Fish oil to improve school performance and delay cognitive decline: how strong is the evidence of benefit?

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Daily Mail

Plan to hand out 'brain food' supplements in primary school

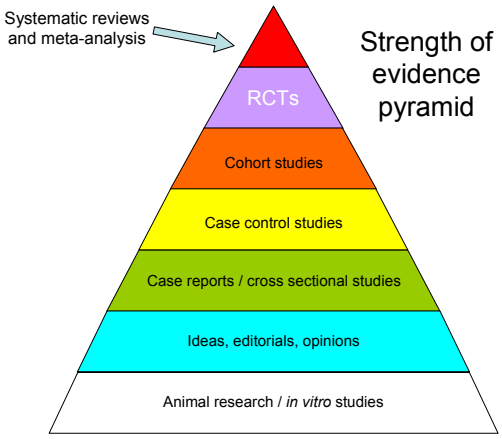
FISH OIL FOR EVERY CHILD

By Sean Poulter
Consumer Affairs Correspondent

CHILDREN may be given food supplements at school to improve their behaviour and studying performance.

A daily shot of Omega 3 fish oil would be supplied to pupils as young as five.

Ministers are considering the move amid growing concern about the poor diets of many of the nation's youngsters.

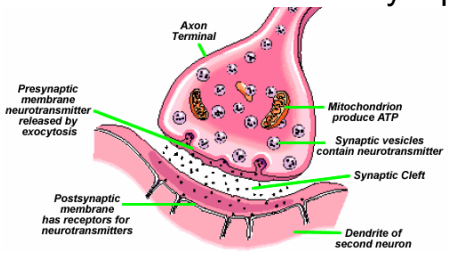


Strength of evidence pyramid

Mechanisms?

- Brain is 22-24% lipid, high concentrations of n-3 LCPs (DHA) in brain and retinal phospholipids
- Clear need for DHA *in utero* (and first 2 years) for optimal brain and retinal development
- DHA effects gene expression, neurogenesis, membrane structure and function, protein lipid interactions and receptor binding
- Very new data (Innis 2007) suggest effect on release of neurotransmitters which may have potential impact on mood/behaviour of children

Action of DHA on neuronal synapse



- DHA modulates neurotransmitter release at nerve synapse via actions on SNARE proteins
- Changes in SNARE protein function may be linked to behaviour/learning

University of Teesside review of fish oil trials and childhood performance

- Findings were mixed and therefore inconclusive
- Only the Durham trial reported consistent improvements in both objective and subjective behavioural and educational outcomes
- Caution when translating evidence of effect from children with neurodevelopmental disorders to mainstream school children
- Dosages in supplements given in trials are unlikely to be achieved through diet alone
- Further large scale trials needed

(Summerbell, in press)

NEMO Study

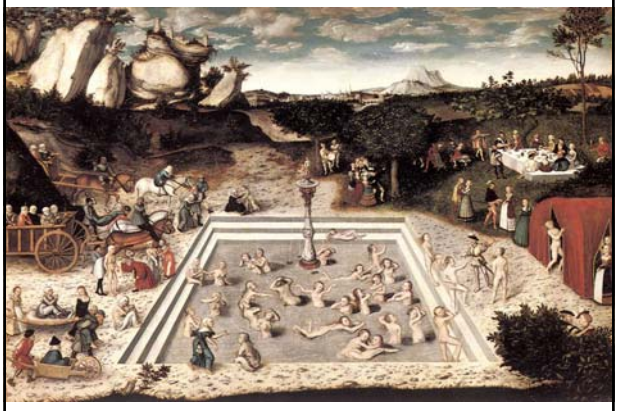
Nutrition Enhancement for Mental Optimisation

- 396 children 6-10yr in Australia (well nourished)
- 384 children in Indonesia (marginally nourished)
- RCT testing effect of multinutrients (Fe, Zn, A, folate, B_6, B_{12}, C), fish oil (110mg/d), both or neither for 12 months on learning and memory
- Blood nutrient profiles improved over 12 months
- Fish oil – no effect on learning outcomes
- Multinutrients – small effect on learning and memory, no effect on intelligence and attention

(NEMO Study group, AJCN, 2007)

Summary of childhood data

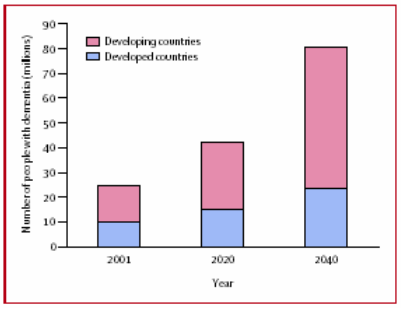
- Some potential mechanisms of effect
- Inconclusive evidence of effect of fish oil on ability and behaviour among school-age children from RCTs
- Small RCTs mostly limited to children with neurodevelopmental disorders
- Issue of importance for public health
- Large RCTs urgently needed



(Lucas Cranach the Elder, 1546)

Global prevalence of dementia: a Delphi consensus study

Cleusa P Ferri, Martin Prince, Carol Brayne, Henry Brodaty, Laura Fratiglioni, Mary Ganguli, Kathleen Hall, Kazuo Hasegawa, Hugh Hendrie, Yueqin Huang, Anthony Jorm, Colin Mathers, Paulo R Menezes, Elizabeth Rimmer, Marcia Scazufca, for Alzheimer's Disease International

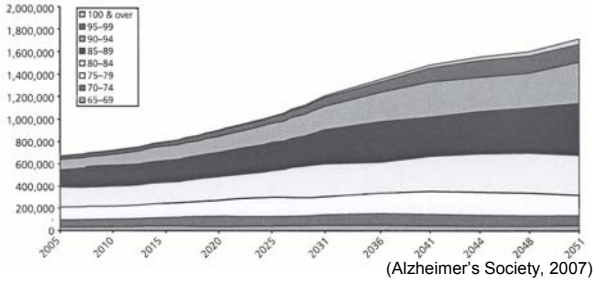


- 24.3 million today
- 4.6 million new cases every year
- 81.1 million 2040
- 100% increase in developed countries
- 300% increase in India and China

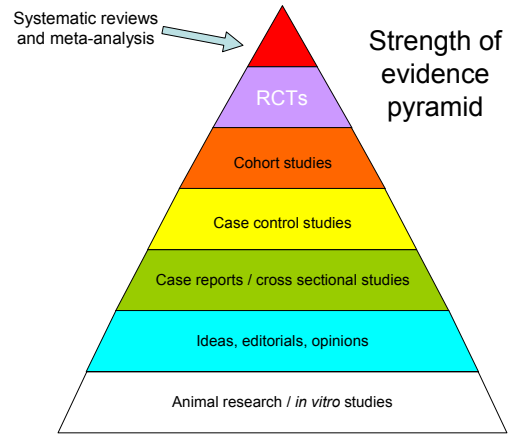
(Ferri, Lancet, 2005)

Dementia in the UK

- 700,000 cases today – 1 in every 88 people
- 940,000 by 2021 – 1 in every 71 people
- 1,735,000 by 2051



(Alzheimer's Society, 2007)



Mechanisms?

- DHA metabolised to *neuroprotectin D1*
- DHA regulates gene expression
- Combined with EPA, actions may:
  - improve vascular integrity
  - reduce microthrombotic obstruction
  - enhance neuronal health and signalling

Role of diet?

- Goodwin (JAMA, 1983)
  - 260 community living adults 60+ years
  - low blood levels of vitamin C and B_{12} associated with worse cognitive function
- Numerous surveys show associations between nutrients and cognitive function

Systematic review of evidence on fish oil and cognitive function

- Inclusion criteria
  - Human
  - RCT, cohort or case-control
  - describe effect of fish oil on cognitive function, or incidence/treatment of dementia
- 5,865 citations
  - 5 relevant (4 cohort studies, 1 RCT)

(Issa, Dement Geriatr Cogn Disord, 2006)

Review conclusions

In four [cohort] studies that assessed the effects of n-3 LCPs on incidence and treatment of dementia, a trend in favour of n-3 LCPs (fish and total n-3 consumption) toward reducing risk of dementia and improving cognitive function was reported.

- One RCT included in the review was small and of poor quality

(Issa, Dement Geriatr Cogn Disord, 2006)

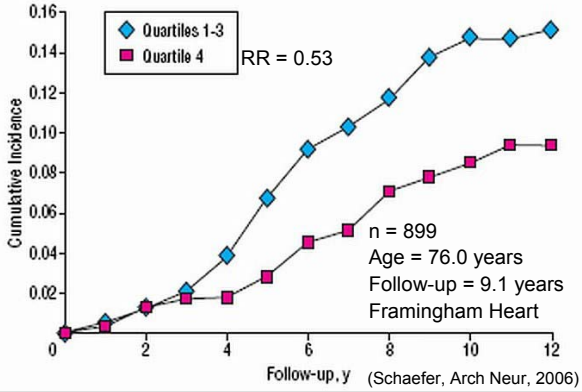
Fish intake and dementia

Fish consumption	n	Cases	Incidence/100 py
Once a day	19	1	1.00 (0.00-2.97)
At least once/wk	1122	124	2.05 (1.69-2.41)
Sometimes	240	35	2.90 (1.94-3.87)
Never	35	10	6.61 (2.51-10.70)

- 1674 free-living French people aged ≥68 years
- Follow-up period - 7 years
- Hazard ratio of at least once/wk vs. less = 0.66 (0.47-0.93)

(Barberger-Gateau, BMJ, 2002)

Plasma DHA and dementia



(Schaefer, Arch Neur, 2006)

Omega 3 fatty acid for the prevention of dementia (Review)

Lim WS, Gammack JK, Van Niekerk J, Dangour AD

THE COCHRANE COLLABORATION®

The Cochrane Database of Systematic Reviews 2006 Issue 2

Cochrane conclusions

There is a growing body of evidence from biological, observational and epidemiological studies that suggests a protective effect of n-3 LCPs against dementia. However, until data from randomized trials become available for analysis, there is no good evidence to support the use of dietary or supplemental n-3 LCPs for the prevention of cognitive impairment or dementia.

ORIGINAL CONTRIBUTION

ω-3 Fatty Acid Treatment in 174 Patients With Mild to Moderate Alzheimer Disease: OmegAD Study

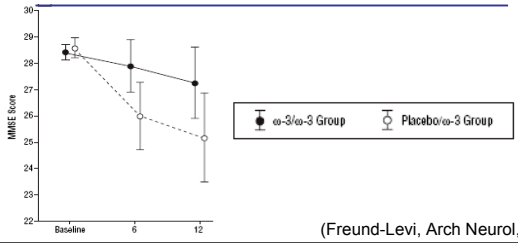
A Randomized Double-blind Trial

Yvonne Freund-Levi, MD; Maria Eriksdotter-Jönhagen, MD, PhD; Tommy Cederholm, MD, PhD; Hans Basun, MD, PhD; Gerd Faxén-Irving, PhD; Anita Garlind, MD, PhD; Inger Vedin, MSci; Bengt Vessby, MD, PhD; Lars-Olof Wahlund, MD, PhD; Jan Palmblad, MD, PhD

- 174 people aged 74 years with Alzheimer's disease and MMSE>15
- RCT of either 1.7g DHA + 0.6g EPA or placebo
- Primary outcome – change in Mini Mental State Examination (MMSE) Score

(Freund-Levi, Arch Neurol, 2006)

	MMSE score (0-30)	
	Baseline	6 months
All subjects (n=174)		
Fish oil	23.6	22.8
Placebo	23.2	22.4
MMSE >27 points (n=32)		
Fish oil	28.4	27.9
Placebo	28.5	26.0



(Freund-Levi, Arch Neurol, 2006)

MEMO study

Mental health in Elderly Maintained with Omega-3

- n=302; 65+ years; MMSE>21
- Randomised for 6 months to:
  - 0.4g n-3 LCPs
  - 2g n-3 LCPs
  - placebo
- Primary outcome: cognitive function and mental well-being

(van der Rest, submitted)

Summary of older people data

- Good mechanistic evidence of potential effect
- Some evidence from surveys
- Good evidence from cohort studies
- No evidence of effect from RCTs
- Large RCTs urgently needed

Why don't trials "work"?

- Residual confounding in cohort studies
- Existing trials are too small or short
- Supplement dose too low
- Outcome measures not sensitive
- Baseline status
- ApoE (other gene) status

OPAL

Older
People
And n-3
Long-chain
polyunsaturated
fatty acids study

FOOD STANDARDS AGENCY

MRC General Practice Research Framework

Hypotheses

- Daily supplementation for 24 months with 0.7g n-3 LCPs (0.5g DHA + 0.2g EPA) will slow cognitive decline in older people
- Daily supplementation for 24 months with 0.7g n-3 LCPs will benefit eye health in older people

N.B. 0.7g = 2 portions of oily fish / week

Study design

- Double-blind placebo-controlled RCT
- 868 cognitively healthy adults 70-79y drawn from 20 GP practices in UK
- Daily capsules for 24 months
- Cognitive function tests at 0 and 24 months
- Retinal function tests on sub-sample
- Results due – Autumn 2008
- www.opal-study.org.uk

Conclusions

- Currently no good quality evidence from RCTs to support the use of fish oil supplements to enhance academic or behavioural performance in school-age children
- Currently no good quality evidence from RCTs to support the use of fish oil supplements to slow or prevent cognitive decline in older people
- Active area of research

Final word

… this should not discourage further research on the relationship between nutrition and cognitive function, [but] it does underscore the critical importance of rigorous experimental design if such studies are to be meaningfully interpreted, and it suggests that nutritional supplementation cannot yet be viewed as a demonstrably effective therapy for cognitive problems in the elderly.

(Raskind, JAMA, 1983)