Functional Approach to Treating Neurodegenerative Disorders

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- Equity interest
  - Dr. Terry Wahls LLC
  - The Wahls Institute PLC
  - [www.terrywahls.com](http://www.terrywahls.com)

Books

- *Minding My Mitochondria* by Terry L. Wahls, M.D.
- *The Wahls Protocol* by Terry Wahls, M.D. and Eve Adamson
- *The Wahls Protocol Cooking for Life* by Terry Wahls, M.D.
Objectives

• Name one mechanisms by which dietary factors may contribute to neuroinflammation and neurodegenerative disease processes and potential worsening of symptoms.

• Name 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.
How many cups of vegetables did you eat in the last 24 hours?
Global Alzheimer's Prevalence

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

WHO 2011

Global MS Prevalence

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)

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)

CLASSIFICATION OF MULTIPLE SCLEROSIS

PRMS Progressive Relapsing MS
Steady decline since onset with super-imposed attacks.

SPMS Secondary Progressive MS
Initial RRMS that suddenly begins to decline without periods of remission and relapses.

PPMS Primary Progressive MS
Gradual progression of the disease from its onset with no relapses or remissions

RRMS Relapsing/Remitting MS
Unpredictable attacks which may or may not leave permanent deficits followed by periods of remission

Progressive Relapsing Multiple Sclerosis | Health Life Media.
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

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

The Cleveland Clinic
Fish oil, creatine and co-enzyme Q 10


2002
# 7 Years of Decline

**NARCOMS QOL Survey**

<table>
<thead>
<tr>
<th></th>
<th>11/23/05</th>
<th>6/2/06</th>
<th>11/28/06</th>
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<tr>
<td><strong>MS Sx Overall</strong></td>
<td>Worse</td>
<td>Worse</td>
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<td><strong>Fatigue</strong></td>
<td>Mod</td>
<td>Severe</td>
<td>Total</td>
<td>Total</td>
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</table>
Neuroprotection:
A Functional Medicine Approach for Common And Uncommon Neurologic Syndromes

Institute For Functional Medicine
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

Personalizing Lifestyle and Environmental Factors

- Sleep & Relaxation
- Exercise/Movement
- Nutrition/Hydration
- Stress/Resilience
- Relationships/Networks
- Trauma
- Microorganisms
- Environmental Pollutants
The Wahls Protocol®

Sleep & Relaxation

Exercise/Movement

Nutrition/Hydration

Stress/Resilience

Personalizing Lifestyle...
The Wahls Protocol®

Terry Wahls MD
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The Wahls Protocol®
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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The Wahls Protocol

Personalizing Lifestyle

- Sleep & Relaxation
- Exercise/Movement
- Nutrition/Hydration
- Stress/Resilience
Sleep Disturbances & MS

N=100

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

Restless legs also more frequent.
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


Exercise Influences Oligodendrocyte Precursor Cell Production and Maturation

Forager - Hunter 500,000 BC
Main Cause of death
- Infection, trauma
Mean age 30s
45% mortality before age 15
Forager-Hunter 2007
Traditional diet, no medical care
Main cause of death
Infection, trauma
Often live into 60s and 80s
Forager-Hunter to Farmer -10,000 BC

↑ fertility, infection; ↓ height

Industrial Revolution 1800s

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

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; •).
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

**Coffee**
- Possible contribution to rheumatoid factor production

**Salt**
- Proinflammatory macrophages
- \(T_\text{H}17\) cell potency and IL-17 levels
- \(T_\text{reg}\) cell function

**Autoimmunity**

**Capsaicin**
- Modulation of neuroimmune inflammatory response
- Pain reduction (topical effect)
- Proliferation and activation of autoreactive T cells
- Anti-inflammatory macrophages

**Omega-3 fatty acids**
- Proinflammatory cytokine production
- \(T\) cell proliferation and IL-2 production
- Autoantibody production

**Curcumin**
- \(T_\text{reg}\) cell proliferation
- \(T_\text{H}1\) cell proliferation
- \(B_\text{reg}\) cell function
- Antioxidants and anti-inflammatory genes

**Resveratrol**
- NF-\(\kappa\)B activation
- Cyclooxygenase 2
- ROS production

**Chocolate**
- Proinflammatory cytokines
- Anti-inflammatory cytokines
- Autoantibody production

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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.
Nutrition in Parkinson's Disease

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
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...
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≤0.00001-0.004).

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 \( \beta \)-casomorphin-7 and exerts its influence on nervous, digestive, and immune functions via the opioid receptor

The Wahls Protocol® Seminar

Dairy & MS
Casein, Gluten & Schizophrenia


8. Transglutaminase-6 is an autoantigen in progressive multiple sclerosis and is upregulated in reactive astrocytes. *Mult Scler.* 2016 Dec 1;1352458516684022.

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


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.”

• **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 of cooking these foods such as soaking, fermenting & cooking will decrease the lectin content.

Paleo Diet Benefits

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


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.


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

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.

**Study** | **Hazard ratio (95% CI)** | **Weight (%)** | **Hazard ratio (95% CI)**
--- | --- | --- | ---
Bellavia 2013 | 0.94 (0.92 to 0.97) | 17 | 0.94 (0.92 to 0.97)
Leenders 2013 | 0.99 (0.98 to 0.99) | 20 | 0.99 (0.98 to 0.99)
Tucker 2005 | 0.95 (0.89 to 1.01) | 10 | 0.95 (0.89 to 1.01)
Genkinger 2004 | 0.91 (0.86 to 0.95) | 13 | 0.91 (0.86 to 0.95)
Steffen 2003 | 0.95 (0.92 to 0.99) | 15 | 0.95 (0.92 to 0.99)
Bazzano 2002 | 0.97 (0.93 to 1.00) | 15 | 0.97 (0.93 to 1.00)
Rissanen 2002 | 0.92 (0.85 to 0.99) | 8 | 0.92 (0.85 to 0.99)
Overall: P<0.001, I²=82% | 0.95 (0.92 to 0.98) | 100 | 0.95 (0.92 to 0.98)
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

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

36 Key Micronutrients


<table>
<thead>
<tr>
<th>Nutrients</th>
<th>Vitamin A, retinol</th>
<th>Alpha carotene</th>
<th>Carnitine</th>
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<tr>
<td>Vitamin B₁ (thiamine)</td>
<td></td>
<td>Beta carotene</td>
<td>Lipoic acid</td>
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<tr>
<td>Vitamin B₂ (riboflavin)</td>
<td></td>
<td>Beta cryptoxanthin</td>
<td>Creatine</td>
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<tr>
<td>Vitamin B₃ (niacin)</td>
<td></td>
<td>Lutein</td>
<td>Cholesterol</td>
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<tr>
<td>Vitamin B₅ (Pantothenic acid)</td>
<td></td>
<td>Lycopene</td>
<td>Alpha-linolenic fatty acid (ALA)</td>
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<tr>
<td>Vitamin B₆ (pyridoxine)</td>
<td></td>
<td>Zeaxanthin</td>
<td>Eicosapentaenoic acid (EPA)</td>
</tr>
<tr>
<td>Vitamin B₉ (folic acid)</td>
<td></td>
<td>Iron</td>
<td>Docosahexaenoic acid (DHA)</td>
</tr>
<tr>
<td>Vitamin B₁₂ (cobalamin)</td>
<td></td>
<td>Copper</td>
<td>Arachidonic acid (AA)</td>
</tr>
<tr>
<td>Vitamin C</td>
<td></td>
<td>Zinc</td>
<td>Gamma-linolenic fatty acid (GLA)</td>
</tr>
<tr>
<td>Vitamin D</td>
<td></td>
<td>Iodine</td>
<td>Linoleic acid (LA)</td>
</tr>
<tr>
<td>Vitamin E</td>
<td></td>
<td>Magnesium</td>
<td>N Acetyl cysteine</td>
</tr>
<tr>
<td>Vitamin K</td>
<td></td>
<td>Selenium</td>
<td>Taurine</td>
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</table>
Sulfur Rich Foods

- Cabbage
- Onion
- Mushroom
Why Brassica and Allium?

• Improve detoxification
• Increase glutathione production
• Increase GABA production
• Enhance Neuroprotection
• Improve endothelial function
Brassica and Allium References


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

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


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.


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


5. Grape juice, berries, and walnuts affect brain aging and behavior. *J Nutr*. 2009 Sep;139(9):1813S-7S.


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.


**Figure 4.** In vitro kinetic analysis of four recombinant human BCMO1 variants. A) Reaction velocity (nmol product formed/mg protein \( \times \) min) as a function of substrate concentration (\( \mu M \)) is plotted for a 15 min reaction with 10.4 \( \mu \)g of recombinant BCMO1 and 2.5–16 \( \mu \)M \( \beta \)-carotene as substrate. Four BCMO1 variants are wild-type, R267/A379, and 3 mutants: 267S (\( \square \)), 379V (\( \triangle \)), and 267S + 379V (\( \diamond \)). 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.
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)

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


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.
The Wahls Protocol®

- **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.


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
The Wahls Protocol® Seminar

Monitor Ketones
Ketosis References


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
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
Thymoquinone-Remyelination

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

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.
3. Effect of low saturated fat diet in early and late cases of multiple sclerosis.
5. Multiple sclerosis: twenty years on low fat diet.
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
Fasting-mimicking diet and aging, diabetes, cancer, and cardiovascular disease

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

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.

Reversal of early and moderate dementia using functional medicine approach
Reversal of Cognitive Decline: 100 Patients

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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 cognitive function. The underlying brain mechanism driving cognitive recovery that I have determined the potential is...
**Table 1. Therapeutic System 1.0**

<table>
<thead>
<tr>
<th>Goal</th>
<th>Approach</th>
<th>Rationale and References</th>
</tr>
</thead>
<tbody>
<tr>
<td>Optimize diet. minimize simple CHO, minimize inflammation</td>
<td>Patients given choice of several low glycemic, low inflammatory, low grain diets</td>
<td>Minimize inflammation, minimize insulin resistance.</td>
</tr>
<tr>
<td>Enhance autophagy, ketogenesis</td>
<td>Fast 12 hr each night, including 3 hr prior to bedtime.</td>
<td>Reduce insulin levels, reduce Aβ.</td>
</tr>
<tr>
<td>Reduce stress</td>
<td>Personalized—yoga or meditation or music, etc.</td>
<td>Reduction of cortisol, CRP, stress axis.</td>
</tr>
<tr>
<td>Optimize sleep</td>
<td>8 hr sleep per night; melatonin 0.5mg po qhs; Trp 500mg po 30 min of awakening. Exclude sleep apnea.</td>
<td>[36].</td>
</tr>
<tr>
<td>Exercise</td>
<td>30-60’ per day, 4-5 days/wk</td>
<td>[37, 38].</td>
</tr>
<tr>
<td>Brain stimulation</td>
<td>Posit or related</td>
<td>[39].</td>
</tr>
<tr>
<td>Homocysteine &lt;7</td>
<td>Me-B12, MTHF, P5P; TMG if necessary</td>
<td>[40].</td>
</tr>
<tr>
<td>Serum B12 &gt;500</td>
<td>Me-B12</td>
<td>[41].</td>
</tr>
<tr>
<td>CRP &lt;1.0, A/G &gt;1.5</td>
<td>Anti-inflammatory diet; curcumin; DHA/EPA, optimize hygiene</td>
<td>Critical role of inflammation in AD.</td>
</tr>
<tr>
<td>Fasting insulin &lt;7; HgbA1c &lt;5.5</td>
<td>Diet as above</td>
<td>Type II diabetes-AD relationship.</td>
</tr>
<tr>
<td>Hormone balance</td>
<td>Optimize ft3, ft4, E2, T, progesterone, pregnenolone, cortisol</td>
<td>[5, 42].</td>
</tr>
<tr>
<td>GI health</td>
<td>Repair if needed; prebiotics and probiotics</td>
<td>Avoid inflammation, autoimmunity.</td>
</tr>
<tr>
<td>Reduction of A-beta</td>
<td>Curcumin, Ashwagandha</td>
<td>43-45.</td>
</tr>
<tr>
<td>Cognitive enhancement</td>
<td>Bacopa monniera, MgT</td>
<td>[46, 47].</td>
</tr>
<tr>
<td>25OH-D3 = 30-100ng/ml</td>
<td>Vitamins D3, K2</td>
<td>[48].</td>
</tr>
<tr>
<td>Increase NGF</td>
<td>H. erinaceus or ALCAR</td>
<td>[49, 50].</td>
</tr>
<tr>
<td>Provide synaptic structural components</td>
<td>Cricotline, DHA</td>
<td>[51].</td>
</tr>
<tr>
<td>Optimize antioxidants</td>
<td>Mixed tocopherols and tocotrienols, Se, blueberries, NAC, ascorbate, α-lipoic acid</td>
<td>[52].</td>
</tr>
<tr>
<td>Optimize Zn/Cu ratio</td>
<td>Depends on values obtained</td>
<td>[53].</td>
</tr>
<tr>
<td>Ensure nocturnal oxygenation</td>
<td>Exclude or treat sleep apnea</td>
<td>[54].</td>
</tr>
<tr>
<td>Optimize mitochondrial function</td>
<td>CoQ or ubiquinol, α-lipoic acid, PQO, NAC, ALCAR, Se, Zn, resveratrol, ascorbate, thiamine</td>
<td>[55].</td>
</tr>
<tr>
<td>Increase focus</td>
<td>Pantothenic acid</td>
<td>Acetylcholine synthesis requirement.</td>
</tr>
<tr>
<td>Increase Sht1 function</td>
<td>Resveratrol</td>
<td>[52].</td>
</tr>
<tr>
<td>Exclude heavy metal toxicity</td>
<td>Evaluate Hg, Pb, Cd, chelate if indicated</td>
<td>CNS effects of heavy metals.</td>
</tr>
<tr>
<td>MCT effects</td>
<td>Coconut oil or Axiona</td>
<td>[56].</td>
</tr>
</tbody>
</table>

CHO, carbohydrates; Hg, mercury; Pb, lead; Cd, cadmium; MCT, medium chain triglycerides; PQO, polyquinoine quinone; NAC, N-acetyl cysteine; CoQ, coenzyme Q; ALCAR, acetyl-L-carnitine; DHA, docosahexaenoic acid; MgT, magnesium threonate; T3, free triiodothyronine; T4, free thyroxine; E2, estradiol; T, testosterone; Me-B12, methylcobalamin; MTHF, methyltetrahydrofolate; P5P, pyridoxal 5-phosphate; TMG, trimethylglycine; Trp, tryptophan.
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
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

<table>
<thead>
<tr>
<th>Food</th>
<th>Instruction</th>
<th>Servings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Green leafy vegetables</td>
<td>Recommended*</td>
<td>3 cups cooked/6 cups raw=3srvg</td>
</tr>
<tr>
<td>Sulfur-rich vegetables</td>
<td>Recommended*</td>
<td>3 cups raw or cooked=3srvg</td>
</tr>
<tr>
<td>Intensely colored fruits or vegetables</td>
<td>Recommended*</td>
<td>3 cups raw or cooked =3srvg</td>
</tr>
<tr>
<td>Omega-3 oils</td>
<td>Encouraged</td>
<td>2 tablespoons</td>
</tr>
<tr>
<td>Animal protein</td>
<td>Encouraged</td>
<td>4 ounces or more</td>
</tr>
<tr>
<td>Gluten-containing grain</td>
<td>Excluded</td>
<td></td>
</tr>
<tr>
<td>Dairy</td>
<td>Excluded</td>
<td></td>
</tr>
<tr>
<td>Eggs</td>
<td>Excluded</td>
<td></td>
</tr>
</tbody>
</table>
Stop processed foods, gluten, dairy, eggs
The Wahls Protocol® Seminar

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.

Nutritional Adequacy (%RDA)

US Diet Vs. Study Diet

- Vitamin D
- Calcium
- Vitamin E
- Magnesium
- Zinc
- Folate
- Iron
- Vitamin A
- Vitamin C
- Niacin
- Vitamin B6
- Vitamin B12
- Thiamin
- Riboflavin

[Bar chart showing nutritional adequacy of various nutrients between US Diet and Wahls* Study Diet]
Methyl B12, Methyl Folate, Vitamin D, Fish Oil

Meditation
<table>
<thead>
<tr>
<th>Stretching Exercises</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gastro-soleus</td>
</tr>
<tr>
<td>[Image of Gastro-soleus exercise]</td>
</tr>
<tr>
<td>Hamstring</td>
</tr>
<tr>
<td>[Image of Hamstring exercise]</td>
</tr>
<tr>
<td>Quadriceps</td>
</tr>
<tr>
<td>[Image of Quadriceps exercise]</td>
</tr>
<tr>
<td>Erector spinae</td>
</tr>
<tr>
<td>[Image of Erector spinae exercise]</td>
</tr>
</tbody>
</table>
Electrical Stimulation of Muscles Builds Muscle Mass
Multimodal intervention improves fatigue and quality of life in subjects with progressive multiple sclerosis: a pilot study

Babita Bisht1
Warren G Darling2
E Torage Shivapour3
Susan K Lutgendorf4
Linda G Snetseela7
Catherine A Chenard1
Terry L Wahl1

1Department of Internal Medicine, Carver College of Medicine, University of Iowa, 2Department of Health and Human Physiology, College of Liberal Arts and Sciences, University of Iowa, 3Department of Neurology, Carver College of Medicine, University of Iowa, 4Department of Anesthesiology, Carver College of Medicine, University of Iowa, 5Department 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 effect 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=0.563, P=0.005) and EDSS scores (r=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
Side effect – Overweight and obese subjects lost weight and got to a healthy weight
Multimodal intervention improves quality of life

Scores

<table>
<thead>
<tr>
<th></th>
<th>SF-36 general health</th>
<th>SF-36 energy</th>
<th>FSS</th>
</tr>
</thead>
<tbody>
<tr>
<td>B</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3M</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>6M</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>9M</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>12M</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

$r = -0.968, p = 0.003$

**p<0.0005
*p<0.05
Mood and Cognition

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

Jennifer E. Lee, PhD, MAa,b, Babita Bisht, PhD, BPTc, Michael J. Hall, PhDd,e, Linda M. Rubenstein, PhD, MSe, Rebecca Louison, BSA, Danielle T. Klein, BSt, and Terry L. Wahls, MDc,g

*Department of Psychology, Mount Mercy University, Cedar Rapids, Iowa; bCollege of Nursing, The University of Iowa, Iowa City, Iowa; cDepartment of Internal Medicine, Carver College of Medicine, The University of Iowa, Iowa City, Iowa; dDepartment of Psychiatry, Iowa City VA Health Care System, Iowa City, Iowa; eDepartment of Psychiatry, Carver College of Medicine, University of Iowa, Iowa City, Iowa; fCollege of Public Health, The University of Iowa, Iowa City, Iowa; gExtended 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 strength training); (3) cognitive behavioral therapy; (4) yoga and meditation; (5) a personal support system; (6) a stress management program; and (7) a mindfulness program.

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

<table>
<thead>
<tr>
<th>Variables 0 to 12 months</th>
<th>Mood (BDA/BDI)</th>
<th>Cognition (Verbal reasoning)</th>
<th>Fatigue</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vegetables/ fruits</td>
<td>0.0001</td>
<td>&lt;0.0001</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Gluten, dairy, egg free</td>
<td>0.001</td>
<td>0.005</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>
Relapsing Remitting MS

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

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

A

FSS

FSS score

Control

MPDI

Baseline

Postprotocol

B

Change in FSS

C1 C2 C3 C4 C5 C6 C7 C8 C9 D1 D2 D3 D4 D5 D6 D7 D8

Control

MPDI
Improved Mental and Physical QoL
Improved Motor Function

A. 9-HPT (dominant)

B. 9-HPT (nondominant)

C. 25-FW

D. 6-MW
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

<table>
<thead>
<tr>
<th>Diet</th>
<th>Basic Guidelines</th>
<th>Restrictions</th>
<th>Possible Deficiencies</th>
<th>Evidence for Benefit in Multiple Sclerosis</th>
<th>Evidence for Benefit in Other Diseases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Paleolithic diet</td>
<td>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</td>
<td>Processed food, domesticated meats, dairy, eggs</td>
<td>Folic acid, thiamine, vitamin B6, calcium and vitamin D, insufficient caloric intake</td>
<td>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)</td>
<td>Single study showed improvement in cardiovascular risk factors</td>
</tr>
<tr>
<td>Mediterranean diet</td>
<td>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)</td>
<td>No specific exclusions</td>
<td>None expected</td>
<td>None</td>
<td>Extensive evidence for a benefit on cardiovascular health, diabetes, and possibly on cancer risk</td>
</tr>
<tr>
<td>McDougall diet</td>
<td>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</td>
<td>Dairy, eggs, meat, poultry, fish, and all oils</td>
<td>Iron, vitamin B12, vitamin D, calcium, and n3-fatty acids</td>
<td>None</td>
<td>One study showed improvement in cardiovascular risk factors with 1 week of the diet (did not look at long-term effects)</td>
</tr>
<tr>
<td>Gluten-free diet</td>
<td>Avoidance of all foods containing wheat, barley, and triticales or their derivatives</td>
<td>Foods containing wheat, barley, or triticales or their derivatives</td>
<td>None expected</td>
<td>None</td>
<td>Treatment for celiac disease and non-celiac gluten sensitivity</td>
</tr>
<tr>
<td>Swank diet</td>
<td>Low-fat diet that advocates reduction in the intake of saturated fats. Whole-grain cereals are recommended daily intake</td>
<td>Processed food with saturated fats, high-fat dairy products, red meat</td>
<td>None expected (possibly vitamin A, D, and folate)</td>
<td>Observational data from a single cohort of patients treated with this diet</td>
<td>None</td>
</tr>
</tbody>
</table>
• 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
The Wahls Protocol®
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
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.

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

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 to 1 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
The Wahls Protocol® Seminar
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
The Wahls Protocol Seminar

- 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.

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.
How many cups of vegetables did you eat in the last 24 hours?
In Person Seminar
Wahls Protocol® Seminar
Health Professional Workshop
Certification program

www.terrywahls.com

• Instagram
  – drterrywahls
• Facebook
  – Terry Wahls MD
• Twitter
  – @TerryWahls
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

<table>
<thead>
<tr>
<th>Goal</th>
<th>Approach</th>
</tr>
</thead>
<tbody>
<tr>
<td>Optimize diet: minimize simple CHO, minimize inflammation. Fasting insulin &lt;7; HgbA1c &lt;5.5</td>
<td>Low glycemic, low inflammatory, gluten free; low grain <strong>TW</strong> – ketogenic, modified paleo, eat 6 to 9 cups vegetables/day, push fiber to poop 2 snakes/day</td>
</tr>
<tr>
<td>Provide synaptic structural components</td>
<td>CDP choline DHA <strong>TW</strong> Phosphatidylcholine, organ meats</td>
</tr>
</tbody>
</table>
# Interventions - Exercise and Movement

<table>
<thead>
<tr>
<th>Goal</th>
<th>Approach</th>
</tr>
</thead>
<tbody>
<tr>
<td>Exercise</td>
<td>30-60’ per day, 4-6 days/wk</td>
</tr>
<tr>
<td></td>
<td><strong>TW</strong> – strength training, balance training, High intensity interval training, PT or OT referral, consider adding NMES=Electrical stimulation of muscles</td>
</tr>
<tr>
<td></td>
<td>DO NOT over train</td>
</tr>
</tbody>
</table>
# Interventions- Sleep/ Stress/ Relationships

<table>
<thead>
<tr>
<th>Goal</th>
<th>Approach</th>
</tr>
</thead>
<tbody>
<tr>
<td>Support sleep</td>
<td>Melatonin 0.5 to 5 mg, full spectrum lighting</td>
</tr>
<tr>
<td>Ensure nocturnal oxygenation</td>
<td>Exclude or treat sleep apnea</td>
</tr>
</tbody>
</table>
| Reduce stress             | Personalized—yoga or meditation or music, etc.  
**TW** gardening, fishing, hunting, Epsom salts |
| Improve relationships     | **TW** – create social connections |
# Mitochondria Energy

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

<table>
<thead>
<tr>
<th>Goal</th>
<th>Approach</th>
</tr>
</thead>
<tbody>
<tr>
<td>Optimize Zn: Cu ratio</td>
<td>Depends on values obtained</td>
</tr>
<tr>
<td>Exclude heavy metal toxicity</td>
<td>Evaluate Hg, Pb, Cd, Mn, As address if indicated</td>
</tr>
<tr>
<td><strong>TW</strong> – ↑ bacterial biotransformation</td>
<td><strong>TW</strong> – ↑ fiber to 2-3 soft BM day</td>
</tr>
<tr>
<td><strong>TW</strong> correct nutrient mineral lacks</td>
<td><strong>TW</strong> nutrient minerals, stomach acid, sea salt, Epsom salts, sea salt, Na bicarbonate soaks</td>
</tr>
</tbody>
</table>
# The Wahls Protocol

## Communication - Hormone

<table>
<thead>
<tr>
<th>Goal</th>
<th>Approach</th>
</tr>
</thead>
<tbody>
<tr>
<td>Optimize hormone balance</td>
<td>Optimize fT3, fT4, E2, T, progesterone, pregnenolone, cortisol.</td>
</tr>
<tr>
<td>TW optimize progenitor (stem cells)</td>
<td>TW – Diet, exercise, sleep, stress, social bonding, fasting, CDP choline, PC, DHA</td>
</tr>
<tr>
<td>Increase NGF</td>
<td>Lion’s mane mushrooms Or ALCAR (acetyl-L-carnitine)</td>
</tr>
<tr>
<td>Brain stimulation</td>
<td>Posit or related</td>
</tr>
<tr>
<td></td>
<td>TW – brain age, lumosity, juggling, do not over train</td>
</tr>
</tbody>
</table>
# Immune - Defense and Repair

<table>
<thead>
<tr>
<th>Goal</th>
<th>Approach</th>
</tr>
</thead>
<tbody>
<tr>
<td>GI health</td>
<td>Repair if needed; prebiotics and probiotics; target 2-3 poop snakes per day</td>
</tr>
<tr>
<td></td>
<td><strong>TW</strong> – address food sensitivities</td>
</tr>
<tr>
<td>Infections, dysbiosis</td>
<td><strong>TW</strong> – check for mold, water damaged buildings, infections, Lyme etc. Floss teeth, add mushrooms, vitamin D, K2mk7</td>
</tr>
</tbody>
</table>
## Other Interventions

<table>
<thead>
<tr>
<th>Goal</th>
<th>Approach</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serum B12 &gt;500</td>
<td>Me-B12</td>
</tr>
<tr>
<td>TW – prefer top quartile of ref. range</td>
<td>TW organ meat 2 to 3 X week</td>
</tr>
<tr>
<td>h.s. CRP &lt;1.0</td>
<td>Anti-inflammatory diet; curcumin; DHA/EPA; optimize hygiene (floss teeth, coconut oil + essential oils to brush teeth, oil pulling)</td>
</tr>
<tr>
<td></td>
<td>TW – 6 to 9 cups vegetables / day</td>
</tr>
<tr>
<td>Homocysteine &lt;7</td>
<td>Me-B12, MTHF, P5P; TMG if necessary</td>
</tr>
<tr>
<td>25OH-D3 = 50-100ng/ml</td>
<td>Vitamins D3, K2</td>
</tr>
<tr>
<td>Reduction of A-beta</td>
<td>Curcumin, Ashwagandha</td>
</tr>
<tr>
<td>Increase focus</td>
<td>Pantothenic acid</td>
</tr>
<tr>
<td>Cognitive enhancement</td>
<td>Bacopa monniera, Mg threonate</td>
</tr>
</tbody>
</table>
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Dietary Approaches to Treating MS Related Fatigue

**NCT02914964**

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- Contact [MSDietStudy@healthcare.uiowa.edu](mailto:MSDietStudy@healthcare.uiowa.edu)
- Post doctoral with an interest in nutrition and multiple sclerosis: [terry-wahls@uiowa.edu](mailto:terry-wahls@uiowa.edu)
- Copies of Wahls MS papers and links to video of gait changes [www.terrywahls.com/papers](http://www.terrywahls.com/papers)