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Biomarkers of Prenatal Exposure to Air Pollution and Children's Health and Development

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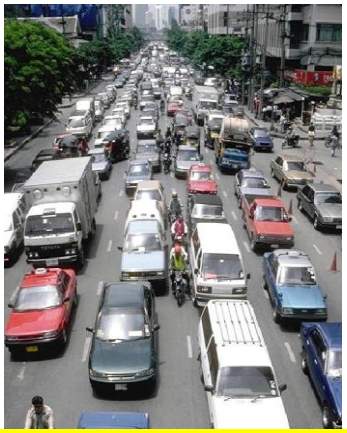
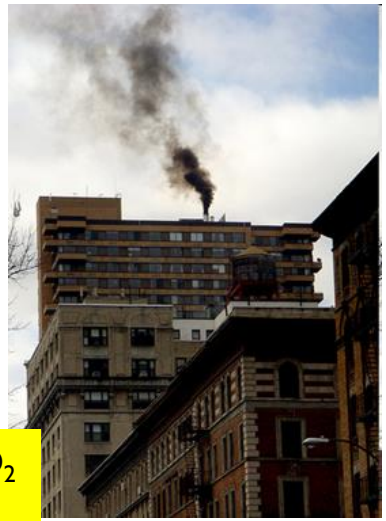
Emissions from Fossil Fuel Combustion





>80% of toxic air pollutants and CO_2

Worsening State of the Air and the Climate

- As much as 90 percent of the total global population is exposed to air pollution above World Health Organization guidelines for health protection.

- We are on track to reach the IPCC "threshold"* for avoiding the most catastrophic effects of climate change within the next two decades

*no greater than 1.5 °C increase in temperature above preindustrial levels by end of the century

Combined Effects and Synergy

Air Toxics

$PM_{2.5}$, PM_{10}

PAH

NO_2

Black Carbon

Mercury, SO_2,

Ozone precursors (NOx, VOCs)

Climate Change

Temperature changes

Precipitation extremes (rain bombs or drought)

Extreme weather events

More forest fires

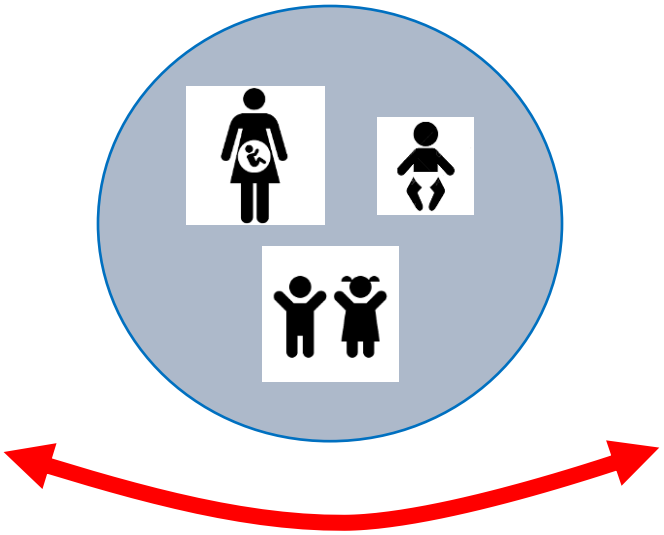
More allergens

Higher levels of O_3, $PM_{2.5}$, BC

Multiple/ Cumulative Health Effects

Air Toxics

- Infant mortality
- Preterm birth
- Low birth weight
- Asthma exacerbation
- New cases of asthma
- Decreased lung function
- Immune disorders
- Neurodevelopmental effects (IQ, ASD, ADHD)
- Mental health disorders
- Alterations in brain structure



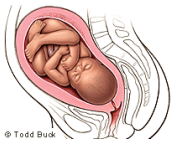
...And the two can interact to heighten risks

CO_2/Climate Change

- Preterm birth
- Low birthweight
- Allergy/asthma exacerbation
- Neurodevelopmental effects
- Heat-related illness
- Malnutrition/stunting
- Infectious disease
- Forced migration
- Trauma
- PTSD, chronic stress
- Mental health disorders

Susceptibility of the Fetus

- Complex and rapid development of the brain, respiratory and other systems
- Immature detoxification, DNA repair and immune systems
- Vulnerability to maternal stress
- Life course impacts
- "Seeding" of chronic diseases *in utero*
- Possible transgenerational inheritance



Timing of Maturational Events in Human Brain Development

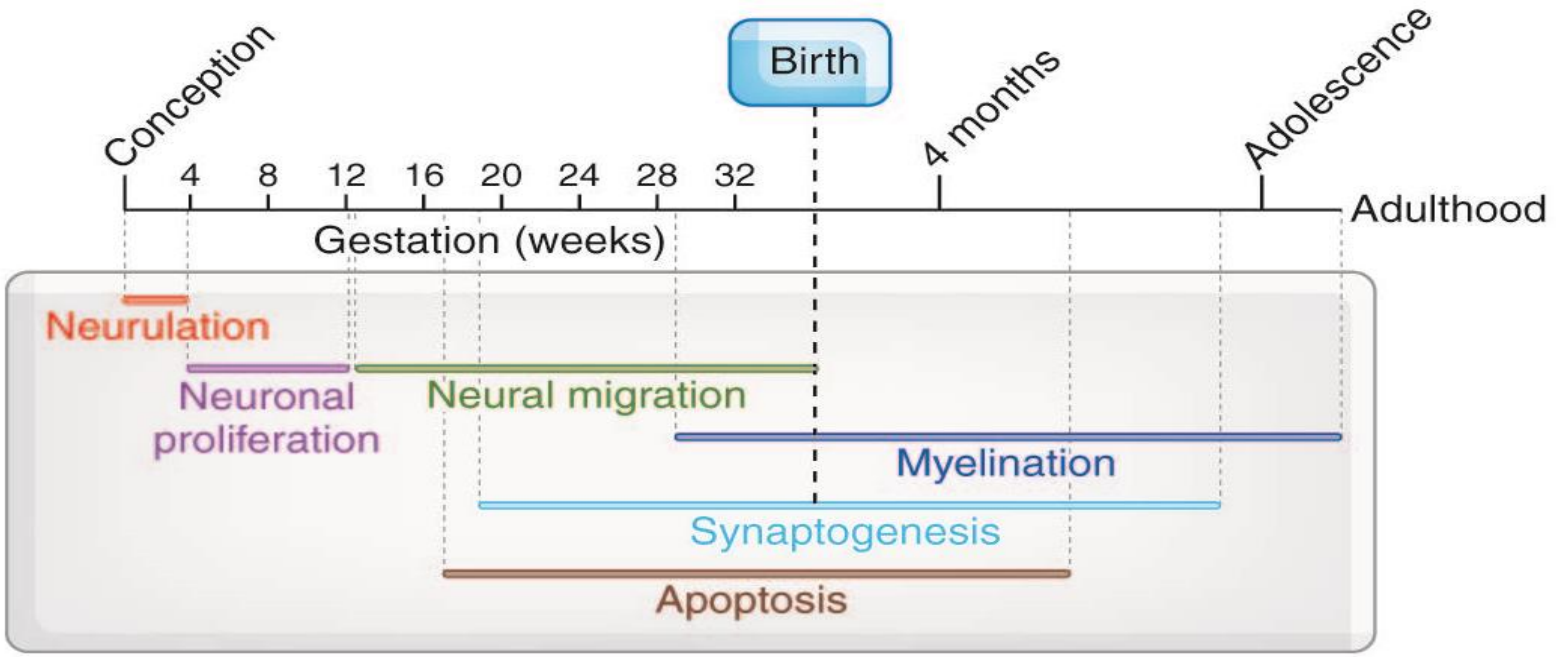


Fig.1. Timing of Maturational Events in Human Brain Development

(Giedd J. Brain development, IX: human brain growth. Am J Psychiatry. 1999;156(1):4)

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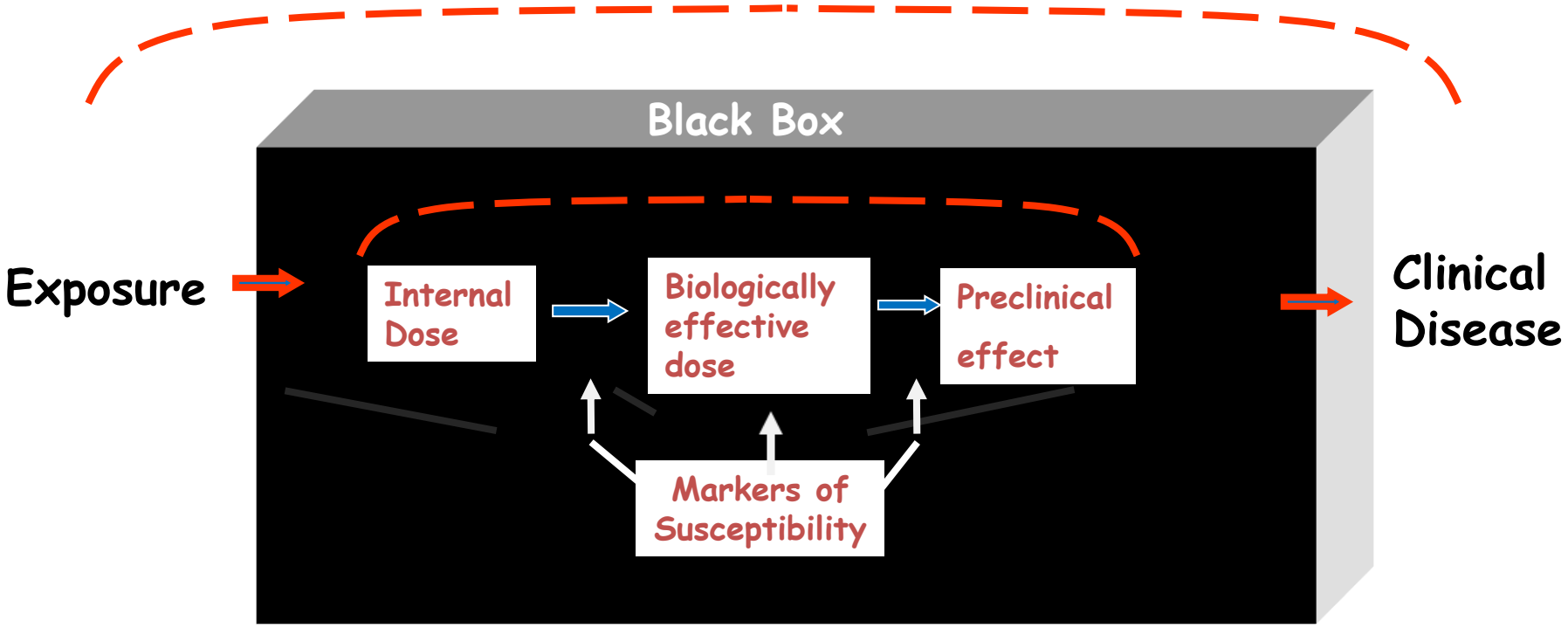
Environmental/Climate Injustice

- The young bear the brunt.
- Disproportionate exposure to toxic air pollution and climate change risks in developing countries and disadvantaged communities in rich countries
- Environmental and socioeconomic/ psychosocial "stressors" interact to magnify adverse health effects

Molecular Epidemiology and Biomarkers



(Perera and Weinstein, J Chron Dis 35:581, 1982, NAS 1987)

Biomarkers of Prenatal Air Pollution Exposure

Biomarker	Prenatal Exposure	Outcome	Type of Study	Reference
Shortened telomere length (cord)	PAH		Cohort study (China)	
Shortened telomere length (placenta)	TRAP		Twin study (Belgium)	Bijnens et al., 2015
Decreased mitochondrial (mt) DNA content; increased mtDNA methylation (placenta)	PM2.5, PM10	Lower birth weight	Cohort study: ENVIRONAGE (Belgium)	Janssen et al., 2015
Decreased mtDNA content (placenta)	NO2	Lower birth weight	Cohort studies: INMA (Spain) and ENVIRONAGE (Belgium)	Clemente et al., 2015
Increased 3-nitrotyrosine levels (placenta)	PM2.5		Cohort study: ENVIRONAGE (Belgium)	Saenen et al., 2016
15-F2t-isoprostane (cord)	PM2.5, benzo[a]pyrene		Case-control study (Czech Republic)	Ambroz et al., 2016
Increased mitochondrial 8-hydroxy-2′-deoxyguanosine (8-OHdG) levels (maternal blood); increased 8-OHdG (cord)	PM10, PM2.5		Cohort study: ENVIRONAGE (Belgium)	Grevendonk et al., 2016
Increased maternal C-reactive proteins (serum); elevated CRP (cord)	PM10		Cohort study (PA)	Lee et al., 2011

Biomarkers of Prenatal Air Pollution Exposure

Biomarker	Prenatal Exposure	Outcome	Type of Study	Reference
Decreased CD4, CD25 , CD8 cells (cord)	PM10.NO2		Cohort study: EDEN (France)	Baiz et al., 2011
Decreased global methylation, inversely associated with PAH-DNA adducts (cord)	PAH		CCCEH cohort study (NYC)	Herbstman et al., 2012
DNA methylation changes (EWAS) (cord)	PAH, PM2.5		CCCEH cohort study (NYC)	In prep.
Decreased global DNA methylation (placenta)	PM2.5		Cohort study: ENVIRONAGE (Belgium)	Janssen et al., 2013
Increased PAH-DNA adducts (cord)	PAH	Reduced head circumference	Cohort study (China)	Tang et al., 2006
Increased PAH-DNA adducts (cord)	PAH	Reduced IQ scores	Cohort study (NYC)	Vishnevesky et al., 2015
Increased PAH-DNA adducts (cord)	PAH	Decreased birth length, weight, and head circumference	Cohort study (Poland)	Perera et al., 1998
Increased PAH-DNA adducts (maternal blood)	PAH	Delayed self-regulatory development and autistic traits	Cohort study (NYC)	Margolis et al., 2016

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CCCEH: International Cohort Studies

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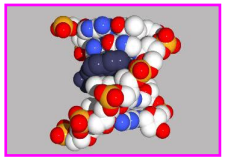
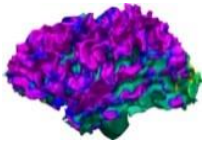
Effects of Prenatal Exposure to PAH and/or PAH-DNA Adducts* Observed in NYC and/or Krakow Children



- Reduced birth weight and head circumference*
- Asthma and allergic sensitization
- Developmental delay
- Reduced IQ*
- Behavioral problems*
- Symptoms of anxiety/depression *
- ADHD*
- Decreased emotional regulation capacity and autistic traits*
- Interaction of PAH and material hardship on IQ and ADHD
- Interaction of PAH and early life stress on attention problems and ADHD*
- MRI brain changes

All significant (<0.05) after adjusting for potential confounders



* Perera et al., 1998, 2011;2011, 2012, 2014; Vishnevetsky et al., 2015; Margolis et al., 2016

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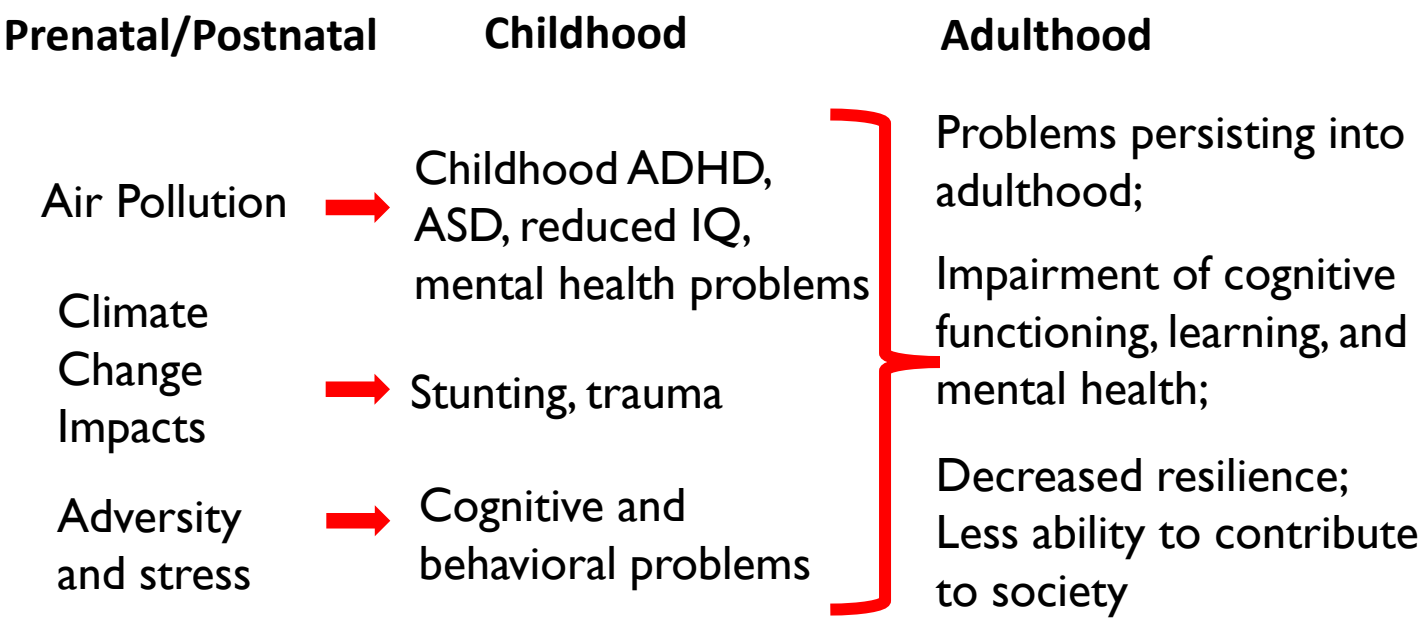
Long-Term Impacts



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Biomarkers Can Support Policy Interventions

- NYC
- Krakow, Poland
- Chongqing, China

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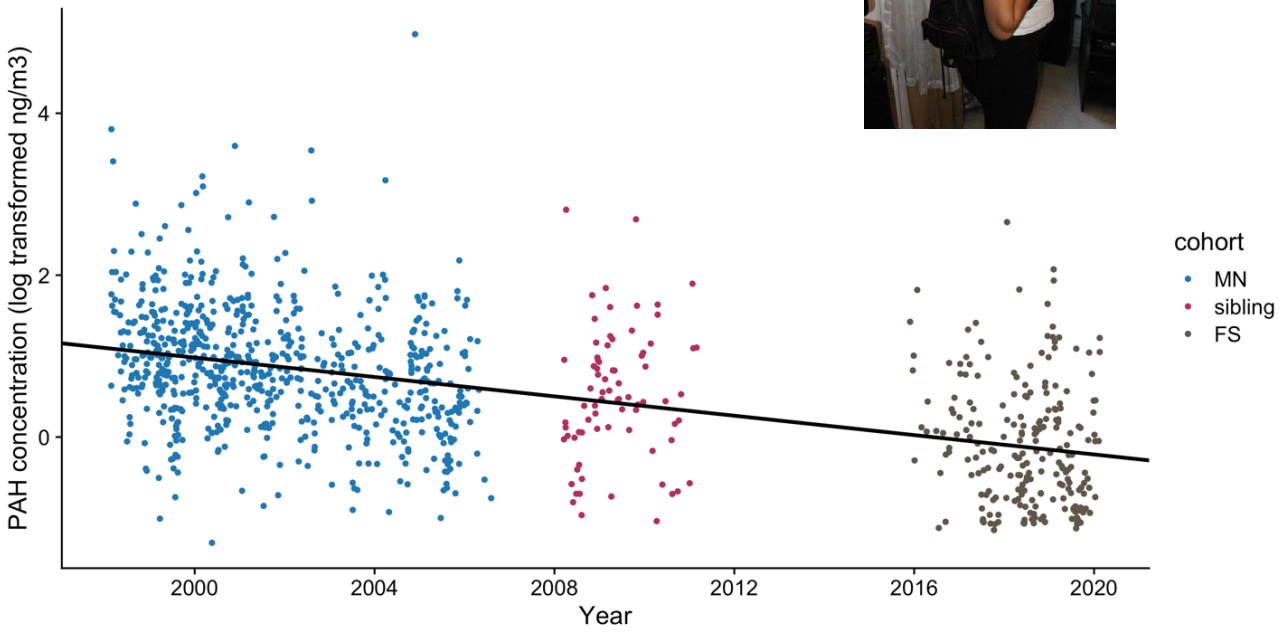
CCCEH Data Credited with Supporting City-Wide Policies to Reduce Air Pollution

Personal prenatal exposure to PAH in the NYC cohort declined from 1998 to 2021 ($p<0.00001$)

NYC regulations (e.g.):

Clean taxi, diesel buses and trucks

Clean heat program



" CCCEH findings ... encouraged our Administration's ongoing commitment to reducing traffic and other airborne contaminants throughout the five boroughs." (Michael R. Bloomberg, March 30, 2009)

[In preparation]

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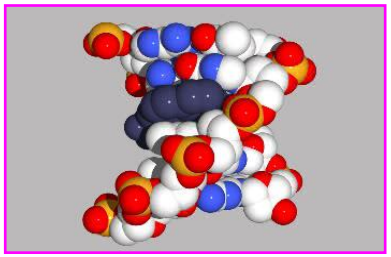
Interventions Work: Pre- and Post- Closure of a Coal Burning Power Plant in Chongqing, China

Cohort I
3/02-6/02
150 pairs

Cohort II
3/05-6/05
150 pairs

At Birth

Taking Gesell test at age 2



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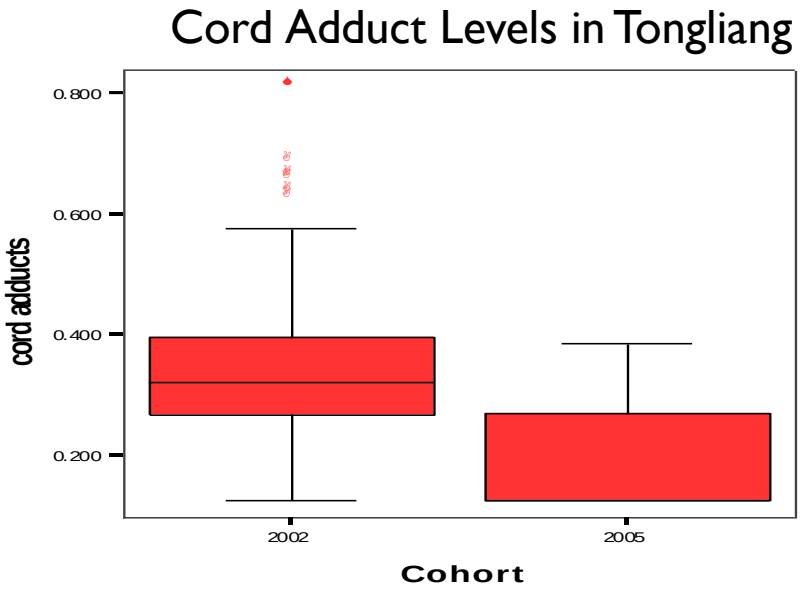
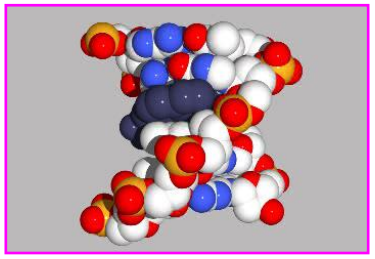
Benefits of Coal Plant Closure





- Ambient air levels of PAH significantly reduced between 2002 and 2005
- PAH-DNA adduct levels in newborns significantly lower in second (2005) cohort
- Mean level of the neurotrophin BDNF significantly higher in the 2005 cohort (1267 pg/ml vs. 753 pg/ml, $p<0.05$)
- We no longer observed significant associations between exposure (adducts) and lower developmental scores at age 2 in the 2005 cohort

[Tang et al. 2008; Perera et al. 2008; Tang et al., 2014]

Research needs

More studies using biomarkers in assessing effects:

- Life course and transgenerational effects
- Cumulative effects
- Interactions between air pollution and climate change
- Interactions of air pollution and stress

More studies incorporating biomarkers into assessment of benefits of regulation and other interventions

More focus on pregnant women and children in environmental justice communities

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Vulnerability to Epigenetic Dysregulation