The Myriad Ways Glyphosate Causes Autism and the Myriad Ways You can Heal Your Child

Stephanie Seneff
MIT CSAIL
AutismOne
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Outline

• Introduction
• Glyphosate and the Gut
• Glutamate Excitotoxicity
• Mineral Disruption
• Glyphosate Displacing Glycine in Protein Synthesis
• Dysfunctional PEP Carboxykinase (PEPCK): Multiple Consequences
• How to Safeguard Yourself and Your Family
Roundup and GMO Crops

GMO Roundup-Ready corn, soy, canola, sugar beets cotton, tobacco and alfalfa

What is glyphosate?
**Roundup as a Desiccant/Ripener just before Harvest**

Wheat, Oats, Barley, Rye, Sugar cane, Beans, Lentils, Peas, Flax, Sunflowers, Pulses, Chick Peas

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**Glyphosate!!**

- Glyphosate is now the #1 herbicide in use in the U.S. and is increasingly used around the world
  - Patented by Monsanto in the mid 1970’s

- Introduced into the US food chain in 1974
- Came out from under patent in 2000

- Inhibits an enzyme in the shikimate pathway involved in the synthesis of tyrosine, tryptophan and phenylalanine (the three aromatic amino acids)

- Huge expansion of GMO corn, soy, cotton and canola crops has led to sharp increases in the last two decades
Shikimate Pathway Disruption

Glyphosate

\[
\text{shikimate} \quad \rightarrow \quad \text{chorismate}
\]

Phenylalanine, tryptophan, 
\(\rightarrow\) Neurotransmitters, thyroid hormone

vitamin K

folate

Evaluating glyphosate use in soybean production

Increased use of glyphosate on herbicide tolerant soybean by farmers (1996-2014)

Late-season spraying increases residues 10-20 fold

Food crops accumulate glyphosate residues

- Thousands of tonnes of glyphosate are introduced into the food chain
- Risk assessment is based on non-representative plants (sprayed less)
- Knowledge gaps points to potentially serious underestimation of health risks

Environmental Working Group Results*

*www.ewg.org/childrenshealth/glyphosateincereal/

Some Foods Containing Glyphosate
Glyphosate in Human Urine Samples*

*Monika Krüger et al., J Environ Anal Toxicol 2014, 4:2

Paper Showing Strong Correlations between Glyphosate Usage and Chronic Disease


Genetically engineered crops, glyphosate and the deterioration of health in the United States of America

Nancy L. Swanson¹, Andre Leu²*, Jon Abrahamson³ and Bradley Wallet⁴

¹ Abacus Enterprises, Lummi Island, WA, USA
² International Federation of Organic Agricultural Movements, Bonn, Germany
³ Abacus Enterprises, Lummi Island, WA, USA
⁴ Crustal Imaging Facility, Conoco Phillips School of Geology and Geophysics, University of Oklahoma, USA

* Corresponding author: andreleu.ai@gmail.com
In 2015, WHO IARC declared glyphosate a “probable carcinogen”
“Although correlation does not necessarily mean causation, when correlation coefficients of over 0.95 (with p-value significance levels less than 0.00001) are calculated for a list of diseases that can be directly linked to glyphosate, via its known biological effects, it would be imprudent not to consider causation as a plausible explanation.”

*NL Swanson et al. Journal of Organic Systems 9(2), 2014, p. 32,

America’s Children are in Trouble!

- It is now "normal" for a kindergarten child to have 12 colds every year and for a baby to have nine
- Fourfold increase in childhood obesity
- Double the asthma rate since the 1980's
- "Chronic illnesses" rose from 1.8% in 1960 to 7% in 2004
  - Today, 43% of US children are chronically ill
- 1 in 6 children in the USA has a neurodevelopmental disability
  - 1 in 38 boys are autistic
- US has the worst neonatal death rate of all industrialized countries
- Today's children in the US will have a shortened life span compared to their parents

Source: http://www.vaccineviolence.com/
Glyphosate and the Gut

Inflammatory bowel disease, autoimmune arthritis, obesity and metabolic syndrome, and nonalcoholic fatty liver disease can all be traced to imbalances in gut microbiome*

*Figure 1. RS Goldszmid and G Trinchieri. Nat Immunol 2012;13(10):932-8.
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, ulcerative colitis as well as Celiac disease (gluten intolerance)


*Figure 20, NL Swanson et al. Journal of Organic Systems 9(2), 2014, p. 25.
**Glyphosate and Celiac Disease**


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**Impaired 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
- Glyphosate induces release of zonulin which opens up gut barrier**
- Undigested proteins in the general circulation induce autoimmune 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 (multiple ongoing lawsuits).

**** M. Eriksson et al., Int J Cancer. 2008 Oct 1;123(7):1657-63.

Pathogen Overgrowth in Poultry Microbes Exposed to Glyphosate*

* Plot provided by Dr. Martin Michener
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

### CASE REPORT

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 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.
“In this work, we state a possible link between Gly-induced dysbiosis and cognitive and motor aggravations in neurodegenerative and neurodevelopmental pathologies, such as autism spectrum disorder (ASD). Hence, we review the negative impact that Gly-induced dysbiosis may have on depression/anxiety, autism, Alzheimer’s and Parkinson’s diseases.”

Recapitulation

- Glyphosate contamination in digestive enzymes makes them defective
  - Undigested proteins induce leaky gut barrier and inflammatory bowel disease
- Celiac disease is associated with increased risk to non-Hodgkin’s lymphoma, which is also linked to glyphosate exposure.
- Glyphosate induces overgrowth of Clostridia species in gut
  - Clostridia release toxins that induce an inflammatory response and prevent dopamine metabolism
  - Clostridia overgrowth can lead to autism
- Inflammation in the brain and excessive neurostimulation by dopamine damages neurons
- Gut-brain axis leads to neurological disease following gut dysbiosis
Glutamate Excitotoxicity

Glyphosate and Glutamate*

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

* Daiane Cattani et al. Toxicology 2014; 320: 34-45.
“Is Agriculture’s Use of Glyphosate Feeding Lake O’s Explosive Algae Blooms?”*

• Sugar cane agriculture is extensive all around Lake Okeechobee in S. Florida, and glyphosate is used both to control weeds and as a desiccant.

• Cyanobacteria can break down the C-P bond in glyphosate and use its phosphorus atom as a fuel source**


Cyanobacteria Feed Red Tide Algae

“Both the coastal red tide and the inland blue-green algae have beset South Florida through the summer, killing vast numbers of fish and other wildlife, including dozens of dolphins, manatees, sea turtles, sharks and eels.” *

• Cyanobacteria feed off of glyphosate (phosphorus source) and produce nitrates from nitrogen

• Red Tide algae flourish, supplied with nitrates produced by cyanobacteria**

  **https://www.sailorsforthesea.org/programs/ocean-watch/nutrients-feed-red-tide
“What California Sea Lions Exposed to Domoic Acid might Teach us about Autism”*

- Toxin domoic acid produced by the Red Tide species, Pseudo nitzschia, is a glutamate analogue
  - It causes behavioral symptoms in sea lions that resemble autism
  - It is neurotoxic, especially in the amygdala and hippocampus
- Autism rates are high in the Pacific Northwest and S. Korea, where domoic acid is a contaminant in seafood
- Glutamate additives in processed foods may also be problematic


Test of Glyphosate Levels in Florida Waterways*

Water sample taken from the coast of Cape Coral, at the mouth of the Caloosahatchee River, where cyanobacteria were present

*https://www.momsacrossamerica.com/orange_juice_positive_forGlyphosate_again
Glyphosate Depletes Iron, Manganese and Zinc in Plants*

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

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 Displacing Glycine in Protein Synthesis
What if Glyphosate could Insert itself into Proteins during Synthesis???

-- Any proteins with conserved glycine residues are likely to be affected in a major way

Extra Piece Sticks Out at Active Site

Substrate no longer fits in active site
Extra Piece Sticks Out at Active Site

Substrate no longer fits in active site

Glyphosate Alanine Proline

glycine

Active Site

Peptide chain

Extra Piece Sticks Out at Active Site

Substrate no longer fits in active site

Glyphosate Alanine Proline

glycine

Active Site

Extra Stuff

Peptide chain
Extra Piece Sticks Out at Active Site

This explains how glyphosate disrupts EPSPS in the shikimate pathway:
Multiple bacteria have developed resistance by replacing active site glycine with alanine and this is the basis for GMO Roundup Ready crops*

*T Funke et al., Molecular basis for the herbicide resistance of Roundup Ready crops. PNAS 2006;103(35):13010-13015.

Inhibition of EPSPS by glyphosate:
Resistant E coli mutant*

*Figure 3, S Eschenburg et al. Planta 2002;216:129-135.
**DowDupont Experiments on Maize**

- Designer gene introduced into maize using CRISPR technology
- Tweaked native EPSP synthase to produce glyphosate-resistant version
- First step: mutate glycine to alanine at residue 101 (GNAG $\rightarrow$ GNAA)
  - Completely erases any glyphosate sensitivity
  - [corresponds to 96 in E coli]
- Modify additional nearby residues to increase space for EPSP substrate


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**Monsanto Study (1989)**

- Study exposed bluegill sunfish to carbon-14 radiolabelled glyphosate
- Measured radiolabel in tissues greatly exceeded measured glyphosate levels
- Proteolysis recovered more glyphosate
  - 20% yield $\rightarrow$ 70% yield

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"Proteinase K hydrolyses proteins to amino acids and small oligopeptides, suggesting that a significant portion of the 14C activity residing in the bluegill sunfish tissue was tightly associated with or incorporated into protein."


Some Predicted Consequences*

- Neural tube defects
- Autism
- Impaired collagen → osteoarthritis
- Steatohepatitis (fatty liver disease)
- Obesity and adrenal insufficiency
- Hypothyroidism
- Impaired iron homeostasis and kidney failure
- Insulin resistance and diabetes
- Cancer

• Glyphosate severely suppresses CYP enzymes in rat liver
• CYP enzymes have a unique FGXGXRCXCXG motif with two and often three critical glycine residues**

Dysfunctional PEP Carboxykinase (PEPCK): Multiple Consequences

Overview of PEP Carboxykinase (PEPCK)

• PEPCK is a crucial enzyme in gluconeogenesis
  – It is a major regulatory enzyme in metabolism
• Defective PEPCK is linked to many diseases and conditions
  – Fatty liver disease
  – Neonatal hypoglycemia
  – Type 1 diabetes
  – Sudden Infant Death Syndrome
  – Fungus overgrowth
  – High oxalate and kidney stones
Basic Chemistry

PEPCK
Oxalacetate + GTP $\rightleftharpoons$ PEP + GDP + CO$_2$

- PEPCK is a *cataplerotic* enzyme and a feeder reaction for downstream metabolic processes
  - Cataplerosis: the removal of intermediate metabolites in the citric acid cycle, to prevent their accumulation in the mitochondrial matrix.
- PEPCK supports the synthesis of many important metabolites by “stealing” oxaloacetate from the citric acid cycle

PEPCK Mimics EPSP Synthase

- EPSP synthase is the enzyme that is disrupted by glyphosate to kill weeds
  - It binds PEP at a site with a highly conserved glycine residue and multiple cationic amino acids
- PEPCK also binds PEP at a site with a highly conserved glycine residue and multiple cationic residues
  - *Glyphosate disrupts PEPCK as well??*
PEPCK and Fatty Liver Disease*

• Mice with defective PEPCK develop dramatic hepatic steatosis
  – TCA cycle intermediates build up and this blocks fatty acid metabolism
• Glucocorticoids in response to physical exercise stimulate gluconeogenesis in liver by promoting PEPCK synthesis**

* Shawn C Burgess et al. JBC 2004; 279(47): 48941-48949

Is Glyphosate Causing an Epidemic in Fatty Liver Disease?

• We have a worldwide epidemic in fatty liver disease today*
• “Multiomics reveal non-alcoholic fatty liver disease in rats following chronic exposure to an ultra-low dose of Roundup herbicide”**
• Glyphosate causes fatty liver disease in humans***

*** PJ Mills et al. Clinical Gastroenterology and Hepatology 2019 [Epub ahead of print].
“Glyphosate Excretion is Associated With Steatohepatitis and Advanced Liver Fibrosis in Patients With Fatty Liver Disease”*

- Patients with liver disease at UC San Diego were carefully screened for NASH
- Glyphosate excretion was significantly higher in patients with NASH than in patients without NASH
  - Patients with advanced fibrosis had significantly higher glyphosate than patients with less fibrosis


Sugar Addicted Newborns: the Silent Epidemic*

- Diabetic moms with high blood sugar supply too much sugar to their fetus during pregnancy
- Infant produces too much insulin, which induces hypoglycemia following birth
  - Symptoms include lethargy, tachycardia, poor feeding, seizures, and even coma
- Excessive growth in utero leads to complicated birth
- Infant normally upregulates PEPCK at birth, but glyphosate exposure could be inhibiting protein activity

*www.dunkthejunk.org/blog/2016/1/19/sugar-addicted-newborns-the-silent-epidemic
Glycine mutation in PEPCK leads to hypoglycemia and liver disease

- Three cases of homozygous mutation of PEPCK in Finland
- All three had a mutation of glycine at residue 309 to arginine which produced a nonfunctional version of the enzyme
- Clinically presented as childhood hypoglycemia, liver dysfunction, and elevations of fumarate and other citric acid cycle intermediates in the urine


Critical diaphragm failure in sudden infant death syndrome*

- “Critical Diaphragm Failure” hypothesis for SIDS
  - Weak diaphragm → breathing difficulties
    (due to PEPCK impairment?)
- PEPCK deficiency in liver → impaired gluconeogenesis
- SIDS often occurs at night after child begins to sleep through the night → acute hypoglycemia

**PEPCK Deficiency: Metabolic Derailments***

Fish exposed to glyphosate had low liver glucose, elevated ALT and AST, and elevated lactate and triglycerides**

*Parvin Hakimi et al. Nutrition and Metabolism 2005: 2:33

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**Could PEPCK Deficiency Cause High Serum Oxalate and Fungus Overgrowth?**

- We have a worldwide epidemic in fungus diseases*
- PEPCK converts oxaloacetate to PEP
- PEPCK deficiency leads to excess oxaloacetate
- White rot fungus synthesizes oxalate from oxaloacetate**
- This leads to accelerated growth and a more pathogenic form

Low Sulfate, High Oxalate Phenotype*

- Gut Dysbiosis
  - Decreased sulfomucins, colitis, IBD, leaky gut
  - Increased susceptibility to pathogens
- Fatty liver disease
  - Reduced detox of heavy metals and toxic chemicals
  - Elevated serum LDL
- Decreased insulin function
- Adrenal insufficiency
- Increased cancer risk
- Stunted growth, slow metabolism
- Serotonin deficiency in brain
- Autism linked to sulfate wasting in kidneys

*Dr. Rostenberg

www.beyondmthfr.com/side-high-oxalates-problems-sulfate-b6-gut-methylation

Autism Linked to Oxalate Crystals*

- Crystals of oxalate form kidney stones and cause great discomfort
- Study has shown at least 3-fold higher serum and urinary levels of oxalate in autistic kids**

*William Shaw, The Role of Oxalates in Autism and Chronic Disorders WAPF, March 26, 2010

Oxalate Causes Sulfate Flush through Urine*

• Sulfate is essential for:
  – Synthesis of extracellular matrix glycoproteins
  – Synthesis of cerebroside sulfate, in myelin in nerve fibers
  – Detoxification of many environmental toxins

• Sulfate is flushed (lost) when kidney oxalate levels are high

• Oxalobacter microbes degrade oxalate but they are killed by antibiotics such as Cipro
  – Oxalate decarboxylase depends on manganese as catalyst**

**A Tanner et al. J Biol Chem. 2001;276(47):43627-34

Recapitulation

• Glyphosate may be disrupting PEPCK in the same way it disrupts EPSP synthase

• If so, it explains glyphosate's well established association with fatty liver disease

• It also explains the epidemic we see today in:
  – autism
  – neonatal hypoglycemia
  – sudden infant death
  – oxalate overload
  – fungus infection
  – type 1 diabetes
How to Safeguard Yourself and Your Family

Go Organic!
Avoid Processed Foods

• Free glutamate (e.g., MSG) is a very common ingredient in processed foods
  – It is neurotoxic, and glyphosate increases its effects
• Other artificial ingredients (artificial flavors and colors) may also cause harm

Some Important Nutrients

• Curcumin
• Garlic
• Vitamin C
• Probiotics
• Methyl tetrahydrofolate
• Cobalamin
• Glutathione
• Taurine
• Epsom salt baths
Biochar, Bentonite and Zeolite to maintain healthy microbial distribution in poultry*


Extracts from Common Plants Can Treat Glyphosate Poisoning*

- Roundup is toxic to hepatic and embryonic cells at doses far below those used in agriculture and at residue levels present in some GM food.
- Extracts from common plants such as dandelions, barberry, and burdock can protect from damage, especially if administered prior to exposure.

*C Gasnier et al. Journal of Occupational Medicine and Toxicology 2011, 6:3
Eat Foods Containing Sulfur

Supplemental Sources of Sulfur*

- glucosamine sulfate
- chondroitin sulfate
- glutathione
- N-acetylcysteine
- alpha lipoic acid
- taurine
- DMSO, MSM
- S-adenosylmethionine (SAMe)
- Epsom salts (Mg-sulfate)

These can have many beneficial effects and are nearly nontoxic

My personal favorite is Epsom salt baths: Magnesium sulfate uptake through the skin

*S Parcell, Alternative Medicine Review 7(1), 2002, 22-44
Flavonoids and Polyphenols!

- Sauerkraut and apple cider vinegar contain acetobacter, one of the very few microbes that can metabolize glyphosate
- Yogurt and kimchi probably do too
Hang Out in the Water at the Seashore

Recommendations from Dr. Zach Bush*

1. Get out into nature. Walk in the woods, barefoot, feel the sunshine – rich environment, breathe in the nutrients in the air
2. Eat probiotics (naturally fermented foods)
3. Eat organic food
   - Demand is dropping the price.
   - Thrive Market – order online
4. Eat more fruits and vegetables
5. Bathe in natural waters

*https://www.youtube.com/watch?v=jWqnkgYtqnw&feature=youtu.be
Summary

• Glyphosate is pervasive in our food supply, and it is far more toxic than we are led to believe
• I believe glyphosate is the primary cause of the autism epidemic, and of many other diseases alarmingly on the rise
  – Glyphosate disrupts the gut microbiome
  – Glyphosate works synergistically with glutamate to cause neurotoxicity
  – Glyphosate chelates minerals, causing widespread deficiencies
• Glyphosate may have a unique mechanism of toxicity involving its role as an analogue of the coding amino acid glycine
• Glyphosate causes fatty liver disease
  – PEPCK suppression could explain this, as well as multiple other issues such as SIDS, hypoglycemia, fungus overgrowth and sulfate deficiency
• A certified organic diet is the best way to minimize glyphosate exposure