Impact of vitamins & nutrients on neurological function

B-vitamins and aging

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Lecture Outline

- Answer to questions from last class
- Homocysteine
- Vitamin B9: Folates/Folic acid
- Vitamin B12
- Vitamin B6
- Peer Review
- Questions
- BREAK
- Dementia and Alzheimer's disease
- Parkinson's disease
- Stroke
- Review Video
- Questions
How do nerve cells in the body communicate with the brain?

https://www.youtube.com/watch?v=L6w0_j6mWbo
Lecture One: How does alcohol cross the blood brain barrier (blood vessels)?

• Alcohol passes across the blood brain barrier
Lecture One: How does alcohol cross the blood brain barrier (blood vessels)?

Passive transport
Lecture two: methylation

https://www.youtube.com/watch?v=kZXKNYSXBCs
Lecture two: methylation

• Neurotransmitters
  • Dopamine
  • Glutamate
  • GABA
  • Serotonin
Homocysteine

• Is a naturally occurring molecule in the body
• Involved in methylation

• Increased levels of homocysteine associated with cardiovascular disease

• Normal range in plasma is 5 and 15 µmol/L

• More information at:
Homocysteine is what scientists refer to as a non-protein amino acid. In other words, we cannot build protein from homocysteine. It is a substance found in the blood that can be accurately measured with a simple blood test.

https://www.youtube.com/watch?v=GPMdz07Y_0s
How to reduce levels of homocysteine?

• Folates reduce levels of homocysteine
• Other B-vitamins, such as vitamin B12 also 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, such as medication, coffee intake and alcohol consumption
Folates

- Obtained from diet
Folate: natural form
Dietary Folic Acid Requirements

• Folic acid intake for women is 0.4 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?
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

- 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 elderly

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:
  • 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)
How does publishing in science work? What is peer review?
Publishing in Science and Peer Review

Video: https://www.lib.ncsu.edu/tutorials/peerreview/
Questions?
BREAK!
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

Normal vs. Alzheimer’s Diseased Brain

Normal

Alzheimer’s

Neurofibrillary tangles

Amyloid plaques

Neuron
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

- 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
- Caudate Nucleus
- Putamen
- Substantia Nigra
- Locus Ceruleus
- Raphe Nuclei
- Brainstem
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
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,

Vermeer et al 2012
Dietary folic acid deficiency & neurodegeneration

• **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
Questions?
Next week…..

Choline and Autoimmunity