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A 26 Year Old Female With Severe Anxiety

The Role of GAD, COMT, MAO

Root Cause and “Downstream” Effect

Case Study by Jess P. Armine DC, RN
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Chief Complaints

What Concerns Her The Most

- OCD
- Severe, Unremitting Anxiety
- Dysautonomia
Symptoms

Gleaned from Oral History and Narrative Written by Pt.

- OCD
- Exhaustion
- Dizziness
- Nausea
- Headaches
- Heat intolerance
- Excessive sweating
- Indigestion
- Bladder infections

- Constipation and other GI issues leading to tremors and muscle twitches,
- Loss of balance
- Difficulty walking and speaking
- POTS
- Sharp lower back pain
- Muscle, chest and stomach aches
- Heart palpitations
- Hot flashes
- Sensitivity to noise and light
- Severe memory loss
- Chronic sore throat.
Timeline of Illness

- **Childhood:** always weak and sick, severe chronic bladder infections which never fully went away as well as chronic coughs and lung issues. Extensive antibiotic use. Born/raised in Poland, now lives in Hong Kong

- **2006**
  - severe depression & symptoms of hormonal imbalance, mild hirsutism and irregular and painful menstruations.
  - Attempted birth control pills numerous times...worsened her depression.

- **2009**
  - headaches, severe fatigue, dizziness and nausea with depression worsening
  - started antidepressant (tried 3 different ones without improvement).

- **2010**
  - quit her job
Timeline of Illness #2

• 2013
  ➢ severe allergies, developed insomnia.

• 2014
  ➢ more agitated and more nervous than usual. Major personality change. I couldn’t relax despite feeling exhausted. My depression went away completely and was replaced with severe anxiety
  ➢ hirsutism started getting really bad
  ➢ lost more than half of my hair

• July 2014,
  ➢ I had 8 amalgam fillings removed in a matter of 3 weeks and recall getting much sicker after that. All symptoms worse with initiation of dysautonomias

• 2015
  ➢ Unable to leave home or prepare my own meals.
  ➢ Can’t move, speak or think for most of the day, even hearing voices of people outside or TV/music being on brings on panic.
  ➢ Just the effort of getting up and taking a few steps leaves me drenched in sweat.
  ➢ I sleep only a few hours a night and I wake up frequently in panic, especially early in the morning.
Lab Testing
Prior to My Consultation

- U/A
- WBC None
- RBC None

- HA1C
- 5.7 5.3 [<6.0]

CRP:  <0.3  (<5.0)

Thyroid:
TSH 1.6  (3/15) [0.27-4.2]
Ft3 4.38  (3/15) (3.9-8.3)
Ft4 13.19 (3/15) [9-20]

Adrenal:
ACTH  2.4  (<10.1)

Sex Hormones:
LH: 2.4 (1/15); 18.3 (3/15) [1-11.4]
FSH: 2.5 (1/15); 3.5 (3/15) [1.7-7.7]
Estradiol 451 (3/15) [161-774]
Prolactin 159 (1/15); 373 (3/15) [102-496]
# Lab Testing

Prior to My Consultation

<table>
<thead>
<tr>
<th>Collect Date</th>
<th>05/06/14</th>
<th>14/08/14</th>
<th>22/10/14</th>
<th>11/11/14</th>
<th>28/03/15</th>
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</thead>
<tbody>
<tr>
<td>Collect Time</td>
<td>13:02</td>
<td>16:53</td>
<td>18:02</td>
<td>09:21</td>
<td>20:26</td>
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<tr>
<td>Arrive Date</td>
<td>05/06/14</td>
<td>14/08/14</td>
<td>22/10/14</td>
<td>11/11/14</td>
<td>28/03/15</td>
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<tr>
<td>Request No.</td>
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<td>C4402260</td>
<td>E4210407</td>
<td>C4559214</td>
<td>E3069771</td>
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<td>Urgency</td>
<td></td>
<td></td>
<td>URGENT</td>
<td></td>
<td>URGENT</td>
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<table>
<thead>
<tr>
<th></th>
<th>Reference Range</th>
<th>Units</th>
</tr>
</thead>
<tbody>
<tr>
<td>Urea</td>
<td>(2.8-8.1)</td>
<td>mmol/L</td>
</tr>
<tr>
<td>Creatinine</td>
<td>(44-80)</td>
<td>umol/L</td>
</tr>
<tr>
<td>Sodium</td>
<td>(136-145)</td>
<td>mmol/L</td>
</tr>
<tr>
<td>Potassium</td>
<td>(3.5-5.1)</td>
<td>mmol/L</td>
</tr>
<tr>
<td>Total Bilirubin</td>
<td>&lt;21</td>
<td>umol/L</td>
</tr>
<tr>
<td>ALP</td>
<td>(35-104)</td>
<td>IU/L</td>
</tr>
<tr>
<td>Total Protein</td>
<td>(66-87)</td>
<td>g/L</td>
</tr>
<tr>
<td>Albumin</td>
<td>(35-52)</td>
<td>g/L</td>
</tr>
<tr>
<td>Globulin</td>
<td>(18-38)</td>
<td>g/L</td>
</tr>
<tr>
<td>ALT</td>
<td>&lt;33</td>
<td>IU/L</td>
</tr>
<tr>
<td>Calcium</td>
<td>(2.15-2.55)</td>
<td>mmol/L</td>
</tr>
<tr>
<td>Phosphate</td>
<td>(0.81-1.45)</td>
<td>mmol/L</td>
</tr>
<tr>
<td>LD</td>
<td>(135-214)</td>
<td>IU/L</td>
</tr>
<tr>
<td>CK</td>
<td>(26-192)</td>
<td>IU/L</td>
</tr>
</tbody>
</table>
Lab Testing
Prior to My Consultation

Borderline anemia based on RBC and H/H.
Relatively low platelet count can mean adrenal issues.
ACTH Stimulation Test

Of all the interventions or tests she was exposed to, this made her feel normal for about 2 days

<table>
<thead>
<tr>
<th>Collect Date</th>
<th>Collect Time</th>
<th>Arrive Date</th>
<th>Arrive Time</th>
<th>Request No.</th>
<th>Time (min)</th>
<th>Cortisol (nmol/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>01/04/15</td>
<td>14:25</td>
<td>01/04/15</td>
<td>14:56</td>
<td>C5170289</td>
<td>0</td>
<td>90</td>
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<tr>
<td></td>
<td>15:25</td>
<td>01/04/15</td>
<td>15:52</td>
<td>C5170290</td>
<td>30</td>
<td>553</td>
</tr>
<tr>
<td></td>
<td></td>
<td>01/04/15</td>
<td>15:52</td>
<td>C5170291</td>
<td>60</td>
<td>782</td>
</tr>
</tbody>
</table>
Genetic SNP’s

- COMT v158m
- COMT (multiple) +/-
- MAO-A r297r
- MAO (multiple)
- GAD C14541T
- GAD C2627A
- DBH (multiple)
- DRD1
- DRD2
- DAO +/-
- DAO +/-
- DAO +/+ - COX
- NUDFS (multi) +/-
- PEMT +/+ - PEMT +/+ - CYP1B1 +/+
- UGT1A1 +/+ - Estrogen Dominance
- Histamine
- Mitochondria
- Choline: Membrane Integrity
Pathway Planner Application

COMT
MAO
GAD
PEMT
DAO
COMT, MAO, DBH

Take Away: A significant level of SNPs gives indication that catecholamines will be slow to metabolize yielding excitatory states

In this case I would be suspicious of hypodopaminergic function based on inflammation, COMT, MAO, DBH and DRD2


Hypodopaminergic Function Impairs Reward-Dependent Behaviors

- Inability to cope with stress
- Increased carbohydrate cravings
- Increased macro-selection of fatty foods
- Reduction of energy expenditure
  - Lower BMR (energy conservation) and Fatigue
- Increased blood pressure
- Increased percent body fat
- Higher Body Mass Index
- Blunted reward response to pleasurable experiences
- Intensified bingeing behavior
- Addictive behaviors
- Impulsive behaviors
- Compulsive behaviors
- Personality disorders
- Poor executive function
- Reduced global cognition

**Reward Deficiency Syndrome: A Function of the DRD2 Gene**

<table>
<thead>
<tr>
<th>Addictive Behaviors</th>
<th>Impulsive Behaviors</th>
<th>Compulsive Behaviors</th>
<th>Personality Disorders</th>
</tr>
</thead>
<tbody>
<tr>
<td>severe alcoholism</td>
<td>attention-deficit disorder hyperactivity</td>
<td>aberrant sexual behavior</td>
<td>conduct disorder</td>
</tr>
<tr>
<td>polysubstance abuse</td>
<td>tics &amp; Tourette Syndrome</td>
<td>Internet gaming</td>
<td>antisocial personality</td>
</tr>
<tr>
<td>smoking</td>
<td>autism</td>
<td>pathological gambling</td>
<td>aggressive behavior</td>
</tr>
<tr>
<td>obesity</td>
<td>Obsessive/Compulsive Disorder</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Take Away:
INCREASED GLUTAMATE CAUSES EXCITATION
Using Glutamine to heal the gut may be ill advised

Association between glutamic acid decarboxylase genes and anxiety disorders, major depression, and neuroticism.
Hettema JM, An SS, Neale MC, Bukszar J, van den Oord EJ, Kendler KS, Chen X.
DAO: Histamine

Take Away: The pt may have difficulty metabolizing histamine resulting in leaky cells.
Take Away: pt. may have trouble re-building her cell walls
Mitochondrial Complex 1 - The Most Important

- **COX** +/-
- **NUDFS** +/-

GSSG gets stuck here

NADH-ubiquinone oxidoreductase (NDUFS) - GSSG will block the entry of the electron donors into the electron transport chain
Oxidized GSH
Time to Think

• Clearly, the patient's neurological system is upregulated
• The genetics point to difficulties in the:
  – Break down of catecholamines (COMT, MAO)
  – Break down of histamine (creation of cell wall hyper permeability)
  – The re-establishment of cell wall integrity (PEMT)

REMEMBER!!!

The Foundation of Life Happens in THE CELL!!
Keep Asking Why?

• Why is there neural upregulation? (etiology*)

• What is the root cause(s) of the dysautonomia?

• Do we need more information to adequately target her treatment?

Etiology “the cause, set of causes, or manner of causation of a disease or condition”.
Lab Testing Adrenal

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Low</th>
<th>Normal</th>
<th>Elevated</th>
<th>High</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serotonin</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>GABA</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Glutamate</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PEA</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dopamine</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Norepinephrine</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Epinephrine</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Cortisol

DHEAS
Initial Immune Pattern.

Global Excitation

Let's look at the sequence of NT patterns as the neuro system’s ability to compensate over time.

About 1 year later. Note: indication of adrenal fatigue.

About 3 years later. Inhibitory NTs are lower & more definite adrenal fatigue.

10 years later, ALL NT’s are on their way down.

15-20 Years. Pretty Much Exhausted.
### Lab Testing

#### HPA/HPT/HPO Axis

<table>
<thead>
<tr>
<th>Test Name</th>
<th>Result</th>
<th>Units</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Estradiol (Saliva)</td>
<td>0.7</td>
<td>L</td>
<td>1.3-3.3 Premenopausal (Luteal)</td>
</tr>
<tr>
<td>Progesterone (Saliva)</td>
<td>66</td>
<td>L</td>
<td>75-270 Premenopausal (Luteal)</td>
</tr>
<tr>
<td>Ratio: Pg/E2 (Saliva)</td>
<td>94</td>
<td>L</td>
<td>Optimal: 100-500 when E2 1.3-3.3 pg/mL</td>
</tr>
<tr>
<td>Testosterone (Saliva)</td>
<td>52</td>
<td>pg/mL</td>
<td>16-55 (Age Dependent)</td>
</tr>
<tr>
<td>DHEAS (Saliva)</td>
<td>4.9</td>
<td>ng/mL</td>
<td>2-23 (Age Dependent)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Test Name</th>
<th>Result</th>
<th>Units</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Free T4 (Blood Spot)</td>
<td>1.9</td>
<td>ng/dL</td>
<td>0.7-2.5</td>
</tr>
<tr>
<td>Free T3 (Blood Spot)</td>
<td>2.8</td>
<td>pg/mL</td>
<td>2.5-6.5</td>
</tr>
<tr>
<td>TSH (Blood Spot)</td>
<td>0.8</td>
<td>µU/mL</td>
<td>0.5-3.0</td>
</tr>
<tr>
<td>TPO (Blood Spot)*</td>
<td>40</td>
<td>IU/mL</td>
<td>0-150 (70-150 borderline)</td>
</tr>
</tbody>
</table>

Again...why?
Lyme Testing

6/3/2014

6/22/2015

IgM

IgG
Assessment of Findings

- **Chronic Lyme disease leading to:**
  - Neural up regulation *(COMT, MAO, GAD)*
  - Neurotransmitter imbalance *(COMT, MAO, GAD)*
  - Adrenal fatigue *(COMT, MAO, GAD)*
  - Hormonal imbalance *(CYP1B1, UGT1A1)*
  - Mitochondrial Dysfunction *(NDUFS, COX)*
  - Leaky gut syndrome (leaky blood brain barrier, leaky mitochondria, etc.) *DAO, Stress, microbes (remember CDR)*
  - Resulting in chronic inflammation causing:
  - Dysautonomias *(POTS, balance, heart palp, heat intolerences, etc.)*
Symptoms Revisited

- OCD (NT Imbalance)
- Exhaustion (multiple etiologies)
- Dizziness (LGS)
- Nausea (LGS)
- Headaches (multiple)
- Heat intolerance (Dysautonomia)
- Excessive sweating (Dysautonomia)
- Indigestion (LGS)
- Bladder infections (? Parasite)
- Constipation and other GI issues leading to tremors and muscle twitches (leaky gut = chronic Inflammation leading to the below)
- Loss of balance
- Difficulty walking and speaking
- POTS
- Sharp lower back pain
- Muscle, chest and stomach aches
- Heart palpitations
- Hot flashes
- Sensitivity to noise and light
- Severe memory loss
- Chronic sore throat.
Order of Treatment

• “Reduce Stress,
• Heal the Cells,
• Heal the Gut,
• Kill the Bugs!!”
Unfortunately this patient lived, at the time, in Hong Kong which is one of the most toxic cities in the world and was in a situation where she had no significant emotional support.

We tried several things to reduce her overall stress but ultimately she needed to move back to her native country (Poland) which turned out to be the final piece of the puzzle that allowed her to heal.
Heal the Cells

- Phospholipids (sunflower lecithin, phosphatidylcholine, preferably liposomal, if possible)

- In numerous consultations generally find that the need for phospholipids is not given a very high priority.

- Often, if we pay attention to cell wall integrity, we correct the major reason that a body will not heal
Heal the Gut

- Digestive enzymes to break down foods to their constituent parts and not create antigens
- Colostrum, serum derived bovine immunoglobulin isolate (reestablish gastrointestinal cell wall patency)
- Demulcent Herbs (Slippery Elm, organic prickly pear, marshmallow root, etc.) to re-create the mucus layer
- Probiotics to reestablish the gut microbiome

Serum derived bovine immunoglobulins:
http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3754419/
http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4020402/
Correct Neurotransmitter Imbalance and Adrenal Fatigue

- Considering the extensive anxiety I began with a pheylated GABA and 5 hydroxy tryptophan to raise GABA and serotonin respectively.
- The result was better control over anxiety but it was not eradicated.
- Use of almost any adrenal substance created neural up regulation so I put that on hold until we could get the microbial issue controlled.
- Eventually, adrenal cortex was successfully utilized.
- DAO enzyme for histamine metabolism.
- Wasn’t able to use SAMe as she reacted upon each trial.

This was a "Band-Aid".

Remember, “There is no dishonor in using a Band-Aid when the patient is bleeding. The dishonor occurs when uses a Band-Aid never look for the cause of bleeding”
Kill the Bugs

• This patient has chronic Lyme disease with numerous downstream effects.
• Once her condition was stabilized sufficiently and she could handle antimicrobials, I explained all choices in treating Lyme disease.
• Including antibiotics, intravenous therapy, numerous alternative methods including herbal treatment, broad biocidal approaches and bio resonance.

Our job is to empower the patient with honest, accurate information that allows them to make informed choices.
In this case...

- The patient chose a broad biocidal approach
- We utilized MMS (chlorine dioxide solution) and very slowly built towards a therapeutic dose of 24 drops per day
- After 2 months she was about 50% better. Followed up with:
  - Colloidal Silver, Biocidin and Artemesia (parasites) for 3 months.
  - Improvement was slow with many exacerbations

Ultimately, the final puzzle piece (as mentioned above) was absenting herself from the toxic environment. This eradicated the ongoing stressors and allowed the almost complete resolution of her condition.
Key Insights

1. The etiology is usually multifactorial
2. Think Root Cause(s) and Downstream effects and be flexible in your treatment approach.
3. Keep the basics in mind. Treat from the foundation upward.
4. Reassess your diagnosis and treatment at intervals.
5. Remember always:

   “When you have eliminated the impossible whatever remains, however improbable, must be the truth” - Sherlock Holmes.
Thank You!