Parkinson’s Foundation

Expert Briefing:

Nutrition and Parkinson’s Disease

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Tuesday, September 12, 2017 at 1:00 PM ET.

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Disclosure Statement

• I have no personal financial conflicts of interest from the pharmaceutical or food industries - no honoraria, no paid advisory boards, no speakers bureaus

• I am not being compensated to give this presentation

• I get research grant support from the VA, NIH, Michael J. Fox Foundation and DOD

• I am personally biased by anecdotal experience in how a healthy lifestyle can impact wellbeing
Learning Objectives

• Understand how dietary choices can affect symptom control in PD

• Discuss how the gut microbiome may be involved in PD

• Explore the possibility that sound nutritional choices may provide disease-modifying effects in PD
Can diet interfere with PD medications?

- Levodopa is a large neutral amino acid (LNAA) which is absorbed in the small intestine and transported into the brain by the same mechanisms as other LNAAs
- Some people with PD will notice less efficacy of carbidopa/levodopa if taken with a high protein meal
- Generally, we recommend people take carbidopa/levodopa 30 minutes before or 60 minutes after meals
- Also, can’t take iron supplements or multivitamins with iron within 2 hours of carbidopa/levodopa
- Some people with motor fluctuations may benefit by a change in diet
Dietary management of motor fluctuations

- Low protein diet and protein redistribution diets have been tried
- Meta-analysis in 2010 included 16 studies
- No support for low protein diet
- However, over two-thirds of studies reported >80% response rates for protein redistribution
- All studies reported reductions in motor impairment or improvements in fluctuations

Mov Disord 2010;25:2021-34
Which patients respond best

- Three studies addressed this question

<table>
<thead>
<tr>
<th>Source (year)</th>
<th>Reference</th>
<th>Feature</th>
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<tbody>
<tr>
<td>Riley et al. (1988)</td>
<td>24</td>
<td>Shorter duration of Parkinson’s disease</td>
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<td>Shorter length of levodopa treatment</td>
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<td>Bracco et al. (1991)</td>
<td>26</td>
<td>Shorter duration of fluctuations</td>
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<tr>
<td>Giménez-Roldán et al. (1991)</td>
<td>28</td>
<td>Older age at onset and shorter duration of fluctuations</td>
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- Efficacy and benefits appeared to be higher when started early
- Long term compliance was possible
Caffeine for the treatment of sleepiness in PD

- 6-week randomized controlled trial of 100-200mg of caffeine in PD with daytime somnolence
- The equivalent of 2-4 cups of coffee a day clearly improved daytime sleepiness
- This has been confirmed in a second unpublished trial called CafePD

*Neurology* 2012;79;651
Dietary management of orthostatic hypotension

- Orthostatic hypotension, (a drop in blood pressure upon standing) that often causes lightheadedness, occurs in up to 50% of people with PD

- Dietary management includes:
  - Avoiding large meals
  - INCREASE dietary salt intake
  - Increase fluid intake
  - Decrease alcohol
How much water?

• Unless there are medical reasons not to like heart or kidney disease, aim for 1.5-2 quarts of liquid a day

• Graduated containers like those from Hydr-8 can help assure adequate hydration

http://hydr-8.com/
Avoiding malnourishment and weight loss in PD

• Malnourishment occurs in up to 25% of people with PD

• One reason may be the loss of sense of smell that occurs in nearly everyone with PD, as taste is mostly driven by smell, so food can taste bland

• Any patient with significant weight loss should consult a nutritionist

• One possible solution is increasing the amount of amount of herbs, spices, and other flavors in food
Dietary management of constipation

• Constipation and hard stools are very common in people with PD

• Dietary management includes:
  • Increasing fluid intake - including coffee
  • Increase intake of dietary fiber from fruits, vegetables, beans, whole grains, nuts, seeds

How much fiber?

- Aim for 30-40 grams per day
- Look at nutrition labels
  - ≥ 5 grams/serving is excellent source of Fiber
  - 3 grams/serving is good
- Ideally, the ratio of total carbohydrates to dietary fiber should be 5 or less
- Carbs 27g/ fiber 3 = 9 Too high!
Mediterranean diet likely reduces risk of dementia

Mediterranean Diet, Cognitive Function, and Dementia

A Systematic Review

Ilianna Lourida, Maya Soni, Joanna Thompson-Coon, Nitin Purandare, Iain A. Lang, Obioha C. Ukoumunne, and David J. Llewellyn

Adherence to a Mediterranean-Style Diet and Effects on Cognition in Adults: A Qualitative Evaluation and Systematic Review of Longitudinal and Prospective Trials

Roy J. Hardman, Greg Kennedy, Helen Macpherson, Andrew B. Scholey, and Andrew Pipingas

Mediterranean Diet, Cognitive Function, and Dementia: A Systematic Review of the Evidence

Sara Danuta Petersson and Elena Philippou

Epidemiology (2013) 24:479
Front Nutr (2016) 3:22
Adv Nutr (2016) 7:889–904
Parkinson’s disease and bone health

- People with PD are more likely to have low Vitamin D levels
- Low vitamin D levels can lead to osteoporosis which can make bones more likely to break
- Everyone with PD should have their vitamin D level checked
- It is very difficult to reach adequate levels of vitamin D with dietary intake and sun exposure so most patients should take supplements to reach a 25-Hydroxyvitamin D [25(OH)D] levels of approximately 40-60 ng/ml
Learning Objectives

• Understand how dietary choices can affect symptom control in PD

• Discuss how the gut microbiome may be involved in PD

• Explore the possibility that sound nutritional choices may provide disease-modifying effects in PD
The gut microbiome

- The gut microbiome are all the bacteria, yeast, viruses and other organisms living in our digestive system.
- It is essential for health.
- We suspect it may play a role in the risk of Parkinson’s disease.

*npj Parkinson's Disease 3, Article number: 3(2017)*
The gut microbiome is different in PD

- 72 PD and 72 controls
- 16S ribosomal RNA analysis of stool samples
- 77.6% reduction in abundance of *Prevotella* in patients with PD
- *Prevotella* have been shown to be health-promoting and anti-inflammatory by the production of short chain fatty acid compounds (SCFAs)

Mov Dis 2015;30:351-8
Second study suggests SCFA-producing bacteria under-represented in PD

- Second study with 38 PD samples and 34 controls
- Assessed sigmoid colonic biopsies and stool
- Found a non-significant 50% decrease in *Prevotella* in biopsies but no difference in stool
- SCFA- producing *Blautia*, *Coprococcus*, and *Roseburia* were significantly more abundant in feces of controls than PD patients
- Some bacteria which are thought to be “proinflammatory” were significantly more abundant in mucosa of PD than controls

Mov Dis 2015;30:1351-1360
Third confirmatory study in PD

Control Young n=10
Control old n=34
PD n=34
Also, short chain fatty acids decreased in PD stool

- Acetate
- Butyrate
- Valerate
- Propionate
- i-Butyrate
- i-Valerate

In general people have different types of microbiome

- 3 distinct enterotypes identified
- One of the distinguishing factors is prevalence of *Prevotella*

Long term diet patterns are strongly associated with enterotype

- 100 healthy controls
- Segregated into two enterotypes
- Protein and animal fat consumption - Bacteroides
- Carbohydrate consumption - Prevotella

Science 2011;334:105-8
Adherence to Mediterranean diet increases Prevotella and SCFAs

- 153 vegan, vegetarian or omnivore Italians
- The majority of vegans and vegetarians and 30% of omnivores had high Mediterranean diet scores
- There were significant associations between consumption of Mediterranean-type diets and increased levels of fecal SCFAs and Prevotella, despite overall diet type
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‘there appears to be sufficient reason for hoping that some remedial process may ere long be discovered, by which, at least, the progress of the disease may be stopped’

James Parkinson, 1817
Molecular Mechanisms involved in PD

Alpha-synuclein misfolding and aggregation
Oxidative stress
Mitochondrial dysfunction
Inflammation
How can nutrition change any of this?
Phytochemicals are Medicine!

http://www.bmrbb.wisc.edu/featuredSys/flavonoids/
The possibilities are tremendous!

mTOR inhibition results in increased autophagy, that may help to clear alpha-synuclein aggregates. Caffeine, curcumin and resveratrol inhibit mTOR.

EGCG converts large alpha-synuclein aggregates into small non-toxic ones.

Curcumin inhibits alpha-synuclein oligomerization into higher molecular weight aggregates.

Phytochemicals in strawberries inhibit COX-2 enzymes

Flavonoids have been shown to stabilize alpha-synuclein in vitro.

Flavonoids inhibit inflammation by inhibiting release of NO, PD-preferring enzymes.

Phytochemicals in strawberries inhibit COX-2 enzymes

Genistein, an isoflavone found in soybeans, protects dopaminergic neurons by inhibiting microglial activation

Some flavonoids directly scavenge ROS.
Dietary modifications in Parkinson's disease: A neuroprotective intervention?

Shital P. Shah \textsuperscript{a,*}, John E. Duda \textsuperscript{a,b}
So what do I tell my patients to do?
I believe that Parkinson’s disease might be treated by increasing the levels of anti-oxidant and anti-inflammatory compounds in your blood and brain.

The best way to do that is to eat more sources of these compounds from whole, unprocessed foods, including fruits, vegetables, mushrooms, nuts, seeds, beans, legumes, whole grains, teas and spices.

Avoid highly processed foods as much as possible.

The more variety and color in your diet the better!
Simple Nutritional Recommendations for patients with PD

- Eat more nuts and seeds, (whichever ones you like) and optimally 1-2 tablespoons ground flax seeds daily.
- Eat what you need to eat to be happy, but eat it as a ‘treat’, not all the time, and eat more of the food that is good for your health.
- Every healthy lifestyle change helps and most people do better making minor changes gradually that become major changes over time.
- Consult your own physician before making major changes.
What about organics?

- Not clear that eating organics will clearly affect PD
- However, it is plausible that it might, so..
- The Environmental Working Group analyzed pesticide residue testing data from the U.S. Department of Agriculture and Food and Drug Administration to come up with rankings for the following popular fresh produce items.
  - Generated the ‘Clean 15’ and ‘Dirty Dozen’ for consumers
  - However, they actually rank 48 foods that are listed from worst to best - lower numbers indicate more pesticides.
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<tr>
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<tr>
<td>1</td>
<td>Strawberries</td>
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<td>Spinach</td>
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<td>Nectarines</td>
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<td>Tomatoes</td>
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<td>Sweet bell peppers</td>
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<td>Potatoes</td>
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<td>Snap peas - imported</td>
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<td>Blueberries - domestic</td>
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<td>Blueberries - imported</td>
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<td>Oranges</td>
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<td>28</td>
<td>Green beans - Imported</td>
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<td>Snap peas - domestic</td>
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<td>Green onions</td>
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<td>Mushrooms</td>
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<td>Sweet potatoes</td>
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<td>Broccoli</td>
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<td>Grapefruit</td>
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<td>Cauliflower</td>
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<td>Kiwi</td>
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<td>Onions</td>
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<td>49</td>
<td>Avocados</td>
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<td>Sweet Corn</td>
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Adapted from www.EWG.org
Side effects of a whole food plant based diet

- GI discomfort/flatulence
- Change bowel movements - less constipation!
- Medication interactions
  - Warfarin and leafy greens
  - Grapefruit
- Don’t forget:
  - Less heart disease, diabetes, stroke, cancer, depression, dementia, insomnia, hypertension, etc, etc, etc
I don’t know everything, and these are just my opinions, so Educate yourself about health and wellness! Get better informed about nutrition and wellness by checking out the these books:

- **How Not to Die**, by Dr. Michael Greger
- **The Get Healthy, Go Vegan Cookbook**, by Dr. Neal Barnard
- **The Forks Over Knives Plan**, by Alona Pulde M.D. and Matthew Lederman M.D.
Or these websites:

- www.nutritionfacts.org - my favorite website! A great resource
- www.forkoverknives.com
- www.straightupfood.com
- www.happyhealthylonglife.com
- www.pcrm.org/health/diets
- http://www.vegetariantimes.com/recipe/vegan/
- https://www.happycow.net/vegetarian-recipes.html
- http://www.choosveg.com/recipes
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Resources

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