Integrative Strategies for Supporting Patients with Mental Health Disorders

Presented by Charles Gant, M.D., PH.D.
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Charles Gant, M.D., Ph.D.
Technical Issues & Clinical Questions

Please type any technical issue or clinical question into either the “Chat” or “Questions” boxes, making sure to send them to “Organizer” at any time during the webinar.

We will be compiling your clinical questions and answering as many as we can the final 15 minutes of the webinar.

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Integrative Strategies for Supporting Patients with Mental Health Disorders

Presented by Charles Gant, M.D., PH.D.
“About half of Americans will meet the criteria for a DSM-IV disorder sometime in their life, with first onset usually in childhood or adolescence. Interventions aimed at prevention or early treatment need to focus on youth.”

Prevalence of Mental Disorders

This chart illustrates the percentage of people in the United States who experience a particular class of mental illness at some point during their lives. The figures are derived from the National Comorbidity Survey, in which researchers interviewed more than 9,000 people over 18 years of age.


Source: National Institute of Mental Health, National Comorbidity Study
Mental Disorders

• An estimated 26.2 percent of Americans ages 18 and older — about one in four adults — suffer from a diagnosable mental disorder in a given year.
• When applied to the 2004 U.S. Census residential population estimate for ages 18 and older, this figure translates to 57.7 million people.
• The main burden of illness is concentrated in a much smaller proportion — about 6 percent, or 1 in 17 — who suffer from a serious mental illness.
• Mental disorders are the leading cause of disability in the U.S. and Canada for ages 15-44.
• Nearly half (45 percent) of those with any mental disorder meet criteria for 2 or more disorders, with severity strongly related to comorbidity.
What does a Diagnosis of a Mental Disorder Actually Mean?

Two Definitions for the Term “Diagnosis”

“When there is no explanation, then give it a name, which immediately explains everything”


1. To recognize a disease or condition by its outward signs and symptoms
2. To analyze the underlying physiological/biochemical cause disease or condition
   – Example – diagnose a brake problem in car
Advantage of diagnosing the underlying biochemical causes of any condition?

- Uncovering biochemical, toxicological, immune, genetic risk factors (definition #2) opens the door to reversing the root causes, as opposed to “sealing over” symptoms (definition #1) with palliative therapy.
  - Example, pneumonia was diagnosed as pneumonia for 1000’s of years before the discovery of germs – palliative therapies prevailed until root causes were discovered
  - Treating the cause (germs) led to “cures” (antibiotic therapies)
How the DSM-IV (Diagnostic and Statistical Manual of Mental Disorders-IV) published by the American Psychiatric Association defines the diagnosis of mental disorders
“...Whatever its original cause, it (a mental disorder) must currently be considered a manifestation of a behavioral, psychological, or **biological dysfunction** in the individual...”
“The clinician using the DSM-IV should therefore consider that individuals sharing a diagnosis are likely to be heterogeneous even in regard to the defining features of the diagnosis and that boundary cases will be difficult to diagnose in any but a probabilistic fashion.”
Heterogeneous  (het-er-o-je’ne-us)
[G. eteros, other, + gennos, type]

- Of unlike natures and composed of unlike substances. In contrast to homogeneous.
- Consisting of dissimilar elements or parts.
- Completely different; incongruous.
DSM IV Uses the Descriptive Definition of the Term Diagnosis, not the Causal

- Example
  - 3 mineral deficiencies, 2 fatty acid deficiencies, 1 heavy metal toxicity, GI dysbiosis

- Risk factor analysis
- Why cardiologists coined this term
- Begin RF discussion with the GI
The Gut Brain Connection

1. Malabsorption
2. Inflammation Uses Up Precurisers
3. GI Toxins are Neurotoxic
4. Immune Challenge
5. Pancreatic Insufficiency

Brain

Lumen GI

Pancreas

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Your Backup Brain

“There’s a "second brain” in your stomach. It influences your mood, what you eat, the kinds of diseases you get, as well as the decisions you make. And you thought it was all in your head!”

By Dan Hurley, published November 1, 2011 – Psychology Today
“The gut can work independently of any control by the brain in your head—it's functioning as a second brain,” says Michael Gershon, professor and chair of pathology and cell biology at Columbia. “It's another independent center of integrative neural activity.”
“There is now evidence that the gut microflora plays a role in autism. Modulation of the gut microflora by reducing the numbers of certain clostridia in ASD patients, while stimulating more beneficial gut bacteria, may help alleviate some of the related symptoms.”


http://jmm.sgmjournals.org/cgi/content/full/54/10/987
Elevated DHPPA

**Bacterial Dysbiosis Markers**

- **Dihydroxyphenylpropionic Acid (DHPPA)**
  - Value: 18.1
  - Reference: <= 12.8
# Stool test with a Positive *clostridium difficile*

**Methodology:** EIA, Fecal Immunochemical Testing (FIT)

<table>
<thead>
<tr>
<th>Additional Results</th>
<th>Result</th>
<th>Expected Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fecal Occult Blood♦</td>
<td>Negative</td>
<td>Negative</td>
</tr>
<tr>
<td>Color††</td>
<td>Brown</td>
<td></td>
</tr>
<tr>
<td>Consistency††</td>
<td>Formed/Normal</td>
<td></td>
</tr>
<tr>
<td><strong>HpSA - <em>H. pylori</em></strong></td>
<td>Negative</td>
<td>Negative</td>
</tr>
<tr>
<td><strong>Campylobacter spp♦</strong></td>
<td>Negative</td>
<td>Negative</td>
</tr>
<tr>
<td><strong>Clostridium difficile♦</strong></td>
<td>Positive</td>
<td>Negative</td>
</tr>
<tr>
<td>*<em>Shiga toxin <em>E. coli♦</em></em></td>
<td>Negative</td>
<td>Negative</td>
</tr>
<tr>
<td>Fecal Lactoferrin♦</td>
<td>Negative</td>
<td>Negative</td>
</tr>
</tbody>
</table>

††† Results provided from patient input.
Q: Is there an integrative model to address the causal risk factors of mental disorders?

A: Stress

– At least 12 kinds of stressors (next slide) – which stressors causative of illness in your patient(s) do you not want to know about?
The primary cause or exacerbating factor of most (perhaps all) mental (& medical) disorders (including addiction & violent behaviors) is:

**FIGHT** (anger)  
**FLIGHT** (fear)

**CHRONIC STRESS**

**Dictionary definition of stress:** Mental or bodily tension resulting from factors that tend to alter an existent equilibrium.
Both Parts of the Autonomic Nervous System are Ideally Balanced

1. **Sympathetic Nervous System** (degenerative)
   - “Fight or Flight” – for survival, brief emergencies
   - AKA - the *accelerator* in the nervous system

2. **Parasympathetic Nervous System** (regenerative)
   - the “Rest and Digest” response when no survival threat or stress exists
   - The *brakes* in the nervous system

• **Autonomic Nervous System** imbalances are called **Dysautonomia** (technical term)
  - Usually excessive sympathetic (fight or flight)
Why does **CHRONIC STRESS** cause injury to the Body & Brain?

- When chronic stress occurs from overuse of the fight (anger) or flight (flight) sympathetic nervous system, burnout can occur.

- **Example:** A car engine is only supposed to be revved up briefly for an emergency passing on the highway.

  - **QUESTION:** What happens to an engine if it is revved up indefinitely?
  
  - **ANSWER:** It **BURNS OUT**.
22 Well-studied Consequences of Chronic Stress & Burnout

1. Addiction
2. Nausea
3. Headache
4. Backache
5. Insomnia
6. Anxiety
7. Depression
8. Anger (cynicism)
9. Cancer
10. Ulcers
11. Fatigue
12. Depersonalization
13. Other GI Problems
14. Eating Disorders
15. Adrenal exhaustion
16. Heart arrhythmias, AMI
17. (Auto) Immune injury
18. Clotting problems
19. Panic Disorder
20. Heart Disease
21. Worsening of all medical and psychiatric disorders
22. AD/HD
Note how stressors are all connected on last slide, so how do we begin to integrate these stressors together and test for them – will connect stressors #5, 6, 9, and 10

Begin with (upper right hand corner next slide):

5) Toxic stressors – RBC minerals/toxic elements, pre-post provocation testing, hair, dental, Phase I & II Detoxigenomics

6) Immune stressors – food allergy/leaky gut

9) Infectious stressors
   a. Candida/mold first – 4 ways to test: candida antibody profile, dysbiosis markers, stool C&S, mycotoxins (even a 5th way – mold plates in house)
   b. Chronic sinusitis is mold (candida Ab/mycotoxins)
   c. Dental cavitations – anaerobes - DHPPA
   d. Lyme/babesia/bartonella – ILADS docs – your patients will never get well until mold/candida is under control – brief discussions of Rx protocols

10) Oxidative stressors - markers on NutrEval
Example of Toxic Stressors (#5)

### Toxic Elements

<table>
<thead>
<tr>
<th>Element</th>
<th>Reference Range</th>
<th>Reference Range</th>
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</thead>
<tbody>
<tr>
<td>Lead</td>
<td>0.024</td>
<td>&lt;= 0.048 mcg/g</td>
</tr>
<tr>
<td>Mercury</td>
<td>0.0376</td>
<td>&lt;= 0.0039 mcg/g</td>
</tr>
<tr>
<td>Antimony</td>
<td>0.003</td>
<td>&lt;= 0.002 mcg/g</td>
</tr>
<tr>
<td>Arsenic</td>
<td>0.061</td>
<td>&lt;= 0.071 mcg/g</td>
</tr>
<tr>
<td>Cadmium</td>
<td>&lt;dl</td>
<td>&lt;= 0.001 mcg/g</td>
</tr>
<tr>
<td>Tin</td>
<td>&lt;dl</td>
<td>&lt;= 0.0009 mcg/g</td>
</tr>
</tbody>
</table>

### Methylation

<table>
<thead>
<tr>
<th>Result</th>
<th>Gene</th>
<th>SNP Location</th>
<th>Internet Information</th>
<th>Affects</th>
</tr>
</thead>
<tbody>
<tr>
<td>+</td>
<td>COMT</td>
<td>V158M</td>
<td><a href="#">www.genovations.com/gdv158m</a></td>
<td>Liver/Gut</td>
</tr>
<tr>
<td>-</td>
<td></td>
<td></td>
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</table>

### Acetylation (N-acetyl transferase)

#### SLOW METABOLIZER POLYMORPHISM

<table>
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<th>Gene</th>
<th>SNP Location</th>
<th>Internet Information</th>
<th>Affects</th>
</tr>
</thead>
<tbody>
<tr>
<td>-</td>
<td>NAT1</td>
<td>R64W</td>
<td><a href="#">www.genovations.com/gdv64w</a></td>
<td>All Cells</td>
</tr>
<tr>
<td>-</td>
<td>NAT1</td>
<td>R187Q</td>
<td><a href="#">www.genovations.com/gdv187q</a></td>
<td>Liver/Gut</td>
</tr>
<tr>
<td>-</td>
<td>NAT2</td>
<td>I114T</td>
<td><a href="#">www.genovations.com/gdv114t</a></td>
<td>Liver/Gut</td>
</tr>
<tr>
<td>++</td>
<td>NAT2</td>
<td>R197Q</td>
<td><a href="#">www.genovations.com/gdv197q</a></td>
<td>Liver/Gut</td>
</tr>
<tr>
<td>++</td>
<td>NAT2</td>
<td>G286E</td>
<td><a href="#">www.genovations.com/gdv286e</a></td>
<td>Liver/Gut</td>
</tr>
<tr>
<td>-</td>
<td>NAT2</td>
<td>R64Q</td>
<td><a href="#">www.genovations.com/gdv64q</a></td>
<td>Liver/Gut</td>
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<tr>
<td>-</td>
<td>NAT2</td>
<td>K268R</td>
<td><a href="#">www.genovations.com/gdk268r</a></td>
<td>Liver/Gut</td>
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#### FAST METABOLIZER POLYMORPHISM

<table>
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<th>Result</th>
<th>Gene</th>
<th>SNP Location</th>
<th>Internet Information</th>
<th>Affects</th>
</tr>
</thead>
<tbody>
<tr>
<td>-</td>
<td>NAT1</td>
<td>G620</td>
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<td></td>
</tr>
</tbody>
</table>

### Glutathione Conjugation (Glutathione s-transferase)

<table>
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<th>Gene</th>
<th>SNP Location</th>
<th>Internet Information</th>
<th>Affects</th>
</tr>
</thead>
<tbody>
<tr>
<td>-</td>
<td>GSTM1</td>
<td>1p13.3</td>
<td><a href="#">www.genovations.com/gdgstm1</a></td>
<td>Liver/Kidney</td>
</tr>
<tr>
<td>-</td>
<td>GSTP1</td>
<td>I105V</td>
<td><a href="#">www.genovations.com/gdgs1</a></td>
<td>Brain/Skin</td>
</tr>
<tr>
<td>-</td>
<td>GSTP1</td>
<td>A114V</td>
<td><a href="#">www.genovations.com/gda114v</a></td>
<td>Brain/Skin</td>
</tr>
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</table>

### Oxidative Protection

<table>
<thead>
<tr>
<th>Result</th>
<th>Gene</th>
<th>SNP Location</th>
<th>Internet Information</th>
<th>Affects</th>
</tr>
</thead>
<tbody>
<tr>
<td>-</td>
<td>SOD1</td>
<td>G93A</td>
<td><a href="#">www.genovations.com/gdg93a</a></td>
<td>Cytosol</td>
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<tr>
<td>-</td>
<td>SOD1</td>
<td>A4V</td>
<td><a href="#">www.genovations.com/gda4v</a></td>
<td>Cytosol</td>
</tr>
<tr>
<td>-</td>
<td>SOD2</td>
<td>A16V</td>
<td><a href="#">www.genovations.com/gda16v</a></td>
<td>Mitochondrion</td>
</tr>
</tbody>
</table>
Example of Immune Stressors (#6)

<table>
<thead>
<tr>
<th>Dairy</th>
<th>Vegetables</th>
<th>Fish/Shellfish</th>
<th>Nuts and Grains</th>
</tr>
</thead>
<tbody>
<tr>
<td>Casein</td>
<td>Alfalfa</td>
<td>Clam</td>
<td>Almond</td>
</tr>
<tr>
<td>Cheddar cheese</td>
<td>Asparagus</td>
<td>Cod</td>
<td>Buckwheat</td>
</tr>
<tr>
<td>Cottage cheese</td>
<td>Avocado</td>
<td>Crab</td>
<td>Corn</td>
</tr>
<tr>
<td>Cow's milk</td>
<td>Beets</td>
<td>Lobster</td>
<td>Corn gluten</td>
</tr>
<tr>
<td>Goat's milk</td>
<td>Broccoli</td>
<td>Oyster</td>
<td>Gluten</td>
</tr>
<tr>
<td>Lactalbumin</td>
<td>Cabbage</td>
<td>Red snapper</td>
<td>Kidney bean</td>
</tr>
<tr>
<td>Yogurt</td>
<td>Carrot</td>
<td>Salmon</td>
<td>Lentil</td>
</tr>
<tr>
<td>Fruits</td>
<td>Celery</td>
<td>Sardine</td>
<td>Lima bean</td>
</tr>
<tr>
<td>Apple</td>
<td>Cucumber</td>
<td>Shrimp</td>
<td>Oat</td>
</tr>
<tr>
<td>Apricot</td>
<td>Garlic</td>
<td>Sole</td>
<td>Peanut</td>
</tr>
<tr>
<td>Banana</td>
<td>Green Pepper</td>
<td>Sole</td>
<td>Pecan</td>
</tr>
<tr>
<td>Blueberry</td>
<td>Lettuce</td>
<td>Trout</td>
<td>3+</td>
</tr>
<tr>
<td>Cranberry</td>
<td>Mushroom</td>
<td>Tuna</td>
<td>0</td>
</tr>
<tr>
<td>Grape</td>
<td>Olive</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Grapefruit</td>
<td>Onion</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Lemon</td>
<td>Pea</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Orange</td>
<td>Potato, sweet</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Papaya</td>
<td>Potato, white</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Peach</td>
<td>Spinach</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Pear</td>
<td>String bean</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Pineapple</td>
<td>Tomato</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Plum</td>
<td>Zucchini</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Raspberry</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Strawberry</td>
<td>0</td>
<td>0</td>
<td>0</td>
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</table>

<table>
<thead>
<tr>
<th>Total IgE</th>
<th>Inside</th>
<th>Outside</th>
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</tr>
</thead>
<tbody>
<tr>
<td>Total IgE</td>
<td>298.0</td>
<td></td>
<td>&lt;=87.0 IU/mL</td>
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</table>

Immune Markers

| Chronic Inflammation
<table>
<thead>
<tr>
<th>IL-1β</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
</tr>
</tbody>
</table>

| TH-1 Cytokine |
| IL-4 |
|       |

| TH-2 Cytokines |
| IL-6 |
|       |

| IL-10 |
|       |

| IL-13 |
|       |

| Miscellaneous |
| Yeast |
| 1+    |

| Cane sugar |
| 1+         |

| Chocolate |
| VL         |

| Coffee |
| VL      |

| Honey |
| 0      |
Examples of Infectious Stressors (#9)

Microscopic Exam Results:

Blastocystis hominis: Many

Mycology (Culture)

*Candida albicans/cabliniensis*  +2 PP

Yeast, not *Candida albicans*  +1 NP

Bacterial Dysbiosis Markers

<table>
<thead>
<tr>
<th>Marker</th>
<th>Value</th>
<th>Reference Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dihydroxyphenylpropionic Acid (DHPPA)</td>
<td>18.1</td>
<td>&lt;= 12.8</td>
</tr>
<tr>
<td>3-Hydroxyphenylacetic Acid</td>
<td>5.8</td>
<td>&lt;= 8.1</td>
</tr>
<tr>
<td>4-Hydroxyphenylacetic Acid</td>
<td>22</td>
<td>&lt;= 29</td>
</tr>
<tr>
<td>Benzoic Acid</td>
<td>0.05</td>
<td>&lt;= 0.05</td>
</tr>
<tr>
<td>Hippuric Acid</td>
<td>600</td>
<td>&lt;= 603</td>
</tr>
</tbody>
</table>

Anti-Candida Antibody

<table>
<thead>
<tr>
<th>Test</th>
<th>Value</th>
<th>Reference Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Candida Immune Complex (serum)</td>
<td>1.2</td>
<td>&lt;= 0.9</td>
</tr>
<tr>
<td>Candida Antibody, IgA (serum)</td>
<td>22</td>
<td>&lt;= 10</td>
</tr>
<tr>
<td>Candida Antibody, IgG (serum)</td>
<td>11</td>
<td>&lt;= 10</td>
</tr>
<tr>
<td>Candida Antibody, IgM (serum)</td>
<td>4</td>
<td>&lt;= 10</td>
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</tbody>
</table>
Examples of Oxidative Stress (#10)

### Oxidative Stress Markers

<table>
<thead>
<tr>
<th>Marker</th>
<th>Reference Range</th>
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</thead>
<tbody>
<tr>
<td>Glutathione (whole blood)</td>
<td>&gt;= 669 micromol/L</td>
</tr>
<tr>
<td>Lipid Peroxides (urine)</td>
<td>&lt;=10.0 micromol/g Creat.</td>
</tr>
<tr>
<td>8-OHdG (urine)</td>
<td>&lt;=16 mcg/g Creat.</td>
</tr>
<tr>
<td>Coenzyme Q10, Ubiquinone (plasma)</td>
<td>0.43-1.49 mcg/mL</td>
</tr>
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</table>

### Cytochrome P-450

<table>
<thead>
<tr>
<th>Result</th>
<th>Gene</th>
<th>internet information</th>
</tr>
</thead>
<tbody>
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<td>📊</td>
<td>CYP1A1 *</td>
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<td>CYP1B1 *</td>
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<td>☑</td>
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<td>☑</td>
<td>CYP2E1</td>
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<td>☑</td>
<td>CYP3A4 *</td>
<td><a href="http://www.genovations.com/gdgen07">www.genovations.com/gdgen07</a></td>
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</tbody>
</table>
Noradrenalin (slowly metabolized) [fight/flight sympathetic]

Adrenalin, VMA (rapidly metabolized) [34 other methylations]
• Oxidative stress from toxins, leaky gut/food allergy, pathogens, other causes, up-regulates transulfuration and down-regulates transmethylation (see Diagram)

• Not incurring oxidative stress via diversion of homocysteine to glutathione may be more important than incurring ravages of hypomethylation

• Methylation defective patients will be more sensitive to oxidative stress from toxicity, allergy and infections
Phase II: COMT heterozygous

<table>
<thead>
<tr>
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<tbody>
<tr>
<td>+ -</td>
<td>COMT</td>
<td>V158M</td>
<td><a href="http://www.genovations.com/gdv158m">www.genovations.com/gdv158m</a></td>
<td>Liver/Gut</td>
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# Heterozygous c677 MTHFR

## MTHFR

<table>
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<tr>
<th>Location: Chromosome 1</th>
<th><em>C677T</em></th>
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<tbody>
<tr>
<td>Your Genotype:</td>
<td>+</td>
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## 5,10-methyltetrahydrofolate reductase: METHYLATION

5,10-methylenetetrahydrofolate reductase (MTHFR) is a key enzyme in folate metabolism, facilitating the formation of methyltetrahydrofolate, a required cofactor in the remethylation of homocysteine (Hcy) to methionine.

### Health Implications
- Heterozygosity for 677 (+/-) results in 30-40% reduction in MTHFR enzyme activity
- Increased risk of elevated homocysteine, esp. if low levels of B vitamins
- Possible methylation impairment, including disrupted neurotransmitter metabolism and synthesis of DNA, carnitine and coenzyme Q10
- Increased risk of autism, depression, schizophrenia, neural tube defects, cardiovascular disease, essential hypertension, diabetic retinopathy, osteoporosis, and cancers of the stomach
- Low levels of vitamins B2, B6, B12, and/or folate often determines the risk of these associated disorders

### Treatment Options
- Ensure adequate intake of folate-rich green vegetables
- Consider supplementation with folic acid (or folic acid or 5-methyltetrahydrofolate), vitamins B2, B3, B6 (pyridoxal 5-phosphate), B12 (or methylcobalamin), and betaine (trimethylglycine)
1) Emotional Stress (e.g., losses, PTSD, vocational, interpersonal, anxiety, depression)

2) Cognitive Stress (e.g., irrational demands and expectations, awfullizing and catastrophizing, victim thinking, blame games, lack of gratitude)

3) Sensory Stress (e.g., pain syndromes, joint/back, phantom pain, sensory processing defect)

4) Metabolic Stress (e.g., ↓ exercise, ↑ pH syndrome X, ↑↓ blood sugar methylation & nutritional [vitamin, amino/fatty acid] abnormalities, osteopenia)

5) Toxic Stress (e.g., heavy metals [e.g., mercury], halogens, porphyrrias, food additives, trans fats, herbicides, petrochemicals, insecticides, fungicides, CO)

6) Immune Stress (e.g., allergies [food and contact], inflammatory and autoimmune disorder, asthma/eczema)

7) Endocrine & Neurotransmitter Stress (e.g., hormonal and cell-to-cell molecules, PMS, aging, andro-menopause, osteoporosis, ↑↑ thyroid, ↑↑ cortisol, ↑ estrogen, ↑ progesterone, ↓ DHEA, ↓ serotonin, ↓ dopamine, ↓ taurine, ↓ endorphins, ↑↑ noradrenalin, ↑ insulin, ↑ GABA, endocannabinoids)

8) Purposelessness Stress (e.g., meaninglessness, inability to live in the Now, lack of spirituality, “higher purpose,” empathy, serenity)

9) Infectious Stress (e.g., lyme, candida, parasites, viral, [nano]bacteria, sinuses, prions, dental, gastrointestinal, other)

10) Oxidative Stress (e.g., vein or arterial blockage, ↓ antioxidants, ↓ fresh air, sleep apnea, ↑↓ Phase I&II detox, CAD, emphysema)

11) Energetic Stress (e.g., microwaves, cell phones, electromagnetic pollution, meridians, geopathic)

12) Structural stress (e.g., TMJ, cancer, ↑↓ joint flexibility, structural & postural abnormalities, obstructions)

What is Your TSL (Total Stress Load)?
Noradrenalin
(slowly metabolized)
[fight/flight sympathetic]

Adrenalin, VMA
(rapidly metabolized)
[34 other methylations]

**From Lord and Bralley text, few items added by presenter**

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Toxins, Phase 1 & 2 SNPs, infections, hypoxia, antioxidant deficiency

Oxidative Stress
Inflammation

---

Noradrenalin
(slowly metabolized)
[fight/flight sympathetic]

Adrenalin, VMA
(rapidly metabolized)
[34 other methylations]
Neurotransmitter Metabolites

Reference Range

Vanilmandelic Acid

0.8

0.4-3.6
What is the relationship between hypomethylation, stressors (such as #5, 6, 9, 10 in diagram above) and mental disorders?

- Why are these factors epidemiologically connected?
  - Noradrenaline is a very important sympathetic driver of fight flight response, perhaps the most important, and hypomethylation of noradrenaline may account for the sympathetic stress observed in hypomethylators and individuals incurring a high load of stressors (such as #5, 6, 9, 10 in diagram above)
• Natural selection advantage of hypomethylation – perhaps why these SNPs are so common
• Hypomethylation “driven” individuals during younger adult, reproductive years are more physiologically adaptive to extra stress
• Analogy to sickle cell trait (malarial resistance heterozygous, homozygous = sickle cell disease)
• To much of a good thing = a bad thing
• Severe hypomethylators in an age of oxidative stress, toxicities, food allergy, chronic infections (Lyme, candida, co-infections) could seriously predispose to mental illness
Noradrenalin (slowly metabolized) [fight/flight sympathetic]

Adrenalin, VMA (rapidly metabolized) [34 other methylations]

**From Lord and Bralley text, few items added by presenter**

Toxins, Phase 1 & 2 SNPs, infections, hypoxia, antioxidant deficiency

Oxidative Stress

Inflammation

Tryptophan, Arginine, PA, Tyrosine

Dihydrofolate (from food)

BH4

BH2

Neurotransmitters (NO, DA, Ser., NE)

BH4

DHFR

Dihydrobiopterin

DHFR   Dihydrofolate reductase
BH2     Dihydrobiopterin

MAT     Methionine adenosyltransferase
SAHH    S-Adenosylhomocysteine hydrolase
CBS     Cystathionine β-Synthase
CGL     Cystathionine γ-lyase
MTHFR   Methylene-tetrahydrofolate reductase
MS      Methionine synthase
BHMT    Betaine homocysteine methyltransferase

α-Ketobutyrate

α-Hydroxybutyrate (Glutathione synthesis)

Fat Digestion

Neurotransmitter

Antioxidant

Sulfated derivative

(Activated Sulfate)

Oxidized

Glutathione

Reduced

Glutathione

Oxidative balance

Detoxification

Pyroglutamate

(Glutathione-wasting)
The Locus Ceruleus Secretes Noradrenalin, a Neurotransmitter, which Ignites Fight/Flight Response

ONE LC NEURON CAN POTENTIALLY IGNITE ALL CELLS IN THE BODY INSTANTLY!

1) Locus Ceruleus - source of **NA** (noradrenalin), the “fuse” which ignites the explosion of the fight or flight emergency response

2) Amygdala – fear (flight), anger, hate (fight), survival emotion

3) Hypothalamus – stimulates **pituitary** which releases **ACTH** (adrenocorticotropin hormone) which stimulates adrenals to release cortisol

4) Spinal cord to preganglionic sympathetic neurons and adrenal medulla - epinephrine

5) Frontal Lobes

6) Cerebral Cortex

ONE LC NEURON CAN POTENTIALLY IGNITE ALL CELLS IN THE BODY INSTANTLY!
IRON, NADH (VIT B3) & BH4 → Phenylalanine → Tyrosine → L-DOPA → Dopamine → NORADRENALINE

NORADRENALIN can be “drained away” via methylation with SAMe and magnesium.
8 Stress-modifying ("anti-NA") Neurotransmitters

Importance of Plasma AA and Urine OA

1. Serotonin – the brain’s “natural Prozac”
2. Dopamine – the brain’s “natural Ritalin”
3. GABA – the brain’s “natural Xanax”
4. Enkephalins/endorphins – the brain’s “natural heroin”
5. Acetylcholine – the brain’s “natural nicotine”
6. Endocannabinoids – the brain’s natural marijuana or THC
7. Taurine – GABAnergic
8. Histamine – no psychototropic drug analogue
TRYPTOPHAN

5-HP
(5-hydroxy tryptophan)

SEROTONIN

N-ACETYL-SEROTONIN

MELATONIN

IRON, BH4
VITAMIN B3 (NIACIN)

PYRIDOXAL-5-PHOSPHATE
VITAMIN B6 (P5P)

PANTETHINE
VITAMIN B5

SAM-e (s-adenosyl methionine)

COPPER INHIBITS

Tryptophan hydroxylase
Synthesis of Dopamine
the neurotransmitter of
frontal lobe activation,
mindfulness, happiness,
motivation and reward

IRON, NADH (VIT B3) & BH4

Phenylalanine

Iron, NADH (VIT B3) & BH4

Tyrosine

Iron, NADH (VIT B3) & BH4

L-DOPA

Pyridoxal-5-phosphate
Vitamin B6

Dopamine

Phenylalanine → Tyrosine → L-DOPA → Dopamine

Genova Diagnostics
The Dilemma

How to downregulate effects of Noradrenalin while upregulating effects of Dopamine, Enkephalins and Thyroid Hormone – SAMe and Magnesium

Tyrosine

Dopamine

Noradrenaline

Thyroid Hormone

Enkephalins
Enkephalins

Met- & Leu-enkephalins, endorphins

D-phenyl-alanine (DPA)

Amino acid precursors tyrosine, glycine, L-phenylalanine, methionine, leucine

Metabolites

synthesis

inhibits

breakdown
Acetylcholine
The Brain’s “Natural Nicotine”

- **Eggs, soy and liver**
- **Deficiency**
- **Vitamin B5 (Pantethine)**
- **AcetylCoA, Choline acetylase (enzyme)**
- **Phosphatidyl Choline (Lecithin)**
- **Choline**
- **Acetylcholine (Ach)**
- **Nicotine**

Nicotine stimulates Ach receptors.
Anandamide is synthesized from N-arachidonoyl phosphatidylethanolamine (NAPE), which synthesized by transferring arachidonic acid from lecithin to the free amine of phosphatidylethanolamine through an N-acyltransferase enzyme.
Ethanolamine and Arachidonate Availability for Anandamide Synthesis

Arachidonic Acid

Pro-inflammatory Eicosanoids
Practical Takeaways - Simple Tobacco Rx

1. SAMe 200 mg. (Jarrow brand is s,s isomers) – 1 bid, 1 hour before meals, and work up to 2-3 capsules 1 hour before meals over first few days
2. Lecithin 1000 mg. – 3 bid
3. 5HTP 50 mg. bid (if on SSRIs or antidepressants), 300 mg. bid if not on antidepressants
4. After on at least 400 mg. of SAMe twice a day, begin Tyrosine 500 mg. – 2-5 bid, 1 hour before meals (don’t want to increase NA)

- Protocol works well even without SAMe or 5HTP
- Rx of other mental disorders more involved
• DSM IV – all mental disorders are “heterogeneous”
• DSM IV Diagnosis of Mood Disorder Patients - 293.83 –
  – Mood disorder secondary to a medical condition (risk factors)
• Can a mental disorder even exist at all which does not have biophysical, diagnosable, “heterogeneous” causes?
In an ideal world - All Mental Health Rx could start with the nutrigenomics evaluation, work towards optimizing genetic expression of common, important and modifiable SNPs, and then use functional medicine and other diagnostic testing to measure outcome success of nutrigenomic Rx.
My Two Favorite DSM Diagnoses of all Time

• 313.1: Misery & unhappiness disorder
  – That’s no one I know!

• 313.23: Selective Mutism
  – Formerly Elective Mutism, AKA deciding to keep yo’ mouth shut!

Which causes which?
Q & A Session
Additional Education Materials:
www.gdx.net

Sample Reports, Interpretive Guides, Kit Instructions, FAQs, Payment Options, and much more!
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- Nutrition

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<td>December 18, 2013</td>
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Additional Questions?

US Client Services: 800-522-4762

Genova Diagnostics offers Medical Education phone appointments for more specific inquiries or questions we did not have time to answer during the webinar.

We look forward to hearing from you!
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Presented by Charles Gant, M.D., PH.D.