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New research uncovers mercury's long-term health effects

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Methylmercury (MeHg) is a well-known neurotoxin that can impact brain development, particularly in utero. A series of new studies from researchers at the University of Rochester Medical Center (URMC) indicate that exposure may disrupt the early development of the connections between muscles and the brain, which could lead to motor control problems later in life.

MeHg enters in the environment in the form of industrial pollution and natural sources, settles in the oceans and is eventually absorbed in plants and other small organisms like plankton. Mercury bio-accumulates as it moves up the food chain and eventually reaches humans in the form of fish consumption, which is a major food source in many parts of the world.

Much of our understanding of the impact of mercury exposure comes from major 20th century industrial accidents in Japan and Iran, which poisoned thousands of people with high levels of mercury exposure. Many victims of these accidents exhibited a range of neurological symptoms similar to cerebral palsy, including muscle weakness and impaired motor control. While these accidents document the dangers of high levels of mercury, the long-term cumulative effects of exposure to smaller amounts are not well understood, especially during the important and vulnerable period of early development of the central nervous system.

The new studies—which come from the lab of Matthew Rand, Ph.D.,

with the URMC Department of Environmental Medicine and appear in the journals *Neurotoxicology and Teratology* and *Toxicological Sciences*—begin to shed light on the mechanism by which mercury may damage developing muscles and motor control.

The new research was conducted in the fruit fly Drosophilia, a long-established and important research tool in neuroscience because it enables researchers to study the entire nervous system. The researchers—which included graduate students Ashley Peppriell and Jakob Gunderson—found that when fruit fly larva were exposed to MeHg it impacted the early formation of flight muscles and ultimately impaired flight ability when the flies reached adulthood. The researchers identified a gene called Nlg1 that encodes a protein found in muscles that plays an important role in forming the connections between muscles and neurons, known as the neuromuscular junction. The Nlg1 gene expression is altered when exposed to MeHg during the larva stage.

"What we have to appreciate is that the musculoskeletal system is really sort of a continuation of the nervous system," said Rand. "They're connected and neural impulses are responsible for the muscle contractions that move our body. These are integrated systems and when a fetus is forming, muscle tissue and neural tissue need to talk to each other to get wired up. These findings indicate that mercury exposure disrupts this process, with effects that may not appear until adulthood."

The analysis of the risk/benefit of fish consumption during pregnancy is complicated. Fish are a rich source of omega-3 acids and other nutrients that are important brain development. The U.S. Food and Drug Administration and Environmental Protection Agency currently acknowledges the health benefits of nutrients in fish, but also recommends that pregnant mothers limit consumption and avoid fish with higher concentrations of MeHg.

However, decades of study involving mothers and children in the Seychelles Islands in the Pacific Ocean, where residents consume a wide variety of ocean fish resulting in MeHg exposure that is about 10 times greater than in the populations of the U.S. and Europe, have muddled the scientific consensus. Research conducted by the Seychelles Child Development Study—an international research consortium consisting of University of Rochester and the Seychelles Ministries of Health and Education, Ulster University in Northern Ireland, and the Karolinska Institute in Sweden—has shown that the fatty acids in fish enhance developmental and educational outcomes and may even help protect the developing brain from the harmful effects of mercury.

Researchers in the Rand lab are currently working to translate these new findings into animal models—in collaboration with the lab of Deborah Cory-Slechta, Ph.D. Rand is also collaborating with the Seychelles research team to see if muscle weakness, loss of motor skills, and other symptoms can be observed in the mothers and their children—many of whom are now adults—that are a part of the study.

More information: Ashley E. Peppriell et al, Latent effects of early-life methylmercury exposure on motor function in Drosophila, *Neurotoxicology and Teratology* (2021). DOI: 10.1016/j.ntt.2021.107037

Jakob T Gunderson et al, Neuroligin-1 Is a Mediator of Methylmercury Neuromuscular Toxicity, *Toxicological Sciences* (2021). DOI: 10.1093/toxsci/kfab114

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