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WE STILL NEED TO FIND MORE EFFICIENT WAYS TO GROW OUR CROPS TO KEEP A FOOD SUPPLY FOR EVERYBODY

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ENVIRONMENT, CHEMICALS AND DISEASE:

finding exposure triggers that cause Parkinson's, other diseases

by MADELINE CLARK *and* RODRIGO FRANCO-CRUZ

To most, chemicals that are sprayed on crops or home gardens just keep pests and weeds away. To Rodrigo Franco-Cruz, they are more than just chemicals. They are part of the environment and the foundation of his research on how environmental toxicity impacts human and animal health.

Franco-Cruz, an assistant professor in the School of Veterinary Medicine and Biomedical Sciences at the University of Nebraska–Lincoln, earned his Ph.D. in Biomedical Sciences at the National Autonomous University of Mexico, focusing on the chemical aspect of the neuronal response to stress (neurochemistry). His research at UNL now looks at how environmental exposures to toxins (natural) or toxicants (human-made) affect neuronal function. One of the diseases that has been largely associated with environmental toxicants is Parkinson's disease, Franco-Cruz said. During part of his post-doctoral research training at the National Institutes of Environmental Health Sciences (NIEHS), he became interested in how the environment affects human health and since starting his own independent research program in 2009, he has uncovered novel molecular mechanisms by which exposures to environmental contaminants can affect neuronal cell function.

ENVIRONMENTAL EXPOSURES AND HEALTH

Environmental exposures have been linked to a number of diseases, such as asthma and cardiovascular disorders, Franco-Cruz said; with pesticides the evidence is particularly strong for a link with Parkinson's disease. Parkinson's disease is a progressive neurodegenerative disorder that primarily affects motor movement and coordination. "Unfortunately, to date we don't know exactly what's triggering it," he said. Only around 10 percent of the cases have a hereditary aspect. Ninety percent are completely sporadic – meaning there is no clear cause associated with them, he added.

The pesticides themselves are likely not the single cause of Parkinson's disease, "but it is pretty much clear that they are altering neuronal function and eventually or progressively leading to neuronal cell death," he said. "My research group at the UNL Institute of Agriculture and Natural Resources is trying to understand how agricultural pesticides lead to human disease and what makes an individual susceptible to them," Franco-Cruz said.

NEURONAL DYSFUNCTION, PESTICIDES AND AGE

Two primary pesticides have been linked to Parkinson's disease: paraquat and rotenone. Within the last five years, the evidence linking those two pesticides to neuronal dysfunction has strengthened, Franco-Cruz said. Although there is evidence linking those pesticides to Parkinson's neurodegeneration, they are most likely not the only ones, he added. This is because there is a general association with pesticide exposure and Parkinson's disease but in agriculture, many different pesticides are used. This leads to multiple hypotheses in which a combination of different stressors and different pesticides, along with different habits of an individual, can act in conjunction to cause Parkinson's disease.

Even though pesticides and other toxicants are linked to this disease, the major risk factor is age. "For Parkinson's disease, after 60 years the risk of presenting Parkinson's disease just increases exponentially. So, the major risk factor is age. But not everybody who ages gets Parkinson's, so we and many other research groups think that together with genetics, the environment plays an important role," he said.

"It is evident that we still need to find more efficient ways to grow our crops to keep a food supply for everybody, so there is no way to avoid the use of pesticides. However, we need to understand the risk of exposure," he said. Franco-Cruz and his research team aim to understand how pesticides cause neuronal dysfunction. They have found that the mechanisms by which pesticides promote neuronal degeneration are very diverse and depend on their interaction with other risk factors (genes).

"This disease is more like a syndrome in which the intrinsic susceptibility of neuronal cells to the combination of different risk factors, including pesticides, can trigger the degeneration," Franco-Cruz said.

UNDERSTANDING PARKINSON'S VIA AN INTERDISCIPLINARY APPROACH

Approximately 4 million people worldwide suffer from Parkinson's disease and about one in 20 are diagnosed when they are younger than 40. Parkinson's disease selectively targets "dopaminergic" neurons in a region called the substantia nigra, localized in the midbrain. Dopamine, the neurotransmitter used by these cells to communicate, is involved in the control of movement and coordination. By the time Parkinson's disease is detected, 50-80 percent of the neuronal population is lost. "By the time symptoms start to appear, there is not much prevention you can do, unfortunately," Franco-Cruz said. Currently, there is no therapeutic approach to stop the disease progression or cure it. Current research efforts are aimed at restoring those neuronal populations and identifying biomarkers for its early diagnosis.

Another important area of research is attempting to understand the mechanisms of the disease. "By understanding the basic mechanisms involved, we may be able to learn ways to diagnose it early and prevent or reduce the degenerative process," he explained.

ONE HEALTH: INTERDISCIPLINARY COLLABORATIONS

"The One Health concept is a strategy for expanding interdisciplinary research collaborations between scientists and other health and environmentally related disciplines in all aspects of health, including research, for humans, animals and the environment," he said. "Research at our school places an emphasis on collaborative efforts toward the advancement of biomedical knowledge. My research program is very interdisciplinary as we collaborate with chemists, engineers, veterinarians and the medical college in Omaha to understand how the environment contributes to disease progression."

Franco-Cruz's research aims to identify novel mechanisms of disease. "We have made important contributions in three major areas: redox biology, energy metabolism and protein quality control. For example, we have recently demonstrated that impairment in the ability of the cells to tag and degrade proteins regulates cellular homeostasis and death. Furthermore, we have also uncovered a very important role of energy metabolism. Glucose is the obligatory energy substrate of the adult brain. Neurons require energy for a number of functions, including communication, homeostasis and antioxidant defense. Dopaminergic neurons in the substantia nigra consume a significant amount of energy. Energy failure is the hallmark of Parkinson's disease and we have demonstrated that alterations in energy metabolism have important implications for neurogeneration," he said. Franco-Cruz's research also looks at genetic traits that can increase the risk of acquiring the disorder. Many kinds of pesticides are used in agriculture, so one idea used in the Franco-Cruz team's research is that multiple factors may combine to cause the disease. It could be many different types of pesticides, combined with the different habits of an individual. The pesticides that have been most commonly used in the past now are used less often due to more stringent regulations. However, the prevalence of Parkinson's disease is increasing, he said. "While our research is primarily focused on determining the basic mechanisms involved in neuronal dysfunction, eventually, I will hopefully see this research evolving so we can identify individuals that can be more susceptible to pesticides and try to avoid or reduce their exposure, and also identify potential exposure combinations (genes and environment) that will make an individual more susceptible to develop Parkinson's disease," he said. +