

The Societal and Economic Costs of Cognitive and Behavioral Impairments due to Developmental Neurotoxicity Across the Lifespan

The Case of Lead

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Prelude

Dr. Leila Denmark
(1898-2012)



"...when you love what you do, it's not work, it is play."

Dr. Leila Denmark, Atlanta Journal-Constitution.

Prelude

Dr. Herbert L. Needleman

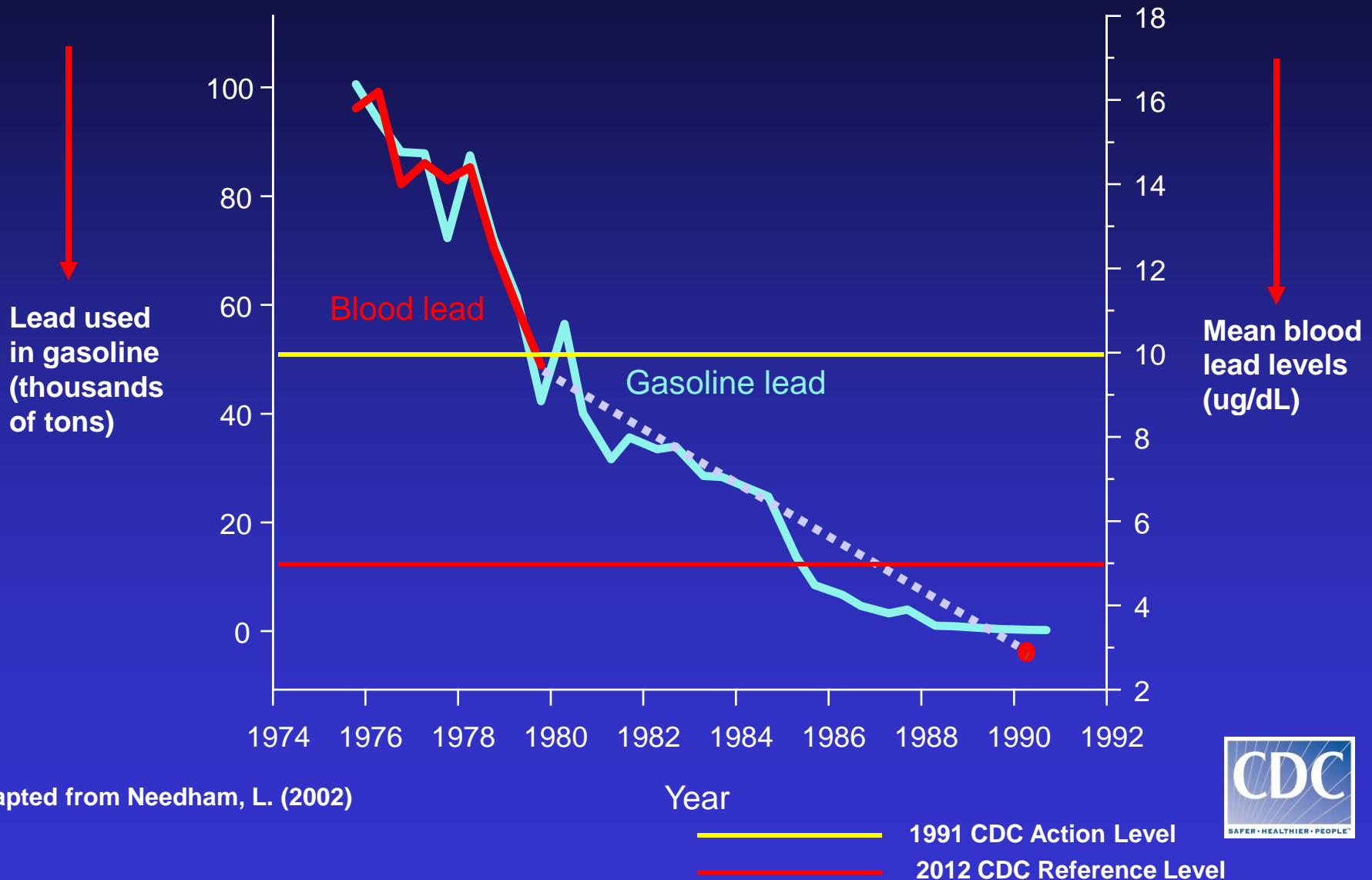


Herbert L. Needleman, M.D.

'Sometimes the data speak clearly'

Personal communication and many scientific press interviews and talks.

Decline in Blood Lead Levels in the United States NHANES II AND NHANES III



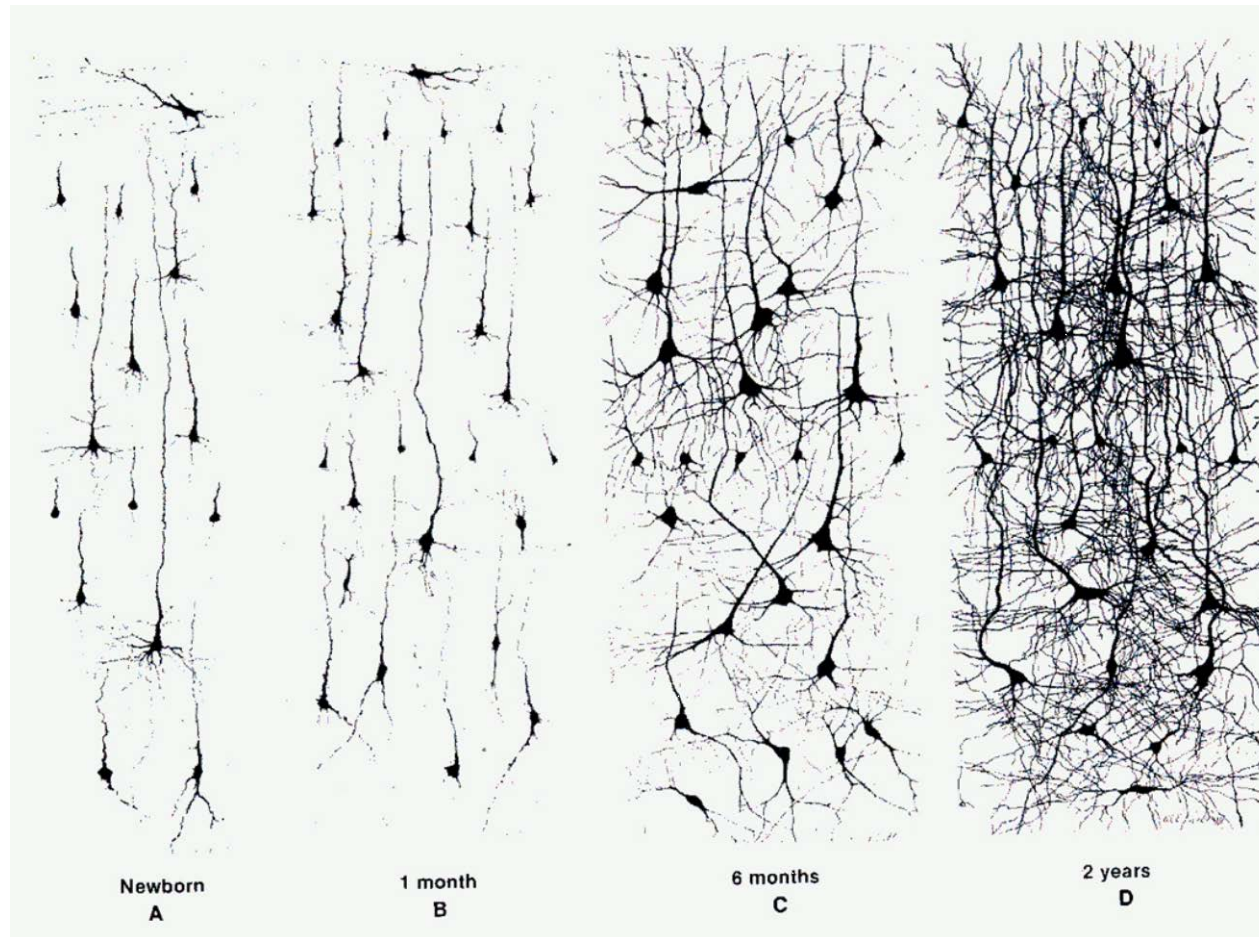


Old, deteriorating and peeling paint is a continual source of lead in our inner-cities.

Age of Maximum Ingestion of Environmental Lead



The Age of Maximum Lead Ingestion and Early Cerebral Development



From Nolte (1993). The Human Brain

Expert Quantitative and Theoretical Assessments of the Societal and Economic Costs of Lead Exposure

- Estimated Costs in Terms of Intelligence as Measured by Lowered Full-Scale IQ

Bellinger, D.C. (2012). A strategy for comparing the contributions of Environmental chemicals and other risk factors to neurodevelopment in children. *Environmental Health Perspectives*, 120, 501-507).

- Economic Impacts of Lead Exposure as Measured by Health Care, Special Education, Lower Earnings, and Crime

The PEW Center on the States (2010). Cutting lead poisoning and public costs. www.pewcenteronthestates.org.

The Cincinnati Lead Study (1979 – 2016)



Blood Lead Concentrations in the Cincinnati Lead Study

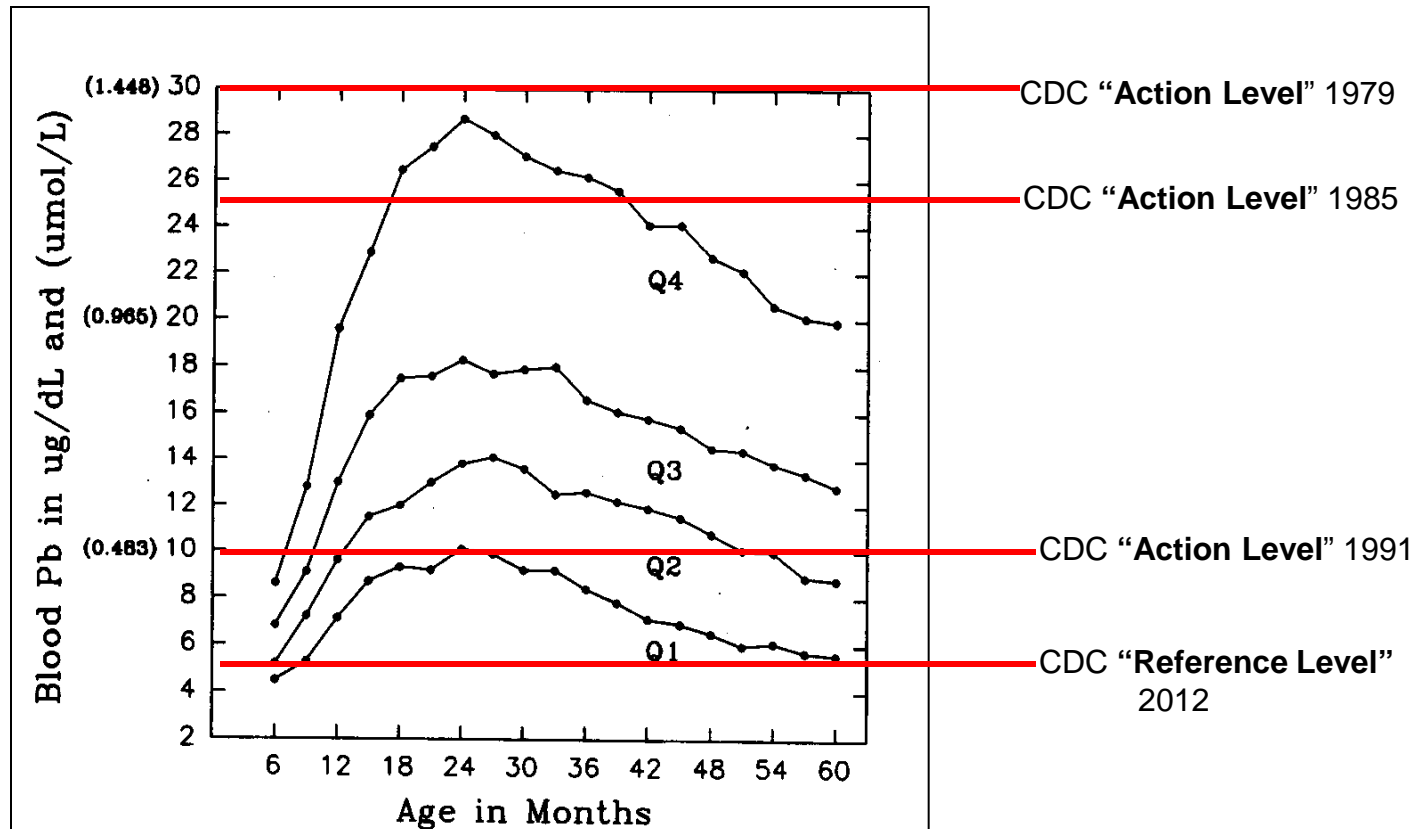


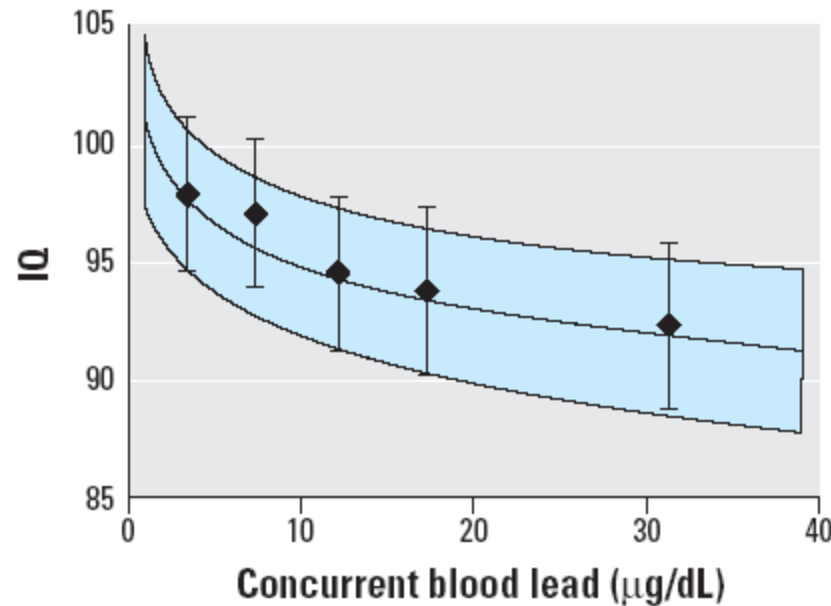
Fig 1. Blood lead concentrations obtained quarterly for children divided into four quartiles (Q1-4) based on average lifetime blood lead concentration (ie, the mean of 20 quarterly blood lead concentrations from 3 to 60 months). Age in months has been abbreviated to 6-month intervals rather than 3-month intervals for clarity of presentation.

Dietrich, et al. *Pediatrics*, 1993.

Early Exposure to Lead and Child IQ

Medscape®

www.medscape.com



N = 1,333

Source: Environ Health Perspect © 2005 National Institute of Environmental Health Sciences

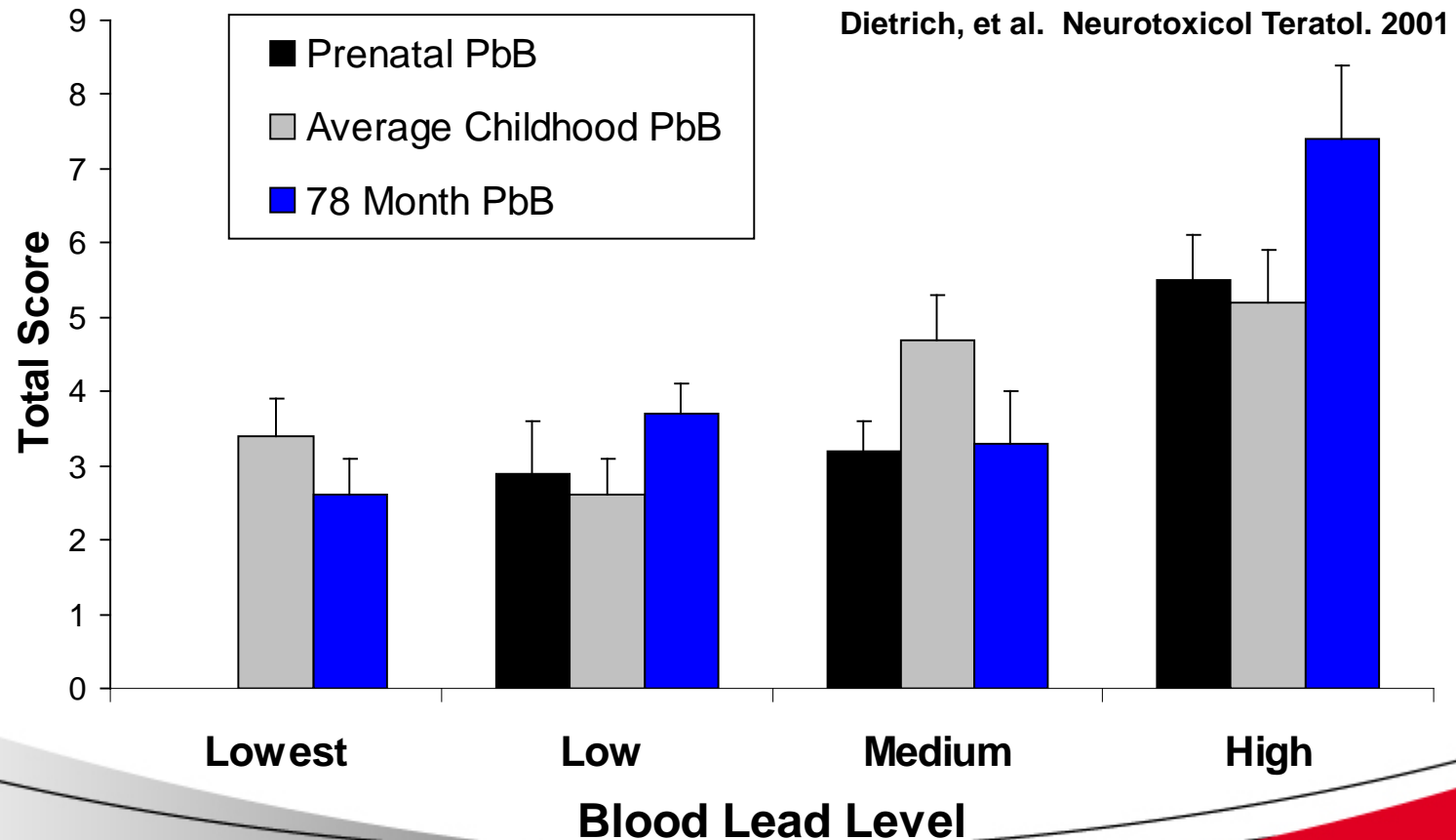
Low-Level Environmental Lead Exposure and Children's Intellectual Function: An International Pooled Analysis

[Bruce P. Lanphear](#),^{1,2} [Richard Hornung](#),^{1,2,3} [Jane Khoury](#),^{1,2} [Kimberly Yolton](#),¹ [Peter Baghurst](#),⁴ [David C. Bellinger](#),⁵ [Richard L. Canfield](#),⁶ [Kim N. Dietrich](#),^{1,2} [Robert Bornschein](#),² [Tom Greene](#),⁷ [Stephen J. Rothenberg](#),^{8,9} [Herbert L. Needleman](#),¹⁰ [Lourdes Schnaas](#),¹¹ [Gail Wasserman](#),¹² [Joseph Graziano](#),¹³ and [Russell Roberts](#)¹⁴

Beyond IQ



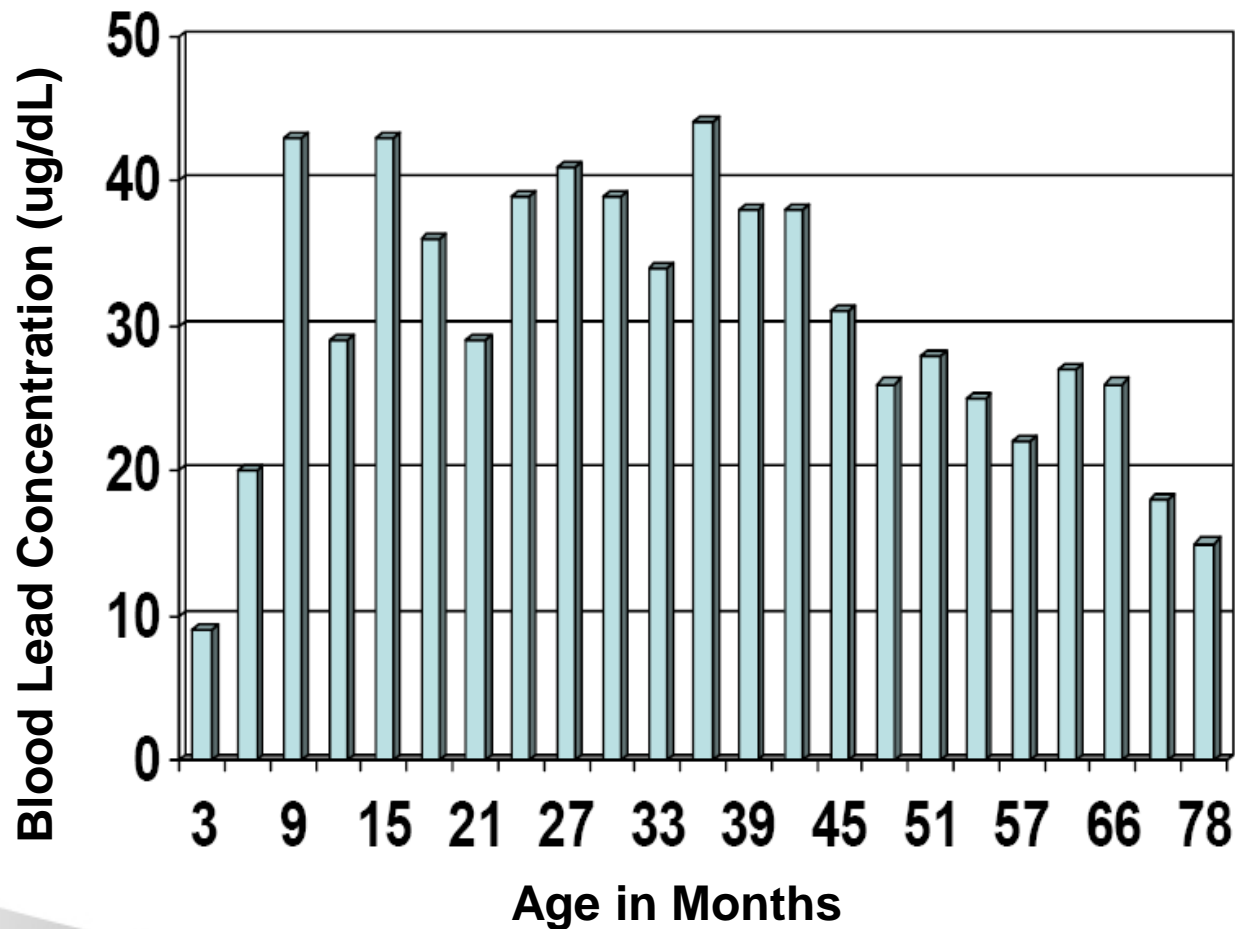
Association of Blood Lead Levels and Self-Reported Delinquency in 16 Year-Old Adolescents in the Cincinnati Lead Study



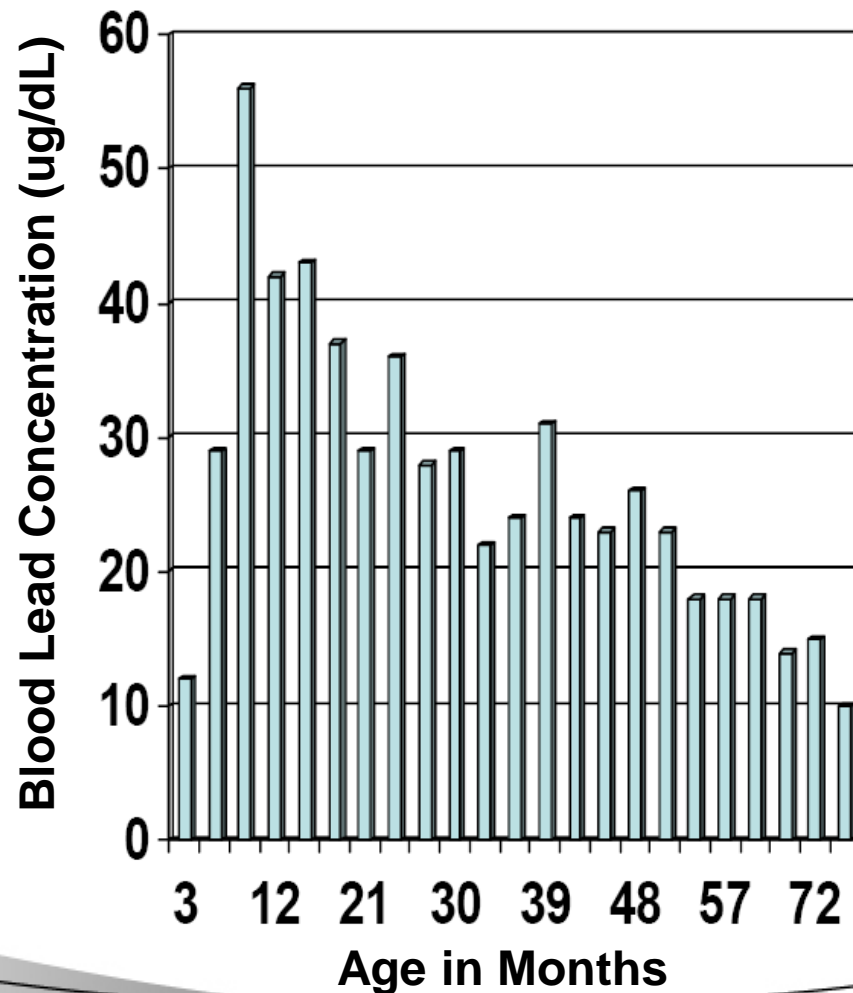
Questions from a Lead Study Cohort

- Why can't I hold onto a job?
- Why can't I get along with my girl friend/wife?
- Why am I angry all of the time?
- Why can't I concentrate?
- Why can't my son/daughter stay out of trouble?

Blood Lead Concentration Profile of a 26 Year-Old CLS Male Subject with a History of Domestic Violence and Delinquent/Criminal Behavior



Blood Lead Concentration Profile of a 26 Year-Old CLS Male Subject with a History of Adult Criminal Behavior and Repeated Incarcerations



Does Early Exposure to Pb Leave a Long-Term Signature in the Brains and Behavior of Adults?

The Cincinnati Lead Study (1979-2016)

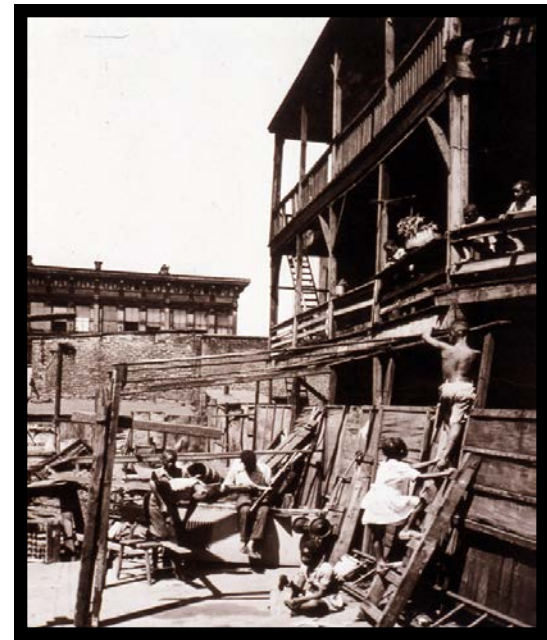
- Neuroimaging studies
- Criminality studies

Early Exposure to Lead and Adult Criminality



Environmental Factors in Criminal Disposition

- Parental dysfunction
- Community violence
- Poverty
- Media
- **Lead**
- Nutrition
- Alcohol
- Illicit Drugs

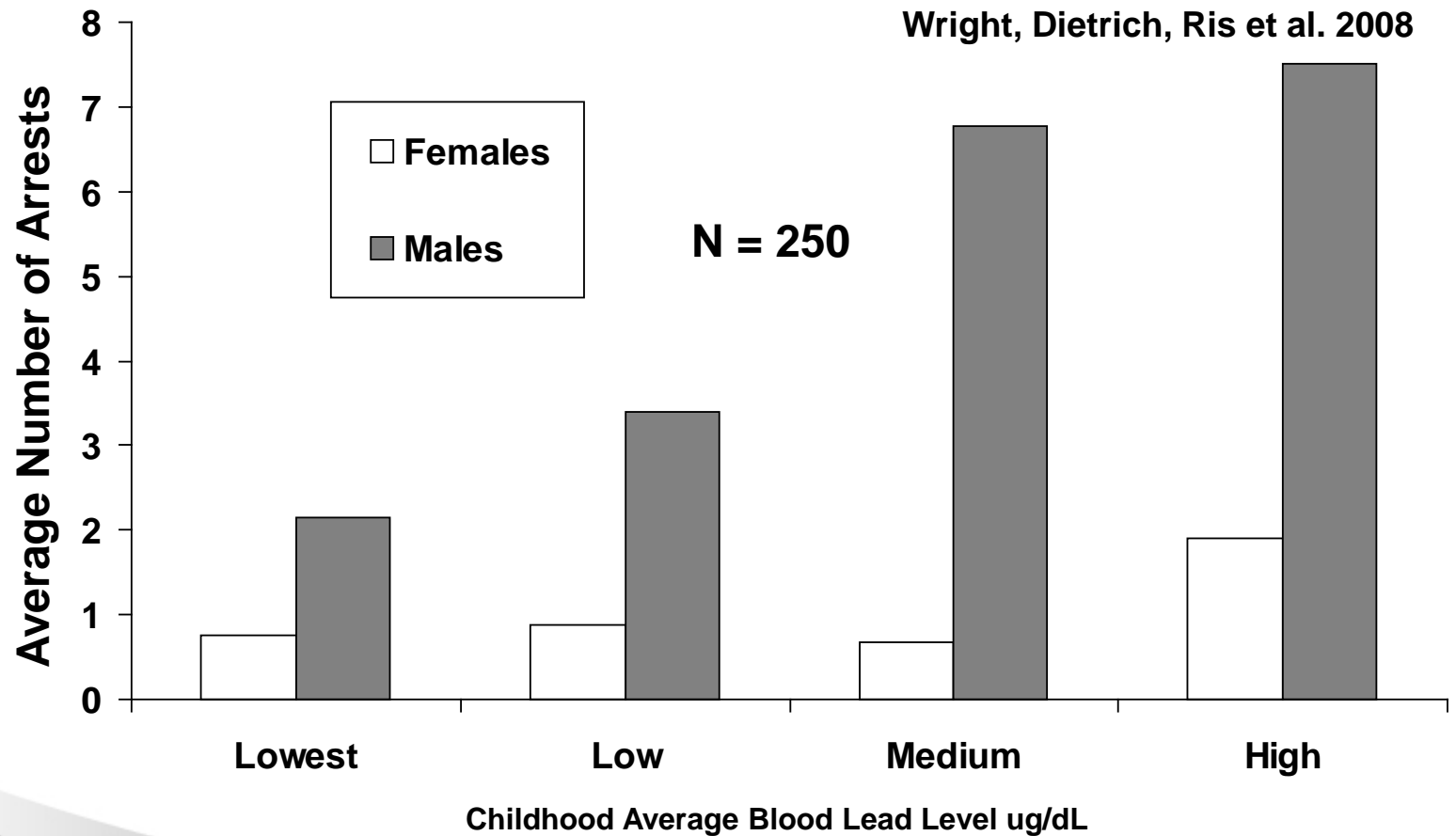


Cincinnati, 1956

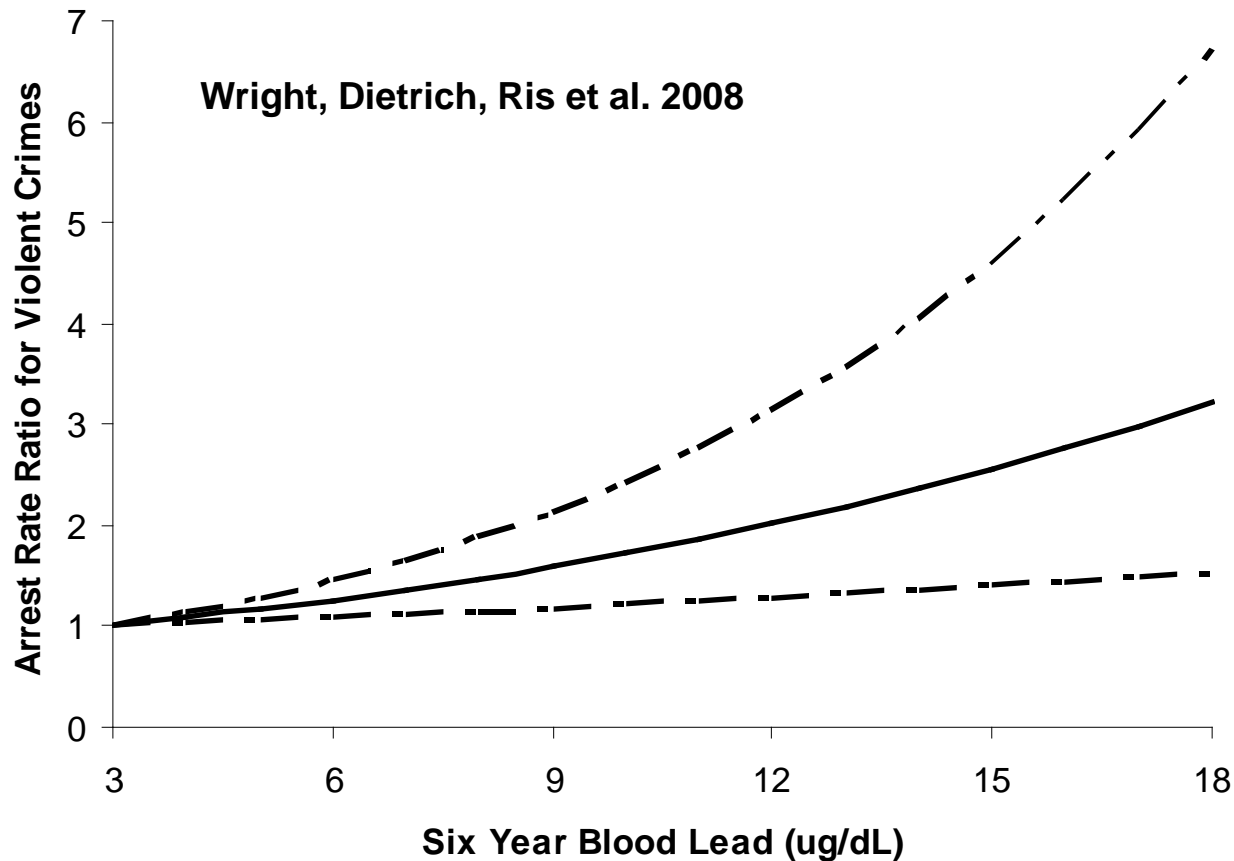
Covariates in Analyses of Adult Criminality Data

- Home Environment (HOME score)
- Birth Weight
- Gender
- Age
- Maternal Smoking During Pregnancy
- Maternal Drug/ETOH Use During Pregnancy
- Maternal Education
- Maternal IQ
- Total Prior Maternal Arrests
- Socioeconomic Status
- Household Size
- Public Assistance

Average Number of Criminal Arrests in the Cincinnati Lead Study Cohort (M Age = 22 years) by Average Blood Lead Concentration and Gender (Unadjusted)



Blood Lead Concentrations to Six Years and Arrest Rate Ratio for Violent Offenses*

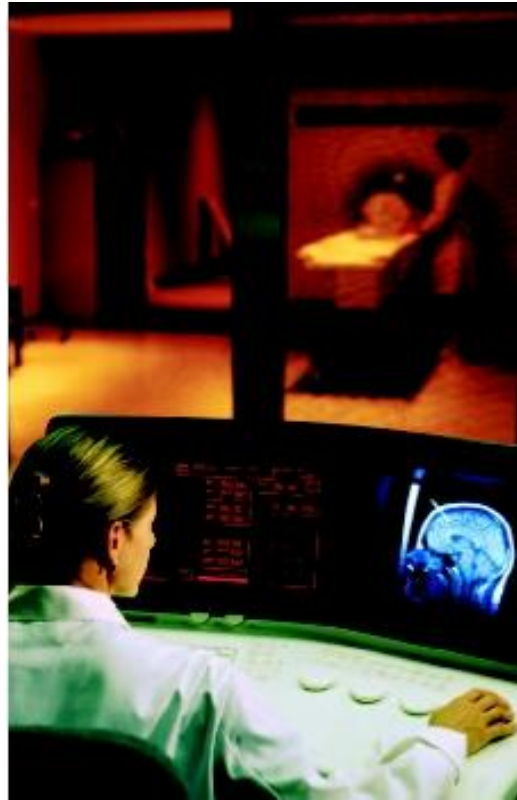


*Any 5 ug/dL elevation in blood lead increased the rate of arrests for violent offenses by 48 percent.

Early Exposure to Lead and Career Criminality



Imaging Studies of the Cincinnati Lead Study Cohort (MRI, MRS, fMRI, DTI)



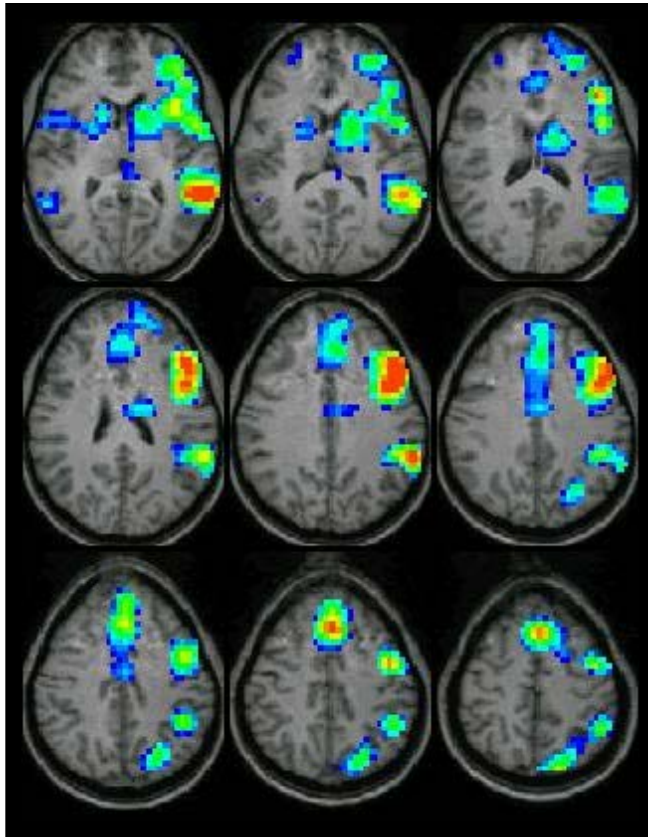
Covariates in Analyses of CLS Adult MRI Data

- **Home Environment (HOME score)**
- **Birth Weight**
- **Gender**
- **Maternal Smoking During Pregnancy**
- **Maternal Drug/ETOH Use During Pregnancy**
- **Maternal Education**
- **Maternal IQ**
- **Socioeconomic Status**
- **Household Size**
- **Public Assistance**
- **Age at time of imaging**
- **Positive drug screen**

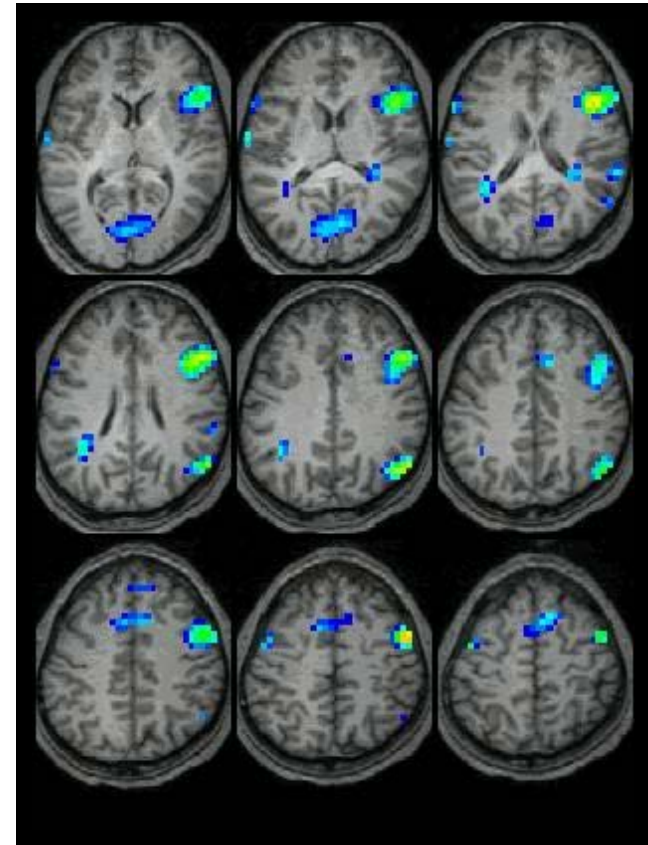
Cincinnati Neuroradiological Studies of Childhood Lead Exposure and Adult Brain Outcomes

- fMRI – dose-dependent reductions in brain activation in the traditional language areas (Yuan et al. 2006).
- HR Anatomical MRI – dose-dependent reductions in cortical gray matter in the frontal lobe (Cecil et al. 2008).
- DT MRI – dose dependent injury to both myelin and axonal structures (Brubaker et al. 2008).
- Proton MRS – dose-dependent reduction in gray matter NAA along with white matter choline declines (Cecil et al. 2011).

Verb Generation Task by Average Childhood Lead Exposure in the Cincinnati Lead Study



Low Average Mean Blood Lead (7.6 $\mu\text{g/dL}$)

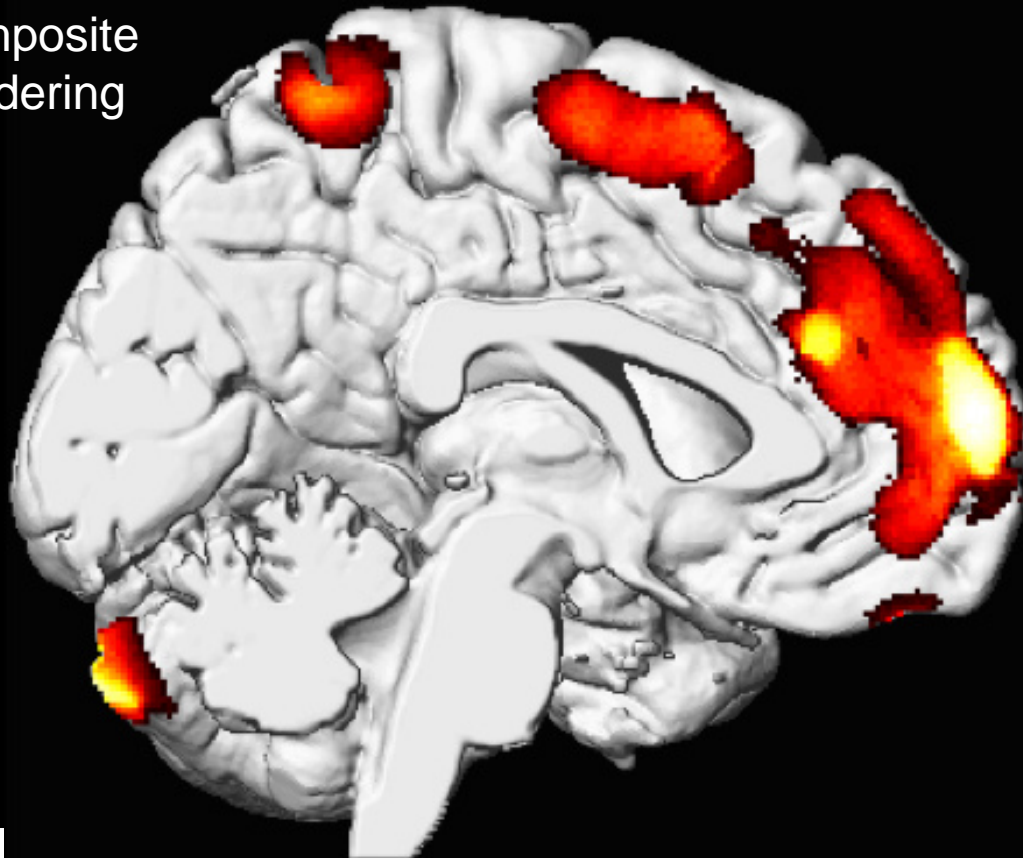


High Average Mean Blood Lead (26 $\mu\text{g/dL}$)

Yuan, et al. *Pediatrics*, 2006.

Adult Cortical Gray Matter Loss in Cincinnati Lead Study Subjects in Relationship to Postnatal Lead Exposure to Six Years

Composite rendering



Single voxel significance more significant



less significant

Cecil K.M., Brubaker C.J., Adler C.M., Dietrich K.N., et al. (2008). Decreased brain volume in adults with childhood lead exposure. *PLoS Medicine*, 5m 741-750.

International Implications

Fatal and Severely Disabling Infant and Childhood Lead Poisoning in Zamfara State Nigeria from Artisanal Gold Mining



Human Rights Watch (2012). A heavy price: Lead poisoning and gold mining.

Funding for This Research



NIEHS

**National Institute of
Environmental Health Sciences**