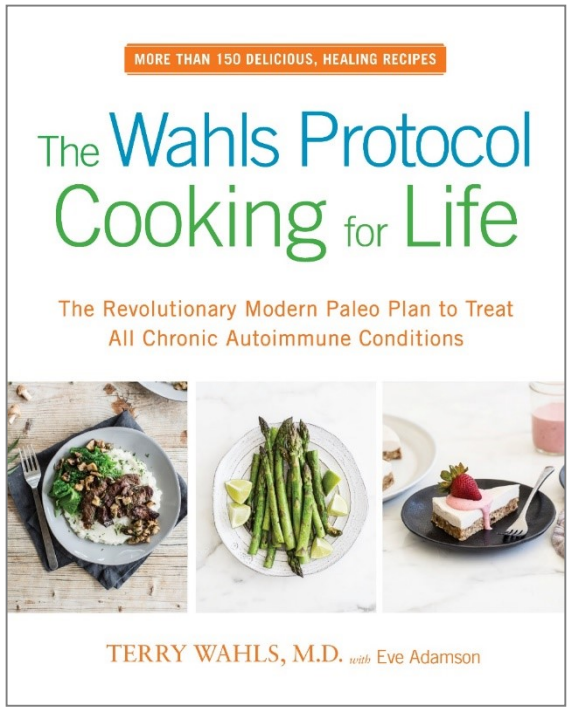
- Martin Seligman
- Positive Psychology

- 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-happinessorg*. 2018. Available at: http://www.pursuit-of-happiness.org/history-of-happiness/martin-seligman-psychology/. Accessed May 21, 2018.

1. **Pleasant life** - appreciate such basic pleasures as companionship, the natural environment and our bodily needs.
2. **Good Life** - achieved through discovering our unique virtues and strengths, and employing them creatively to enhance our lives.
3. **Meaningful Life** – achieved by employing our unique strengths for a purpose greater than ourselves.





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Dietary Approaches to Treating MS Related Fatigue

NCT02914964

- Recruiting - Fatigue + Relapsing-remitting MS
- Live within 500 miles of Iowa City
- Contact MSDietStudy@healthcare.uiowa.edu
- Post doctoral with an interest in nutrition and multiple sclerosis: terry-wahls@uiowa.edu
- Copies of Wahls MS papers and links to video of gait changes www.terrywahls.com/papers

Appendix
Doses – Bredesen

- **Methylfolate/B12/ trimethyl glycine/ B complex**
  - Titrate to homocysteine < 7
- **Curcumin**
  - 500 mg to 2000 mg/ day with 4mg bioperine
- **Resveratrol**
  - 100 to 250 mg/ day
- **PQQ (polyquinoline quinone)**
  - 20 mg/ day

Doses – Bredesen

- **Balance Zn: Cu Ratio**
  - (20-50mg Zn + 6mg Cu or less)
- **DHA / cod liver oil**
  - 1 – 2 grams/ monitor EFA levels in cell membranes
  - (Consider GLA 300mg / 1-5 grams cod liver oil)
- **ALCAR, acetyl-L-carnitine**
  - 500 mg to 1000 mg (with Lipoic Acid 600 mg)
- **P5P, pyridoxal-5-phosphate (50 mg)**
  - Monitor levels

Doses – Bredesen

- **NAC, N-acetyl cysteine**
  - 500 mg to 2 grams/Day
- **Citicholine (CDP)**
  - 250 mg to 1000 mg BID
- **CoQ10**
  - 200 mg to 2400 mg/Day
- ***Bacopa Monnieri*** (brahmi, water hyssop)
  - 300 mg extract/Day
- **Lion's Mane mushroom** 1 tsp
- **Melatonin**
  - 0.5 mg to 5 mg
  - Full spectrum light morning
  - Evening amber light

Nutrition/ Assimilation /Structure

Goal	Approach
Optimize diet: minimize simple CHO, minimize inflammation. Fasting insulin <7; HgbA1c <5.5	Low glycemic, low inflammatory, gluten free; low grain **TW** – ketogenic, modified paleo, eat 6 to 9 cups vegetables/ day, push fiber to poop 2 snakes day
Provide synaptic structural components	CDP choline DHA **TW** Phosphatidylcholine, organ meats

Interventions- Exercise and Movement

Goal	Approach
Exercise	30-60’ per day, 4-6 days/wk **TW** – strength training, balance training, High intensity interval training, PT or OT referral, consider adding NMES=Electrical stimulation of muscles DO NOT over train

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 or meditation or music, etc. **TW** gardening, fishing, hunting, Epsom salts
Improve relationships	**TW** – create social connections

Mitochondria Energy

Goal	Approach
Enhance autophagy, ketogenesis	Fast 12 hr + each night, including 3 hr prior to bedtime, longer fasts
Optimize mitochondrial function	CoQ or ubiquinol, α-lipoic acid, PQQ, NAC, Acetyl carnitine, Se, Zn, resveratrol, ascorbate, thiamine **TW** – eat organ meats 2-3 X week
Optimize antioxidants	Mixed tocopherols and tocotrienols, Se, blueberries, NAC, ascorbate, α-lipoic acid **TW** 6 to 9 cups vegetables (Greens, sulfur, color)/D

Biotransformation - Detoxification

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

Communication - Hormone

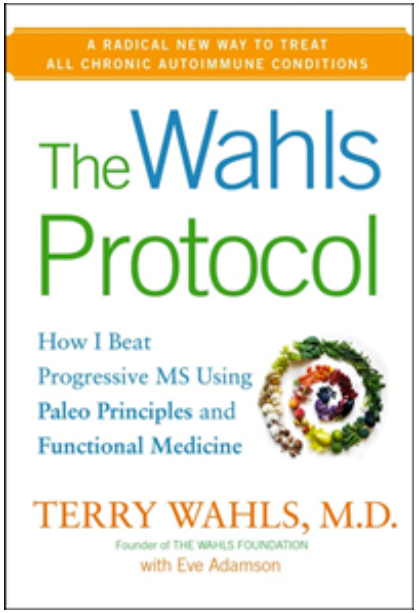
Goal	Approach
Optimize hormone balance	Optimize fT3, fT4, E2, T, progesterone, pregnenolone, cortisol.
TW optimize progenitor (stem cells)	**TW** – Diet, exercise, sleep, stress, social bonding, fasting, CDP choline, PC, DHA
Increase NGF	Lion's mane mushrooms Or ALCAR (acetyl-L-carnitine)
Brain stimulation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

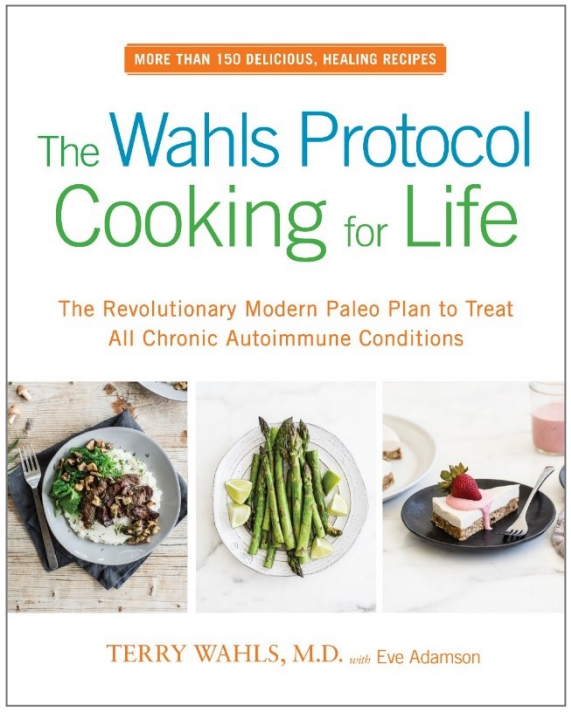
Immune - Defense and Repair

Goal	Approach
GI health	Repair if needed; prebiotics and probiotics; target 2-3 poop snakes per day **TW** – address food sensitivities
Infections, dysbiosis	**TW** – check for mold, water damaged buildings, infections, Lyme etc. Floss teeth, add mushrooms, vitamin D, K2mk7

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





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