

Eating to Live Well: Nutrition and Metabolic Therapies for Parkinson's

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Who are we, and what is the mission of Neurology Solutions Consultants?



TEAM NSC!



TEAM NSC!



- Internationally recognized deep brain stimulation (DBS) program in close collaboration with Medtronic and Dr. Anant Patel, neurosurgeon
- Largest private practice DBS center in the country, and 4th largest overall per neurosurgeon (Medtronic data, 2018)
- On-site training center with Medtronic for neurologists and neurosurgeons in the US and from as far away as China and Brazil
- Most experienced DBS programming team offering frequent visits for troubleshooting and to optimize system performance, **same or next day**
- Second Opinion/Tertiary Referral Center for challenging or urgent **cases**

TEAM NSC!



- Integrative and holistic approach to diagnosis and treatment.
- Frequent visits with NSC team enhances diagnostic accuracy, optimizes symptomatic treatment, and relieves suffering as quickly as possible.
- Research grade scales track treatment outcomes which include cognitive, behavioral and physical function as well as activities of daily living.
- Implementation of advanced metabolic therapies is a high priority.
- Our mission is to reverse disability and suffering wherever possible, stabilize progression of disease and improve long term outcomes.

Disclosures

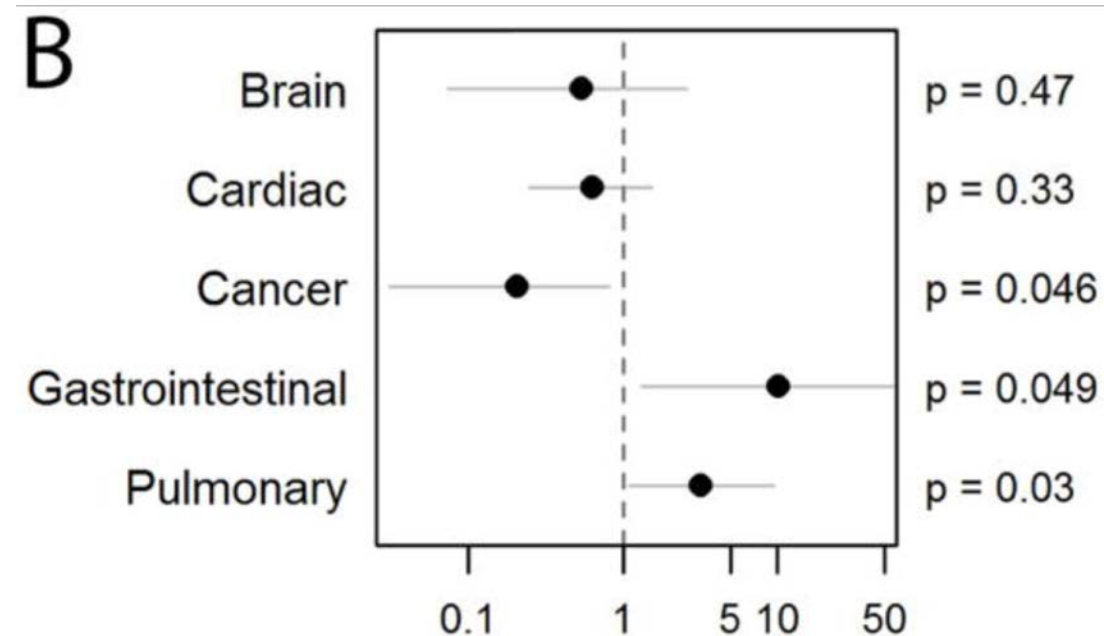
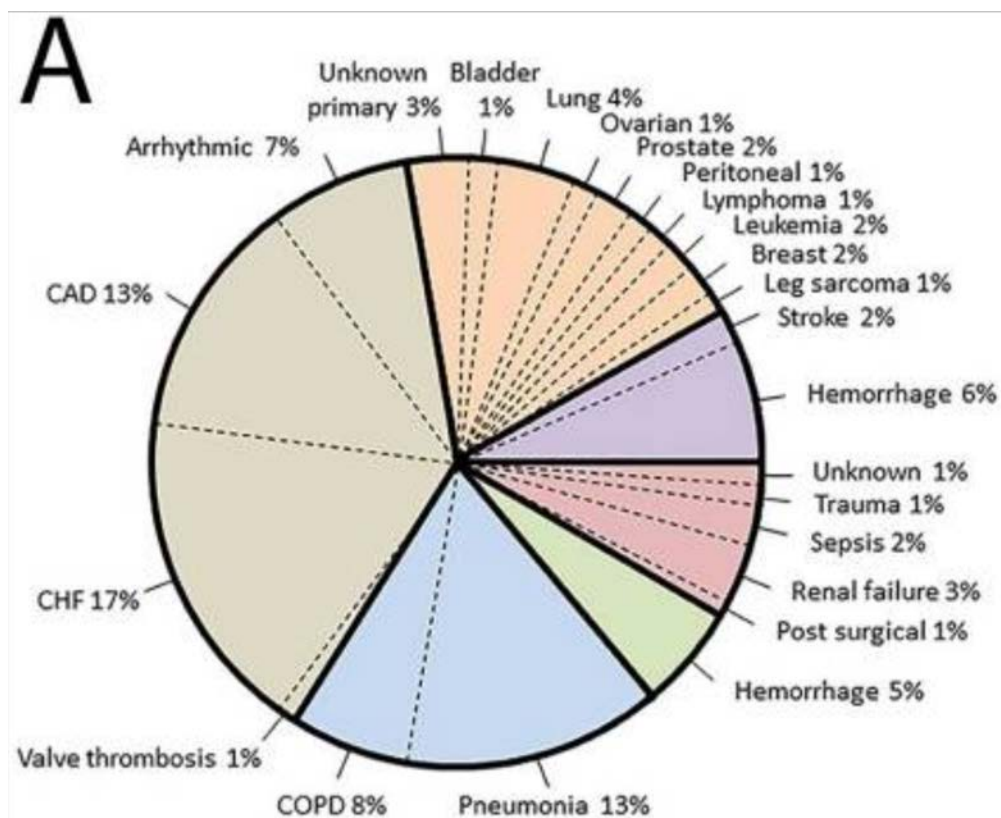


- Consultant for Medtronic product development and training programs
- Mother passed from Alzheimer's in 2013; FHx of early heart disease and cancer; Career of caring for neurodegenerative patients like Parkinson's
- Adopted “well-formulated” ketogenic diet in 2017; intermittent fasting; quarterly prolonged fasting; and resistance/circuit training 3-4x/wk
- Magnesium, Metformin, melatonin, nicotinic acid, lithium, and Vit D as neuroprotective and vascular risk management strategies
- Maintain a balanced catabolic/anabolic state to enhance autophagy and restorative sleep through a multi-mechanistic approach

Why Consider Nutrition, Lifestyle and Metabolic Therapies?

Brain tau deposition linked to systemic causes of death in normal elderly.

Josephs KA¹, Tosakulwong N², Weigand SD², Murray ME³, Whitwell JL⁴, Parisi JE⁵, Dickson DW³, Petersen RC⁶.

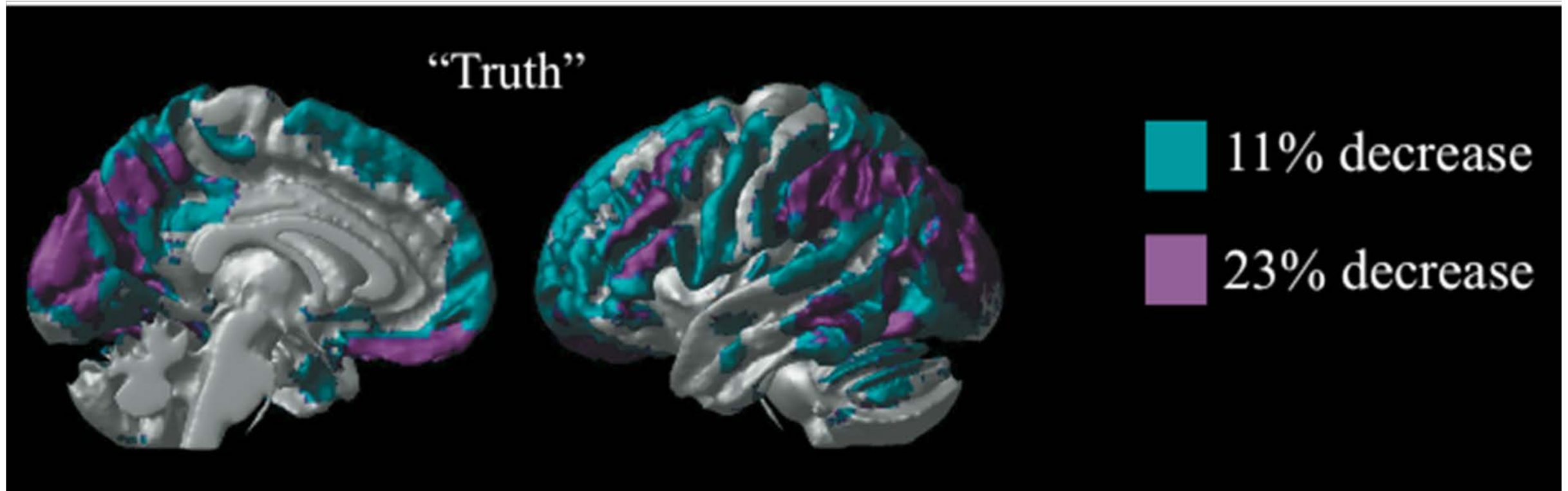


Diabetes/Insulin Resistance and Association with Parkinson's

- Increased rate of Parkinson's following diagnosis of type 2 diabetes (De Pablo-Fernandez, 2018) - HR 1.5x for complicated DM and 3.8x for younger onset PD
- Cross-talk between pathological amyloidogenic proteins in type-2 diabetes and Parkinson's (Horvath I, 2016)
- Dementia associated with insulin resistance in patients with Parkinson's (D'Amelio M, 2009)
- Diabetes and progression of rigidity and gait disturbance in older persons (Arvanitakis Z, 2004)
- Parkinson's patients have higher rates of diabetes & hypertension (National survey data from Medicare)

Cortical hypometabolism and hypoperfusion in Parkinson's disease is extensive: probably even at early disease stages.

Borghammer P¹, Chakravarty M, Jonsdottir KY, Sato N, Matsuda H, Ito K, Arahata Y, Kato T, Gjedde A.



Does Insulin Resistance or Prediabetes Contribute to Parkinson's?

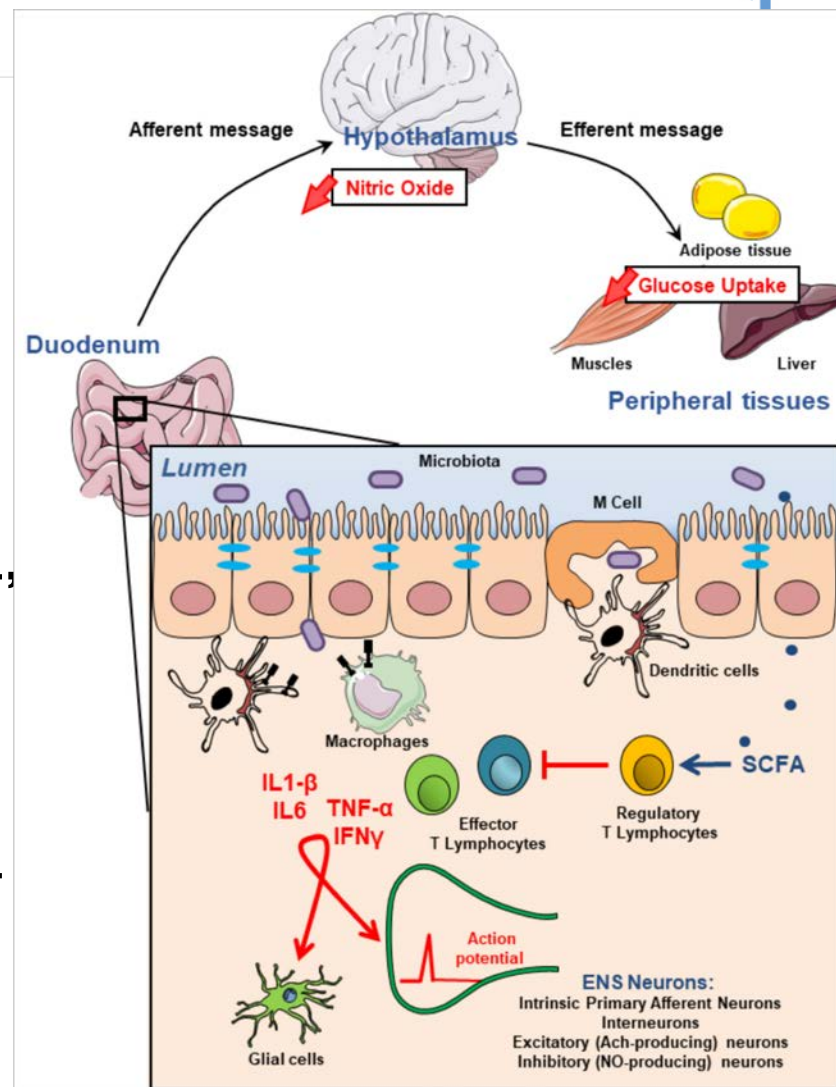
- There is an association between insulin resistance and age-related neurodegenerative disorders including Parkinson's and Alzheimer's...AS WELL AS heart disease, stroke, and cancer risk.
- There are still a lot of Parkinson's patients who do not have overt signs of insulin resistance.
- Susceptibility to chronic diseases is influenced by many factors including genetics and environmental exposures/toxins.
- What could be the lowest common denominator between these disorders?

Inflammation and Gut-Brain Axis During Type 2 Diabetes: Focus on the Crosstalk Between Intestinal Immune Cells and Enteric Nervous System.

Bessac A^{1,2}, Cani PD^{1,3}, Meunier E⁴, Dietrich G^{1,2}, Knauf C^{1,2}.

INFLAMMATION

- Gut microbiome/dysbiosis
- LPS and "leaky gut"
- Inflammatory cytokines TNF- α , IL-1 and IL-6
- TNF- α contributes to insulin resistance
- TNF- α blockers reduce insulin resistance
- LPS endotoxemia induces tau and amyloid in rat brain



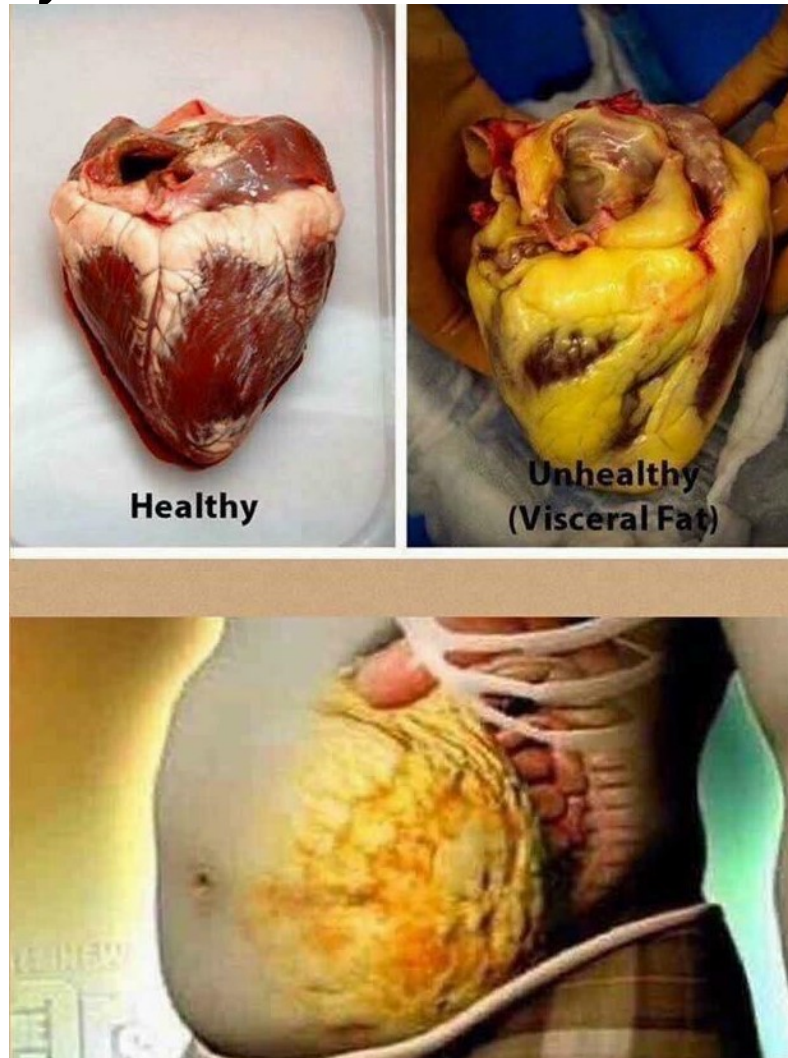
Metabolic Syndrome (MetS)

Criteria meet 3 out of 5 of following:

- Insulin Resistance; Fasting Glucose > 100 mg/dL
- Visceral Obesity; Waist Circumference
 > 37 -40 inches for men
 > 32 -35 inches for women
- Blood Pressure $> 130/85$ mmHg
- Triglyceride > 150 mg/dL
- HDL < 40 mg/dL/men, 50 mg/dL/women
- Microalbuminuria (excess protein in urine)



Metabolic Syndrome (MetS)

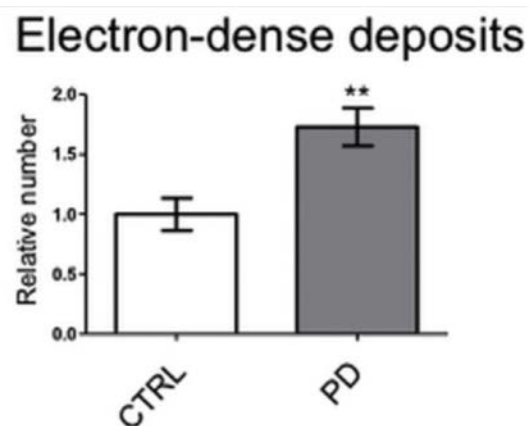
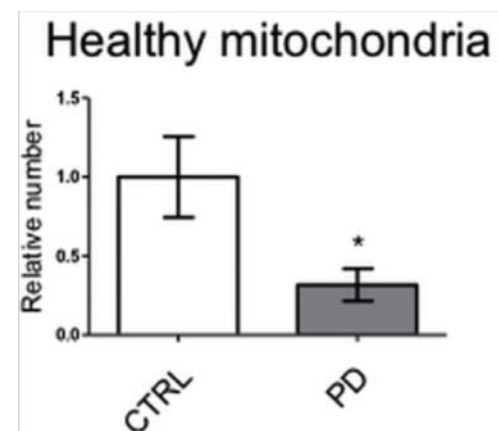
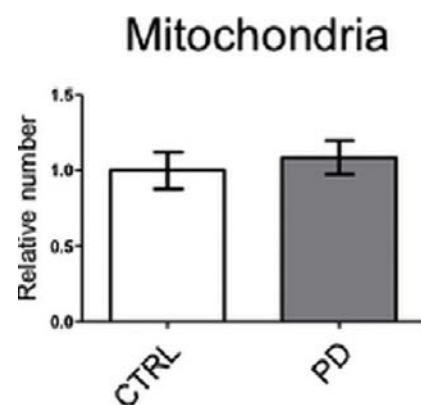


Central Features

- Insulin Resistance
- Visceral Adiposity
- Atherogenic Dyslipidemia
- Endothelial Dysfunction
- **Inflammatory cytokines are present in all MetS patients regardless of obesity**

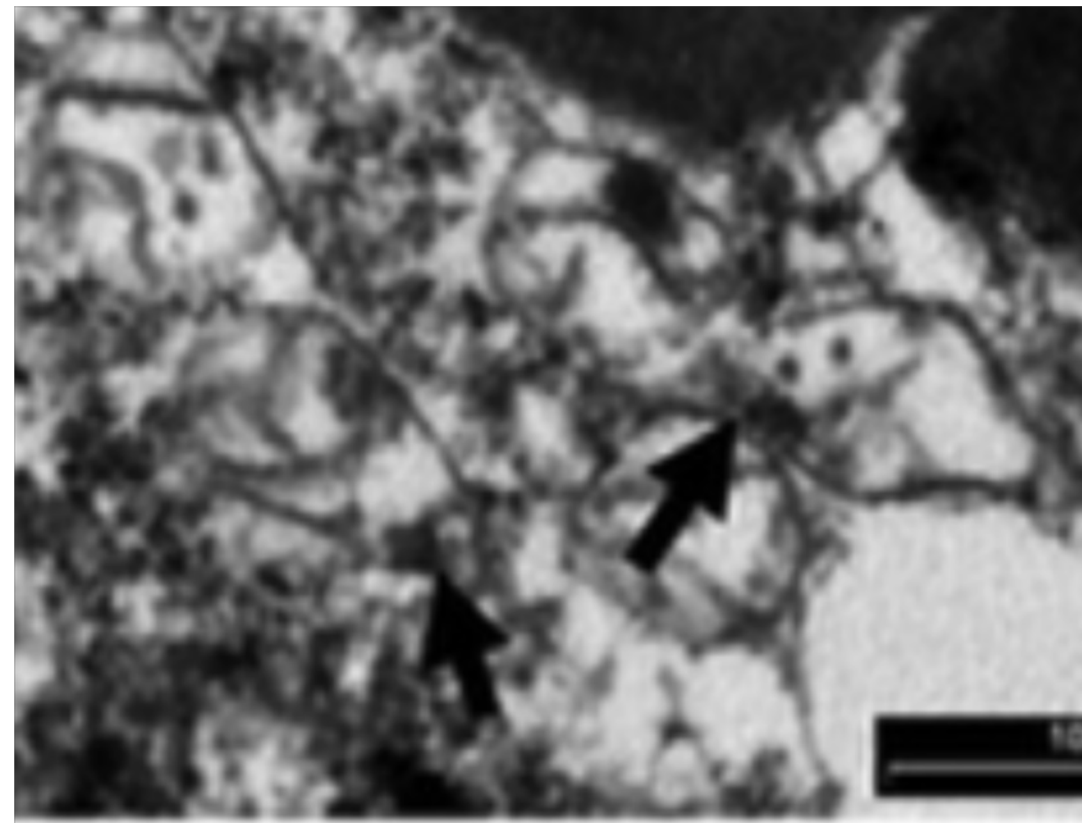
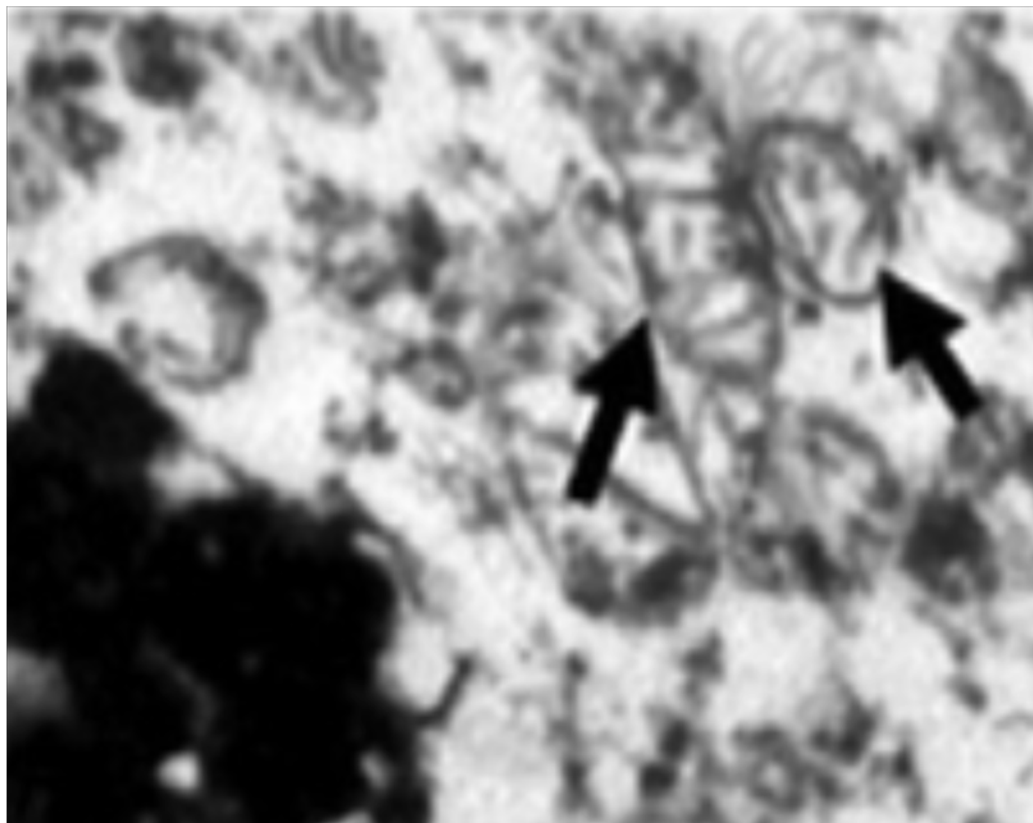
Mitochondrial alterations in Parkinson's disease human samples and cellular models.

Zilocchi M¹, Finzi G², Lualdi M¹, Sessa F², Fasano M¹, Alberio T³.



Mitochondrial alterations in Parkinson's disease human samples and cellular models.

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What Should We Do?

Strategies to Reduce Inflammation, Improve Insulin Sensitivity and Mitochondrial Function

- **RESTORE METABOLIC FLEXABILITY!**
- MEND Protocol
- Ketogenic Diet vs. Mediterranean Diet vs. low fat DASH Diet
- Enhance sleep, promote autophagy
- Resistance and HIIT exercise
- MCT oil/Exogenous Ketones
- Anti-diabetic supplements and even **prescription diabetic medications**



French and Mediterranean-style diets: Contradictions, misconceptions and scientific facts-A review.

Ndlovu T¹, van Jaarsveld F², Caleb OJ².

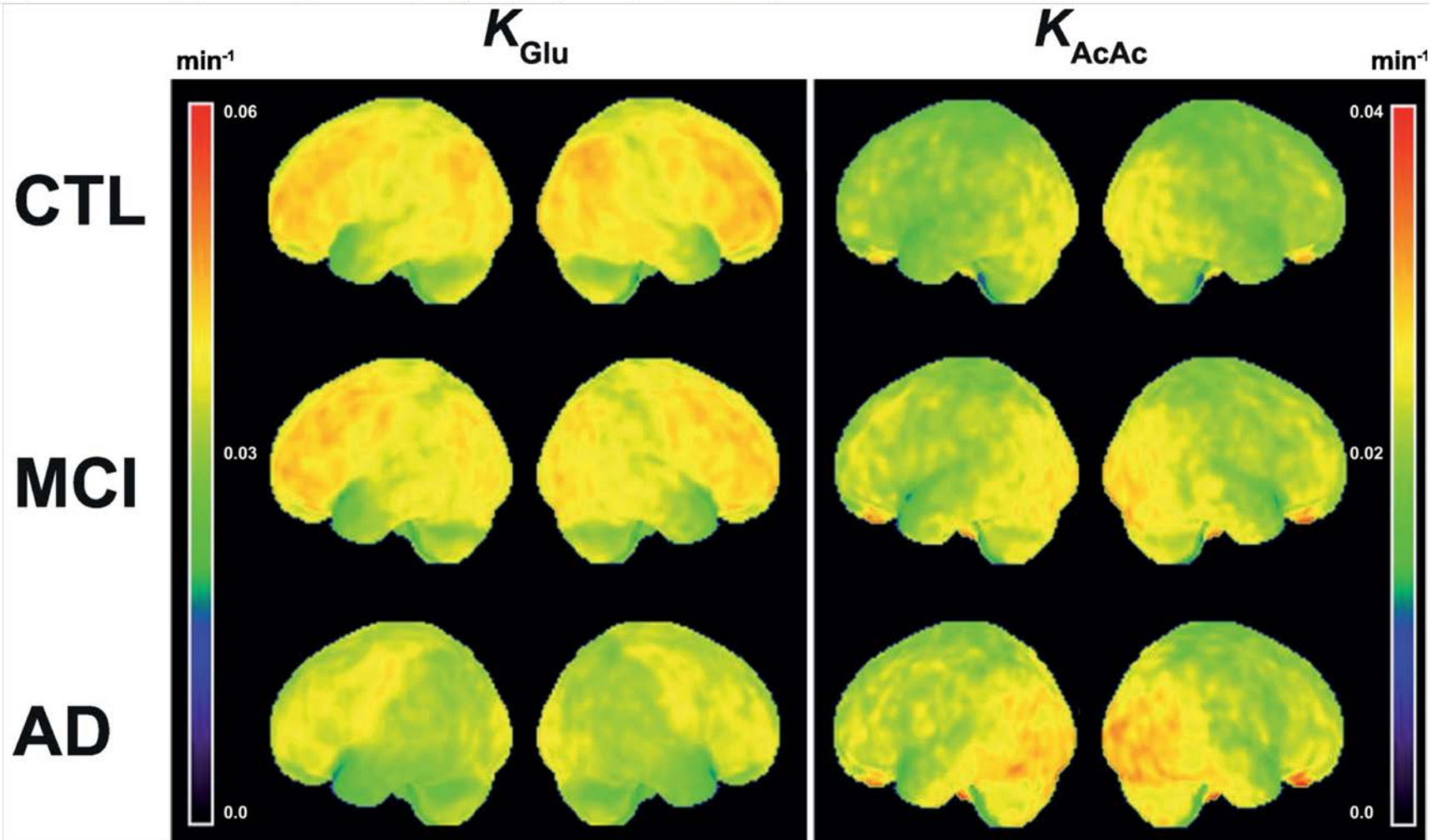
Whole Organic and Fermented Foods with Bioactive Nutrients

- Broccoli, Kale, Spinach, Artichoke...
- Tomato, Olive, Avocado, Berries...
- Beans, Nuts, Seeds, Whole Grains...
- Cinnamon, Cacao, Coffee, Tea, Curcumin, Cloves, Sumac, Baobab...
- What about Cheese? Butyric Acid
- Goal is to reduce oxidative stress, inhibit gut/brain axis inflammation and related mitochondrial dysfunction



A cross-sectional comparison of brain glucose and ketone metabolism in cognitively healthy older adults, mild cognitive impairment and early Alzheimer's disease.

Croteau E¹, Castellano CA², Fortier M², Bocti C³, Fulop T³, Paquet N⁴, Cunnane SC⁵.



Ketogenic Medium Chain Triglycerides Increase Brain Energy Metabolism in Alzheimer's Disease.

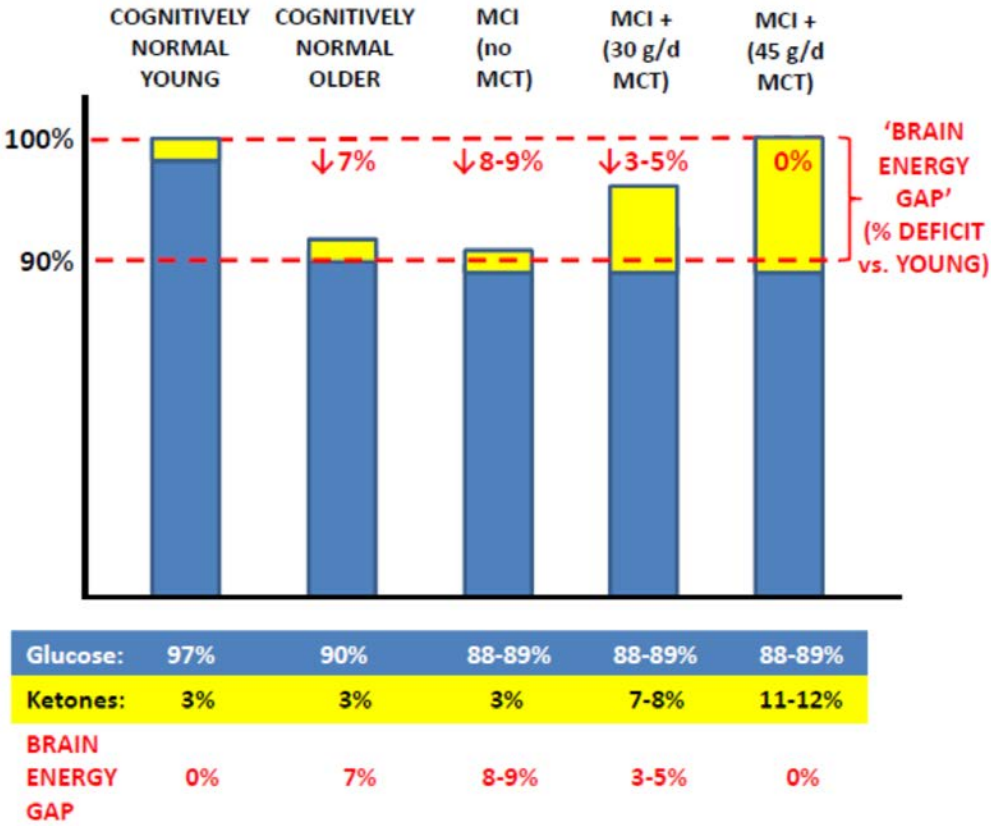
Croteau E¹, Castellano CA¹, Richard MA², Fortier M¹, Nugent S³, Lepage M², Duchesne S^{3,4}, Whittingstall K⁵, Turcotte EE², Bocti C⁶, Fülöp T^{1,6}, Cunnane SC^{1,6}.



every victory counts.

Ketones Improve Mitochondrial Function Bypassing Complex I

- Pushed freely into cells without insulin
- MCTs, Ketone Esters, butyrate
- Improves gut/brain axis inflammation, TNF-a
- Reverses type II diabetes and insulin resistance, stabilizes glucose control in type I diabetes
- Reduces oxidative stress directly and indirectly by increasing SOD/glutathione
- Powerful anticonvulsant



Neurosci Lett. 2019 Jan 18;690:232-236. doi: 10.1016/j.neulet.2018.10.048. Epub 2018 Oct 24.

Effects of a medium-chain triglyceride-based ketogenic formula on cognitive function in patients with mild-to-moderate Alzheimer's disease.

Ota M¹, Matsuo J², Ishida I², Takano H³, Yokoi Y³, Hori H², Yoshida S³, Ashida K⁴, Nakamura K⁴, Takahashi T⁴, Kunugi H².

J Cereb Blood Flow Metab. 2016 Sep;36(9):1603-13. doi: 10.1177/0271678X15610584. Epub 2015 Oct 13.

Ketogenic diet decreases oxidative stress and improves mitochondrial respiratory complex activity.

Greco T¹, Glenn TC², Hovda DA³, Prins ML⁴.

Science. 2013 Jan 11;339(6116):211-4. doi: 10.1126/science.1227166. Epub 2012 Dec 6.

Suppression of oxidative stress by β -hydroxybutyrate, an endogenous histone deacetylase inhibitor.

Shimazu T¹, Hirschey MD, Newman J, He W, Shirakawa K, Le Moan N, Grueter CA, Lim H, Saunders LR, Stevens RD, Newgard CB, Farese RV Jr, de Cabo R, Ulrich S, Akassoglou K, Verdin E.

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

Low-fat versus ketogenic diet in Parkinson's disease: A pilot randomized controlled trial.

Phillips MCL¹, Murtagh DKJ², Gilbertson LJ¹, Asztely FJS^{1,3}, Lynch CDP¹.



Exenatide once weekly versus placebo in Parkinson's disease: a randomised, double-blind, placebo-controlled trial.

[Athauda D](#)¹, [MacLagan K](#)², [Skene SS](#)², [Bajwa-Joseph M](#)², [Letchford D](#)², [Chowdhury K](#)², [Hibbert S](#)², [Budnik N](#)³, [Zampedri L](#)³, [Dickson J](#)⁴, [Li Y](#)⁵, [Aviles-Olmos I](#)¹, [Warner TT](#)⁶, [Limousin P](#)¹, [Lees AJ](#)¹, [Greig NH](#)⁵, [Tebbs S](#)², [Foltynie T](#)⁷.

Metabolic Enhancement Options

- B12, Folate/MTHF, B6 (GSH, methyl)
- Magnesium (GSH, methyl, TNF-a)
- Nicotinic Acid (BHBr, TNF-a, NAD, autophagy)
- Lithium (GLP1R, TNF-a, autophagy)
- Melatonin (TNF-a, NF-kB, Nrf2, GSH, autophagy)
- Treat Sleep Disorders (TNF-a, HGH, autophagy)
- Fasting (TNF-a, HGH, autophagy)
- Rx: Metformin, Acarbose, GLP-1 agonists (Exenatide)



Effects of levodopa/carbidopa intestinal gel versus oral levodopa/carbidopa on B vitamin levels and neuropathy.

[Loens S¹](#), [Chorbadzhieva E¹](#), [Kleimann A²](#), [Dressler D¹](#), [Schrader C¹](#).

[Neurology.](#) 2019 Feb 22. pii: 10.1212/WNL.00000000000007189. doi: 10.1212/WNL.00000000000007189. [Epub ahead of print]

Levodopa-induced dyskinesia is closely linked to progression of frontal dysfunction in PD.

[Yoo HS¹](#), [Chung SJ¹](#), [Lee YH²](#), [Lee HS¹](#), [Ye BS¹](#), [Sohn YH¹](#), [Lee PH²](#).

[Mov Disord.](#) 2018 May;33(5):762-770. doi: 10.1002/mds.27301. Epub 2018 Mar 6.

Vitamin B12 and Homocysteine Levels Predict Different Outcomes in Early Parkinson's Disease.

[Christine CW¹](#), [Auinger P²](#), [Joslin A³](#), [Yelpaala Y³](#), [Green R³](#); [Parkinson Study Group-DATATOP Investigators.](#)

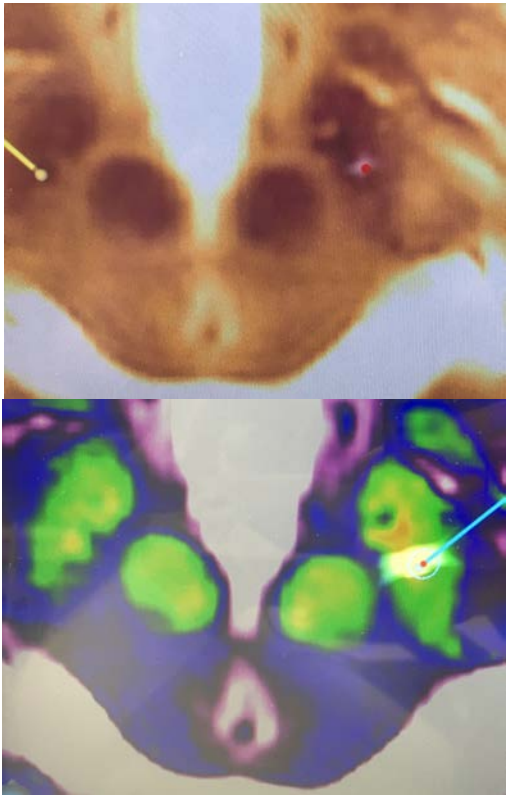
Tailor Treatment Protocols to Limit Inflammatory, Oxidative, Energetic Stress

- Dyskinesia and L-dopa increase oxidative stress
- Sinemet (carbidopa) interferes with Vitamin B6, increases homocysteine
- ELLDOPA failed to prove any protective effect, and treatments that result in later and/or lower dose of Sinemet improve outcomes, DATATOP trial



Post mortem examination of Parkinson's disease brains suggests decline in mitochondrial biomass, reversed by deep brain stimulation of subthalamic nucleus.

Mallach A¹, Weinert M¹, Arthur J¹, Gveric D¹, Tierney TS^{1,2}, Alavian KN^{1,3}.



Summary/Action Steps

- Comprehensive evaluation to help reverse Metabolic Syndrome
- **Mediterranean Ketogenic Diet:** organic high fiber and low net carbohydrate whole foods; free range organic meats; >70-80% calories from primarily monounsaturated and polyunsaturated fats (e.g. olives, avocados, macadamia)
- Customize salt/electrolyte intake (2-5 grams a day)
- Use pure stevia 1/8 teaspoon with 1-2 tablespoons of erythritol per 32oz drink
- **Minimize** animal saturated fat including dairy fat
- **AVOID** sugars including fructose and common artificial sweeteners (e.g. most sodas/diet drinks, aspartame, saccharine, sucralose)

Summary/Action Steps

- Once MetS reversed, you may include limited amounts of the following:
 - Low glycemic load high fiber grains and beans (steel cut oats, white and black beans, lentils, peas, etc.)
 - Sourdough whole grain breads (Mestermacher)
 - Fermented dairy (greek yogurt, kieferr)
 - Saturated animal fats (lard, cream, butter)
- Virgin coconut oil and/or MCT oil, butyrate, ketone salts/esters
- Magnesium, melatonin, B vitamins, Vit D, probiotics, apple cider vinegar
- Intermittent fasting (time restricted feeding), low temp cooking
- Resistance exercises, high intensity interval training