The inadequacy of current pesticide regulations for protecting brain health: the case of glyphosate and Parkinson's disease

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Parkinson's disease is undergoing the fastest rise in prevalence among neurological diseases worldwide.[1] This growth is caused in part by exposure to environmental toxicants, with a particular concern revolving around exposure to pesticides. Many pesticides cause nigrostriatal cell death and produce parkinsonian signs in exposed animals. Moreover, farmers have an increased risk of developing Parkinson's disease.[1]

There is an intense debate in Europe around glyphosate, with a vote in November, 2023, on renewing its marketing authorisation. Glyphosate is a controversial herbicide because of concerns around public health risks, including cancer. Many individuals are exposed to glyphosate, with the international SPRINT study finding glyphosate residues in faeces of 70% of participants (farmers, their neighbours, and urban residents).[2]

We urgently appeal to governments and policy makers throughout the European Union to vote against extending the marketing authorisation of glyphosate by another 10 years. Our opinion is based on two considerations, illustrated here using Parkinson's disease as an example, although similar concerns apply to other neurodegenerative diseases (eg, Alzheimer's, motor neuron disease) and intellectual disabilities in children.

Current regulatory actions are inadequate. It is impossible to estimate the safety of glyphosate in relation to Parkinson's disease because current regulatory actions—defined by the European Food Safety Authority (EFSA)—have serious shortcomings. First, procedures to test for neurotoxicity are too crude. Experimental animals are exposed to pesticides, and neurotoxicity is assessed primarily by evaluating the occurrence of clinically discernible neurological symptoms in exposed animals. However, in case of the nigrostriatal system, parkinsonian signs arise only after extensive damage has been inflicted, after loss of 60–70% of nerve cells. If, for example, 40% of those cells have died, the test animal seems healthy, but the tested pesticide is anything but safe. Therefore, absence of neurological signs in these animal experiments does not exclude relevant damage. Targeted post-mortem cell counts in relevant brain regions are necessary, but are not part of current regulatory actions.

This shortcoming had long been recognised by international researchers, but was also acknowledged in a recent working conference organised by the EFSA:[3] "Overall, there was broad consensus that the currently existing procedures, that are part of existing regulatory actions, are likely to give us an inadequate insight into the actual neurotoxic actions of specific pesticides for the substantia nigra, and consequently, offer an inadequate assessment of the risk of developing Parkinson's disease in case of human exposure."

Second, glyphosate doses in animal experiments were probably too low and not representative of everyday exposure. The present experiments test glyphosate concentrations that typically reach humans after dietary exposure. However, glyphosate can travel long distances through the air and there are high concentrations of glyphosate and other pesticides in house dust in homes of farmers and residents living nearby farmland,[4] thus creating exposure via skin and inhalation. These entry routes and such high concentrations should be considered explicitly when assessing glyphosate's neurotoxicity.

Third, pesticides can cause neurodegeneration by affecting gut microbiome, as shown in animal studies where glyphosate exposure produced changes in intestinal bacteria.[5] Such microbial changes could act as the first event that triggers a cascade of neurodegenerative processes, spreading from intestinal neurons via the vagal nerve to the brain. Evaluation of changes in gut microbiome and downstream neurodegenerative processes should therefore become part of improved regulatory actions.

Fourth, only isolated pesticides are presently being assessed. However, the reality is that individuals are exposed to so-called cocktails which contain multiple pesticides.[2] Recent work showed that co-exposures to different pesticides results in greater neurotoxicity to dopaminergic neurons than any single pesticide.[6] The identified cocktail included pesticides with different mechanisms of action, including compounds that had not raised concerns previously when tested in isolation. These findings indicate that little can be said about the safety of currently used pesticides, including glyphosate.

Finally, much research on glyphosate has thus far been conducted by industry itself, but they have been shown to omit at least some relevant findings from the evaluation dossier. For example, a relevant study was omitted that linked glyphosate exposure to neurotoxicity in young rats that had been exposed in utero.[7] Independent studies should therefore be part of the risk evaluation.

Taken together, there is a serious data gap when it comes to glyphosate and the risk of neurological diseases. However, this important knowledge gap was not addressed in the reassessment of glyphosate and the risk of neurological diseases.

Glyphosate might be a cause of Parkinson's disease, as indicated by four case studies (summarised here[8]) and one epidemiological study.[9] In an animal experiment, co-exposure to glyphosate plus MPTP, a potent neurotoxin that kills dopaminergic neurons, was associated with greater neurotoxicity than exposure to MPTP alone.[10] Furthermore, exposure to glyphosate is associated with higher levels of urinary neurofilament light protein, an indicator of neural damage in neurodegenerative diseases.[11] These latter effects were seen in the general population—that is, among people not working with glyphosate professionally. Finally, in vitro studies suggest that glyphosate can cause oxidative stress, neuroinflammation and mitochondrial dysfunction, processes that have all been associated with neurodegeneration in the context of Parkinson's disease.[12]

Overall, the evidence is inconclusive, but sufficient to suggest that there is a biologically plausible link between glyphosate exposure and nigrostriatal cell death, and hence a risk of Parkinson's disease. Together with the identified shortcomings in regulatory actions and the rapid growth of Parkinson's disease, this is cause for serious concern.

We offer the following advice to European Union governments and policy makers: first, vote against renewing the marketing authorisation for glyphosate by 10 years, but consider an admission for a briefer period of time, maximally 5 years. Second, urge European authorities to release funding for rapid development of improved regulatory actions, specifically targeting the risk of Parkinson's disease and other neurodegenerative diseases. Third, have glyphosate evaluated according to this new framework by independent scientific institutions, and immediately include other pesticides currently used in Europe in the same evaluation. Only pesticides that demonstrate safety according to these new criteria may continue to be used. In parallel, alternatives to the use of pesticides must be pursued vigorously. Such measures will be likely to help protect our population from Parkinson's disease and other health risks.

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