Obesity, Diabetes & Cognitive Function

Louise Dye

Chair in Nutrition & Behaviour
Nutrition & Behaviour Group
Human Appetite Research Unit
Institute of Psychological Sciences
University of Leeds

l.dye@leeds.ac.uk
Overview

Conditions

• Obesity
• Type 2 Diabetes (IGT)
• Alzheimer’s Disease ~ Type 3 diabetes

Impact on Cognitive Function

• Cognitive Domains

Potential impact of Nutrition

• Prevention of cognitive decline
• Therapeutic potential?
Obesity & Overweight in Europe

Proportion of men (upper) & women (lower) who were overweight or obese, 2008 or nearest year in each EU country

Source: Eurostat (online data code: hith_ehis_de1)
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 10 7 5 3 2

10% 17% 58% 15%

14% 18% 55%

Total: 500 million

Total: 517 million

Louise Dye, HARU, Leeds
Population aged 65 years and more as a share of population aged 15-64 years:

- > 35.0
- 30.0 - 35.0
- 25.0 - 30.0
- 20.0 - 25.0
- 15.0 - 20.0
- < 15.0
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

Louise Dye, HARU, Leeds
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)
Obesity and Cognitive Function

Obese adults perform worse than normal weight on:

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

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

Selbom & Gunstad (2012)
Obesity & Cognitive Function:
Data from Framingham

Four findings:

1. Effects of Obesity & HT on learning & memory in men not women.

2. Indpt of other CVD risk.

3. Suggest similar pathophysiological mechanisms.


Elias et al. (2002)

Louise Dye, HARU, Leeds
Obesity related Neuropsychological changes

Fig. 1. A preliminary integrative model of obesity-related neuropsychological changes.

Selbom & Gunstad (2012)
High inter-individual variation
More tightly regulated in young healthy
Smaller in individuals who show better memory performance
Suggests optimal range for cognitive enhancement

Korol, D. & Gold P. (1998) AJCN
OGTT: Oral glucose tolerance test is the diagnostic test (75g glucose solution)
Diabetes Prevalence

UK prevalence 3.5 million people diagnosed
0.5 million undiagnosed
235,000 diagnosed in 2015

(Diabetes UK)

90% Type 2 DM
Earlier onset – teens/20s
Genetic predisposition – Afro-Caribbean & Asian
Prenatal exposure to high sugar levels

Healthy diet & exercise can halve risk of developing diabetes in people with IGT
Type 2 Diabetes and cognitive function

- Evidence that type 2 diabetes (T2DM) associated with cognitive impairments
- Early onset, poor regulation & micro-, macrovascular disease - early deficits
- Reduced hippocampal volume - memory (Convit, 2009)
- Some evidence that IGT associated with cog. Impairments

BUT… Difficult to rule out cognitive effects of ageing
T2DM and cognitive function

Type 2 diabetes - impairments in:

- Verbal memory,
- Spatial memory,
- Psychomotor skill,
- Executive function

Compared to NGT adults matched for education, age, depression, & IQ.

Prevalence of Impaired Glucose Tolerance 2013
Effects of glucose on cognition in relation to glucose regulation

- Epidemiological studies of IGT—clear association with impaired cognitive function (Kalmijn et al., 1995)

- Systematic review

NGT –
Normal glucose tolerance

Clear effects on cognition
Memory – worse
- specific tests
Only in poor regulators in the normal range

IGT –
Impaired glucose tolerance

Pre Diabetic state – losing regulation
Unaware, not on treatment
Middle aged
Few effects on cognition
Poor range of insensitive tests (e.g. MMSE)

Recruited 65 females aged 30-50 years from general population

- Screening
  - OGTT (oral glucose tolerance test)
    - normal glucose tolerance (NGT)
      - N = 47
    - Impaired glucose tolerance (NGT)
      - N = 18

Lamport et al. (2014)
Glycaemic response to the OGTT

Lamport et al. (2014)
IGT and Memory

IGT greater retroactive interference at Session 2 relative to Session 1

IGT poorer delayed recall & recognition of verbal material - deficit in hippocampal function

Lamport et al. (2014)
IGT and cognitive function

IGT group impaired on...

- VVLT (immediate & delayed)
- Word recognition
- VSLT (immediate & delayed)
- Corsi block tapping
- Psychomotor Test

IGT impaired on 12 / 27 cognitive test outcomes

Subtle impairments in prolonged concentration in ostensibly healthy middle aged women

Lamport et al. (2014)
Attention Switching Task: People with CF-related diabetes have significantly slower processing speed than non-diabetic people with CF and healthy controls.

Mean reaction time (ms) for correct trials

- CF-related diabetics
- CF non-diabetics
- Controls

* * p < .001
** * p = .077

Chadwick et al. (2015)
Cognition throughout life

prevention of cognitive aging

ABILITY

infant  child  adult  elderly

Louise Dye, HARU, Leeds
Fish consumption is negatively related to the risk of dementia.

Barberger-Gateau (2002)
Devore et al (2012) Nurses Health Study

16010 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?
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
Mediterranean Diet (PrediMed)

Middle age/high CVD risk

Valls-Pedret et al. (2015) JAMA
Nutrients & Glycaemic Control/Vascular Function: Polyphenols

CBF & Age/Dementia

Cocoa Flavanols

Blueberries

Brickman et al. (2015) Nat Neurosci

Rodriguez-Mateos et al. (2013) AJCN

Cocoa Flavanols – Improved IR & Lipid Peroxidation

Mastroiacovo et al. (2015) AJCN
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>
<td>-</td>
</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)
# Nutrients & Cognitive Decline

<table>
<thead>
<tr>
<th>Nutrient</th>
<th>Effect</th>
<th>Sample</th>
<th>Sources</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>n-3 (DHA, EPA)</strong></td>
<td>Benefits cog decline</td>
<td>Elderly, mouse model of AD</td>
<td>Fish (salmon), flax, krill, chia</td>
</tr>
<tr>
<td>Curcumin</td>
<td>Benefit cog decay</td>
<td>Mouse AD, rodent brain injury</td>
<td>Turmeric</td>
</tr>
<tr>
<td><strong>Ca+, Zinc, Selenium</strong></td>
<td>High Ca+-faster cog decline; lower zinc better cog; lifelong low selenium –better cognitive function</td>
<td>elderly</td>
<td>Ca+ dairy; Zinc-oysters, beans, nuts, seeds, selenium- nuts, cereals, meat, fish, eggs</td>
</tr>
<tr>
<td>Antioxidant vitamins C, E, carotene</td>
<td>Delay cog decline</td>
<td>elderly</td>
<td>Fruit, veg, calf/beef liver</td>
</tr>
<tr>
<td>Vitamin E</td>
<td>+ve cog brain trauma Delay cog decline</td>
<td>Rodents Elderly</td>
<td>Asparagus, avocado, nuts, olives, seeds, spinach, wheatgerm</td>
</tr>
<tr>
<td>Copper</td>
<td>Cog decline correlated with plasma copper</td>
<td>Elderly with AD</td>
<td></td>
</tr>
<tr>
<td>Sat Fat</td>
<td>exacerbate cog decline</td>
<td>Rodents, aging humans, brain injury</td>
<td>Butter, ghee, oils, dairy, meat</td>
</tr>
</tbody>
</table>
Future Directions

- Changing nature of diet, health & population
  - Understand effects of ageing AND eating patterns
  - Effects of under & overnutrition
- 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
Use it or lose it?

Thank You
Thank You!

Professor Louise Dye
Dr Clare Lawton – Appetite control, satiety & weight management
Dr Katie Adolphus – Breakfast & cognition/academic outcomes in children
Claire Champ – Dairy intervention & cognition in children/elderly
Dr Neil Boyle – Stress and dietary protection, dairy components
Dr James Stone – Nutritional intervention in children

Dr Dan Lamport – IGT, T2DM & Cognition;
Polyphenols & Cognition (Reading Uni)

Dr Amy Weeks – Exercise interventions and cognitive function in obesity
Iria Myrissa – Fibre and wellbeing – predictors of weight loss/maintenance
Denise Hofman – PKU & cognitive function/Insulin/Hunger & cognitive function

Dr Ann Lanham – Predictors of long term outcome of bariatric surgery
Fiona Croden – research dietitian
Kate Earl – Cognitive function, muscle mitochondria & Chronic Fatigue Syndrome
(Institute of Aging, Univ o Liverpool – Profs McArdle & Jackson
Dr Eleanor Scott – Gestational Diabetes, Eating Behaviour & Sleep