Cognition – The new frontier for nuts

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Disclosures

- Research grand from CWC
Outline

- Introduction
- Review
  - Animal studies
  - Long term studies (observational)
- Experimental study
Nuts & Functional Food

- Excellent source of plant protein
- **Optimal fat composition** (blend of mono and poly saturated fatty acids)
- **Omega-3 fatty acids** (seafood stock as a source of EPA and DHA is in danger of depletion, while land-based sources of ALA like walnuts are plentiful)
- Excellent source of vitamin E
- Folic acid
- Melatonin
Nuts & Functional Food

- **Mineral** (Calcium, Magnesium, Potassium, Phosphorus)
- **Trace elements** (Zinc, Copper, Selenium)
- **Antioxidative phytochemical** (flavonoids, anthocyanidins, phenolic acids)
Cognition

- Cognition is a group of mental processes that includes **attention, memory, producing and understanding language, learning, reasoning, problem solving and decision making**
Cognition

- Narrowly: perception, recognition, reasoning, deduction, intuition, processing speed
- Broadly: Intelligence, memory, mood (affect)
Animal studies

• Rats fed almond paste demonstrated better results in the elevated-plus maze test (J Am Osteopath Assoc 2005; 105:145-58)
  • Almonds fed rats exhibited pro-cholinergic activity
  • Cholinergic systems play an important role in cognitive dysfunction associated with Alzheimer's disease and aging
Animal studies

• Improvement of cognitive and motor performance with dietary walnuts supplementation in aged rats (Br J Nutr 2009; 101:1140-4)

• 0, 2, 6, 9% walnut diet for 8 weeks

• Improvement on 2 and 6% in test of balance, on 6% improvement of working memory version of Morris water maze

• 6% - \( \frac{1}{4} \) of cup (1 oz)

• 9% diet impaired balance test, reference memory
Animal studies

- Feeding 19-months-old rats with 6% and 9% walnut diet significantly reduced the aggregation of polyubiquitinated proteins and activated autophagy in striatum and hippocampus (J Nutr Biochem 2012; 60:1084–93)

- Accumulation of polyubiquitinated proteins is hallmark of many age-related neurodegenerative diseases

- Hippocampus and striatum are critical regions for memory
Animal studies

- Rats fed walnuts solution demonstrated significantly better memory retention in water maze tests (Plant Foods Hum Nutr 2011; 66:335–40)
- Tryptophan – serotonin – increase in memory retention
## Large Neutral Amino Acids Content of Nuts in g/100g

<table>
<thead>
<tr>
<th>Name</th>
<th>TRP</th>
<th>ISO</th>
<th>LEU</th>
<th>MET</th>
<th>PHE</th>
<th>TYR</th>
<th>VAL</th>
<th>Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Almonds</td>
<td>0.281</td>
<td>0.677</td>
<td>1.210</td>
<td>0.179</td>
<td>0.281</td>
<td>0.87</td>
<td>0.551</td>
<td>0.07</td>
</tr>
<tr>
<td>Pistachio</td>
<td>0.271</td>
<td>0.893</td>
<td>1.542</td>
<td>0.335</td>
<td>1.054</td>
<td>0.412</td>
<td>1.230</td>
<td>0.05</td>
</tr>
<tr>
<td>Hazelnuts</td>
<td>0.193</td>
<td>0.545</td>
<td>1.063</td>
<td>0.221</td>
<td>0.663</td>
<td>0.362</td>
<td>0.701</td>
<td>0.05</td>
</tr>
<tr>
<td>Walnuts</td>
<td>0.170</td>
<td>0.625</td>
<td>1.170</td>
<td>0.236</td>
<td>0.711</td>
<td>0.406</td>
<td>0.753</td>
<td>0.04</td>
</tr>
<tr>
<td>Peanuts</td>
<td>0.131</td>
<td>0.475</td>
<td>0.875</td>
<td>0.166</td>
<td>0.700</td>
<td>0.549</td>
<td>0.566</td>
<td>0.04</td>
</tr>
<tr>
<td>Pecans</td>
<td>0.096</td>
<td>0.348</td>
<td>0.619</td>
<td>0.189</td>
<td>0.441</td>
<td>0.223</td>
<td>0.426</td>
<td>0.04</td>
</tr>
<tr>
<td>Macadamias</td>
<td>0.066</td>
<td>0.309</td>
<td>0.592</td>
<td>0.023</td>
<td>0.654</td>
<td>0.503</td>
<td>0.357</td>
<td>0.03</td>
</tr>
</tbody>
</table>

TRP = tryptophan, ISO = isoleucine, LEU = leucine, MET = methionine, PHE = phenylalanine, TYR = tyrosine, VAL = valine. The ratio was calculated as following: TRP/ISO+LEU+MET+PHE+TYR+VAL; Source: USDA National Nutrient Database for Standard Reference – Release 23 (2010). Beltsville, MD.
Nuts & Honey

- Tryptophan hydroxylase
- Tryptophan competes with LNAA for blood-barrier transport
PREDIMED studies

- PREDIMED – men+women 55–80 years – effects of Mediterranean diet on cardiovascular risk factors
  - Low fat control
  - Mediterranean + olive oil
  - Mediterranean + 15g walnuts/15 g almonds daily
PREDIMED studies

- Brain-derived nerve growth factors significantly elevated in nut groups (Nutr Neurosci 2011; 14:195-201)
  - Affect neurotransmitter release, presynaptic structure, axonal elongation, “Miracle grow for the brain”
- Improvements of working memory with walnuts (J Alzheimers Dis 2012; 29:773–82)
Short term studies

• Effects of walnuts consumption on cognitive performance in young adults (Br J Nutr 2011; 19:1–9)
32-32-32
Placebo-Walnuts group
3 withdrew first week
3 flu

Walnuts-Placebo group
3 withdrew first week
5 flu

Environmental control group
1 withdrew first week
1 dropped

Placebo-Walnuts group
3 withdrew first week
3 flu
2 transferred
1 dropped
Experimental group
Walnuts
8 weeks

Control group
Placebo
8 weeks

Environmental control group
No dietary intervention
8 weeks

Washout period
8 weeks

Experimental group
Walnuts
8 weeks

Control group
Walnuts
8 weeks

Experimental group
Placebo
8 weeks

Environmental control group
No dietary intervention
8 weeks
## Gender distribution

<table>
<thead>
<tr>
<th>Category</th>
<th>n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Males</td>
<td>39 (41)</td>
</tr>
<tr>
<td></td>
<td>33 (43)</td>
</tr>
<tr>
<td>Females</td>
<td>57 (59)</td>
</tr>
<tr>
<td></td>
<td>44 (57)</td>
</tr>
</tbody>
</table>
## Selected characteristics

<table>
<thead>
<tr>
<th></th>
<th>Experimental</th>
<th>Placebo</th>
<th>Environmental</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age (years)</strong></td>
<td>20.6 ± 2.0</td>
<td>20.7 ± 2.1</td>
<td>20.0 ± 1.9</td>
<td>0.362</td>
</tr>
<tr>
<td><strong>Hours of sleep (h/day)</strong></td>
<td>7.2 ± 1.3</td>
<td>7.0 ± 0.7</td>
<td>7.0 ± 1.0</td>
<td>0.747</td>
</tr>
<tr>
<td><strong>BMI (kg/m^2)</strong></td>
<td>22.6 ± 3.3</td>
<td>23.2 ± 3.5</td>
<td>23.1 ± 4.1</td>
<td>0.776</td>
</tr>
<tr>
<td><strong>Omega-3 intake (g)</strong></td>
<td>0.7 ± 1.1</td>
<td>0.6 ± 0.6</td>
<td>0.7 ± 1.0</td>
<td>0.788</td>
</tr>
<tr>
<td>Category</td>
<td>n</td>
<td>(%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>------------------</td>
<td>-----</td>
<td>-----</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Caucasian</td>
<td>41</td>
<td>(43)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>African–american</td>
<td>21</td>
<td>(22)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hispanic</td>
<td>13</td>
<td>(14)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Asian</td>
<td>10</td>
<td>(11)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mixed</td>
<td>9</td>
<td>(10)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
- 385 kcal
  - 20 g walnuts
  - 2.52 g ALA
    - 3 slices 1040 kcal / 60 g (1/2 cup) walnuts

- 287 kcal
  - No walnuts
  - 0.21 g ALA
    - 3 slices 775 kcal
Food displacement

- Males – less milk, cereal, pasta, bread
- Females – less milk, cheese, dried fruits, cereals
WMS–III
The Wechsler Memory Scale

- Memory test
  - Immediate
  - Delayed
  - Working memory

- Auditory
- Visual
- Recall (unprompted)
- Recognition (prompted)
WMS–III
The Wechsler Memory Scale

Memory test
- Logical memory
- Faces
- Verbal memory
- Numbers
- Family pictures
- Auditory memory

Immediate memory
- Delayed memory
- General memory
- Auditory memory
- Visual memory
WMS-III The Wechsler Memory Scale

- No changes
  - Differences – –3.7 to 2.8%
- No significance
- Norms – 50th to 80th percentile
• APM
Raven’s Advanced Progressive Matrices

• Fluid (decontextualized) intelligence
• Non-verbal, clear thinking abilities, logical reasoning, symbolic thinking, identifying relationships
APM
Δ 0.55% (95CI% -2.70 – 3.80), p=0.735
**APM**
Raven’s Advanced Progressive Matrices

- Fluid intelligence very stable
- Norms
  - Males – 81st percentile, IQ 113
  - Females – 64th percentile, IQ 105
WGCTA
The Watson–Glaser Critical Thinking Appraisal

- Crystalized intelligence (contextualized)
- Verbal, defining problem, selecting relevant information, recognizing assumption, formulating hypothesis, evaluate conclusions
WGCTA
The Watson–Glaser Critical Thinking Appraisal

- Inference
- Recognition of Assumption
- Deduction
- Interpretation
- Evaluation of Arguments
- Total score
WGCTA
Both sexes

- Walnuts
- Placebo

<table>
<thead>
<tr>
<th></th>
<th>Inference</th>
<th>Recognition</th>
<th>Deduction</th>
<th>Interpretation</th>
<th>Evaluation</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Walnuts</td>
<td>9.8</td>
<td>12.4</td>
<td>11.7</td>
<td>12.1</td>
<td>12.2</td>
<td>45.7</td>
</tr>
<tr>
<td>Placebo</td>
<td>8.8</td>
<td>12.1</td>
<td>11.6</td>
<td>12.1</td>
<td>12</td>
<td>44.1</td>
</tr>
</tbody>
</table>
WGCTA – Inference – Both Sexes

Δ 11.2% (95CI% 2.86 – 19.55), p=0.009
POMS
Profile of mood states

- 65 adjectives
- 5 point Likert scale – “not at all” to “extremely”
POMS
Profile of mood states

Six mood domains

- Tension–Anxiety (T)
- Depression–Dejection (D)
- Anger–Hostility (A)
- Vigor–Activity (V)
- Fatigue–Inertia (F)
- Confusion–Bewilderment (C)

Total Mood Disturbance (TMD) = (T+D+A+F+C)−V
POMS
Both sexes – all differences non-significant

- Walnuts
- Placebo
POMS
Males – Anger–Hostility p=0.013; TMD p=0.043
Conclusion

- No effect on memory
- No effect on intuition
- Selective effect on critical thinking
- Selective effect on mood in males
Conclusion

- Depression, ADHD, aging, Alzheimers, neurogenerative disorders
- More research is needed to observe short and long terms effects of nuts consumption on cognition