The role of diet and exercise in cognition in multiple sclerosis

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NOTE: THESE SLIDES FOCUS ON THE ROLE OF DIET AND EXERCISE ON COGNITION. PLEASE SEEK ADVICE FROM YOUR GP, NEUROLOGIST, REGISTERED DIETICIAN OR PHYSIOTHERAPIST BEFORE MAKING EXTREME LIFESTYLE CHANGES
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

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
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
DIET & MULTIPLE SCLEROSIS QUALITY OF LIFE, DISABILITY & RELAPSE

- 2087 people with MS
- USA (663), Aus (550), UK (356), NZ (178), Canada (92), Other (248)
- Higher overall dietary health score (foods as described on next slide) =
  Better Physical QoL
  Better Mental QoL
  Lower disability
  Links to relapse rate not as clear


WHAT DIET PATTERN WAS HEALTHY IN THE SOUTH AUSTRALIA STUDY?

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
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 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

FAT IS NOT SO BAD

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, Eicosapentanoic 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, vegetables, 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 turmeric) reduces inflammation induced by Western diet, and protects against cognitive impairment in Alzheimer’s disease and traumatic brain injury

RICHEST DIET SOURCES OF POLYPHENOLS

<table>
<thead>
<tr>
<th>Cloves</th>
<th>Herb/Spice</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peppermint, dried</td>
<td>Herb/Spice</td>
</tr>
<tr>
<td>Star anise</td>
<td>Herb/Spice</td>
</tr>
<tr>
<td>Cocoa powder</td>
<td>Cocoa products</td>
</tr>
<tr>
<td>Mexican oregano, dried</td>
<td>Herb/Spice</td>
</tr>
<tr>
<td>Celery seed</td>
<td>Herb/Spice</td>
</tr>
<tr>
<td>Black chokeberry</td>
<td>Herbs</td>
</tr>
<tr>
<td>Dark chocolate</td>
<td>Cocoa products</td>
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<tr>
<td>Flaxseed meal</td>
<td>Seeds</td>
</tr>
<tr>
<td>Black elderberry</td>
<td>Fruits</td>
</tr>
<tr>
<td>Chestnut</td>
<td>Seeds</td>
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<td>Common sage, dried</td>
<td>Herb/Spice</td>
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<tr>
<td>Spearmint, dried</td>
<td>Herb/Spice</td>
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<tr>
<td>Common thyme, dried</td>
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<tr>
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<tr>
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<td>Black olive</td>
<td>Vegetables</td>
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<tr>
<td>Highbush blueberry</td>
<td>Fruits</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
- 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
- Vitamin D has a positive effect on the immune system (reduces the chance that the immune system will attack the myelin sheath)

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


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**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.

EXERCISE AND COGNITION
GENERAL BENEFITS OF EXERCISE

- General Health Benefits
- Increases metabolic function
- Reduction of metabolic syndrome
- Reduction in dementia risk
- Improves life satisfaction
- Reduces depression

EXERCISE LEADS TO ANATOMICAL AND PHYSIOLOGICAL ALTERATIONS IN THE BRAIN

Anatomical:
- Increased physical activity is associated with increased hippocampal volume

EXERCISE REDUCES INFLAMMATION

• Exercise activates an adaptive cellular stress response, mobilising defense mechanisms against oxidative stress, metabolic stress and inflammation.


EXERCISE AND AGING

Most recommendations suggesting physical activity to improve cognition come from studies showing exercise benefits cognition in older adults.

Benefits in older adults include:
• Improvement of existing cognitive function
• Maintenance of optimal cognitive function
• Reduced risk of neurodegenerative conditions such as Alzheimer’s disease
WHAT TYPE OF EXERCISE

- Aerobic
  - Running
  - Cycling
  - Swimming
- Muscle-strengthening
  - Heavy weights
  - Pilates
  - Barre
- Meditative movement
  - Yoga
  - Tai Chi

AEROBIC EXERCISE & COGNITION

STRENGTH TRAINING & COGNITION

• More muscle mass associated with more brain mass
• Just 20 minutes of leg strength training enhanced long-term memory by 10%

INCIDENTAL MOVEMENT & COGNITION

Maintaining an exercise program can be difficult
Benefits even of simply moving around a lot and avoiding sitting for too long
Physical movement (e.g. gardening, walking, moving around the house) associated with:
• Higher brain oxygenation
• Patterns of brain activity associated with better cognitive function
EXERCISE & COGNITION IN MS

In people with multiple sclerosis, higher levels of physical activity predicted:
• more cortical plasticity
• preserved cognitive capabilities


WEBSITE/TELEPHONE BASED EXERCISE PROGRAMS

• 6 month program
• Website and one-on-one coaching sessions aimed at increasing physical activity.
• Those with mild disabilities showed improvement in processing speed. Those with moderate disabilities showed only minimal improvement.

• 12 week program
• Telephone based health promotion intervention.
• Those who physically improved, also showed improvement on processing speed.

Beier (2014) Sandroff et al. (2014)
Garrett et al (2012) 60 minute group exercise sessions, once per week for 10 weeks. Exercise consisted of standard physical therapy, yoga, combined aerobic and resistance training all compared to a control group. All 3 exercise groups improved on the cognitive subscale of the Modified Fatigue Impact Scale.

PHYSICAL THERAPY, YOGA OR AEROBIC+WEIGHT TRAINING


STATIONARY BICYCLE

• Training sessions gradually increasing from 15-45 minutes.
• 2-3 times per week for 8-10 weeks.
• Three exercise interventions (arm ergometry, rowing, bicycle ergometry)
• Bicycle training group showed significant improvement on tests of attention.

**YOGA AND COGNITION**

Metanalysis of 15 Randomised Controlled Trials:

- Moderate beneficial long term effect of yoga on cognition
- Strongest effects for attention and processing speed, then executive function and memory
- Also acute (immediate effects) on these same cognitive domains


**YOGA AND COGNITION IN MS**

- Hatha yoga, 1 day per week for 10 weeks
- PwMS aged 26-50
- Improvements in:
  - Attention
  - Processing speed
  - Executive function
EXERCISE & COGNITION IN MS – A SUMMARY

• Exercise well-established to be beneficial for neuroplasticity and neurogenesis
• Exercise benefits cognition
• This appears to be true for people with MS too
• Benefits have been shown in a variety of exercise programs so do what suits you
• Seek advice of physio, exercise physiologist or trainer

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