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Most Popular Herbicide
Glyphosate Causes Autism

Stephanie Seneff
MIT CSAIL
April 28, 2014
A Frightening Trend*

AUTISM DIAGNOSES RISING
Almost 1.5% of US children are now diagnosed with autism, according to data from 11 regions in the United States.

If it is an environmental cause contributing to an increase, we certainly want to find it.”*

“Autism is a single-factorial condition”
Outline

• Autism and glyphosate: Introduction
• Glyphosate is TOXIC to humans
• My earlier papers reexamined
• Glyphosate and aluminum
• Glyphosate and arsenic
• Glyphosate and manganese
  – Lactobacillus and anxiety
  – Glutamate and ammonia
  – Mitochondrial disorder
  – Thyroid hormone
  – Impaired bone development
• Recommendations and Summary
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Glyphosate and Autism*

Pearson Correlation Coefficient = 0.99

Glyphosate and Autism*

![Graph showing correlation between glyphosate use and autism](image)

**Pearson Correlation Coefficient = 0.99**


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**Is Glyphosate Nontoxic?**

- Monsanto has argued that glyphosate is harmless to humans because our cells don’t have the shikimate pathway, which it inhibits
- However, our gut bacteria DO have this pathway
  - We depend upon them to supply us with essential amino acids (among many other things)
- Other ingredients in Roundup greatly increase glyphosate’s toxic effects
- Insidious effects of glyphosate accumulate over time
  - Most studies are too short to detect damage
Main Toxic Effects of Glyphosate*

- Kills beneficial gut bacteria and allows pathogens to overgrow
- Interferes with function of cytochrome P450 (CYP) enzymes
- Chelates important minerals (iron, cobalt, manganese, etc.)
- Interferes with synthesis of aromatic amino acids and methionine
  – Leads to shortages in critical neurotransmitters and folate
- Disrupts sulfate synthesis and sulfate transport

*Samsel and Seneff, Entropy 2013, 15, 1416-1463

The Enhancing Effect of Adjuvants*

“Adjuvants in pesticides are generally declared as inerts, and for this reason they are not tested in long-term regulatory experiments. It is thus very surprising that they amplify up to 1000 times the toxicity of their APs [Active Principles] in 100% of the cases where they are indicated to be present by the manufacturer.”

Some Biomarkers for Autism

• Disrupted gut bacteria; inflammatory bowel
• Low serum sulfate
• Methionine deficiency
• Serotonin and melatonin deficiency
• Defective aromatase
• Zinc and iron deficiency
• Urinary p-cresol
• Mitochondrial disorder
• Glutamate toxicity in the brain

These can all be explained as potential effects of glyphosate on biological systems.
Dementia and Autism Have Much in Common

Deaths from Senile Dementia (ICD F01, F03 & 290) plotted against glyphosate applications on corn & soy (R = 0.9933, p <= 1.947e-09) sources: USDA NASS, CDC

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Roundup Safety Claims Disputed*

“It is commonly believed that Roundup is among the safest pesticides. ... Despite its reputation, Roundup was by far the most toxic among the herbicides and insecticides tested. This inconsistency between scientific fact and industrial claim may be attributed to huge economic interests, which have been found to falsify health risk assessments and delay health policy decisions.”


Glyphosate Test Report: Findings in American Mother's Breast milk, urine and water*

• Moms Across America initiative!
• Breast milk levels ranging from 76 ug/l to 166 ug/l are 760 to 1600 times higher than the European Drinking Water Directive allows
• Urine testing shows glyphosate levels over 10 times higher than in Europe
• Monsanto is wrong regarding bioaccumulation

*Posted on Apr 6 2014 - 4:19am by Sustainable Pulse
“Another claim of Monsanto's has been that residue levels of up to 5.6 mg/kg in GM-soy represent "...extreme levels, and far higher than those typically found" (Monsanto 1999).”

*Soy Formula Linked to Seizures in Autism*

"There was a 2.6-fold higher rate of febrile seizures, a 2.1-fold higher rate of epilepsy comorbidity and a 4-fold higher rate of simple partial seizures in the autistic children fed soy-based formula"

*CJ Westmark, PLOSOne March 12, 2014, DOI: 10.1371/journal.pone.0080488.*
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Two Papers

**Is Cholesterol Sulfate Deficiency a Common Factor in Preeclampsia, Autism, and Pernicious Anemia?**
Stephanie Seneff \(^1\), Robert M. Davidson \(^2\) and Jingjing Liu \(^3\)

**Is Encephalopathy a Mechanism to Renew Sulfate in Autism?**
Stephanie Seneff \(^1\), Ann Lauritzen \(^2\), Robert M. Davidson \(^3\) and Laurie Lentz-Marino \(^4\)
The First Paper

• This paper used the US CDC VAERS database to link together preeclampsia, autism and pernicious anemia
• Pernicious anemia is due to cobalamin (B12) deficiency
• Preeclampsia is a strong risk factor for autism
• The symptoms in adverse reactions linked to anemia recapitulate preeclampsia

Glyphosate chelates cobalt which prevents gut bacteria from producing cobalamin

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Figure from Our First Paper*

Figure 1. Feedback loop leading to excess production of nitric oxide and *Desulfovibrio* overgrowth in the gut in autism, resulting in inflammatory bowel disease.

* S. Seneff et al., Entropy 2012, 14, 2265-2290.

Figure from Our Second Paper*

Figure from Our Second Paper*

* Glyphosate depletes glutathione and methionine
* Glyphosate increases ammonia
* Glyphosate increases glutamate

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Autism, Glyphosate, Vaccine Reactions*

Glyphosate application to corn and soy, US

Children with Autism, US

# Adverse Reactions in VAERS

*Collaboration with Nancy Swanson
MIT Computer Science and Artificial Intelligence Laboratory

Glyphosate makes the aluminum (and mercury?) in vaccines much more toxic

# Adverse Reactions in VAERS

*Collaboration with Nancy Swanson
MIT Computer Science and Artificial Intelligence Laboratory
Glyphosate enhances aluminum toxicity

Glyphosate interferes with acetaminophen metabolism

*M. Purgel et al., Journal of Inorganic Biochemistry 103 (2009) 1426–1438

Aluminum & Mercury
Autism & PDD & Anxiety

formula: \( Al + 1.5 \times (Al \text{ w/ } Hg) + 2.0 \times Hg \)

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Glyphosate chelates many metal cations: I suspect many adverse health effects from chelation of aluminum, arsenic, manganese, and cobalt.
Sri Lanka is the first Country to Ban Glyphosate

Hypothesis

Glyphosate, Hard Water and Nephrotoxic Metals: Are They the Culprits Behind the Epidemic of Chronic Kidney Disease of Unknown Etiology in Sri Lanka?

This problem did not exist in Sri Lanka prior to the 1990s.

Acute Kidney Disease Death Rate Plotted Against Glyphosate and GMOs*

*Plot prepared by Nancy Swanson from available data online
Acute Kidney Disease Death Rate Plotted Against Glyphosate and GMOs*

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“The mechanism by which glyphosate disrupts the EPSPS enzyme in plants and microorganism is by chelating the manganese metal co-factor of this enzyme. In other words it steals the ‘ignition key’ of the enzyme.”

Dr. Arden Andersen, D.O.,
Food Plague Primer: Glyphosate and Genetically Engineered Crops
“Fundamentally the herbicidal effect of glyphosate is ultimately due to soil pathogens gaining access to the “weed” thanks to glyphosate’s weakening of the plant and killing of beneficial microbes by the chelation of manganese and other trace elements.”

Dr. Arden Andersen, D.O.,
Food Plague Primer: Glyphosate and Genetically Engineered Crops

This is analogous to glyphosate’s effect on gut bacteria: killing the beneficial bacteria and allowing the pathogens to overgrow.
Glyphosate Depletes Iron, Manganese and Zinc in Plants*

![Bar chart showing the effect of glyphosate on nutrient uptake and translocation by "non-target" plants, Eker, et al. 2008. (*2.5% of recommended herbicidal rate of glyphosate.)](image)


Severe Deficiency in Serum Manganese and Cobalt in Cows*

Eight different farms: all cows tested had glyphosate in the urine

* M. Krüger et al., *J Environ Anal Toxicol* 2013, 3:5
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**Glyphosate Kills Beneficial Bacteria**

- Examined effect of glyphosate and Roundup on three food microorganisms widely used as starters in dairy technologies
  - Two are species of *Lactobacillus*
- Roundup is always more potent than glyphosate, and in all cases, toxic from levels 10–100 times below the lowest agricultural uses (10,000 ppm).
- Unpredictable consequences of Roundup on soil microorganisms have to be considered


**Lactobacillus Depends on Manganese!**

- Many lactic acid bacteria contain very high intracellular manganese levels
  - Scavenges toxic oxygen species, particularly superoxide
- Manganese deprivation suppresses growth

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*Lactobacillus levels are low in the gut in association with autism


Lactobacillus Alleviate Anxiety*

- Patients suffered from chronic fatigue syndrome and associated anxiety
- Patients were treated with probiotic strain of Lactobacillus (control group got a placebo)
- Significant rise in both Lactobacillus and Bifidobacteria in gut
- Significant decrease in anxiety symptoms ($p = 0.01$)
- Supports concept of gut-brain axis (communicate with brain via vagal nerve)

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Anxiety and Autism*

- Specific Phobia: 30%
- Obsessive-Compulsive Disorder: 17%
- Social Anxiety Disorder/Agoraphobia: 17%
- Generalized Anxiety Disorder: 15%
- Separation Anxiety Disorder: 9%
- Panic Disorder: 2%

Glyphosate Application on Corn and Soy Plotted against Anxiety, Panic Disorder and Phobias*

Plots provided by Dr. Nancy Swanson

Bacteria Incorporate Cobalt and Iron into Cobalamin and Heme

Cobalamin

Heme Iron
Bacteria Incorporate Cobalt and Iron into Cobalamin and Heme

Glyphosate chelates cobalt and iron and prevents bacteria from producing these important molecules.

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Glyphosate and Glutamate*

- Acute exposure activates NMDA receptors and voltage-dependent calcium channels
  - Oxidative stress and neural cell death
  - Increased glutamate released into the synaptic cleft → *excessive extracellular glutamate levels*
  - Decreased glutathione content
  - Increased peroxidation of lipids (fats)

- Chronic exposure:
  - Decreased glutamate uptake and metabolism
  - Induced calcium uptake
  - Induced oxidative stress

*http://www.greenmedinfo.com/blog/roundup-weedkiller-brain-damaging-neurotoxin

Glutamine Synthesis Depends on Manganese!

Glutamine synthetase

\[ \text{glutamate} + \text{ATP} + \text{Mn}^{2+} \rightarrow \text{glutamine} + \text{ADP} + \text{PPi} \]

Ammonium and glutamate toxicity in the brain can arise because of insufficient manganese
Glutamate and ammonia both build up to toxic levels because of manganese deficiency

“Alteration of Plasma Glutamate and Glutamine Levels in Children with High-Functioning Autism”*

<table>
<thead>
<tr>
<th>Amino acid</th>
<th>Control</th>
<th>HFA</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Norepinephrine</td>
<td>326.1±61.6</td>
<td>300.3±55.0</td>
<td>0.145</td>
</tr>
<tr>
<td>e-Norepinephrine</td>
<td>168±3.8</td>
<td>167±3.4</td>
<td>0.971</td>
</tr>
<tr>
<td>Arginine</td>
<td>401±17.6</td>
<td>352±16.3</td>
<td>0.079</td>
</tr>
<tr>
<td>Asparagine</td>
<td>408±4.3</td>
<td>451±15.0</td>
<td>0.011</td>
</tr>
</tbody>
</table>

Glutamate: 20.9±4.5 vs 27.9±7.4 <0.002*  
Glutamine: 513.1±48.5 vs 445.8±50.6 <0.0004**

* C. Shimmura et al.
PLoSone October 2011 6(1):e25340

Journal of Personal Science: One Child’s Autism Eliminated by Removal of Glutamate From Her Diet*

By Katherine Reid

First Round:
- Kale, cucumber, cilantro, nuts, seeds, fruits
- Magnesium B-complex, vitamin D3, omega 3 fats (EPA, DHA)
- Probiotics
- Gluten free and casein free (no wheat, no milk)

Child improved significantly but still had autistic behaviors

Second Round:
- ADD: ELIMINATE FREE GLUTAMATE

Child lost the "autism" label!

* blog.sethroberts.net/2013/05/17/journal-of-personal-science-one childs-autism-eliminated-by-removal-of-glutamate-from-her-diet
Glyphosate depletes glutathione and methionine

Glyphosate increases ammonia

Glyphosate increases glutamate

Glyphosate activates NMDA receptors

Glyphosate depletes serotonin

Vitamin D hormone regulates serotonin synthesis. Part 1: relevance for autism

Rhonda P. Patrick and Bruce N. Ames

- Autism is associated with low activated vitamin D and low brain serotonin
  - Vitamin D activates serotonin receptors in the brain
- Estrogen rescues females by boosting serotonin levels in brain
- Recommendation is supplements in both vitamin D and tryptophan (*precursor to serotonin*)

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Autism and Mitochondrial Disorder*

“Five of 11 patients studied were classified with definite mitochondrial respiratory chain disorder, suggesting that this might be one of the most common disorders associated with autism”

Manganese superoxide dismutase plays a critical role in protecting mitochondria from oxidative damage

The iron sulfur cluster in aconitase is highly sensitive to oxidation by superoxide.*

Aconitase Dysfunction and Brain Inflammation in Autism*

- Frozen samples of post-mortem tissues from cerebellum and temporal cortex of autism patients compared with controls.
- Compared to controls:
  - Aconitase activity was significantly reduced in the cerebellum and correlated with low glutathione levels
  - Biomarkers of inflammation were increased


Aconitase & Glutathione in Cerebellum in Autism*

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Maternal Low Thyroid and Autism*

“Severe maternal hypothyroxinemia early in gestation increased the likelihood of having an autistic child by almost 4-fold.”

Thyroid hormone is derived from tyrosine, one of the three aromatic amino acids produced via the shikimate pathway

Dopamine and Thyroid Hormone*

- Like thyroid hormone, dopamine is derived from the aromatic amino acid tyrosine
- Dopamine inhibits thyroid stimulating hormone
  - Corollary: insufficient dopamine leads to overactive thyroid → burnout
- Thyroid hormone promotes synaptogenesis, synaptic vesicle and receptor recycling, neurotransmitter reuptake, and growth factor receptor signaling


Glyphosate and Thyroid Cancer*

Glyphosate applied to Corn & Soy % GE soy & corn crops

[Graph showing Thyroid Cancer Incidence Rate plotted against glyphosate applied to U.S. corn & soy crops (R = 0.988, p <= 7.612e-09) along with %GE com & soy crops R = 0.9377, p <= 2.152e-05. Sources: USDA/NASS; SEER.]*

*Graph kindly provided by Nancy Swanson
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Glyphosate and Bone Development*

• Dams treated with glyphosate in water from days 6 to 15 of their pregnancy
• Effects on pups:
  – Lack of development of the ossification centers of the terminal phalanges (bones in fingers and toes)
  – Larger fontanelles ("soft spot") and incomplete development of skull bones
  – Absence of important bones or parts of bones, shortenings, bendlings, asymmetry, fusions or clefts.
  – Surfactant polyoxyethyleneamine increased glyphosate's toxicity

**Manganese and Bones**

“The multiple cellular effects of Mn deficiency include: decreased bone resorption, production of labile bone, and decreased synthesis of organic matrix. The serum level of Mn in a group of osteoporotic postmenopausal women was significantly lower than age-matched controls.”

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**Osteoblasts build “Ground Substance”**

- Ground substance is made of chondroitin sulfate and osteocalcin – collagen is layered over this
- Poor mineralization results from impaired chondroitin sulfate synthesis

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Chondroitin Sulfate Synthesis in Cartilage depends on Manganese*

• Two critical enzymes are manganese dependent:
  – Polymerase enzyme forms the polysaccharide
  – Galactotransferase incorporates galactose that links the polysaccharide to the protein associated with it.


Perineuronal Nets*

• Perineuronal nets (PNs) formed from chondroitin sulfate attached to hyaluronan, modulate GABAergic inhibitory signaling
• Removal of PNs increased excitability of interneurons in cultures
• They provide an environment rich in anions (negative charge)

Perineuronal Nets*

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- They provide an environment rich in anions (negative charge).

*Might manganese deficiency lead to impaired synthesis of perineuronal nets and increased neuronal excitability leading to cell death?*


Coral Die-Off & Chondroitin Sulfate*

- Large amounts of chondroitin sulfate are adsorbed onto coral.
- Sulfate groups are of paramount importance to the adsorption process.
- Adsorption rate is a direct function of the amount of negative charge.

“Disease Causes Starfish to Lose Arms, Dissolve into White Blobs of Goo” *

- Glyphosate is used to kill seagrass in oyster beds
- "Glyphosate and diuron are among the most frequently detected herbicides in oyster production areas"**
- Starfish eat oysters

**F. Akcha et al. Aquatic Toxicology. 106-107 (pp 104-113), 2012

Recapitulation

- Glyphosate chelates manganese
- Manganese deficiency leads to:
  - Disrupted gut bacteria → anxiety
  - Tyrosine depletion → thyroid disease
  - Glutamate and ammonium toxicity in the brain as well as glutamine deficiency
  - Mitochondrial damage
  - Impaired bone development and osteoporosis
  - Impaired development of perineuronal nets
- Many of these pathologies are associated with autism
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Foods High in Sulfur
Foods High in Manganese

Go Organic!
Summary

• Contrary to popular belief, glyphosate is toxic to humans and is likely the number one factor in the autism epidemic
• Glyphosate’s chelation of rare minerals is a core component of its toxicity
  – Disrupted gut bacteria leads to multiple problems
  – Aluminum and manganese pathology can account for many aspects of autism
• Dementia may well be the same story
• Autism may be treatable through organic diet enriched in sulfur and manganese