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UC Systemwide Toxic Substances Research and Teaching Program

Exposure to Manganese May Contribute to Parkinson's Disease

a UC Santa Cruz press release

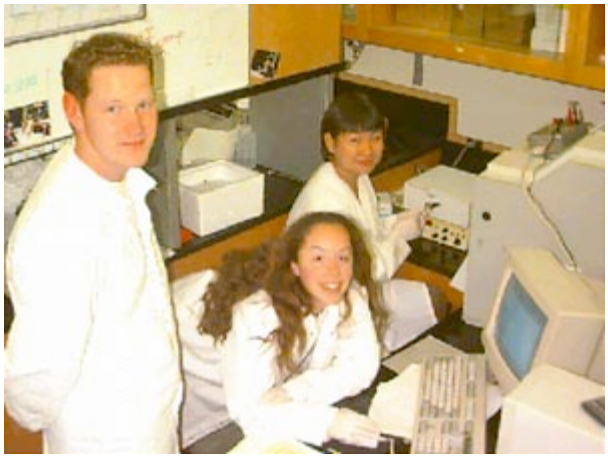
Editor's Note: This research has been partly funded by the TSR&TP.

SANTA CRUZ, CA--A new study suggests that too much manganese, an essential element required by the body in tiny amounts but toxic at elevated levels, may contribute to the early development of Parkinson's disease symptoms in susceptible people. Recent epidemiological studies have suggested an association between Parkinson's disease and elevated exposure to manganese. The new study in animals shows that exposure to low levels of manganese does not directly contribute to the disease, but affects a different part of the brain in a way that exacerbates the effects of Parkinson's.

Researchers at the University of California, Santa Cruz, evaluated the effects of low-level exposure to manganese using rats with a condition that mimics pre-Parkinsonism, an early stage of the disease in which no symptoms are apparent. Their findings were published in the current issue of the scientific journal Neurotoxicology and Teratology.

The study highlights the importance of looking at the effects of toxic substances on sensitive subsets of the population who may be most vulnerable, said Donald Smith, an associate professor of environmental toxicology at UC Santa Cruz and a coauthor of the paper.

"We are concerned about how chronic low-level exposures to toxic substances may accelerate the emergence of neurodegenerative diseases like Parkinson's," Smith said.



UC Santa Cruz students Josh Sheridan, Isabelle Haller, and Donna Lee analyzing the neurotransmitter dopamine on the HPLC as part of the manganese study. They have all since moved on: Josh is entering medical school this year, Isabelle is working in the biotech industry, and Donna is a doctoral student in the Environmental Toxicology program at Rochester University in New York.

The possibility that people in the early stages of Parkinsonism could be especially sensitive to moderately increased levels of manganese is disturbing for several reasons, he said. Manganese is ubiquitous in the environment, and its increasing use in industrial processes may cause some people to take in greater amounts from water, food, and airborne sources. In addition, increased exposure to airborne manganese could result from the use of the manganese compound MMT as a gasoline additive. MMT gained approval for use in the U.S. after its manufacturer, Ethyl Corporation, sued the Environmental Protection Agency and won. Currently, none of the major oil refineries are using MMT, but that could change, Smith noted. "We need better information about the potential risk to sensitive populations when we make decisions about things like MMT," Smith said.

Parkinson's disease and manganese toxicity seem to affect different parts of the neurological pathway involved in muscle control, he said. In Parkinson's disease, loss of brain cells in a region called the substantia nigra results in reduced production of dopamine, a chemical involved in communication between nerve cells. The substantia nigra is part of the basal ganglia, the brain region responsible for fine muscle control. Other parts of the basal ganglia, including the striatum and globus pallidus, are the targets of manganese toxicity.

"If two areas in the same pathway are weakened, you get an additive impact, and that's what we believe occurred in this experiment," Smith said.

In the experiment, rats were treated with a substance toxic to dopamine-producing nerve cells to induce a pre-Parkinson's condition. The treatment moderately reduced

dopamine levels in the substantia nigra region of the rats' brains, but did not cause symptoms detectable in a battery of neurobehavioral tests. This created a condition of pre-Parkinsonism mimicking the early neurodegenerative state in the progression of Parkinson's disease. Treated and untreated rats were then given low doses of manganese. The manganese had no effect on dopamine levels in the substantia nigra, but caused significant impairment of neurologic functions. Furthermore, some of the neurologic effects of manganese were more pronounced in the rats with pre-Parkinsonism.

The toxic effects of manganese have long been known from studies of miners, steelworkers, and others with high occupational exposures. Chronic overexposure to manganese can lead to a disease known as manganism with symptoms similar to Parkinson's disease. But lower doses of manganese that can cause more subtle health effects are not well known, said Roberto Gwiazda, a research toxicologist at UCSC and coauthor of the study.

In the new study, rats showed impaired muscle control at manganese doses much lower than those used in previously published animal studies of manganese toxicity. But Gwiazda cautioned that the exposure regimen and route (a series of injections) were not comparable to typical environmental exposures in humans.

Smith and his coworkers are currently conducting follow-up studies to determine the effects of different doses of manganese and to better understand the mechanisms underlying those effects. In addition to Smith and Gwiazda, the paper is coauthored by Ryan Witholt, who worked on the project as a UCSC undergraduate researcher.

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