Investigating the Role of Paraquat on the Pathogenesis of Parkinson's Disease

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TOHS AP Research STEM

Abstract

The effects of the herbicide paraquat in the pathogenesis of Parkinson's Disease (PD) was investigated. Paraquat is a common pesticide known for its toxicity in humans, but recent studies suggest that exposure can induce PD. Data was collected through a systematic literature review in 12 papers. Results showed a positive correlation between exposure to paraquat and death of dopaminergic neurons, suggesting that pesticide exposure is a risk factor for Parkinson's Disease.

Introduction

Parkinson's Disease (PD) is a progressive neurodegenerative disease that causes physical tremors and impairs movement. This arises through the degeneration of dopamine-containing cells in the central nervous system. Although the exact cause of PD is unknown, the misfolding of alpha-synuclein, a protein abundant in the substantia nigra pars compacta (SNpc) part of the basal ganglia of the midbrain, was discovered to be a pathogenesis of PD. Of all the factors increasing the risk for a person to develop PD, the newest proposed element involves exposure to pesticides. Scientifically, paraquat (N, N′-dimethyl-4,4′-bipyridinium dichloride) is considered a viologen, and the chemical is known to cause toxicity among organisms. One postulated mechanism of paraquat in regards to PD is its ability to increase the aggregation of alpha-synuclein proteins, thus inducing neuronal cell death in the SNpc. Thus, paraquat may reduce dopaminergic neuronal cells in humans, leading to PD.

Fig 1: The figure shows the difference in dopamine production between a normal person and a PD patient.

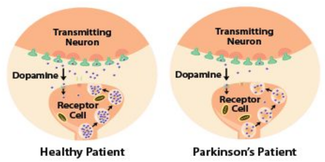
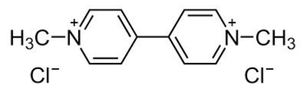


Fig. 2: The diagram shows the chemical structure of paraquat.



Purpose

The purpose of this study is to investigate the effect of paraquat on the death of dopaminergic neuron cells in mice. By addressing the in vivo connections between the pesticide and the disease, scientists can make necessary warnings regarding the use of paraquat. Also, the pathogenesis of neurodegenerative diseases can be more fully understood, which may promote the discovery of new treatments or cures for the disease.

Research Question and Hypotheses

Research Question: Does exposure to paraquat result in the loss of dopaminergic neuronal cells? Should paraquat be considered as an environmental risk factor of PD?

Alternative Hypothesis: Considering articles covering the various mechanisms of paraquat and its interactions with the human body, paraquat is hypothesized to result in the loss of dopaminergic neuronal cells. Therefore, the role of paraquat in the pathogenesis of PD must be an environmental risk factor to consider when exposing oneself to pesticides.

Null Hypothesis: Exposure to paraquat does not result in the loss of dopaminergic neuronal cells. Thus, the need to label paraquat as an environmental risk factor is not necessary.

Methodology

Theoretical Systematic Literature Review was used as the primary research strategy to evaluate the effectiveness of paraquat on PD across multiple authors. When separating these studies into blinded and unblinded tests, a count of n=7 was determined relevant for unblinded studies while a count of n=5 was determined for blinded studies. The data was graphed using Excel in the form of a bar graph, comparing the amount of TH^+ neurons before and after the administration of paraquat. Variability of dosage frequency was not taken into consideration because the p-values which are going to be determined are based on the ratio of affected mice to unaffected mice.

Age of mice was considered irrelevant due to meta analysis of the studies comparing the null and positive results which determined age was not predictive of the outcome between positive or null results. Using these limitations, data was collected from C57BL/6J male mice, and data was separated from unblinded and blinded studies.

Results

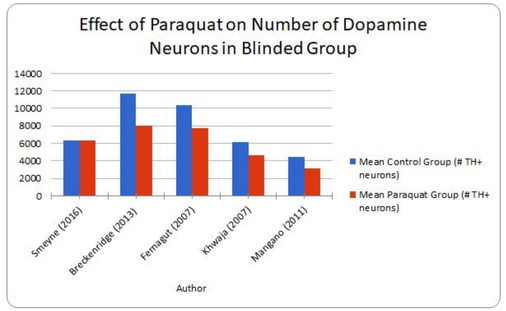


Fig. 8: This figure shows the relationships between paraquat and the number of dopamine neurons in a blinded setting.

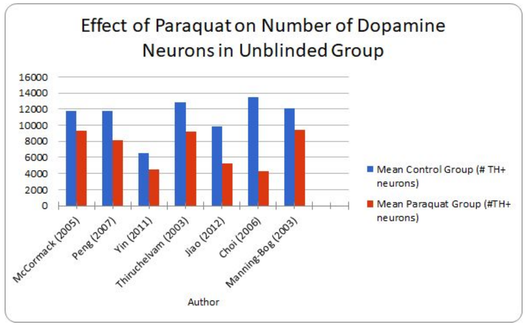


Fig. 9: This graph shows the relationship between paraquat and the number of dopamine neurons in an unblinded setting.

Discussion

When conducting a T-test in the blinded tests, a p-value of 0.02 was found. Since a p-value of $P<.05$ indicates statistical importance, this number indicates that the dosage of paraquat on C57BL/6J male mice results in significantly less TH^+ neurons present, compared to the control mice who did not take any dosage of paraquat. Similarly, when analyzing the effects in a blinded study environment, results indicate a significant P-value of 0.002 as shown in figure 9. In figure 9, all seven papers analyzed showed a decrease in dopaminergic neuronal cells compared to figure 8 in which one study found null results. Both T-tests indicate positive results regarding the possible connection between the effects of paraquat and the death of dopaminergic neuron cells, and whether the studies were blinded or unblinded was found negligible to the overall results between all experiments. Because of the decrease in dopaminergic neurons in mice, it is reasonable to infer that paraquat should be considered as an environmental risk towards PD. Seen through the consistent death of dopaminergic neurons in vivo, paraquat is likely to impose environmental risks to the human population which should be taken into consideration when regulating future pesticides.

Conclusion

Ultimately, this systematic literature review showed the connections between paraquat and its role in the pathogenesis of PD. When this review was conducted, a positive correlation was found due to an overall decrease in TH^+ neurons in the SNpc of mice. In sum, the evidence collected from the data suggests that paraquat is linked to PD by prompting hallmark signs of a person who has PD, with the death of dopaminergic neurons being the focus of the review. Thus, paraquat should be considered as an environmental risk which aids in the development of PD.

Acknowledgements

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