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Plant protection products and Parkinson's: confirmation of previous findings

The German Federal Institute for Risk Assessment (BfR) reassesses the possibility of occupational diseases in agriculture

Once again the BfR has assessed the risk of Parkinson's disease as a result of the occupational use of plant protection products (PPP). So far, there are no new findings compared with the previous assessments of the BfR (Opinions 033/2006 and 042/2012).

Epidemiological studies from France show that people working in viticulture suffer from Parkinson's disease more frequently than people who work in livestock farming or agriculture. It should be emphasised that this observation has so far been based on correlations (i.e. on observed statistical relationships). However, the causes of this statistical correlation have not yet been analysed.

With regard to the trigger for Parkinson's disease, causal links have so far only been proven for the insecticide rotenone and the herbicide paraquat. However, both active substances are no longer approved in the EU. Although other pesticides (PPP or biocides) are also associated with Parkinson's disease, there is not yet sufficient evidence to establish a direct link between exposure to these active substances and an increased risk of developing Parkinson's disease.

The BfR consider it possible that there may be an association between prolonged and high occupational exposure to certain pesticides and the development of Parkinson's disease. Further research is needed to better understand the causal links between the occurrence of Parkinson's disease and exposure to pesticides.

1 Subject of the assessment

The BfR has reassessed the risk of Parkinson's disease resulting from the exposure of farmers to PPP. Two questions were central to this:

1: How does the BfR assess the risk to users with regard to Parkinson's disease caused by PPP?

2: Does the BfR have any studies on Parkinson's disease caused by PPP (in general or specifically for certain PPP or active ingredients in PPP) that confirm or refute such an assessment?

2 Result

The development of Parkinson's disease (hereinafter referred to as "Parkinson's") is a complex process that is not yet fully understood. Various epidemiological studies indicate a possible link between chronic high occupational exposure to pesticides (PPP or biocides) and the probability of developing Parkinson's. Occupationally exposed users (e.g. winegrowers) have a higher risk of Parkinson's than farmers in livestock farming or arable farming. However, this observation has so far been based on correlations only. A clear aetiology or cause analysis is currently not available.

In principle, pesticides can also have neurotoxic effects. However, their use is then restricted with a view to health protection through appropriate regulatory measures and, if necessary, risk mitigation measures. For example, the insecticide rotenone and the herbicide paraquat both are linked to the development of Parkinson's. This has been proven by animal experiments and mechanistic studies. Therefore, both active substances are no longer approved in the EU. Although other classes of pesticides have also been linked to Parkinson's, there is insufficient experimental or epidemiological evidence to establish a direct link between exposure to these active substances and an increased risk of Parkinson's. Further research is needed in order to better understand causal relationships between pesticide exposure and Parkinson's and to identify active substances or classes of substance that could pose a particular risk.

3 Rationale

An association between exposure to pesticides and the development of Parkinson's in occupationally exposed users has been known for some time (Ascherio et al., 2006; Elbaz et al., 2009; Li et al., 2023; Moisan et al., 2023). Some studies have shown that winegrowers have a higher risk of developing Parkinson's than farmers working in other agricultural sectors (Kab et al., 2017; Perrin et al., 2021).

The insecticide rotenone and the herbicide paraquat – both of which are no longer approved in the EU – have been identified as possible triggers for the development of Parkinson's disease. The experimental data on these active substances as well as on some other substances such as MPTP (a contaminant of the opioid meperidine) were used by the EFSA as the basis for the development of an "Adverse Outcome Pathway" (AOP). This AOP provides a mechanistic understanding of how pesticides can contribute to the development of Parkinson's (Choi et al., 2016; EFSA PPR Panel, 2017; Terron et al., 2018). This enabled further pesticides to be identified as potential neurotoxins (Kan et al., 2022).

Other classes of pesticides such as dithiocarbamates, organochlorines, and organophosphates have also been linked to the development of Parkinson's (Freire and

Koifman, 2012; Hatcher et al., 2008; Narayan et al., 2017). However, clear identification proves to be challenging. Paul et al. (2023) recently published a study in which 68 pesticide active substances were identified showing a strong association with the risk of Parkinson's. To do this, the authors matched the area of agricultural use of each active substance using pesticide use reports from 1974 to 2017 with the lifetime, residential, and workplace addresses of participants in a case-control study in California ("Parkinson's Environment and Genes Study" consisting of 829 Parkinson's patients and 824 controls). The substances mentioned in this study were identified without recall bias based on the exposure reported by the Parkinson's patients themselves and without pre-selection of specific pesticides.

However, no direct causal link between exposure to certain pesticides and the development of Parkinson's was established here or in other case-control studies. The exposure of Parkinson's patients to chemical mixtures (including non-pesticide substances) and the lack of direct and repeated exposure measurements over time pose a considerable challenge in identifying possible pesticides that may be involved in the development of Parkinson's.

In summary, the BfR considers an association between chronic occupational exposure to pesticides and the development of Parkinson's disease to be possible. However, except for rotenone and paraquat, the BfR is currently unable to derive a causal relationship with sufficient certainty. The BfR has already commented on this issue several times in the past (Opinion no. 033/2006 of 27 June 2006 and Opinion no. 042/2012 of 6 December 2012). The BfR currently does not have any new findings that could lead to a change in the previous assessment. However, more research is needed here.

Further information on Parkinson's disease on the website of the BfR

BfR Opinion 042/2012 Association between Parkinson's disease and rotenone
<https://www.bfr.bund.de/cm/343/assoziation-zwischen-der-parkinson-krankheit-und-rotenon.pdf>

BfR opinion 033/2006 Pesticide exposure and Parkinson's disease: The BfR sees an association but no causal link
https://www.bfr.bund.de/cm/343/pestizidexposition_und_parkinson_bfr_sieht_a_ssoziation_aber_keinen_kausalen_zusammenhang.pdf

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About the BfR

The German Federal Institute for Risk Assessment (BfR) is a scientifically independent institution within the portfolio of the Federal Ministry of Food and Agriculture (BMEL) in Germany. The BfR advises the Federal Government and the States ('Laender') on questions of food, chemicals and product safety. The BfR conducts independent research on topics that are closely linked to its assessment tasks.

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