Nutrition & the (un)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 - claims
• Need for Markers
Cognition throughout life

- **Cognitive development**
- **Prevention of cognitive aging**
- **Optimalization of cognitive performance**

**ABILITY**

infant, child, adult, elderly
EU population by age and sex

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

Thousands, UK

2008 2018 2028 2038 2048 2058

Government Actuary’s Department

Millions of persons

25 15

Government Actuary’s Department

2060

Total: 500 million

Total: 517 million

10% 14%

17% 18%

58% 55%

15% 14%
Ageing and dementia

Morbidity Rate in %

Age (years)

Alzheimer's-related dementia

Total dementias

German Alzheimer's Association 2011
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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Vascular Dementia

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)
Increased visceral fat may induce cognitive decline (Type III DM?)

Stress promotes deposition of visceral fat

Jagust et al. (2005)

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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)

Bariatric surgery – prompt, sustained improvement in EF & Memory

Obesity related cognitive dysfunction is partly reversible but the mechanisms/physiological processes responsible are not determined
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
Hippocampal Neurogenesis

Occurs throughout life in humans – 700 new neurons/day

Dentate gyrus contains neurostem cells which migrate, differentiate, receive input and integrate into circuitry

New hippocampal neurons cells:
- Increase spatial memory capacity,
- Reduce interference between memories pattern separation i.e. helps us to distinguish similar memories

Thuret, 2017 ILSI Workshop on Ageing Brain
Modulation of hippocampal neurogenesis

Decrease HNG

Increase HNG

Diet can affect HNG

Zainuddin and Thuret, 2012

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Overview of the four different levels at which diet impacts on Adult Hippocampal Neurogenesis. The grey dots represent newborn neurons in the dentate gyrus of the hippocampus.

Zainuddin M S A, Thuret S Br Med Bull 2012; bmb.lds021
Cocoa Flavanols improve Pattern Separation in the dentate gyrus

Brickman et al. (2015) Nat Neurosci
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)

prevention of cognitive aging

infant child adult elderly
Midlife - critical period to prevent cognitive decline?
Mediterranean Diet (PrediMed)

Figure 2. Changes in Cognitive Function Measured With Composites by Intervention Group

Middle age/high CVD risk

Valls-Pedret et al. (2015) JAMA
Concord grape juice, cognitive function, and driving performance: a 12-wk, placebo-controlled, randomized crossover trial in mothers of preteen children

Crossover, n = 25
4 week washout

Baseline 6 weeks 12 weeks

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

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

Grape juice flavonoids

**Figure 1: VVLT immediate recall averaged across three trials (A1-A3)**

- For VVLT immediate recall, a significant Condition*Study Phase interaction was observed ($F[1,20]=4.61$, $p<0.05$). Post hoc tests indicated an initial benefit of the CGJ in arm 1 which endured into arm 2 when the placebo was consumed (see Figure 1).

**Figure 2: Tower of Hanoi completion time for each Condition and Study Phase**

- ToH completion time showed a significant Condition*Study Phase interaction ($F[1,21]=14.12$, $p<0.01$). As shown in Figure 2, post hoc tests revealed that completion time was significantly faster for the CGJ relative to the placebo in arm 1 ($p<0.01$) whereas this difference was not significant in arm 2.

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*

de Jager et al, 2014
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
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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BioPsychology Group

Professor Louise Dye
Dr Clare Lawton – Appetite control, satiety & weight
Dr Neil Boyle – Stress and dietary protection, dairy
Dr James Stone – Polyphenols and cognition/gut
Dr Katie Adolphus – Breakfast & cognition/academic
Claire Champ – Dairy phospholipids & cognition in
Helen Chadwick – Cognition and glycaemic control
Iria Myrissa – Fibre and wellbeing – predictors of
Denise Hofman – PKU & cognitive function/Insulin
Fiona Croden – research dietitian
Dr Arief Gusnanto – Statistician
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Chronic Fatigue Syndrome (Institute of Aging, Uni)
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