Impact of vitamins & nutrients on neurological function

Impact of diets on brain function

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Outline

• Supplement Study!
• Follow-up from last lecture
  • Cholesterol and choline interaction
  • Vitamin D & Microglial
• High Fat: Ketogenic
• Mediterranean
• Vegetarian/Vegan
• Questions?
• Break
• Low Fat
• Low Carbohydrate: Atkins/Paleo
• Gut Microbiota
• Questions
Supplementation Study

Annals of Internal Medicine

ORIGINAL RESEARCH | 9 APRIL 2019

Association Among Dietary Supplement Use, Nutrient Intake, and Mortality Among U.S. Adults: A Cohort Study

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Article, Author, and Disclosure Information
Background: The health benefits and risks of dietary supplement use are controversial.

Objective: To evaluate the association among dietary supplement use, levels of nutrient intake from foods and supplements, and mortality among U.S. adults.

Design: Prospective cohort study.


Participants: 30,899 U.S. adults aged 20 years or older who answered questions on dietary supplement use.

Measurements: Dietary supplement use in the previous 30 days and nutrient intake from foods and supplements. Outcomes included mortality from all causes, cardiovascular disease (CVD), and cancer.
Limitations: Results from observational data may be affected by residual confounding. Reporting of dietary supplement use is subject to recall bias.

Conclusion: Use of dietary supplements is not associated with mortality benefits among U.S. adults.

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Cholesterol and choline interaction

• Lipid (fat) transport and metabolism
• Fat and cholesterol consumed in the diet are transported to the liver
• Liver, fat and cholesterol are packaged into very-low-density lipoproteins (VLDL) for transport in the bloodstream to extrahepatic tissues
• Choline metabolites are required for packaging and transport
• If there isn’t enough, then fat and cholesterol accumulate in liver
Vitamin D and Neurological Function

• Neuroimmunodulation
  • Microglial cells
Respiratory burst

- Also called oxidative burst
- Rapid release of reactive oxygen species from different cells
- Can include immune cells
Ketogenic diet
Ketogenic Diet

- Water Consumption
- Low Amount of Carbohydrates
- Monounsaturated and Saturated Fats
- Fats
- Proteins
Ketogenic Diet

• Increase fat and decrease carbohydrates

• 3 to 4 grams of fat for every 1 gram of carbohydrate and protein

• Fat converted to fatty acids and ketone bodies in liver

• Body to go into a metabolic state called ketosis

• Lowers glucose levels and decreases insulin resistance

• The liver becomes the sole provider of glucose for organs
HOW DOES KETOSIS WORK?

TRADITIONAL DIET: HIGHER CARB

GLUCOSE LEVELS RISE
PANCREAS SECRETES INSULIN
INSULIN SHUTTLES GLUCOSE INTO CELL

ENERGY

KETO DIET: HIGHER FAT

GLUCOSE LEVELS FALL
LIPASE RELEASES STORED TRIGLYCERIDES
FATTY ACIDS TRAVEL TO THE LIVER
LIVER PRODUCES KETONES

ENERGY

http://www.bodybuilding.com/fun/keto.htm
Ketogenic summary video

https://www.youtube.com/watch?v=OFD2q5iqevY&feature=youtu.be
What is Epilepsy?

• is the fourth most common neurological disorder and affects people of all ages.
• means the same thing as "seizure disorders."

https://www.epilepsy.com/learn/about-epilepsy-basics/what-epilepsy
What is Epilepsy?

• is characterized by unpredictable seizures and can cause other health problems.

• is a spectrum condition with a wide range of seizure types and control varying from person-to-person.

• public misunderstandings of epilepsy cause challenges that are often worse than the seizures.

https://www.epilepsy.com/learn/about-epilepsy-basics/what-epilepsy
Epilepsy & Nutrition

• Steady energy release foods
• People with epilepsy should have a balanced diet (carbs, fats, proteins, veg and fruit)
• Avoid swings of blood sugar
• Anticonvulsants may interfere with body’s ability to absorb vitamin B12, K, D, Calcium and Magnesium
• Large amounts of alcohol are concerning – may interfere with anticonvulsants medication
Ketogenic Diet & Epilepsy

• Used to treat drug-resistant epilepsy in children since the 1920s

• Several studies have shown that the ketogenic diet does reduce or prevent seizures

• The diet works well for children with focal seizures, but may be less likely to lead to an immediate seizure-free result

http://www.charliefoundation.org/explore-ketogenic-diet/explore-1/introducing-the-diet
Ketogenic Diet & Alzheimer's disease

• double-blind, placebo-controlled study

• 152 patients with mild- to moderate Alzheimer’s disease

• ketogenic agent or a placebo, maintaining a normal diet

• 90 days later, those receiving the drug showed marked cognitive improvement compared to placebo

• correlated with the level of ketones in the blood

Mediterranean diet
Key Components of Mediterranean diet

• Eating primarily plant-based foods, such as fruits and vegetables, whole grains, legumes and nuts

• Replacing butter with healthy fats such as olive oil

• Using herbs and spices instead of salt to flavor foods

• Limiting red meat to no more than a few times a month
Key Components of Mediterranean diet

• Eating fish and poultry at least twice a week

• Enjoying meals with family and friends

• Drinking red wine in moderation (optional)

• Getting plenty of exercise
How to implement the Mediterranean diet

1) Re-think meat
2) Increase plant based meals
3) Batch cook whole grains
4) Eat Vegetables
5) Snack on fruits and nuts
6) Change your fats
7) Add herbs and spices, decrease salt

Globe and Mail, 2018
Mediterranean diet

• Does it prevent disease?

• Scientific research is inconclusive

• Components of the diet have benefits
Omega 3 & 6 fatty acids

- Omega 6 fatty acids → some are pro-inflammatory
- Diet needs to be balance of omega 3 & 6 fatty acids

- Examples

<table>
<thead>
<tr>
<th>Omega 3</th>
<th>Omega 6</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fish (e.g. tuna, cod)</td>
<td>Corn oil</td>
</tr>
<tr>
<td>Flax</td>
<td>Poultry</td>
</tr>
<tr>
<td>Hemp</td>
<td>Nuts</td>
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<td></td>
<td>Cereal</td>
</tr>
<tr>
<td></td>
<td>Eggs</td>
</tr>
</tbody>
</table>
Docosahexaenoic acid (DHA)

- Risk of dementia double every 5 years after 65
- Docosahexaenoic acid (DHA), omega-3 fatty acid

- Neuroprotective
- Reduced production beta amyloid peptide (thought to start AD)
- Reduction of neuro inflammation
- Decrease oxidative damage
- Increase brain derived neurotrophic factor (BDNF)

Cole & Frautschy, 2010
Docosahexaenoic acid (DHA)

- Clinical trials suggest DHA or fish oil can slow early stages of progression
- BUT maybe specific to lipid metabolism
- Larger trials needed to determine efficacy

Cole & Frautschy, 2010
Polyphenols

- Blueberry, strawberry, grape, and plum juices/extracts
- Positive effects in rodents (cognition)
- Polyphenols in juice/extracts maybe causing positive effects
- Grapes – resveratrol
- Blueberries - pterostilbene

Improve cognition in rodents

Cherniack et al., 2012
Polyphenols

Fig. 1. Potential mechanisms for polyphenol activity against dementing illness.

Cherniack et al., 2012
Polyphenols

• Mechanisms of action
  • Anti-inflammatory
    • Reduce vascular inflammation by decreasing producing of adipocyte generated inflammatory cytokines
  • Protect brain vasculature against pro-inflammatory state induced by metabolic syndrome
  • Neuroprotective effects, e.g. resveratrol, reduce neuron loss
  • Clinical trials underway in US of polyphenols

Cherniack et al., 2012
Polyphenols

- Improve insulin sensitivity, glucose, and insulin levels in rodent and preliminary human trials

Cherniack et al., 2012
Polyphenols

• Consideration for therapy
  • Optimum aged for initiation of therapy
  • Bioavailability – proportion of drug enters circulation when introduced into the body
  • How do they cross blood brain barrier
  • Sugar (comorbidities, diabetes)

Cherniack et al., 2012
Vegetarian & Vegan Diets
What is a vegetarian diet?

• Is plant-based, excluding the consumption of meat and sometimes animal by-products.
• Ovo- and lacto-vegetarian diets (those that include eggs and dairy, respectively)

• Research shows it can be a lot harder to get all the vitamins, minerals, and nutrients essential for proper health with a limited diet
What is a vegan diet?

• Is a stricter form of the vegetarian diet. It excludes all meat and animal-derived products (e.g., eggs and dairy)
Vegan Diet: Vitamin D and Brain Function

• Vitamin D is particularly important for vegans
• Not found in many vegan foods

• 2009 study by researchers at the University of Manchester
  • adults with lower vitamin D levels processed information much slower than those who had adequate levels
Vegan Diet: Vitamin D and Brain Function

• Vitamin D3 (cholecalciferol) – needed by our bodies

• Vitamin D3 important:
  • in brain growth and development
  • regulates calcium levels within the brain
  • helps protect brain cells from damaging oxidation
  • supports the health of the hippocampus (the brain’s memory center)

• Get Vitamin D3 from sunshine or obtain it from animal products
Vegan Diet: Vitamin D and Brain Function

• Plant foods is vitamin D2 (ergocalciferol)
• Bodies can convert some D2 to D,
• D2 is less potent, doesn’t last as long in the bloodstream
• Harder to store in our body fat for rainy days and dark winters

• Most studies have found that vegans have lower blood levels of vitamin D3 compared to people that eat animal products
Vegan Diet: Vitamin B12

- Vegan diets contain virtually no vitamin B12
- Severe, prolonged B12 deficiency is fatal
- Vegans and vegetarians take supplements
- Consume fortified yeast (unfortified yeast doesn’t naturally contain any vitamin B12)

- Vegetarians tend to have lower B12 levels than omnivores
- Vegans on average tend to have the lowest B12 levels
Vegan Diet: Prenatal Period

• 2009 study by researchers from Emory University in Georgia found that infants of mothers who don't get enough vitamin B-12, or cobalamin, may be at increased risk for developmental delays
• B-12 is also an important nutrient for neurological development of the fetus during pregnancy
Vegan Diet: Iron

• When people think of iron deficiency, they think of anemia (lower numbers of red blood cells in the circulation), but the truth is that the brain needs iron just as much as red blood cells do

• Iron in the brain is required for:
  • neurotransmitter production (serotonin, dopamine and norepinephrine)
  • generation of brain energy
  • hippocampal function (memory)
  • cell signaling
  • infant brain development.
Vegan Diet: iron

• Many plant foods are lower in iron than animal foods
• Plants contain a form of iron that is far more difficult to absorb than the form found in animal foods
• Vegans and vegetarians have about the same amount of iron in their blood as people that eat animal products
• Iron stores (how much they have in reserve) do tend to be lower
Vegan & Vegetarian Diets: Fatty Acids

- Vegan diets contain low amounts of omega-3 (DHA or EPA), and vegetarian diets contain only small amounts from eggs and dairy.

- Comparison to omnivores, DHA and EPA levels can be about 30% lower in vegetarians and more than 50% lower in vegans.
Questions?
Break
Low Fat Diet
What is a low fat diet?

• Restricts fat
• ↓ Saturated fat
  • Examples include: fatty beef, lamb, pork, butter, lard and cream
What is a low fat diet?

• ↓ Cholesterol
  • Can be increased by
    • saturated fat, found in animal products
    • trans fats, found in some commercially baked cookies and crackers and microwave popcorn
    • red meat and full-fat dairy products

• Fat 1g = 9 calories
• 1g of protein or carbohydrates = 4 calories
Low Fat

• Brains need certain fats
• Fattiest organ is brain
• Composed of 60% fat,
• ~ 25% of your body's cholesterol is found in the brain
Cell Membrane

Phospholipid Bilayer

- external environment
- internal environment
- cholesterol
- phospholipid
- molecule
Importance of fat in the diet

• Cell membranes are made of it, but the type of fat is very important

• Omega-3, polyunsaturated fats especially important

• Vital components of cell membranes
  • keep them flexible
  • allows molecules embedded in them more freedom to change shape
High Protein Diet
What is a high protein diet?

• Is low in fat and carbohydrate intake

• Example foods in a high-protein diet include lean beef, chicken or poultry, pork, salmon and tuna, eggs, and soy

• A diet is considered "high in protein" if daily protein consumption exceeds 15% of total energy intake
Impact of high protein diet on the body

• Can result in **nutritional deficiencies or insufficient fiber**
  • cause problems such as bad breath, headache and constipation

• Some high-protein diets include foods such as red meat and full-fat dairy products
  • increase your risk of heart disease

• A high-protein diet may worsen **kidney function** in people with **kidney disease** because your body may have trouble eliminating all the waste **products of protein metabolism**
Impact of high protein diet on the body

• If you want to follow a high-protein diet, choose your protein wisely.
  • Good choices include soy protein, beans, nuts, fish, skinless poultry, lean beef, pork and low-fat dairy products
  • Avoid processed meats

• The quality of the carbohydrates (carbs) you eat is important too.
  • Cut processed carbs from your diet
  • Choose carbs that are high in fiber and nutrient-dense, such as whole grains and vegetables and fruit
Impact of High Protein Diet on Brain Function

- Research from Dr. Heather Leidy has shown that eating a high protein breakfast leads to reductions in the activation of reward areas of the brain when study subjects were shown sweet or savory snacks like pizza, french fries, and/or cookies.
Impact of High Protein Diet on Brain Function

• Another study found that when people ate less protein, their brains were more responsive to reward-driven eating cues (e.g. seeing pizza and then wanting to eat pizza) versus when on a higher protein diet.

• When presented with a variety of foods, people eating the lower protein diet also ate more protein, seemingly in an effort to restore protein balance.
Take Away of 2 studies

• higher protein diet can lead to decreased activity in the reward centers of the brain

• means that if you’re full of protein, you may not desire a pizza or cookie treat
High Protein

• when protein you have eaten reaches your small intestine it causes the release of cholecystokinin (CCK).
• CCK’s *primary* job it to aid in the digestion of fat and protein
• But CCK also travels up to your brain and acts as an appetite suppressant.
High Protein

• the fullness you feel after eating protein is actually driven in large part by your brain signaling your body that you don’t need to eat anymore

• Takeaway: A higher protein diet releases CCK, which can act as an appetite suppressant
Summary Video: How the food you eat affects your brain

https://www.youtube.com/watch?v=xyQY8a-ng6g
Human Microbiome
Microbiota

- Microbial cells and genetic material
- Involved in digestion, growth, immunity and brain
- 10^14 microorganisms reside in the GI tract
- Sensitive to diet, stress, infection and medicines
- Changes during different milestones in life
Gut-brain axis

The ability of the brain to influence the intestinal microbiota

The ability of the microbiota to influence brain and behavior
Microbiome – gut brain axis

• Maintains homeostasis
• Regulation of satiety and digestive function
• Modulation linked to stress
• Communication via neurons and hormones

• Disruption of bacteria in gut may be linked to development of autoimmune diseases
Brain-Gut Axis Research

Probiotics

2016 small clinical trial showed potential benefits of available strains of probiotics on CNS disorders

*Bifidabacterium*

*Lactibacillus genera*
Brain-Gut Axis Research

Anxiety and Mood Disorders

• People with anxiety and mood disorders have gastrointestinal problems

• Contradictory results: people with major depressive disorders and healthy people gut flora comparison

• 2004 study, germ free mice have exaggerated HPA axis in response to stress, add *Bifidobacterium* to gut reverse effect
Brain-Gut Axis Research

Anxiety and Mood Disorders

• bacteria in gut produce neurotransmitters

Noradrenalin: *Escherichia Bacillus*, *Saccharomyces*

Serotonin: *Candida*, *Streptococcus*, *Escherichia*
Brain-Gut Axis Research

Parkinson’s disease (PD)

GI dysfunction has a high prevalence in preclinical PD

PD patients have altered gut changes in bacteria

Bacteria produce short chain fatty acids, permeate the blood brain barrier
Brain-Gut Axis Research

Parkinson’s disease (PD)

Bacteria produce short chain fatty acids, permeate the blood brain barrier

Generate inflammation in brain and alpha-synuclein levels
Conclusions

• High Fat: Ketogenic
• Mediterranean
• Vegetarian/Vegan
• Low Fat
• Low Carbohydrate: Atkins/Paleo
• Gut Microbiota $\rightarrow$ still investigating the impact!
Next week (April 19th)……..NO LECTURE, because it’s GOOD FRIDAY!

April 26th LAST LECTURE!
Effect of over supplementation of vitamins and nutrients
Questions?