Developmental PCB Exposure

Parallels with ADHD

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Why ADHD?

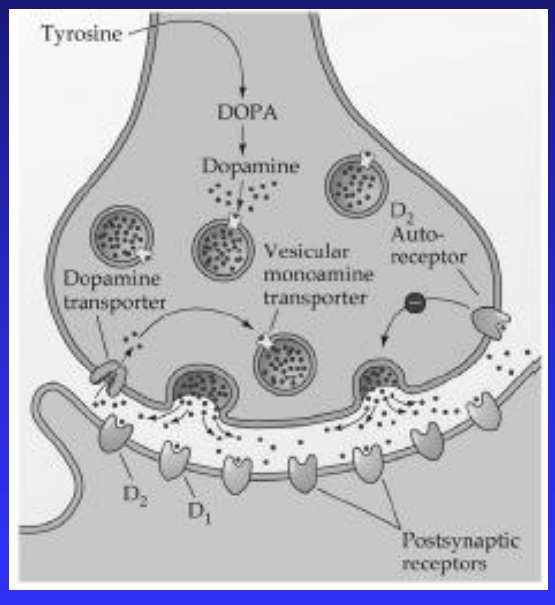
- Most commonly diagnosed neuropsychiatric disorder of childhood.
- Affects ~ 9% of boys and 3-4% of girls.
- Evidence that environmental exposures may play a role.

Key behavioral features of ADHD..

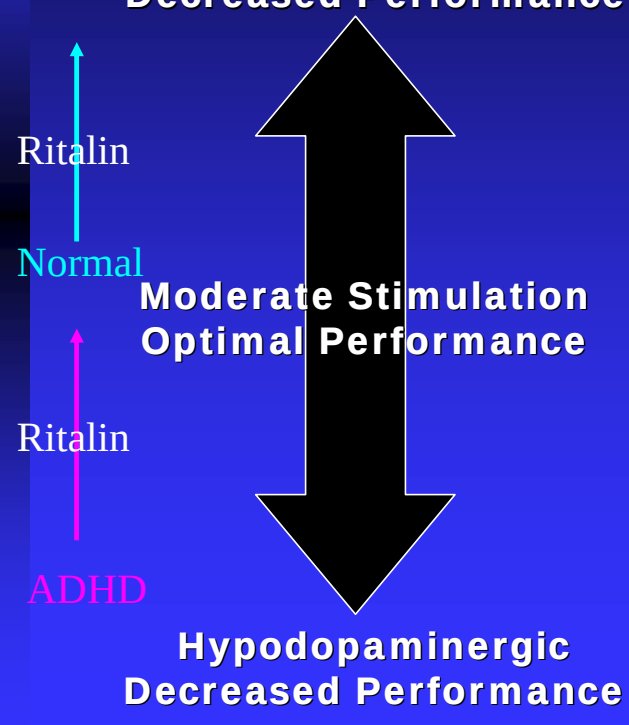
- Impulsivity (impaired behavioral inhibition)
- Attentional Problems
- Hyperactivity

Role of Dopamine (DA) in ADHD

- ADHD is associated with hypo-function of DA in the PFC.
- Evidence is indirect.
  - Behavioral profile suggests PFC.
  - Enhancing DA activity has a therapeutic benefit.



Walking a fine line…

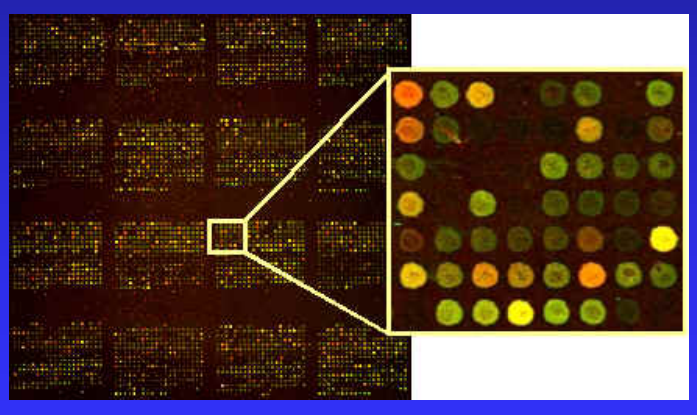


A moderate level of DA stimulation in the PFC is optimal.

Either too much or too little can impair executive functioning.

Genes……

- Genetics accounts for roughly 70% of the prevalence.
- Majority of polymorphisms associated with ADHD are in DA pathway.
  - DAT
  - D4 and D5
  - DA ß-hydroxylase
  - NET
  - SNAP 25



- Multiple genes involved.

…..and Environment..

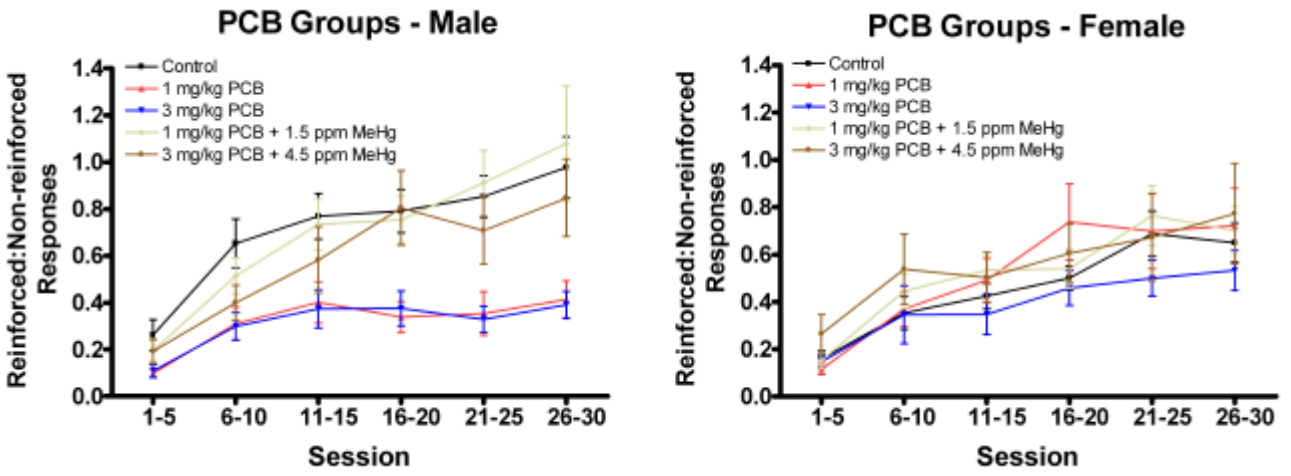
- lead
- maternal smoking
- maternal alcohol consumption
- Pesticide exposure
- low birth weight
- psychosocial adversity
- **PCBs??**

Key Behavioral Features of Developmental PCB Exposure…

- PCB-exposed animals:
  - show deficits on learning tests that require inhibitory control.
  - are hyperactive (fail to habituate; or extinguish).
- Males may be more affected.

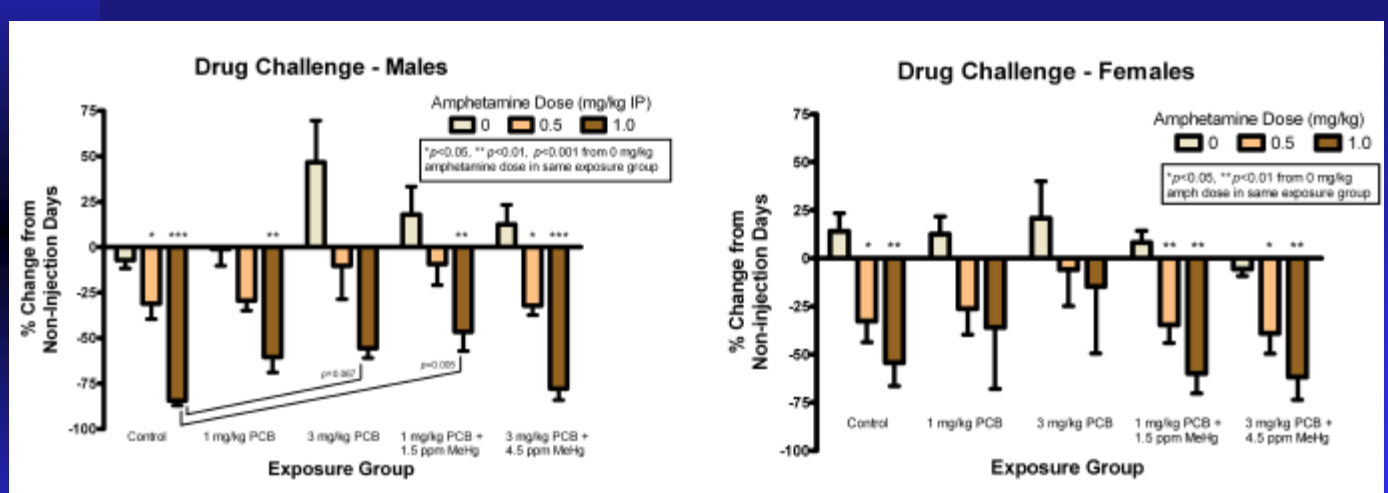
Sable and Schantz, 2006

DRL Ratio of Reinforced to Non-Reinforced Presses



Sable, Eugib et al., unpublished

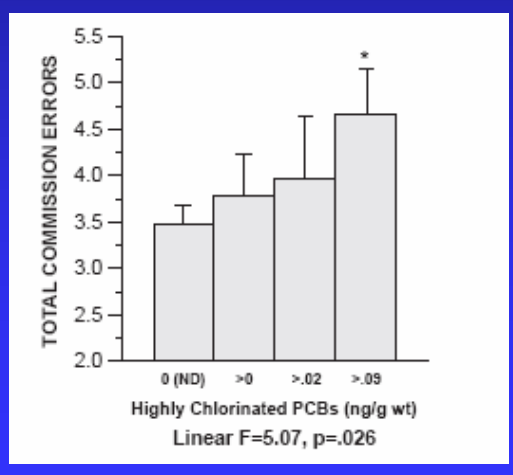
Amphetamine Challenge: Change in Ratio of Reinforced:Non-reinforced Trials



In kids PCB exposure is also associated w/ deficits in behavioral inhibition.

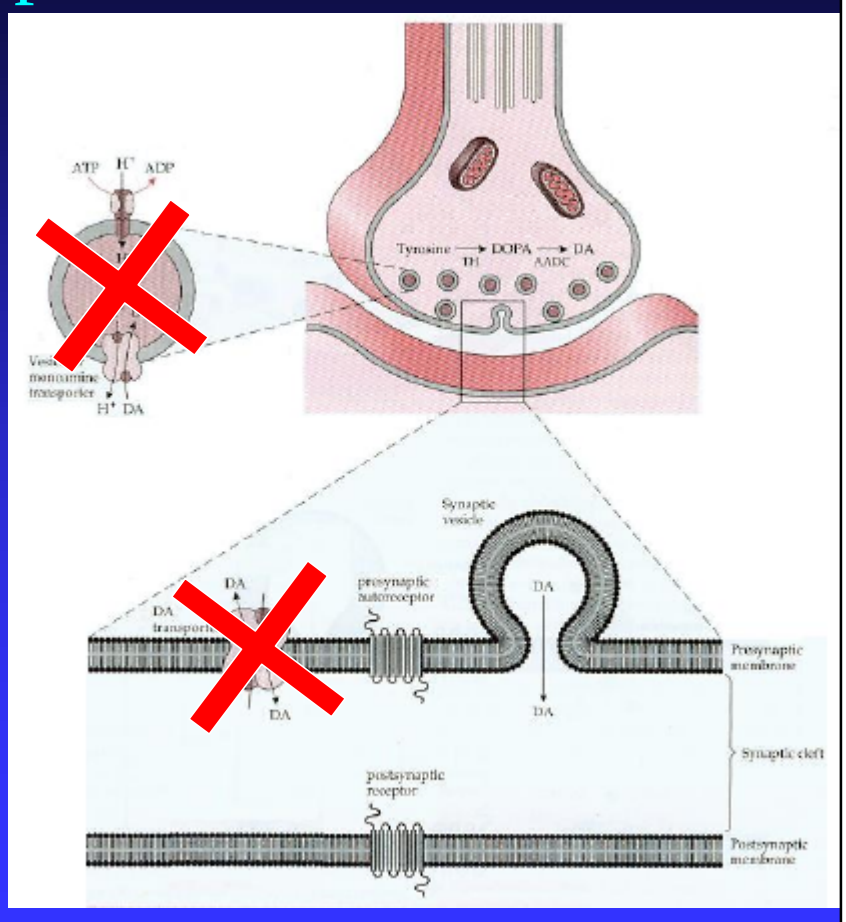
- Increased errors of commision on CPTs; especially when frequency of targets is high.
- Increased responding, decreased IRTs and fewer reinforcers earned on a DRL task.

Jacobson and Jacobson, 2003; Stewart et al. 2005, 2006



PCBs and Dopamine

- PCBs inhibit both the DAT and the VMAT2.
- Extracellular DA increases initially.
- With prolonged exposure DA decreases.
- Probably due to end product inhibition of DA synthesis.



Summary

- The behavioral and neurochemical effects of PCBs show important parallels with ADHD.
- Studies of developmental PCB exposure in animal models may help us to gain a better mechanistic understanding of the disease.
- Studies of exposures and gene-exposure interactions in ADHD children are needed to help us to understand whether PCBs (or other chemicals) play a role in the disease.
- In humans the story is never simple. Exposures to mixtures of chemicals can lead to unexpected effects.