B-Vitamins and the Ageing Brain

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Presentation Outline

• The Ageing Brain

• Evidence linking B-vitamins with Cognition in ageing

• Results from the TUDA study (island of Ireland)

• Future directions and Conclusions
Dementia: Incidence

The number of people with the condition will double in the next 20 years and treble in the next 35 years.

Genio Dementia Learning Event
Dementia: The Costs

UK
850,000

ROI
74,468

World
46.8 million

£26.3 billion

€1.7 billion

$818 billion

Cognitive Impairment Spectrum

TIME (Years)

NORMAL AGEING
MILD COGNITIVE IMPAIRMENT
DEMENTIA

Cognitive Function

65
75
85

50%
1. Smith, *Food Nutr Bull* 2008; 29, 2, S143
Specific nutrients and brain health

- B Vitamins
- Carbohydrates
- Fatty acids
- Protein
- Vitamin C
- Polyphenols
- B Vitamins
# B-vitamins in Relation to Cognition in Ageing

<table>
<thead>
<tr>
<th>Biomarker</th>
<th>Epidemiological Evidence</th>
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<tbody>
<tr>
<td>Plasma homocysteine 1-4, 6</td>
<td>✔✔✔✔</td>
</tr>
<tr>
<td>Folate 1-4,7</td>
<td>✔✔✔</td>
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<tr>
<td>Vitamin B12 1-5</td>
<td>✔✔✔</td>
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<tr>
<td>Vitamin B6 5, 8</td>
<td>✔</td>
</tr>
<tr>
<td>Riboflavin</td>
<td>?</td>
</tr>
</tbody>
</table>

1. Selhub et al., *AJCN* 2000; 71, 614S-620S.
5. Moorthy et al., *J. Nutr* 2012; 142, 1554-1560
6. Almeida et al., *Arch Gen Psychiatry* 2008; 65(11), 1286-1294.
8. Skarupski et al., *AJCN* 2010; 92(2), 330-335
<table>
<thead>
<tr>
<th>Author</th>
<th>Dose (mg/d)</th>
<th>Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>McMahon 2006</td>
<td>B12 (0.5), FA (1) and B6 (10) for 2 years n=253</td>
<td>No effect</td>
</tr>
<tr>
<td>Durga 2007</td>
<td>FA (0.8) for 3 years n=836</td>
<td>Improved cognition</td>
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<tr>
<td>Kwok 2010</td>
<td>B12 (1) and FA (5) for 2 years n=140</td>
<td>No effect</td>
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<tr>
<td>Walker 2012</td>
<td>B12 (0.1) and FA (0.4) for 2 years n=900</td>
<td>Improved cognition</td>
</tr>
<tr>
<td>VITACOG Study</td>
<td>B12 (0.5), FA (0.8) and B6 (20) for 2 year n=266</td>
<td>Improved cognition MRI: ↓ grey matter ↓ brain atrophy by 30%</td>
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<tr>
<td>Smith 2010</td>
<td>B12 (0.5), FA (0.8) and B6 (20) for 2 year n=266</td>
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<tr>
<td>De Jager 2012</td>
<td>B12 (0.5), FA (0.8) and B6 (20) for 2 year n=266</td>
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<tr>
<td>Douaud 2013</td>
<td>B12 (0.5), FA (0.8) and B6 (20) for 2 year n=266</td>
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<td>Jernerén 2015</td>
<td>B12 (0.5), FA (0.8) and B6 (20) for 2 year n=266</td>
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<tr>
<td>Van der Zwaluw 2014</td>
<td>B12 (0.5), FA (0.8) and B6 (20) for 2 year n=266</td>
<td>No effect</td>
</tr>
</tbody>
</table>
The VITACOG Study

A: Placebo
Rate of Atrophy: 2.5% per year

B: B Vitamins
Rate of Atrophy: 0.46% per year

Significantly greater loss in Grey Matter Volume in the placebo group

Smith et al., *Plos One* 2010; 5(9):e1224
Douaud et al., *Proc of Natl Acad Sci of USA* 2013; 110(23):9523-9528
Anthropometric details

Demographic details

Lifestyle variables
Smoking, alcohol, dietary habits, sun exposure

Measures of frailty
Physical self maintenance, daily living activities, mobility

Medical history,
Heart disease, stroke, diabetes, hypertension, falls, anxiety, depression

Clinical parameters
BP, liver function, kidney function, haematology, lipids, electrolytes

Medications, supplements, fortified foods

The Trinity Ulster Department of Agriculture (TUDA) Ageing Study n = 5,186
Trinity Ulster Department of Agriculture Ageing Cohort Study (TUDA)

1. TUDA \( n \) 5186
2. TUDA +5 \( n \) 587
3. TUDA RCT \( n \) 328
Cognitive Assessment

Mini-Mental State Examination (MMSE)
• Quick method for global cognition; widely used
• <24 mild cognitive impairment; <20 dementia

Repeatable Battery for Neuropsychological Assessment (RBANS)
• Screening battery for attention, language, constructional abilities, immediate and delayed memory
• <80 cognitive impairment

Frontal Assessment Battery (FAB)
• Designed to test frontal lobe function
• <15 cognitive impairment
# TUDA - General Characteristics

<table>
<thead>
<tr>
<th></th>
<th>Males n 1699</th>
<th>Females n 3487</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>73.4±8.1</td>
<td>74.3±8.4</td>
<td>0.001</td>
</tr>
<tr>
<td>Educations (years)</td>
<td>16.0±3.2</td>
<td>16.0±2.9</td>
<td>0.968</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>28.5±20.5</td>
<td>27.6±5.8</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>FA Fortified Food Consumer (%)</td>
<td>71</td>
<td>71.8</td>
<td>0.607</td>
</tr>
<tr>
<td>B-vitamin Supplement user (%)</td>
<td>11.5</td>
<td>13.2</td>
<td>&lt;0.001</td>
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<tr>
<td>Hypertension (%)</td>
<td>78.9</td>
<td>68.0</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Diabetes (%)</td>
<td>18.8</td>
<td>9.8</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Stroke (%)</td>
<td>11.4</td>
<td>5.9</td>
<td>&lt;0.001</td>
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</tbody>
</table>

Data presented as mean ± SD unless otherwise indicated. Differences assessed using an independent t test and chi-square analysis p<0.05 considered significant.
Trinity Ulster Department of Agriculture Ageing Cohort Study (TUDA)

1. TUDA n 5186
2. TUDA +5 n 587
3. TUDA RCT n 328
Aim:
• Examine role of baseline folate and related B-vitamins as predictors of cognitive decline in ageing

Hypothesis:
• Suboptimal status of folate and/or related B-vitamins, will be associated with a greater rate of cognitive decline over a five year follow-up period.
Older adults who do not consume fortified foods or supplements have sub-optimal B vitamin status.

In relation to cognition:

- Findings add to emerging evidence supporting role of B-vitamins in maintaining cognitive health in ageing. They show:
  - Suboptimal status of vitamin B6 or riboflavin are each associated with an increased risk of accelerated cognitive decline by up to 75%.
  - No significant relationship between rate of cognitive decline and folate or vitamin B12 status in this cohort.
- Vitamin B6 and riboflavin may be much more important than previously appreciated for cognition in ageing (yet overlooked in most studies).
Low riboflavin status is a global health issue

[Unpublished data from Ulster in collaboration with UBC, Vancouver Canada]
Trinity Ulster Department of Agriculture Ageing Cohort Study (TUDA)

1. TUDA n 5186
2. TUDA +5 n 587
3. TUDA RCT n 328
Participants from the TUDA North cohort and their partners identified as cognitively intact (n 715).

Recruitment (n 328)

Cognitive Assessment (MMSE, RBANS+ FAB)

Other Neuropsychiatric tests (HAD + CED-S)

Biochemical Analysis

General Health + Lifestyle Assessment

Dietary Assessment (4 day food diary + FFQ)

Baseline & Post-treatment Assessment (Week 0 & 104)

Randomisation (Week 0)

Placebo (n 164)

Combined B-vitamin Supplement (Low dose FA, B12, B6 + B2; n 164)

Brain Imaging (n 25)

Brain Imaging (n 25)
Magnetoencephalography (MEG)

MEG maps brain activity by measuring the magnetic fields produced by neuronal activity with sub-millisecond precision.
Preventing or delaying the onset of cognitive impairment is a major public health priority.
Public Health Impact of findings

• Optimising B-vitamin status may offer a public health strategy for maintaining cognition in ageing

• Implications for public health policy
  ➢ Emerging dietary recommendations
  ➢ Food fortification
  ➢ Potential to decrease health care costs and disease burden
Take Home Messages

B vitamins and Cognition in Ageing?

• Strong evidence supports a role for B-vitamins in maintaining better cognitive health in ageing.
• Further well-designed RCTs are required to confirm these effects
  ◆ combined B vitamin supplementation
  ◆ targeted at those who need the supplements

Can supplementation with B vitamins help?

• Older adults who do not consume fortified foods or supplements have sub-optimal B vitamin status

• Supplementation and food fortification with B-vitamins represent effective, low cost options to promote better health in ageing