Nutrition & the healthy ageing of the brain

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Overview

Effects of Diet on Cognitive Function/Decline

- Extent of the problem – dementia prevalence increasing
- Ageing population – greater old age dependency
- Nutrient intake - modifiable
- Demonstrate effective dietary interventions
- Valid measures of cognition/cognitive decline
- Sensitivity to Nutrient Intervention
- Suitability for different age groups
- Establish mechanisms of effects
- Need for expertise in the assessment of cognitive function in nutritional studies
Cognition throughout life

- Cognitive development
- Prevention of cognitive aging
- Optimization of cognitive performance

- Infant
- Child
- Adult
- Elderly

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EU population by age and sex

Telegram overload - centenarians will continue to be the fastest growing age group

Thousands, UK

Government Actuary's Department

Millions of persons

Total: 500 million

Total: 517 million

10% 14%
17% 18%
58% 55%
15% 14%

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Ageing and dementia

German Alzheimer's Association 2011

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Alzheimer’s disease

Alzheimer’s disease: a progressive problem

Earliest Alzheimer’s-changes may begin even 20 years before the diagnosis
Mild to moderate Alzheimer’s stage: last from 2 to 10 years
Severe Alzheimer’s: last from 1-5 years

Type 3 Diabetes?
- metabolic disease
Impairment in brain insulin responsiveness, glucose utilization & energy metabolism,
Insulin-like growth factor (IGF) resistance

80% of AD patients have problems with glycaemic control

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Relative risk of VD in those with T2DM
RR: 2.49,
95% CI: 2.09–2.97

For AD:
RR: 1.46,
95% CI: 1.20–1.77

Cheng et al. (2012)
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Possible Mechanisms: effects of diet on cognitive function

• Improved insulin (gluco) regulation
• Reduced Inflammation
• Reduced Oxidative stress
• Improved cardiovascular status
• Improved/maintained neurogenesis

Reduce Obesity

Direct Effects Of Nutrients?
Micronutrients & potential mechanisms for effects on cognitive function

Inflammation
Micronutrients influence cytokine production or free radical scavenging (reduce CRP).

Oxidative Stress
Antioxidant micronutrients (Vit C, E, Selenium, Zinc, β–Carotene, Flavonoids) associated with mitochondrial function influence cognitive function & limit oxidative stress in neuronal cells.

Influence neurotrophins
Polyphenols affect BDNF (Neshatdoust et al. 2016); High Flavonoid F&V improved cognition & increased BDNF in serum.

SuViMax study – 8 years AO showed improved verbal memory 5 years later cf placebo recipients.
Devore et al (2012) Nurses Health Study

16,010 women aged 70+

Follow up – 2yr intervals

Greater intake of

&

Slower rate of cognitive decline
(6 cognitive tests)

infant  child  adult  elderly

prevention of cognitive aging

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Midlife - critical period to prevent cognitive decline?

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Mediterranean Diet (PrediMed)

Middle age/high CVD risk

Valls-Pedret et al. (2015) JAMA
Can obesity related deficits in cognitive function be reversed?

Weight loss through diet & exercise – improve cog function
e.g. Hypertensives on the DASH diet, aerobic exercise and reduced calories showed improvements in multiple measures of cognitive function (Smith et al., 2010)

Overweight & obese people who lost 14kg over 1 year showed improvements in working memory (Brinkworth et al., 2009)

Obesity related cognitive dysfunction is partly reversible but the mechanisms/physiological processes responsible are not determined
Dietary fibre, exercise & cognition in elderly with IGT /T2DM

2 year intervention: exercise 2-4/wk + Dietary fibre >30g/day

<table>
<thead>
<tr>
<th></th>
<th>NGT (n=74)</th>
<th>IGT (n=36)</th>
<th>T2DM (n=19)</th>
</tr>
</thead>
<tbody>
<tr>
<td>FPG</td>
<td>0</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>2hr OGTT</td>
<td>0</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>HOMA</td>
<td>0</td>
<td>-</td>
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</tr>
<tr>
<td>MMSE</td>
<td>0</td>
<td>0</td>
<td>+</td>
</tr>
<tr>
<td>Dementia scale</td>
<td>0</td>
<td>0</td>
<td>+</td>
</tr>
<tr>
<td>Delayed recall</td>
<td>0</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Block design</td>
<td>0</td>
<td>+</td>
<td>0</td>
</tr>
</tbody>
</table>

Dietary fibre & exercise improved cognitive function via improved glucoregulation

Yamamoto et al. (2009)
Effects of nutrition on mood & cognition will be subtle

- Nutritional interventions with enduring effects on cognition or mood may take months or even years to manifest

E.g. 6 months fish oil consumption (1.7 g DHA, 0.7 g EPA) increased recall of word lists by ~1 word

Authors concluded the treatment had no effect

But:

*decreased recall of 1 word may equal 1 year of cognitive decline*
Where should we focus our research & public health efforts?

- younger populations (aged 40–65 years) – key demographic
- Longer prospective studies
- use of biomarkers
- account for potentially harmful dietary components,
- use of neuroimaging data/ cognitive tests sensitive to diet
- Additive/synergistic effects of other behaviour e.g. physical activity, body weight change
Crossover, n = 25
4 week washout

Baseline

6 weeks

12 weeks

12oz daily serving CGJ or placebo
777mg total polyphenolics
167mg anthocyanins & 334mg proanthocyanidins
Matched for energy (223kcal), appearance, taste and volume

• Cognitive battery
• Mood
• Stress and anxiety
• Blood pressure
• Driving performance

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Future Directions

- Changing nature of diet, health & population
  - Understand effects of altered eating patterns
  - Effects of under & over-nutrition
- Cognitive benefits could be conferred directly –specific nutrients or overall intake
- Or via other effects on health e.g. better gluco-regulation, reduced triglycerides or other markers
- Important to preserve cognitive capacity in ageing
- Need functional foods/nutrients to help maintain brain function
Use it or lose it?

Thank You

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Thank You!

BioPsychology Group

Professor Louise Dye
Dr Clare Lawton – Appetite control, satiety & weight management
Dr Neil Boyle – Stress and dietary protection, dairy
Dr James Stone – Polyphenols and cognition/gut
Dr Katie Adolphus – Breakfast & cognition/academic outcomes
Claire Champ – Dairy phospholipids & cognition in children
Helen Chadwick – Cognition and glycaemic control in Cystic Fibrosis
Iria Myrissa – Fibre and wellbeing – predictors of weight loss/maintenance
Denise Hofman – PKU & cognitive function/Insulin/Hunger & cognitive function
Fiona Croden – research dietitian
Dr Arief Gusnanto – Statistician
Prof Anne McArdle & Prof M Jackson – Cognitive function, muscle mitochondria & Chronic Fatigue Syndrome (Institute of Aging, Univ of Liverpool)
Dr Daniel Lamport – IGT, T2DM & Cognition; Polyphenols & Cognition (Reading Uni)
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Dr Eleanor Scott – Gestational Diabetes, Eating Behaviour & Sleep
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### Significant effects of selected nutritional interventions on tests of cognitive domains/ no of tests applied

De Jager et al. 2014

<table>
<thead>
<tr>
<th>Cognitive Domain</th>
<th>Isoflavones</th>
<th>Polyphenols</th>
<th>B Vitamins</th>
<th>N-3 Fatty Acids</th>
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</thead>
<tbody>
<tr>
<td>Immediate verbal memory</td>
<td>3/15</td>
<td>2/7</td>
<td>3/7</td>
<td>0/3</td>
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<tr>
<td>Delayed verbal memory</td>
<td>0/9</td>
<td>0/4</td>
<td>2/2</td>
<td>1/3</td>
</tr>
<tr>
<td>Immediate spatial memory</td>
<td>4/15</td>
<td>4/8</td>
<td>1/1</td>
<td>1/2</td>
</tr>
<tr>
<td>Delayed spatial memory</td>
<td>3/4</td>
<td>0/1</td>
<td>-</td>
<td>1/1</td>
</tr>
<tr>
<td>Executive Function</td>
<td>10/30</td>
<td>0/3</td>
<td>4/6</td>
<td>0/3</td>
</tr>
<tr>
<td>Working memory</td>
<td>1/8</td>
<td>1/5</td>
<td>0/2</td>
<td>2/6</td>
</tr>
<tr>
<td>Attention/info processing</td>
<td>3/12</td>
<td>2/15</td>
<td>1/4</td>
<td>0/9</td>
</tr>
<tr>
<td>Global (adult)</td>
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<td>-</td>
<td>3/7</td>
<td>0/2</td>
</tr>
<tr>
<td>Global (child)</td>
<td>0/4</td>
<td>-</td>
<td>2/2</td>
<td>1/1</td>
</tr>
<tr>
<td>Psychomotor</td>
<td>1/3</td>
<td>-</td>
<td>-</td>
<td>0/1</td>
</tr>
</tbody>
</table>
Few effects of these nutrients on various cognitive domains

- Quite sparse amount of research using cognitive outcomes
- Poor choice of tests?
- Tests not sensitive
- No real effect of intervention
- Intervention inadequate to exert cognitive effects – too short/low dose
- Inappropriate sample (too healthy/ young etc)
- Enduring effect of active treatment affects comparison in crossover designs
Obese adults perform worse than normal weight on:

**Learning & Memory:**
- List learning
- Delayed recall
- Recognition

**Frontal lobe tasks:**
- Executive Function
- Complex attention
- Psychomotor speed

Selbom & Gunstad (2012)
Increased visceral fat may induce cognitive decline (Type III DM?)

Jagust et al. (2005)

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Increased WHR is associated with a reduction in spatial recognition memory in middle-aged males exposed to stress.

Lasikiewicz et al, 2012