THE CINCINNATI LEAD STUDY



AUTHORS

- Kim Dietrich, Environmental Epidemiology
- Kim Cecil, Children's Hospital
- Michelle Coyne, Criminal Justice
- Lisa Tully, Children's Hospital
- Bruce Lanphear, Simon Fraser University
- Many other scholars have made this study possible over the decades

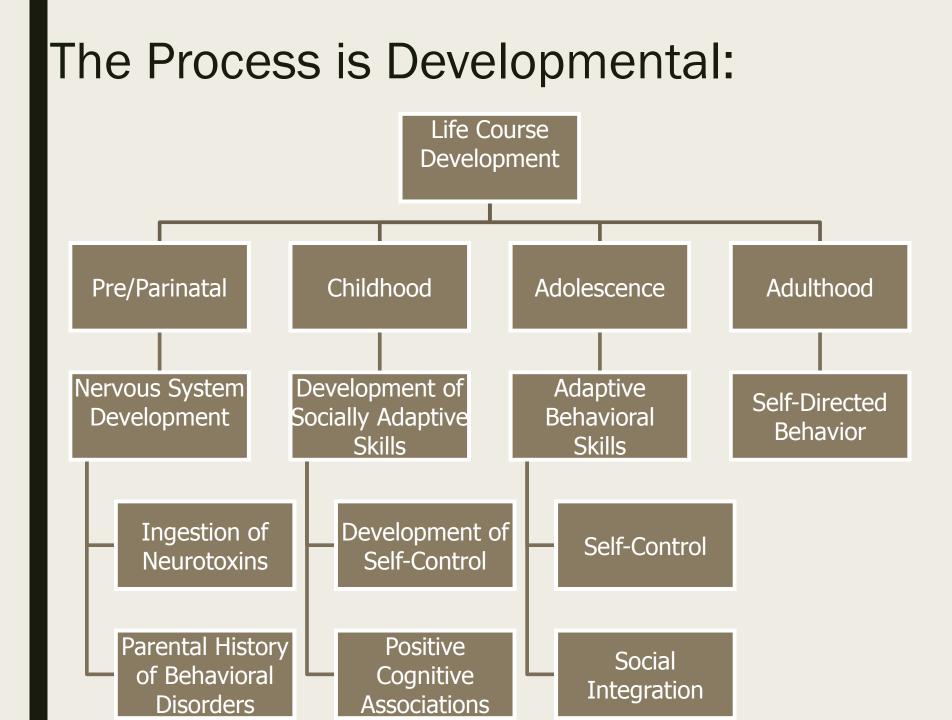
Biosocial Criminology

- Criminal behavior is the product of genetic, biological, and specific environmental influences
- These influences create brain-based predispositions, including propensities towards criminal/antisocial behavior

Exposure to neurotoxins along the developmental pathway may impact these proclivities directly or indirectly through other variables, such as selfcontrol or IQ

What Do Adult Offenders Look Like?

- <u>Persistent</u> pattern of hostile interactions with others.
- <u>Persistent</u> pattern of poor impulse control and emotional regulation.
- <u>Significant</u> cognitive distortions (attribution biases).
- <u>Significant</u> impairment in various social arenas (social failures).
- <u>Inability</u> to effectively adapt behavior to novel situations and contexts.

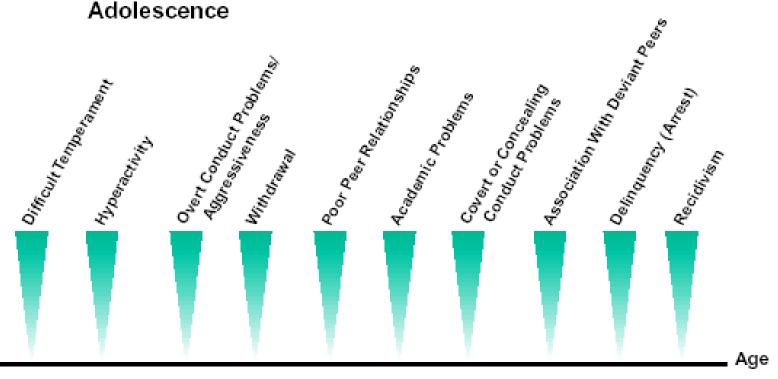


The Process is Cumulative \rightarrow

Infancy	Childhood	Adolescence	
Poor CNS Development	Hyperactive	Limited Impulse Control	
Fussy/Irritable	Impulsive	School failure	
Difficult to soothe	Peer Rejection	Poor relationships	
Less Parental Bonding	Language/Reading Probs.	Deviant peers	
	Physical Aggression Aggressive bias		
	Lying	Drugs/Alcohol	
	Theft	Manipulation of others	
		Arrest	

The Process is Somewhat Sequential:

Figure 1: Approximate Ordering of the Different Manifestations of Disruptive and Antisocial Behaviors in Childhood and Adolescence



Adolescence

The Process is Identifiable Early in Life.



- Low IQ
- Low Self-Control
- Having Criminal Parents
- Concentration of Offending in Families
- **Generational Continuity**
- Genetic/Biological **Risk Factors**
- MAO-A
- Low Resting Heart Rate —

Leads to Outcomes in Childhood: Bullying

- Peer rejection
- Learning problems
- Limited vocabulary
- Repetition of grade
- School discipline
- Poor health, poor diet

- Vandalism and destructiveness
- Stressful parent-child relationship
- Conflict ridden relationships with others

To Outcomes in Adolescence:

- Violence
- Early onset drugs/alcohol
- Delinquent peers
- Motor-vehicle accidents
- Physical injuries
- Early onset of sexual relations
- Multiple sexual partners

- Smoking
- Suicide (6x higher)
- Mortality (all forms)
- School failure/dropping out
- Inadequate speech, language, and social skills
- Arrest
- Incarceration

To Outcomes in Adulthood:

- **O** Arrest
- **O** Imprisonment
- **O** Heavy drug use/addiction **O**
- Motor-vehicle wrecks/fatalities
- **O** Multiple divorces
- Multiple offspring with no visible means of support or interest

- Very poor employability, limited job history, long-term unemployment
 - Malingering (workman's comp)
- Very poor credit history, credit unworthiness
- **O** Venereal disease
- Criminal lifestyle.....frequent, highly versatile offending

Which Means That Maladaptive Behavior Becomes Very, Very Stable...

Individual differences in antisocial behavior can emerge early in the life-course. Some traits are measurable by 6 months of age!

At age 4 we can predict who will likely become a high-rate juvenile offender. By age 12 we can predict who will likely become a high-rate adult offender.

 ADULT CRIMINAL BEHAVIOR IS BETTER PREDICTED BY EARLY MISBEHAVIOR THAN BY ANY OTHER FACTORS (SES, family origin, or anything else).

 ADULT criminal behavior ALMOST REQUIRES early antisocial behavior.

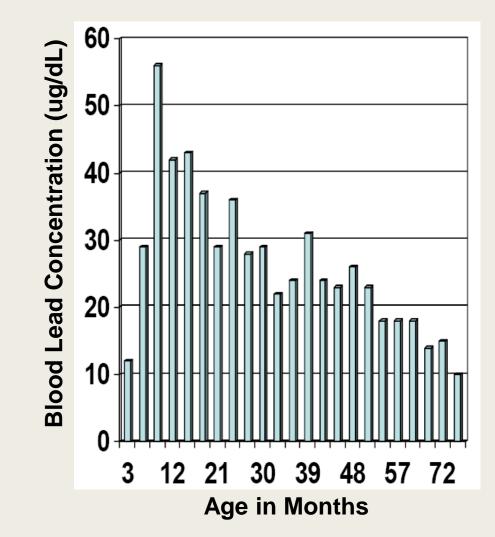
A Quick Note: Interviews with CLS Subjects Echoed This Pattern

- Interviews conducted by trained staff and by Kim Dietrich
- All were blinded to childhood blood profiles

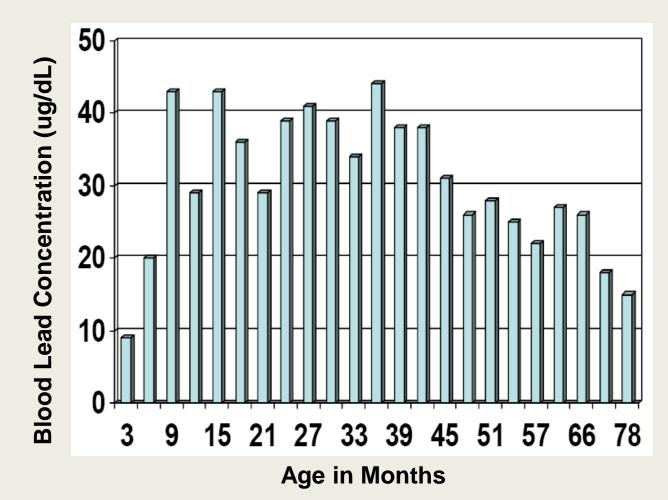
Adult CLS Subjects Commonly Reported the Same Problems....

- 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 Adult Criminal Behavior and Repeated Incarcerations



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



Standards of Evidence

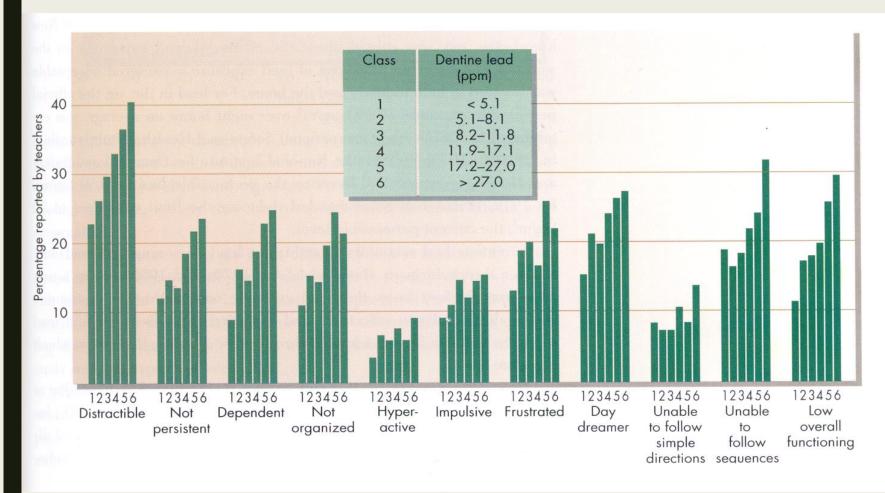
- Theory linking exposure and mechanism to outcome
 - Low Birth Weight
 - Low IQ
 - Structural and Functional Anomalies in the Brain
 - Neurotransmission
 - **Toxicokinetics**
- Diversity in the measurement of the risk variable (blood lead, dentine levels, bone lead, air lead)
- Diversity in the measurement of theoretically specified outcomes (IQ, emotional stability, school performance, delinquency, criminal behavior)
- Diversity across and within samples and types of samples (longitudinal, cohort, snowball....gender, race, SES)
- Measurement of potential operative mechanisms (fMri, x rayfluoroscopy)
- Diversity of analytical approaches under varied statistical assumptions

Isolating a "True" Lead Effect is Methodologically Difficult

- From a research perspective, any neurotoxin may affect a wide range of phenotypes in very complex ways. The interdependencies we see in the life-course—where independent variables at one time period become dependent variables later—mean that any number of confounders and moderators may be at work along the causal pathway.
- $Pb \rightarrow IQ \rightarrow Criminal Behavior$
- $Pb \rightarrow Self-Control \rightarrow Criminal Behavior$

Isolating a "true" lead effect becomes methodologically difficult

Lead-associated Behavioral and Emotional Problems in Children



Needleman HL, et al. N Engl J Med 1979;300:689-95.

Bone Lead Levels and Percentage of Children Scoring in the Clinical Range for Aggression, Delinquency, and Attention on the Achenbach Child Behavior Check List

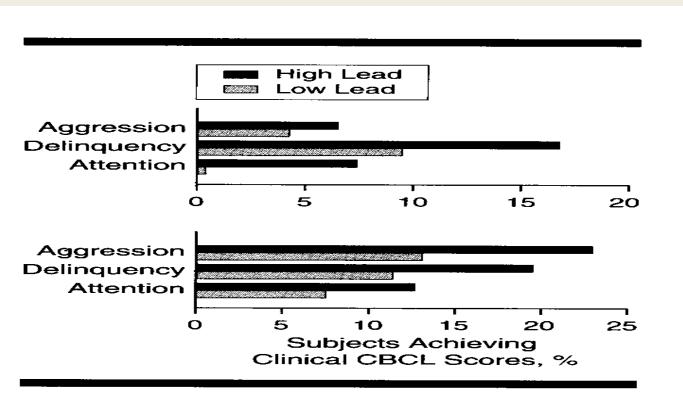


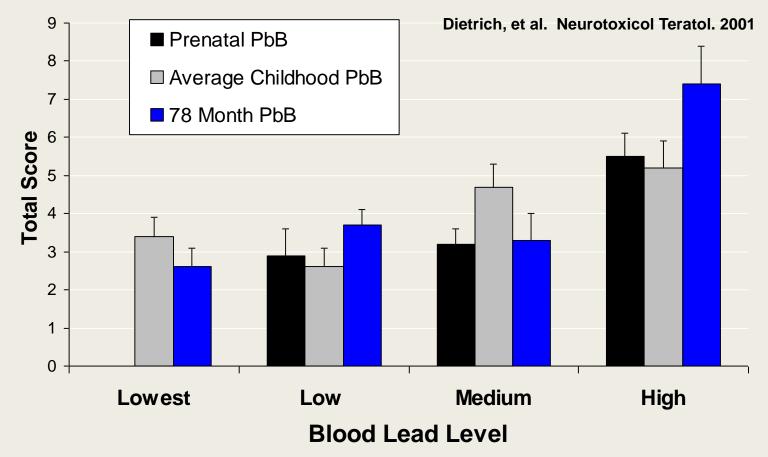
Figure 4.—The association between bone lead concentation and clinical Child Behavior Checklist (CBCL) (T>70) scores for aggression, delinquency, and attention. Subjects are classified as "high lead" (above the median) and "low lead" (below the median). Both parents' CBCL scores (top) and teachers' scores (bottom) are displayed.

Needleman, et al., JAMA, 1996. *Bone lead concentrations Measured in-vivo with K X-ray fluorescence spectroscopy. Bone Lead Levels (ppm) in Adjudicated Delinquents: A Case Control Study*

	Cases		Con	trols	P value
	n	Mean (SD)	n	Mean (SD)	
All Subjects	195	11.0 (32.7)	150	1.5 (32.1)	0.007
African-Americar	า 158	9.0 (33.6)	51	-1.4 (31.9)	0.05
White	36	20.0 (27.5)	95	3.5 (32.6)	0.008

*Needleman, et al. 2002, Neurotoxicology and Teratology.

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



Ecological Studies

Stretesky and Lynch (2001) reported positive correlations between homicide rates and air lead contamination levels for 3111 counties in the US. Even after adjustment for 15 confounding variables, a four-fold increase in homicides in the counties with the highest air lead concentrations compared to counties with the lowest air lead concentrations was found.

Stetesky & Lynch, Arch Pediatr Adolesc Med., 2001

Nevin (2000) reported a statistically significant relationship between trends in sales of leaded gasoline and violent crime after adjustment for such variables as unemployment rates and percent of population in the age range where is a higher risk for criminal behavior.

Nevin, Environ Res., 2000

CINCINNATI LEAD STUDY 1979-2014

Studies of Juvenile Delinquency and Adult Criminality



Cincinnati Lead Study catchment area

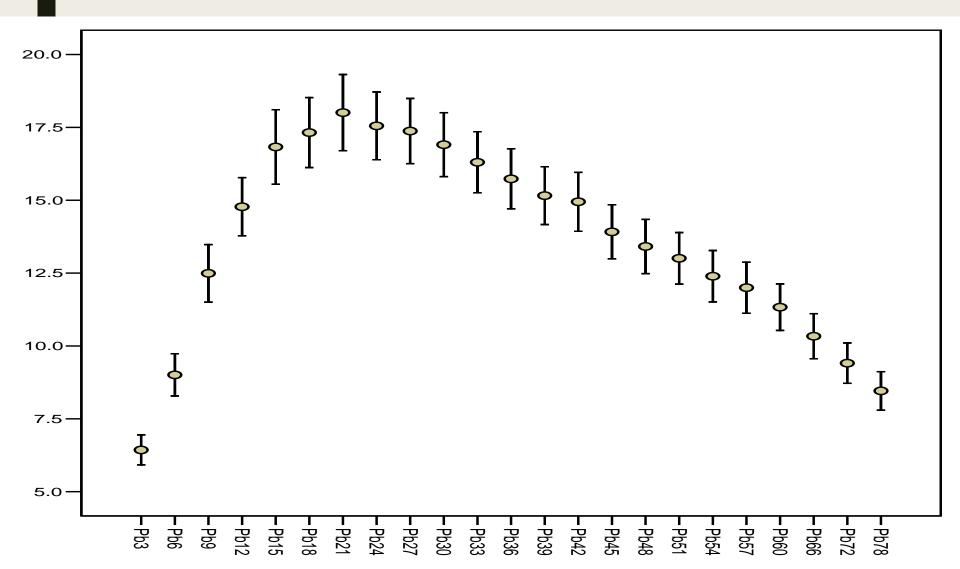
THE CINCINNATI LEAD STUDY

- A prospective study of offspring born to mothers in the catchment area (N=~250)
- Multiple measures of blood lead taken at regular intervals through 16 years
- Multiple neuropsychological measures
- Official measures of offspring and maternal criminal histories
- ACASI surveys including self-control, SR criminal behavior, urine tests, drug-use batteries
- fMRI scans

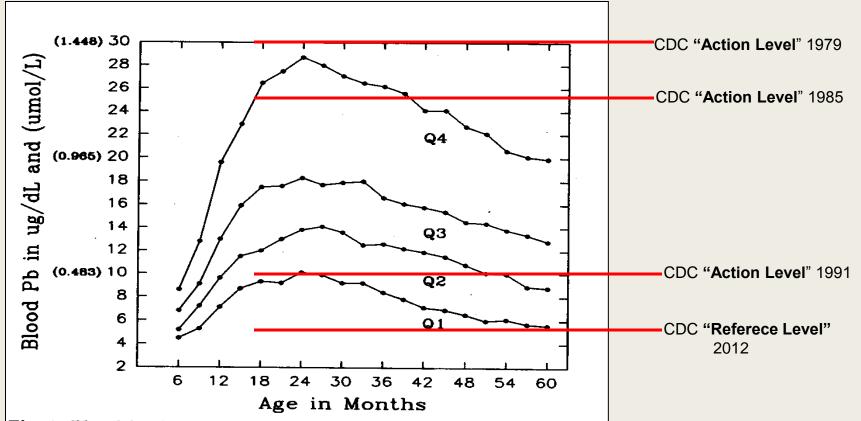
The Sample:

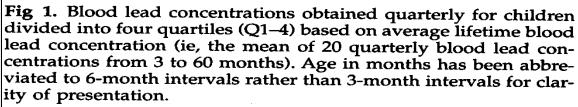
- Almost all are African-American
- Sample mothers scored in the lowest 2 categories on Hollingshead SES
- Average maternal IQ = 75
- Males 52% / Females 48%
- The latest wave of measurement concluded in 2013
- Subjects were between the ages of 27 and 33
- There was non-random selection out of the sample

Blood Lead Profiles:



Blood Lead Concentrations in the Cincinnati Lead Study





Dietrich, et al. Pediatrics, 1993.

Criminal Profiles

- We identified a total of 1129 arrests from 2003 to 2013
- We identified a total of 1429 lifetime arrests from 1997 to 2013
- A number of subjects with available childhood lead data were killed or imprisoned during the study
- Average male 8.1 lifetime arrests, sd=10.65 (n=986)
- Almost 85% of all males had an arrest record
- Average female 3.3 lifetime arrests, sd=4.1 (n=443)
- Almost 77% of all females had an arrest record

Negative Binomial Regression with Robust SE's: 2003-2013

Table 2: Association Between Childhood Blood Lead Measures in 5 mg/dL Increments and Adult Arrests 2003-2013

	Blood Lead Variable	Adult Arrests	Violent Arrests	Drug Arrests
-		RR (95% C.I.)		
	Prenatal Blood Lead	1.14 (1.03-1.26)*	* 1.17 (1.00-1.38)*	1.22 (1.02-1.47)*
-	Average Childhood Blood Lead	1.06 (1.01-1.12)*	1.05 (.96-1.15)	1.10 (.99-1.21)*
-	Average Late Childhood Blood Lead	1.10 (1.03-1.18)*	1.08 (.96-1.20)	1.18 (1.03-1.34)*
•	6-Year Blood Lead	1.10 (1.02-1.19)*	1.12 (1.00-1.26)*	1.16 (1.01-1.35)*

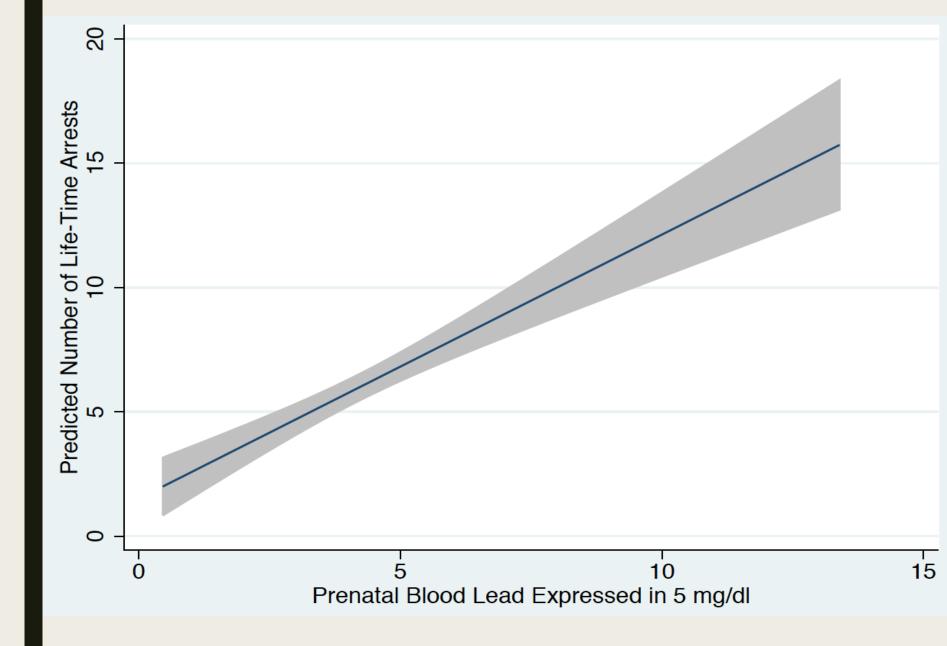
Coefficients significant at P<.05, one-tailed, age, race, sex, and previous arrests (1998-2003) controlled in each equation. Rate ratios are reported and reflect percentage changes in expected counts of arrest associated with a unit change in the dependent variable.</p>

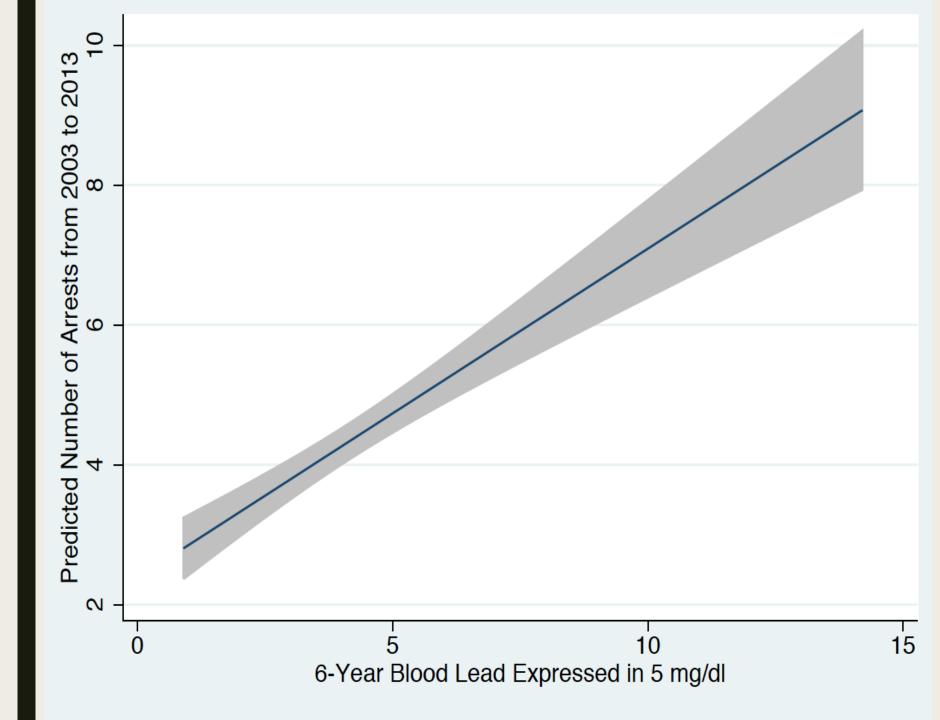
Negative Binomial Regression with Robust SE's: Life-Time

Table 3: Association Between Childhood Blood Lead Measures in 5 mg/dL, Total Life Arrests, and Changes in Adult Arrests Over Time

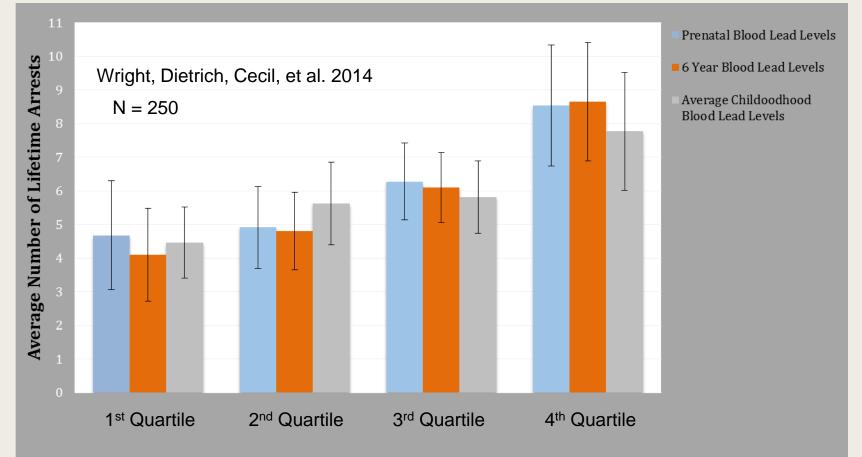
	Blood Lead Variable	Total Life-Time Arrests	Controlling for Prior Arrests
•		RR (95% C.I.)	RR (95% C.I.)
	Prenatal Blood Levels	1.15 (1.05-1.27)	* 1.07 (1.03-1.11)*
•	Average Childhood Blood Lev	els 1.05 (1.00-1.11)	* 1.05 (1.01-1.09)*
•	Average Late Childhood Blood	d Levels 1.10 (1.02-1.17)	* 1.08 (1.02-1.14)*
•	6-Year Blood Levels	1.11 (1.04-1.20)	* 1.06 (1.00-1.12)*

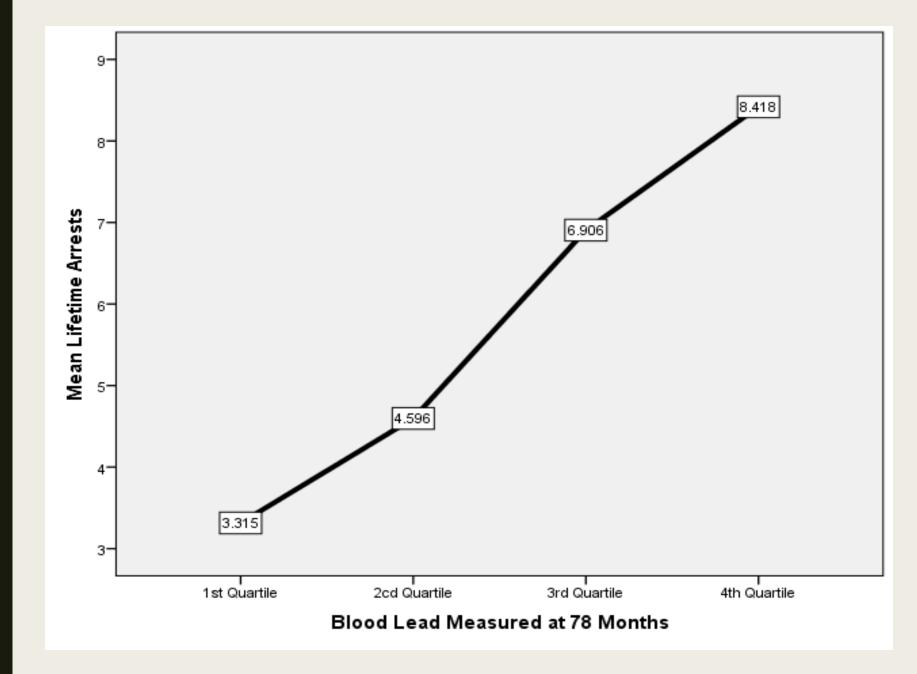
- Coefficients significant at P<.05, one-tailed, age, race, sex controlled in each equation. Rate ratios are reported and reflect percentage changes in expected counts of arrest associated with a unit change in the dependent variable.

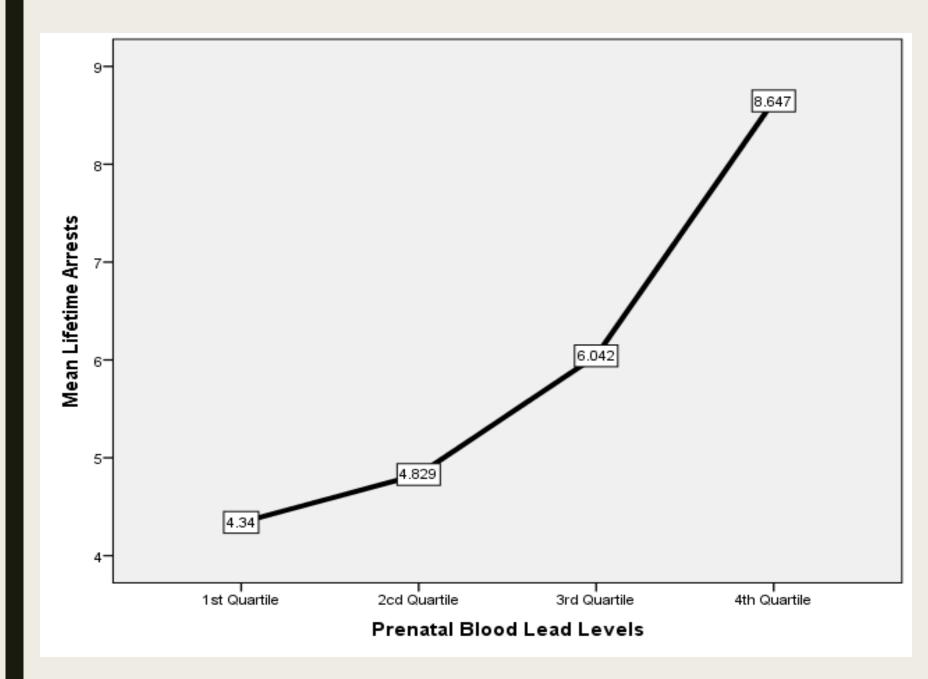




Adjusted Adult Lifetime Average Criminal Arrests 18 to 33 years by Blood Pb Quartiles in







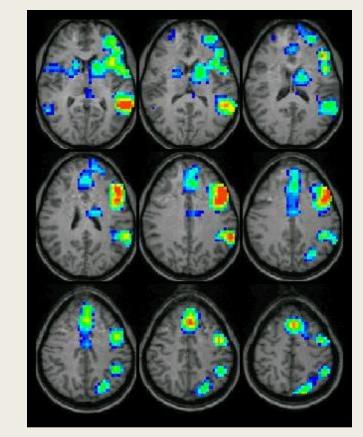
Number of Arrests by Blood Pb Quartile



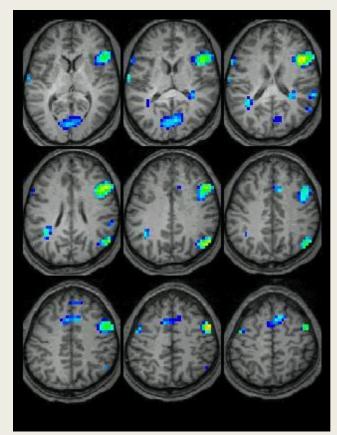
Cincinnati Neuroradiological Studies of Childhood Lead Exposure and Adult Brain Outcomes

- 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).

Functional MRI During a Verb Generation Task: The Cincinnati Lead Study Cohort



Lower Lifetime Mean Blood Lead (7.6 µg/dL)

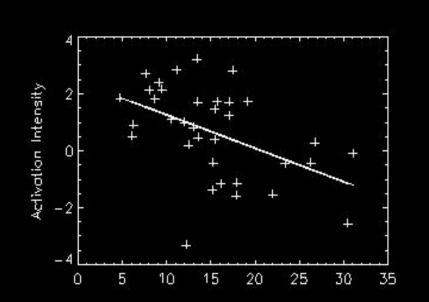


Higher Lifetime Mean Blood Lead (26 µg/dL)

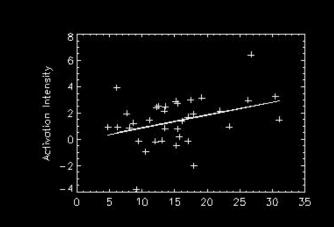
Decreased activation of Wernicke's and Broca's areas in the left cerebral hemisphere in young adults with a history of higher postnatal lead exposure.

Contralateral reorganization of language functions

BROCA'S AREA DEACTIVATION (LEFT) WERNIKES ON RIGHT: STRIKING DOSE DEPENDENCY



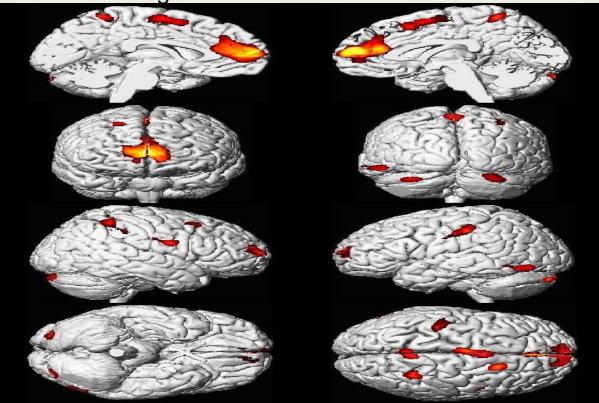
R = -0.480980, p = 0.00344588



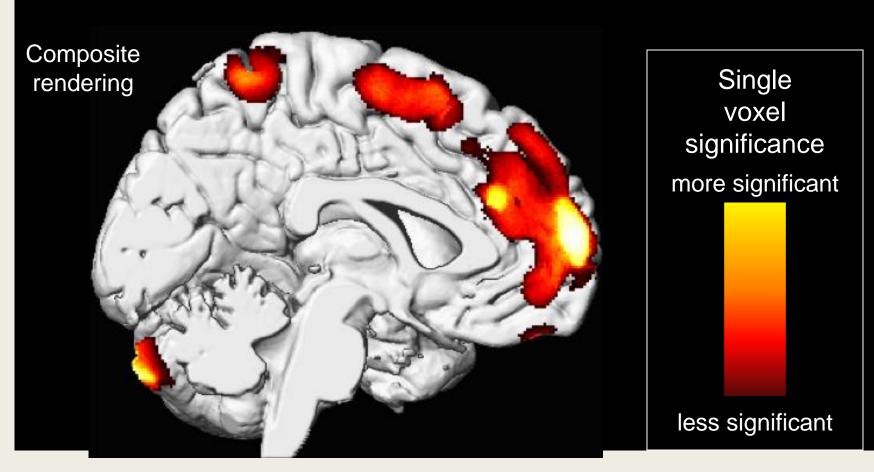
R = 0.356293, p = 0.0356582

Lead Associated Gray Matter Loss in Brain: Cincinnati Lead Study Cohort

Average Childhood Blood Lead



Lead-associated gray matter loss most severe in the frontal regions of brain involved in attention, executive functions, and regulation of social behaviors. Brighter areas indicate greater loss. Adult Cortical Gray Matter Loss in Cincinnati Lead Study Subjects in Relationship to Postnatal Lead Exposure to Six Years



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.

Standards of Evidence: Revisited

- Theory linking exposure and mechanism to outcome
 - Low Birth Weight
 - Low IQ
 - Structural and Functional Anomalies in the Brain
 - Neurotransmission
 - **Toxicokinetics**
- Diversity in the measurement of the risk variable (blood lead, dentine levels, bone lead, air lead)
- Diversity in the measurement of theoretically specified outcomes (IQ, emotional stability, school performance, delinquency, criminal behavior)
- Diversity across and within samples and types of samples (longitudinal, cohort, snowball....gender, race, SES)
- Measurement of potential operative mechanisms (fMri, x ray-fluoroscopy)
- Diversity of analytical approaches under varied statistical assumptions

CONCLUSIONS

Data from the Cincinnati Lead Study indicate a robust prospective association between prenatal and early postnatal exposure to lead and adult criminal behaviors. This includes violent behavior.

Neuroimaging studies indicate a contralateral reorganization of language functions based on dosage.

Neuroimaging studies indicate hypoactive right hemispheric metabolism in verb generation task based on dosage.

Neuroimaging studies of the Cincinnati Lead Study cohort indicate lead-associated losses in gray matter of the cerebral cortex in areas of the brain that regulate attention, executive functions, judgment and social behaviors.