Research uncovers how pesticides increase risk for Parkinson's disease

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New research looks at the relationship between pesticides and Parkinson's. Credit: UCLA

Previous studies have shown the certain pesticides can increase the risk for developing Parkinson's disease. Now, UCLA researchers have now found that the strength of that risk depends on an individual's genetic makeup, which in the most pesticide-exposed populations could increase the chances of developing the debilitating disease by two- to six-fold.

In a previous study published January 2013 in the *Proceedings of the National Academy of Sciences*, the UCLA research team discovered a link between Parkinson's and the pesticide benomyl, a fungicide that has been banned by the U.S. Environmental Protection Agency. That study found that benomyl inhibited an enzyme called aldehyde dehydrogenase (ALDH), which converts aldehydes highly toxic to dopamine cells into less toxic agents, and therefore contributed to the development of

Parkinson's.

In this study, UCLA researchers tested a number of other pesticides and found 11 that also inhibit ALDH and increase the risk of Parkinson's, and at much lower levels than those at which they are currently being used, said study lead author Jeff Bronstein, a professor of neurology and director of movement disorders at UCLA.

Bronstein said the team also found that people with a common genetic variant of the ALDH2 gene are particularly sensitive to the effects of ALDH-inhibiting pesticides, and were two to six times more likely to develop Parkinson's than those without the variant when exposed to these pesticides.

The results of the epidemiological study appear Feb. 5, 2014 in the online issue of *Neurology*, the medical journal of the American Academy of Neurology.

"We were very surprised that so many pesticides inhibited ALDH and at quite low concentrations, concentrations that were way below what was needed for the pesticides to do their job," Bronstein said. "These pesticides are pretty ubiquitous, and can be found on our food supply and are used in parks and golf courses and in pest control inside buildings and homes. So this significantly broadens the number of people at risk."

The study compared 360 patients with Parkinson's in three agriculture heavy Central California counties to 816 people from the same area who did not have Parkinson's. Researchers focused their analyses on individuals with ambient exposures to pesticides at work and at home, using information from the California Department of Pesticide Regulation.

In the previous PNAS study, Bronstein and his team determined the mechanism that leads to increased risk. Exposure to pesticides starts a cascade of cellular events, preventing ALDH from keeping a lid on DOPAL, a toxin that naturally occurs in the brain. When ALDH does not detoxify DOPAL sufficiently, it accumulates, damages neurons and increases an individual's risk of developing Parkinson's.

"ALDH inhibition appears to be an important mechanism by which these environmental toxins contribute to Parkinson's pathogenesis, especially in genetically vulnerable individuals," said study author Beate Ritz, a professor of epidemiology at the Fielding School of Public Health at UCLA. "This suggests several potential interventions to reduce Parkinson's occurrence or to slow its progression."

In this study, the research team developed a lab test to determine which pesticides inhibited ALDH. Then the researchers found that those participants in the epidemiologic study with a genetic variant in the ALDH gene were at increased risk of Parkinson's when exposed to these pesticides. Just having the variant alone, however, did not increase risk of the disease, Bronstein said.

"This report provides evidence for the relevance of ALDH inhibition in Parkinson's disease pathogenesis, identifies pesticides that should be avoided to reduce the risk of developing Parkinson's disease and suggests that therapies modulating ALDH enzyme activity or otherwise eliminating toxic aldehydes should be developed and tested to potentially reduce Parkinson's disease occurrence or slow its progression particularly for patients exposed to pesticides," the study states.

Provided by University of California, Los Angeles

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