Overview

Part 1
- Nutrition & Brain Development
- Gut-Brain Axis
- Chronic Inflammation
- Neuroinflammation

Part 2
- Nutripsychiatry
- Depression
- Anxiety
- ADHD
- Autism
- Anti-Inflammatory Diet

Depression Stats

- Affects 350 million people globally
- 3,000 suicide deaths occur daily
- 25% of those diagnosed with major depressive disorder (MDD) are <19 years old
- 40% do not respond to current meds
Depression Etiology

- Genetics
  - Hypermethylation of ZBTB20

- Epigenetics
  - Immune dysregulation

- Stress & anxiety
  - Green spaces

- Immune dysregulation
  - Gut microbiome dysfunction
  - Excessive Alistipes
  - Inadequate Faecalibacterium

- Discount the future

Characteristics of Depression

- Monoamine depletion
- Increased # microglia
- Over-activation of microglia
- Elevated inflammatory markers
- Oxidative stress

GI Abnormalities & Brain Disorders

Co-morbidities

- Depression
  - IBS = 61%; IBD = 16%
- Anxiety
  - IBS = 54%; IBD = 11%
- Panic disorder
  - IBS = 61%; IBD = 11%

Davies et al. 2014. Genome Biol. 15:R56.
Tryptophan

Stimulated by LPS

Kynurenine

5-HT

Serotonin

Nicotinamide

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Neurodevelopmental Disruptions & Depression

- Altered fetal period
- Maternal malnutrition
- Maternal stress
- Child abuse
- Child malnutrition

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Diet & Depression

Dietary inflammation increases the likelihood of depression by 31%

- ↑ Bifidobacteria
- ↓ Bacteroides
- ↑ Prevotella
- ↓ Firmicutes

SCFA

- ↑ Butyrate
- ↑ Acetate
- ↑ Propionate

- ↓ Butyrate
- ↓ Acetate
- ↓ Propionate

Improved mood disorders

Induction of depression

Firth et al. 2019.

Molendijk et al. 2018.

Sandhu et al. 2016.
Diet & Depression

**Macronutrients**

- Omega-3s from fish (60% EPA & 40% DHA)
- Fish contain many other nutrients
- Protein
  - Need amino acid precursors for neurotransmitters

**Micronutrients**

- Zinc – most favorable research outcomes
- Iron
- Magnesium
- Folate & B12
  - Patients with depression have lower serum folate
  - Supplementation enhances antidepressant effect

**Phytochemicals**

- Cocoa, coffee, green tea, honey, blueberries & curcumin are associated with a decreased risk of depression and/or cognitive decline
- All increase *Bifidobacterium & Lactobacillus*
- Most phytochemical are too large to be absorbed in the small intestine and are fermented in the gut
Diet & Depression

**Prebiotics**
- Did not differ from placebo

**Probiotics**
- Small, but significant decrease in depression (d=0.24)

Herbal Supplements
- *Crocus sativus* (Saffron) – 30-100 mg/d
- *Echium amoenum* (Borage) – 375 mg/d
- *Hypericum perforatum* (St. John’s Wort) – 300 mg 3x/d
- *Piper methysticum* (Kava) – 250 mg kavalactones/d
- *Rhodiola rosea* (Rose Root) – 340-680 mg/d
- *Lavandula angustifolia* (lavender) – cream or aromatherapy

Exercise & Depression

**Meta-analysis data**
- Exercise is more beneficial than no treatment
- Not as beneficial as therapy or medications
- Moderate effect on depression when added to meds


Anxiety Stats

- Affects 40 million adults in U.S.
- 50% of those with depression also have an anxiety disorder

Stress & Anxiety

- Prenatal & postnatal stress induce anxiety
- Psychological stress induces both intestinal and BBB permeability
- Maternal obesity or high-fat consumption increased anxiety in offspring
  - Activation of microglia
  - Found to be due to increased cortisol
  - Mediated by mast cells
  - Caused permanent neurodevelopmental changes

Anxiety & the Gut

- Gut inflammation stimulates anxiety-like behavior
- High prevalence of anxiety in IBD patients
- Fermentation products are protective
- Lactobacillus rhamnosus has the most evidence to support
Diet & Anxiety

**Macronutrients**
- Carbohydrates
  - Low blood sugar is a contributing factor
- Omega-3s
  - Significantly decrease anxiety in doses >2 g/d

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**Micronutrients**
- Magnesium
  - At least 100 mg/d
- Zinc
  - Serum levels reduced in pts with anxiety
  - Supplementation does not seem to help
  - Could be an artifact of elevated inflammation

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**Herbs & Anxiety**
- Ashwagandha (*Withania somnifera*)
  - Decreased anxiety by 57% and 44% decrease risk of perceived stress
- Kava
  - Influences GABA synthesis
  - 120-280 mg/d of kavalactones
  - Recommended for no more than 8 weeks
- Passion flower
  - RCTs indicate as effective as benzodiazepines
- Lavender oil aromatherapy
  - Comparable to lorazepam

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Exercise & Anxiety

Meta-analysis data

Exercise had a moderate effect on decreasing anxiety compared to control

Attention Deficit Hyperactivity Disorder (ADHD)

- Found in 3-6% of all kids
- 50-80% persist into adulthood
- Genetics
  - Region on chromosome 16
  - 76% chance of heritability
- Abnormal GABAergic & glutamatergic systems in the brain

Attention Deficit Hyperactivity Disorder (ADHD)

Environmental Risk Factors

- Maternal mental disorder
- Violence
- Stress
- Smoking
- Prenatal alcohol intake
- Family dysfunction
- Intrauterine or postnatal stress
- Premature birth

Schuch et al. 2015. Front Psychiatry. 6:126.
Attention Deficit Hyperactivity Disorder (ADHD)

**Immune changes in ADHD**
- Less Th2
- More Th1
- Cortisol is low in the morning
- Stimulates higher Th1/Th2 ratio

**Food hypersensitivity**
- Cell-mediated food allergies found in some children
- Causes neurologic inflammation
- Elimination diet may be beneficial

Proposed ADHD Mechanism

- Food allergy causes increased production of IgE
- Cytokines bind receptors activating HPA axis
- Increased production of inflammatory cytokines
- Chronic elevation of cortisol causes neuroinflammation
- Cytokines cross BBB
- Negative feedback decreases cortisol production
Diet & ADHD

Restrictive Diets
- Eliminating artificial food coloring has a small effect size
- Few foods diet has a moderate effect size

Omega-3s
- Small effect size

Mediterranean Diet
- Lower adherence increases ADHD symptoms by 600%

Most Common Nutritional Deficiencies in ADHD Patients
- Iron
- Zinc
- Vitamin D

Autism Spectrum Disorder Statistics
- 1-2% of kids
- 40-95% prevalence in identical twins
- 0-30% prevalence in non-identical twins
Autism Spectrum Disorder

GI symptoms
Leaky gut
Leaky blood-brain-barrier
Elevated # microglia
Altered metabolism
Altered microbial composition
Mitochondrial dysfunction

In utero deficiency:
• Iron

Most common nutritional deficiencies:
• Iodine
• Vitamin D
• Folate
• Vitamin B₆
• Vitamin B₁₂

Diet & Autism Spectrum Disorder


In utero deficiency:

Best Practices?
Anti-inflammatory
- Turmeric (most)
- Fiber
- Flavones
- Tea
- Beta-carotene
- Isoflavones
- Magnesium
- Omega-3 FA

Inflammatory
- Trans fat (most)
- Saturated fat
- Total fat
- Calories
- Vitamin B12
- Carbohydrates

Dietary Inflammatory Index

Dietary Inflammatory Index & Mental Health
↑ Inflammation = ↑ Mental Health Issues
- 70% increased risk of depression
- 60% increased risk of anxiety
- More prominent results in women

Anti-Inflammatory Diets
- Mediterranean Diet
- Dietary Approaches to Stopping Hypertension (DASH)
- Plant-based
## Which Fish Are Best?

<table>
<thead>
<tr>
<th>Fish</th>
<th>Omega-3 (mg/4 oz. cooked fish)</th>
<th>Mercury (mg/4 oz. cooked fish)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Salmon (Atlantic, Chinook, Coho)</td>
<td>1200-2400</td>
<td>2</td>
</tr>
<tr>
<td>Anchovies, Herring, Shad</td>
<td>2500-2800</td>
<td>5-10</td>
</tr>
<tr>
<td>Mackerel (Atlantic &amp; Pacific)</td>
<td>1150-2100</td>
<td>8-13</td>
</tr>
<tr>
<td>Tuna (Bluefin &amp; Albacore)</td>
<td>1700</td>
<td>16-18</td>
</tr>
<tr>
<td>Sardines (Atlantic &amp; Pacific)</td>
<td>1100-1600</td>
<td>2</td>
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<tr>
<td>Oysters (Pacific)</td>
<td>1550</td>
<td>2</td>
</tr>
<tr>
<td>Trout (Freshwater)</td>
<td>1000-1100</td>
<td>11</td>
</tr>
<tr>
<td>Tuna (Canned Albacore)</td>
<td>1000</td>
<td>40</td>
</tr>
<tr>
<td>Salmon (Pink, Sockeye)</td>
<td>700-900</td>
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<tr>
<td>Pollock</td>
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<td>6</td>
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<tr>
<td>Tuna (Light canned)</td>
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<tr>
<td>Catfish</td>
<td>100-250</td>
<td>7</td>
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<tr>
<td>Tilapia</td>
<td>150</td>
<td>2</td>
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<tr>
<td>Shrimp</td>
<td>100</td>
<td>&lt;1</td>
</tr>
</tbody>
</table>

Serving sizes should be individualized to meet energy and nutrient needs.

DASH Diet

- Fruits: 4 or more servings each day
- Grains: 4 or more servings each day
- Fats/Oils: Olive Oil, 4 Tablespoons or more each day
- Dried Beans/Nuts/Seeds: 3 or more servings each week
- Fish and Seafood: 2-3 servings each week
- Herbs and Spices: Use daily
- Yogurt/Buttermilk: Choose dairy to weekly
- Alcohol/Wine: Men: 1-2 glasses each day, Women: 1 glass each day

Tips:
- A serving is 1 cup raw or 1/2 cup cooked vegetables. Eat a variety of colors and textures.
- Consume mostly whole grains. 1 serving = 1 slice bread or 1/2 cup cooked cereal.
- Choose extra virgin olive oil (EVOO) and use in salad dressings and cooking; choose avocados or natural peanut butter instead of butter or margarine.
- Choose salmon, sardines, and tuna which are rich in Omega-3 fatty acids.
- Season foods with herbs, garlic, onions, and spices instead of salt.

Choose low-fat yogurt and cheese; choose skinless chicken or turkey in place of red meat.

Always ask your medical team if alcohol is ok for you to consume.

Red meats, processed meats, and sweets should be limited.
What does my plate look like?