Diet: Neurodegeneration and Neuro-Restoration

Dr. Terry Wahls
University of Iowa
The Wahls Institute PLC
Disclosures

Terry Wahls, MD grant support – Direct MS, National MS Society

In kind support DJO Inc., Pinnaclife Inc., TZ Press LLC

Book Royalties: Minding My Mitochondria; The Wahls Protocol, Cooking for Life

Equity Interest: TZ Press LLC, Dr. Terry Wahls LLC, The Wahls Institute PLC

Website: www.terrywahls.com
7 years of steady decline due to MS
Fish oil, creatine and co-enzyme Q 10


The Paleo Diet

Loren Cordain, Ph.D.
author of The Paleo Diet Cookbook

Over 100,000 copies sold!
7 Year conventional therapy

1 Year FM therapy

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Case report

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

David Reese¹,², ET Shivapour³, Terry L Wahls⁴,⁵,⁶*, Shauna D Dudley-Javoroski² and Richard Shields²

Addresses: ¹Performance Therapies, PC, Ridgeway Drive, Coralville, Iowa, USA
²Department of Physical Therapy, University of Iowa Carver College of Medicine, Iowa City, Iowa, 52246, USA
³Department of Neurology, University of Iowa Carver College of Medicine, 200 Hawkins Drive, Iowa City, Iowa, 52246, USA
⁴Veterans Administration (VA), Iowa City VA Medical Center, 601 Highway 6 West, Iowa City, Iowa, 52246, USA
⁵Center for Research in the Implementation of Innovative Strategies in Practice (CRIISP) VA HSR&D Center of Excellence, Iowa City VA Medical Center, 601 Highway 6 West, Iowa City, Iowa, 52246, USA
⁶Division of General Medicine, Department of Internal Medicine, University of Iowa Carver College of Medicine, 200 Hawkins Drive, Iowa City, Iowa, 52246, USA

Email: DR - DReese@pentrex.com; ETS - et-shivapour@uiowa.edu; TLW - Terry.Wahls@va.gov; SD - shauna-dudley@uiowa.edu; RS - richard-shields@uiowa.edu

* Corresponding author

Received: 5 May 2009   Accepted: 17 July 2009   Published: 2009


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

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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)
World map illustrating the global distribution of deaths caused due to Alzheimer’s Disease/Dementia. WHO 2011.
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 aims of this study were to investigate the efficacy 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 an Expanded Disability Status Scale (EDSS) score of 4.2 (range: 3.3-5.0) 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 analysis at 1 month, 3 months, 6 months, 9 months, and 12 months.

Results: Subjects showed good adherence (mean ± SD) with this intervention and did not report any serious side effects. Fatigue Severity Scale (FSS) and Performance Status Scale-fatigue subscale scores decreased in 12 months (P<0.0003). Average FSS scores of eleven subjects showed clinically significant reduction (more than two points, high response) at 3 months, and this improvement was maintained 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=0.31, P=0.01), and lower baseline Patient-Reported Outcome (PRO) scales (r=0.36, P=0.003) and EDSS score (r=0.36, P=0.01). Compared to low responders, high responders had lower level of physical disability (P=0.05) and lower levels of fatigue, energy, productivity, and mood (P=0.05) at baseline. High responders underwent longer duration of massage and stretches per week (P=0.05) in 12 months.

Conclusions: A multimodal intervention may reduce fatigue and improve quality of life of subjects with progressive MS. Larger randomized controlled trials with blinded scores 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
Subject 3- Baseline and 12 Month Walk
Subject 3- Stair Climbing at 12 months
### Effects of nutrients (in food) on the structure and function of the nervous system

<table>
<thead>
<tr>
<th>36 Key Nutrients - Food First</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Vitamin A, retinol</strong></td>
</tr>
<tr>
<td><strong>Vitamin B₁ (thiamine)</strong></td>
</tr>
<tr>
<td><strong>Vitamin B₂ (riboflavin)</strong></td>
</tr>
<tr>
<td><strong>Vitamin B₃ (niacin)</strong></td>
</tr>
<tr>
<td><strong>Vitamin B₅ (Pantothenic acid)</strong></td>
</tr>
<tr>
<td><strong>Vitamin B₆ (pyridoxine)</strong></td>
</tr>
<tr>
<td><strong>Vitamin B₉ (folic acid)</strong></td>
</tr>
<tr>
<td><strong>Vitamin B₁₂ (cobalamin)</strong></td>
</tr>
<tr>
<td><strong>Vitamin C</strong></td>
</tr>
<tr>
<td><strong>Vitamin D</strong></td>
</tr>
<tr>
<td><strong>Vitamin E</strong></td>
</tr>
<tr>
<td><strong>Vitamin K</strong></td>
</tr>
</tbody>
</table>

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

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
• 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
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
Brassica and Allium References


The Wahls Protocol® Seminar

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.


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


• Reversing the deleterious effects of aging on neuronal communication and behavior: beneficial properties of fruit polyphenolic compounds. *Am J Clin Nutr*. 2005 Jan;81(1 Suppl):313S-316S.
Eat 9 Cups Vegetables/Fruit Daily

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
## 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>
</tr>
</thead>
<tbody>
<tr>
<td>Calcium</td>
<td>72</td>
<td>26</td>
<td>6</td>
<td>94</td>
</tr>
<tr>
<td>Iron</td>
<td>0.9</td>
<td>1.79</td>
<td>6.54</td>
<td>1.17</td>
</tr>
<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>
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<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</td>
<td>0.85</td>
<td>0</td>
<td>0.51</td>
<td>1.1</td>
</tr>
<tr>
<td>(alpha-tocopherol)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vitamin K1 µg</td>
<td>817 (K1)</td>
<td>1.3</td>
<td>3.3 (K2)</td>
<td>0.5</td>
</tr>
<tr>
<td>(phyloquinone)</td>
<td></td>
<td></td>
<td></td>
<td></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 effect individual vitamin A status.

The frequency of a rare missense mutation in the **BCMO1** gene that caused a dramatic decrease in the enzyme activity is so low that this SNP cannot explain the high occurrence of the poor converter phenotype. The present report shows for the first time that two common nonsynonymous SNPs that exist in the **BCMO1** gene occur at frequencies similar to those of the poor converter trait observed in human intervention studies and that they lead to impaired function of the BCMO1 enzyme in vitro and in vivo.

The 267S/H11001379V double mutation indicated a reduced catalytic activity of BCMO1 in vitro by 57%. The in vivo results from this intervention trial are consistent with the biochemical characterization of the 267S/H11001379V double mutant and indicate that female volunteers carrying the combined 267S/H11001379V variant alleles show a 69% lower ability to convert H9252-carotene into retinyl esters. Although in vitro results did not indicate that the 379V mutant would affect the catalytic activity of BCMO1, female volunteers carrying the 379V variant allele showed a reduced ability to convert H9252-carotene by 32%.

**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) Km and Vmax 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 $3.4:1$ ($\omega-6$ to $\omega-3$)
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

• Essential fatty acids are mediators of brain biochemistry and cognitive functions J Neurosci Res. 1999 Jun 15;56(6):565-70.
• Essential fatty acids in visual and brain development. Lipids. 2001 Sep;36(9):885-95.
## Nutrition Takeaways

### Assessment
- IFM DNL journal
- Homocysteine
- B12, folate
- A1c, insulin

### Treatment
- Modified paleo OR MCT keto
- Both $\omega$-6 and $\omega$-3 fats
- Meat
  - Grass fed / wild / organ
- Vegetables
  - 6-9 cups / day
  - Greens
  - Color
  - Brassica, Allium, Mushrooms
- Seaweed, ferments
Nutrition Takeaways

Assessment
• Diet Diary
• GI symptoms from ROS

Treatment
• Food as discussed
• 5R Treatments
The role of microbiome in central nervous system disorders.

Yang Y. The role of microbiome in central nervous system disorders. *Brain Behav Immun.*, 2014
Diet rapidly and reproducibly alters the human gut microbiome.
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)
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

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
Multiple Sclerosis patients have gut dysbiosis

- MS (n=31) More Psuedomonas, Mycoplana, Haemophilus, Blautia, and Dorea
- Control (n=36) more Parabacteroides, 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)
<table>
<thead>
<tr>
<th>Type</th>
<th>Description</th>
<th>Condition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Type 1</td>
<td>Separate hard lumps</td>
<td>Very constipated</td>
</tr>
<tr>
<td>Type 2</td>
<td>Lumpy and sausage like</td>
<td>Slightly constipated</td>
</tr>
<tr>
<td>Type 3</td>
<td>A sausage shape with cracks in the surface</td>
<td>Normal</td>
</tr>
<tr>
<td>Type 4</td>
<td>Like a smooth, soft sausage or snake</td>
<td>Normal</td>
</tr>
<tr>
<td>Type 5</td>
<td>Soft blobs with clear-cut edges</td>
<td>Lacking fibre</td>
</tr>
<tr>
<td>Type 6</td>
<td>Mushy consistency with ragged edges</td>
<td>Inflammation</td>
</tr>
<tr>
<td>Type 7</td>
<td>Liquid consistency with no solid pieces</td>
<td>Inflammation</td>
</tr>
</tbody>
</table>
Microbiome References

• Hoban AE, Stilling RM, Ryan FJ, Shanahan F, et al. Regulation of prefrontal cortex myelination by the microbiota. Transl Psychiatry. 2016 Apr 5;6:e774


• Mulak A, Bonaz B. Brain-gut-microbiota axis in Parkinson's disease. World J Gastroenterol. 2015 Oct 7;21(37):10609-20

• Miyake S, Kim S, Suda W, Oshima K et al. 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
Microbiome Takeaways

Assessment
• Bristol Stool Chart

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

A mitochondrial bioenergetic etiology of disease

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

Progressive bioenergetic decline

Immunological disease
- Infection
- Inflammation
- Fever
- Autoimmunity

Cancer
- Initiation
- Promotion
- Metastasis

Metabolic disease
- Diabetes and obesity
- Thermoregulation stress and trauma

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

Aging
- Apoptosis
- Senescence
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 References


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, organophosphates, 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
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 References

- Valero J, Paris I, Sierra A. Lifestyle shapes the dialogue between environment microglia and neurogenesis. *ACS Chem Neurosci.* 2016 Mar 1
- Simon C, Götz M, Dimou L. Progenitors in the Adult Cerebral Cortex: Cell Cycle Properties and Regulation by Physiological stimuli and injury *Glia.* 2011 Jun;59(6):869-81
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
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
TBI References


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


• Freedman R, Ross RG. Prenatal choline and the development of schizophrenia Shanghai Arch Psychiatry. 2015 Apr 25;27(2):90-102
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
Seligman’s conclusion is that happiness has three dimensions that can be cultivated.
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
Introduction To Clinical Medicine

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

Babita Bisht1
Warren G Darling2
E Torge Shivapour3
Susan K Lutgendorf4
Linda G Snelsonar7
Catherine A Chenard1
Terry L Wahls1,

1Department 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 Pediatrics, College of Liberal Arts and Sciences, University of Iowa, Department of Obstetrics and Gynecology, Carver College of Medicine, University of Iowa, Department of Pediatrics, 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 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
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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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

**p<0.0005
*p< 0.05
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
TBI Clinic

- Interdisciplinary - Speech Path, SW, Psychiatry, PM&R, Primary Care, Neuro-psychology
- 20 minutes with patient
- No labs
- Seen every 6 months
- Blast exposure and current neuropsychiatric symptoms
• 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
• FH brain, heart and autoimmune issues
• 20 + antibiotics as a child and young adult
• Pesticides (farm)
• Solvent exposure (work)
• Frequent steroid use (asthma)
• Very poor sleep (pain)
• No exercise (pain)
• Comfort food =↑Sugar, white flour, no vegetables
• Sober 22 years with AA
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.

Rebound Relapses After Ceasing Another Disease-Modifying Treatment in Patients With Multiple Sclerosis Are There Lessons to Be Learned?

Rhonda Voskuhl, MD

“Do no harm” is the timeless tenet of the Hippocratic Oath. It applies not only to how patients tolerate prescribed treatments but also to how they tolerate treatments after discontinuation. The sum of both events must be considered in the overall risk-benefit ratio before starting any given treatment.

The article by Hatcher et al, published in this issue of JAMA Neurology describes a rebound in multiple sclerosis (MS) relapses after ceasing fingolimod treatment. Rebound occurred in 5 of 46 patients (10.9%) at their center, with additional reports identified by the authors’ literature search. Rebounds in relapses were clinically severe and accompanied by magnetic resonance imaging lesion activity that surpassed the level of activity before starting treatment. The first step during postmarketing experience is to report adverse events to increase awareness and provide a rationale for a registry to be created to establish frequency. This is addressed by Hatcher et al. The next step is to understand why rebound is occurring in order to prevent it from happening to other patients in the future. Finally, a discussion of the altered risk-benefit ratio of fingolimod within the context of currently evolving schools of thought regarding disease-modifying treatments in relapsing-remitting MS (RRMS) is warranted.

The present article documenting rebound relapse activity after stopping fingolimod treatment is particularly important because a similar rebound of disease activity after stopping natalizumab treatment has been well documented. Why would fingolimod and natalizumab be associated with a rebound in disease activity after ceasing treatment compared with other MS disease-modifying therapies that have not been associated with a rebound? It may have to do with targeting immune cell trafficking. Fingolimod acts on sphingosine-1-phosphate receptors, which results in sequestration of lymphocytes in secondary lymphoid tissues and leads to less infiltration of these cells into the brain during MS. In turn, this reduces inflammatory lesions in white matter and reduces MS relapses. Natalizumab acts on α4 integrin receptors on lymphocytes to block their passage across the blood-brain barrier and reduce their infiltration into the brain. Perhaps treatments that are designed to block immune cells from entering the brain, either at the level of the blood-brain barrier with natalizumab or at the level of lymphoid tissues with fingolimod, can be associated with rebound relapses after ceasing treatment. In contrast, rebound disease activity over and above pretreatment levels is not an issue for first-line disease-modifying treatments for MS (eg, glatiramer acetate and interferon-β), despite extensive use for decades. These safely, long-standing disease-modifying injectable treatments do not directly target immune cell trafficking but instead act indirectly through a variety of immunomodulatory mechanisms to reduce the proinflammatory profile of immune cells in peripheral blood, with a downstream effect of less inflammation in the brain.

In many biological systems, chronic receptor blocking and/or receptor stimulation can eventually affect not only the expression of target receptors but also the expression of transcription factors involved in receptor stimulation. Accordingly, chronic targeting of the receptor interactions related to trafficking immune cells from lymphoid organs could lead to compensatory changes in other molecules redundant in such trafficking. It is tempting to speculate that chronic sphingosine-1-phosphate receptor blocking with fingolimod could have unexpected effects on receptor physiology in secondary lymphoid tissues. Therefore, sudden cessation of fingolimod treatment could result in lower efficacy of lymphocytes from lymph nodes than during pretreatment as a consequence of these upregulated compensatory pathways. This effect would involve immune cells that are not otherwise immunomodulated, paving the way for rebounds of disease activity even higher than pretreatment. Future studies are needed to discern the mechanism of rebound relapses with cessation of fingolimod treatment, as Hatcher et al acknowledge. However, these future studies will require much more than quantification of immune cell types in the blood during rebound; they will likely entail assessment of receptor physiology within secondary lymphoid tissues. Such mechanistic studies are important because there may be implications for treatments beyond fingolimod, both currently and in the future.

Given the new finding of the potential for rebound relapses after ceasing fingolimod treatment, a discussion of the altered risk-benefit ratio is salient and should be considered in the context of larger treatment-related issues in MS. Indeed, this is timely in light of evolving opinions regarding the selection of the best disease-modifying treatment approach for early RRMS. There are 2 schools of thought regarding how aggressive treatments should be in patients with early RRMS. In the past, most physicians started patients with the safest MS treatments. If they “failed” such treatments, as evidenced by relapse frequency at or near pretreatment levels, then escalating Benefits to Be Learned? JAMA Neurol. 2016 May 2. doi: 10.1001/jamaneurol.2016.0934. [Epub ahead of print]
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