NeuroRestoration:
Using Food and Lifestyle Choices to Stabilize and Reverse Neurodegenerative Disease Processes

Terry Wahls, MD
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Website: www.terrywahls.com
Learning Objectives

1. Name at least four mechanisms by which environmental factors contribute to accelerated aging and neurodegenerative disease processes.

2. Name specific food and lifestyle interventions that can stabilize and or reverse neurodegenerative disease processes.

3. Introduce three resilience factors into their patient conversations that contribute to improved success rates in adopting and sustaining health behavior changes.
7 years of steady decline due to MS
Fish oil, creatine and co-enzyme Q10.


The Paleo Diet
REVISED EDITION
Updated to include the latest guidelines and research
Over 100,000 copies sold!

Lose Weight and Get Healthy by Eating the Foods You Were Designed to Eat

Loren Cordain, Ph.D.
author of The Paleo Diet Cookbook
Neuroprotection:
A Functional Medicine Approach for Common
And Uncommon Neurologic Syndromes

Institute For Functional Medicine
7 Year conventional therapy

1 Year FM therapy

http://www.casesjournal.com/content/2/1/7601
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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Common Neurodegenerative Conditions:

Examples include:

- Alzheimer’s disease (AD)
- Parkinson’s disease (PD)
- Multiple Sclerosis (MS)
- Amyotrophic Lateral Sclerosis (ALS)
- Traumatic Brain Injury (TBI)
- Post CVA Brain Injury (PCVABI)
- Non-Alzheimer's Cognitive Decline (NACD)
Global Alzheimer's Prevalence

World map illustrating the global distribution of deaths caused due to Alzheimer’s Disease/Dementia. WHO 2011.
Global MS Prevalence

How MS Progresses

- 10% benign
- 10% Primary Progressive MS (PPMS)
- Optic Neuritis / Clinically isolated syndrome BUT 50% progress to MS
- 80% diagnosed with Relapsing–Remitting MS (RRMS)
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
- PPMS – no approved treatments

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 NH care
- Leading diagnosis for those requesting assisted suicide from Dr. Kevorkian
Neurodegeneration

• Goal of therapies:
  – Slow the decline
    (Lost functions not expected to return)
• Examples:
  – Alzheimer’s
  – Secondary Progressive MS (SPMS)
  – Primary Progressive MS (PPMS)
Neuroprotection vs. NeuroRegeneration

• Restoring function is the goal
• Restore the brain / mitochondria
Multimodal intervention improves fatigue and quality of life in subjects with progressive multiple sclerosis: a pilot study

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 ($r=0.563$, $P=0.005$) 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 3- Baseline and 12 Month Walk

SPMS
TUG-127 sec.
FSS-5.6
Subject 3 - Baseline and 12 Month Walk

SPMS
TUG-41.8 sec.
FSS-4.4
Subject 3- Stair Climbing at 12 months
### Effects of nutrients (in food) on the structure and function of the nervous system

#### 36 Key Nutrients - Food First

<table>
<thead>
<tr>
<th>Vitamin A, retinol</th>
<th>Alpha carotene</th>
<th>Carnitine</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vitamin B&lt;sub&gt;1&lt;/sub&gt; (thiamine)</td>
<td>Beta carotene</td>
<td>Alpha-Lipoic acid (ALA)</td>
</tr>
<tr>
<td>Vitamin B&lt;sub&gt;2&lt;/sub&gt; (riboflavin)</td>
<td>Beta cryptoxanthin</td>
<td>Creatine</td>
</tr>
<tr>
<td>Vitamin B&lt;sub&gt;3&lt;/sub&gt; (niacin)</td>
<td>Lutein</td>
<td>Cholesterol</td>
</tr>
<tr>
<td>Vitamin B&lt;sub&gt;5&lt;/sub&gt; (Pantothenic acid)</td>
<td>Lycopene</td>
<td>Alpha-linolenic fatty acid</td>
</tr>
<tr>
<td>Vitamin B&lt;sub&gt;6&lt;/sub&gt; (pyridoxine)</td>
<td>Zeaxanthin</td>
<td>Eicosapentaenoic acid (EPA)</td>
</tr>
<tr>
<td>Vitamin B&lt;sub&gt;9&lt;/sub&gt; (folic acid)</td>
<td>Iron</td>
<td>Docosahexaenoic acid (DHA)</td>
</tr>
<tr>
<td>Vitamin B&lt;sub&gt;12&lt;/sub&gt; (cobalamin)</td>
<td>Copper</td>
<td>Arachidonic acid (AA)</td>
</tr>
<tr>
<td>Vitamin C</td>
<td>Zinc</td>
<td>Gamma-linolenic acid (GLA)</td>
</tr>
<tr>
<td>Vitamin D</td>
<td>Iodine</td>
<td>Linoleic acid (LA)</td>
</tr>
<tr>
<td>Vitamin E</td>
<td>Magnesium</td>
<td>N Acetyl cysteine</td>
</tr>
<tr>
<td>Vitamin K</td>
<td>Selenium</td>
<td>Taurine</td>
</tr>
</tbody>
</table>


Oregon Brain Aging Study
(n=104, $\bar{x} = 88$ years)

Two nutrient biomarker patterns (NBPs) were especially associated with more favorable cognitive and MRI measures:

1) High plasma B1, B2, B6, B9 (folate), B12, C, D, and E

2) High plasma marine n-3 fatty acids

Combined nutrient patterns predicted 75% of cognition / brain structure

Diet Quality & MS

Of 2469 participants with confirmed MS, 2087 (84.5%) provided complete data on their dietary habits (DHQ total score).

Every 10-point ↑ on the DHQ total score was associated with:

• 6-point ↑ in physical HRQOL
• 5-point ↑ in mental HRQOL
• 30% ↓ likelihood of a ↑ disability

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).

Nutrition in Parkinson's Disease

Sulfur Rich Foods

Cabbage

Onion

Mushroom

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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


Why Brassica and Allium?

- Improve detoxification
- Increase glutathione production
- Increase GABA production
- Enhance Neuroprotection
- Improve endothelial function
Why Greens?

• Vitamin K1 metabolized to K2-mk7 in gut
• K2 important in ….
  – Myelin production
  – Calcium influx into bones and teeth
• Carotenoids, magnesium
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.
Eat 9 Cups Vegetables/Fruit Daily

3 Greens
3 Colored
3 Sulfur
# Phytonutrient Spectrum Foods

## RED

<table>
<thead>
<tr>
<th>Foods</th>
<th>Benefits</th>
<th>Benefits</th>
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</thead>
<tbody>
<tr>
<td>Apples</td>
<td>Anti-cancer</td>
<td>Gastrointestinal health</td>
</tr>
<tr>
<td>Beet</td>
<td>Anti-inflammatory</td>
<td>Heart health</td>
</tr>
<tr>
<td>Grapes</td>
<td>Cell protection</td>
<td>Hormone health</td>
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<tr>
<td>Blood oranges</td>
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<td>Liver health</td>
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<tr>
<td>Cranberries</td>
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<td>Cherries</td>
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<td>Grapefruit</td>
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<td>Goji berries</td>
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<td>Pomegranate</td>
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<td>Potatoes</td>
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<td>Radishes</td>
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<td>Raspberries</td>
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<td>Strawberries</td>
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<tr>
<td>Sweet red peppers</td>
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<tr>
<td>Rhubarb</td>
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<td>Rooibos tea</td>
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<td>Tomato</td>
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<td>Watermelon</td>
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## ORANGE

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<tr>
<td>Apricots</td>
<td>Anti-cancer</td>
<td>Reduced mortality</td>
</tr>
<tr>
<td>Bell peppers</td>
<td>Anti-cancer</td>
<td>Reproductive health</td>
</tr>
<tr>
<td>Carrots</td>
<td>Anti-bacterial</td>
<td>Skin health</td>
</tr>
<tr>
<td>Mango</td>
<td>Turmeric root</td>
<td>Source of vitamin A</td>
</tr>
<tr>
<td>Nectarine</td>
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<tr>
<td>Orange</td>
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<td>Papaya</td>
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<td>Penicillmons</td>
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<td>Pumkin</td>
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<td>Squash (aam)</td>
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<td>Sweet potato</td>
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<tr>
<td>Tangerines</td>
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<tr>
<td>Tumeric root</td>
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<tr>
<td>Yuzu</td>
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## YELLOW

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<tbody>
<tr>
<td>Apple</td>
<td>Anti-cancer</td>
<td>Eye health</td>
</tr>
<tr>
<td>Asian pears</td>
<td>Anti-cancer</td>
<td>Heart health</td>
</tr>
<tr>
<td>Banana</td>
<td>Anti-inflammatory</td>
<td>Skin health</td>
</tr>
<tr>
<td>Bell peppers</td>
<td>Cell protection</td>
<td>Vascular health</td>
</tr>
<tr>
<td>Corn</td>
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<tr>
<td>Corn on-cob</td>
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<tr>
<td>Ginger root</td>
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<tr>
<td>Lemon</td>
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<tr>
<td>Millet</td>
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<tr>
<td>Pineapple</td>
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<tr>
<td>Summer squash</td>
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## GREEN

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<tr>
<th>Foods</th>
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</thead>
<tbody>
<tr>
<td>Bok choy</td>
<td>Anti-inflammatory</td>
<td>Skin health</td>
</tr>
<tr>
<td>Broccoli</td>
<td>Anti-inflammatory</td>
<td>Hormone balance</td>
</tr>
<tr>
<td>Broccolini</td>
<td>Brain health</td>
<td>Heart health</td>
</tr>
<tr>
<td>Brussel sproum</td>
<td>Cell protection</td>
<td>Liver health</td>
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<tr>
<td>Cabbage</td>
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<tr>
<td>Celery</td>
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<tr>
<td>Cucumber</td>
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<tr>
<td>Edamame/Soy beans</td>
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<td>Ginger root</td>
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<tr>
<td>Green pear</td>
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<tr>
<td>Green tea</td>
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<tr>
<td>Greens (arugula, bok choy, radicchio, kale, lettuce, mustard, spinach, tomatoes)</td>
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<td>Okra</td>
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<td>Olives</td>
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<td>Peas</td>
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<tr>
<td>Snow peas</td>
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<td>Watercress</td>
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<tr>
<td>Zucchini</td>
<td>Anti-cancer</td>
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## BLUE/PURPLE/BLACK

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<tr>
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</thead>
<tbody>
<tr>
<td>Bell peppers</td>
<td>Anti-cancer</td>
<td>Cognitive health</td>
</tr>
<tr>
<td>Berries (Blue, Black, boysenberries, huckleberries, maravannes)</td>
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</tr>
<tr>
<td>Carrots</td>
<td>Anti-inflammatory</td>
<td>Heart health</td>
</tr>
<tr>
<td>Cabbage</td>
<td>Cell protection</td>
<td>Liver health</td>
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<td>Cigars</td>
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<td>Eggplant</td>
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<tr>
<td>Figs</td>
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<td>Pimientos</td>
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<td>Prunes</td>
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<td>Raisins</td>
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<tr>
<td>Rice (Black or purple)</td>
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<tr>
<td>Shallots</td>
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<tr>
<td>Soy</td>
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<tr>
<td>Tahini</td>
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<tr>
<td>Tea (black, white)</td>
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<tr>
<td>Whole grains</td>
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<tr>
<td>Hazelnut, pine, walnuts</td>
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</tr>
<tr>
<td>Seeds (flax, hemp, pumpkin, sunflower, sunflower)</td>
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<tr>
<td>Spinach, asparagus</td>
<td></td>
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<td>Swede, kale, turnip</td>
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## WHITE/TAN/BROWN

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<tbody>
<tr>
<td>Dates</td>
<td>Anti-cancer</td>
<td>Heart health</td>
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<td>Garlic</td>
<td>Anti-inflammatory</td>
<td>Hormone health</td>
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<tr>
<td>Ginger</td>
<td>Cell protection</td>
<td>Liver health</td>
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<td>Jicama</td>
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<tr>
<td>Leagumes (chickpeas, dried beans or peas, lima beans, lentil, pinto beans, peas)</td>
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<tr>
<td>Mushrooms</td>
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<tr>
<td>Nuts (almonds, walnuts, pecans, peanuts)</td>
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<td>Onion</td>
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<td>Pears</td>
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<tr>
<td>Sauskraut</td>
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<tr>
<td>Seeds (flax, hemp, pumpkin, sunflower, sunflower)</td>
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<tr>
<td>Shallots</td>
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<td>Soy</td>
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<td>Tahini</td>
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<tr>
<td>Tea (black, white)</td>
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<tr>
<td>Whole grains</td>
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<tr>
<td>Hazelnut, pine, walnuts</td>
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<tr>
<td>Seeds (flax, hemp, pumpkin, sunflower, sunflower)</td>
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<tr>
<td>Spinach, asparagus</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Swede, kale, turnip</td>
<td></td>
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</tr>
</tbody>
</table>

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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
Organ Meat = Superfood

<table>
<thead>
<tr>
<th>Minerals (mg/100g)</th>
<th>Kale</th>
<th>Turkey (roasted)</th>
<th>Beef Liver</th>
<th>Beef Heart</th>
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<tbody>
<tr>
<td>Calcium</td>
<td>72</td>
<td>26</td>
<td>6</td>
<td>94</td>
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<tr>
<td>Magnesium</td>
<td>18</td>
<td>25</td>
<td>21</td>
<td>23</td>
</tr>
<tr>
<td>Phosphorus</td>
<td>28</td>
<td>203</td>
<td>497</td>
<td>36</td>
</tr>
<tr>
<td>Potassium</td>
<td>228</td>
<td>280</td>
<td>352</td>
<td>296</td>
</tr>
<tr>
<td>Sodium</td>
<td>23</td>
<td>68</td>
<td>79</td>
<td>30</td>
</tr>
<tr>
<td>Zinc</td>
<td>0.24</td>
<td>2.96</td>
<td>5.3</td>
<td>0.31</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Vitamins (per 100g)</th>
<th>Kale</th>
<th>Turkey roasted</th>
<th>Beer Liver</th>
<th>Beef Heart</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vitamin C, mg</td>
<td>41</td>
<td>0</td>
<td>1.9</td>
<td>53.3</td>
</tr>
<tr>
<td>Thiamin mg</td>
<td>0.053</td>
<td>0.057</td>
<td>0.194</td>
<td>0.069</td>
</tr>
<tr>
<td>Riboflavin mg</td>
<td>0.07</td>
<td>0.177</td>
<td>3.425</td>
<td>0.091</td>
</tr>
<tr>
<td>Niacin mg</td>
<td>0.5</td>
<td>5.088</td>
<td>17.525</td>
<td>0.65</td>
</tr>
<tr>
<td>Vitamin mg B-6</td>
<td>0.138</td>
<td>0.41</td>
<td>1.017</td>
<td>0.179</td>
</tr>
<tr>
<td>Folate, mcgDFE</td>
<td>13</td>
<td>7</td>
<td>253</td>
<td>17</td>
</tr>
<tr>
<td>Vitamin B-12µg</td>
<td>0</td>
<td>0.35</td>
<td>70.58</td>
<td>0</td>
</tr>
<tr>
<td>Vitamin A, RAE</td>
<td>681 mcg</td>
<td>0</td>
<td>9442 mcg</td>
<td>885 mcg</td>
</tr>
<tr>
<td>Vitamin A, IU</td>
<td>13621 *</td>
<td>0.34</td>
<td>31714</td>
<td>17707</td>
</tr>
<tr>
<td>Vitamin E mg (alpha-tocopherol)</td>
<td>0.85</td>
<td>0</td>
<td>0.51</td>
<td>1.1</td>
</tr>
<tr>
<td>Vitamin K1 µg (phyloquinone)</td>
<td>817 (K1)</td>
<td>1.3</td>
<td>3.3 (K2)</td>
<td>0.5</td>
</tr>
</tbody>
</table>
Grass-fed Meats, Organ Meats, and Wild Fish
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 affect individual vitamin A status.

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 mutations: 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.
EFAs Mediate Cognitive Function and Brain Biochemistry

- FA 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 3.4:1 (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
## Nutrition Takeaways

<table>
<thead>
<tr>
<th>Assessment</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>IFM DNL journal</td>
<td>• Modified paleo OR MCT keto</td>
</tr>
<tr>
<td>Homocysteine</td>
<td>• Both $\omega-6$ and $\omega-3$ fats</td>
</tr>
<tr>
<td>B12, folate</td>
<td>• Meat</td>
</tr>
<tr>
<td>A1c, insulin</td>
<td>– Grass fed / wild / organ</td>
</tr>
<tr>
<td></td>
<td>• Vegetables</td>
</tr>
<tr>
<td></td>
<td>– 6-9 cups / day</td>
</tr>
<tr>
<td></td>
<td>– Greens</td>
</tr>
<tr>
<td></td>
<td>– Color</td>
</tr>
<tr>
<td></td>
<td>– Brassica, Allium, Mushrooms</td>
</tr>
<tr>
<td></td>
<td>• Seaweed, ferments</td>
</tr>
</tbody>
</table>
# Diet, Nutrition, and Lifestyle Journal

## 1 Day

<table>
<thead>
<tr>
<th>Day Event</th>
<th>Food &amp; Drink Intake (Include type, amount, brand)</th>
<th>Macronutrients (PFC) and Phytonutrients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Raising Time</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Breakfast Time</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mid-AM Snack Time</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lunch Time</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mid-PM Snack Time</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dinner Time</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PM Snack Time</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bed Time</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Sleep & Relaxation

<table>
<thead>
<tr>
<th>Time</th>
<th>Type</th>
<th>Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sleep</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Quantity:</td>
<td>(hours)</td>
<td></td>
</tr>
<tr>
<td>Quality:</td>
<td>Poor</td>
<td>Fair</td>
</tr>
<tr>
<td>Relaxation</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Time</td>
<td>Type</td>
<td>Amount</td>
</tr>
<tr>
<td>Mental</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Emotional</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Exercise & Movement

<table>
<thead>
<tr>
<th>Time</th>
<th>Type</th>
<th>Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sleep</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Quantity:</td>
<td>(hours)</td>
<td></td>
</tr>
<tr>
<td>Quality:</td>
<td>Poor</td>
<td>Fair</td>
</tr>
<tr>
<td>Relaxation</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Time</td>
<td>Type</td>
<td>Amount</td>
</tr>
<tr>
<td>Mental</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Emotional</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Stress

- Reduce: Aerobic
- Reduce: Strength

### Relationships

- Supporting
- Non-supporting
Nutrition Takeaways

Assessment
• Diet Diary
• GI symptoms from ROS

Treatment
• Food as discussed
• 5R Treatments
Role of the Microbiota in Immunity and Inflammation

Diet, Microbiota and Autoimmune Diseases

The role of microbiome in central nervous system disorders.

Diet rapidly and reproducibly alters the human gut microbiome.

Microbiome and Myelination

“The microbiome is necessary for appropriate and dynamic regulation of myelin-related genes.

The microbiota is therefore a potential therapeutic target for psychiatric disorders involving dynamic myelination in the PFC.” (Pre-Frontal Cortex)

AE Hoban, RM Stilling, FJ Ryan, F Shanahan, TG Dinan, MJ Claesson, G Clarke, and JF Cryan. Regulation of prefrontal cortex myelination by the microbiota. Translational Psychiatry (2016) 6, e774; doi:10.1038/tp.2016.42
Microbiome and MS

- 20 MS patients
- 40 Controls
- Depletion of clostridia species related to priming the regulatory Th17 cells
- Loss of T regulatory cells / tolerance

Multiple Sclerosis patients have gut dysbiosis

- **MS (n=31)**
  More Psuedomonas, Mycoplana, Haemophilus, Blautia, and Dorea

- **Control (n=36)**
  more Parabacteroide s, Adlercreutzia and Prevotella

Miyake S. *Dysbiosis in the Gut Microbiota of Patients with Multiple Sclerosis, with a Striking Depletion of Species Belonging to Clostridia XIVa and IV Clusters.* PLoS One. 2015 Sep 14;10(9):e0137429.
<table>
<thead>
<tr>
<th>Type</th>
<th>Description</th>
<th>Condition</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Separate hard lumps</td>
<td>Very constipated</td>
</tr>
<tr>
<td>2</td>
<td>Lumpy and sausage like</td>
<td>Slightly constipated</td>
</tr>
<tr>
<td>3</td>
<td>A sausage shape with cracks in the surface</td>
<td>Normal</td>
</tr>
<tr>
<td>4</td>
<td>Like a smooth, soft sausage or snake</td>
<td>Normal</td>
</tr>
<tr>
<td>5</td>
<td>Soft blobs with clear-cut edges</td>
<td>Lacking fibre</td>
</tr>
<tr>
<td>6</td>
<td>Mushy consistency with ragged edges</td>
<td>Inflammation</td>
</tr>
<tr>
<td>7</td>
<td>Liquid consistency with no solid pieces</td>
<td>Inflammation</td>
</tr>
</tbody>
</table>
Microbiome Takeaways

Assessment
• Bristol Stool Chart

Treatment
• Microbiome diversity
• Vegetable fiber (Not potato starch)
• Psyllium
Mitochondrial Energy

Environmental factors
- Energy resources
- Energy demands
- Toxins

mtDNA variation
- Ancient adaptive polymorphisms
- Recent deleterious mutations

nDNA variation
- Deleterious mutations
- Polymorphisms
- Epigenomic changes

OXPHOS dysfunction
- Decreased energy, increased ROS, altered REDOX regulation of gene expression and metabolism, altered calcium homeostasis

Mitochondrial damage and somatic mtDNA mutations

Immunological disease
- Infection
- Inflammation
- Fever
- Autoimmunity

Progressive bioenergetic decline

Metabolic disease
- Diabetes and obesity
- Thermoregulation stress and trauma

Cancer
- Initiation
- Promotion
- Metastasis

Degenerative disease
- Neurological
- Muscular
- Cardiac
- Renal
- Gastrointestinal

Aging
- Apoptosis
- Senescence

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

- 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.
Ketosis vs. Low Glycemic Index

• Arctic dwellers have a summer season

• Problems with long-term ketosis:
  – It is difficult to sustain
  – Increases risk for nutrient deficiencies, microbiome issues, hormone disruptions.

Terry’s Opinion and Experience


Mitochondria Energy Takeaways

**Assessment**
- History
- (Optional) Blood Ketosis monitoring

**Treatment**
- Low-Glycemic Index
- Ketogenic (MCT)
- 60-80 g / carbs
- MCT/ Coconut oil
- Avoid dairy-based ketogenic based diets (CHO too low).
Pesticides and Neurodegeneration

- PD, AD and ALS Risk factors: Pesticides (e.g. paraquat, maneb, dieldrin, pyrethroids, organo-phosphates, glyphosate)
- These pesticides share common features:
  - Induce oxidative stress
  - Induce mitochondrial dysfunction
  - Promote α-synuclein fibrillization
  - Cause neuronal cell death


Parkinson’s & Parkinsonian: 
*It’s not just Pesticides Anymore*

- Pesticides have repeatedly been identified as risk factors for PD
- Non-pesticide contaminants: metals, solvents, PCBs, other halogenated organic compounds are also implicated

Deaths from Parkinson's disease (ICD G20 & 332.0)
plotted against glyphosate use on corn & soy ($R = 0.9006$, $p \leq 5.063e-07$)
and percent GE corn & soy planted ($R=0.9676$, $p \leq 2.714e-06$)
sources: USDA: NASS; CDC

Biotransformation

“Our findings suggest that simvastatin inhibits central nervous system remyelination by blocking progenitor differentiation.”

# Toxin Exposure Questionnaire (TEQ-20)

**Patient Name**: ___________________________  
**Date**: ___________________________

**Please check YES or NO for each of the following questions. Your provider will discuss your answers with you.**

<table>
<thead>
<tr>
<th>QUESTIONS</th>
<th>YES</th>
<th>NO</th>
</tr>
</thead>
</table>
| 1. Do you consume conventionally grown (non-organic) fruits and vegetables regularly?  
If so, which ones do you eat most often? |     |    |
| 2. Do you consume conventionally raised animal products (meat, dairy, eggs) regularly?  
If so, which ones do you eat most often? |     |    |
| 3. Do you consume fish or seafood more than twice a week? If so, please describe what you eat and whether it is farmed or wild. |     |    |
| 4. Do you consume fast foods, canned/packaged foods, soda, or foods with artificial colors, flavor, preservatives or sweeteners more than three times a week? |     |    |
| 5. Have you lived in a mobile home, boat, or RV, or in a very old or brand-new home?  
If so, please describe: |     |    |
| 6. Have you recently been exposed to new construction materials or furniture (e.g., paint, laminate flooring, particle board, new carpeting, bedding, furniture, etc.)? |     |    |
| 7. Does your home or workplace have cracking paint or decaying insulation or foam, visible mold, water damage, or damp windows, basement, or crawlspaces? |     |    |
| 8. Are you often exposed to adhesives, paints, flea treatments, varnishes, solvents, welding/soldering materials, or other air-borne chemicals at home or work? |     |    |
| 9. Have you been exposed to treated lumber, lead paint, paint chips or dust, broken mercury thermometers or fluorescent bulbs, or other toxic substances you know of? |     |    |
| 10. Do you drink water from a well, spring, or cistern, or from plumbing pipes or fixtures installed before 1986? |     |    |
| 11. Do you regularly use conventional cleaning chemicals, disinfectants, air fresheners, scented candles, or other scented products at home or work? |     |    |
| 12. Are your health concerns related to time spent living or working adjacent to a highway, factory, incinerator, gas station, power plant, or other industrial pollution source? |     |    |
| 13. Have you lived in an agricultural area or often been exposed to herbicides, pesticides, fungicides at home, work, parks & golf course, or roadside? |     |    |
| 14. Do you live near a cell phone tower, high-voltage power lines, or other known source of electromagnetic radiation? |     |    |
| 15. Do you live or work in a sealed building with recirculated air or a building that has wood, propane, or gas stoves or appliances? |     |    |
| 16. Do you smoke or are often exposed to second-hand smoke, fly often, or run or bike to work along busy streets? |     |    |
| 17. Are you highly sensitive to smoke, perfumes, fragrances, cleaning products, gasoline, or other fumes?  
If so, please explain: |     |    |
| 18. Have you had root canals, tooth extractions, "silver" fillings, crowns, dental sealants, dentures, retainers, aligning trays, braces, mouth guards, dental implants, etc.? |     |    |
| 19. Have you had any unusual reactions to anesthesia or to prescription or over-the-counter medications?  
If so, please describe: |     |    |
| 20. Do you have a history of heavy use of alcohol or recreational or prescription drugs?  
If so, please describe or discuss with your provider: |     |    |
Biotransformation & Elimination Takeaways

Assessment
• Assume inefficient detox enzymes
• Use the IFM TEQ-20
• (Optional) SNP testing
• (Optional) Body Burden testing

Treatment
• Fix the gut
• Brassica, Allium
• Curcumin
• Algae
• Intermittent charcoal, clay, zeolite
• Saunas if tolerated
Stem Cells

• Trophic support to our stems cells needed
• Diet, exercise, stress all communicate to our stem cells via microglia
• Lion’s Mane mushrooms stimulate nerve growth factor production (BDNF).
  • Hericium erinaceus

Stem Cell Takeaways

Assessment
• Use DNL Journal
• Cortisol, sex steroids, thyroid hormones as needed

Treatment
• Exercise
• Sleep
• Stress reducing activities
• Optimize nutrition
• Lion’s Mane mushrooms
• Correct persisting hormonal imbalances
Traumatic Brain Injury (TBI)

TBI is associated with:

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

- **Terry’s Take Home:** Left unaddressed, Brain, GI and systemic symptoms can be expected to persist and/or worsen with TBI.

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)

TBI and Omega-3 Fatty Acids

- N-3s in severe TBI (comatose) after MVI
- Glasgow coma score 3
- Patient was Not expected to survive
- DAY 10 began: 15 ml twice a day (30ml/day); 9,756 mg EPA, 6,756 mg DHA, and 19,212 mg total n-3FA daily
- Patient was Not on fish oil previously

TBI and Omega-3 Fatty Acids

• 3-months after injury attended his high school graduation.
• 4-months after injury, discharged to home.
• Three years – working with athletic trainer.
• Four years – has a small business.

Acute Traumatic Brain Injury

- Brain Health Education Non-profit
- Printable protocol
- Acute injury through maintenance
- NOT on fish oil prior to injury
- Check EPA/AA membrane ratio
- www.brainhealtheducation.org

If you've been diagnosed with a concussion or other head injury,

CLICK HERE TO READ THE

Omega-3 Protocol
Traumatic Brain Injury
Chronic Traumatic Encephalopathy

- For patients with repeated concussions
- Worsening psychiatric, motor, sensory symptoms, must be taken seriously
- Increases risk for Chronic Traumatic Encephalopathy (CTE)
  - Acute Tx: Lipid therapy, intensive nutrition, antioxidants, fiber
  - Long Term Tx: Address the matrix
Rebuild Myelin

• Conventional neuroprotective approaches for CNS regeneration have generally not been successful.

• Cytidine 5’diphosphocholine (CDP) choline had beneficial effects on myelin, oligodendrocytes and axons.

• CDP-choline enhanced myelin regeneration through an increase in oligodendrocyte precursor cells and oligodendrocytes.

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

Structural Takeaways

Assessment
• RBC AA:DHA ratios
• Concussion history
• Nutritional status
• Is patient at risk for CTE?

Treatment
• For Acute TBI
  – Fish oil, matrix
• For Remyelination
  – CPD Choline  500 mg to 1 gram bid
  – Or PC 1 to 4 tbs day as liposomes
Martin Seligman: The new era of positive psychology

• Seligman’s conclusion is that happiness has three dimensions that can be cultivated.

Martin Seligman. The Pursuit of Happiness
http://www.pursuit-of-happiness.org/history-of-happiness/martin-seligman-positive-psychology
Martin Seligman: The Pursuit of Happiness

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.
“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
What was I going to model for them
Changing the Narratives

I could still model resilience to my kids
Introduction to Clinical Medicine

• Cased-based learning in small groups

• 4 weekly discussions

• Capstone lecture
“Patient experience through the eyes of a physician colleague”

My MD colleagues thought it was crazy

Became the highest rated lecture in medical school

This was another key step in my recovery
I Changed My Narrative

• Still no hope of cure or recovery – but I choose to seek and find meaning in my life as it was going to unfold
Hero’s Journey

- Society faces an adversary and is losing
- The hero separates and learns some key truths
- Returns to society to re-engage in the ‘fight’
- **ASK:** What is your Hero’s Journey?
Resilience Factors
Mental-Emotional-Spiritual Takeaways

Assessment
• Identify Learned Helplessness
• Ask about pts higher purpose
• Ask about the meaning of their illness experience ("honoring the symptoms")

Treatment
• Cognitive behavioral Tx
Multimodal intervention improves fatigue and quality of life in subjects with progressive multiple sclerosis: a pilot study

Babita Bisht, Warren G Darling, E Torage Shivapour, Susan K Lutgendorf, Linda S Smetzelaar, Catherine A Chenard, Terry L Wahls

Department of Internal Medicine, Carver College of Medicine, University of Iowa, Department of Health and Human Physiology, College of Liberal Arts and Sciences, University of Iowa, Department of Neurology, Carver College of Medicine, University of Iowa, Department of Obstetrics and Gynecology, Carver College of Medicine, University of Iowa, Department of Urology, Carver College of Medicine, University of Iowa, Department of Epidemiology, College of Public Health, University of Iowa, 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 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 11 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=0.56, 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
Modified Paleolithic Diet

Home Exercise Program
  + Neuromuscular Electrical Stimulation

Vitamins & Nutritional supplements

Stress Management

Multimodal Intervention
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

US Diet
Wahls*

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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)
Subjects’ intake of recommended and excluded foods during the study
Multimodal intervention improves fatigue and quality of life in subjects with progressive multiple sclerosis: a pilot study

![Graph showing improvement in scores over time with statistical significance markers.]

- **p<0.0005
- *p<0.05

Scores

- SF-36 general health
- SF-36 energy
- FSS

\( r = -0.968, p = 0.003 \)

Degenerative Neurological and Neuromuscular Disease 2015:5
Subject 17- Baseline and 3 Month Walk

PPMS
TUG-21 sec.
FSS-6.7
Subject 17- Baseline and 3 Month Walk

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
Subject 11- Baseline and 3 Month Walk

SPMS
TUG- 8.6 sec.
FSS-1.4
Subject 11- Jogging & Jumping at 6 months
Subject 11- Jogging & Jumping at 6 months
Reversal of cognitive decline: A novel therapeutic program

Dale E. Bredesen

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Key words: Alzheimer’s, dementia, mild cognitive impairment, neurobehavioral disorders, neuroinflammation, neurodegeneration, systems biology

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Abstract: This report describes a novel, comprehensive, and personalized therapeutic program that is based on the underlying pathogenesis of Alzheimer’s disease, and which involves multiple modalities designed to achieve metabolic enhancement for neurodegeneration (MEND). The first 10 patients who have utilized this program include patients with memory loss associated with Alzheimer’s disease (AD), amnestic mild cognitive impairment (aMCI), or subjective cognitive impairment (SCI). Nine of the 10 displayed subjective or objective improvement in cognition beginning within 3–6 months, with the one failure being a patient with very late stage AD. Six of the patients had to discontinue working or were struggling with their jobs at the time of presentation, and all were able to return to work or continue working with improved performance. Improvements have been sustained, and at this time the longest patient follow-up is two and one-half years from initial treatment, with sustained and marked improvement. These results suggest that a larger, more extensive trial of this therapeutic program is warranted. The results also suggest that, at least early in the course, cognitive decline may be driven in large part by metabolic processes. Furthermore, given the failure of monotherapeutics in AD to date, the results raise the possibility that such a therapeutic system may be useful as a platform on which drugs that would fail as monotherapeutics may succeed as key components of a therapeutic system.

INTRODUCTION

Magnitude of the problem

Cognitive decline is a major concern of the aging population, and Alzheimer’s disease is the major cause of age-related cognitive decline, with approximately 5.4 million American patients and 30 million affected globally[1]. In the absence of effective prevention and treatment, the prospects for the future are of great concern, with 13 million Americans and 160 million globally projected for 2050, leading to potential bankruptcy of the Medicare system. Unlike several other chronic illnesses, Alzheimer’s disease prevalence is on the rise, which makes the need to develop effective prevention and treatment increasingly pressing. Recent estimates suggest that AD has become the third leading cause of death in the United States [2], behind cardiovascular disease and cancer. Furthermore, it has been pointed out recently that women are at the epicenter of the Alzheimer’s epidemic, with 65% of patients and 60% of caregivers being women [3]. Indeed, a woman’s chance of developing AD is now greater than her chance of developing breast cancer [4].

Failure of monotherapeutics

Neurodegenerative disease therapeutics has been, arguably, the field of greatest failure of biomedical therapeutics development. Patients with acute illnesses such as infectious diseases, or with other chronic illnesses, such as cardiovascular disease, osteoporosis, human immunodeficiency virus infection, and even cancer, have access to more effective therapeutic options than do patients with AD or other neurodegenerative diseases such as Lewy body disease.
Small Mutation 7 Million Years Ago

Gibbon  Human  Chimpanzee  Gorilla  Orangutan
Evolutionary Advantage ApoE4

• 7,000,000 – AoE4 (96% history)
  – Carries fat
  – 1700 genes impacted
  – Ramps up NFkappaB, NGF, apoptosis, microtubules – infection risk, thinking, survival

• 200,000 – AoE3

• 80,000 – ApoE2

• All “Pre-agriculture”
# APOE Status and Alzheimer’s risk

<table>
<thead>
<tr>
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</thead>
<tbody>
<tr>
<td>Disease risk</td>
<td>40% less likely</td>
<td>40% less likely</td>
<td>2.6 X more likely</td>
<td>Average risk</td>
<td>3.2 times more likely</td>
<td>14.9 times more likely</td>
</tr>
</tbody>
</table>

# APOE Status and Alzheimer’s risk

<table>
<thead>
<tr>
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</tr>
</thead>
<tbody>
<tr>
<td>Disease risk</td>
<td>40% less likely</td>
<td>40% less likely</td>
<td>Average risk</td>
<td>2.6 X more likely</td>
<td>3.2 times more likely</td>
<td>14.9 times more likely (90%)</td>
</tr>
</tbody>
</table>

### 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, CRF, stress axis.</td>
</tr>
<tr>
<td>Optimize sleep</td>
<td>8 hr sleep per night; melatonin 0.5mg po qhs; Trp 500mg po 3x/wk if awakening. Exclude sleep apnea.</td>
<td></td>
</tr>
<tr>
<td>Exercise</td>
<td>30-60' per day, 4-6 days/wk</td>
<td></td>
</tr>
<tr>
<td>Brain stimulation</td>
<td>Posit or related</td>
<td></td>
</tr>
<tr>
<td>Homocysteine &lt; 7</td>
<td>Me-B12, MTHF, PSP; TMG if necessary</td>
<td></td>
</tr>
<tr>
<td>Serum B12 &gt; 500</td>
<td>Me-B12</td>
<td></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>
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<tr>
<td>Hormone balance</td>
<td>Optimize T3, T4, E2, T, progesterone, pregnenolone, cortisol</td>
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</tr>
<tr>
<td>GI health</td>
<td>Repair if needed; prebiotics and probiotics</td>
<td>Avoid inflammation, autoimmunity</td>
</tr>
<tr>
<td>Reduction of Aβ</td>
<td>Curcumin, Ashwagandha</td>
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</tr>
<tr>
<td>Cognitive enhancement</td>
<td>Bacopa, monniera, MgT</td>
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</tr>
<tr>
<td>25OH-D3 = 50-100ng/ml</td>
<td>Vitamins D3, K2</td>
<td></td>
</tr>
<tr>
<td>Increase NGF</td>
<td>H. erinaceus or ALCAR</td>
<td></td>
</tr>
<tr>
<td>Provide synaptic structural components</td>
<td>Citicoline, DHA</td>
<td></td>
</tr>
<tr>
<td>Optimize antioxidants</td>
<td>Mixed tocopherols and tocotrienols, Se, blueberries, NAC, ascorbate, a-lipoic acid</td>
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</tr>
<tr>
<td>Optimize Zn:Fe ratio</td>
<td>Depends on values obtained</td>
<td></td>
</tr>
<tr>
<td>Ensure nocturnal oxygenation</td>
<td>Exclude or treat sleep apnea</td>
<td></td>
</tr>
<tr>
<td>Optimize mitochondrial function</td>
<td>CoQ or ubiquinol, a-lipoic acid, PQQ, NAC, ALCAR, Se, Zn, resveratrol, ascorbate, thiamine</td>
<td></td>
</tr>
<tr>
<td>Increase focus</td>
<td>Pantothenic acid</td>
<td>Acetylcholine synthesis requirement</td>
</tr>
<tr>
<td>Increase SirT1 function</td>
<td>Resveratrol</td>
<td></td>
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<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 Axona</td>
<td></td>
</tr>
</tbody>
</table>

**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, methylene tetrahydrofolate; PSP, pyridoxal-5-phosphate; TMG, trimethylglycine; Trp, tryptophan.**
TBI Clinic

- Interdisciplinary - Speech Path, SW, Psychiatry, PM&R, Primary Care, Neuropsychology
- **20 minutes with patient**
- **No labs**
- Seen every 6 months
- Blast exposure and current neuropsychiatric symptoms
• 32 y/o WM deployed X 3
• Multiple IEDs, dazed 2007 x2
• 1 LOC brief, dazed for hours 2008
• Issues – HA, poor memory, hypervigilant, can’t get along, fatigue, back pain, ↑ 80lbs, nightmares, marriage failing, flunking out
TBI

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

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

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

• Modified Paleo diet
  – (9 cups – Greens, sulfur, color)
  – Organ meat

• Cut out energy drinks / caffeine

• Walking

• Epsom salts soak

• Stress reducing activity of choice
Outcome

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

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

- CBC, Creatinine, hs-CRP, Lipids, 25-OH Vitamin D, Homocysteine, B12, folate
Neuropathy Case

- Referred from Pain clinic
- Progressive Neuropathic Pain
- Neuromas
- Contemplating Suicide
Neuropathic Pain
10 vets in class + spouses

- 55 y/o WM S/p BKA (military), nerve stimulators not controlling pain any more, multiple ER visits, continual electrical pain
- PMH hx of substance abuse, depression, obesity, hyperlipidemia, HTN, asthma, constipation,
- Supportive wife
- MSQ score 64
<table>
<thead>
<tr>
<th>Timeline / Matrix</th>
</tr>
</thead>
<tbody>
<tr>
<td>• FH brain, heart and autoimmune issues</td>
</tr>
<tr>
<td>• 20 + antibiotics as a child and young adult</td>
</tr>
<tr>
<td>• Pesticides (farm)</td>
</tr>
<tr>
<td>• Solvent exposure (work)</td>
</tr>
<tr>
<td>• Frequent steroid use (asthma)</td>
</tr>
<tr>
<td>• Very poor sleep (pain)</td>
</tr>
<tr>
<td>• No exercise (pain)</td>
</tr>
<tr>
<td>• Comfort food =↑Sugar, white flour, no vegetables</td>
</tr>
<tr>
<td>• Sober 22 years with AA</td>
</tr>
</tbody>
</table>
Labs/ Intervention

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

• Reports 100% GF, DF, Sugar free
• Using smoothies “to get the 9 cups in”
• Swimming 3x week
• Pain much more manageable
• Sleep is good
• Mood much better
• Family life even better
• MSQ 11
Interrupting treatments that have been working predictably causes rebound relapses. This is true with drugs and modifiable lifestyle factors (MLF).

If a patient wants to transition from drug interventions to MLF interventions, you must employ MLF for at least 6 months with good effect before even attempting to gradually reduce the drug therapy.
NMSS funded Clinical Trial

- Relapsing-remitting MS with fatigue, living in the Midwest
- Dietary Approaches to Treating MS Related Fatigue

MSDietStudy@healthcare.uiowa.edu
Catherine-chenard@uiowa.edu
Summary

• From Wahls and Bredesen papers


• Bisht B, Darling WG, Shivapour ET, Lutgendorf SK, Snetselaar LG, Chenrad CA TL. Multimodal intervention improves quality of life in subjects with progressive MS. Degenerative Neurological and Neuromuscular Disease 2015, 5:91-92
## 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>
<tr>
<td>Reduce stress</td>
<td>Personalized—yoga or meditation or music, etc. TW gardening, fishing, hunting, Epsom salts</td>
</tr>
<tr>
<td>Improve relationships</td>
<td>TW — create social connections</td>
</tr>
<tr>
<td>Goal</td>
<td>Approach</td>
</tr>
<tr>
<td>--------------</td>
<td>--------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Exercise</td>
<td>30-60’ per day, 4-6 days/wk</td>
</tr>
<tr>
<td>TW – strength training, balance training, High intensity interval training, PT or OT referral, consider adding NMES=Electrical stimulation of muscles</td>
<td></td>
</tr>
<tr>
<td></td>
<td>DO NOT over train</td>
</tr>
<tr>
<td>Goal</td>
<td>Approach</td>
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<tr>
<td>-------------------------------------------</td>
<td>--------------------------------------------------------------------------</td>
</tr>
<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 TW – 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 TW Phosphatidylcholine, organ meats, cod liver oil</td>
</tr>
<tr>
<td>Goal</td>
<td>Approach</td>
</tr>
<tr>
<td>-----------------------------</td>
<td>--------------------------------------------------------------------------</td>
</tr>
<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.</td>
</tr>
<tr>
<td></td>
<td>Floss teeth, add mushrooms, vitamin D, K2mk7</td>
</tr>
</tbody>
</table>
# Mitochondria Energy

<table>
<thead>
<tr>
<th>Goal</th>
<th>Approach</th>
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</thead>
<tbody>
<tr>
<td>Enhance autophagy, ketogenesis</td>
<td>Fast 12 hr + each night, including 3 hr prior to bedtime, longer fasts</td>
</tr>
</tbody>
</table>
| 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                                                 |
# Biotransformation

<table>
<thead>
<tr>
<th>Goal</th>
<th>Approach</th>
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</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>TW – ↑ bacterial biotransformation</td>
<td>TW – ↑ fiber to 2-3 soft BM day</td>
</tr>
<tr>
<td>TW correct nutrient mineral lacks</td>
<td>TW nutrient minerals, stomach acid, sea salt, soaks in Epsom salts, sodium bicarbonate</td>
</tr>
<tr>
<td>Goal</td>
<td>Approach</td>
</tr>
<tr>
<td>-------------------------------------------</td>
<td>----------------------------------------------</td>
</tr>
<tr>
<td>Optimize hormone balance</td>
<td>Optimize fT3, fT4, E2, T, progesterone, pregnenolone, cortisol.</td>
</tr>
<tr>
<td><strong>TW</strong> optimize progenitor (stem cells)</td>
<td><strong>TW</strong> – 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 <strong>TW</strong> – brain age, lumosity, juggling, do not over train</td>
</tr>
</tbody>
</table>
### Other Interventions

<table>
<thead>
<tr>
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<th>Approach</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serum B12 &gt;500 TW – prefer top quartile of ref. range</td>
<td>Me-B12 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) 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>
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## Other Interventions

<table>
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<tr>
<th>Goal</th>
<th>Approach</th>
</tr>
</thead>
<tbody>
<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>
NMSS funded Clinical Trial

- Relapsing-remitting MS with fatigue, living in the Midwest
- Dietary Approaches to Treating MS Related Fatigue

MSDietStudy@healthcare.uiowa.edu
Catherine-chenard@uiowa.edu
**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.
- **Addendum A** has more on 5 critical β-carotene SNPs.


**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.
BCMO1 SNPs & β-carotene Conversion

- **A379V; rs7501331 (C>T)** 24% Allele frequency
- **R267S; rs12934922 (A>T)** 42% Allele frequency
- **379V alone = 32% decreased efficiency**
- **379V + 276S = -69% decreased efficiency**

SNPs Upstream from BCMO1 and β-carotene conversion

FIGURE 1  TRL response and baseline plasma concentration in 28 female volunteers depending on genotype. TRL retinyl palmitate:β-carotene ratios and baseline fasting plasma b-carotene concentrations after intake of a b-carotene-rich meal (120 mg) in 28 female volunteers depending on genotype. Data are displayed as mean ± SEM. * Different from other homozygous allele at P < 0.05; ** different from other homozygous allele at P < 0.01 (ANOVA). Black square, reference allele; white square, other allele. rs6420424 was analyzed using rs12597639 as the tag SNP. #, no SEM due to small n. BCMO1, b-carotene 15,15'-monooxygenase; SNP, single nucleotide polymorphism; TRL, TG-rich lipoprotein fraction.

β-carotene SNP Summary

- rs7501331 (C>T); T Decrease 32%
  CT incidence = 39%, TT incidence = 5%
- rs7501331 + rs12934922 (A>T); Decrease 69%
  AT incidence = 40%, TT incidence = 22%
- rs6420424 (G>A); AA Decrease 59%
  A allele frequency = 45%
- Rs11645428 (A>G); GG Decrease 51%
  G allele frequency = 71% (i.e. most people are GG)
- rs6564851 (T>G); GG Decrease 48%
  G allele frequency = 48%


How Do You Use this Data?

Load your raw SNP data file to Interpretome.com (free), and lookup the specific rs tags:

1. rs7501331
2. rs12934922
3. rs6420424
4. rs11645428
5. rs6564851

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<th>Genotype</th>
<th>Reference</th>
<th>Reference Frequency</th>
<th>Alternate</th>
<th>Alternate Frequency</th>
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<td>C</td>
<td>0.707</td>
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</tr>
<tr>
<td>6564851</td>
<td>TT</td>
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<td>G</td>
<td>0.563</td>
<td>16</td>
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