WebMD

How PCBs May Hurt the Brain

New Studies Shed Light on Exposure to Environmental Toxin and Development of Brain Cells

By Kathleen Doheny

FROM THE WEBMD ARCHIVES

April 13, 2009 -- Exposure to environmental toxins known as PCBs have long been linked with behavioral and developmental problems in children, but scientists could never say exactly how PCBs (polychlorinated biphenyls) might adversely affect the brain and lead to the problems.

Now, scientists think they may know.

The chemicals adversely affect the development of brain cells and also make brain circuits "overexcited," which has been linked in previous research to developmental problems, according to researcher Isaac N. Pessah, PhD, a professor of molecular biosciences and director of the University of California Davis Center for Children's Environmental Health.

"We think we have identified the way in which a broad class of environmental contaminants influences the developing nervous system and may contribute to neuro-developmental impairments such as hyperactivity, seizure disorders, and autism," says Pessah, a co-author on a trio of new studies examining the issue. The latest of the three is published online today in *PLoS-Biology.*

The findings of the three studies are called a "turning point" by another expert in the field.

One surprise finding: low levels of PCB exposure sometimes have greater ill effects than high-dose exposures.

PCBs were widely used for years in many products such as electronic components, pesticides, caulking, and flame retardants, but their production was banned in the U.S. in 1979.

Even so, the chemicals persist in the environment because they don't break

down easily, explaining why high levels of PCBs can still be detected in people and in animals. PCBs are found in air, water, soil, and contaminated foods such as fish.

PCB Exposure and Effect on Learning and Brain Cells

In one of the three new studies, exposures to low doses of PCBs in animals hampered their ability to learn to swim a maze, a common test of animal learning.

The low PCB doses also adversely affected the plasticity of the animals' dendrites -- small projections branching out from the neurons or nerve cells that get signals from other cells in the body.

"This plasticity is very important for learning and memory," says study researcher Pamela Lein, PhD, associate professor of neurotoxicology at the UC Davis School of Veterinary Medicine.

The study was published in March in *Environmental and Health Perspectives.*

Problems in dendrite plasticity and growth have already been implicated in disorders such as autism , schizophrenia, and mental retardation, Lein says.

Lein and colleagues compared the effects of low-dose PCB exposure, high-dose exposure, and no exposure in three groups of rats that had been trained to swim and find an escape platform in a maze, and three groups not trained to swim the maze.

"The PCB treatments did affect the learning and memory," she says. "The effects were seen in the low-dose group but not the high-dose." Those in the low-dose trained group took longer to learn to swim and escape the maze, she says.

In the high-dose group, she says, the exposure may have triggered a compensatory mechanism that protected the brain cells from harm.

PCB Exposure: The Tissue Study

In a second study, the researchers looked at tissue from the animals' hippocampus, an area of the brain that regulates memory and emotion, and measured the "excitability" of neurons there before and during exposures to two different PCBs.

With one of them, says Pessah, "we can get an enhancement of excitability." Normally, information processing in the brain depends on a balance between excitation and inhibition of the neurons.

"Too much excitability is bad for the brain," Pessah says. Many neuro-developmental disorders, he says, including autism and attention deficit hyperactivity disorder or ADHD , "are thought to involve an imbalance between inhibition and excitability."

What they found in this study, he says, is that "even low levels [of PCBs] can tip the balance in the brain." The report is published in March in *Toxicology and Applied Pharmacology.*

PCB Exposure: The Cellular Level Clues

Finally, the researchers went to the cellular level, trying to find out more specifically how the PCBs change brain cell development as they found in the animal study and how they change the neurons' excitability, as seen in the study on brain tissue.

In the lab, they exposed receptors within the cells that regulate the release of calcium, crucial to maintain normal signaling from cell to cell, to PCBs. When they used electron microscope to create high-resolution images of the interaction between the receptors and the PCBs, they found the chemical binds to the receptors and adversely affects the calcium release. This interference accounts for the findings in the other two studies, Pessah says.

PCB Studies: Second Opinion

"I think that these studies represent a kind of a turning point for our recognition of how these chemicals, PCBs, can interfere with brain development," says R. Thomas Zoeller, PhD, professor of biology at the University of Massachusetts, Amherst. He was a journal reviewer for one study and reviewed the other two for WebMD.

"They are looking at a limited number of forms of PCB chemicals and they are linking exposures to very specific changes in proteins in the nervous system that impact brain development and behavior," he says. Because the animal model studied developmental events that are akin to human developmental events, "for the first time we are getting a clear view of how these chemicals can impact the brain in humans," he says.

PCB Studies: Practical Applications

The new findings will add weight to the studies finding a link between exposures to PCBs and developmental problems, Lien says. "For the first time, we now have a plausible biological mechanism to explain the effect of PCBs on behavior."

One practical application of the research? Scientists may use the findings to evaluate the safety of numerous chemicals produced to take the place of PCBs, Zoeller says. "Science can't keep up with the rapid kinds of chemical changes that industry can manufacture," he says. "It would be great if we could get out in front of it and identify dangerous chemicals before people are being exposed."

The research findings may also make experts who thought lower-dose PCB exposures were not a problem think again, Pessah says.