

A SOUND MIND IN A SOUND BODY

The Impact of Nutrition on Cognition

SEPTEMBER 12, 2019 2-3:30 PM ET

A Becky Dornier & Associates & *Today's Dietitian* joint webinar presented by **SANGEETA PRADHAN, RD, LDN, CDE**

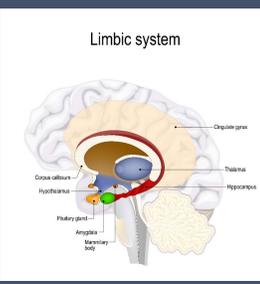


Objectives

- 1 Define neurogenesis, neuroplasticity, and the role of neurotrophins in influencing cognitive function.
- 2 Describe the role of dietary patterns, dietary components, exercise, gut bacteria, gut peptides, and epigenetics in the cognitive process and neuroplasticity.
- 3 Explore how type 2 diabetes (T2DM) and Alzheimer's Disease (AD) may be linked, and describe their common features.
- 4 Analyze how oxidative stress may be associated with dementia and how antioxidants may potentially mitigate this process.
- 5 Explain how dietitians can leverage scientific research on cognitive function to encourage patients to eat healthfully.

Hippocampus

- Seat of learning
- Higher thinking
- Memory consolidation
- Mood



Limbic system

SYNAPSE

How
Signals Are
Transmitted
from Neuron
to Neuron

Neuroplasticity, Neurogenesis and LTP

- Neuroplasticity is the ability of the brain to change in response to every experience
- Neurogenesis is the production of new neurons and neural pathways or connections
- Repeated signals strengthen neural connections in a process called long term potentiation, or LTP
- This is also how habits form over time
- LTP is a key mechanism underlying learning and memory

Neurons That Fire Together, Wire Together!

- **100 billion neurons** in the human brain
- **Each neuron** has thousands of synapses
- **Neurons connect** to each other through their synapses
- **Leads** to the formation of complex, intricate neural circuits in the brain
- **The brain** is like a complex, electrical grid
- **The wiring** of complex neural networks leads to memory consolidation and learning



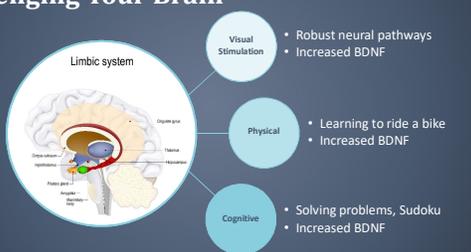
You Can Teach an Old Dog New Tricks

Every thought, every action changes the brain.

We experience neuroplasticity every day!

7

Harness the Power of Neurogenesis by Challenging Your Brain



- Visual Stimulation**
 - Robust neural pathways
 - Increased BDNF
- Physical**
 - Learning to ride a bike
 - Increased BDNF
- Cognitive**
 - Solving problems, Sudoku
 - Increased BDNF

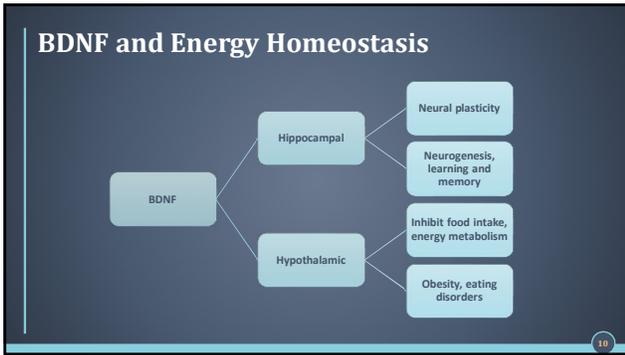
8

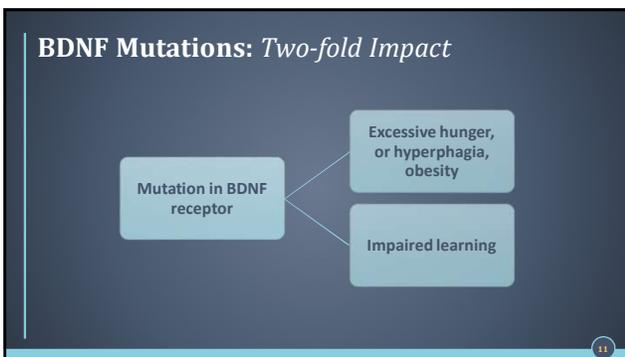
BDNF: The Mastermind Behind Neuroplasticity

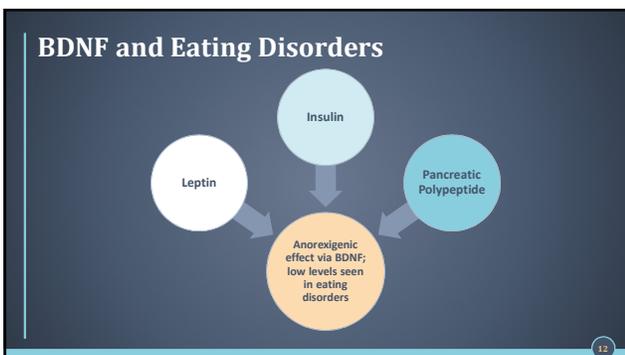
 **Brain-derived Neurotrophic Factor, or BDNF:**

- Growth of new neurons and synapses through neurogenesis
- Bridge between diet and mental health: anti-toxic
- Neuroplasticity
- Mood disorders
- Microbiota-link
- Anti-depressant activity
- Anxiolytic (reduces anxiety)
- Learning and memory, includes spatial memory
- Eating disorders

9







Insulin and Ghrelin: Peripheral Hormones Modulating Memory and Hippocampal Function

Insulin
Receptors in hippocampus
Hippocampal memory
Synaptic plasticity

Ghrelin
Receptors in hippocampus
Hippocampal memory
Anxiety

13

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

14

BDNF: Multiple Effects - A Metabotrophin?

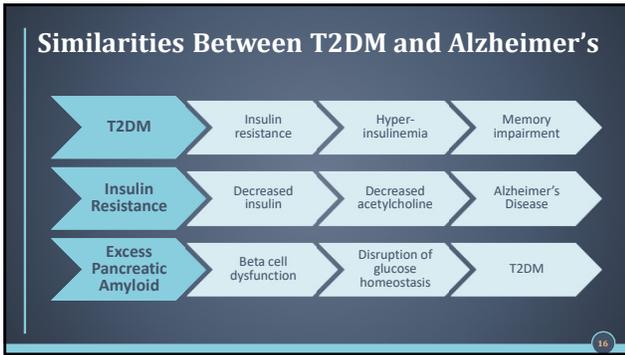
BDNF, an important mediator of synaptic plasticity: memory and learning

Energy homeostasis: suppresses hepatic glucose production

Genetic deletion of the BDNF gene in animals: hyperphagic and develop obesity

Infusion of BDNF: reduces body weight, normalizes glucose levels, increases insulin sensitivity

15



Free radical **Antioxidant**

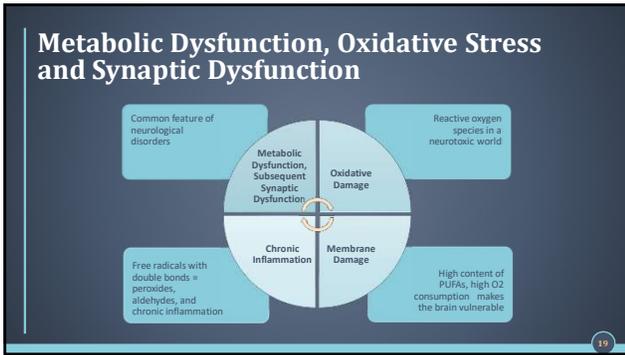
Unpaired electron

- Free radicals have unpaired electrons
- Unstable
- Strip electrons from various cells in the body
- This "oxidizes" the target cell
- Antioxidants are free radical scavengers
- They can be vitamins, minerals, or enzyme systems
- Dynamic state between free radicals and antioxidants
- Determines the course of disease

The War Within: Antioxidants and Free Radicals

- Consumes 25% of the body's energy reserves
- High PUFA content makes it very vulnerable to oxidative stress

The Brain: The Energy Guzzler!



DHA and Risk of Alzheimer's Disease (AD)

- Prospective study 1993-2000
- Total 815 residents unaffected by AD initially
- Participants consuming fish once a week or more had 60% decreased chance of developing AD
- Strong correlation between DHA (but not EPA) and a decreased risk for AD
- Prevents formation of beta amyloid
- DHA supplementation may be effective in Apolipoprotein E (APOE4) carriers, i.e. those with a higher risk for AD



Morris MC, Evans DA, Bienias JL, et al. Consumption of fish and n-3 fatty acids and risk of incident Alzheimer disease. *Arch Neurol.* 2003;60(7):940-946.

20

DHA and Learning: Coping After Brain Injury

Rats Fed a Regular Diet

- Traumatic brain injury
- Decreased BDNF
- Neurological disorders: AD, PD, bipolar disease, and schizophrenia

Rats Supplemented with Omega-3 for 4 Weeks and Given Exercise

- Traumatic brain injury
- Protection against impaired learning ability in water maze

21

DHA and Learning: Coping After Brain Injury

Rats Fed a Regular Diet

- Fluid percussion injury (FPI) in water maze
- Decreased BDNF
- Neurological disorders

Supplemented with Omega-3 for 4 Weeks and Given Exercise

- FPI in water maze
- Protection against impaired learning

22

Randomized Controlled Study with DHA

- 402 patients with mild to moderate AD
- Randomly assigned to Algal-DHA at a dose of 2 g/day or an identical placebo for 18 months
- 51 US clinical research sites of the Alzheimer's Disease Cooperative Study
- Supplementation with DHA compared with placebo *did not slow* the rate of cognitive and functional decline
- Similar result with a three-year, multi-center, randomized, placebo-controlled trial with 800 mg DHA and 225 mg EPA across 1,680 participants

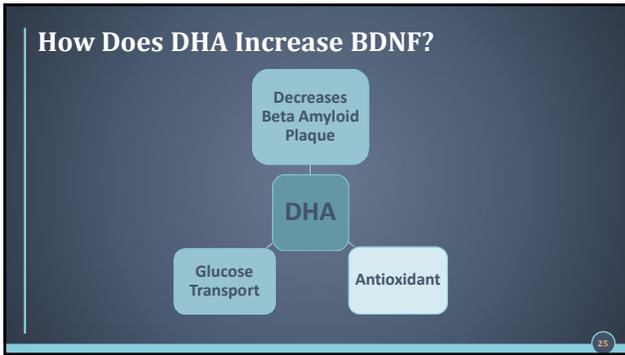
Quinn JF, Raman R, Thomas RG, et al. Docosahexaenoic acid supplementation and cognitive decline in Alzheimer disease, a randomized trial. *JAMA*. 2010;304(17):1932-1938.

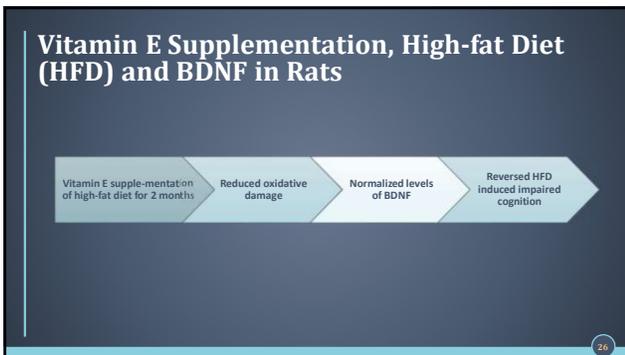
23

DHA and Exercise Synergy

DHA + Exercise → Neuroplasticity and Improved Cognition

24









Folate

- The Baltimore Longitudinal Study of Aging
- Study examined whether total intake of antioxidant vitamins (E, C, carotenoids) and B vitamins (folate, B6, and B12) are associated with a reduced 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

Corrada MM, Kawanishi H, Hallfrisch J, Muller D, Brookmeyer R. Reduced risk of Alzheimer's disease with high folate intake: the Baltimore Longitudinal Study of Aging. *Alzheimers Dement*. 2005;1(1):11-18

Mediterranean Diet (Med)



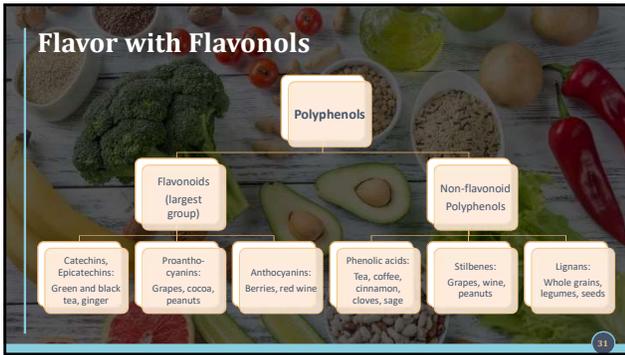
- Mediterranean Diet¹
 - Predimed randomized trial, n=243, control (low fat), Med + EVOO, (1 L/wk), Med + nuts (30 g/day)²
 - Nonsignificant increases in BDNF
 - Significant increases in BDNF in the Med + nuts diet in those with depression
 - (2) Chicago Health and Aging Project, n= 3502²
 - 98.6% lower rate of depressive symptoms

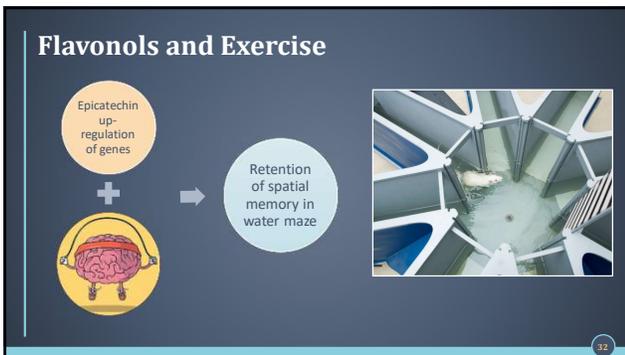
1. Sanchez-Villegas A, Galbete C, Martinez-Gonzalez MA, et al. The effect of the Mediterranean diet on plasma brain-derived neurotrophic factor (BDNF) levels: the PREDIMED NUTRISA randomized trial. *Nutr Neurosci*. 2013;14(9):199-203.
2. Skarupski KA, Tangney CC, Li H, Evans DA, Morris MC. Mediterranean diet and depressive symptoms among older adults over time. *J Nutr Health Aging*. 2013;17(5):441-445.

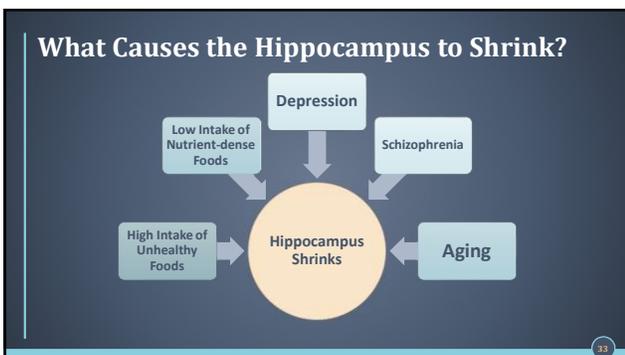


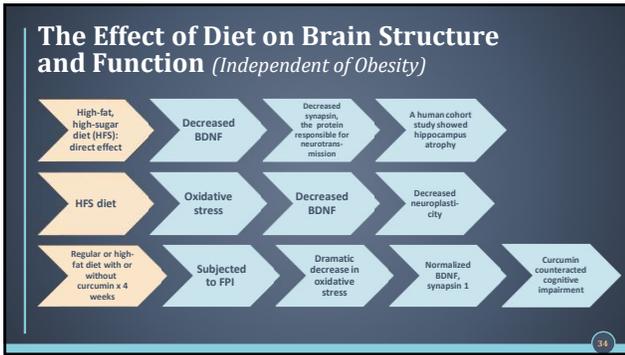
The Mediterranean Diet, BDNF and Depression

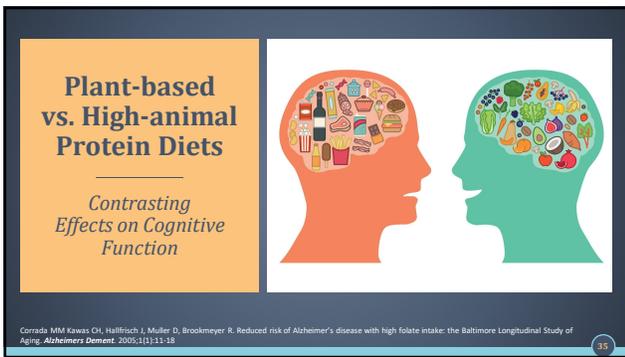
- Improved cognitive function in Med plus nuts and Med plus EVOO diet in an older population
- Among those with prevalent depression, BDNF increased in Mediterranean diet plus nuts

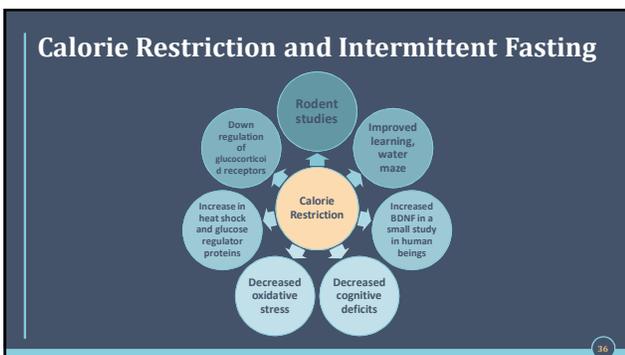












What is Epigenetics?

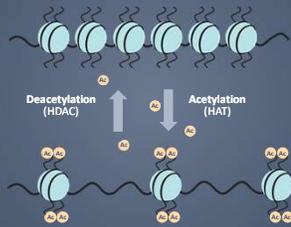
Epigenetics refers to external modifications to DNA that turn genes "on" or "off." These modifications do not change the DNA sequence, but instead they affect how cells "read" genes.

Some experts like to refer to the DNA sequence as the text and epigenetics as a pack of highlighters.

Methyl groups are associated with inactivation.

37

Epigenetics: *The Histone Wraps Itself Around DNA*

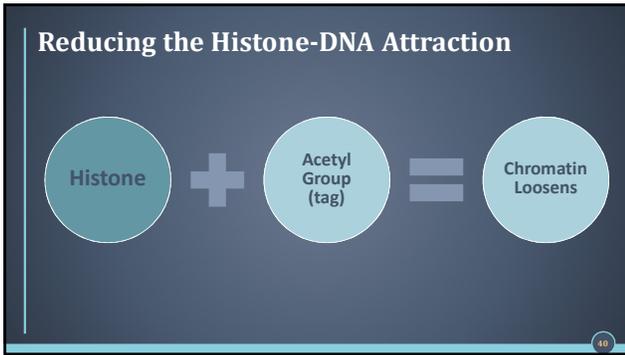


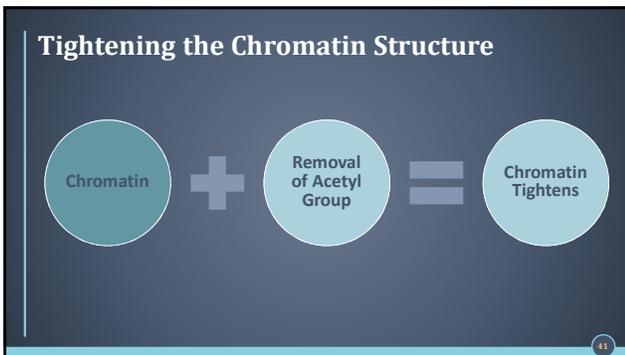
38

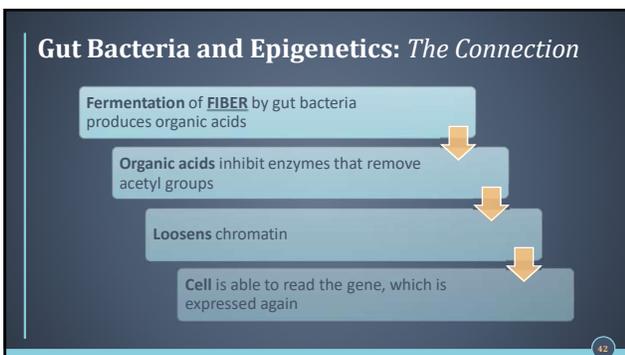
Histone, DNA, and Chromatin

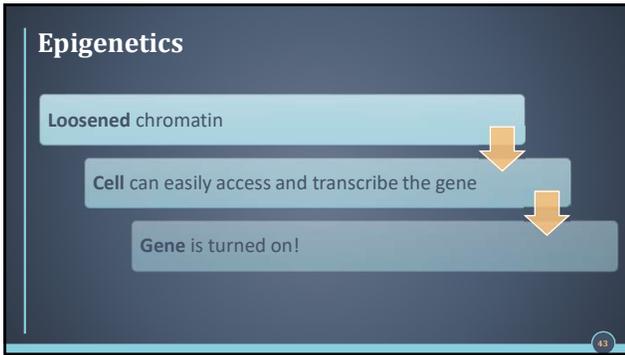


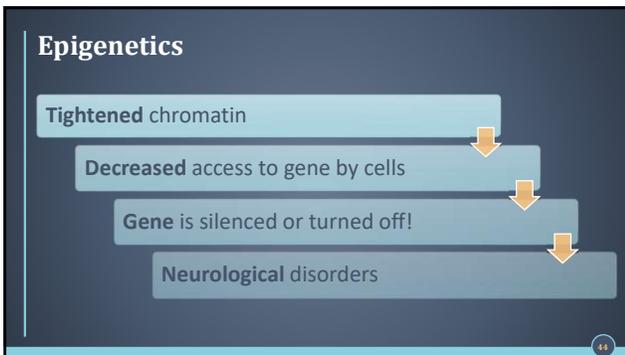
39

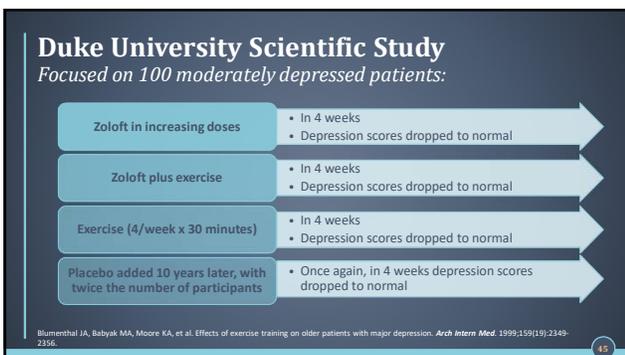












The Effect of Exercise on BDNF Through Epigenetics

Exercise → Remodeling of chromatin containing BDNF gene → Enhanced learning, memory through epigenetics

Sieman SF, Henry J, Al-Hudissi R, et al. Exercise promotes the expression of brain derived neurotrophic factor (BDNF) through the action of the ketone body 3-hydroxybutyrate. *Elife*. 2016;5:e15092

46

The Enteric Nervous System: A Second Brain?

```
graph TD
    CNS[Central Nervous System (CNS)] --- Brain[Brain and Spinal Cord]
    PNS[Peripheral Nervous System (PNS)] --- Afferent[Afferent Neurons]
    PNS --- Efferent[Efferent Neurons]
    Afferent --- Sensory[Sensory Input]
    Efferent --- Autonomic[Autonomic Neurons]
    Efferent --- Somatic[Somatic Motor Neurons]
    Autonomic --- Sympathetic[Sympathetic]
    Autonomic --- Parasympathetic[Parasympathetic]
    Enteric[Enteric Nervous System] --- Parasympathetic
```

47

The Gut-Brain Connection: Bi-directional, Primal Communication

Alterations in the communication between the enteric nervous system and the central nervous system can lead to classic disorders of the gut-brain axis:

- IBS
- behavioral disorders
- neurological disorders

48

Interface Between the Gut Lumen and Lamina Propria

- Intestinal microbiota lies strategically at the interface of the internal and external environment of the gut
- Cross talk between microbes in the lumen and immune cells

The diagram illustrates the anatomical and cellular components of the gut wall. It shows the stomach, small intestine, and large intestine (colon) with labels for the stomach, small intestine, large intestine, and rectum. A detailed view of the intestinal wall shows the lumen, mucus layer, epithelial cells, and lamina propria. A 'Healthy Small Intestine' inset shows a normal microbial community, while a 'Dysbiotic Small Intestine' inset shows an overgrowth of harmful bacteria. A diagram below shows the interaction between microbes and immune cells, including the production of antimicrobial peptides and the role of the gut barrier.

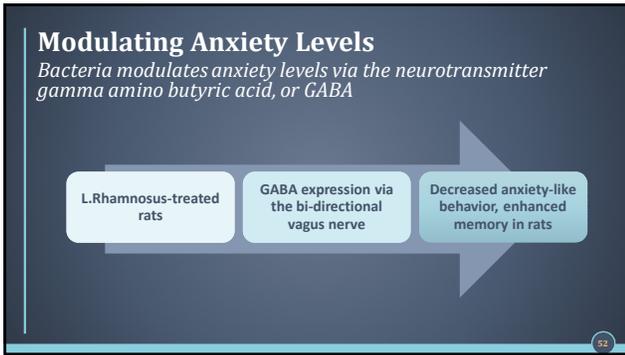
The Microbiome: A Therapeutic Target for Modulating Cognitive Disorders

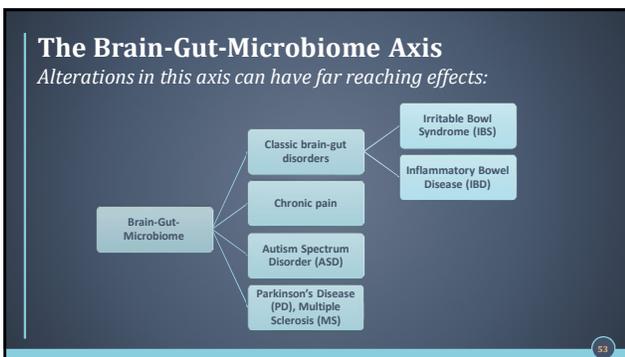
The diagram shows a cross-section of the brain with the limbic system highlighted. The limbic system is connected to three main areas: Neural, Immune, and Endocrine. The limbic system includes the amygdala, hippocampus, and hypothalamus. The diagram illustrates how the microbiome influences these systems and how they in turn affect cognitive function.

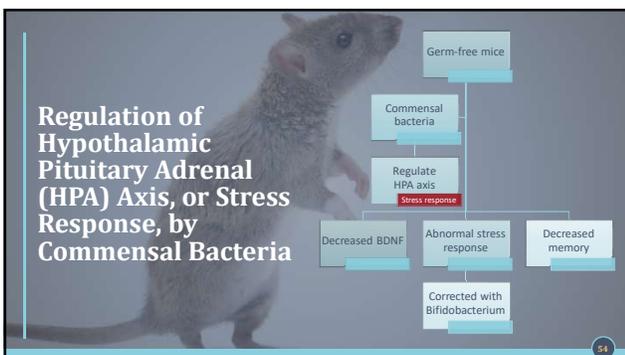
Serotonin Modulation by Gut Bacteria

The flowchart shows the following process:

- Gut microbes** cross talk with **enterochromaffin cells (ECs)**.
- ECs (signal transducers)** produce serotonin.
- Under the influence of microbes**, ECs produce serotonin.
- ECs synapse with the **vagus nerve**, the superhighway of the CNS.
- The **vagus nerve** has a direct line into the brain stem.
- From food to feelings in seconds!
- Disruption of serotonin signaling may cause IBS symptoms.**







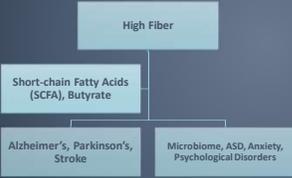
Fiber to the Rescue, Again!

- **Bacteria** produce butyrate as an end point in the gut lumen by fermenting carbs
- **Primary** energy source of colon cells
- **Butyrate** can protect the brain and enhance plasticity in neurological models
- **High-fiber** foods that supply prebiotics:
 - **Resistant starches:** whole grain, legumes
 - **Fructo-oligosaccharides (FOS)** from bananas, onions, garlic, artichokes, asparagus
 - **A diverse, rich microbiome** comes from a diverse, rich, plant-based diet high in fiber



55

Gut Microbiome Modulation of Neurological Disorders

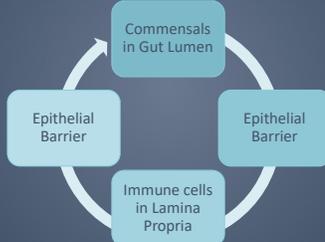


```
graph TD; A[High Fiber] --> B[Short-chain Fatty Acids (SCFA), Butyrate]; B --> C[Alzheimer's, Parkinson's, Stroke]; B --> D[Microbiome, ASD, Anxiety, Psychological Disorders];
```



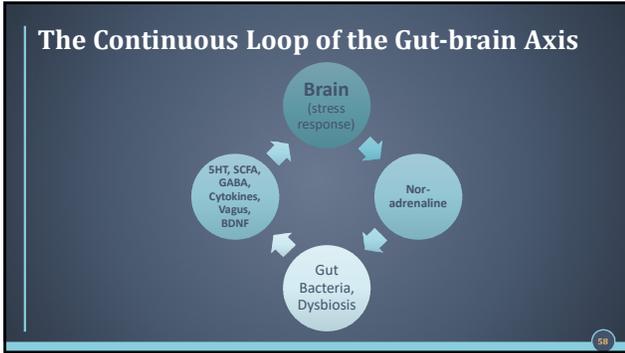
56

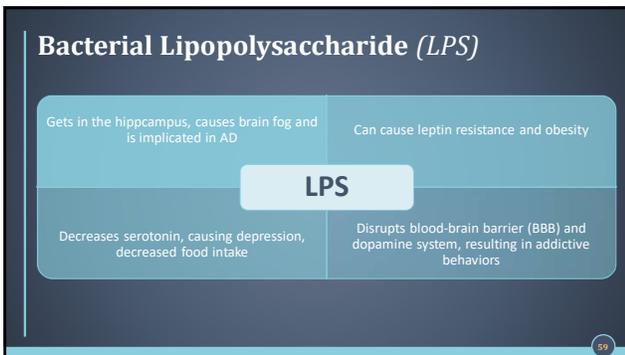
Microbiota: The Interface of the Environment in the Gut



```
graph TD; A[Commensals in Gut Lumen] --> B[Epithelial Barrier]; B --> C[Immune cells in Lamina Propria]; C --> D[Epithelial Barrier]; D --> A;
```

57





Meditation

- **Increases** BDNF
- **Decreases** pro-inflammatory cytokines
- **Increases** anti-inflammatory cytokines
- **Improves** stress resilience

100

Which Increases Neurogenesis via BDNF?

 Stress	 Sleep	 Typical Western Diet
 Brisk Walking	 Salmon	 Meditation
 Depression	 Learning to Play the Guitar	

61

Mind-altering Take-aways

- **Healthy weight** (note the relation between obesity and inflammation)
- **Diet has a direct effect** on brain structure and function, independent of insulin resistance (IR) and obesity
- **Mediterranean-style diet**
 - Antioxidant-rich fruits, veggies, fatty fish, limited sugars, and unhealthy fats
 - DHA
 - Probiotics and prebiotics
 - Curcumin (not Mediterranean)
- **Ace card:** exercise!
- **Become** a life-long learner
- **Reduce stress** through mindfulness and meditation
- Evidence is compelling, but more comprehensive studies needed

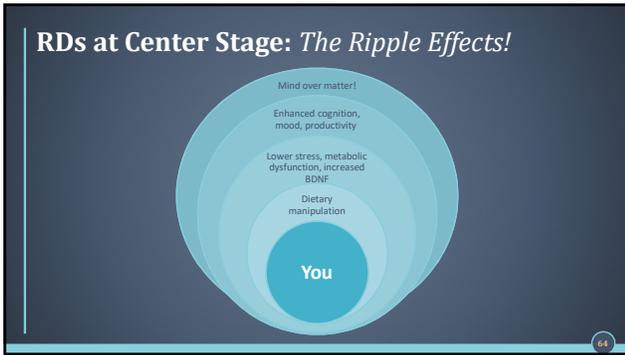


62

Your Incredible, Moldable Brain!

- **Leverage** the power of neurogenesis and neuroplasticity: neurotrophins are the bridge between diet and mental health
- **Your behaviors** drive neuroplasticity
- **Neuroplasticity** follows the “use it or lose it” rule
- **You can alter** your brain's chemistry at any age
- **Whole foods and exercise** can synergistically create *positive* mind-altering changes in the brain
- **You can use modifiable** risk factors to build the brain that you want!

63



Questions?

Sangeeta Pradhan, RD, LDN, CDE
<https://webdietitian.wordpress.com>
@Webdietitian
@spradhanrd
spradhanrd@gmail.com

65

Credit Claiming

You must complete a brief evaluation of the program in order to obtain your certificate. The evaluation will be available for 1 year; you do not have to complete it today.

CREDIT CLAIMING INSTRUCTIONS:

1. Login to www.CE.TodaysDietitian.com.
2. Click "My Courses" and select this webinar's title.
3. Click "Take Course" on the webinar description page.
4. Select "Start/Resume" to complete the course and submit the evaluation.
5. Download and print your certificate.

66

Appendix: Glossary of Abbreviations

- **AD:** Alzheimer’s disease
- **ASD:** Autism Spectrum disorder
- **BBB:** Blood-brain barrier
- **BDNF:** Brain-derived neurotropic factor
- **EC:** Enterochromaffin cells
- **FPI:** Fluid percussion injury
- **HC:** Hippocampus
- **HD:** Huntington’s disease
- **LTP:** Long-term potentiation
- **MS:** Multiple sclerosis
- **PD:** Parkinson’s disease
- **TBI:** Traumatic brain injury

67

Appendix: Glossary of Terms

- **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:** 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.

68

Appendix: Glossary of Terms

- **GABA:** gamma-Aminobutyric acid 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 structure and allowing gene transcription.
- **HDACs:** Histone deacetylases remove acetyl groups and repress gene transcription.
- **SCFA:** Short-chain fatty acids are produced by bacterial fermentation such as butyrate.
- **BGM:** Brain gut microbiome.

69
