A developmental perspective on early-life exposures to neurotoxicants

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Making the Link Between Environmental Exposures and Neurodevelopmental Disorders More Compelling to Stakeholders (public, regulators, politicians)

• Importance of developing a broader and more integrated story about how early-life exposure to a neurotoxicant can impact a child’s developmental trajectory in multiple domains, the downstream effects: example of childhood lead exposure and criminal offending in young adulthood

• Early-life exposure to neurotoxicants affects how effectively an individual is able to respond to later neurological insults, i.e., an effect modifier that reduces resilience or cognitive reserve

• A focus on population rather than individual risk produces a more veridical assessment of the societal impact of neurotoxicant exposures (the “prevention paradox”)
Association Between Childhood Lead Exposure and Criminal Behaviors in Adolescence and Young Adulthood

- Emer et al. Environ Res, 2020;180: article 108882
- Coulton et al. (2020)
Relationship of Concurrent Blood Lead Level and IQ:
Lanphear et al. *Environ Health Perspect* 2005;113:894-899

![Graph showing the relationship between concurrent blood lead level (µg/dL) and IQ. The graph includes a log-linear model and a 5-knot restricted spline.](image_url)
Blood Lead Level and ADHD: NHANES 1999-2002

Figure 1. AOR for ADHD among U.S. children, NHANES 1999–2002, by blood lead concentration (µg/dL). The model was adjusted for child’s age, sex, race/ethnicity, preschool attendance, serum ferritin, prenatal ETS exposure, smoker in the household, and insurance status. p-value for trend = 0.012.

Needleman et al., 1979
Nigg et al., 2008
Wang et al., 2008
Froehlich et al., 2009
Nigg et al., 2010
Goodlad et al., 2013
Kim et al., 2013
Park et al., 2016
Choi et al., 2016
Darneshparvar et al., 2016
Nigg et al., 2016

Braun et al. Environ Health Perspect 2006;114:1904-1909
Blood Lead Levels and Performance on End-of-Grade Reading Achievement Test, 2000-2004, NC 4th graders (N=8,600)

Figure 4. Percent of students failing 4th-grade Reading EOG.

Miranda et al., Environ Health Perspect 2007;115:1242-1247
Blood Lead Level and “Exceptionality Designations” in 4th Graders (Miranda et al. Int J Child Health Hum Dev 2010:3:77-84)

AIG: advanced and intellectually gifted
LBED: learning and behavioral exceptional
EDO: designated exceptional for other reasons (sensory, physical, ASD, severe IDD)
Change in IQ and SES: 11 to 38 Years by Blood Lead Concentration at 11 Years: Dunedin Study (Reuben et al. JAMA 2017;317:1244-51)
Developmental Cascade Linking Childhood Lead Exposure to Adverse Outcomes in Adulthood: for some individuals, reduction in IQ might be the beginning, not the end of the story.

Children who, prior to age 3 years, had a blood lead concentration above 5 ug/dL (current CDC reference value) were:

- 27 percent less likely to be ready for kindergarten
- 30 percent more likely to enter the juvenile justice system
- 34 percent more likely to be incarcerated as young adults
- 40 percent more likely to experience some level of homelessness
Early-Life Neurotoxicant Exposure as an Effect Modifier: Early Lead Exposure Alters Adult Rat Response to a Photothrombotic Stroke in Hind Limb Parietal Sensorimotor Cortex

Square: lead-exposed
Circle: controls

A: beam walking;
B: proprioceptive limb placing

Roots of Environmental Injustice

• Disadvantaged children tend to be:

  • more highly exposed to neurotoxicants

  • the same magnitude of exposure has greater adverse impact than on more advantaged children

  • early life exposures appear to make them less resilient in responding to later neurological insults and, perhaps, less able to benefit from environmental factors that support optimal development
Focusing on Population Rather than Individual Risk in Quantifying Impact of Neurotoxicants

Total IQ Losses Associated with Medical Events/Conditions, US Children 0-5 Years (Bellinger, *Environ Health Perspect* 2012; 120:501-7)

<table>
<thead>
<tr>
<th>Event/Condition</th>
<th>Total Number of IQ points Lost</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brain tumors</td>
<td>37,288</td>
</tr>
<tr>
<td>Duchenne muscular dystrophy</td>
<td>68,850</td>
</tr>
<tr>
<td>Congenital heart disease</td>
<td>105,805</td>
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<tr>
<td>Chemotherapy (ALL)</td>
<td>135,788</td>
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<tr>
<td>Type 1 diabetes</td>
<td>185,640</td>
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<tr>
<td><strong>Methylmercury</strong></td>
<td><strong>1,385,785</strong></td>
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<tr>
<td>Pediatric bipolar disorder</td>
<td>2,203,200</td>
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<tr>
<td>Traumatic brain injury</td>
<td>4,856,086</td>
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<tr>
<td>Nonorganic failure to thrive</td>
<td>5,355,000</td>
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<tr>
<td>Autism spectrum disorders</td>
<td>7,018,563</td>
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<tr>
<td>Iron deficiency</td>
<td>9,409,510</td>
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<tr>
<td>ADHD</td>
<td>16,799,400</td>
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<tr>
<td><strong>Organophosphate pesticides</strong></td>
<td><strong>18,978,019</strong></td>
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<tr>
<td>Lead</td>
<td><strong>22,947,853</strong></td>
</tr>
<tr>
<td>Preterm birth</td>
<td>34,031,025</td>
</tr>
</tbody>
</table>
Estimated Loss of IQ in US Children at Different Intervals of Blood Lead (µg/dL)

- Current Reference Value = 5 µg/dL
- 0.5 Million children with 6.1 IQ points lost
- 5.7 Million children with 1.6 IQ points lost
- 6.4 Million children with 0.9 IQ points lost
- 12.7 Million children with 0.3 IQ points lost

Total Estimated IQ Points Lost:
- 3.1 Million
- 9.3 Million
- 5.7 Million
- 4.7 Million

- 13%
- 41%
- 25%
- 21%