Parkinson's and Pesticides:

Exploring the Link Between Glyphosate and Parkinson's Disease

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Abstract

Parkinson's Disease (PD) is a progressive neurodegenerative disorder characterized by accumulation of misfolded α-synuclein and the loss of dopaminergic neurons in the substantia nigra and accumulation of misfolded α-synuclein. While age is the strongest risk factor, environmental exposures to toxic compounds such as pesticides are increasingly recognised as a risk factor for PD. Glyphosate, one of the most widely used herbicides, is currently under scrutiny for its possible link with PD development
Case reports show individuals developing PD after acute or chronic glyphosate exposure. Similarly, epidemiological studies have found correlations between glyphosate exposure and PD. However, the evidence is not conclusive. Other epidemiological studies have found no association between glyphosate and PD. Animal studies have found associations between glyphosate exposure and motor and memory symptoms. Several mechanisms have been proposed for the link between glyphosate and PD. Glyphosate has been shown to affect the gut microbiome, which is highly implicated in PD. Testosterone, which is neuroprotective and lowered in PD, might also be affected by glyphosate. Leydig cells were shown to be damaged in response to glyphosate exposure. Lastly, glyphosate might affect mitochondrial functioning, which in turn leads to oxidative stress, which has been implicated in PD.
Unfortunately, it is unclear whether the effects observed are from glyphosate or rather from glyphosate-based herbicides, a mixture of glyphosate and co-formulants. These co-formulants often have unknown or proprietary compositions and may enhance toxicity.
All in all, while there may be a potential association between glyphosate and PD development, further research is needed to clarify causality and mechanisms.

Table of contents

Introduction

Parkinson's disease (PD) is a progressive neurodegenerative disease where the dopaminergic neurons in the substantia nigra die. PD is most well-known for its motor symptoms such as tremor and bradykinesia, and in addition PD is characterised by non-motor symptoms such as dementia or loss of smell. It is characterised by the buildup of α-synuclein inside nerve cells in PD. α-Synuclein aggregates are the main component of Lewy bodies (Spillantini et al., 1997), of which the exact role is still uncertain.

PD was first discovered in 1817 by Dr. Parkinson (Parkinson, 2002). At the time, PD did not occur very frequently, however, through the years an increase in the cases of PD incidence can be seen (Savica et al., 2016; Willis et al., 2022), so much so that people now speak of the Parkinson Pandemic (Dorsey et al., 2018). Part of this increase in prevalence can be explained by an ageing population – age is the biggest risk factor for PD – and a decrease in smoking , since smoking seems to prevent development of PD (Dorsey & Bloem, 2018; Rossi et al., 2018). Another phenomenon thought to play a big role in the increase of PD prevalence is the increased use of toxins due to industrialisation and intensified agriculture.

Exposure to pesticides has been associated with the development of PD, and it has been shown that pesticide exposure is associated with the development of PD (Reynoso et al., 2024)(Brouwer et al., 2017). Farming – an occupation in which pesticides are often used – is also associated with the development of PD (Petit et al., 2025)(Moisan et al., 2011). Similarly, clear links were found between residential exposure to agricultural chemical application and premature mortality from PD in Washington State (Caballero et al., 2018). Pesticides such as paraquat and rotenone are believed to have links with PD for some time (Sharma & Mittal, 2024; Tanner et al., 2011), however these compounds are not the only pesticides under scrutiny.

While for quite some time research has focused on pesticides like rotenone and paraquat for their potential role in PD, limited research has been conducted to other broadly used pesticides (Liu et al., 2020). Specifically glyphosate is one of the pesticides that is also suspected of playing a role in the development of PD. Glyphosate is an inhibitor of 5-enolpyruvylshikimate-3-phospate synthase (EPSP synthase), an enzyme found in plants but not in animals (Schönbrunn et al., 2001). Glyphosate is the most used pesticide worldwide , and is the main active ingredient in well-known pesticides like RoundUp or TouchDown. Many people are exposed to glyphosate, with glyphosate residues being found in various biofluids of not just the occupational, but also in the general population (Gillezeau et al., 2019). Despite its widespread use, glyphosate remains a controversial chemical in toxicological and health research. It is believed that glyphosate may potentially be neurotoxic (J. Lee et al., 2017), and there is also worry about glyphosate's bioaccumulation in the food chain. Glyphosate was initially thought to be relatively safe since it acts on an enzyme found in plant systems only. However, recent studies are now questioning this assumption, suggesting that its long-term effects, especially at low doses, may have been underestimated (Bloem et al., 2024).

There is much debate about whether or not glyphosate should be allowed to use. On 28 November 2023, the use of glyphosate in the EU was authorised for 10 more years by the European Commission (European Commission, 2023). This was not without controversy (Mie & Rudén, 2022).

The aim of this essay is to create an overview of existing evidence for a link between glyphosate exposure and PD incidence, focusing on epidemiological studies, case reports and animal studies. It is hypothesised that exposure to glyphosate is associated with an increase in PD prevalence in epidemiological studies, and motor function and memory impairments in animal studies. Furthermore, possible mechanisms of how glyphosate can contribute to PD development will be discussed.

Results

Epidemiology

Epidemiological studies

Epidemiological studies find little results between glyphosate exposure and PD development. Of 5 epidemiological studies where subjects had direct exposure to glyphosate, no association was found with PD. Also the 6 studies in which subjects experienced indirect glyphosate exposure did not find an association with PD (reviewed in Chang et al., 2023).

There are however some studies that do find a conservative link between glyphosate exposure and PD mortality. In Washington state, it was found that individuals that had passed away and who were previously were diagnosed with PD and were likely exposed to herbicides associated with glyphosate were 33% more likely to die before the average life expectancy upon PD diagnosis (9.1 years) at 65 years of age (Caballero et al., 2018). This could among others indicate that the disease progress of PD in those exposed to glyphosate is worse. It might also be that people exposed to glyphosate develop PD earlier than those not exposed, leading to more people dying below the 75 years of age. Unfortunately the authors did not investigate the age at PD diagnosis.

Another epidemiological study focussed on smallholding farmers exposed to pesticide and neurobehavioral outcomes in Uganda. Glyphosate exposure was correlated with impaired visual memory (Fuhrimann et al., 2021). The study unfortunately did not look at PD incidence among the farmers. PD is associated with reduced working memory, and therefore not surprisingly, visual memory is often impaired in PD (Lee et al., 2010). Visual memory impairments have also been associated other forms of dementia such as Alzheimer's disease (AD) (Lee et al., 2010; Pavisic et al., 2021), however it is also affected in the healthy ageing process (Ko et al., 2014). Of course, visual impairment is only one of the possible symptoms of PD, and it can also have many other causes. Therefore the significance of this research is limited, it is however interesting that of all the pesticides tested, glyphosate was the only pesticide found to have an effect.

Of course, these epidemiological studies are limited. There could be other factors at play that account for the correlations found between glyphosate use and PD onset. Furthermore, farmers often admit to using a cocktail of pesticides, and this could of course also be a cause of PD development, as opposed to glyphosate use alone being the cause (Fuhrimann et al., 2021).

Exposure levels

Limited evidence in epidemiological studies might be because reference values for exposure to glyphosate are rarely crossed. Glyphosate can be present in food such as breakfast cereal (Liao et al., 2018) and therefore it can reach the gut microbiome through ingestion. Human exposure to glyphosate is usually low and below relevant threshold values. Measuring urinary levels can be useful for estimating actual exposure of humans to substances. This can be compared to reference values such as the acceptable daily intake (ADI) (0.125 mg kg^{-1} bw). ADI is the daily maximum amount of a substance that can be ingested over a lifetime without adverse health effects. To calculate an estimated daily intake, urine samples can be used since this contains traces of glyphosate. It was found that exposure estimates to glyphosate in humans were much lower than the ADI (Niemann et al., 2015). In addition, exposure estimates were lower than concentrations used in EU studies. However, these studies assumed that 20% of glyphosate would be excreted in urine. More recent studies found that only around 1% of ingested glyphosate is excreted in urine (Zoller et al., 2020). A more recent study using the same calculations used by Niemann et al., found that with this new excretion factor, apart from a few cases, glyphosate exposure in non-occupational populations is still well below the ADI.

Therefore it is unlikely that glyphosate exposure will lead to health risks, since most people do not ingest glyphosate in levels that exceeds safety thresholds such as the ADI. However, the ADI is often only tested on acute effects, while long term effects are not taken into consideration. One of the problems with diagnosing PD, is that it develops over a long time and effects only become seeable after extensive damage has already been done. Therefore the question is whether these thresholds are correct.

Case reports

A possible link between glyphosate exposure and PD is further underlined by a number of case reports. Though these are limited, there are multiple case reports of people coming into contact with glyphosate and developing PD several years later. A Japanese man attempted suicide by ingesting glyphosate and developed PD 4 years later (Eriguchi et al., 2019). Another example is the case of a 44 year old woman who developed PD 3 years after having started working in a glyphosate producing chemical factory (Wang et al., 2011). Other case reports showed development of PD after the skin coming into contact with glyphosate. In one of the cases, a man developed a parkinsonian syndrome only a month after he accidentally sprayed himself with glyphosate (Barbosa et al., 2001). One month is remarkably fast to develop parkinsonian syndrome and seems unlikely. The patient's occupation in this case was a gardener who did not wear protective clothing while using herbicides. Therefore, it is likely that he was previously exposed to glyphosate on a regular basis, and that this is the reason for the quick onset of PD. Unfortunately the report does not show how long the patient has been working with glyphosate or other possible herbicides. As for the other case reports, the time between glyphosate exposure and PD onset is much longer and realistic, but because of that it is also harder to exclude other possible causes of PD development.

Animal studies

Glyphosate could possibly be linked to neurological damage. A significant positive association between urinary glyphosate levels and serum neurofilament light chain (NfL) – an indicator of neurodegeneration – was found (Yang et al., 2024), in addition to the elevation of S100B protein – an indicator of nervous system damage – in patients with glyphosate poisoning , indicating that glyphosate is neurotoxic (Lee et al., 2017). Glyphosate can enter the blood, as it was shown that prolonged exposure to low-doses of glyphosate leads to residues of glyphosate in the blood among others (Liu et al., 2022). Furthermore, it has been demonstrated that glyphosate can cross the blood brain barrier (BBB) in mice, where it can elevate pro- and anti-inflammatory cytokins and chemokines in brains of mice exposed to glyphosate, even after a 6 month recovery period (Bartholomew et al., 2024) pro-inflammatory cytokines (Bartholomew et al., 2024).

Once in the brain, glyphosate appears to influence motor behaviour and the dopaminergic system, however the effects of glyphosate on dopamine levels are contradictory. After intraperitoneal injections of glyphosate, a study found a reduction of basal extracellular dopamine levels in the striatum and there was less binding of a specific D1 antagonist in the nucleus accumbens, and this was accompanied by decreases in exploratory behaviour and spontaneous locomotor activity (Hernández-Plata et al., 2015). A reason for this may be a reduced expression of receptors, or that receptor binding is affected by glyphosate. However, it may also be that there is an increase in dopamine release, which was found by other studies that have found that administering glyphosate in the striatum of rats increases dopamine levels (Costas-Ferreira et al., 2024; Faro et al., 2022). On a side not, dopamine was however immediately measured following the injection, which is not representative for exposure in

humans, who are often exposed to low doses for a longer period of time, therefore the translatability of these studies is questionable.
Behaviour was also affected by glyphosate. Injections with glyphosate based herbicides – not pure glyphosate -in mice also resulted in impaired memory and learning (Bali et al., 2019). A well-known animal model for PD is obtained by injecting rodents with the metabolite of 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP). This metabolite is converted in the body to a structure that resembles the herbicide paraquat, and is believed to damage cells in the substantia nigra and thus cause PD (Langston et al., 1983). MPTP- induced dopaminergic neurotoxicity has been widely used as an animal model for PD. Glyphosate-based herbicides in addition to MPTP reduced the number of dopamine transporter (DAT) in the striatum and it reduced the number of tyrosine hydroxylase (TH) in the substantia nigra compared to MPTP alone, but glyphosate-based herbicides on their own showed no effect (Pu et al., 2020). This suggests that glyphosate might perhaps increase the likelihood of developing PD in response to exposure to PD risk factors.

Cell studies

Neurodegeneration in PD is in part believed to be caused by the aggregation of α-synuclein in the brain. Human neuroblastoma cell lines can express endogenous α-synuclein, and are therefore often used to test α-synuclein aggregation in response to certain chemicals. While herbicides with prominent links to PD like paraquat and rotenone led to α-synuclein aggregation, this was not found for neuroblastoma cells treated with glyphosate (Chorfa et al., 2013). However, different research found that glyphosate exposure had cytotoxic effects by increasing oxidative stress and led to activation of apoptotic pathways (Martínez et al., 2020).

Mechanisms

Gut microbiome

Glyphosate specifically works by inhibiting the enzyme 5-enolpyruvylshikimate-3-phosphate synthase (EPSP synthase). This enzyme is an important step in the shikimate pathway in plants, which creates the precursor of three aromatic amino acids. Though human cells do not express the shikimate pathway which glyphosate inhibits, a number of bacteria in the human microbiome do (Puigbò et al., 2022), and these can be affected when water or food containing glyphosate is consumed (fig.1).
The gut microbiome is believed to play an important role in PD progression. Braak's hypothesis suggests that α-synuclein is originally produced in the intestine (Braak et al., 2003). Changes in the gut microbiome might lead to increased α-synuclein. In idiopathic PD, α-synuclein aggregates in the gastrointestinal (GI) tract at least 8 years before motor symptoms occur (Hilton et al., 2014). Changes to the gut microbiome might cause the misfolding and aggregation of α-synuclein. From here, it then spreads to the CNS through the nervus vagus, where it accumulates in the substantia nigra (Holmqvist et al., 2014). Disruption of the gut microbiota is associated with

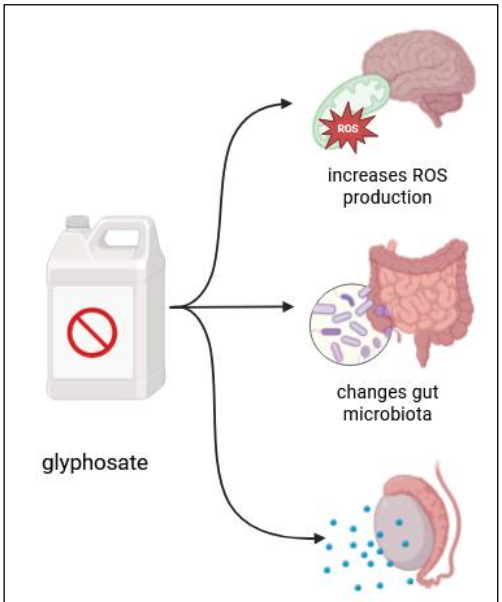

Figure 1. ways in which glyphosate might lead to PD. Glyphosate can lead to an increased ROS production in the brain, changes to gut microbiota and decreases in testosterone production, processes which are all implicated in PD.

neuroinflammation and neurodegenerative disorders (Benakis et al., 2020), and it is also found in PD and its related preclinical models (Morais et al., 2024; Sampson et al., 2016). Generally, the gut microbiome in PD has fewer anti-inflammatory bacteria while pathogenic bacteria are increased (Romano et al., 2021; Wallen et al., 2022). Lactobacilli and Bifidobacteria make up the vast majority of the gut microbiota. Apart from breaking down dietary compounds and its uptake, they also play an important role in protection against infectious, allergic and inflammatory conditions. Lactobacilli and Bifidobacteria are known to be affected by glyphosate (Lehman et al., 2023). This was accompanied by an increase in inflammatory markers and activation of immune cells in rats. These findings suggest that environmental exposures such as glyphosate could indirectly contribute to PD pathology by altering the gut microbiome. Targeting gut dysbiosis through diet, probiotics, or microbiota-directed therapies may be promising research areas for the link between glyphosate and PD.

Though a link between glyphosate and microbiome alterations is suggested which might be related to the development of PD, it appears as if parts the microbiome landscape associated with PD is affected in the opposite way by glyphosate. Lactobacilli and Bifidobacteria, which are increased in PD (Romano et al., 2021), are decreased after glyphosate exposure (Lehman et al., 2023), though an increase in lactobacillus has been found as well (Buchenauer et al., 2022). Similarly, dams that were given glyphosate showed a decrease in abundance of *Akkermansia* (Buchenauer et al., 2022), and offspring of mice that were fed glyphosate during gestation and lactation showed a decreased abundance of *Akkermansia* (Buchenauer et al., 2023). However, in PD, *Akkermansia* appears to be increased (Fang et al., 2021). Of course there can be multiple explanations for this, for example the changes in gut microbiome caused by glyphosate can give rise to the PD phenotype, which could alter the gut microbiome in turn. The changes in microbiome in response to both glyphosate and PD are an interesting topic that hopefully will be explored more in future research. For now however, seeing as how important parts of the gut microbiome change in opposite directions in both PD and glyphosate exposure, a link between glyphosate, the gut microbiome and PD development seems unlikely, though not impossible.

Endocrine changes

Another way in which glyphosate might contribute to the development of PD is by affecting neuroprotective factors like testosterone (fig.1). Testosterone deficiency is a common non-motor symptom in PD, and multiple symptoms like dopamine deficiency, energy loss, depression and other hormonal imbalances are correlated with testosterone deficiency symptoms. Replacement of testosterone has been found to improve motor symptoms in a case study (Mitchell et al., 2006). An animal study that induced catalepsy – a symptom of PD – in rats by giving a D2 antagonist found that testosterone deficiency increased catalepsy, and that replacement was effective in catalepsy remission (Majidi Zolbanin et al., 2014). Androgens such as testosterone and its metabolite dihydrotestosterone have neuroprotective and anti-neuroinflammatory effects (Yang et al., 2020). Leydig cells are responsible for the production of testosterone in the presence of luteinising hormone. Glyphosate was found to decrease testosterone production (Clair et al., 2012; Zhao et al., 2021). A study that looked at the effects of glyphosate on microglia in Leydig cells found that microglia of glyphosate treated cells showed morphological damage, and that ATP production was significantly lowered (Lu et al., 2022). Furthermore, reactive oxygen species (mtROS) were upregulated, a sign of oxidative stress-mediated mitochondrial dysfunction. Interestingly, sex may influence the link between mortality and urinary glyphosate. Men were found to have a higher all-cause mortality compared to females. This could be related to glyphosates effect on testosterone, however in women on a whole lower glyphosate concentrations were found, and other factors such as environment, lifestyle and heredity could also explain this phenomenon (Chen et al., 2025).

Following research by the EPA's Endocrine Disruptor Screening Program (EDSPP and the European Food Safety Authority (EFSA), no interaction of glyphosate with oestrogen, androgen, thyroid and steroidogenic pathways was found (Levine et al., 2020). One of the studies included looked at the effect of glyphosate on testosterone production of Leydig cells and in this case found no effect (Forgacs et al., 2012). The reason that this study did not find an effect and other studies did (Lu et al., 2022; Zhao et al., 2021), might be because this study only looked at testosterone production after 4h, while the other studies looked at long term exposure of glyphosate (24h and 48h). Of course, most people are exposed to glyphosate for a longer time then 4 hours and therefore the studies that look at 24 and 48 hours might be more representative. However whether or not this exposure duration is actually the cause of these conflicting results should be further studied before anything conclusive can be said about this topic. In any case, glyphosates effect on endocrine disruption – which in turn may have an effect on PD development – remains questionable.

Oxidative Stress & Mitochondria

As mentioned before, an important mechanism of action of glyphosate on disruption of neuronal functioning seems to be oxidative stress and mitochondrial dysfunction. When mitochondrial function is impaired, cells may have reduced energy production, which could lead to cellular stress and contribute to diseases linked to mitochondrial dysfunction, such as neurodegenerative disorders and metabolic diseases. Chronic injections of glyphosate in rats were associated with reduced mitochondrial cardiolipin content in the substantia nigra and the cerebral cortex (Astiz et al., 2009). Mitochondrial dysfunction is prominent in PD and is believed to precede neuron degeneration. Through glyphosates impact on mitochondria it can increase ROS production, which in turn leads to oxidative stress and which has been implicated in neurodegenerative disorders. In cell cultures it has been shown that glyphosate and AMPA resulted in more reactive oxygen species (ROS), nitric oxide (NO) and malondialdehyde (MDA) (Martínez et al., 2020)(Kwiatkowska et al., 2014).

Limitations

It is hard to isolate the role of a specific herbicide in the possible development of PD. Farmers are likely to use a multitude of pesticides, and this mixture can present a danger to human health when this was not the case when the substances were tested individually. Co-treatments can be more toxic then individual treatments (Paul et al., 2023). Furthermore, while most research focusses on oral ingestion of glyphosate, glyphosate can also travel through the air and therefore be inhaled (Bifaroni et al., 2024). Ultimately, it appears as if the possible mechanisms in which glyphosate may contribute to PD development are quite indirect – such as by affecting endocrine signalling, inflammation or microbiome disruption. These processes are known to implicate dopaminergic neurons, however a causative effect is harder to test for such indirect pathways.

A previous herbicides that was under scrutiny for having links with PD was paraquat. However, unlike glyphosate, this herbicide causes immediate oxidative stress and is therefore more easily picked up by toxicity studies. Toxicity studies focus mainly on acute effects, even though most farmers and people living in rural areas are exposed to glyphosate for a long time. Another problem is that most tests are on the basis of animal studies, however, PD signs only show after loss of 60-70% of nerve cells. This means that by the time people show potential signs in behaviour, most of the damage has already been done. This is similar for most animal studies, which often look at motor function and memory.

Another big problem in the safety regulations of herbicides is that the companies that produce these chemicals are responsible for proving safety data. Of course, this leads to quite some conflicts of interest, since these companies make money with the sales of these products. Recently, Bayer – the producer of roundup – was found to have withheld brain toxicity studies from EU authorities as opposed to USA authorities (Mie & Rudén, 2023). Following that line, Syngenta – producer of paraquat – still states that their product is safe to use (Tomenson & Campbell, 2011). This raises questions about the trustworthiness of their claims that their products are safe to use.

There is much uncertainty about a possible connection between glyphosate and PD, and this is further complicated by the fact that many studies do not necessarily focus on glyphosate, but rather use glyphosate based herbicides in their studies, which has additional elements and can therefore have different effects (Spulber et al., 2024). While this essay has tried to mainly focus on the effects of pure glyphosate, research should also focus on the glyphosate-based herbicides. This is very relevant for public health, since glyphosate as an herbicide is always used in combination with surfactants, for example as RoundUp®, and it is relevant for future research to investigate the effect of glyphosate on its own, but also how it is generally used and if toxicity changes in this form. This is however complicated by the facts that many of the co-formulants are not disclosed, as is explained further on.

Finally, and most importantly, this essay has mainly focussed on the links between pure glyphosate and PD. In real life however, glyphosate mainly occurs in the form of glyphosate based herbicides, which consist of the active ingredient glyphosate in addition to other chemicals that can help absorption. As a result, the final composition can have a different toxicological profile compared to pure glyphosate. For example, in cell lines it was found that polyoxyethylene 15 tallow amine (POE-15) – a co-formulant of the glyphosate-based herbicide RangerPro – resulted in endoplasmatic reticulum stress, as did RangerPro, however no effects were seen for pure glyphosate (Mesnage et al., 2022). This can explain the differences in effect found between glyphosate-based herbicides and pure glyphosate. It was found that glyphosate-based herbicides produced an effect on glucocorticoid receptor signalling, whereas pure glyphosate had almost no effect (Spulber et al., 2024). This was likely because of the added co-formulants present in the glyphosate-based herbicides, however this could not be checked since the co-formulants are kept secret. Similarly, it was found that glyphosate based herbicides resulted in a more immature neuronal profile in neuroepithelial stem cells (NES) derived from induced pluripotent stem cells (iPSC), and that the differentiation process of these cells was shifted to glial cell fate as

opposed to mature neurons, whereas no effects were found for cells treated exclusively with glyphosate (Reis et al., 2022). This is unsurprising since glyphosate-based herbicides contain surfactants, which will make it easier for glyphosate to enter the cell, however this would also suggest that glyphosate-based herbicides can be more harmful then glyphosate on its own. Unfortunately the type of glyphosate-based herbicide that was used in this study, Roundup Transorb®, has unknown co-formulants, so it is impossible to determine a possible mechanism of action. What makes it even harder to test toxicity is that the composition of co-formulants are kept secret from public and researchers under European and United States law (Straw, 2024). An example of the problems that arise with this policy is the example of co-formulant polyoxyethylene tallow amine (POEA). POEA was found to be more toxic than glyphosate alone in human cell lines (Mesnage et al., 2022). Another study claims that POEA has no adverse effects when used in proper dosages . To determine this, the study looked into previous research of irritation of the skin, eyes, respiratory tract and the gastro-intestinal tract. Most studies find irritation as a result of POEA, however most the concentrations used and that found irritation as a response are not representative of concentrations in which POEA is used, which are much lower. Following this they claim that people are not exposed to values above reference values like the ADI or the no-observed-adverse-effect level (NOAEL), which was based on a single study; 13-week oral toxicology study in rats (Stout, 1990). Whether the study indeed found the NOAEL claimed by Mesnage et al., can however not be checked, and neither can proper research practices be checked, since it concerns an unpublished study by Monsanto Company, a major producer of glyphosate-based herbicides. On a side note, all authors of the study are employed by Bayer or formerly employed by Monsanto, big glyphosate producing companies, therefore since POEA is a beneficial product for the efficacy of glyphosate based herbicides. This may raise questions about the reliability of the study though this does not have to be the case.

POEA is forbidden to be used in glyphosate based products in the EU because in glyphosate based herbicides it was found to be more toxic than the active ingredient glyphosate (European Commission, 2016). This of course can explain why some studies find contradicting results, when one of them focusses on the glyphosate based herbicides while the other uses pure glyphosate. This also makes epidemiological studies less relevant, since they concern exposure to glyphosate-based herbicides instead of pure glyphosate. Rather than testing whether pure glyphosate leads to PD, it is of importance that research focusses on the complete herbicide, since it appears as if this has a much stronger effect. Preferably research can also have access to the co-formulants in the herbicides so that toxicity can be tested.

Conclusion

The aim of the study was to look for associations between glyphosate exposure and PD development. Ultimately, while there is some evidence for an association between glyphosate and PD development, causality has not been proven yet.

Research shows conflicting results. While epidemiological studies find no correlation between glyphosate exposure and PD development, another study found that patients exposed to glyphosate had an increased chance of dying prematurely of PD. There exist a number of case reports in which people exposed to glyphosate developed PD, however on of these cases had a remarkably fast onset time, and the expected delay in onset of PD in the other cases makes it hard to rule out other factors that might cause PD. The lack in evidence found in the epidemiological studies may be because research has found that reference values for glyphosate exposure like the ADI are rarely crossed.

Possible mechanisms through which glyphosate can have an effect are by altering the gut microbiome, increasing oxidative stress, and by affecting the endocrine system. These processes are all implicated in PD pathology. However, the microbiome seems to be affected in a different way after glyphosate exposure than in PD. Furthermore, some studies find no effect of glyphosate on endocrine signalling, though this may in part be explained because of the short exposure time to glyphosate.

Most importantly, some studies suggest that the observed effects of glyphosate may be due to the co-formulants in glyphosate-based herbicides rather than through glyphosate alone.

Based on the current available evidence, it is not possible to say if glyphosate contributes to the development to PD. However, it is clear that glyphosate has an effect on neurotoxicity, the gut microbiome and endocrine signalling.

The lack of consecutive findings might in part be due to the fact that mixing herbicides – including glyphosate – is common practice (Argüelles & March, 2023; Barbieri et al., 2022). These so-called tank-mixes with adjuvants have different properties and can therefore have unknown effects on human health, which can result in conflicting epidemiological data.

Currently, research towards this topic is limited, with many studies focussing on the short term effects of glyphosate, while chronic studies would be more relevant to the topic. Furthermore, there are limited studies done in rodents, and often in these studies glyphosate-based herbicides are used instead of pure glyphosate. Furthermore, it might be beneficial if studies focussed on neurodegeneration instead of neurobehavioral outcomes. Future research might consider comparing neurobehavioral outcomes of a rodent exposed to chronic glyphosate to an established animal model of PD. In addition, future research should focus on the possible mechanisms , including the gut microbiome, oxidative stress and endocrine changes.

All in all, the current body of research underlines the need for more targeted, long-term studies that distinguish between glyphosate and its formulations and clarify underlying mechanisms. Until then, the link between glyphosate and Parkinson's disease remains a topic of ongoing scientific investigation.

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