Nutritional intervention in early Alzheimer’s disease

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Nutricia
• Nutrition and brain function
• Single nutrient intervention
• Diet and risk of Alzheimer’s disease
• What is an FSMP?
• Souvenaid as a viable management option for AD
Nutritional need to maintain brain function

• The brain needs specific nutrients to build and maintain its structure\(^1\)

• Nutritional deficiencies are associated with impaired brain function, for example:
  – Omega 3 fatty acid levels affect mood, behaviour, stress, depression and dementia\(^1\)\(^3\)
  – Vitamin B deficiency is linked to neurologic disorders and psychologic disturbances\(^1\)

• The need to supply specific nutrients to the brain may be increased in neurological disease, such as AD\(^4\)

## Single nutrient interventions in AD/MCI: in general no beneficial effects on cognition

<table>
<thead>
<tr>
<th>Nutrient</th>
<th>Author</th>
<th>Journal</th>
<th>#Subjects/Duration</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>n3 PUFAs</td>
<td>Quinn 2010</td>
<td>JAMA</td>
<td>402/18 months</td>
<td>DHA compared with placebo <strong>did not slow the rate of cognitive and functional decline</strong> in mild-moderate AD patients.</td>
</tr>
<tr>
<td></td>
<td>Freund-Levi 2006</td>
<td>Arch Neurol</td>
<td>174/6 months</td>
<td>Administration of n3PUFA in mild -moderate AD patients did <strong>not delay the rate of cognitive decline</strong> according to the MMSE or the cognitive portion of the ADAS. However, positive effects were observed in a small group of patients with very mild AD (MMSE&gt;27).</td>
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<tr>
<td>B-vitamins</td>
<td>Aisen 2008</td>
<td>JAMA</td>
<td>409/18 months</td>
<td>This regimen of high-dose B vitamin supplements does <strong>not slow cognitive decline</strong> in individuals with mild to moderate AD.</td>
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<tr>
<td></td>
<td>McMahon 2006</td>
<td>N Eng J Med</td>
<td>276/24 months</td>
<td>The results of this trial do **not support the hypothesis that homocysteine lowering with B vitamins improves cognitive performance.</td>
</tr>
<tr>
<td>Vitamin E / Antioxidants</td>
<td>Dysken 2014</td>
<td>JAMA</td>
<td>304/27 months</td>
<td>Among patients with mild to moderate AD, 2000 IU/d of **alpha-tocopherol compared with placebo resulted in slower functional decline.</td>
</tr>
<tr>
<td></td>
<td>Petersen 2005</td>
<td>N Eng J Med</td>
<td>769/36 months</td>
<td>Vitamin E had <strong>no benefit in patients with mild cognitive impairment</strong>.</td>
</tr>
<tr>
<td></td>
<td>Galasko 2012</td>
<td>Arch Neurol</td>
<td>52/16 weeks</td>
<td>However, this treatment (vitamin E + vitamin C plus α-lipoic acid) raised the caution of <strong>faster cognitive decline</strong>.</td>
</tr>
<tr>
<td>Vitamin D2</td>
<td>Stein 2011</td>
<td>J Alz Disease</td>
<td>32/8 weeks</td>
<td>We conclude that high-dose vitamin D provides <strong>no benefit for cognition</strong> or disability over low-dose vitamin D in mild-moderate AD.</td>
</tr>
<tr>
<td>Ginkgo biloba</td>
<td>DeKosky 2008</td>
<td>JAMA</td>
<td>3069/6.1 Y</td>
<td>Ginkgo biloba at 120 mg twice a day was <strong>not effective in reducing either the overall incidence rate of dementia or AD incidence</strong> in elderly individuals with normal cognition or those with MCI.</td>
</tr>
</tbody>
</table>
Diet and AD risk

- Epidemiological data has shown an association between certain dietary patterns and a lower risk of AD, e.g.\(^4\)
  - Regular intake of fish (providing PUFAs)\(^5,6\)
  - Mediterranean diet
  - Adherence to nutritional recommendations in middle-age adults is associated with future memory performance\(^7\)
- These data suggest that supplementation with specific combinations of nutrients is more effective in improving cognitive performance than single nutrient supplementation
- AD is multifaceted and heterogenous disease so it is unlikely that a single intervention will be the answer

1. Malouf et al., Cochrane Database Syst Rev. 2008;(4):CD004514
Regulatory overview

Product

Does it prevent, treat, or cure a disease? Or present itself as capable of doing so?

- No
- Yes

Food

Is it for the dietary management of a disease?

- Yes
- No

Dietary Food for Special Medical Purpose (FSMP) / Medical Food*

Is it a food fortified with micronutrients?

- Yes
- No

Fortified Food

Is it a product intended to supplement a normal diet?

- Yes
- No

Food Supplement

Conventional Food

* For individuals with distinctive/special dietary needs which cannot be met by modification of normal diet.
Definition of FSMP

European Union

“.. a category of foods for particular nutritional uses specially processed or formulated and intended for the **dietary management of patients and to be used under medical supervision**. They are intended for the exclusive or partial feeding of patients with a limited, impaired or disturbed capacity to **take, digest, absorb, metabolize or excrete** ordinary foodstuffs or certain nutrients contained therein or metabolites, or with other medically-determined nutrient requirements, whose dietary management **cannot be achieved only by modification of the normal diet**, by other foods for particular nutritional uses, or by a combination of the two” (Directive 1999/21/EC).

FSMPs must be based on sound medical and nutritional principles and that its use in accordance with the manufacture’s instructions is **safe, beneficial and effective in meeting the particular nutritional requirements of the patients** for which it is intended, as **demonstrated by generally accepted scientific data** (Directive 2009/39/EC, repealed/replaced by Regulation 609/2013).
Souvenaid: an FSMP

Fortasyn™ Connect

- UMP
- Omega-3 fatty acids
- Choline
- Phospholipids
- B vitamins
- Antioxidants

Designed to:

Support the formation of synapses

Ingredients:

- DHA 1200 mg
- EPA 300 mg
- UMP 625 mg
- Choline 400 mg
- Folic acid 400 µg
- B6 1 mg
- B12 3 µg
- Vit C 80 mg
- Vit E 40 mg
- Se 60 µg
- Phospholipids 106 mg
Dietary precursor control of neural membrane synthesis

The Kennedy pathway for biosynthesis neuronal membrane

Phospholipids are main constituents of synapses
# Full clinical trial programme

<table>
<thead>
<tr>
<th>Prodromal</th>
<th>Mild</th>
<th>Moderate</th>
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</table>
| WMS-r & ADAS-cog  
MMSE 20-26, drug-naïve  
28 sites | ADAS-cog  
MMSE 14-24, stable on AD drugs  
48 sites | NTB + MRI/CSF  
MMSE ≥ 24, drug-naïve  
13 sites |
| NTB + EEG/MEG  
MMSE ≥ 20, drug-naïve  
27 sites | | |

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Souvenir I: this project receives funding from NL STW.  
Souvenir II: This project receives funding from the NL Food & Nutrition Delta project, FND N° 10003.  
LipiDiDiet: Funded by the EU FP7 project LipiDiDiet, Grant Agreement N° 211696.
Significantly more responders in mild AD after 12 weeks ($p=0.021$)*

Significantly more responders in very mild (MMSE 24-26) AD after 12 weeks ($p=0.019$)*

* Chi-square - skewed distribution: 40% scored 0 on WMS-r @

S-Connect: Primary endpoint
ADAS-cog 24 weeks, MMSE 14-24, stable on AD drugs

No significant effect* (p=0.513) during 24 weeks

ITT, MMRM, data are mean ±SE.
*Statistical analysis run by Rush Alzheimer’s Disease Center, Rush University Medical Center.

**Exploratory Outcome:** Sustainable NTB memory domain improvement

**Significant increase from week 24 to week 48 in both groups.**

- **Active - Active:** $p=0.038$
- **Control - Active:** $p=0.029$

<table>
<thead>
<tr>
<th></th>
<th>Control (N)</th>
<th>Active (N)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>12</td>
<td>100</td>
<td>107</td>
</tr>
<tr>
<td>24</td>
<td>103</td>
<td>103</td>
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<tr>
<td>36</td>
<td>85</td>
<td>83</td>
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<tr>
<td>48</td>
<td>83</td>
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</tbody>
</table>
Thank you for your attention

Any questions?