Understanding the link between Cognition, Obesity and Type 2 Diabetes

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Overview

Conditions which alter glucose regulation

- Obesity
- Impaired Glucose Tolerance (IGT) and Type 2 Diabetes
- Impact on Cognitive Function
- 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)
Central obesity and risk of MetS

waist-to-hip ratio (WHR)

<table>
<thead>
<tr>
<th>Male</th>
<th>Female</th>
<th>Health Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤0.95</td>
<td>≤0.80</td>
<td>Low</td>
</tr>
<tr>
<td>≥1.0</td>
<td>≥0.85+</td>
<td>High</td>
</tr>
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</table>

‘subcutaneous’ adipose

‘visceral’ adipose

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Prevalence of the Metabolic Syndrome (MetS)

MetS
waist:hip ratio > 0.90 (male)
> 0.85 (female)
+ dysglycemia

NHANES III: n=8814 adults
Increased visceral fat may induce cognitive decline (Type III DM?)
Obesity and Cognitive Function

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)
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.


Figure 1  Relation of number of CVD risk factors (0 = none; 1 = either obesity or hypertension present; 2 = both obesity and hypertension present) to cognitive test performance in men.

Elias et al. (2002)
Obesity related Neuropsychological changes

Selbom & Gunstad (2012)

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

Selbom & Gunstad (2012)
OGTT: Oral glucose tolerance test is the diagnostic test (75g glucose solution).
Prevalence of Impaired Glucose Tolerance 2013
Effects of glucose on cognition in relation to glucose regulation

<table>
<thead>
<tr>
<th>NGT – Normal glucose tolerance</th>
<th>IGT – Impaired glucose tolerance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clear effects on cognition</td>
<td>Pre Diabetic state – losing regulation</td>
</tr>
<tr>
<td>Memory – worse</td>
<td>Unaware, not on treatment</td>
</tr>
<tr>
<td>- specific tests</td>
<td>Middle aged</td>
</tr>
<tr>
<td>Only in <strong>poor regulators</strong> in the <strong>normal range</strong></td>
<td>Few effects on cognition</td>
</tr>
<tr>
<td></td>
<td>Poor range of insensitive tests (e.g. MMSE)</td>
</tr>
</tbody>
</table>


- Epidemiological studies of IGT–clear association with impaired cognitive function (Kalmijn et al., 1995)
- Systematic review
IGT and cognition

Recruited 65 females aged 30-50 years from general population

• Screening

• OGGTT (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)
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.

Cognition throughout life

infant  child  adult  elderly

prevention of cognitive aging
Midlife - critical period to prevent obesity & 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
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 OGGTT</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)
Fish consumption is negatively related to the risk of dementia

Barberger-Gateau (2002)
Dietary Flavonoids

A wide array of Fruits and vegetables

Green & Black Tea: (Flavanols)

Red wine: (Flavanol, Flavonols)

Citrus: (Flavanone)

Cocoa: (Flavanols and procyanidins)

Berries: (Anthocyanins)
Effects of Flavonoids on Health

- Reduced cancer risk
  - Steinmetz et al. 1993 Am J Epid

- Lower stroke risk

- Reduces Blood Pressure
  - Morand, C 2011. Am Clin Nutr vol. 93 no. 1 73-80
  - Asgary & Keshvari 2013. ARYA Atheroscler 9-1

- Improves blood lipid profile
  - Kurowska et al 2000. Am J Clin Nutr. 72 no. 5 1095-1100

- Cognition and psychological condition

- Improves endothelial function
  - Morand, C 2011. Am Clin Nutr vol. 93 no. 1 73-80

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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
Crossover, n = 25
4 week washout

- 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
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).

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.
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

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<table>
<thead>
<tr>
<th>Nutrient</th>
<th>Effect</th>
<th>Sample</th>
<th>Sources</th>
</tr>
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<tbody>
<tr>
<td>n-3 (DHA, EPA)</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>Ca+, Zinc,</td>
<td>High Ca+-faster cog decline; lower zinc</td>
<td>elderly</td>
<td>Ca+ dairy; Zinc-oysters, beans, nuts, seeds,</td>
</tr>
<tr>
<td>Selenium</td>
<td>better cog; lifelong low selenium –better</td>
<td></td>
<td>selenium- nuts, cereals, meat, fish, eggs</td>
</tr>
<tr>
<td></td>
<td>cognitive function</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Antioxidant</td>
<td>Delay cog decline</td>
<td>elderly</td>
<td>Fruit, veg, calf/beef liver</td>
</tr>
<tr>
<td>vitamins C, E,</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>carotene</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vitamin E</td>
<td>+ve cog brain trauma</td>
<td>Rodents</td>
<td>Asparagus, avocado, nuts, olives, seeds,</td>
</tr>
<tr>
<td></td>
<td>Reduce cog decay</td>
<td>Elderly</td>
<td>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>
Use it or lose it?

Thank You

Louise Dye, HARU, Leeds
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 – Nutrients and cognition in children
Dr Amy Weeks – Exercise interventions and cognitive function in obesity
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
Dr Ann Lanham – Predictors of long term outcome of bariatric surgery
Fiona Croden – research dietitian
Dr Dan Lamport – IGT, T2DM & Cognition; Polyphenols & Cognition (Reading Uni)
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