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# Glyphosate and Dopaminergic Neurotoxicity: Herbicide Impacts on Parkinson's Disease Development

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## Introduction

- Glyphosate (*N*-(phosphonomethyl) glycine) is the world's most used herbicide [9]. It is the active ingredient in Roundup, the most popular product for pre-sowing weed control [4]
- Agricultural application of glyphosate in the U.S. reached 36 million kg by 2000 [2].
- Parkinson's disease (PD) was first described by Dr. James Parkinson in 1817 as a "shaking palsy." It is a chronic, progressive neurodegenerative disease characterized by both motor and nonmotor features [3]

## Study Aims

- Recent research done in the field has found glyphosate to affect many mechanisms with implications towards.
- Glyphosate is banned or phasing out has begun in at least 10 countries including Mexico, Germany, Saudi Arabia, and Vietnam [8]. According to the Human Rights Watch, cities within the United States, such as Los Angeles, have restricted glyphosate's use.
- The purpose of this meta-analysis is to utilize research from recent years to provide an updated source of information on exactly how glyphosate exposure and PD onset are linked and to propose federal policy to mandate glyphosate restriction in the United States.

## Results/Discussion

❖ Glyphosate exposure causes synaptic terminal alterations which affect the synaptic assembly and neuronal connectivity which triggers the impairment of cognitive function and induces neurotoxicity [6].
- Neuronal exposure to Glyph impairs dendritic development and synaptic spine morphogenesis. It is clearly seen that glyphosate impairs neuron development, including dopaminergic neurons which are first to seen affected by Parkinson's disease [6].
- Glyphosate increased single and double strand-breaks in DNA from concentration of 0.5 mM [5].
- Roundup 360 PLUS, glyphosate and AMPA increased DNA damage (SSBs, DSBs and ALSs formation, alkaline version of comet assay) from the concentration of 5 µM, 250 µM and 500 µM, respectively [11].

❖ Glyphosate exposure alters adaption of gene expression by crossing the blood-brain barrier which may cause tissue injury.
- Two of the most frequently used enzyme biomarkers for cellular damage (LDH and -GT) indicate strong association of pesticides provoking tissue injury, even in low doses (from 125% to 186% over control values) [1].
- Glyphosate exposure increases levels of pro-inflammatory cytokine TNFa in the brain which represents a neuroimmune response to glyphosate exposure [10].
- Glyphosate treatment showed a significant decrease in claudin-5 relative expression at 100 and 1000 µM concentrations [7].

❖ Because glyphosate can diffuse across the blood-brain barrier and high doses of glyphosate (100 uM) can affect BMECs glucose uptake and neurons' metabolic activity, glyphosate may alter brain signals.
- There is dose-dependent glyphosate accumulation in the brain [10].
- Glyphosate decreases claudin-5 so the blood-brain barrier can't be regulated properly [10].

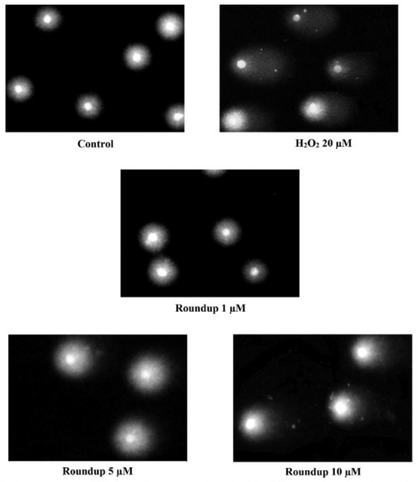


**Fig. 1:** Selected photographs of DNA (comets) of human PBMCs incubated with different concentrations of Roundup 360 PLUS for 24 h and PBMCs incubated with hydrogen peroxide (20 uM) for 15 min on ice (positive control) (comet assay, alkaline version). The photos were achieved using fluorescent microscope with 200 x magnification. Wozniak et al. (2018)

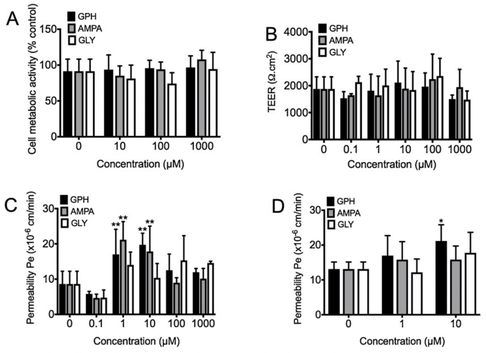


**Fig. 2:** Effects of glyphosate and AMPA on the blood-brain barrier integrity. Martinez A, & Al-Ahmed A. (2019)

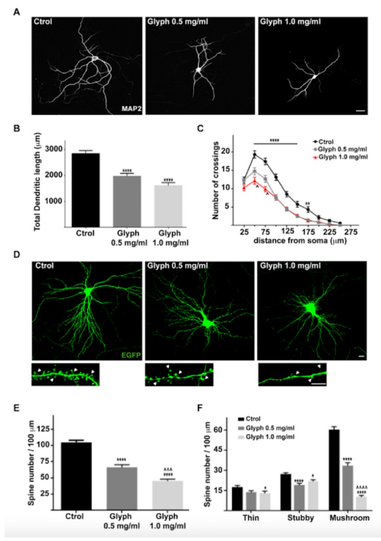


**Fig. 3:** Neuronal exposure to Glyph impairs dendritic development and synaptic spine morphogenesis. Luna et al. (2021)

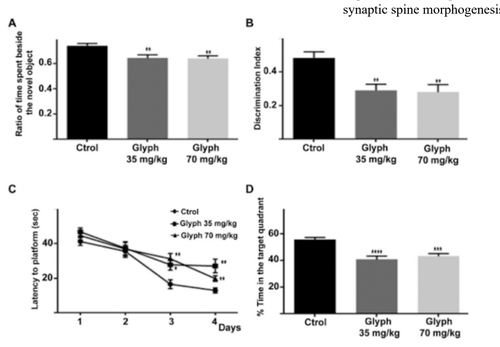


**Fig. 4:** Exposure to Glyph alters cognitive function. Luna et. al (2021)

## Methodology

The purpose of this meta-analysis is to utilize research from 2015-2022 to provide an updated source of information on exactly how glyphosate exposure and PD onset are linked and to propose federal policy to mandate glyphosate restriction in the United States.

## Conclusions

Glyphosate causes public health risks as it has been concluded that its exposure causes synaptic terminal alterations, alter adaption of gene expression by crossing the blood-brain barrier, and affect BMECs glucose uptake and neurons' metabolic activity. Similarly, DDT has been shown to cause significant alterations in vesicular handling of dopamine. In the 1960s, there was a peak in significant research that related DDT with risks to human health; because of this, the EPA was created in 1970 to ban the chemical. Between 2017 and 2022, a wealth of knowledge has been gained with the rapid increase in research of glyphosate's effect on humans. With this rapid increase in research, it is critical that the EPA reevaluate their stance on the chemical's role on public health.

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