A Sound Mind in a Sound Body: The Link between Diet and Cognition

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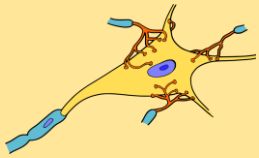
Objectives

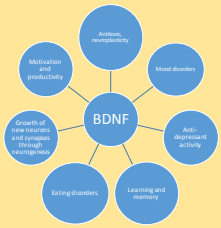
- Define neurogenesis and neuroplasticity
- Define and describe the role of BDNF in cognitive function and homeostasis
- Describe the roles of dietary components in influencing neuroplasticity
- Describe the role of gut bacteria and gut peptides in neuroplasticity
- Describe the similarities between diabetes, Alzheimer's disease and mental disorders
- Describe the role that epigenetics might play in the cognitive process
- State why dietitians must, and how they can leverage the scientific research on nutrition and cognitive function to get their patients to eat healthfully

Hippocampus: Seat of learning and memory

What is neuroplasticity and neurogenesis?



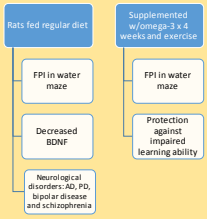
BDNF : The Master Mind behind neuroplasticity!



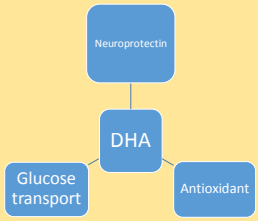
DHA and risk of Alzheimer's disease

- Prospective study 1993-2000
- Total 815 residents unaffected by AD initially
- Participants consuming fish 1x/week of more had 60% decreased chance of developing AD
- Strong correlation between DHA and decreased AD risk, but not EPA

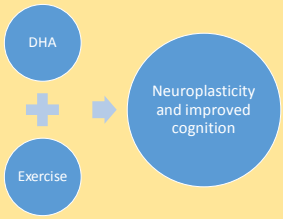
DHA and learning/coping after brain injury



Mechanisms by which DHA increases BDNF



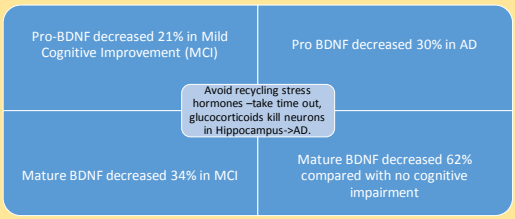
DHA and exercise synergy



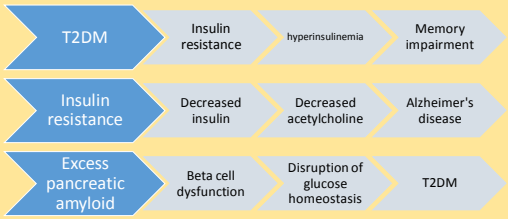
Folate

- Study examined whether total intake (diet plus supplements) of antioxidant vitamins (E, C, carotenoids) and B vitamins (folate, B6, and B12) is associated with a reduced risk of AD.
- 579 nondemented elderly volunteers from the Baltimore Longitudinal Study of Aging. After a mean follow-up of 9.3 years, AD developed in 57 participants. Only total intake of folate at or above the RDA was associated with a significant decreased risk of AD. No association was found between total intake of vitamins C, carotenoids, or vitamin B12 and risk of AD.
- Additional studies are necessary to further investigate whether folate or other unmeasured factor(s) may be responsible for this reduction in risk.

Study measuring the relative amounts of BDNF proteins in AD



T2 DM and AD



BDNF and hyperglycemia

Insulin independent
- BDNF administration in rats
- Intracerebroventricular administration

Independent of changes in food intake
- Hepatic glucose suppression
- Decreased glucagon

- Decreased glucose levels
- Independent of insulin and tissue glucose uptake

High fat, high sugar

HFS diet : direct effect	Decreased BDNF	Decreased Synapsin I	
HFS diet	Oxidative stress and inflammation	Decreased BDNF	Decreased neuroplasticity
Antioxidants curcumin	Dramatic decrease in oxidative stress	Normalized BDNF, synapsin 1	Curcumin counter acted cognitive dysfunction caused by TBI

High saturated fat and BDNF

Vitamin E supplementation of high fat diet → Reduced oxidative damage → Normalized levels of BDNF, synapsin I → Reversed HF induced impaired cognition

BDNF and energy homeostasis?

- BDNF
  - Hippocampal
    - Neural plasticity
    - Neurogenesis, learning and memory
  - Hypothalamic
    - Inhibit food intake, energy metabolism
    - Obesity, eating disorders

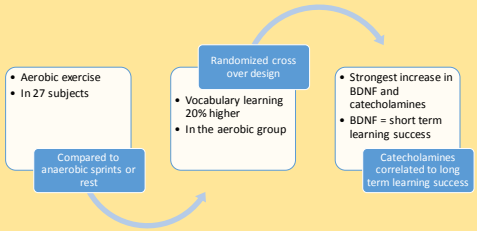
BDNF

- BDNF, an important mediator of synaptic plasticity: memory and learning
- Energy homeostasis
- Genetic deletion of the *Bdnf* gene in animals: hyperphagic and develop obesity
- Infusion of BDNF :reduces body weight, normalizes glucose levels, increases insulin sensitivity

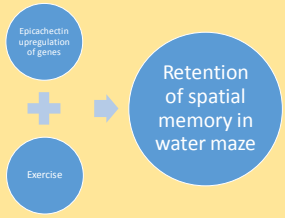
Caloric restriction and intermittent fasting

Rodent studies
- Decreased oxidative stress
- Improved learning, water maze
- Calorie restriction
- Decreased cognitive deficits
- Increased BDNF

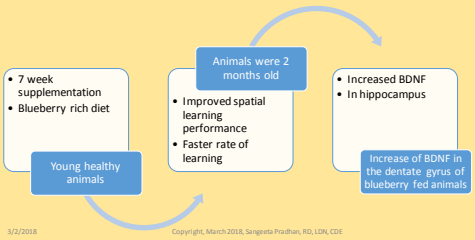
Aerobic exercise improves learning.



Flavonols and Exercise

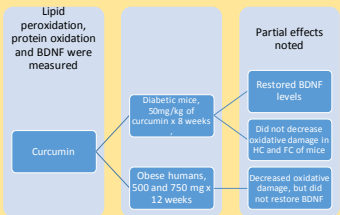


polyphenols

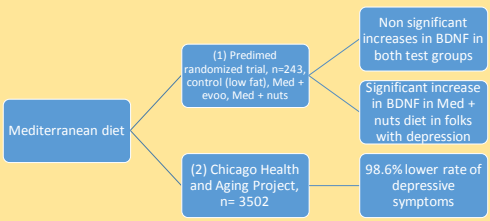


Curcumin

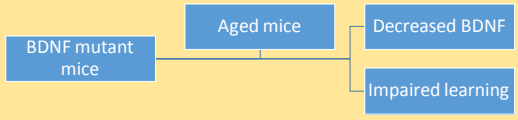
Curcumin: May combat oxidative damage and low BDNF levels in DM and obesity



Mediterranean diet and BDNF, depression



BDNF and learning: Learning deficit in BDNF mutant mice.



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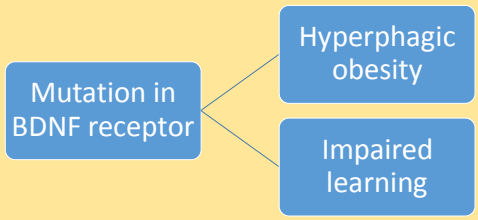
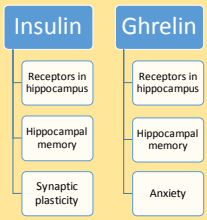


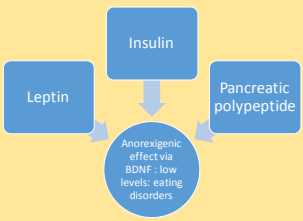
Insulin and ghrelin: peripheral hormones modulating memory and hippocampal function.



Leptin, ghrelin and GLP1

- Leptin receptors in brain areas, the hypothalamus, the cerebral cortex and the hippocampus.
- Dysfunctional leptin receptors and impairment in LTP, spatial learning
- Hippocampal plasticity
- Peripheral administration of ghrelin increases food intake in normal rodents and humans whereas chronic administration: adiposity
- Ghrelin: LTP? enhanced spatial learning and memory formation.
- GLP1:
  - pancreatic insulin secretion and subsequent glucose uptake by muscle cells,
  - suppressing food intake through actions on the hypothalamus.
  - spatial memory

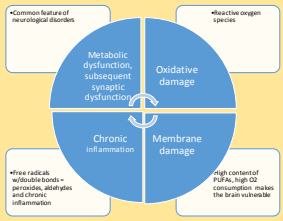
BDNF and eating disorders



? Link between disruption in energy homeostasis and mental disease

Abnormal metabolism (T2DM, metabolic syndrome)	• Psychiatric disorders, Depression • Role for MNT
Difficult to establish cause -effect	• Poor quality of life • Anti-psychotic medications

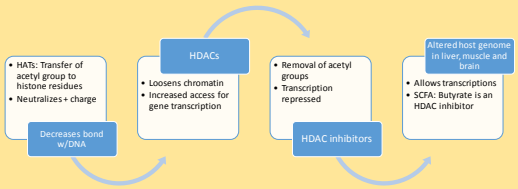
Metabolic dysfunction, oxidative stress and synaptic dysfunction



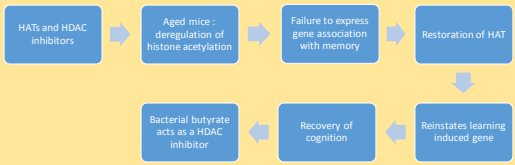
Epigenetics

- Epigenetics is essentially additional information layered on top of the sequence of letters (A, C, G, and T, nucleotide bases in DNA) that makes up DNA.
- DNA sequence is the text, epigenetics is a pack of highlighters
- Different types of epigenetic marks
- Methyl groups: associated with inactivation.

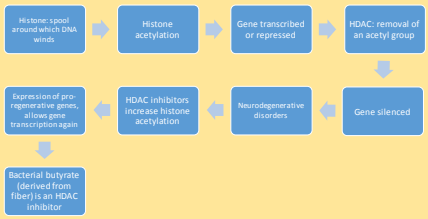
Short chain fatty acids (SCFA) from gut bacteria, and gene expression



Altered histone acetylation is associated with age-dependent memory impairment in mice.



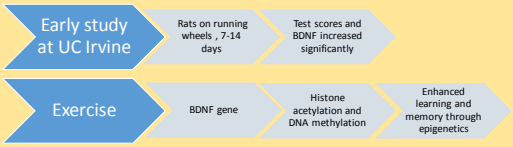
Butyrate and histone acetylation



BDNF: Miracle Grow for the brain!

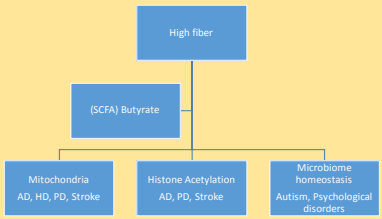
- The King of all nerve growth factors
- Evolution's greatest gift: you increase it just by using your brain!!
  - Be a life long leaner!
  - Antitoxic and antidepressant
- Intelligence and memory
- Lessens AD risk
- Improves scores at any age
- Improves mood, motivation and energy
- Exercise has one of the most potent impacts:10,000 steps per day

Exercise effect on BDNF through epigenetics



Gut-microbial axis: Are bacteria calling the shots?

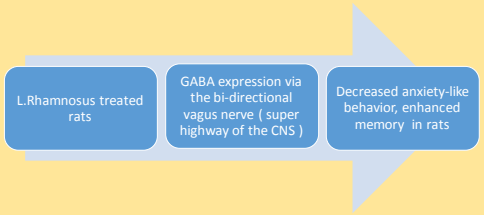
Gut microbiome



Fiber and butyrate

- Bacteria produce butyrate as an end point in the gut lumen
- Fermentation intermediates: lactate, succinate or formate, which are used by the bacteria themselves to proliferate and survive
- Primary energy source of colonocytes, mutually beneficial relationship.
- High fiber foods: resistant starches and fructo-oligosaccharides (FOS)
- Butyrate production in rats fed 2 weeks of a high FOS diet and starch free wheat bran
- Different strokes for different folks: Butyrate level depends upon type of fiber

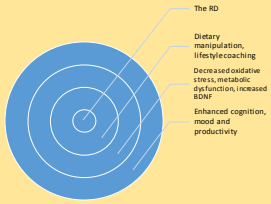
L.rhamnosus and anxiety reduction via vagus nerve



Mind-Altering take-aways

- Healthy weight (Note relation between metabolic dysfunction and mental health)
- Mediterranean style diet
  - Antioxidant rich fruits veggies, fatty fish, whole grains, limited sugars and unhealthy fats
  - DHA
  - Probiotics
- Ace card: Exercise
- Become a Life long learner
- Reduce stress/cortisol levels: Mindfulness and meditation
- Tap into the power of neuroplasticity and epigenetics
- Remind your patients that cognitive function can be largely influenced by *modifiable* risk factors

The RD: Ripple effects from what we can do!



Appendix A: Glossary of terms and abbreviations

- AD: Alzheimer's disease
- BDNF: Brain derived neurotropic factor
- FPI: Fluid percussion injury
- HC: Hippocampus
- HD: Huntington's disease
- PD: Parkinson's disease
- TBI: Traumatic brain injury
- GABA: is an inhibitory neurotransmitter, which means that it weakens or slows down signals and reduces anxiety
- HATs: Histone Acetyl Transferases transfer acetyl groups to highly conserved N-terminal L-lysine residues, thereby loosening the chromation structure and allowing gene transcription
- (HDACs): Histone deacetylases remove acetyl groups and repress gene transcription
- Histone: They are the chief protein components of chromatin, acting as spools around which DNA winds, playing a role in gene regulation.

Appendix B: Glossary of terms and abbreviations :

- Acetylcholine: Acetylcholine is a neurotransmitter—a chemical released by nerve cells to send signals to other cells. Low insulin levels and low insulin sensitivity can contribute to a decrease in acetylcholine synthesis, leading to AD.
- Adipogenesis: The process of cell differentiation by which pre-adipocytes become adipocytes
- Beta-amyloid: Peptides that are the main components of the plaques found in the brain of patients with AD
- Dentate gyrus: The dentate gyrus is part of the hippocampus and is thought to contribute to the formation of new episodic memories
- Epigenetics literally means "above" or "on top of" genetics. It refers to external modifications to DNA that turn genes "on" or "off." These modifications do not change the DNA sequence, but instead, they affect how cells "read" genes
- Neuroprotectin: A DHA derived mediator that protects the brain against oxidative stress
- Synapsins: A family of proteins that have been known to regulate neurotransmitter release at synapses
- Synapse: is a junction between neurons, consisting of a minute gap across which impulses pass by diffusion of a neurotransmitter
- SCFA: Short chain fatty acids produced by bacterial fermentation such as butyrate

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