“Nutraceuticals” in Psychiatry

Elise Leonard, MD
Phoenix Indian Medical Center
Introduction

• Patients and parents use many practices, herbs, vitamins, and ‘food additives’ in the hope of better brain function
• These vary widely in safety and quality
• We should find out what our patients are taking, document these treatments, and may sometimes recommend safe and appropriate OTC therapies
Objectives

• Review commonly used non-prescription remedies for psychiatric illness
• Consider available data on efficacy, tolerability, and safety
• Discuss how to integrate safe, efficacious complementary therapies into the psychiatric toolbox
Omega-3 Fatty Acids

• Widely taken for a number of medical problems
  – Hypertriglyceridemia
  – Autoimmune d/o (RA, lupus, Crohn’s)
  – Hypertension
  – Cognitive decline
  – Cancer prevention (colon, prostate, breast)
  – ADHD, depression, psychosis prevention
Fatty Acids: Brief Review

• Make up cell membranes
• Connected to glycerol, make up fats
  – Important energy source)
• “Essential” fatty acids are those we cannot synthesize and must ingest
Fatty Acids

- **Estearic acid** (C18:0)
- **Oleic acid** (C18:2, ω-9)
- **Linoleic acid** (C18:2, ω-6)
- **alpha-linolenic acid** (C18:3, ω-3)
The bad, the good, and the twisted...

**Saturated**

![Saturated diagram]

**Unsaturated**

![Unsaturated diagram]
Trans fats: the twisted

- Start with inexpensive vegetable fat
- Twist it at a double bond
- Voila! It acts like saturated (animal) fat
  - Solid at room temperature, stays crispy
Our Relationship with Fat

Simopoulos AP
Omega-3 and Omega-6

• Position of the first double bond, counting back from the methyl end

• Polyunsaturated (more than one double bond) fatty acids, or PUFA’s
Omega-3 Fatty Acids

- Alpha-linoleic acid (ALA)
  - Vegetable
- Eicosapentanoic acid (EPA)
- Docosahexanoic acid (DHA)
Omega-6 Fatty Acids

- Linoleic acid (LA)
- Gamma-linoleic acid (GLA)
- Dihomo-gamma-linoleic acid (DGLA)
- Arachidonic acid (AA)
Omega-6 Fatty Acids

- Lend fluidity to cell membranes
- Precursors to eicosanoids, which are potent lipid mediator signaling molecules
  - Inflammation, immunity, CNS
- Those derived from omega-6’s tend to be pro-inflammatory
  - AA is converted to prostaglandin
Omega-6 Fatty Acids

• Higher linoleic acid (LA) levels – but not other omega 6’s- were associated with lower cardiovascular death rate*

• In another study, higher omega-6 levels were not associated with risk for heart failure in physicians**


Omega-3 Fatty Acids

• Lend fluidity to cell membranes
• Precursor to eicosanoids
  – Modulate signal transduction, possibly by Ca- channel effects and inhibition of protein kinase A- cAMP signal transduction
• $\omega$-3 form eicosanoids that are less, non-, or anti-inflammatory
ω-6 to ω-3 Ratio in Foods

- Tuna in H2O: 0.2
- Salmon: 0.2
- Flax seed oil: 0.2
- Butter: 1.55
- Canola oil: 2.18
- Beef-alfalfa fed:
  - Grain fed: 20
- Walnuts: 5.2
- Eggs: 1.6 to 19*
- Soybean oil: 7.5
- Lard: 10
- Olive oil: 13
- Tuna in oil, drained: 13
- Pistachios: 55
- Corn, safflower oil: 60-80
- Sunflower oil: 199

* feed-dependent
Omega-3 to Omega-6 Ratio

- Arctic traditional diet 6 : 1
- Hunter-gatherer diet 1 : 1
- Japanese traditional diet 1 : 6
- Current ‘western’ diet 1 : 30
All nuts are not alike

<table>
<thead>
<tr>
<th>Nuts and Seeds</th>
<th>Omega 6 per ounce</th>
<th>Omega 3 per ounce</th>
<th>Ratio of omega 6 to omega 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>English walnuts</td>
<td>10,666 mg</td>
<td>2,542 mg</td>
<td>4 to 1</td>
</tr>
<tr>
<td>Pecans</td>
<td>5,777 mg</td>
<td>276 mg</td>
<td>21 to 1</td>
</tr>
<tr>
<td>Pistachio nuts</td>
<td>3,818 mg</td>
<td>73 mg</td>
<td>52 to 1</td>
</tr>
<tr>
<td>Sesame seeds</td>
<td>7,063 mg</td>
<td>74 mg</td>
<td>96 to 1</td>
</tr>
<tr>
<td>Poppy seeds</td>
<td>7,921 mg</td>
<td>76 mg</td>
<td>104 to 1</td>
</tr>
<tr>
<td>Pumpkin seeds*</td>
<td>5,797 mg</td>
<td>51 mg</td>
<td>114 to 1</td>
</tr>
<tr>
<td>Pine nuts</td>
<td>9,410 mg</td>
<td>31 mg</td>
<td>300 to 1</td>
</tr>
<tr>
<td>Brazil nuts</td>
<td>5,758 mg</td>
<td>5 mg</td>
<td>1150 to 1</td>
</tr>
<tr>
<td>Almonds</td>
<td>3,378 mg</td>
<td>2 mg</td>
<td>1987 to 1</td>
</tr>
<tr>
<td>Peanuts</td>
<td>4,393 mg</td>
<td>&lt;1 mg</td>
<td>5500 to 1</td>
</tr>
</tbody>
</table>
ω-3 to ω-6 Ratio

– Center for Genetics, Nutrition, and Health data

• 1: 2.5 ratio reduces cell proliferation in colorectal Ca
• Breast Ca risk lower as denominator decreases
• 1: 2-3 ratio suppresses inflammation in RA
• 1: 5 ratio beneficial for asthma (>10:1 adverse)

Omega-3 Fatty Acids

• NIH reports ‘A’ level (strong scientific) evidence for benefit in hypertriglyceridemia, cardiovascular disease prevention, hypertension
• ‘B’ level (good scientific) evidence for benefit in primary prevention of cardiovascular disease, rheumatoid arthritis
• ‘Preliminary’ evidence of benefit in various psychiatric disorders
Why Wild Fish?

• They eat the phytoplankton that synthesize long-chain omega-3 fatty acids
• They store loads of EPA and DHA
  — Fatty fish store it all over (salmon)
  — Less fatty fish keep it in their livers (cod)
• Fish oil supplements are basically “squeezed” fatty fish
• Distillation process removes heavy metals
How about farmed fish?

• Fish do not make their own omega-3’s
  – They ingest the phytoplankton that produce it
• Farmed fish are usually fed terrestrial feeds (grain, meat protein)
  – Recently, fish feed is sometimes supplemented with fish oil to ‘pump up’ omega-3 content
Other Sources of Omega-3

• Wild game and grass-fed meats: provide some omega-3, though much less than wild fish
• Flax, chia, hemp seed, cauliflower, brussels sprouts
  – Plant sources have mostly ALA
  – Some metabolic conversion to EPA occurs (<10%)
  – Very restricted conversion to DHA occurs (<5%)
• We are dependent on wild fish for most of our EPA and DHA
Collapse of Fish Populations

A Future Without Fish

A new study suggests that overfishing could lead to a catastrophic loss of marine species as soon as the middle of the century.

Percentage of species collapsed (defined as less than 10% left)

![Graph showing percentage of species collapsed over time]


Source: SeaWeb

The New York Times
Other Sources of Omega-3

• Dupont has patented a genetically modified yeast (yarrowia lipolytica) which produces EPA

• Martin Marietta and NASA, in working on an algae-based life support system, discovered that the resulting fatty acids (especially DHA) could be produced on a large scale
Omega 3’s and Mental Health

• mood
• ADHD
• psychosis
• cognition
National Fish Consumption and Prevalence of Bipolar d/o

A Fish a Day...
A cross-national comparison of the relationship between seafood consumption and lifetime prevalence rates of bipolar spectrum disorders shows a positive correlation, but proof of a causal relationship is absent.

Source: American Journal of Psychiatry, December 2003
ω-3 Treatment of Childhood Depression

• 20 children, mean age 10
• All having first depressive episode, mean duration of symptoms 3 months
• Comorbid conditions allowed
• Randomized to receive 400mg EPA + 200 mg DHA or identical capsule filled with olive or safflower oil
• CDRS (childhood depression rating scale) used to assess outcome

ω-3 Treatment of Childhood Depression

Differences significant at weeks 8, 12, and 16
Omega-3 Treatment of Adult Depression

• Only a trend toward improvement over placebo in patients with comorbid anxiety
• Clear improvement in patients with depression but not anxiety

Lesperance F et al. J Clin Psychiatry 2011, 72 (8); 1054-1062
Meta-analysis of Omega 3’s in Bipolar D/O

• Strong evidence that bipolar depressive symptoms are reduced by *adjunctive* omega-3 use

Omega-3 Supplementation for ADHD

- Meta analysis of RPCT’s
- Omega 3 supplementation, especially higher EPA, modestly effective in treatment of ADHD
- EPA dose areound 450 mg/d

ω-3 Treatment of Childhood Bipolar Disorder

• One open label trial, n=20, ages 6 to 17
• Doses varied with size
• Outpatient, 8 weeks
• “Statistically significant but modest” reduction in YMRS

Omega-3 Fatty acid monotherapy in bipolar disorder: survival analysis


N=8, 9.6 gm omega-3 vs. olive oil
Omega-3 fatty acids in psychosis prodrome

- N= 81, age 13-25 in Vienna
- Randomized, dbl-bl, pbo-cont
- 700mg EPA, 480mg DHA vs. coconut oil capsules (with added vitamin E to match fish oil content) daily for 12 weeks

Amminger GP et al. Long-Chain Omega-3 Fatty Acids for Indicated Prevention of Psychotic Disorders. Arch Gen Psychiatry Vol 67(2), Feb 2010
Omega-3 fatty acids in the prodrome

- 12-week treatment trial
- Weekly assessments for 4 weeks, then at 8 and 12 weeks, then at 6 and 12 months
- Number progressing to psychosis
- Time to psychosis
- At 12 months, 4.9% of treatment group converted to psychosis vs. 27.5% of control group
Time to Psychosis

Kaplan-Meier survival curve
Recommending or Prescribing Nutraceuticals

• Don’t use in lieu of mainstream treatment - use as an enhancement of treatment
• Document discussion of risks and benefits
• If patient requests ‘nutraceutical’ treatment in lieu of medication
  – Consider in mild-moderate illness
  – Document offer of mainstream treatment, an patient/parent’s preference for non- prescription intervention
  – Use in conjunction with ongoing therapy