The role of diet and exercise in cognition in multiple sclerosis

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COGNITION IN MULTIPLE SCLEROSIS

• Multiple sclerosis typically known as affecting physical function
• The impact on cognition is less well known and recognised
• Nevertheless, occurs in about 58% of pwMS in Australia
• Not everyone with MS will have cognitive difficulties
• Pattern and severity vary
COGNITION IN MULTIPLE SCLEROSIS

Processes most affected:
- Speed of thinking
- Attention
  - Complex
  - Sustained
- Memory
- Executive functioning
  - Working memory
  - Problem solving
  - Abstract reasoning

Processes least affected:
- General knowledge
- Long-term memories
- Language skills

INFLAMMATION AND MULTIPLE SCLEROSIS

- Multiple sclerosis is an immune-mediated and neurodegenerative disease of the central nervous system
- Characterized by areas of inflammation in the brain, causing demyelination
USE OF COMPLEMENTARY & ALTERNATIVE MEDICINE IN MS

• CAM use is prevalent in MS at 33-70% (64.7% in a South Australian study)
• Usually used in adjunct to pharmacological therapies
• Most widely used CAMs are:
  • Diet
  • Omega-3 polyunsaturated fatty acids supplements
  • Antioxidants
• Reasons for use include:
  • General health
  • Reduce muscle weakness
  • Alleviate memory problems
  • Improve mobility

DIET AND COGNITION
WHY AM I INTERESTED IN DIET AND COGNITION?

My research...

• Rats given a high saturated fat and refined sugar diet had impaired memory and changes in proteins in the hippocampus
• Healthy young adults who habitually consume a high fat and refined sugar diet have poorer memory function
• Consumption of 4 unhealthy breakfasts causes memory impairments, which correlate with changes in blood sugar levels and inflammatory markers

ROLE OF DIET IN MS
(A COUPLE OF EXAMPLES)

Norway, 1952:

- incidence of MS in coastal towns with high fish intake
- risk in cities where animal fat consumption is high

Iran, 1989-2006:

- 8.3 fold incidence of MS from 1989-2006
- Genetic changes unlikely of that period
- Environmental factors being explored

DIET & MULTIPLE SCLEROSIS

Epidemiological studies show a link between MS prevalence and particular diets

Lower risk of MS:
• Omega-3 and Omega-6 polyunsaturated fatty acids
• Fibre
• Whole grains

Higher risk of MS:
• Saturated animal fat
• Sugars
• Alcohol


POSSIBLE MECHANISM LINKING DIET TO MULTIPLE SCLEROSIS

HIGH-FAT / SUGAR WESTERN DIET

Immunological action
Post-prandial inflammation
Low-grade chronic inflammation

systemic chronic inflammation
↑ inflammatory cascade
loss of immune self-tolerance

Dysbiosis in Gut Microbiota
Enteric inflammation
epithelium permeabilization
Endotoxicemia

DIET & MULTIPLE SCLEROSIS:
QUALITY OF LIFE, DISABILITY & RELAPSE

- 2087 people with MS
- Higher overall dietary health score =
  Better Physical QoL
  Better Mental QoL
  Lower disability
  Links to relapse rate not as clear


WHAT IS A “HEALTHY” DIET PATTERN?

Healthy Fruit & vegetable group
- 5 serves vegetable
- 2 fruit servings
- Legumes
- Raw nuts or seeds

Healthy fat group:
- Frequent consumption of:
  - Fish
  - Avocado
  - Mono/polyunsaturated oil for salads
    (e.g. olive oil)
- Minimal consumption of:
  - Oil in cooking
  - Processed or fatty meats
  - Cakes, biscuits, sweets
  - Take away foods

DIET & MULTIPLE SCLEROSIS: DISABILITY, MOOD, COGNITION, FATIGUE & PAIN

- 6,989 individuals with multiple sclerosis

Healthier diet pattern associated with less self-reported:
- Disability
- Depression
- Fatigue
- Pain
- Cognitive difficulties

What is a “healthy” diet pattern?
- ↑ High in fruit & vegetables
- ↑ High in legumes & whole grains
- ↓ Low in sugar
- ↓ Low in red meat


THE WAHLS DIET

- Fruits and vegetables (especially dark leafy green and intensely coloured)
- Omega-3 oils
- Animal & plant protein
- Gluten
- Dairy
- Eggs

THE WAHLS DIET

- A single-arm study has shown that participants who go on the Wahls diet show mood and cognitive improvements over 12 months.
- BUT there is no control arm of the study so improvements on cognitive tests could be due to practice effects.
- HOWEVER, the greater the adherence to diet, the better the mood and cognitive outcomes (suggests it is not just due to practice effects).
- Improvements in mood and cognition may be mediated by improvements in fatigue.


MEDITERRANEAN DIET

Largely consists of:
- Fish
- Variety of fruits & vegetables
- Olive oil
- Whole grains
- Legumes

Compared to other diets:
Higher
- Omega-3 fatty acids
- Lean protein
- Magnesium
- Antioxidants
- Polyphenols

Lower
- Processed foods
- Refined carbohydrates & saturated fats

Mediterranean Food Pyramid

- Mediterranean Oil (Olive)
- Meats and Sweets (in moderation)
- Seafood, Eggs, Cheese, and Yogurt
- Poultry, Legumes, Beans, and Whole Grains
- Fruits, Vegetables, Herbs, Spices, and Nuts

Daily Physical Activity

Olive Oil, Beans, Nuts, Legumes and Seeds, Herbs and Spices ( daily intake)

Fish and Seafood (daily intake)

Fruits, Vegetables, Herbs, Spices (handy supply)

Meats and Sweets (in moderation)

Seafood, Eggs, Cheese, and Yogurt

Poultry, Legumes, Beans, and Whole Grains

Fruits, Vegetables, Herbs, Spices, and Nuts

Dairy Products, Nuts, Legumes, Beans, Herbs and Spices (daily intake)

Dry Fruits

Meats and Sweets (in moderation)

Meat, Poultry, and Seafood

Eggs, Cheese, and Yogurt

Pantry Items

Daily Physical Activity

Drink Water

Meats and Sweets (in moderation)

Seafood, Eggs, Cheese, and Yogurt

Poultry, Legumes, Beans, and Whole Grains

Fruits, Vegetables, Herbs, Spices, and Nuts

Dairy Products, Nuts, Legumes, Beans, Herbs and Spices (daily intake)

Dry Fruits

Meats and Sweets (in moderation)

Meat, Poultry, and Seafood

Eggs, Cheese, and Yogurt

Pantry Items

Daily Physical Activity

Drink Water
MEDITERRANEAN DIET & COGNITION

In healthy older and younger adults:
• Improvement in cognition
  • Attention
  • Memory
• Slower rate of cognitive decline with age
• Reduced risk of dementia (e.g. Alzheimer’s disease)

• Note: some studies found no effects but:
  • Didn’t control for baseline diet
  • Used brief/easier cognitive tasks (ceiling effects)

• Higher adherence to Mediterranean diet associated with reduced risk of multiple sclerosis

OMEGA-3 & OMEGA-6 POLYUNSATURATED FATTY ACIDS

- Omega-3 PUFAs
  - Fish oils

- Omega-6 PUFAS
  - Sunflower oils
  - Soybean oils
  - Wheat germ

- PUFAs reduce inflammation
- PUFAs are decreased in plasma and CSF of pwMS
- EPA improves myelin self-repair capability
- In animal models, increasing PUFAs in the diet reduced the inflammation and demyelination, improved the quality of the myelin sheath

OMEGA-3 SUPPLEMENTATION TRIALS IN MS

- Clinical trials have shown:
  - Reduced disease progression
  - Decreased inflammatory cytokines
  - Decreased secretion of inflammatory eicosanoids
  - Improved physical & mental quality of life

- Note:
  - Not all trials have found a significant effect
  - Quality of supplement?
  - Baseline diet & other health behaviour
  - Seems to be better when dietary recommendations are given to participants
  - Greater EPA concentration seems to be best
COMBINATION OF PUFA, MUFA, SFA, VIT A & VIT E

For 30 months, people with MS were given a formulation containing:
- Omega 3 (Docosahexaenoic acid, Eicosapentaneoic acid)
- Omega 6 (linoleic acid, gamma-linoleic acid)
- Monounsaturated fatty acids
- Small quantity saturated fatty acids
- Vitamin A
- Vitamin E
- G-tocopherol

Compared to placebo, the formulation reduced:
- Annual relapse rate
- Time to disability progression
- New or enlarging lesions on MRI


POLYPHENOLS & COGNITION

- Polyphenols are naturally occurring chemicals found in foods
- Sources = fruits, veges, red wine, green tea, spinach, walnuts, spices, herbs
- Generally involved in the plants own defense against UV rays or pathogens
- Research shows consumption of polyphenols offers protection against cancer, diabetes, osteoporosis &neurodegenerative diseases
- Antioxidant and anti-inflammatory
- RA (found in herbs e.g. rosemary, thyme, sage) improved cognitive function in 13-15 year olds
- Resveratrol (found in dark berries, grapes, red wine) reduces oxidative stress & neurodegeneration, increases blood flow to PFC during cognitive tasks
- Curcumin (yellow spice tumeric) reduces inflammation induced by Western diet, and protects against cognitive impairment in Alzheimer’s disease and traumatic brain injury
RICHEST DIET SOURCES OF POLYPHENOLS

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<thead>
<tr>
<th>RICHEST DIET SOURCES OF POLYPHENOLS</th>
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<tbody>
<tr>
<td>Cloves</td>
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<tr>
<td>Peppermint, dried</td>
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<tr>
<td>Star anise</td>
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<tr>
<td>Cocoa powder</td>
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<tr>
<td>Mexican oregano, dried</td>
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<tr>
<td>Celery seed</td>
</tr>
<tr>
<td>Black chokeberry</td>
</tr>
<tr>
<td>Dark chocolate</td>
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<td>Flaxseed meal</td>
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<td>Black elderberry</td>
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<tr>
<td>Chestnut</td>
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<td>Common sage, dried</td>
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<td>Rosemary, dried</td>
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<td>Common thyme, dried</td>
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<td>Blackcurrant</td>
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<td>Capers</td>
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<td>Black olive</td>
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<td>Highbush blueberry</td>
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VITAMIN D & MS

- The further away someone lives from the equator, the higher the risk of MS (thought to be because of the reduced sun exposure)
- Maintaining adequate levels of vitamin D may have a protective effect and lower the risk of developing MS
- Vitamin D has a positive effect on the immune system (reduces the chance that the immune system will attack the myelin sheath)
VITAMIN D SUPPLEMENTATION

- Risk of MS substantially less for women taking >400 IUs Vit D/day
- For people who already have MS, vitamin D may lessen the frequency & severity of symptoms
- Level of supplementation depends on blood levels
- Ideal range is 40-80ng/ml

FASTING AND THE BRAIN

Period of fasting can:
- Increase brain cell activity
- Increase strength of connections between brain cells
- Promote growth of new brain cells
- Induce repair of brain cells
- Reduce inflammation
- Improve cognitive function

Note: I am not aware of any studies examining the effects of fasting in people with MS, only animal studies, however, please see the following slides regarding diets that mimic the effect of fasting and promising results regarding their safety and tolerability in people with multiple sclerosis.
KETOGENIC DIET & MEMORY IN MS

In an animal model of MS, ketogenic diet:
- Improved spatial learning and memory
- Reduced brain inflammation
- Reduced reactive oxygen species


FASTING MIMICKING DIET & MS

The fasting mimicking diet is low protein, low essential amino acid, low sugar and high in fat.

In an animal model of multiple sclerosis, fasting mimicking diet for 3/7 days over 3 weeks:
- Reduced disease severity
- Reduced immune cell infiltration
- Reduced demyelination
- Stimulated oligodendrocyte regeneration (repair of the myelin sheath)

PILOT TRIAL TO TEST THE EFFECTS OF A FMD OR KD IN RRMS PATIENTS

- 60 patients with relapsing-remitting MS randomised to either
  1. Fasting Mimicking diet for 7 days, then mediterranean diet for 6 months
  2. Ketogenic diet for 6 months
  3. Normal diet for 6 months

- Fasting Mimicking diets and ketogenic diets hold promise for cognition in MS and initial pilot studies to investigate their safety for use by people with MS are positive, however, the research literature is still emerging with respect to this

- If you are interested in following the progress, see the researcher’s website (Dr Valter Longo): http://longevityinstitute.usc.edu/
DIET AND COGNITION IN MS – A SUMMARY

- Not to be used to replace medically advised treatments
- Eat lots of fish, fruits, vegetables, nuts, seeds, wholegrains
- Avoid processed foods, eat foods in their whole form
- Get Vitamin D (via sunlight, as well as fish and diary)
- Little evidence that any one aspect of diet can be a cure all. A focus on whole diet is necessary.

I hope the information in this presentation will inspire and motivate you. Remember, my expertise is as a neuropsychologist and my focus is on benefits to cognition so make sure you seek expert advice regarding other physiological effects.

Dr Heather Francis