FOOD FOR THOUGHT:
Diet, Nutrition &
The Future of PD

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Nutrition
- Human dependence on the planet.
- Exogenous supply of molecules, minerals, etc.

Latin: to nourish
We think of ourselves as self-contained separate from our environment

Me  Environment

NUTRITION is not food
The study of where nourishment comes from

That which nourishes:
- Air
- Water
- Electromagnetic waveforms
- Social connection
- Phytonutrients (epigallocatechin gallate, flavonoids, terpenoids)
- Supplements (coenzyme Q10, fish oil)
- Medications (insulin, levodopa, glutathione)

Nutrients from food

Macronutrients:
- Fat, Protein, Carbohydrates (alcohol?)

Micronutrients
- Vitamins: vit A, Bs, C, D, E, etc.
- Minerals: potassium, magnesium, calcium, etc.

Fiber

Accessory Nutrients: Q10, glutathione, flavonoids

Microorganisms: fermented foods, prebiotics, etc.

What do we know about PD?
- Syndrome
  - Non-Motor Symptoms (usually first)
    - Fatigue, seborrhea, constipation, slowness, tremor, drooling, sleep problems, anxiety.
  - Motor
    - Tremor, rigidity, slowness
- Long pre-clinical phase
  - 5-10 years
Nutritional Deficiency Syndromes

- Dermatitis, dementia, diarrhea, and eventual death → ?
- Lethargy, Easy bruising, bleeding gums, death → ?
- Painful sensations, tingling, confusion, dementia, loss of balance, emotional instability, → ?
- Goiter, mental retardation, growth disorder… → ?

Memory loss reversed!

First 10 patients to use this program:
- All had mild cognitive impairment or AD
- 9/10 had improvement within 3-6 months (1 was late AD)
- Of the 6 patients who had stopped work or having work problems, all were able to return to work/ improved performance at work.
- All results have been sustained
- Longest patient being followed currently 2.5 years…

Alzheimer’s reversed!

Systems-based approach
- DIET:
  - Minimize simple carbohydrates
  - Minimize inflammation with low grain diets
  - Fast 12 hours each night, including 3 hours prior to bedtime
- OPTIMIZE SLEEP
  - 8 hr/night, melatonin & tryptophan if necessary
- EXERCISE
  - 30-60 min/ day, 4-6 d/ week
- STRESS REDUCTION
  - Yoga, meditation, etc.

Alzheimer’s reversed! (cont.)

- SUPPLEMENTS
  - Kaap homocysteine below 7
  - Curcumin
  - DHA/ EPA
  - Probiotics/ Prebiotics
  - Ashwaganda
  - Citicoline
  - Vit D
  - Bacopa
  - CoQ10, Ipoic acid, vit C, etc for mitochondrial function
  - Coconut oil
  - Resveratrol

PD Protection: “The Prudent Diet”

High intakes of:
- Coffee
- Tea
- Legumes (beans)
- Vegetables
- Whole grains (rice, quinoa)
- Nuts
- Fish
- Poultry
- Fruit

Low intake of:
- Saturated fat (cream, red meat, pork)

Moderate intake of:
- Alcohol

Am J Clin Nutr 2007;86:1486-1494
**Flavonoids / Berries are Protective**

- Health professional follow-up study; N=805 PD
- Intakes of anthocyanins AND berries were sig associated with lower PD risk (0.77 berries, 0.76 anthocyanins, p <0.02) for those in the highest vs. lowest quintiles
  
  (Gao 2012)

**Green & Black Tea are Protective**

- Consumption of 3+ cups/day of tea delayed motor symptom onset by 7.7 years.
  

**Coffee**

- One of the most consistently identified nutrients associated with PD protection
- ~28% reduction in risk of developing PD
- Maximum benefit reached at approximately 3 cups of coffee daily.
  
  (Qi H, Li S 2014)

**Dairy Increases Risk**

- Nurses’ Health Study (121000) & Health Professional Follow-up Study (51000)
- Honolulu Heart Program (7500 men)
- American Cancer Society’s Cancer Prevention Study II Nutrition Cohort (57000 men, 73000 women)
- EPIC-Greece Cohort (26,173)
- Strong positive association with milk but not cheese or yogurt.

“CAM Care in PD” is the first study to ask the question: “Do people who consume dairy progress at a different RATE than those who avoid it?”

**NEW IN NUTRITION**

Symptom Management
Disease Modification Therapy

**“Treat the gut”**

- Irritable Bowel Syndrome
  - Taiwan Natl Health Insurance Program 2000-2010
  - 23,875 pts with IBS; 95,500 non-IBS controls
  - Adjusted HR of PD was 1.48 (95% CI 1.27, 1.72)
    
  
  - Small intestine bacterial overgrowth (SIBO)
    - Investigators used urea breath test & lactulose
    - Prevalence of overgrowth was significantly higher in pts than in controls (54.5% vs. 20%; P<0.01)
      
      (Fasano A, et al, Mov Disorders 2014)
50% of body dopamine is produced in the gut

Where do good bugs come from?
- Vaginal canal during birth
- Implications for C-sections?
- Fiber & other plant-based nutrients
- Fermented foods
  - Yogurt with “active cultures”
  - Book: *Wild Fermentation*
- Supplements

Increasing Digestive Enzymes
- Less stress
  - Fight/Flight OR Rest/Digest
  - Meditate
  - Stress management (e.g. MBSR program)
- Chew your food better, eat slower
  - Consume less food, concentrate nutrients
- Softer (partially predigested)
  - Soups, stews
  - Crockpots
  - Sashimi, tartare

*Lactobacillus acidophilus*
Use of probiotics for the treatment of PD constipation
- 40 pts with PD + constipation
- 65 mL fermented milk drink containing $6.5 \times 10^9$ CFU of *Lactobacillus casei* Shirota daily x 5 weeks
- Probiotic group: Significant improvements in:
  - Stool consistency
  - Days per week patients felt bloated
  - Abdominal pain
  - Sensation of incomplete emptying (all $P < 0.01$)


LIPDS: MCT & Coconut Oil

Parkinson’s is a Metabolic Disease
**DIABETES OF THE BRAIN**
- Brain does not use sugar efficiently
- Disruption of cellular metabolism
- Not burning sugar efficiently (Type 3 Diabetes)
- Free radical formation
- Inflammation
- Accumulation of cellular debris (impaired autophagy)
- Apoptosis
- Microglial activation

Photo: http://www.quinzanisbakery.com/breads.html
Carbohydrates

Why do we eat?

• Addicted to it
• Food tastes good
• Bored
• Nervous or upset
• Depressed
• Celebrating
• Mindless

Movie: FED UP

If your belly is bigger than your hips…
this one’s for you.

Calorie Restriction

American’s tend to:
• Eat too much
• Eat for reasons other than to nourish

CR is typically defined as 10-25% fewer calories than the average Western diet.

Calorie Restriction: Mechanisms of Action

• Reduces cellular oxidative stress
• Protects genes from damage
• Enhances detoxification
• Improves energy homeostasis

(Roledle ON, 2006)
Nutrient Dense Foods:

- Nutrient-Dense Foods (usually bright colors)
  - Kale, spinach, chard
  - Carrots, beets, tomatoes
  - Broccoli
  - Berries, cherries
  - Salmon, sardines, herring
  - Eggs

- NOT nutrient-dense
  - Donuts
  - Potato chips
  - French fries
  - Bread
  - Pasta
  - Soda
  - Candy, sweets
  - Fast food
  - Ice cream

Omega-3 fats

**Sources**
- Anchovies
- Herring
- Mackerel
- Wild salmon
- Sardines
- Tuna
- Sturgeon

**Benefits**
- Reduced triglycerides
- Arthritis
- Depression
- Asthma
- Attention deficit disorder
- Alzheimers disease
- Dementia

Omega-3 FA & Risk of Dementia

Estimated 40-50% reduced risk of dementia associated with high n-3 intake.

- N/A to ApoE4 carriers


(Cole 2010, MacLean 2005)

DHA (Fish Oil) for Dyskinesia

Reduces dyskinesia in primate model

Does it work in humans?

Mischley 2013

Choline

Essential nutrient for learning and memory!
- Humans can synthesize it in small amounts
- Must be consumed in the diet to maintain health
- Adequate Intake for adults:
  - Females: 425 mg
  - Males: 550 mg

Dietary Sources:
- Beef liver (3oz 355 mg)
- Wheat germ (1c 172mg)
- 1 large egg (126 mg)
- Cod, brussel sprouts, shrimp

CDP-Choline

- 4 caps/day has been shown to reduce levodopa requirement
- Precursor for Acetylcholine
  - Important neurotransmitter involved in learning, memory, & muscle control
- Component of membrane phospholipids
  - All play a role in cell signaling: precursors for intracellular messengers (diacylglycerol, ceramide)
  - Role in membrane structure and stability

Curcumin (from Turmeric)

- Active ingredient from the Indian spice turmeric
- Makes mustard yellow
- Available over-the-counter
- Formulations with added lipids, pepper, etc. are being studies for ways to optimize absorption.

Curcumin (from Turmeric)

- Antioxidant
- Prevents alpha-synuclein aggregation
- Prevents fibril formation
- Inhibits monoamine oxidase B
  - Ji HF, et al. CNS Neurol Dis Drug Targets 2013
- Local inflammation: protects neurons from degeneration
  - Tegenge MA et al, 2013

Cinnamon

- 2 impressive studies in animal models of PD
- Benefit due to sodium benzoate
- Prevented alpha-a-synuclein from misfolding in rodents and fruit flies
- In fruit flies that ALREADY HAD PD, the cinnamon supplement led to reduction in misfolded fibrils!
L-dopa in food?
- Levodopa occurs naturally in Mucuna & fava beans

Timing your fava bean salad/ Mucuna supplement:
- Levodopa is lost from your bloodstream faster than carbidopa. If your medicine doesn’t last as long as you’d like, but you don’t want to take another C/L, try eating fava beans/ Mucuna ~ 2 hours after C/L.

Levodopa raises homocysteine
- Keep homocysteine below 10
  - Check you homocysteine levels 1-2 x year ($35 blood test)

If your levels are above 10, you should take:
- Rx: Homocysteine Factors
  - MethyB12
  - 5-MTHF
  - B6
  - Betaine
  - Choline

Glutathione Deficiency in PD?
Options for Supplementation
- IV
- Oral NAC
- Oral glutathione
- Transdermal
- Intranasal

Conclusion: Safe & Tolerable
Recommendation to continue on to efficacy studies.

Symptom improvement?

CNS Absorption following (in)GSH?
The Secret to Success

“CAM Care in PD”

Who are the POSITIVE DEVIANTS??

Can we identify diet, lifestyle, and supplements associated with those doing unusually well?

Are there behavior patterns associated with a more rapid progression?

Study Goals:
1. Describe lifestyle habits and therapies being used by individuals with PD.
2. Identify what those who are doing unusually well have in common.

For more information:
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“Heterogeneous disease”

How are these groups different?

First peek at positive deviants
- Those who report the fewest symptoms, based on years since diagnosis, are more likely to:
  - Not be lonely
  - Not be overweight
  - Exercise - the more often the better
  - Avoid soda
  - Avoid artificial sweeteners
  - Make more money (not education)

THE FUTURE OF NUTRITIONAL NEUROLOGY
Start upstream- use what we know

- Practice Prevention
  - Take politics out of public health

- Identify those at increased risk (prevention)
  - Family members, Assoc Conditions (AD, CVD)
  - Screen for early sx: Constipation, Loss of smell

- ID modifiable risk factors that increase/ decrease risk
  - Dairy, tea, coffee, smoking, well water, obesity.
  - (CAM Care is trying to do this)

Paradigm Shift in Research Strategy

**Pragmatic** (vs. Explanative)

- Neuroprotection studies should NOT be done on untreated patients
- We need results that can be translated to patients ASAP
- Less focus on dopamine, more on systemic & non-motor symptoms

Homocysteine Monitoring on Levodopa

- Keep homocysteine below 10
  - Check you homocysteine levels 1-2 x year ($35 blood test)

If your levels are above 10, you should take:

- Rx: Homocysteine Factors
  - MethylB12
  - 5 MTHF (nice part of 23andme)
  - B6
  - Betaine
  - Choline

Multi-Modal Interventions

- PD community needs to come up with “What works”
  - Identify the conditionally essential nutrients in PD (apply them all)

- Discourage irritation, inflammation

- Encourage cellular detoxification, growth factors, and neurorepair

Social contact as a nutrient

- Do NOT withdraw
  - Find new hobbies, new friends, new experiences

- Attend PD support groups
  - Dance, singing, yoga, etc.

- Ask for help
  - By doing so, you give others permission to do the same.

- Be a resource
  - “My tremor goes away when I’m helping someone else.”

- Shared meals
- Human touch
Rx:
Sleep

In summary

MORE
• Vegetables
• Fruits
• Beans
• Nuts, seeds
• Fish
• Shared meals
• Slow chewing
• Exercise

LESS
• Sugar
• Artificial sweeteners
• White foods
• Processed foods
• Mindless eating
• Beef, pork
• Dairy
• Obesity

Sleep Drives Metabolite Clearance from the Adult Brain
Lulla Kist et al.
Science 342, 273 (2013);
DOI: 10.1126/science.1241224