Environmental endocrine disruptors, the developing brain, and behavior

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The world is contaminated and will never return to conditions that existed prior to the industrial and chemical revolutions.

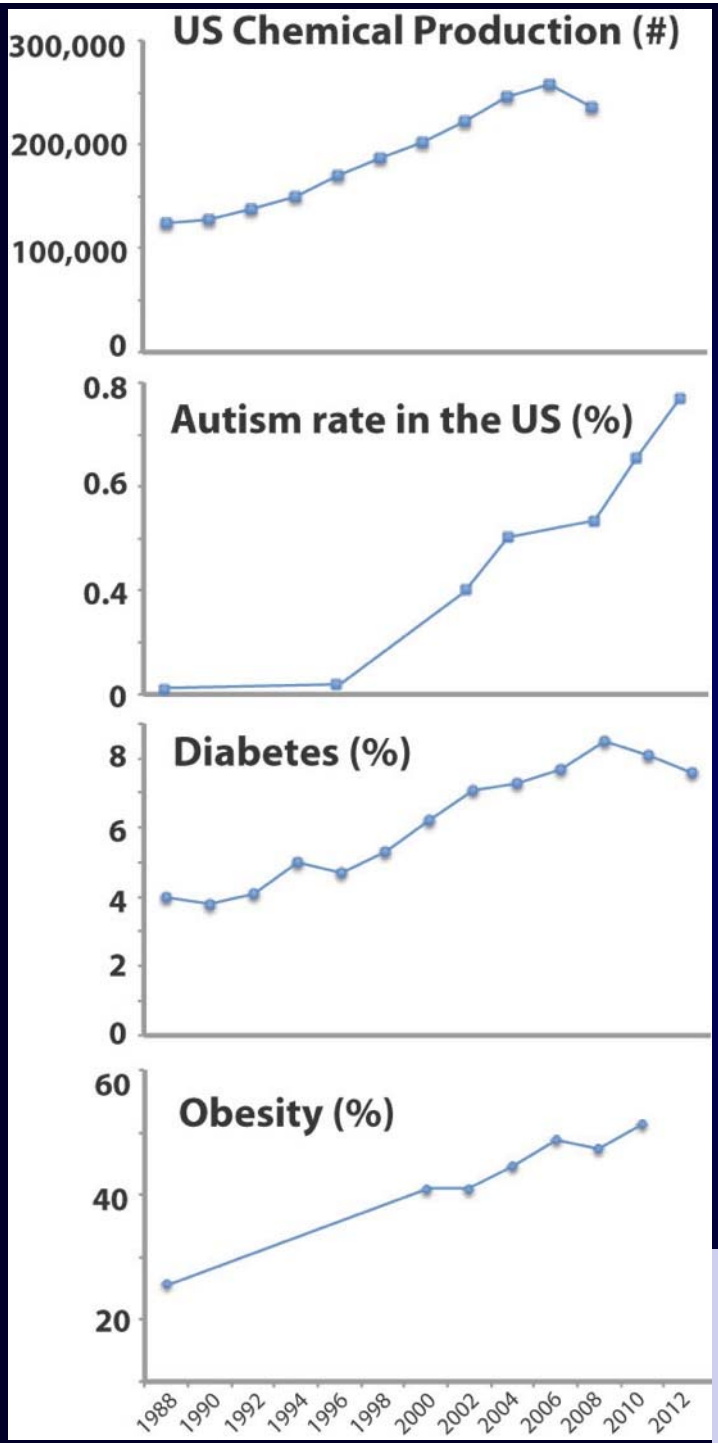
Although some local remediation of contamination has occurred, at a global level this is simply not possible.

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**



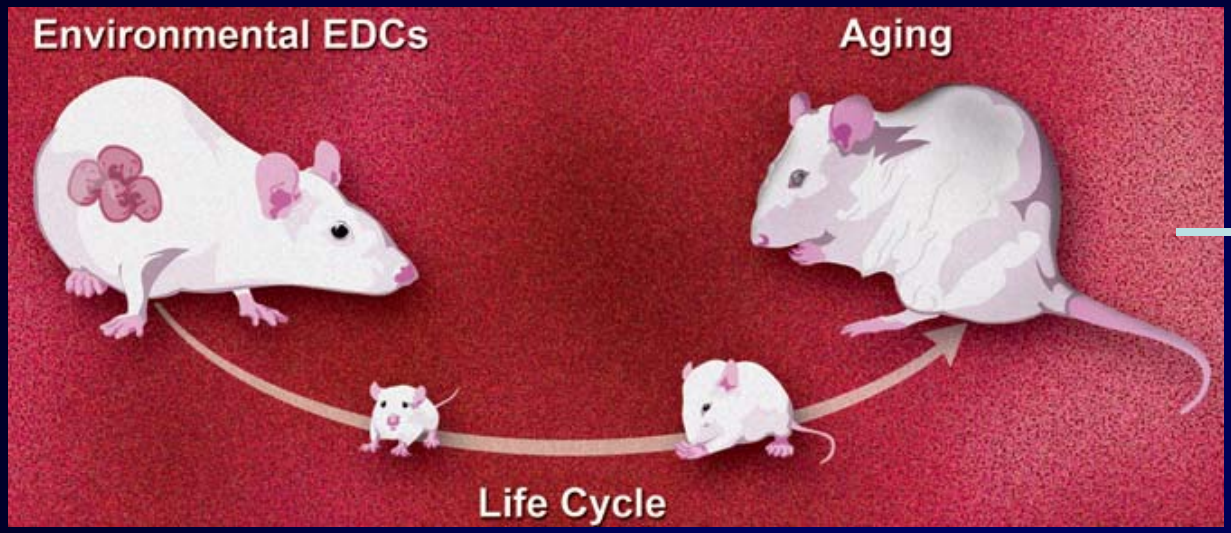
EDCs: Links to human health?

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%

Gore et al. *Endocrine Reviews,* In Press (2014)

Prenatal EDCs and the Developing Brain

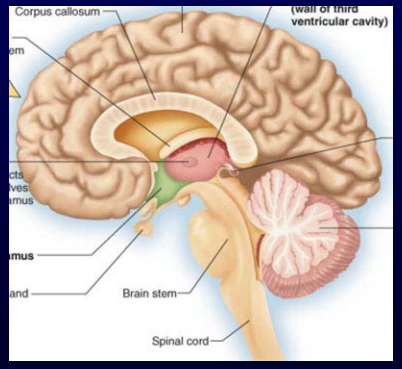


Transgenerational

Gore et al. *Molecular Endocrinology* 25: 2157 (2012)

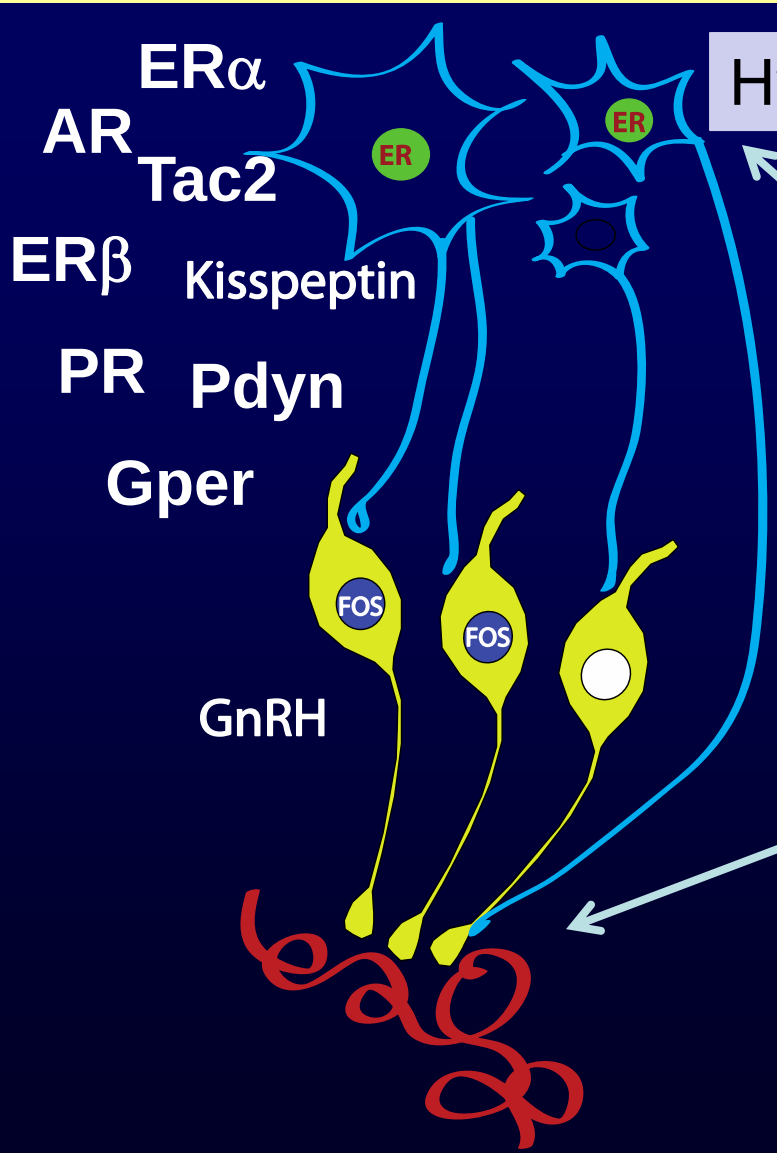
Brain sexual differentiation, gene/protein expression, HPG axis physiology, hormones, & behaviors

Developmental Hormones, EDCs



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

Central Hypothesis: EDC exposures during critical windows reprogram hypothalamic development



PCBs

Hypothalamus

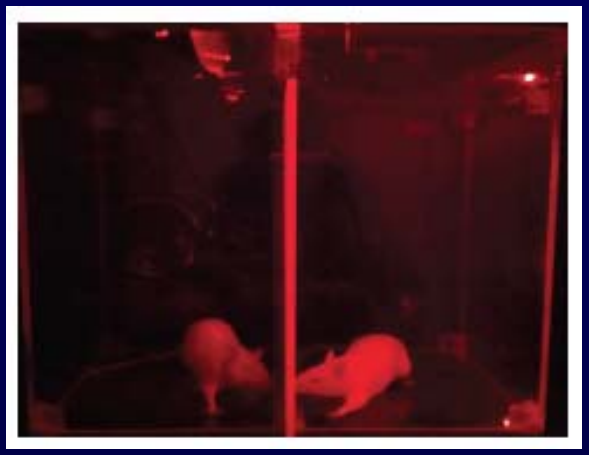
Other brain regions

Gonadal Steroids

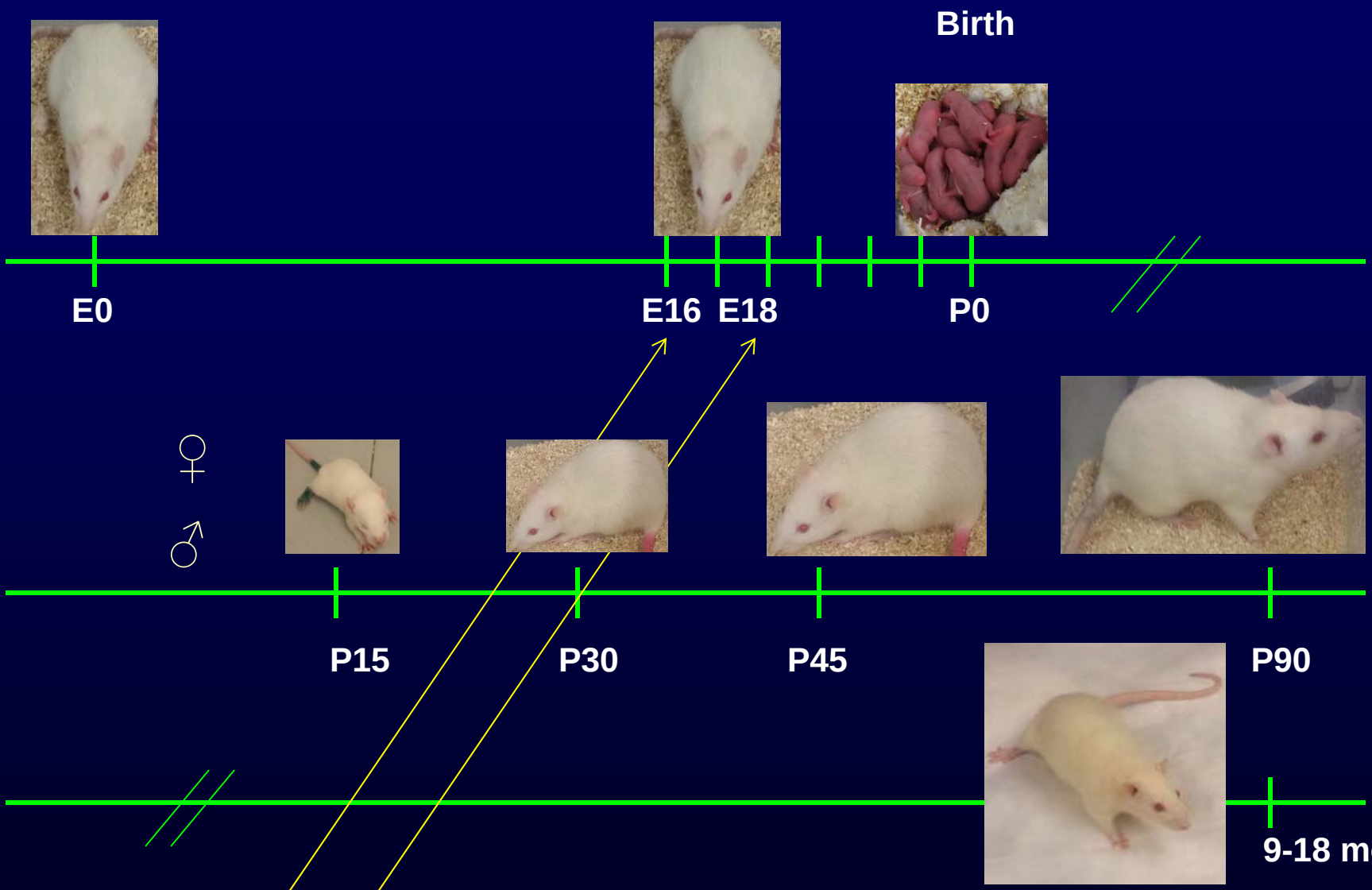
Developmental changes in gene and protein expression; DNA methylation; hormonal and physiological effects

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

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.

NIH RO1 ES023254
NIH RO1 ES020662

Thank you!

Our happy rats