Nutritional Considerations in Bipolar Disorder

Simon J. Evans, Ph.D.
“Leave your drugs in the chemist’s pot if you can heal the patient with food.”

– Hippocrates, circa 400 B.C.
Overview

- The Brain as a Physical Organ
  - The brain has high metabolic demands and requires delivery of oxygen, energy and nutrients

- Foods and Mood Disorders
  - There is a relationship between the diet and the incidence of mood disorders

- Fatty Acids and Bipolar Disorder
  - Omega-3s and -6 may play roles in bipolar risk, severity and response to medications
The Brain is Metabolic Machine
The Brain Needs Nutrients, Too

- Your Brain weighs about 2% of your body weight but uses more than its share of energy and nutrients.
  - 15% of cardiac output (blood supply)
  - 20% of oxygen consumption
  - 25% of glucose utilization (energy supply)

- Your Brain is about 65% Fat!
  - Large amounts of polyunsaturated fat
  - High concentration of the omega-3, DHA
The Brain is Influenced by Metabolic Health of the Body
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<table>
<thead>
<tr>
<th>Vitamins</th>
<th>Minerals</th>
<th>Essential Nutrients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Folic Acid</td>
<td>Calcium</td>
<td>Omega-3s</td>
</tr>
<tr>
<td>Vitamin D</td>
<td>Selenium</td>
<td>Tryptophan</td>
</tr>
<tr>
<td>Vitamin B12</td>
<td>Zinc</td>
<td>Other Amino Acids</td>
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<tr>
<td>Vitamin B6</td>
<td>Magnesium</td>
<td></td>
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<tr>
<td>Thiamin</td>
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<tr>
<td>Vitamin E</td>
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</table>
Acute Mood Effects of High Glycemic Meals

Blood sugar over time:

- Elevated mood (increased dopamine)
- Irritable mood
- Hunger cravings, energy crash

High glycemic diet versus low glycemic diet:

- Target blood sugar

Source: University of Michigan Depression Center
Dietary pattern and depressive symptoms in middle age

Tasnime N. Akbaraly, Eric J. Brunner, Jane E. Ferrie, Michael G. Marmot, Mika Kivimaki and Archana Singh-Manoux

In middle-aged participants, a processed food dietary pattern is a risk factor for CES-D depression 5 years later, whereas a whole food pattern is protective.

Statistical models adjusted for:
• gender
• age
• marital status
• energy intake
• employment grade
• education level
• physical activity
• diabetes
• heart disease
• cognitive function
• antidepressants use

the lowest tertile. In contrast, high consumption of processed food was associated with an increased odds of CES-D depression (OR = 1.58, 95% CI 1.11–2.23).

Conclusions
In middle-aged participants, a processed food dietary pattern is a risk factor for CES-D depression 5 years later, whereas a whole food pattern is protective.

Declaration of interest
None.

Bipolar Patients have Increased Risk for Poor Metabolic Health

• Bipolar Patients as a group have poorer eating habits than the general population.
  – Eat less regular daily meals
  – Report difficulty in obtaining or cooking food
  – Eat foods of poorer nutritional quality
  – Eat foods with an increased glycemic load

• Bipolar Patients on anti-psychotic medications are at increased risk for metabolic health problems.
  – Increased weight gain
  – Insulin resistance
  – Endothelial dysfunction
It’s a Balancing Act

Genetics

Risk Factors

Poor Sleep Habits

Sedentary Behavior

Poor Diet

Quality Sleep Habits

Healthy Diet

Exercise

Protective Factors

Experiences
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How Do Fats Fit Into the Picture?

- The Brain has a high concentration of fat
  - 65% fatty acids by dry weight
  - 15% Polyunsaturated fatty acid
  - 6% omega-3 (DHA)
- Low serum omega-3s *associate* with mood and cognitive disorders
  - Major Depression
  - Bipolar Disorder
  - Schizophrenia
  - Suicidal Behavior
  - Violent Behavior
  - Child and Adult ADHD
  - Alzheimer’s Dementia and Cognitive Impairment
All Omega Fats Are Not Created Equal

Omega-6s

Omega-3s

plant oils

short chain fats

long chain fats

Dietary Omega-3 to Omega-6 Ratios Have Changed

Omega-3 Intake Correlates with Mood Disorders

Major Depression

Bipolar Disorder


Dietary Omega-3 Deficiency Alters Brain Chemistry

Diet Effects Changes in Behavior and Neurochemistry
- Anxiety-Like Behavior
- Dopamine Activity
- Serotonin Activity
- Endocannabinoid Activity
Conceptual Mechanisms of Omega-3 and Omega-6 Actions

extracellular signaling (endocannabinoids, eicosanoids)
cleavage from membrane
intracellular signal transduction

Cross Section of Neuronal Membrane

w-3s and w-6s compete for:
• membrane incorporation
• synthesis of eicosanoids
• elongation by enzymes
• Intracellular signaling

This effects:
• Immune responsivity
• Cardiovascular tone
• Mood circuits
• Insulin sensitivity

receptor kinetics
Genetic Variants Influence Omega-3 and Omega-6 Levels

Mood Stabilizers Inhibit Omega-6 Activity in Neurons

Omega-3 Profiles Associate with Personality Traits

Omega-3 Profiles

<table>
<thead>
<tr>
<th>Serum ALA:EPA</th>
<th>Serum EPA:DHA</th>
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<td>Extraversion Factor</td>
<td>Agreeableness Factor</td>
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- **Serum ALA:EPA**
  - $r = -0.39$
  - $p = 0.045$

- **Serum EPA:DHA**
  - $r = -0.44$
  - $p = 0.022$

- **Extraversion Factor**
  - $r = 0.38$
  - $p = 0.052$

- **Agreeableness Factor**
  - $r = 0.43$
  - $p = 0.025$
Omega-3 Profiles Associate with Personality Traits

**Graph 1:**
- Serum ALA:DHA
- Openness Factor
- Correlation: $r = 0.498$, $p = 0.008$

**Graph 2:**
- FADS2 Activity
- Openness Factor
- Correlation: $r = 0.41$, $p = 0.034$

**Note:**
- ALA → FADS2 → EPA → DHA
Omega-3 and -6 Profiles Differ in Suicide Attempters

**Graph 1:**
- **Y-axis:** Serum Concentration
- **X-axis:** AA, EPA
- **Legend:**
  - non-attempters (yellow)
  - attempters (blue)

**Graph 2:**
- **Y-axis:** n6:n3 serum ratios
- **X-axis:** LA:ALA, AA:EPA, AA:DHA, n6:n3
- **Legend:**
  - non-attempters (yellow)
  - attempters (blue)
The brain is a physical organ, requiring:
- A healthy neurovascular system.
- A supply of quality nutrients and energy.

Dietary patterns associate with the development of major depression.

Fatty acid intakes associate with the rate of depression and bipolar disorder and alters neurochemistry involved in mood regulation.

Diet and genetics interact to control fatty acid profiles.

Mood stabilizing medications used to treat bipolar disorder inhibit omega-6 activity.

Omega-3 profiles associate with personality factors that may influence the burden of bipolar disease and suicide risk.
Research Questions (Studies in Progress)

• Does a diet high in omega-6 or low in omega-3…
  – influence the burden of disease in bipolar disorder?
  – inhibit medications used to treat mood disorders?

• Do specific genetic variants that control fatty acid profiles either increase risk for mood disorders or influence the efficacy of mood stabilizing medications?

• Can dietary interventions aimed at increasing specific fatty acids be protective against developing mood disorders or at least reduce the severity of mood disorders and improve patients’ responses to medications?