Extramural papers of the month

By Nancy Lemontagne

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Children's lungs grew stronger as pollution declined in California

New research from NIEHS grantees found that as air quality improved in the Los Angeles basin, children's lung health also improved. Improving lung function during developmental years could lead to better lung function in adulthood, and potentially reduce risk for adverse health outcomes.

The improving air quality of the Los Angeles basin, over the last several decades, provided an opportunity to study its potential benefits to human health. As part of the Children's Health Study, researchers measured lung function in 2120 children, from three different cohorts, who lived in the same five communities. Measurements were taken each year between the ages of 11 and 15, but during different calendar periods — 1994-1998, 1997-2001, and 2007-2011. After adjusting for age, gender, ethnicity, height, respiratory illness, and other variables, the researchers found large improvements in lung development for children studied in 2007-2011, compared to children studied in 1994-1998 or 1997-2001. Regional air quality improved dramatically over the course of the study, and lung function gains strongly correlated with lower levels of particulate matter (PM2.5 and PM10) and nitrogen dioxide in the communities studied. For example, lung growth was more than 10 percent greater for children breathing the lower levels of nitrogen dioxide in 2007-2011, compared to those breathing higher levels in 1994-1998.

Citation: Gauderman WJ, Urman R, Avol E, Berhane K, McConnell R, Rappaport E, Chang R, Lurmann F, Gilliland F *(http://www.ncbi.nlm.nih.gov/pubmed/25738666)*. 2015. Association of improved air quality with lung development in children. N Engl J Med. 372(10):905-913. (Story)

Prenatal window of susceptibility for genetic damage

A new mouse study, funded in part by NIEHS, quantitatively links prenatal DNA damage from the liver carcinogen aflatoxin B1 (AFB1) with risk of cancer later in life. The new results point to the prenatal period as a critical window of susceptibility to genetic damage from toxins.

AFB1, a toxin produced by fungi that contaminate food supplies, is a potent carcinogen that leads to a type of liver cancer known as hepatocellular carcinoma. It is especially problematic in the developing world. To quantify the link between AFB1 damage and later development of cancer, the researchers exposed mice embryos to AFB1 and compared the rates of cancer-causing mutations in these mice with adult mice exposed to the same dose.

The data revealed that the DNA adducts produced in the livers of exposed embryos were twentyfold more likely to lead to mutations than in adults that received the same dose of aflatoxin. These results correlated with Ki67 staining of the liver, which indicated that the fetal liver cells were dividing much faster than adult liver cells.

Based on these findings, the researchers noted that it is especially important to prevent maternal exposures to aflatoxins. They also pointed to the need to explore preventive measures that improve maternal pathways of metabolism and detoxification, to prevent effects from unavoidable exposures to food contaminated with aflatoxins.

Citation: Chawanthayatham S, Thiantanawat A, Egner PA, Groopman JD, Wogan GN, Croy RG, Essigmann JM *(http://www.ncbi.nlm.nih.gov/pubmed/25070670)*. 2015. Prenatal exposure of mice to the human liver carcinogen aflatoxin B1 reveals a critical window of susceptibility to genetic change. Int J Cancer 136(6):1254-1262.

More evidence that lead plays a role in schizophrenia

An NIEHS grantee and colleagues report strong similarities between the brains of people with schizophrenia and the brains of rats chronically exposed to lead from the prenatal period through adolescence, adding evidence that early lead exposure primes the brain for schizophrenia later in life.

The researchers found that rats with chronic lead exposure during development showed detriments in three brain areas known to be involved in schizophrenia — the medial prefrontal cortex, hippocampus, and striatum. Compared to control rats that were not exposed to lead, the exposed rats showed a decrease of approximately one-third in the density of parvalbumin-positive GABAergic interneurons (PVGI), which are critical to cognitive function. Using imaging technology, the researchers identified higher levels of D2-dopamine receptor, a hallmark of schizophrenia, in the striatum of lead-exposed rats.

Psychosis, a characteristic symptom of schizophrenia, has been linked to subcortical dopaminergic hyperactivity. To determine whether lead-exposed animals expressed this hyperactivity, the researchers administered cocaine to both control and lead-exposed rats and measured their locomotor response. The lead-exposed rats showed hyperactivity in the subcortical dopaminergic system.

Overall, the study in rats showed that developmental lead exposure reproduces the specific neuropathology and dopamine system changes seen in people with schizophrenia.

Citation: Stansfield KH, Ruby KN, Soares BD, McGlothan JL, Liu X, Guilarte TR *(http://www.ncbi.nlm.nih.gov/pubmed/25756805)*. 2015. Early-life lead exposure recapitulates the selective loss of parvalbumin-positive GABAergic interneurons and subcortical dopamine system hyperactivity present in schizophrenia. Transl Psychiatry 5:e522.

MRI reveals how early life air pollution exposure affects the brain

In one the largest MRI studies to date, NIEHS grantees report how prenatal and postnatal exposure to polycyclic aromatic hydrocarbon (PAH) air pollutants disturbs the developing brain. If confirmed, the findings have important public health implications, as PAHs are widespread in the environment.

The researchers used MRI to study the brains of 40 children from minority communities in New York City that had been followed from before birth until 7 to 9 years of age. The researchers previously reported that prenatal exposure to airborne PAHs during gestation in this cohort was associated with multiple neurodevelopmental problems, including development delay by age 3, reduced verbal IQ at age 5, and symptoms of anxiety and depression at age 7.

The new study showed a dose-response relationship between increased prenatal PAH exposure and later childhood reductions in the white matter surface of the left hemisphere of the brain, which is associated with slower processing of information and externalizing behavioral problems, including ADHD and aggression. For postnatal PAH exposure measured at age 5, the researchers found additional disturbances in development of white matter in the dorsal prefrontal region of the brain, which is associated with concentration, reasoning, judgment, and problem-solving ability. The postnatal affects were spatially distinct and statistically independent from those for prenatal PAH exposure. The researchers are currently undertaking a much larger study to confirm and extend their findings.

Citation: Peterson BS, Rauh VA, Bansal R, Hao X, Toth Z, Nati G, Walsh K, Miller RL, Semanek D, Perera F *(http://www.ncbi.nlm.nih.gov/pubmed/25807066)* . 2015. Effects of prenatal exposure to air pollutants (polycyclic aromatic hydrocarbons) on the development of brain white matter, cognition, and behavior in later childhood. JAMA Psychiatry; doi:10.1001/jamapsychiatry.2015.57 [Online 25 March 2015]. (Story)

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