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Examining a Link between Paraquat, Alpha-Synuclein Fibrillation and Neurodegeneration: A Review

By Nikhil Ailaney, Mentored by Professor Mary Boyes

Abstract

Parkinson's disease is a progressive and chronic disorder that causes motor system dysfunction due to a lack of dopamine in the central nervous system. Although this disorder has been researched extensively, the etiology of Parkinson's disease remains unknown. Paraquat, a commonly used pesticide, is a known neurotoxin and is used extensively worldwide. In order to determine if people who live in agricultural regions that use paraquat are more susceptible to Parkinson's disease I examined a possible link between paraquat, the fibrillation of the protein alpha-synuclein and neurodegeneration. To conduct this review, I analyzed epidemiological studies on the correlation between pesticides and Parkinson's disease, research on the link between pesticides and the protein alpha-synuclein and research on the link between alpha-synuclein and Parkinson's disease. From this review, I found that areas that are exposed to high levels of paraquat experience elevated rates of Parkinson's disease in their populations, that paraquat is positively correlated with the aggregation of alpha-synuclein, and that an increase in alpha-synuclein causes neurodegeneration due to an imposed neurotoxicity or through an oxidative stress pathway. This review clearly points to a strong correlation between paraquat exposure and the pathogenesis of Parkinson's disease. This review leads to the recommendation of future research that solely tests the effect of paraquat on alpha-synuclein fibrillation and neurodegeneration in mice. This work would clarify the definitive link between paraquat and the pathogenesis of Parkinson's disease thus informing the practices of those who use pesticides.

Introduction

Parkinson's disease is a chronic and progressive motor system disorder that is caused by the degeneration of dopaminergic neurons in the central nervous system. At the molecular level, Parkinson's disease works by decreasing the concentrations of the neurotransmitter dopamine, a chemical messenger involved in motor messaging, within the central nervous system. Low levels of dopamine in the central nervous system causes motor system dysfunction because the insufficient levels of dopamine lead to an inability for neurons to successfully transmit motor messages. At the organismal level, Parkinson's disease causes tremors, Bradykinesia, and rigidity. These symptoms ultimately lead to a very difficult lifestyle for a person suffering from the disease. As a result, the etiology of Parkinson's disease must be thoroughly examined to help prevent people from acquiring and suffering from the symptoms of Parkinson's disease.

Scientists have extensively researched the etiology of Parkinson's disease to determine whether it is caused by a genetic or environmental mechanism. However, the absolute etiology of Parkinson's disease remains unknown. Recent studies support a more prominent environmental etiology for Parkinson's disease, rather than a biological etiology for the pathogenesis of Parkinson's disease. This is because researchers have found that agricultural pesticides generally are able to work as neurotoxins, which may degenerate or impede dopamine producing nerve cells if the neurotoxins reach the central nervous system. Therefore, pesticide use in agricultural areas is of great concern because pesticides may increase the risk for the pathogenesis of Parkinson's disease if the pesticides directly cause the degeneration of dopaminergic neurons.

Paraquat is a type of herbicide, but it is also commonly referred to as a pesticide. Industrial farmers expose pesticides, such as paraquat, to the environment by spraying them onto their fields to eliminate weeds. This allows paraquat to accumulate in the soil at high concentrations over time. High concentrations of paraquat in the soil are a danger for entire agricultural societies because paraquat may contaminate well water, which is often the primary source of water in agricultural societies. If the contaminated well water is ingested, the herbicide may diffuse into the bloodstream and eventually reach the central nervous system via systemic circulation. Once in the central nervous system, paraquat is able to come into direct contact with and may degenerate dopaminergic neurons. Since paraquat is a pesticide, and the fact that pesticides are known neurotoxins, paraquat is potentially linked to the pathogenesis of Parkinson's disease.

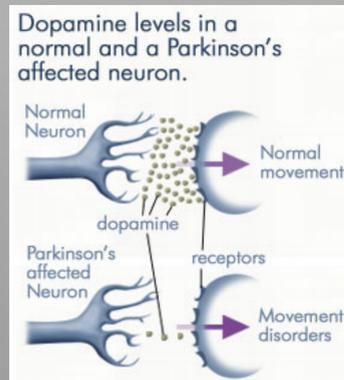
Paraquat may cause Parkinson's disease because of its role as a neurotoxin. A molecular mechanism of neurotoxins is to damage dopaminergic neurons in the central nervous system; this would directly lead to lower concentrations of dopamine in the central nervous system, thus leading to the onset of Parkinson's disease. In order to determine if people living in agricultural regions that use paraquat are at a greater risk of developing Parkinson's disease, this research reviews epidemiological studies on the correlation between pesticides and Parkinson's disease, research on the link between paraquat and the protein alpha-synuclein and research on the link between alpha-synuclein and Parkinson's disease. The goal of this study is to examine the link between paraquat usage and Parkinson's disease, and to recommend areas for future study. A potential future study is one that solely tests the effect of paraquat on alpha-synuclein fibrillation and neurodegeneration in mice to further support the positive link between paraquat and the pathogenesis of Parkinson's disease. Although researchers have concluded that pesticides may cause Parkinson's disease, there is a lack of understanding about which specific pesticides cause the disease and through which molecular pathway the pesticides cause Parkinson's disease. Based on this review that supports a definitive link between paraquat, alpha-synuclein fibrillation, and neurodegeneration, paraquat presents a biological risk because it leads to the pathogenesis of Parkinson's disease, therefore paraquat is a component of the environmental etiology of Parkinson's disease.

Results/Discussion

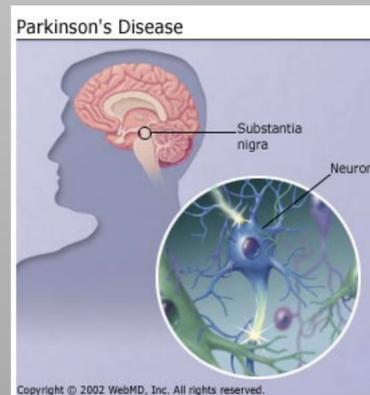
- ❖ According to epidemiological research, there is a positive correlation between pesticide exposure and the pathogenesis of Parkinson's Disease
- ❖ A specific pesticide, paraquat, is associated to neurodegeneration based on its ability to increase alpha-synuclein fibrillation and oxidative stress
- ❖ Alpha-synuclein fibrillation and oxidative stress have been linked to the molecular mechanisms of Parkinson's Disease based on their abilities to degenerate dopaminergic neurons
- ❖ Therefore, paraquat is a cause for the pathogenesis of Parkinson's Disease and is a key component in the environmental etiology of Parkinson's Disease
- ❖ A call for new studies is necessary to further support the claim stated in this research; experiments should be conducted to directly examine paraquat exposure on the degeneration of dopaminergic neurons



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<http://www.webmd.com/parkinsons-disease/parkinsons-faq>

Conclusion

Epidemiological research correlates pesticide exposure to elevated rates of Parkinson's disease in various populations around the world. Research on paraquat and pesticides associates paraquat to neurodegeneration because of its ability to increase alpha-synuclein fibrillation. In addition, research on alpha-synuclein shows that alpha-synuclein is the primary mechanism for Parkinson's disease development at the molecular level. As a result, paraquat is a cause for the pathogenesis of Parkinson's disease and is therefore a key component in the environmental etiology of Parkinson's disease.

Although a conclusion has been made about the environmental etiology of Parkinson's disease, a call for new studies is necessary to further support the claim stated in this research study. An experiment should be conducted to directly test paraquat exposure on the degeneration of dopaminergic neurons. This can be done by exposing mice to water, which would simulate contaminated well water exposure, that varies in paraquat concentrations and then measuring both alpha-synuclein fibrillation and neurodegeneration in the central nervous system of mice. The experimental groups would also be compared to a control group, which consists of mice that are not exposed to paraquat. In this experiment, quantitative data would show paraquat's ability to cause the molecular mechanisms of Parkinson's disease and qualitative data would show the onset of external Parkinson's disease symptoms such as motor dysfunction in the mice. This type of future research would advance Parkinson's disease research to a point where paraquat is widely accepted to be a component in the environmental etiology of Parkinson's disease and thus similar substances to paraquat may come under review because of their potential to cause Parkinson's Disease.

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