Environmental endocrine disruptors, the developing brain, and behavior

Andrea C. Gore, PhD
Pharmacology & Toxicology
College of Pharmacy
The world is contaminated and will never return to conditions that existed prior to the industrial and chemical revolutions.

Although some local remediation of contamination has occurred, at a global level this is simply not possible.
Environmental Endocrine-Disrupting Chemicals (EDCs)

“An endocrine disruptor is an exogenous chemical, or mixture of chemicals, that interferes with any aspect of hormone action”

Zoeller et al. (2012) Endocrinology 153: 4097

- Industry (PCBs, dioxins)
- Pesticides, fungicides (DDT, methoxychlor, vinclozolin)
- Pharmaceuticals (DES, EE)
- Plastics (BPA), Plasticizers (phthalates)
- Phytoestrogens (soy, alfalfa)
- Heavy metals
EDCs: Links to human health?

NHANES & Epidemiological Studies show:

• 287 chemicals in cord blood
• In breast milk (PCBs, dioxins, pesticides, mercury, flame retardants)
• Of people tested by CDC:
  – BPA in 93%
  – Phthalates 50-97%
  – PFCs in 91-99%
  – PBDEs in 100%
  – Triclosan in 80%
  – PCBs in 100%

Prenatal EDCs and the Developing Brain

Brain sexual differentiation, gene/protein expression, HPG axis physiology, hormones, & behaviors

Developmental Hormones, EDCs

Sex differences in ASD, ADHD, cognitive, affective, & neurodegenerative disorders

Central Hypothesis: EDC exposures during critical windows reprogram hypothalamic development

Developmental changes in gene and protein expression; DNA methylation; hormonal and physiological effects
Behavioral consequences of prenatal EDC exposures

Social, sociosexual, anxiety-like behaviors
Involve hypothalamus and other brain regions
Developmental exposure to PCBs

Critical Period of brain sexual differentiation

- E0
- E16, E18
- P0
- P15, P30, P45, P90
- Birth
- 9-18 months
What have we learned from this research?

• Exposure to PCBs during a critical period of brain development reprograms gene expression in the hypothalamus.

• Effects on genes and proteins in the brain are sex-, brain region, and developmental stage-specific.

• These molecular changes are accompanied by changes in physiology, development, and behavior.

• We see substantial alterations in reproductive aging, and lifelong changes in gene expression in the brain.

• There are transgenerational effects of EDCs on brain and behavior, at least 3 generations after exposure.
Thank you!

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Our happy rats