Assessing Neurodevelopment in Parallel Animal and Human Studies

Children's Environmental Health Research Center at Illinois
Researching the impact of bisphenol A (BPA) and phthalates on child development
Focus of the Children’s Health Center at Illinois

- Study the impact of chemicals in consumer products on neurodevelopment.
- Assess exposures during the prenatal and adolescent periods.
- Investigate whether maternal obesity increases risks from prenatal chemical exposure.
Center Investigators—A Diverse Team

Susan Schantz (director)—Neuroscience/Toxicology
Jodi Flaws (associate director)—Reproductive Biology/Toxicology
Jay Ko—Reproductive Biology
Sidonie Lavergne—Immunology
Sharon Donovan—Nutritional Science
Yuan Xiang Pan—Nutritional Science
Andrea Aguiar—Developmental Psychology
Renee Baillargeon—Developmental Psychology
Daniel Hyde—Developmental Psychology/Neuroscience
Janice Juraska—Biological Psychology/Neuroscience
Susan Korrick (Harvard Medical School)—Epidemiology
Joseph Gardiner (Michigan State University)—Biostatistics
Barbara Fiese—Community Outreach
Lizanne Destefano—Community Outreach/Evaluation
Parallel Studies in Animal Models and Exposed Human Populations

• In animal models we aim to:
  – Closely model human exposure.
  – Conduct studies that probe the underlying biological mechanisms.
  – Use results to guide selection of health outcomes for studies of children.
Prospective Birth Cohort Study

• Goal is to develop better tools that will allow us to reliably identify neurodevelopmental risks from prenatal exposures much earlier.

• Use tests that assess core cognitive abilities.
  
  – information processing ability, working memory, attention.

  – predictive of cognitive function later in childhood.
Neonatal Memory & Attention Task

Andrea Aguiar
Event Related Potentials (ERPs)

• Babies see stream of faces with occasional test images that are either the same or novel.

• Compare responses to the same and novel test images (difference scores).

• Five spatial and temporally distinct components that measure:
  • Visual processing
  • Attention
  • Memory
4-5 Month Tasks That Assess Sexual Dimorphisms in Cognition

- **Spatial reasoning**—mental rotation task (Moore and Johnson).
  - Boys out perform girls.

- **Physical reasoning**—magic—real task (Baillargeon).
  - Girls out perform boys.
Set Up for 4-5 Month Tests
Looking Time to the “Magic” and “Real” Events

<table>
<thead>
<tr>
<th></th>
<th>GIRLS</th>
<th>BOYS</th>
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<tbody>
<tr>
<td>Magic</td>
<td>24.5</td>
<td>23.7</td>
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<tr>
<td>Real</td>
<td>20.3</td>
<td>23.2</td>
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Why Does This Difference Exist?

• Binocular vision develops earlier in girls.
  – Learn about physical relationships between objects at earlier age.
  – Slower development in boys mediated by prenatal exposure to androgens.

• Endocrine disruptors (especially anti-androgenic chemicals like phthalates) could affect this process.
Adolescent Cohort Study

New Bedford Birth Cohort Study (NBC)


- Maternal residence in towns next to PCB-contaminated harbor in New Bedford, MA.

- Parent study goal to assess PCBs, OC pesticides, metals and child development.
Study Design and Timeline

Birth 1993-1998 (n=788)

6 months 8 years 15 years
(n=297) (n=607) (n=528)

Exposure (cord blood & maternal hair, nails, milk), behavior, growth

Cognition, growth

Cognition, behavior, growth

Exposure (urine), cognition, behavior, growth

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Outcome Assessment

**Visual Motor Abilities**
- Wide Range Assessment of Visual Motor Abilities (WRAVMA)

**Verbal Abilities**
- Wide Range Achievement Test (WRAT-4: Reading)
- Verbal Memory (WRAML2)

**Math skills**
- Wide Range Achievement Test (WRAT-4: Math)

**Executive Function:**
- Working Memory (WRAML2)

**ADHD-related Behavior**
- Conners’ Attention Deficit Scale (CADS)

**Psychiatric Symptoms**
- Behavioral Assessment System for Children (BASC-2: teacher, parent, self)

**Social Cognition**
- Developmental Social Disorders (BASC-2)
Neuron and glia numbers are increased in the prefrontal cortex of BPA-exposed male rats.
Neuron and Glia Numbers after Adolescent BPA Exposure

Glia numbers were increased in females and decreased in males.

There was no change in astrocytes but microglia were increased in females and decreased in males.
Summary

• Using complementary studies in animal models and humans to identify risks from chemical exposures.

• Studying exposure during two key developmental periods: prenatal and adolescent.

• Focusing on basic building blocks of cognition (information processing, attention and memory) that are relatively stable across time.

• Addressing whether EDCs disrupt typical male-female differences in cognition.

• Using animal models to determine if there are underlying changes in brain development.