LOW LEVEL LEAD EXPOSURE IMPAIRS ATTENTIONAL SET SHIFTING TASK PERFORMANCE DEPENDING UPON SEX AND DEVELOPMENTAL PERIODS OF EXPOSURE

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Human Lead (Pb) Toxicity in Review

Adverse Health Effects of Lead Exposure

- Death
- Encephalopathy
- Nephropathy
- Frank Anemia
- Colic
- Decreased hemoglobin synthesis
- Increased vitamin D metabolism
  - Increased risk of hypertension in adulthood
- Increased nerve conduction velocity
- Increased level of erythrocyte protoporphyrin
- Decreased vitamin D metabolism
- Decreased calcium homeostasis
- Developmental toxicity
  - Delayed puberty
  - Decreased growth & hearing
- Developmental toxicity
  - Decreased IQ levels & academic abilities
  - Attention-related behaviors
  - Anti-social behaviors

100 mL’s = 1 dL

http://www.ehatlas.ca/lead/human-impact/health-concerns
http://brickleyenv.com/services/lead-paint-removal-contractor/
### Chronological Review of the United States CDC’s Threshold for Pb Poisoning Interventions

<table>
<thead>
<tr>
<th>Year of CDC Revision</th>
<th>Number of Years Between CDC Revision</th>
<th>CDC BLL Listed as Threshold</th>
<th>CDC BLL Considered to be Safe /Actionable</th>
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<tbody>
<tr>
<td>1960</td>
<td>10</td>
<td>60 µg/dL</td>
<td>( \leq 59 ) µg/dL</td>
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<tr>
<td>1970</td>
<td>10</td>
<td>40 µg/dL</td>
<td>( \leq 39 ) µg/dL</td>
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<td>1975</td>
<td>5</td>
<td>30 µg/dL</td>
<td>( \leq 29 ) µg/dL</td>
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<tr>
<td>1985</td>
<td>10</td>
<td>25 µg/dL</td>
<td>( \leq 24 ) µg/dL</td>
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<td>1991</td>
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<td>10 µg/dL</td>
<td>( \leq 9 ) µg/dL</td>
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<td>2016</td>
<td>25</td>
<td>5 µg/dL</td>
<td>( \leq 0 ) µg/dL</td>
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</table>

Today BLL’s of 39 µg/dL or greater require immediate chelation therapy.

*BLL = Blood Lead Levels

*CDC = Center for Disease Control

Pb produced consistent aberrant behaviors related to attention, visual-motor reasoning skills, social skills, mathematics and reading abilities at exposures of ~ 10µg/dL (Canfield et al., 2003; Lanphear et al., 2000; 2005; Wasserman et al., 1997) Predicts for lifetime educational and emotional problems, delinquent and anti-social behaviors (Nevin, 2007).
TRADITIONAL IQ TESTS ARE INSENSITIVE IN ASSESSING BRAIN INJURY INDUCED BY PB

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<tr>
<th>Pb</th>
<th>Motor</th>
<th>Fluency</th>
<th>Attention</th>
<th>Verbal memory</th>
<th>Visual Memory</th>
<th>Planning</th>
<th>Concept Form</th>
<th>Cog, Flex</th>
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= impaired test performance

Group Average IQ 95 Assessed By WISC-III

Lidsky & Schneider, (2006)
WISCONSIN CARD SORTING TEST (WCST)

Sort By Color

Sort by Number

Sort By Shape
Attentional Set Shifting Task: From human cognition to using animal models to evaluate neurodevelopmental disabilities

- Wisconsin Card Sorting Test
ATTENTION SET SHIFTING TASK (ASST) EXPERIMENT

Right Choice Chamber (Styrofoam with R+)

Left Choice Chamber (Shredded Paper)

Neutral Chamber

Start Chamber
DIG TRAINING/SHAPING
150ppm Pb Acetate Food Produces The Following:
Early Post Natal (EPN) Rat BLLS ~ 5-7 μg/dL
Perinatal (Peri) Rat BLLS ~ 10-13 μg/dL
ASST Trials To Learn Cognitive Task

<table>
<thead>
<tr>
<th>Discrimination Condition</th>
<th>Cont</th>
<th>Peri</th>
<th>EPN</th>
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<tbody>
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<td>ED-Rev</td>
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</table>

EPN Rats Unable to Complete CD Stages Cannot Proceed Forward in ASST

N=6
N=8
N=8

#
ATTENTIONAL SET SHIFTING: FROM HUMAN COGNITION TO USING ANIMALS TO EVALUATE NEURODEVELOPMENTAL DISABILITIES

• Time of developmental Pb exposure produces different deficits in performance of an attention set shifting task.

• EPN male rats have increased difficulty learning SD tasks and cannot learn CD tasks, whereas females are able to complete the test.

• Peri rats are able to learn SD and CD tasks and can perform ID and ED shifts. However, they exhibit increased trials to learn across most stages, impulsive responding, and perseveration when compared to control rats.

• Sex differences are minimally observed in control rats and Pb exposure produces sex specific deficits in learning.

• Pb exposure may result in different attention/executive-based cognitive deficits depending on the developmental window of exposure and these effects may be evaluated through the ASST.
IN CONCLUSION

- Pb toxicity is a very expensive social problem nationally and internationally.

- Pb is a persistent condition lacking a direct biological mechanism to treat cognitive symptoms induced by this environmental toxin.

- Identifying a direct protein relationship with learning and memory plasticity modeling human Pb cognitive deficits in animals will enhance drug discovery for treating Pb early in life.
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REFERENCES:


