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Air Pollution Linked to Learning and Memory Problems, Depression

July 6, 2011 — Long-term exposure to air pollution can lead to physical changes in the brain, as well as learning and memory problems and even depression, new research in mice suggests.

While other studies have shown the damaging effects of polluted air on the heart and lungs, this is one of the first long-term studies to show the negative impact on the brain, said Laura Fonken, lead author of the study and a doctoral student in neuroscience at Ohio State University.

"The results suggest prolonged exposure to polluted air can have visible, negative effects on the brain, which can lead to a variety of health problems," Fonken said.

"This could have important and troubling implications for people who live and work in polluted urban areas around the world."

The study appears online this week in the journal *Molecular Psychiatry*.

For this study, Fonken and colleagues in Ohio State's Department of Neuroscience collaborated with researchers in the university's Davis Heart and Lung Research Institute.

In previous studies in mice, the Davis research group -- including Qinghua Sun, associate professor of environmental health sciences, and Sanjay Rajagopalan, professor of cardiovascular medicine -- found that fine air particulate matter causes widespread inflammation in the body, and can be linked to high blood pressure, diabetes and obesity. This new study aimed to extend their research on air pollution to the brain.

"The more we learn about the health effects of prolonged exposure to air pollution, the more reasons there are to be concerned," said Randy Nelson, co-author of the study and professor of neuroscience and psychology at Ohio State.

"This study adds more evidence of pollution's negative effects on health."

In the new study, mice were exposed to either filtered air or polluted air for six hours a day, five days a week for 10 months -- nearly half the lifespan of the mice.

The polluted air contained fine particulate matter, the kind of pollution created by cars, factories and natural dust. The fine particulates are tiny -- about 2.5 micrometers in diameter, or about 1/30th of the average width of a human hair. These particles can reach deep areas of the lungs and other organs of the body.

The concentration of particulate matter that the mice were exposed to was equivalent to what people may be

exposed to in some polluted urban areas, according to the researchers.

After 10 months of exposure to the polluted or filtered air, the researchers performed a variety of behavioral tests on the animals.

In a learning and memory test, mice were placed in the middle of a brightly lit arena and given two minutes to find an escape hole leading to a dark box where they feel more comfortable. They were given five days of training to locate the escape hole, but the mice who breathed the polluted air took longer to learn where the escape hole was located. The mice exposed to polluted air also were less likely to remember where the escape hole was when tested later.

In another experiment, mice exposed to the polluted air showed more depressive-like behaviors than did the mice that breathed the filtered air. The polluted-air mice showed signs of higher levels of anxiety-like behaviors in one test, but not in another.

But how does air pollution lead to these changes in learning, memory and mood? The researchers did tests on the hippocampal area of the mice brains to find the answers.

"We wanted to look carefully at the hippocampus because it is associated with learning, memory and depression," said Fonken, who, along with Nelson, are also members of Ohio State's Institute for Behavioral Medicine Research.

Results showed clear physical differences in the hippocampi of the mice who were exposed to polluted air compared to those who weren't.

The researchers looked specifically at branches that grow off of nerve cells (or neurons) called dendrites. The dendrites have small projections growing off them called spines, which transmit signals from one neuron to another.

Mice exposed to polluted air had fewer spines in parts of the hippocampus, shorter dendrites and overall reduced cell complexity.

"Previous research has shown that these types of changes are linked to decreased learning and memory abilities," said Nelson.

In other studies, several of the co-authors of this study from the Davis research center found that chronic exposure to polluted air leads to widespread inflammation in the body, which is linked to a variety of health problems in humans, including depression. This new study found evidence that this low-grade inflammation is evident in the hippocampus.

In mice that breathed the polluted air, chemical messengers that cause inflammation -- called pro-inflammatory cytokines -- were more active in the hippocampus than they were in mice who breathed the filtered air.

"The hippocampus is particularly sensitive to damage caused by inflammation," Fonken said.

"We suspect that the systemic inflammation caused by breathing polluted air is being communicated to the central nervous system."

The research was supported by grants from the National Institutes of Health.

Other co-authors, all from Ohio State, included Qinghua Sun, associate professor of environmental health sciences; Sanjay Rajagopalan, professor of cardiovascular medicine; Xiaohua Xu, in environmental health sciences; Zachary Weil, in neuroscience and psychology; and Guohua Chen, in the Davis Heart and Lung Research Institute.

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1. L K Fonken, X Xu, Z M Weil, G Chen, Q Sun, S Rajagopalan, R J Nelson. **Air pollution impairs cognition, provokes depressive-like behaviors and alters hippocampal cytokine expression and morphology**. *Molecular Psychiatry*, 2011; DOI: 10.1038/mp.2011.76

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