Healthy Ageing: The Importance of Diet and Lifestyle

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The Modern, Western-Type Diet

- Modern, ‘junk food’ diets are seriously damaging our physical health – leading to increased rates of:
  - Obesity
  - Type II Diabetes
  - Heart Disease
  - Cancer
  - Allergies / Immune Disorders

- Diet also affects our brains and behaviour

Increasing Cost Burden of Mental Health Disorders

UK (Government’s own figures)
- In 2007: £77 billion
- In 2010: £105 billion

Europe 2010
- 38% of Europeans (≈165 million) have a fully developed mental or neurological illness

Most Common Mental Health Disorders

Europe
- Anxiety disorders 14.0%
- Insomnia 7.0%
- Major depression 6.9%
- Somatoform 6.3%
- Alcohol and drug dependence 5.4%
- ADHD 5% in the young
- Dementia 1–30%, depending on age

Witthens et al, 2011 Eur Neuropsychopharmacol, 21, 655-679

Age-related Cognitive Decline and Dementia Syndromes

- ARCD, Alzheimer’s Disease and other forms of dementia already affect at least 1 in 5 people over 60 in the US and UK.
- The high rates of these conditions are widely attributed to increased life expectancy (as with physical degenerative diseases such as cardiovascular disease and cancers)

HOWEVER
- Life expectancy in the UK has NOT in fact increased when compared with mid-Victorian times (=1880).
- Rather, the causes of death have changed dramatically - and diet and lifestyle factors are likely to have played key roles in this.

(Chilton and Rossbotham (2008), *An Unsuitable and Degraded Diet*? Parts 1, 2 and 3, HMS)
Changes in Life Expectancy in the UK since mid-Victorian Times

Cause of Death in England and Wales: 1880 and 1997

The role of Nutrition?

- Appropriate nutrition is essential for:
  - The growth and development of brains and bodies
  - Building, maintaining, fuelling and repairing every cell in every part of the brain and body
- At least 39 essential nutrients must be provided by our food
  - These include vitamins and minerals, essential amino acids, and omega 3 and omega 6 fatty acids
- Many of these are lacking from modern diets
- Individual differences affect dietary requirements
  - Specific nutrients may be needed in unusually high quantities
  - There may be allergies or intolerances to certain foods

Typical for UK Population

Fruit & Veg
Protein
Starchy foods
Fatty / Sugary foods
Calcium rich dairy
Many nutritional features of modern western diets are both *evolutionarily novel* and *pathological*:

- High Glycaemic Load
- Altered Fatty Acid Composition
- Altered Macronutrient Composition
- Reduced Micronutrient Density
- Acid-Alkaline Balance
- Sodium-Potassium Ratio
- Dietary Fibre
- Sugar
- Fat
- Vitamins, Minerals etc
- Fibre


Sugar and ‘Refined Carbs’

**Associations with:**
- Obesity, Diabetes, Cardiovascular Disease, Cancers
- ADHD, Depression, Dementia and other Mental Health Problems

Is Sugar Really A Problem?

- High intakes of sugar & refined carbohydrate (sweets, soft drinks, biscuits, cakes, pastries etc) can damage brain function in many different ways:
  - Rapid blood sugar swings affect attention, memory and mood (short-term), and contribute to Type 2 Diabetes (longer-term)
  - Increases risk of deficiencies in many essential micronutrients
    - Displacement of healthier, nutrient-rich foods from the diet
    - Depletion of magnesium, B vitamins, zinc, chromium etc (needed to unlock the energy from sugar, and to stabilise blood glucose)
  - High sugar, high fat diets can stunt brain growth & connectivity (by inhibiting key substances such as BDNF, IGF-1 etc)
  - Sugar also feeds ‘bad bacteria’ and yeasts, impairing digestion and gut health – on which all health depends.

Glucose vs Fructose

- **Glucose**
  - Used by all living cells as a source of energy
  - Absorbed directly into the bloodstream
- **Fructose**
  - Requires processing by the liver before its energy can be used (technically – a ‘toxin’)
  - *NO PROBLEM* if consumed via eating fruits and vegetables (*nature provides the antidote....*)
  - *NOT HEALTHY* if consumed as a ‘white powder’ (i.e table sugar or High-Fructose Corn Syrup - both approx 50% glucose, 50% fructose)

All Calories are NOT equal

- ‘Energy in, energy out’
  - Consuming more calories than are burned for energy leads to fat storage. Yes, BUT:
- Conventional advice to ‘Eat Less, Exercise more’ does not work to reduce obesity – because:
  - Consuming excess sugar can increase appetite and reduce energy
- Excessive calories from sugar (fructose) affect the balance of key hormones that regulate energy metabolism and appetite
  - Insulin resistance, leptin resistance, increased ghrelin etc.

‘Food for Thought: Eat Your Way to Dementia’

- Sugar and Carbs Cause Alzheimer’s Disease’
- New Scientist – Sept 3 2012

- Diabetes is a known risk factor for AD, and also exacerbates cognitive impairment.
- Diabetes induces AD-type pathology in brain and retina in animal models.
- This in turn can exacerbate insulin resistance. • Jones et al. (2011) *Increased DJ-1 production promotes the onset of glucose intolerance and insulin resistance in Diabetic Endothelial Msh.*. 2011(1) EAT2 89
Dietary Omega-3 fatty acids modulate the cognitive and metabolic impairments induced by a high-sugar diet

Many nutritional features of modern western-type diets are evolutionarily novel and pathological

DOES SUGAR MAKE YOU STUPID?

• Water laced with high-fructose corn syrup given to omega-3 deficient rats over 6 weeks led to
  – Learning and memory problems
  – Impaired insulin sensitivity, elevated triglycerides, and reductions in markers of synaptic plasticity in brain tissue
• The addition of dietary omega-3 fatty acids ameliorated all parameters of metabolic dysfunction related to the fructose treatment.

The absolute essentiality of Omega-3 DHA (and Omega-6 AA) for brain development

Professor Michael Crawford, Imperial College School of Medicine, London
Founder, Institute of Brain Chemistry and Human Nutrition, London

1970s: gave warning to W.H.O. and governments: “Brain Disorders will be next”

The Human Brain is 60% FAT and it matters what kind

Omega-3 (and Omega-6) LC-PUFA are Essential for Healthy Brain Development And Functioning

Getting the Fats Wrong

Cheap margarines, ‘takeaways’ and commercially baked or fried foods still often contain hydrogenated and trans fats

These are artificially saturated and ‘twisted’ fats, which have
• no known nutritional benefits
• many health risks.

Trans fats compete with the essential fatty acids (omega-3 and omega-6) needed for brain and body health

Getting the Fats Right

Quality, not Quantity

Some Fats are Essential
Omega-3 and Omega-6 Polyunsaturates
Synthesis of Long-chain from Shorter-chain Polyunsaturated Fatty Acids (PUFA)

**omega-6**

- LA (Linoleic) 18:2
- GLA 18:3
- DGLA 20:3
- AA (Arachidonic) 20:4
- Adrenic 22:4
- DPA(n-6) 22:5

**omega-3**

- ALA (A-linolenic) 18:3
- SDA 18:4
- EPA 20:5
- DPA(n-3) 22:5
- DHA 22:6

Shorter-chain PUFA

Long-chain PUFA

Conversion of short to long-chain PUFA is poor, and is further blocked by:

**Diet and Lifestyle**
- Saturated fats
- Hydrogenated fats
- Trans fatty acids
- Lack of co-factors (e.g. Zinc, magnesium, manganese, Vitamins A, B3, B6, C etc.)
- ‘Stress’ hormones
- Viral infections

**NB: Excess alcohol & smoking: both destroy LC-PUFA via oxidative stress**

**Constitutional factors**
- Aging
- Atopic eczema (& other allergies?)
- Diabetes
- Being male
  - Testosterone blocks conversion
  - Oestrogen helps to protect HUF A from breakdown
- Genetic predisposition

Changes in Dietary Fat Intake

Dramatic increase in Omega-6 / Omega-3 Ratio

Impaired liver conversion of ALA to DHA correlates with cognitive impairment in AD

Dietary Sources of Omega-6
**Dietary Sources of Omega-3**

- **Green leafy vegetables, seaweed, & some nut & seed oils (flax, hemp, rapeseed, chia, walnut)**
- **Fish and seafood**

**Omega-3 and Vision**

Omega-3 fatty acids from fish oils are absolutely **essential** to the visual system:
- 30-50% of the retina should be made of the omega-3 DHA
- DHA deficiency can reduce retinal signalling to 1/1000 normal levels
- Omega-3 deficiency is associated with poor night vision and other problems with visual, spatial and attentional processing.

**Why we need omega-3 (and omega-6) fats (1)**

1. **The structure of all cell membranes**
   - The long-chain omega-3 DHA (and omega-6 AA) increase membrane fluidity, essential for optimal cell signalling
   - 6-10% of the dry mass of the brain should be DHA
   - DHA is particularly concentrated in nerve terminals, where chemical signals between cells are exchanged
   - Concentrations of dopamine, serotonin, noradrenalin, acetylcholine etc are influenced by omega-3 status

**Omega-3 DHA deficiency impairs synapse development**

- Adequate DHA
- Deficient in DHA

**Why we need omega-3 (and omega-6) fats (2)**

1. **The structure of all cell membrane**
   - Omega-3 (and omega-6 LC-PUFA) increase membrane fluidity, essential for optimal cell signalling

2. **Brain development**
   - Omega-3 and Omega-6 LC-PUFA make up around 20% of dry brain mass, and affect brain growth and connectivity
   - DHA and AA are preferentially transferred via the placenta, and are found in breastmilk (so are important in infant formula)

**The Critical Importance of Early Life Nutrition**

- ‘**Nutritional programming**’ studies suggest that deficiencies of omega-3 may ‘prime’ the next generation for:
  - Reduced visual, motor and cognitive / intellectual development
  - Increased anxiety, stress, depression and related mental health disorders.

- **Other nutrients already established as critical for brain development in early life (0-2 years)**
  - Folic acid, iodine, vitamin A, vitamin B12, iron, Vitamin D, (Zinc ?)
Why we need omega-3 (and omega-6) fats (3)

1. The structure of all cell membranes
   - Omega-3 (and omega-6) increase membrane fluidity, essential for optimal cell signalling

2. Brain development
   - Omega-3 and Omega-6 LCPs make up around 20% of dry brain mass, and affect brain growth and connectivity
   - DHA and AA are preferentially transferred via the placenta, and are found in breastmilk (so are important in infant formula)

3. Maintenance of optimal brain function throughout life
   - Cell signalling depends on membrane fluidity
   - Omega-3 and omega-6 LCPs and their derivatives influence almost all brain signalling systems
   - They also profoundly affect hormonal balance, blood flow and immune system function

Omega 6 and Omega-3 ‘functional fats’ – a matter of balance

The Omega-6 AA
(from meat, eggs and dairy products – or converted from LA in vegetable oils)
gives rise to substances that
- promote inflammation
- promote blood clotting
- narrow blood vessels

The Omega-3 EPA & DHA
(from fish and seafood – or converted from ALA in green leafy vegetables, flax seed etc)
gives rise to substances that
- reduce inflammation
- reduce blood clotting
- relax blood vessels

A few simple dietary changes can make a big difference
- Eat more: fish and seafood, green vegetables, nuts, seeds
- Eat less: meat, dairy products, refined vegetable oils

If dietary intake of omega-3 is increased, will it help?
Evidence from Randomised Controlled Trials

Dysfunctions of Body and Mind that long-chain Omega-3 (EPA and DHA) may help to prevent or ameliorate
- Cardiovascular Disease
  - Heart Disease and Stroke
- Inflammatory / Auto-immune Disorders
  - e.g. Rheumatoid Arthritis
- Visual Problems
  - ‘Retinopathies’ of Prematurity, Diabetes, Old Age
- Disorders of Behaviour, Learning and Mood
  - ADHD and related childhood developmental disorders?
  - Depression, Schizophrenia and other mental health problems?
  - Age-related cognitive decline and dementia?

Omega-3 from fish oils are effective in reducing ADHD symptoms

<table>
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<th>Study or Subgroup</th>
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<th>Weight</th>
<th>Std. Mean Difference (95% CI)</th>
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<td>Brawner 2007*</td>
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<td>Hawkey &amp; Niggs 2014, Clin Psychol Rev</td>
<td>1.7%</td>
<td>0.49</td>
<td>0.11 (0.01, 0.21)</td>
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</table>

Total (95% CI) 100.0%: 0.23 [0.16, 0.30]

Heterogeneity: Chi^2 = 5.25, df = 10, P = 0.86; I^2 = 0.2%

Test for overall effect: Z = -0.13 (P = 0.898)

Omega-3 for ADHD symptoms (2)

Hawkey & Niggs 2014, Clin Psychol Rev

Bloch and Qawasmi 2011, JAACAP
Omega-3 for Depression

- Many clinical trials show that Omega-3 LC-PUFA can reduce depression in adults
- In 2006, the American Psychiatric Association made a treatment recommendation*
  > 1000 mg/day EPA+DHA for adults with clinical depression (& other major psychiatric disorders)
- NB: this is in addition to any standard treatment, not as a substitute.

(Freeman et al. J. Clin Psychiat. 2006)

Prevention of Psychosis (Schizophrenia)

Amminger et al (2010) Archives of General Psychiatry 67(2) 146-54
- 81 young people at ultra-high risk for psychosis
  - Age 13-25 yrs
- 12 weeks treatment with 1.2g long-chain omega-3
  - 700mg EPA, 500mg DHA from fish oils
- Assessments over 12 months
  - Baseline, 1, 2, 3, 4, 8, 12 weeks, then 6 & 12 months
- Primary outcome:
  - Transition to psychosis
- Secondary outcomes:
  - Measures of symptoms & functioning
  - Blood fatty acids

Results at 12 month follow-up

Primary outcome: transition to psychosis (p=0.007, NNT=4).
- Omega-3: 2/41 (4.9%)
- Placebo: 11/40 (27.5%)

Advice from the Psychiatric Associations

RCPsych website

<table>
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<th>Depression</th>
<th>Bipolar</th>
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<th>ADHD</th>
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<td>No clear advice</td>
<td>Eat ketogenic diet (Atkins)</td>
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<td>Calcium, Tryptophan</td>
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</table>

APA advice (2006)

*All adults should eat fish twice a week
*Patients with mood, impulse and psychotic disorders should consume >1g / day EPA / DHA

Other psychological / psychiatric conditions?

- Autistic Spectrum Disorders
- Anxiety Disorders
- Borderline Personality Disorder
- Self-harm
- Stress / Hostility /Aggression
- Age-related Cognitive Decline
- Alzheimer’s Disease (early stage)

In each case, pilot RCTs have provided some preliminary evidence of possible benefits, but more research is needed
Age-Related Cognitive Decline and Dementia

• Epidemiological evidence
  – Higher intakes of omega-3 from seafood (EPA + DHA) are protective against dementia, and associated with higher intelligence and mental agility in older adults (Whalley et al. 2006)

• Biochemical and MRI studies
  – Low blood omega-3 is associated with impaired attention, memory and other aspects of cognitive function in adults – and with reduced brain volume in older adults (Yam et al. 2012)

• Controlled treatment trials
  – Initial pilot study: EPA+DHA beneficial in early-stage, but not late-stage Alzheimer’s disease. (Yordanova et al. 2008)
  – Memory / Mild Cognitive Impairment in older adults: significant benefits in only one of 3 recent RCTs (Parko-Mauro et al. 2010)
  – Prevention of AD: 3 RCTs show no evidence of benefit (Yordanova et al. 2012) although study design is a major problem (Dominguez 2012)

Fish and seafood provide other essential nutrients that few other foods contain

In addition to providing long-chain Omega-3 (EPA and DHA), fish and seafood is also an important dietary source of other key nutrients:
  – Vitamin D
  – Iodine
  – Selenium
  – Zinc
  – B vitamins
  – high-quality protein etc.

Nutrient Status in AD: Lower Plasma B Vitamins

The ‘Vitacog’ study (Oxford & Oslo)
• RCT of high-dose B vitamins for 2 years in people aged 70+ yrs with MCI
• B vitamins vs placebo
  ➢ Improved mental function on some tests
  ➢ Reduced brain shrinkage

Dietary need for Omega-3 (EPA/DHA)*

*Shorter-chain omega-3 (ALA) from plant sources do NOT have the same health benefits

Recommendations from international scientific & health organisations

• General population - cardiovascular health:

• Depression or other mental health conditions:
  – > 1000mg / day EPA+DHA (APA Freeman et al. 2006, Hibbeln & Davis 2009)

In the UK, Australia and Canada, most people consume < 150mg/day

Cognitive Decline and Alzheimer’s Disease: Multiple Nutritional Issues

• Blood Sugar Regulation / Insulin Resistance
• Fatty Acid deficiencies / imbalances
• Other micronutrient deficiencies or imbalances
  – B Vitamins (B6, B12, folate)
  – Vitamin C, Vitamin E
  – Other substances from food with antioxidant /anti-inflammatory effects (e.g. Polyphenols, curcumin etc)
• Reduced Uptake and Metabolism of Key Nutrients

Can B Vitamins prevent dementia?

Research Summary (1)

- Modern, western-type diets are associated with many degenerative physical and mental health conditions. Pathogenic characteristics include:
  - Excessive sugar and refined carbohydrates
  - Deficiencies of long-chain Omega-3 (EPA and DHA), which are essential for brain development and function
  - Low levels of other key micronutrients (vitamins, minerals, antioxidants)
- RCTs of dietary supplementation with Omega-3 alone have shown modest benefits for
  - ADHD and related developmental conditions
  - Depression (and other Mood/Anxiety Disorders?)
  - Prevention / early treatment of Schizophrenia

Lessons from the Mid-Victorians?

Clayton & Rowbotham
J. Royal Soc Med 2008

The Mid-Victorian ‘Golden Age’

- c1850 – c1885
- Mid-Victorians had similar life expectancy
- Better health expectancy
- Required significantly less healthcare
- 90% lower incidence of cancer
- 90% less degenerative disease

Key facilitators

- The ‘Agricultural Revolution’
Key facilitators

- The expansion of the railways

How the mid-Victorians worked

- Society mostly working class
- Working class – predominantly blue collar
- 10 hrs / day, 5.5 - 6 days / week
- 6 miles / day walking to & from work
- Leisure 5-6 hours / week
- 60 – 75 hours of physical activity / week

How the mid-Victorians Ate

- High level physical activity (>4000 cals/day)
- High intake: omega 3, prebiotic fiber, wholegrain
- Fruit & veg: 10 or more portions / day
- Low intake: salt, alcohol
- V low intake: tobacco, spirits, processed foods
- A ‘super-Mediterranean’ diet

How the mid-Victorians Died

- Infection: individual and epidemic
- Child-birth
- Industrial accidents, domestic fires
- Heart failure (after rheumatic fever)
- Cancer, coronary artery disease, dementia, allergy …. rare / very rare

Mid-Victorian diet rich in …

- Anti-inflammatory compounds (various)
- Innate immuno-primers (ie 1-3, 1-6 β-g)
- Prebiotics (Jerusalem artichoke, chicory)
- Phase-2 upregulators (water-cress, brassica)
- Re-differentiators
- Mid cell cycle arresters
- Apoptosis-inducers (fruit / veg organic, bitter varieties)
- Matrix stabilisers / angiotostats
Mid-Victorian diet low in …

- Tobacco
- Spirits
- Cooked meat carcinogens
- AGE’s, ALE’s

- Low incidence of diabetes, obesity, dementia
- High levels of physical exercise

How did it all go wrong?

- Growth of the British Empire
- International trade & shipping technology
- Mass imports of salted meats
- Mass imports of cheap sugar: fruits in syrup, confectionery, condensed milk
- Mass imports of tobacco
- Industrial cigarette production 1884

How did it all go wrong?

- 1850: navvies routinely lifting 20 tons/day
- 1900: army rejects 50% of recruits

  Minimum height of army recruits
  - 1800 – 1880: 1.68m
  - 1885: 1.6m
  - 1900: 1.52 (= 10% reduction)

1885: first automobile (Karl Benz)

1912: first traffic jams

1929: first parking problems
Obesogenic culture (AHA '03)

Large US adult sedentary 8 hours / day, < 2,000 steps / day (NYS Public Health Assocn '05)

Amish 16,000 steps / day: obesity 9% women, 0% men (Bassett et al '04)

Reduced energy expenditure

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Positive energy balance

- Reduced activity / calorie requirements
- Institutional diet
- Financial hardship
- Poor dentition
- Swallowing problems (xerostomia)
- Loss of sense of taste

‘Type B’ Malnutrition worsens with age

- Progressive depletion of anabolic factors
  (vits C, B’s, D; Zn, Cu, Se, Fe, Ca, Mg; amino acids etc)
- Progressive depletion of anti-catabolic factors
  (vit E; Zn, Cu, Mn, Se; sterols, flavonoids, carotenoids etc)

‘Type B’ Malnutrition worsens with age

- Progressive depletion of anabolic factors
  → decreased tissue repair, damage clearance
- Progressive depletion of anti-catabolic factors
  → increased free radical activity, hexosylation, nitrosation, inflammation

= CATABOLIC DOMINANCE

Diseases driven by chronic inflammation

- Arteries --- atheroma, hypertension
- Diabetes --- complications
- Brain --- Dementia (inc AD), Parkinson’s
- Lungs --- COPD
- Skin --- accelerated ageing
- Joints --- arthritis
- Many tissues --- cancer

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<th>Victorians</th>
<th>Us</th>
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<td>1-3, 1-6 β-glucans</td>
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<td>Tobacco, spirits</td>
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<td>Cooked meat carcinogens</td>
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<td>++++++++</td>
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<td>Phase 2 inducers</td>
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<td>AMP-K / MTOR</td>
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### Mediterranean Diet

- Reduces chronic inflammation
- Reduces risk of many non-communicable diseases by 35 - 50%
  - inc. CAD, COPD, Alzheimer’s, Parkinsonism, diabetes, cancer progression

*de Lorgeril et al ’99, Esposito et al ’04, Knoops et al ’04, Varraso et al ’07a, Varraso et al ’07b, Stavitski et al ’08, Gu et al ’10, etc etc*

### Whitehall II Cohort Study

- N = 5350; chronic disease & mortality, 16 years
- "Western" dieters (fried & sugary foods, refined starches): aged faster / died younger than healthier dieters
- Healthy aging (free of chronic illness, high scores in physical and mental agility tests) almost exclusively in the 4% with healthier diet (fruits, vegetables, whole grains, fish)

*(Akbaraly et al AJM ’13)*

### Prevention of Avoidable Death

- HALE Project (multi-centre EU), 13,000 elderly subjects, 10 yr prospective trial
- Mediterranean diet, moderate physical activity / alcohol intake, no smoking
  - Death (from all causes) reduced by 65%

*Knoops et al, JAMA 2004*

### A Neo-Victorian diet

- Higher levels of physical activity & shift to a 'super-Mediterranean' type diet
- Increased micro- & phyto-nutrient density (Supplements and/or functional foods?)
- Glycemic load reduction
  - Less degenerative disease (of both brain and body)
Nutrition and Healthy Ageing, Cognitive Decline, and Dementia - Nov 2014

Professor Michael Crawford (Emeritus Professor, Imperial College, London)
Dr Roger Bullock (Retired NHS Consultant in Old Age Psychiatry, and Research Associate, University of Bristol)
Dr Fredrik Jernerén and Professor David Smith (Dept of Pharmacology, University of Oxford)
Dr Paul Clayton (Senior Research Fellow at the University of Pecs, Hungary, and Institute for Food Brain and Behaviour, UK)
Professor Margaret Rayman (Nutritional Medicine, University of Surrey)

Further Information
For details of this and related research see

Food And Behaviour Research
www.fabresearch.org