

What is “Developmental” About “Developmental Neurotoxicology”

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What We (Think We) Know About Children and Chemicals

Neurodevelopmental Effects

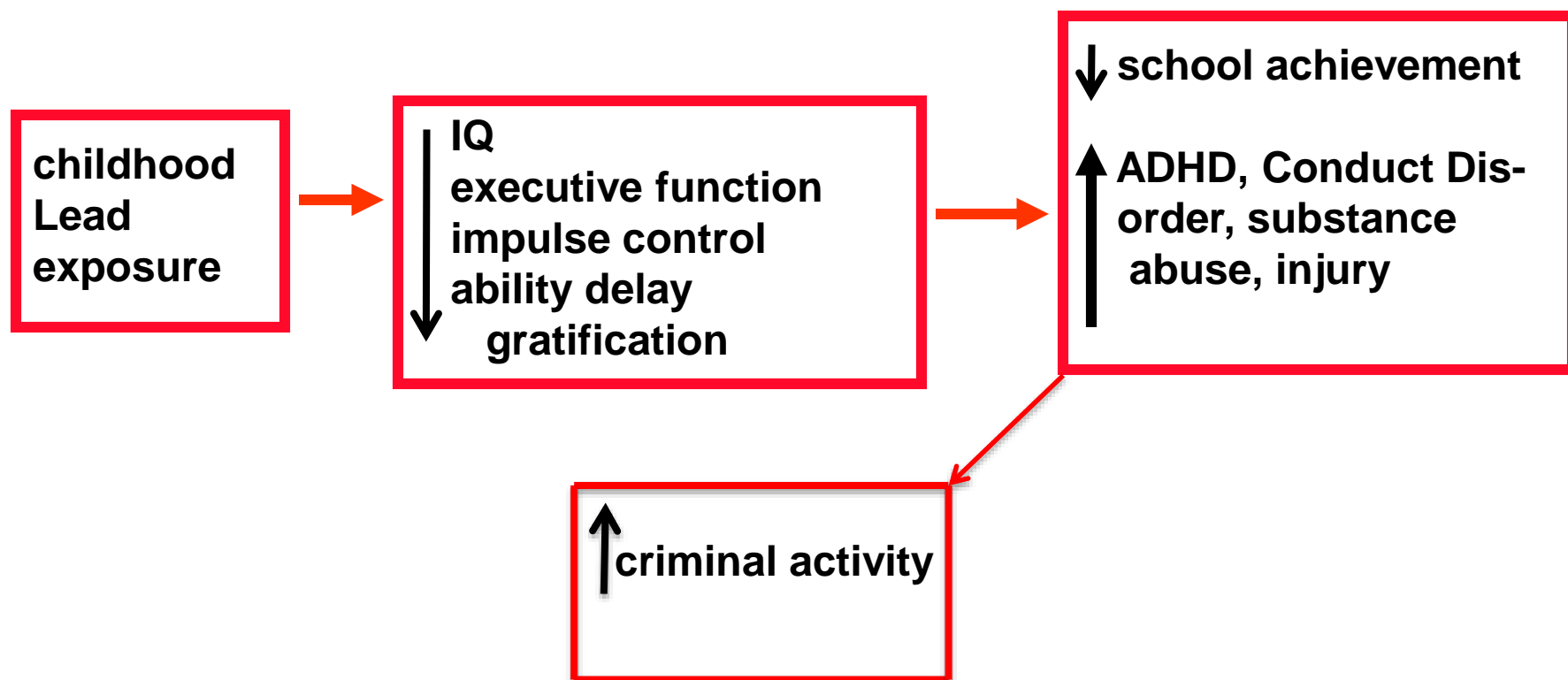
Exposure

	Little or None	Some	Considerable
Little or None	waste sites incinerators solvents	manganese	
Some	cadmium dioxins phthalates bisphenol A PFAAs	OPs arsenic PBDEs inorganic Hg PAHs	
Considerable	Elemental Hg	fluoride	lead MeHg PCBs

Elements of a Developmental Perspective

- 1. Early stages of development shape and constrain the way in which subsequent development unfolds (developmental cascades)**
- 2. Elements of a child's developmental system influence the form and severity of adverse effects of neurotoxicant exposure (effect modifiers)**
- 3. Early-life neurotoxicant exposure becomes an element of the context within which a child's subsequent development occurs (neurotoxicant exposure as an effect modifier itself in later life)**

1. Early stages of development shape and constrain the way in which subsequent development unfolds: “developmental cascades”



2. Form and severity of adverse effects of neurotoxicants influenced by other elements of the developmental system

- **Co-exposures to other neurotoxicants (i.e., mixtures)**
- **Prenatal stress**
- **Nutrition**
- **Extent to which child-rearing environment fosters optimal development**
 - **effects of lead more pronounced on disadvantaged children**
 - **animal data suggest possible remediation strategies**

3. Early-life neurotoxicant exposure reduces resilience to meet later neurological challenges

- **reduces CNS “reserve capacity” available in adulthood**
 - **recovery from a photothrombotic stroke in hind limb parietal sensorimotor cortex slower in rats with early lead exposure (beam walking and proprioceptive limb placing)**
- **produces epigenetic changes eventually expressed as altered gene expression in adulthood**
 - **rats exposed to lead only as newborns show delayed overexpression, as adults, of the gene encoding the β -amyloid precursor protein**
- **accelerating neurodegenerative processes associated with aging**

Conclusions

- **Early-life exposure to neurotoxicants can affect myriad aspects of a child's neurodevelopment;**
 - **adversities evident in childhood are only earliest stage of their unfolding; need to consider downstream effects**
 - **a lifespan approach necessary to appreciate full range of morbidities and burden associated with them; delayed neurotoxicity**
- **Exposure-related adversities responsive to context in which development occurs**
 - **suggests that viewing the adversities as “permanent” unduly pessimistic, ignoring possibilities of remediation by environmental manipulation**
- **Early-life exposure is, itself, a risk modifier, forming part of the context that determines the impacts of later physiologic and pathologic CNS events;**
 - **a child exposed early to a neurotoxicant likely to respond differently to a later insult than a child not similarly exposed**