Fetal exposure to PCBs found to affect hearing health later in life

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Music, mice, and microscopic imaging combine to provide new insight into the effects of environmental chemicals on hearing loss.

Researchers at the Beckman Institute for Advanced Science and Technology found that early exposure to an environmental chemical called polychlorinated biphenyls, or PCBs, made it more difficult for mice to recover from sound-related trauma sustained later in life.

Their paper appears in the *Journal of Neuroscience*.

PCBs are carcinogenic compounds formerly used in industrial and consumer products. Although they were banned in the United States in 1979 and haven't seen industrial use in decades, their highly stable chemical structure makes them difficult to eradicate from the environment. Exposure continues to this day and is most common through consumption of contaminated fish. In particular, exposure to PCBs can be harmful to a developing fetus.

"The most sensitive period in pregnancy for these types of developmental exposures is typically early in the pregnancy, in the first trimester," said Dr. Daniel Llano, an associate professor in the Department of Molecular and Integrative Physiology at the University of Illinois Urbana-Champaign and the corresponding author on the paper. "But PCBs as chemical entities are very permeant to all sorts of membranes. They can cross the placenta and they can get into the brain. That makes them particularly dangerous throughout all phases of pregnancy."

The groundwork for the research was laid several years ago by Susan Schantz, a professor emerita in the Department of Comparative Biosciences who was studying the effects of PCBs on the developing auditory system. She found that rats treated with PCBs experienced seizures in response to certain levels of sound.

This led to a collaboration among Schantz, Llano, and Baher Ibrahim, a research scientist in the Department of Molecular and Integrative

Physiology and the lead author of the paper. Although the researchers had known for years that PCBs altered hearing, they wanted to understand how.

The researchers suspected that if an individual who was exposed to PCBs in utero sustained acoustic trauma later in life (for example, from an occupation associated with high noise levels, or even a recreational activity like a rock concert), their hearing might not recover as would typically be expected.

Instead of continuing to study the auditory cortex, the researchers shifted focus to a lower brain region known as the inferior colliculus. There, they identified damage resulting from the combination of PCBs and noise.

They studied individual neurons in the animals' brains with a technique called multiphoton imaging.

"This is a one-of-a-kind microscope, and we are one of very few labs in the world doing this particular kind of imaging in this brain region," Llano said. "People have shown in the past that if you expose a mouse to loud sound, over time, the neurons in the inferior colliculus become hyper-responsive. But when combining the two toxic exposures, PCBs and noise, and using our imaging technique, that hyperexcitability went away."

The researchers also observed the neurons to become hypo-excitable—a brand-new finding.

The study team used chemical analysis to further understand the mechanisms behind these changes. Their findings centered around a common cellular process called oxidative stress that automatically releases oxygen radicals—or highly reactive chemicals—when cells are

sick or exposed to toxins. Oxygen radicals are eliminated by an intrinsic system within the body.

Mice with higher levels of the intrinsic protective system suffered less damage to the inferior colliculus, suggesting that PCBs and noise could cause a surplus of oxidative stress in the inferior colliculus, suppressing the auditory system's ability to recover from acoustic trauma.

"On its own, PCB exposure in utero may cause only a moderate degree of hearing loss," Llano said. "But that PCB exposure creates a particular vulnerability to later hearing loss. And so someone who is exposed to PCBs during development and has a significant occupational or recreational exposure to sound later in life may suffer greater-than-expected consequences when it comes to hearing."

Compared to many toxicology studies, which look at a single exposure, the Beckman research team accounted for two exposures—PCBs and noise—experienced in separate instances over the course of a lifespan.

"What we found were effects that would not have been predictable based on the separate impacts of the individual exposures," Llano said. "You can't necessarily predict the consequence of combined exposure to two environmental factors by adding up the effects of either one by itself. I think that's one of the more interesting things about this study, and hopefully it can be used as a model for future toxicology studies."

The study team will continue to investigate the connections among PCB exposure, noise exposure, and hearing loss. While oxidative stress appears to be a key mediator of the effect, investigators have yet to measure oxygen radicals in the tissues to confirm this.

"Dr. Llano and I have now co-mentored a graduate student and three postdocs who have carried this research forward," Schantz said. "We are

about to embark on the next stage of our collaboration, co-mentoring a fourth postdoc who will study the microvasculature of key brain regions after PCB and noise exposure."

These research questions will continue to be explored exactly where the study began: at the Beckman Institute.

"This is the kind of study that could only occur at Beckman," Llano said. "Dr. Schantz and I are in entirely different departments. Our home departments are in completely different locations on campus, but our Beckman offices are 10 feet apart. Because of that, it's made it very easy for us to collaborate. I think this is the kind of study that would be almost impossible to do in a different environment where we didn't have easy access to each other's ideas and the various interactions that exist here."

More information: Baher A. Ibrahim et al, Developmental exposure to polychlorinated biphenyls prevents recovery from noise-induced hearing loss and disrupts the functional organization of the inferior colliculus, *The Journal of Neuroscience* (2023). DOI: 10.1523/JNEUROSCI.0030-23.2023

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