HOW NUTRITION CHANGES THE AGING BRAIN

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Lecture Outline

• Introduction
  • Brain
  • Nutrition
  • Peer Review
• Questions
• BREAK
• Dementia and Alzheimer's disease
• Parkinson’s disease
• Choline and Neurodegeneration
• Review Video
• Questions
Nervous System
What does the brain look like?
Cross section of the brain
How is the brain organized?
Structures of the brain
Behaviour

• Kind of movement in a living organism
• Have a cause and function
Behaviour

• Can be learned
• Vary in degree of complexity
Behaviour: Research Example

Skilled Reaching Task In Rodents
Units of Brain Function

• Neurons
• Glial cells
Units of Brain Function: Neurons

dendrites, nucleus, cell body, axon, myelin sheath, axon ending
Units of Brain Function: Glial Cells (support cells)
Components of the Synapse

- Presynaptic Membrane
- Synaptic Vesicle
- Synaptic Cleft
- Neurotransmitter
- Postsynaptic Membrane
How neurons in the cell communicate: the synapse
Neurotransmitters

• Acetylcholine $\rightarrow$ memory, PNS
• Dopamine $\rightarrow$ reward
• Norepinephrine (a.k.a., noradrenaline) $\rightarrow$ stress response
• Serotonin $\rightarrow$ mood balance
How do nerve cells in the body communicate with the brain?

https://www.youtube.com/watch?v=L6w0_j6mWbo
Brain development
Brain Development
What’s going on at the cellular level?

Brain and Behaviour, Kolb & Whishaw, 2001
What’s going on at the cellular level?
What happens to the brain during aging?

- **Preclinical**: Silent phase: brain changes without measurable symptoms. Individual may notice changes, but not detectable on tests. “A stage where the patient knows, but the doctor doesn’t.”
- **MCI**: Cognitive changes are of concern to individual and/or family. One or more cognitive domains impaired significantly. Preserved activities of daily living.
- **Dementia**: Cognitive impairment severe enough to interfere with everyday abilities.

Time (Years)

Normal Aging

Mild - Moderate - Severe
Nutrition
Vitamins

Can be categorized as:

1) FAT SOLUBLE
2) WATER SOLUBLE
Fat Soluble

- Vitamins A, D, E and K
- Soluble in fats
- Stores in body tissues
- They are absorbed by fat globules and moved into circulation (intestine)

- BOTTOM LINE: vitamin stays in your body
Fat Soluble

• Too much vitamins in body can develop hypervitaminosis (too much vitamins)

• Can become deficient in vitamins if:
  • Fat intake is too low
  • Fat absorptions is compromised by certain drugs
Water Soluble

Vitamins B and C

• Require continuous supple to your body
• Steady daily intake required
• Take too much, then your body removes it (e.g. pee it out)
Homocysteine

- Molecule, amino acid

- High levels associated with:
  - Cardiovascular disease, changes blood vessels
  - Pregnancy complications: Neural tube defects
  - Neurodegeneration
What is oxidative stress?

Stable Molecule

Unstable Molecule (Free Radical)

Antioxidants have extra electrons that they can donate to free radicals

Free radical missing an electron in its outer shell

Antioxidants Doing their Job

Healthy Cell Membrane

Damage Free Radicals

Antioxidant neutralizing a free radical

HUMAN CELL

NUCLEUS
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?

• B-vitamins
  • Folic Acid (vitamin B9)
  • Vitamin B12

• Choline
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, such as medication, coffee intake and alcohol consumption
What factors influence homocysteine levels?
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
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

Stated Clearly
Folates play a role in making DNA
Folates: DNA damage and repair

DNA damage:
- Single-strand DNA break
- DNA-binding chemotherapeutic drug
- Radiation

DNA repair:
Vitamin B12

- Helps reduce levels of homocysteine
- Deficiency leads to neurological disorders
- Memory loss
- Fatigue
- 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

<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>
Choline

- Essential Nutrient
- Involved in maintenance of DNA and chromosome stability
Food sources of choline

- food sources of choline are high in fats and cholesterol
- only 20-25% of people get adequate levels of choline

Rich food sources of choline (per 100 gram serving)

<table>
<thead>
<tr>
<th>Food</th>
<th>Choline (mg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Beef liver</td>
<td>350</td>
</tr>
<tr>
<td>Chicken liver</td>
<td>330</td>
</tr>
<tr>
<td>Egg, hard boiled</td>
<td>230</td>
</tr>
<tr>
<td>Salmon, smoked</td>
<td>220</td>
</tr>
<tr>
<td>Salmon, cooked</td>
<td>91</td>
</tr>
<tr>
<td>Soy protein powder</td>
<td>86</td>
</tr>
<tr>
<td>Tilapia</td>
<td>83</td>
</tr>
<tr>
<td>Chicken, roasted</td>
<td>79</td>
</tr>
<tr>
<td>Peanut butter</td>
<td>66</td>
</tr>
<tr>
<td>Almonds</td>
<td>52</td>
</tr>
<tr>
<td>Brussels sprouts</td>
<td>41</td>
</tr>
<tr>
<td>Broccoli</td>
<td>40</td>
</tr>
<tr>
<td>Cauliflower</td>
<td>39</td>
</tr>
</tbody>
</table>

Choline & Neurological Function

- Membrane formation
Neurotransmitter: acetylcholine

\[
\text{Choline} + \text{AcetylCoA} \rightarrow \text{Acetylcholine}
\]
Choline & Neurological Function

- Makes Acetylcholine
  - Acetylcholine is involved in memory and motor function
Choline & Neurological Function

• Metabolism of Homocysteine
  • Reduces levels of homocysteine
  • Interacts with folate metabolism
Factors that affect vitamin and nutrient 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 vitamin and nutrient 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 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 (PD)

• 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
Parkinson’s disease and diet

- Diet affects normal cellular processes,
  - immune system
  - oxidative stress
  - repair
  - 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 as well as controls
- 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)
Choline in Aging and Neurodegeneration

- Significant cholinergic cell loss during aging
Choline in Aging and Neurodegeneration

• Possibly a result of a loss of nerve growth factor (NGF)
• NGF is neurotrophic factor
Neurotrophins

Nerve Growth Factors (shown in green) is required by neurons in order to survive. As they are a limited extracellular resource, some neurons (shown in blue) may uptake a disproportionate share of survival factors, leading to the eventual death of neighboring neurons (shown in red).
Choline in Aging and Neurodegeneration

STUDY
• clinical trial of NGF gene therapy
• individuals with mild Alzheimer disease (AD) for 22 months
• No long-term adverse effects of NGF
• Delayed the rate of cognitive decline

Schliebs et al., 2010
Choline in Aging and Neurodegeneration

STUDY:
• Aged monkeys long-term NGF delivery
• cholinergic basal forebrain (subcortical structure)
• restored cholinergic neuronal markers to levels of young monkeys
• extended NGF support to neurons may reverse aging-related neuronal loss

Schliebs et al., 2010
Choline in Aging and Neurodegeneration

- Late stage of Alzheimer’s disease, extensive cholinergic loss in cortex

- Early stages of Alzheimer’s disease and Mild Cognitive Impairment no loss of cholinergic cells
Choline in Aging and Neurodegeneration

Cholinergic function

- Trophic responsiveness
  - TrkA/p75NTR; NGF/proNGF
- Cholinergic signaling
  - Acetylcholine release
  - High affinity choline uptake
  - mACHR, α7 nACHR

Cholinergic signaling:

- AChE
- M1-mACHR
- α7 nACHR
- p75NTR
- Proteome

β-amyloid → GSK-3β → p38-MAPK

P-tau

tau

Cholinergic cell loss:

Shift in isoform ratio

MCI early AD AD advanced AD

Acetylcholine and Alzheimer's disease
B-vitamin supplementation in the elderly
Neurodegeneration Progression

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Folate supplementation in Elderly

Study Background
- 2004-06
- Patients with Mild Cognitive Impairment (MCI) & controls
- Treatment, 2 years; Folic Acid and Vitamin B12

Smith et al., 2010
Folate supplementation in Elderly

Placebo

Treated

Rate of atrophy per year (%)

tHcy (μmol/L) at baseline

Treatment
• Placebo
• Active
Folate supplementation in Elderly

Placebo

Treated
Effect of B-vitamin supplementation on grey matter volume in patients with Mild Cognitive Impairment

**Objective**: investigate whether Alzheimer's disease related gray matter atrophy can be reduced via B-vitamin supplementation

- Patients: Mild Cognitive Impairment
- 2 Years of B-vitamin supplementation
- MRI
Results

B-vitamin supplementation for 2 years reduces brain shrinkages by 7-fold
Results

Treated individuals with the highest levels of homocysteine benefited most from B-vitamin supplementation.
Too much folate

- Exacerbate neurological consequence of vitamin B12 deficiency
- Safe upper limit of 1.0mg/day
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?
Future learning: Nutrition

The Institute of Holistic Nutrition: Ottawa campus
  • [http://www.instituteofholisticnutrition.com](http://www.instituteofholisticnutrition.com)

Text Books Available on Amazon:

Whole: Rethinking the Science of Nutrition
by T. Colin Campbell, Howard Jacobson

The China Study: The Most Comprehensive Study of Nutrition Ever Conducted and the Startling Implications for Diet, Weight Loss and Long-term Health
by T. Colin Campbell

Introduction to Human Nutrition 2nd Edition
by Michael J. Gibney, Susan A. Lanham-New, Aedin Cassidy, Hester H. Vorster
Future Learning: Neuroscience

YouTube Channel: Neuro Transmissions
https://www.youtube.com/user/neurotransmissions

Alzheimer's disease blog (for non-scientists)
https://alzscience.wordpress.com/

List of Neuroscience Blogs:
http://www.prymd.com/blog/the-best-brain-blogs-neuroscience-for-the-non-scientific/
More questions?

E-mail me at NafisaJadavji@Carleton.ca

Please fill out course evaluations!