How Nutrition Changes the Aging Brain

STROKE & DIETARY INFLUENCES ON COGNITION IN AGING

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REMINDER! Purpose of Course

• To present information about how nutrition affects brain function

• Last class discussion and take home points
Outline

• Topics from Lecture #4
• Introduction to Stroke
• Nutrition & Stroke
• Dietary Influences on Cognition
Marijuana – Cannabis Receptors

INTRODUCTION
• Psychoactive drug
  • Alters mood, perception, consciousness and behavior
• Made from Cannabis Plant
• Used for medicinal purposes and recreational use
Marijuana – Cannabis Receptors

• Endocannabinoid system (ECS)
  • Modulates bodily functions
    • Appetite
    • Sleep
    • Cognition
  • Present in the nervous system
Marijuana – Cannabis Receptors

- 2 types of receptors that THC binds to
  1. CB1
  2. CB2
Introduction to stroke video

https://www.youtube.com/watch?v=pcmrgwNCPwM
What is a stroke?

• A stroke is a "brain attack"
• It occurs when blood flow to an area of brain is cut off. When this happens, brain cells are deprived of oxygen and begin to die
• When brain cells die during a stroke, abilities controlled by that area of the brain such as memory and muscle control are lost

http://www.stroke.org/understand-stroke/what-stroke
Types of Stroke

- About 80% of strokes are ischemic caused by the interruption of blood flow to the brain due to a blood clot.

- About 20% of strokes are hemorrhagic caused by uncontrolled bleeding in the brain.
  
  - Can be cortical or sub-cortical.
Ipsilateral vs. Contralateral, Peri-infarct
Patient with stroke

https://www.youtube.com/watch?v=RRJp0204P_s
Who is at risk of a stroke?

- Stroke is not a disease of age anymore
- Profile of stroke patient is changing
- Today stroke patients have multiple conditions:
  - Hypertension
  - Diabetes
  - Coronary artery disease
  - Cancer
- In the next 10 years:
  - Increase by 24% of stroke for people in 50s and 13% for people in 60’s
  - Estimated doubling of strokes in young people

Canadian Heart and Stroke Foundation
Death as a result of stroke

- Stroke is the third leading cause of death in Canada. Six percent of all deaths in Canada are due to stroke.

- Each year, over 14,000 Canadians die from stroke.

- Each year, more women than men die from stroke.

Canadian Heart and Stroke Foundation
Stroke Survival in Canada

Death rate from stroke by province (per 100,000 people)

Average in Canada: 17.9

2011-2012 30-day stroke in-hospital mortality rates standardized per 100,000 population and for age and gender

WHERE YOU LIVE MATTERS

There is a better chance of surviving a stroke in Quebec or Alberta. Reasons for the differences in

Canadian Heart and Stroke Foundation
Public Awareness Campaigns

SIGNS OF STROKE

WEAKNESS:
Sudden loss of strength or sudden numbness in the face, arm or leg, even if temporary.

TROUBLE SPEAKING:
Sudden difficulty speaking or understanding or sudden confusion, even if temporary.

VISION PROBLEMS:
Sudden trouble with vision, even if temporary.

HEADACHE:
Sudden severe and unusual headache.

DIZZINESS:
Sudden loss of balance, especially with any of the above signs.

If you experience any of these symptoms, call 911 or your local emergency number immediately.

Canadian Heart and Stroke Foundation
After stroke, one may have

• Problems using your hand, therefore difficulty to eat and drink
• Problems with memory and thinking, maybe forget to eat and drink
• Loss of appetite
• Swallowing problems, dysphagia

• Difficult to get nutrients you need (malnutrition and dehydration)
• Slow down recovery
Eating after a stroke: Food to Increase

- Fruits and vegetables
  - Contain antioxidants, help reduce damage to blood vessels
  - Potassium to help control blood pressure
  - Fibre in fruit can lower cholesterol

- Dairy
  - Another source of potassium, control blood pressure
Eating after a stroke: foods to decrease

• Salt: too much can raise blood pressure (bp)
• Sugar: increase bp
• Alcohol: too much contributes to stroke, increase blood pressure
• Saturated fats: cause high cholesterol
  • Stick to polyunsaturated fats
  • Monounsaturated fats
Impact of turmeric on diet (2010)

https://www.youtube.com/watch?v=reQM1epROXk
Impact of turmeric on diet (2014)

https://www.youtube.com/watch?v=Ej5nCbp1UYQ
Current therapies for stroke

• tPA (tissue plasminogen activator)
  • Federal Drug Administration approved (undergone clinical trials)
  • Used to treat/stop ischemic strokes
  • Needs to be administered within 3 hours of stroke onset
  • Longer than 3 hours, can cause damage
Current therapies for stroke

- Combination therapies
  - Brain is plastic, ability to change
  - Thrombolytic agents and neuroprotection (e.g. exercise) → treatment of ischemic stroke

Austin et al., 2014
- Exercise 24-48 hour after stroke, reduction is amount of damage
- Long term effects unknown
Neuroprotection – Diet

• Mediterranean diet contributes to prevention and evolution of stroke
• Omega 3 fatty acids and polyphenols exert positive effect on neurovascular disease
• Diets could increase neuroprotection

Ayuso et al., 2017
Current status of stroke research

• hundreds of clinical trials testing neuroprotective agents have failed despite efficacy in experimental models

• several systematic reviews have exposed a number of important deficits in the quality of preclinical stroke research

Dirnagl, 2006
Current status of stroke research

Dirnagl, 2006
Diet and Prevention of Stroke: Folic Acid

• 702 with hypertension history of stroke
• Administer 10mg of enalapril, 0.8mg of folic acid or enalapril alone
• Duration 4.5 years

• Results of enalapril and folic acid reduced incidence of first stroke

• China does not have mandatory folic acid fortification

Huo et al., 2015
B-vitamins reduce homocysteine levels

- High levels of homocysteine increase thrombosis
B-vitamins reduce homocysteine levels

• Vitamin B12 and folic acid reduce homocysteine and reverse effects
• Clinical trials have been conducted but show no benefits
• Lack of results because folic acid controlled, but not vitamin B12 as well as status of patients (e.g. renal failure)

Spence et al., 2006
Mediterranean Diet

• 2 clinical trials shown that Mediterranean diet decreases vascular events compared to Western diet
Mediterranean Diet

• Lyon diet heart study
  • 423 survivors of myocardial infarction
  • 2 groups: Western Diet and Mediterranean diet
  • Calories from fat the same ~30%
• Mediterranean vs Western diet
  • decrease cholesterol and increase in beneficial oils
  • 60% reduction in cardiac death or myocardial infarction

No difference in alcohol consumption
Mediterranean Diet

- Improved endothelial function
- Increases antioxidant rich foods
- Reduces insulin resistance
Questions?
Break!
Folic acid & choline supplementation after stroke

- Ischemic stroke in mice with high levels of homocysteine
- Damage to motor cortex, impaired motor function
- After stroke administered folic acid, vitamin B12 and choline
- Motor function not impaired
- Increase in plasticity

Jadavji et al., 2017
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.

<table>
<thead>
<tr>
<th>Rich food sources of choline (per 100 gram serving)</th>
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</thead>
<tbody>
<tr>
<td>Beef liver 350 mg</td>
</tr>
<tr>
<td>Chicken liver 330 mg</td>
</tr>
<tr>
<td>Egg, hard boiled 230 mg</td>
</tr>
<tr>
<td>Salmon, smoked 220 mg</td>
</tr>
<tr>
<td>Salmon, cooked 91 mg</td>
</tr>
<tr>
<td>Soy protein powder 86 mg</td>
</tr>
<tr>
<td>Tilapia 83 mg</td>
</tr>
<tr>
<td>Chicken, roasted 79 mg</td>
</tr>
<tr>
<td>Peanut butter 66 mg</td>
</tr>
<tr>
<td>Almonds 52 mg</td>
</tr>
<tr>
<td>Brussels sprouts 41 mg</td>
</tr>
<tr>
<td>Broccoli 40 mg</td>
</tr>
<tr>
<td>Cauliflower 39 mg</td>
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</tbody>
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Choline & Neurological Function

• Membrane formation
Neurotransmitter: acetylcholine

Choline + AcetylCoA $\rightarrow$ Acetylcholine

Choline acetyltransferase
**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 folates metabolism
Iron deficiency and stroke

• Iron deficiency anemia (IDA) involved in ischemic attack or stroke

• Study found IDA is a risk factor for stroke

Dubyk et al., 2012
Caloric restriction and Intermittent fasting

- Extends life and decreases age related disease
- Possibly by inducing expression of:
  - Neurotrophic factors
  - Antioxidants
  - Heat shock proteins

Manzanero et al., 2011
Heat Shock Proteins

- Cells produce heat shock proteins in response to stress
- Stabilize new proteins
- Make sure damaged proteins are folder correctly
Figure 2 Protective mechanisms of calorie restriction against neuronal cell death in stroke. Stroke acts in detriment of neuronal health by different mechanisms, including excitotoxicity, calcium overload, oxidative stress and inflammation, which can culminate in neuronal apoptosis. CR prepares neurons to bear each of these forms of stress by modifying the levels of key stress-response proteins. Certain proteins are up-regulated, such as the chaperones Grp78 and Hsp70, which protect from calcium overload and inflammation; neurotrophic factors such as BDNF, whose role is to protect the cells from excitotoxicity but are also key promoters of neurogenesis after stroke; SRT1, a central mediator of many CR beneficial effects such as resistance to oxidative stress and moderation of inflammation (through its down-regulation of NFκB); UCPs, which are thought to decrease the generation of ROS; and HO-1, with anti-oxidant properties. Hence, CR prepares brain cells at many levels to resist stroke-induced neuronal cell death and promote recovery after stroke.

Manzanero et al., 2011
Figure 3. The protective effect of calorie restriction on stroke diminishes with age. In a recent work by our group (47), mice from different age groups were subjected to intermittent fasting for the same time period before suffering ischemic stroke. The adaptive cellular responses, in the form of neurotrophic factors, protein chaperones, anti-oxidant and anti-inflammatory environments, were strongly favoured in young mice. However, aged animals didn’t show such a beneficial response. As a result, if young mice were protected from stroke but the extent of the protection was weak or null in aged mice. These results show that the protective effects of if against stroke are age-dependent.

Manzanero et al., 2011
Dietary influences on cognition in aging
Polyphenols

• Found in plants
• Highly colored fruit and vegetables (e.g. blueberries)
• Flavonoids, most type of polyphenols
Important sources of flavonoids are tea, onions and apples.

Polyphenol family

- Other polyphenols
- Flavonoids
  - Flavanones
  - Isoflavones
  - Flavonols
  - Anthocyanins
  - Flavones

Examples of sources:
- Tea
- Onions
- Apples
Polyphenols

Flavonoids

- Delays or Prevents the onset of diseases caused by free radicals
- Best anti-oxidant
- Anti-inflammatory activity
- Improvement of endothelial functions
- Blood pressure reduction due to its vasodilatory effect
- Inhibits LDL oxidation by free radicals
- Inhibits platelet aggregation
- Anti-viral / Anti-bacterial
- Reduced risk of cardiovascular diseases
Polyphenols

- Polyphenols
  - Absorbed by small intestine
  - Undergo biotransformation
  - Cross blood brain barrier

- Concentration in the brain 1nmol/g (this is low)

- Mode of action is under debate

- Studied in terms of impact on cognition
Polyphenols

• Polyphenols effect may be in the periphery and then this affects the brain

• High levels of flavonoid intake are reported to decrease risk of developing Alzheimer's disease and slow cognitive decline
Polyphenols

- In animal models
  - Decrease microglial activation
  - Decrease proinflammatory molecules
Vitamins

• Aging energy requirements are low
• BUT micronutrient requirements are increased

• Needed for energy production, adenosine triphosphate (ATP)

• Low intakes of:
  • B-vitamins: B12, folic acid and riboflavin
  • Vitamin C

Associated with Poor Memory
Vitamin A, C and E

- Antioxidants
- Oxidative stress, increases as we age

- Studies assessing vitamin A, C, and E on cognitive function show no benefit
Vitamin A, C and E

- Problem with studying vitamin benefits
  - synergy between antioxidant nutrient function

- No reproduction of complex profile of different antioxidants on human diet
Vitamin K

- Role in cognition is limited

- Increased plasma concentration associated with better cognitive performance

- Molecules in the brain dependent on vitamin K are present in the hippocampus
Vitamin D

• Synthesize during skin exposure to sunlight and consumed in diet

• Prevalence high of vitamin D deficiency in elderly

• Patients with Alzheimer's disease have lower circulator levels of vitamin D compared to healthy controls
Vitamin D

• Supplementation studies are not clear
  • Participants from one study
  • Low vitamin D at baseline (start of experiment)
  • Were found to have higher risk of developing cognitive decline
  • Findings not reproduced
Trace Elements: Zinc

- Maintains metabolic homeostasis in elderly
- Protection against oxidative stress
- Proteins involved in DNA damage and repair
- Deficiency affects:
  - DNA repair
  - Antioxidant defense
  - Neuronal death
Trace Elements: Zinc

- Alzheimer's disease patients are often zinc deficient
- Results of zinc supplementation studies are unclear
Trace Elements: Selenium

- Protection against oxidative stress
- Brain is the last organ to be depleted when individual is deficient
Trace Elements: Iron

- Important role in oxygen transport and storage
Trace Elements: Iron

• Deficiency leads to cerebral hypoxia (reduced oxygen going to the brain) and cognitive decline

• Iron deficiency leads to cognitive decline
Trace Elements: Cooper

- Important for antioxidant enzymes
- Toxic at high concentrations
- Causes oxidative cell death
Trace Elements: Cooper

• Impaired cooper homeostasis
  • promotes formation of amyloid beta and neurofibrillary tangles
Summary of how Western Diet affects cognition
Next week…Last Lecture…..
Multiple Sclerosis, Seizures, Diabetes, Arthritis and take home messages
Questions?