Impact of vitamins & nutrients on neurological function

B-vitamins & aging

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Lecture Outline

• Types of B-vitamins
• Folates
• Homocysteine
• BREAK
• Vitamin B12
• B-vitamins and aging
Types of B-vitamins

• Folic Acid/Folates
• Vitamin B12
• Riboflavin
• Thiamin (B1)
• Niacin
• Biotin
• Vitamin B6
• Other types
Folates

- Obtained from diet
Folate: natural form
Folic Acid
Role of folates in the cell

- make DNA
- repair DNA
- methylation
What is DNA?

https://www.youtube.com/watch?v=zwibgNGe4aY
Folates play a role in making DNA.
Folates: DNA damage and repair

DNA damage

DNA repair
Homocysteine

- Molecule, amino acid

- High levels associated with:
  - Cardiovascular disease, changes blood vessels
  - Pregnancy complications: Neural tube defects
  - Neurodegeneration

Chemical structure of homocysteine
Folate and Homocysteine

• Folates reduce levels of homocysteine

• More folate in the body, reduced homocysteine levels

• Less folate in the body higher levels of homocysteine

• Other factors also affect levels of homocysteine
What factors influence homocysteine levels?

Bolander-Gouaille and Bottiglieri, 2007, Homocysteine: Related Vitamins and Neuropsychiatric Disorders
Homocysteine Levels Throughout Lifespan

Life time mean 3-5µmol/L

Bolander-Gouaille and Bottiglieri, 2007, Homocysteine: Related Vitamins and Neuropsychiatric Disorders
Serum plasma homocysteine in alcoholics

Bolander-Gouaille and Bottiglieri, 2007, Homocysteine: Related Vitamins and Neuropsychiatric Disorders
Review: What is oxidative stress?
Hypothesis of homocysteine’s role in oxidative stress

Hoffman et al., 2011
Hypothesis of homocysteine’s role in oxidative stress

Hoffman et al., 2011
Hypothesis of homocysteine’s role in oxidative stress

Hoffman et al., 2011
Questions?
BREAK!
Dietary Folic Acid Requirements

• Folic acid intake for women is 0.4 to 1 mg per day
• Sometimes higher doses are recommended because of other factors
• Should be taken 2 to 3 months before conception, throughout pregnancy and first 4 to 6 weeks after birth (during breast feeding)
• Requirements for everyone else? 0.4mg
Vitamin B12

- Deficiency leads to neurological disorders
- Memory loss
- Fatigue
- Myelopathy: disease of spinal cord
- Neuropathy: disease of the nerves
- Brain atrophy
- Neurodegenerative diseases
- Gait abnormalities
- Molecular level: development of nerve cells, myelination

Vitamin B12 recommendations

<table>
<thead>
<tr>
<th>Life Stage</th>
<th>Recommended Amount</th>
</tr>
</thead>
<tbody>
<tr>
<td>Birth to 6 months</td>
<td>0.4 mcg</td>
</tr>
<tr>
<td>Infants 7–12 months</td>
<td>0.5 mcg</td>
</tr>
<tr>
<td>Children 1–3 years</td>
<td>0.9 mcg</td>
</tr>
<tr>
<td>Children 4–8 years</td>
<td>1.2 mcg</td>
</tr>
<tr>
<td>Children 9–13 years</td>
<td>1.8 mcg</td>
</tr>
<tr>
<td>Teens 14–18 years</td>
<td>2.4 mcg</td>
</tr>
<tr>
<td>Adults</td>
<td>2.4 mcg</td>
</tr>
<tr>
<td>Pregnant teens and women</td>
<td>2.6 mcg</td>
</tr>
<tr>
<td>Breastfeeding teens and women</td>
<td>2.8 mcg</td>
</tr>
</tbody>
</table>

- Some fortified food contain vitamin B12
- Beef liver and clams, which are the best sources of vitamin B12
- Fish, meat, poultry, eggs, milk, and other dairy products, which also contain vitamin B12
- Some breakfast cereals, nutritional yeasts and other food products that are fortified with vitamin B12
Vitamin B6

- Group of chemically similar compounds
- Involved in folate metabolism
- Cognitive development, through biosynthesis of neurotransmitters
- Maintain normal levels of homocysteine
- Deficiency not common, except for alcoholics and in older adults

- More information
https://ods.od.nih.gov/factsheets/VitaminB6-HealthProfessional/
Factors that affect B vitamin absorption

• **Age**
  - Decrease in ability to absorb food

• **Alcohol**
  - Even moderate alcohol consumption can affect your folate status
  - Alcohol interferes with folate metabolism
Factors that affect B vitamin absorption

• Poor Diet:
  • of appetite, health and psychological issues are some of the many factors that can influence food your intake.

• Vegetarian/Vegan Diet:
  • a strict vegan diet, supplementing with vitamin B12 is important to prevent vitamin B12 deficiency
  • Vitamin B12 is only found in animal products and fortified foods

• Medications:
  • Levodopa (L-Dopa)
Review video

https://www.youtube.com/watch?v=Qoz47lYquts
Epidemiological Research
Neurodegeneration

• Folate deficiency and/or elevated levels of plasma homocysteine associated with:
  o Mild Cognitive Impairment
  o Dementia
  o Brain atrophy
  o Alzheimer's disease

• Common for elderly individuals to be folate deficient and have elevated levels of plasma homocysteine

Hooshmand et al., 2011; Herrmann and Obeid, 2011; Annerbo et al., 2005; Seshardi et al., 2002
Neurodegeneration

Mild Cognitive Impairment
- Duration: 7 years
- Disease begins in Medial Temporal Lobe
- Symptoms: Short-term memory loss

Mild Alzheimer’s
- Duration: 2 years
- Disease spreads to Lateral Temporal & Parietal Lobes
- Symptoms include: Reading problems, Poor object recognition, Poor direction sense

Moderate Alzheimer’s
- Duration: 2 years
- Disease spreads to Frontal Lobe
- Symptoms include: Poor judgment, Impulsivity, Short attention

Severe Alzheimer’s
- Duration: 3 years
- Disease spreads to Occipital Lobe
- Symptoms include: Visual problems
Alzheimer’s disease overview

INCREASED LEVELS OF:
- amyloid beta protein
- tau
Clinical study

- Study published in 2002
- 1092 subjects without dementia (667 women and 425 men, ~76 years old)
- Followed for 8 years
- Increased levels of plasma homocysteine risk factor for dementia and Alzheimer’s disease

Clinical studies looking at homocysteine levels in patients with Alzheimer's disease

- Study published in 2005
- 145 patients with AD
- High homocysteine levels and plasma levels of amyloid beta protein were correlated

Reference: NEUROLOGY 2005;65:1402–1408
Clinical studies looking at homocysteine levels in patients with Alzheimer's disease
Clinical study investigating memory and homocysteine levels

- Study published in 2011
- Conducted in US
- 228 individuals (ages 80-101)
- Found no association between homocysteine levels and memory

Am J Geriatr Psychiatry 19:7, July 2011
Parkinson’s disease

• Environmental toxins, such as herbicides like paraquat, have been reported to induce Parkinson’s disease (PD)
• Approximately 55,000 Canadians are affected by PD, 35% of which are older than the age of 45
• PD is the second most common neurodegenerative disorder and is characterized by progressive loss of midbrain dopaminergic (DA) neurons
Parkinson’s disease overview

- Rigidity and trembling of head
- Forward tilt of trunk
- Reduced arm swinging
- Rigidity and trembling of extremities
- Shuffling gait with short steps

Brain Regions Affected by Parkinson’s Disease:
- Motor Cortex
- Globus Pallidus
- Thalamus
- Striatum
  - Caudate Nucleus
  - Putamen
  - Substantia Nigra
- Locus Ceruleus
- Raphe Nuclei
- Brainstem

Substantia Nigra (detail)
- Pars Reticulata
- Pars Compacta
Parkinson’s disease and diet

• Diet affects normal cellular processes, including the immune system, oxidative stress, cellular repair, and regeneration.

• Recent epidemiological studies have found that folates might play a critical role in normal DA neuron functions and PD
Clinical Study

- Human study
- 87 patients with PD
- Blood samples
- Serum levels of homocysteine increased in PD patients
- Changes in methylation correlated with cognitive function

- Reference: Clinical Chemistry 55:10
Animal Study

- Mice with elevated levels of homocysteine
- Injected with paraquat (animal model of Parkinson’s disease)
Cardiovascular disease and homocysteine

• High levels of homocysteine correlated with increased risk of cardiovascular disease
Epidemiological Research

Stroke

- Epidemiological studies indicate that elevated levels of homocysteine results in increased risk of stroke.

- Rotterdam scan study:
  - n = 1077, 60-90 year-old individuals
  - WML = white matter lesions
  - Silent brain infarcts increase with increased plasma homocysteine levels,
Dietary folic acid deficiency & neurodegeneration within the hippocampus

• *In vivo* work:
Controversy......

• Homocysteine easy to measure in blood of humans
• Need high levels of homocysteine to cause damage
• Homocysteine marker for deficiency
Review Video

https://www.youtube.com/watch?v=57QwxhzItbQ
Conclusion

- B-vitamins are water soluble.
- Play important roles in cellular function.
- B-vitamins reduce levels of homocysteine.
- High homocysteine levels have negative health consequences.
Next week....

Choline, Vitamin E, and D
Questions?