

ES/RP 531
Fundamentals of Environmental Toxicology

Lecture 16
Behavioral Toxicity

Behavior

- Represents integration of nervous system control with modulation from the endocrine system
 - Note that behavior is affected only when another fundamental physiological mechanism is affected
 - All exogenous stimuli are perceived through the sensory system that communicates with the brain
 - However, we can study behaviors as toxicological endpoints

Behavioral Toxicology

- Premise: Crucial to evaluate how the whole organism functions when exposed to a chemical
- Presumption: The myriad functions collectively defining behavior can be isolated for study
 - Thus, different behaviors can be observed selectively by appropriate investigative techniques

Why the Fuss Over Behavioral Toxicity?

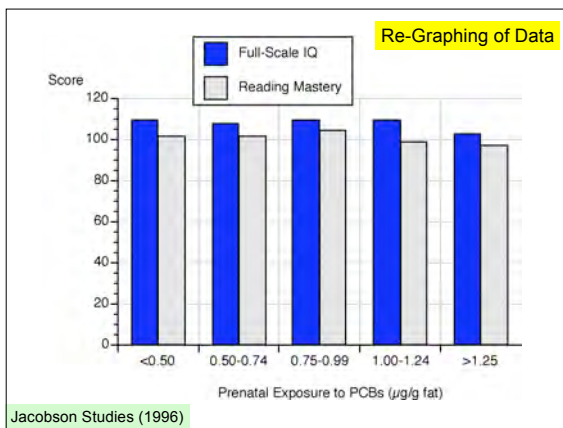
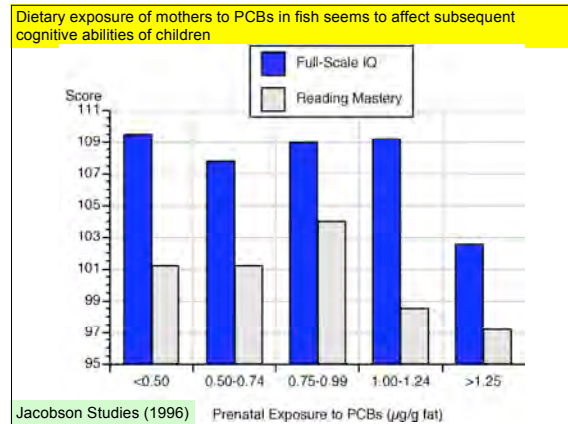
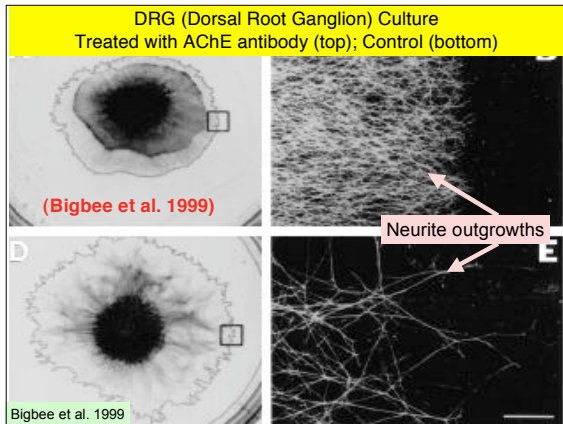
- Historically, many neurotoxic compounds ended up as environmental contaminants
 - Insecticides
 - Heavy metals (copper; lead, mercury)

Concerns About Children's Behavior

- Some have argued that OP insecticides do more than just inhibit acetylcholinesterase
 - Because it can be shown that certain doses affect neurobehavioral functioning of neonatal, juvenile, and adult rats--
 - Then children can be adversely affected in terms of intellectual development
- The concern also extends to PCBs (and Hg and Pb)
 - The Jacobson studies

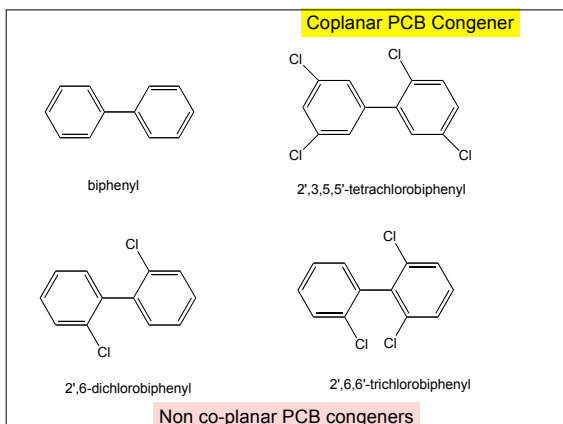
Recent Developments in Knowledge of Effect of OPs on Brain Development

- Chlorpyrifos in particular has been shown to alter neurite outgrowths in cell culture
- The mechanism is not thought to be directly due to acetylcholinesterase inhibition
 - i.e., chlorpyrifos as well as its hydrolytic metabolite are effective, and thus may work at a site distal to the enzyme (perhaps a receptor interaction)
- We now know that acetylcholine titer is important in help structure the patterning of the nerves in the developing brain
 - However, basic morphological studies show that acetylcholinesterase itself may also be important
- We do know that high concentrations of chlorpyrifos affect juvenile rat and adult behavior--but no one has shown that neonate behavior is affected at concentrations that don't inhibit acetylcholinesterase



A PCB Hypothesis?

- Effects on intellectual development through early PCB exposure, if they are occurring at all, are likely to have been mediated through endocrine system effects
 - Organizational vs. activational effects
- A recent hypothesis is that non-coplanar PCBs stimulate calcium influx at nerve terminals
 - Could cause "premature" release (or excessive release) of neurotransmitter during critical developmental periods in the fetus



Main Types of Tests

- Functional Observation Batteries (FOBs)
 - Designed to determine potential neurotoxicity
 - Caveats:
 - Not designed to elucidate underlying toxicological mechanisms
 - Must ensure reliability of measurements by having strict protocols for consistent behavioral observations
 - Examples of behavior: time to first step, gait, reflex, forelimb grip strength

Main Types of Tests

- Motor Activity
 - Observe activity levels of animals as they move in an open space or within a caged environment
 - e.g., mazes, running wheels, unencumbered open "fields"
 - Effects could be due to other systems, not necessarily neurotoxicity
- Naturalistic Behaviors
 - Aggression, mating behavior
 - Used for assessing endocrine system effects
- Ethological analysis
 - Observing animals in natural or quasi-natural environment

Specific Types of Behavioral Tests

- Motor function & coordination
 - Foot splay; rotarod
- Sensory function
 - acoustic startle response
- Cognitive function
 - Avoidance behavior
 - Maze learning for spatial learning
- Operant Behavior
 - Measure of learned or acquired behavior
 - Scheduled learning behavior

Behavioral Toxicity & Fish Categories of Behavior

- Schooling
- Feeding (including predation)
- Migration
- Aggression
- Fear
- Learning
- Rheotropism (orientation toward the current)
- Attraction or Avoidance
- Breathing frequency (may be considered metabolic effect)
- Swimming activity (spontaneous locomotory behavior)

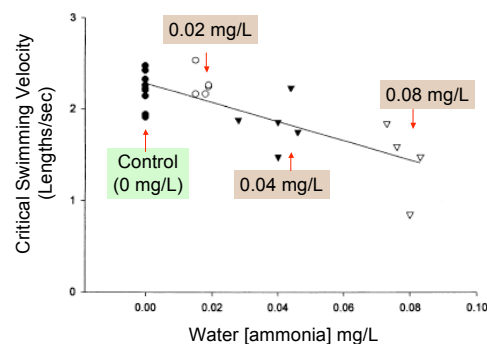
Measuring Behavior in Fish

- Fish placed in tanks divided into chambers
 - Record fish entry into each chamber as measure of locomotory activity, perhaps learning
- Outfit tanks with electrodes or other types of detectors that can detect change in water motion to record swimming activity
- Visual observation
 - Divide chamber in half, separated by a barrier with holes in it to allow fish to pass through
 - Confine fish to one side, expose them to a stressor or contaminant, and then determine the number of fish moving through the barrier per unit of time
 - Use of video cameras for continuous visual monitoring

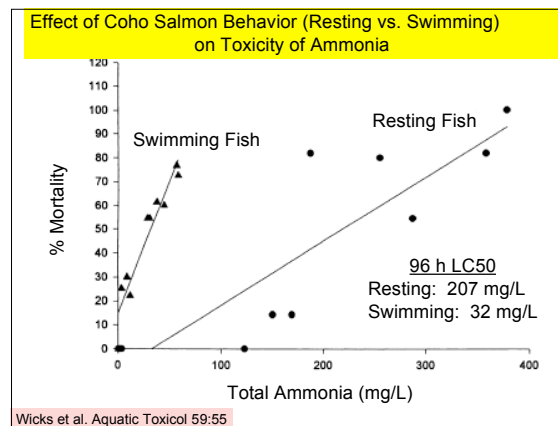
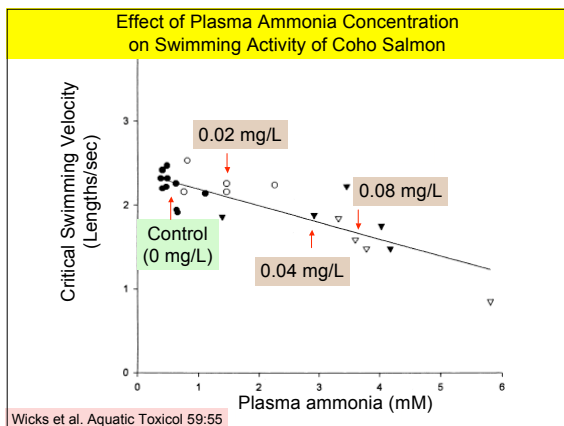
Case Study

- Ammonia affects swimming behavior of coho salmon
 - Wicks et al. 2002
- Measured critical swimming velocity of coho salmon after exposure to four levels of ammonia in water
 - 0, 0.02, 0.04, 0.8 mg/L
- Related plasma levels to swimming velocity
- Observed that behavior affected susceptibility

Effect of Ambient Ammonia Concentration on Swimming Activity of Coho Salmon

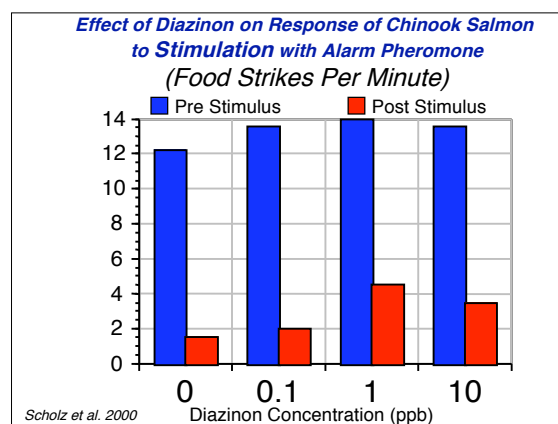
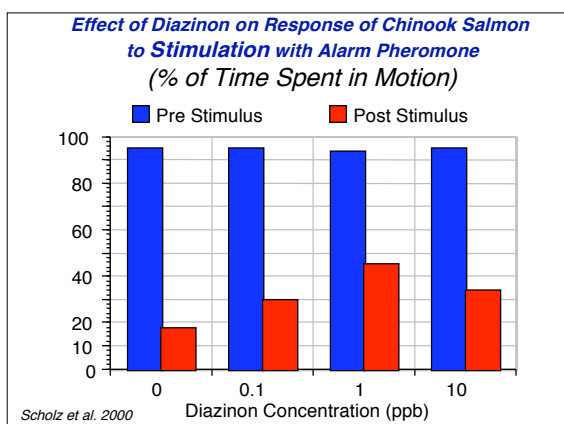


Wicks et al. Aquatic Toxicol 59:55

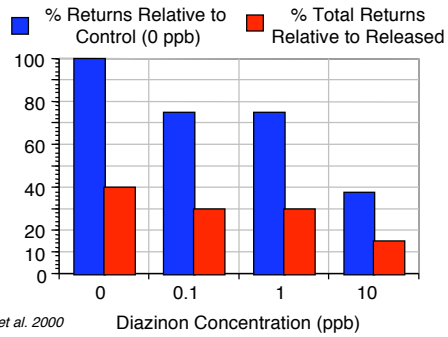


**Salmon Decline
Are Pesticides a Factor?**

- "Diazinon disrupts antipredator and homing behaviors in chinook salmon"
 - Scholz, N. L. et al. 2000
 - Can. J. Fish Aquatic Sciences 57:1911-1918
- Observed alarm pheromone response of salmon exposed to "low" levels of diazinon (formerly a major urban use insecticide)
 - When in the presence of a predator, salmon release an alarm pheromone that should decrease their activity level

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*Effect of Diazinon on Homing Behavior
of Chinook Salmon*



**Concerns About Avian Behavior &
Pesticide Exposure**

- Food searching capabilities
- Ability to avoid predators
- Ability to withstand extremes in cold
- Interestingly, birds are known to avoid contaminated seeds!!