The Gut "Brain" and Eating Disorders: Nutrition Therapy’s Role in the Healing Process

Tammy Beasley, RDN, CEDRD, CSSD
Background and Shout Outs!

• Professional history in ED field (23 of last 30 years)
• Family history of ED, depression and GI disorders
• Hot topic in presentations and ongoing research
• Shout out to recent talks:
  – Pam Kelle, CEDRD (ALDA)
  – Merrily Kuhn, RN PhD (IBP)
  – Janelle Smith, RD (BHN)
Other Common “Gut” Statements

“I had a gut wrenching experience…”

“Put on... BOWELS of mercies, kindness…” (Aramic/Greek root word: heart)

“I just feel it in my gut...”
The Gut-Brain Axis: A Two-way Street

- Emotional signals move from brain to gut and gut to brain
  - Same neurotransmitter receptors in both
- Gut synthesizes and secretes majority of serotonin (90-95%)
- 70-90% of immune system is in the gut
Fantastic Gut Facts

• Ten times more microbial cells (micro-organisms, like bacterium) than human cells
  – Humans shaped by 23,000 genes
  – Gut bacteria shaped by 8 million genes
• Enteric nervous system has 5x # of neurons as spinal cord (500 million!)
• Epithelial layer of our gut = 4000 sq feet
Gut microbiota influence health, mood and behavior

**Microbiota:** organisms living in a community in and on the human body

**Microbiome:** the cumulative genomes of each of these organisms

**Genome:** full set of chromosomes or inheritable traits of an organism

OBJECTIVES

• Simplify the gut brain and hormone connection

• Translate the communication process between the gut brain, food and appetite in relationship to specific hormones

• Connect nutrition’s healing role within the gut brain during stages of eating disorder recovery
Objective 1:
Simplify gut brain & hormone connection

- Comparison: hormone vs neurotransmitter (NT)
- Focus: two specific hormones and/or NTs
  - Serotonin (5-hydroxytryptamine)
  - Dopamine (the “Hollywood” hormone)
Hormones (H) vs Neurotransmitters (NT): Same but Different

• **Similarities**
  – Both signaling molecules
  – Both work together
  – Some work double shifts
    • Can serve both roles depending on release point
    • H when released by adrenal gland/ NT when released by nerve cell
  – Both can be involuntary (although H never voluntary)

• **Differences**
  – Different systems
    • NT uses nervous system
    • H uses endocrine system
  – Different speeds
    • NT is fast
    • H is slow
  – Different transportation
    • NT by neurons
    • H by blood
Serotonin

• **Effect on BRAIN**
  - Maintains mood balance specifically targeting anxiety, depression and “happiness”
  - Direct effect on sleep, social behavior, sexual function
  - Amount used in brain must be made by brain

• **Effect on GUT**
  - Changes how fast food moves through gut
    - Irritating or toxic food increases serotonin which triggers nausea
  - Effects how much fluid is secreted in gut
  - Effects how sensitive gut is to pain and fullness
Dopamine

**Effect on Brain**
- Plays a role in reward-stimulating behavior
  - “Hollywood” hormone
- Guides motor control functions
- Controls release of various hormones

**Effect on Gut**
- Guides gut motility
  - Reduces motility in upper intestine
  - Stimulates motility in colon
- Reduces activity of lymphocytes within immune system
- Protects intestinal mucosa
Objective #2: The Communication Process between Gut Brain, Food & Appetite

• Serotonin in healthy vs anorexic conditions
  – Within individual without anorexia
  – Within individual with anorexia

• Gut Brain in connection w behaviors and weight

• Dopamine in relationship to reward circuitry
  – Related to obesity
  – Related to anorexia
How Serotonin is Made in the Gut: Healthy Population

Notice all the vitamins and minerals?

- Zinc
- B1, B3 and B6
- Folate
- Iron
- Calcium
- Magnesium
Micronutrient Food Sources for Serotonin Production

• Common Food Sources
  – Whole grains/cereals
    • Zinc, Folate, B1/B2, Mg
    • Issues: Calories? Gluten?
  – Dark leafy greens
    • Fe, Mg, B6, Ca
    • Issues: Absorption? Gas?
  – Nuts/seeds
    • Mg, Folate, Zinc
    • Issues: Calories? Fats?
  – Dairy or red meats
    • Ca, Mg, Zinc, B1/B2, Fe
    • Issues: Calories? Lactose? Absorption?
How Serotonin is Made in the Brain
Healthy Population

• Tryptophan (AA) competes for entry into brain w other AA after protein consumed/digested
  • Tryptophan needs carbs to enter brain
• Why? Carbs digested into glucose in intestines
  • Glucose enters blood, insulin released
• Insulin pushes other AAs into organs’ cells except tryptophan, so no longer competing
  • Tryptophan passes through barrier
• Converted to serotonin in brain
The Communication Process:
Serotonin Levels in Anorexia

• Women recovered from AN (both BN and restrictive type) have unusually high levels

• High serotonin levels in recovered women (restrictive) correlated with more harm avoidance
What does this mean?

- Neuroimaging indicates brains had high levels of serotonin *prior* to AN
  - Increased obsessions
  - Harm avoidance
  - Perfectionism
  - Need for symmetry

- Decreased food intake = less serotonin from tryptophan conversion
  - Serotonin drops
  - Starvation feels better
    - Less anxiety
    - Less distress

- Temporary relief until brain increases sensitivity again
  - ># of serotonin receptors
  - Greater restriction to relieve anxiety again
This may be how clients with anorexia get “stuck” in cycle:

Refeeding provides building blocks to make serotonin at the same time brain has increased its sensitivity to serotonin…

Brain “drowning” in serotonin-triggered anxiety?!
The Communication Process: The Gut Brain and Weight Connection

**Intestinal Microbiota May Regulate Common Features**

### OBESITY
- Research study*: transferred microbiota from genetically obese mice to lean mice
- Microbiota from obese mice created similar response in lean:
  - More effective at extracting calories from fat
  - Better at stimulating host storage of fat


### ANOREXIA
- Small culture-based study** of stool sample from AN patient
  - Identified 11 completely new bacterial species in intestinal microbiota
- “Idea worth researching”: Perhaps microbiota in AN influence starvation?

**Pfleiderer et al. Eur J Clin Microbiol Infect Dis 2013**
Integrity of Intestinal Mucosa in Clients with Anorexia

• Study*: investigated diamine oxidase activity (DAO) to determine level of integrity of intestinal mucosa within starved gut
  – DAO is clinical indicator of mucosa integrity
  – 36 AN females (21 AN-R, 15 AN-BP) compared w/ 20 healthy control females
  – Results: DAO levels in AN-R significantly LOWER than AN-BP and healthy controls

The Communication Process: Two-way Behavior Street

“Gut to Brain” in Healthy Controls

- Study*: Significantly more harmful bacterial groups found in gut of depressed vs control groups
- Study**: Healthy mice infected w/ gut pathogen developed memory dysfunction, social impairment
- Both studies indicate direct link to tryptophan/serotonin metabolism and gut microbiota

*Jiang HY Brain Behav Immun; 48 (2015)
**Gareau et al. Gut; 60 (2011); Desbonnet et al. Mol Psychiatry; 19 (2014)
The Communication Process: Two-way Behavior Street

“Brain to Gut” in Healthy Controls

- During stress of exam week, university students’ stool samples contained less healthy bacteria compared to first week

- “Control” mice sharing a cage with more aggressive mice had decreased beneficial bacteria, gut diversity, and immune system

Knowles S. Swinburne Univ of Tech, Australia (2008)


The Communication Process: The Gut Brain, Behaviors and Anorexia

- Study*: Bacterial imbalance in guts of clients with AN is associated with psychological symptoms related to AN
  - Severe limitation of nutritional intake can change gut microbial composition
  - Gut changes can contribute to anxiety and depression and further weight loss

*http://www.med.unc.edu

Public release: 5-oct-2015
Study: Present and Future

“Gut bacteria population, diversity linked to AN”

• Fecal samples 16 women w AN at admission and at weight restoration
  – Significant changes from admission to discharge
  – Gut diversity much less diverse in admission samples
  – Diversity at discharge increased but still significantly less than 12 healthy controls

• Positive change in moods connected to increase in gut diversity

Future NIH grant

• Five year, $2.5 million grant (Natl Institute Mental Health)
  – Fecal samples of large # of clients w AN upon admission and discharge (@85% IBW)
  – Samples transferred into gut bacteria in germ-free mice
  – Study how microbiota of AN clients affect biology and behavior of germ-free mice
Next Up: The Dopamine Pathway

**Dopamine Pathways**
- Frontal cortex
- Nucleus accumbens
- VTA
- Striatum
- Substantia nigra
- Hippocampus
- Raphe nuclei

**Functions**
- Reward (motivation)
- Pleasure, euphoria
- Motor function (fine tuning)
- Compulsion
- Perseveration

**Serotonin Pathways**

**Functions**
- Mood
- Memory processing
- Sleep
- Cognition

---

Castlewood
Treatment Centers for Eating Disorders
ST. LOUIS, MO | MONTEREY, CA | BIRMINGHAM, AL
Dopamine and Reward Circuitry: Chronic Dieting and Obesity

• Dopamine hormone is released in response to food, sex, drugs of abuse
• Dopamine circuits are associated with reward
  – Brain will automate response to behavior if repeated often
  – “Want” it but do not have to “like” it

“How the Brain Forms New Habits: Why Willpower is Not Enough”, February 2013

Bill Kelley, PhD. Center for Cognitive Neuroscience at Dartmouth College
Reward does NOT equal pleasure!

Your reward system in the brain does not differentiate between a good or bad habit.
Dopamine and Reward Circuitry: Chronic Dieting and Obesity

- Both good and bad habits give immediate reward benefits
  - Good habit = immediate AND long term benefits
  - Bad habit = immediate benefit BUT long term harm

- If brain can predict opportunities for reward, it will respond to the dopamine trigger
  - Pictures of “pleasure” food
  - Food-laden environments
Dopamine and Reward Circuitry: Anorexia

• Recovered AN sufferers appear to have differences in reward circuitry compared to controls

• Clients with AN respond less hedonically to palatable food even in a non-fueled state

Dopamine and Reward Circuitry: Anorexia

- Recovered AN sufferers with one year of remission showed no difference in reward circuitry in fed vs unfed state (hunger doesn’t motivate!)
- Recovered AN sufferers showed elevation in cognitive control vs non AN participants

Dopamine and Reward Circuitry: Anorexia

- Study: Variation in brain response to reward and punishment neutralized in anorexia
  - 13 women w AN-R vs 13 healthy controls
  - Gambling game w/ monetary reward if correct guess, monetary loss if missed or took too long
- Graphs of brain activity for reward process function showed variation in controls but **no change** in AN-R subjects

Wagner et al. Amer Jrnl Psych; 164 (2007)
Dopamine and Reward Circuitry: Higher Levels in Anorexic Brain?

• Normal levels of FOXO (genetic transcription factor, like a “dimmer switch”)
  – Triggers increased hunger if food intake is low
  – Controls enzymes that make serotonin and dopamine

• Potential genetic defect in FOXO “switch” in clients with anorexia
  – High FOXO levels can mean extra enzymes that synthesize both serotonin and dopamine
  – Tells body to eat LESS in spite of food restriction

Dwyer et al. Molecular Psych; 16 (2011)
Objective #3: Nutrition’s Healing Role During Stages of ED Recovery

Simply sharing how the brain and gut are connected, and the hormone changes resulting from that connection, can be a starting place to help the client through the difficult stages of recovery.
Understanding the WHY and HOW Restores Healing and Hope

<table>
<thead>
<tr>
<th>The Dietitian’s Role</th>
<th>The Client’s Response</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Translate ED’s physical consequences into real-life, non-judgmental terms</td>
<td>• Develops safe environment of trust</td>
</tr>
<tr>
<td>• Separate the person from the physical consequences</td>
<td>• Removes “surprise element”</td>
</tr>
<tr>
<td>– Replace “lack of willpower” and failure with “inevitable body responses”</td>
<td>• Restores hope within each stage of change</td>
</tr>
<tr>
<td>• Restore HOPE in recovery</td>
<td>– “…so I’m not the only one?”</td>
</tr>
<tr>
<td></td>
<td>– “…this too shall pass”</td>
</tr>
</tbody>
</table>
Nutrition’s Healing Role in Recovery

• Be open to unique twists when goal setting
  – Creative analogies translate science into real world
  – Lateral moves reduce fears about “change” itself
    • Includes food and timing changes
    • Helps break the stronghold of the pattern itself

• Consider use of pre- and probiotics
  – Evidence-base is very limited but growing
  – Clinical effectiveness has been seen
Example of Creative Analogy
Examples of “Lateral Food Moves” to Break a Pattern’s Stronghold

Alternative, and equivalent | Alternative, and more beneficial
“Lateral Timing Moves”
Does Timing Matter?

What We Know:

• Negative impact of long duration between meals/snacks:
  – Increase in physiological cravings (fats, sugars)
  – Changes in body composition
  – Effect on appetite hormones
Research on Meal Timing

• “Adjust mealtimes to help reset body clock.”
  – Your brain is the “clock” for sleep and body temperature
  – Your liver is the “clock” for food metabolism
  – Study: After 2 days of adjusted mealtimes, liver’s rhythm shifted 10 hours.

• “Timed high fat diet resets circadian metabolism and prevents obesity” Hebrew Univ of Jerusalem, FASEB. 2012
  – Mice on scheduled (every 3 hours) high-fat diet had lower final body weight than mice on unscheduled high-fat diet AND mice on unscheduled low-fat diet, although calories same in both groups
Meet Emma:
Lateral Timing and Food Moves

- 19 yr old, AN-R x 1.5 yrs
- H/o competitive swimmer, now distance runner x 6d/ week
- Current: 97# (88%), 5’4”
- Current intake: 800 cal (83% of REE only)
- Med hx: amenorrhea (x15 mon), depression, hypothermia, lethargic, severe bloating
- 3 small veg. meals w/ occasional night snack
- 5-7 hrs* between meals
- Heavy intake bran, soy, cruciferous veggies*
- 5 diet cola*, 2 water/day

• First words: “I’ve seen another RD and hated her”
• “Not going to change any behaviors. NOT going to gain weight”
Consider Use of Pre- and Probiotics

PREBIOTICS
- Non-digestible carbohydrates that FEED the probiotics (bacteria) in the large intestine
  - Three types
    - Fructo-oligosaccharides
    - Inulin
    - Fructan
  - Common foods
    - Wheat/barley/rye/flax
    - Oatmeal
    - Asparagus
    - Garlic/onion
    - Artichokes
    - Bananas/berries

PROBIOTICS
- Organisms, or “good bacteria”, that feed the healthy intestinal microbial community
- Foods containing probiotics
  - Yogurt w/ 3 or more strains live cultures, low in sugar
  - Cottage cheese/kefir
  - Buttermilk
  - Miso/soy sauce
  - Tempeh
  - Fresh sauerkraut

### Which probiotic bacteria produces which hormone/NT?

<table>
<thead>
<tr>
<th>Type of Probiotic Bacteria</th>
<th>Hormone/Neurotransmitter</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Bacillus</strong></td>
<td><em>Dopamine</em> and norepinephrine</td>
</tr>
<tr>
<td>Bifido-bacterium</td>
<td>Gamma aminobutyric acid (GABA)</td>
</tr>
<tr>
<td><strong>Enterococcus</strong></td>
<td><em>Serotonin</em></td>
</tr>
<tr>
<td><strong>Escherichia</strong></td>
<td>Norepinephrine and <em>serotonin</em></td>
</tr>
<tr>
<td>Lactobacillus</td>
<td>Acetylcholine and GABA</td>
</tr>
<tr>
<td><strong>Streptococcus</strong></td>
<td><em>Serotonin</em></td>
</tr>
</tbody>
</table>

www.sciencenews.org/article/microbes-can-play-mind-games

**SOURCE:** TG Divan et al/J. Psych.Res. 2015
Very limited research, but...

• (Per Janelle Smith, RD) Study: Probiotic lactobacillus casei strain Shirota relieves stress-associated symptoms by modulating the gut-brain interaction in human and animal models.

  Neurogastroenterol Motil Feb 20 (Epub ahead of print)

• Study: Mice infected w/ parasite to induce chronic inflammation and anxiety were fed 10 day course Bifidobacterium. Result? Anxiety normalized

Palatable Bacteria (yogurt!) Study

• Study: One month intake, morning and evening, of “carefully concocted yogurt” consumed by 12 healthy women w/o anxiety
  – Control: 11 healthy women consuming yogurt-like food without bacteria

• Trial: Shown pictures of angry or scared faces
  – Brain response determined by functional MRI
What did researchers discover?

• Results: Brain areas in women who ate “special” yogurt were calmed/blunted
  – The processing emotions and sensations such as pain were calmed

• “Human studies have been very small. But coupled w/ increasing # of animal studies, the results are HARD TO IGNORE.”

  https://www.sciencenews.org/article/microbes-can-play-games-mind
  (Epub ahead of April 2, 2016 issue of Science News, “Microbes and the Mind”
Take-Home Points

• The gut-brain axis is a two-way street
  – Hormones and NTs are similar and different
  – Serotonin and dopamine: two messengers of interest

• Translated the communication process between the gut brain, food and appetite
  – Serotonin and dopamine levels are unique in clients w/ anorexia and directly affect appetite and reward signals
  – Gut-brain pathway helps control changes in weight

• “Lateral” moves and creative analogies related to gut-brain health are effective nutrition therapy tools
  – Pre/probiotics are of interest
  – Stay tuned to more research coming soon
Gut Bacteria Might Guide the Workings of Our Minds
Research Publications

- Frank GK, et al. Reduced 5-HT2A receptor binding after recovery from anorexia nervosa, Biolog Psych, 52, 896-906 (2002).
Research Publications

Research Publications

- Microbes can play games with the mind. Sanders L. 03-23-2016. www.sciencenews.org/article/microbes-can-play-games-mind. (Epub)
- Mossman S. This is Your Brain, This is Your Brain on Food. Scan’s Pulse, Spring 2013, Vol 32, No 2. 6-8.
Research Publications