Glyphosate: Is it the Primary Cause of the Autism Epidemic?

Stephanie Seneff
MIT CSAIL
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Outline

• Introduction
• Glyphosate and the Gut
• Glyphosate and Manganese
• What you can do!
• Summary
Autism Prevalence: 6 year olds*

glyphosate is total of year indicated + 3 previous years
R = 0.9972, p <= 2.366e-07

**R = 0.9972**

* Figure 15, Seneff et al., Agricultural Sciences, 2015, 6, 42-70
Some Foods Containing Glyphosate
Is Glyphosate Toxic?

- 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 and are themselves toxic.
- Insidious effects of glyphosate accumulate over time.
  - Most studies are too short to detect damage.
Main Toxic Effects of Glyphosate*

• Disrupts gut microbes leading to overgrowth of pathogens and inflammatory/leaky gut syndrome
• 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
  – Leads to disrupted bile flow and impaired fat digestion

*Samsel and Seneff, Entropy 2013, 15, 1416-1463
Glyphosate vs. Other Pesticides: Usage in the United States*

Sobering Statistics on Glyphosate Residues*

• Parts per *trillion* (*ppt*): increased proliferation of breast cancer cells in vitro

• 0.1 ppb:
  – Altered the gene function of over 4000 genes in the livers and kidneys of rats
  – Severe organ damage in rats
  – Permitted level for glyphosate and all other herbicides in EU tap water

• 10 ppb: demonstrated toxic effects on the livers of fish

• 700 ppb: Permitted level for glyphosate in U.S. tap water

• 11,900 ppb: found in Genetically Modified (GMO) soybeans

*http://detoxproject.org/glyphosate-in-numbers/*
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

Plot kindly provided by Nancy Swanson
Glyphosate and the Gut
Autism and the Gut*

“Prospective, controlled studies suggest that as many as 70% of autistic children exhibit chronic GI-related symptoms [1,5,6] including diarrhea, laxative-dependent constipation, abdominal distension, failure to thrive, weight loss, feeding problems, and abdominal pain related to extreme irritability, aggression, and self-injury.”

LEAKY GUT

undigested food particles / toxins

tight junctions

normal

leaky

inflammatory response to intruders spreads throughout the body

blood vessel

lymphatic vessel
Glyphosate and the Gut: Pathogen Overgrowth*

• Glyphosate is an antimicrobial agent that preferentially kills beneficial microbes, allowing pathogens to flourish in the gut

• Immune cells invade the gut and release inflammatory cytokines
  – This causes increased risk to inflammatory bowel diseases such as Crohn’s and ulcerative colitis

Pathogen Overgrowth in Poultry Microbes Exposed to Glyphosate*

Glyphosate and the Gut: Digestive Enzymes

• Glyphosate has been found as a contaminant in digestive enzymes trypsin, pepsin and lipase*
• Trypsin impairment prevents proteins like gluten in wheat from being digested
• Undigested proteins induce release of zonulin which opens up gut barrier**
• Zonulin lingers because trypsin is defective

Trypsin, Pepsin and Lipase are all contaminated with glyphosate*

<table>
<thead>
<tr>
<th>Enzyme</th>
<th>Glyphosate (PPB)</th>
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<tbody>
<tr>
<td>Pepsin (ELISA)</td>
<td>&lt;40</td>
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<tr>
<td>Pepsin (GC-MS)</td>
<td>430</td>
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<tr>
<td>Pepsin (HPLC-MSMS)</td>
<td>290</td>
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<tr>
<td>Trypsin (ELISA)</td>
<td>62</td>
</tr>
<tr>
<td>Lipase (ELISA)</td>
<td>24</td>
</tr>
</tbody>
</table>

* A Samsel and S Seneff. Journal of Biological Physics and Chemistry 2017;17: 8-32
A Scenario for Gluten Intolerance

- Leaky brain barrier
- Autoimmune neurological disease
- Zonulin
- Trypsin defective
- Zonulin released
- Gliadin
- Leaky barrier
- Systemic immune response induces multiple complex symptoms

- Glyphosate in wheat
Glyphosate and Celiac Disease*

*Glyphosate Use on wheat

*Celiac disease

Celiac Disease, Glyphosate and Non Hodgkin’s Lymphoma

• Glyphosate preferentially kills *Bifidobacteria*
• Bifidobacteria are depleted in celiac disease**
• Celiac disease is associated with increased risk to non Hodgkin’s lymphoma***
• Glyphosate itself is also linked directly to non Hodgkin’s lymphoma****

****M. Eriksson et al., Int J Cancer. 2008 Oct 1;123(7):1657-63.
Hospital discharge diagnoses (any) of Inflammatory Bowel disease (Crohn’s and Ulcerative Colitis ICD 555 & 556) plotted against glyphosate applied to corn & soy ($R = 0.9378$, $p \leq 7.068e^{-08}$)

Sources: USDA & CDC

*Figure 20, NL Swanson et al. Journal of Organic Systems 9(2), 2014, p. 25.*
Glyphosate Induces Antibiotic Resistance*

• Actinobacteria produce a free radical scavenger in response to glyphosate that provides resistance to a wide range of antibiotics, including penicillin.

• E. coli exposed to glyphosate develop an "efflux pump" that increases resistance to the fluoroquinolone Ciprofloxacin and the aminoglycoside Kanamycin.
  – Same effect observed in Salmonella exposed to glyphosate.

Glyphosate Usage and Papers on Antibiotic Resistance

![Graph showing the relationship between glyphosate usage and antibiotics resistance papers over time.]

A BTBR Mouse Model of Autism*

These mice had all the mouse features of autism
They were fed “standard rodent chow” – glyphosate contaminated?

Some features in the gut:

• Reduced levels of bile acids
  – Due to impaired CYP7A1 activity in the liver
• Further reduced levels of secondary bile acids
  – Impaired metabolism by gut microbes
• Reduced levels of Lactobacillus and Bifidobacteria
  – Microbes that metabolize bile acids
  – These microbes are preferentially killed by glyphosate
• Serotonin deficiency
  – Serotonin is derived from tryptophan, a product of the shikimate pathway
    which glyphosate disrupts

BTBR mice have low acetate, and glyphosate disrupts acetate synthesis in gut*

Children with autism had only 3.5 mg/ml acetate in stool samples compared to 5.1 in controls. **

*LN Nielsen et al. Environmental Pollution 2018;233:364e376.
BTBR mice have low acetate, and glyphosate disrupts acetate synthesis in gut*

Elevated pH linked to glyphosate exposure results in small intestinal bacterial overgrowth (SIBO)

*LN Nielsen et al. Environmental Pollution 2018;233:364e376.
**Glyphosate, Pathogens, Autism**

*Figure 2. I Argou-Cardozo and F Zeidán-Chuliá. Med. Sci. 2018; 6: 29.*

**POSTULATION**

Environmental glyphosate levels may deleteriously influence the gut-brain axis by boosting the growth of *Clostridium* bacteria in autistic toddlers.
Evidence Linking Autism to Clostridia Overgrowth*

• 14 autistic children with gut disorder compared to 21 controls
• Significant increase in *Clostridia* species in the gut in autistic children
• Associated with reduced tryptophan levels and increased expression of inflammatory markers
  – Tryptophan is a product of the shikimate pathway, which glyphosate blocks
  – Macrophages in inflamed tissue take up tryptophan, reducing bioavailability to the brain
• Proposed role for antibiotics
  – Glyphosate is a patented antimicrobial agent (2010)

*RA Luna et al., Cellular and Molecular Gastroenterology and Hepatology 2017;3(2): 218-230
Elevated Urinary Glyphosate and Clostridia Metabolites With Altered Dopamine Metabolism in Triplets With Autistic Spectrum Disorder or Suspected Seizure Disorder: A Case Study*

William Shaw, PhD

- Triplets: two boys, one girl. Both boys have autism and girl has seizure disorder
- Very high levels of glyphosate in urine in all three
- *Clostridia* overgrowth due to glyphosate disruption of gut microbes
  - Clostridia produce toxins HPHPA and p-cresol, which block the conversion of dopamine to norepinephrine.
  - Damage to neurons in the brain through oxidative stress

*W. Shaw. Integrative Medicine 2017;16(1);50-57.
Recapitulation

• Glyphosate contamination in food proteins makes them hard to break down
  – This leads to autoimmune disease
• Digestive enzymes are contaminated with glyphosate
  – Undigested proteins induce Celiac disease and leaky gut
• Glyphosate is a key factor in the emergence of antibiotic resistant pathogens
• The BTBR mouse model of autism is consistent with glyphosate damage in the gut
• Glyphosate promotes Clostridia overgrowth
  – This induces inflammatory bowel disease, an epidemic today
  – Autism has been linked to Clostridia overgrowth
  – Clostridia release toxins that induce an inflammatory response
Glyphosate and Manganese
“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

Figure 1. Effect of glyphosate* on nutrient uptake and translocation by “non-target” plants, Eker, et al. 2006. (*2.5% of recommended herbicidal rate of glyphosate.)

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

*M. Krüger et al., J Environ Anal Toxicol 2013, 3:5
Low Manganese in Teeth Linked to Autism*

• Studied lead, mercury and manganese levels in tooth enamel of shed primary teeth in 84 children
• Manganese accumulated after birth was down by 60% in autistic children
• No other result was statistically significant

Some Consequences of Manganese Deficiency

- Lactobacillus critically depend on manganese
- Manganese superoxide dismutase protects mitochondria from oxidative damage
- Manganese is essential for detoxing glutamate (neurotoxin)
- Pituitary depends on manganese to release thyroid stimulating hormone
- Chondroitin sulfate synthesis in bones
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

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)

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
It’s not just deficiency!

- Too little manganese in the cortex
- Too much manganese in the brain stem

Excessive manganese in the brain stem is linked to ADHD*

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 synthetetase

![Chemical diagram showing the synthesis of glutamine from glutamate, water, and ammonium with the involvement of manganese.]

Ammonium and glutamate toxicity in the brain can arise because of insufficient manganese.
“Alteration of Plasma Glutamate and Glutamine Levels in Children with High-Functioning Autism”*

<table>
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<th>Amino acid</th>
<th>Control</th>
<th>HFA</th>
<th>p-value</th>
</tr>
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<tbody>
<tr>
<td>Alanine</td>
<td>326.1±61.6</td>
<td>300.3±55.0</td>
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<tr>
<td>α-Aminobutyric acid</td>
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<td>Asparagine</td>
<td>40.8±8.3</td>
<td>43.1±7.0</td>
<td>0.311</td>
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</tbody>
</table>

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

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<tr>
<th>Amino acid</th>
<th>Control</th>
<th>HFA</th>
<th>p-value</th>
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<td>Leucine</td>
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<td>Lysine</td>
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<td>Serine</td>
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<tr>
<td>Tyrosine</td>
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<tr>
<td>Urea</td>
<td>3976.3±818.7</td>
<td>3759.9±773.3</td>
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<tr>
<td>Valine</td>
<td>200.2±29.4</td>
<td>217.1±29.7</td>
<td>0.062</td>
</tr>
</tbody>
</table>

What you can do!
Go Organic!

Wholefoods: Sign at Entrance

Foodland: organic shelf
Eat Natural Probiotic Foods

• Sauerkraut and apple cider vinegar contain acetobacter, one of the very few microbes that can metabolize glyphosate
• Kombucha and kimchi do too!
Eat Foods Containing Manganese

But be aware of a possibility of too much manganese being toxic → ADHD
Summary

• Glyphosate (from Roundup) is pervasive in our environment
  – I believe it is the primary cause of the autism epidemic
• Glyphosate blocks the shikimate pathway in gut microbes, causing deficiencies in amino acids, neurotransmitters and folate
• Glyphosate induces leaky gut and inflammatory gut, and disrupts digestive enzymes, causing Celiac disease
• Glyphosate causes Clostridia overgrowth leading to neurotoxins that cause excess dopamine
• Glyphosate is a chelator and it binds tightly to manganese, disrupting the liver’s distribution of manganese to the tissues
  – Results in simultaneous manganese deficiency and manganese toxicity, as well as glutamate toxicity
  – Lactobacillus depend on manganese to thrive and they alleviate anxiety
• Organic diet and probiotic foods are strategies to heal