AN ASSESSMENT OF LOW LEVEL LEAD EXPOSURE ON ENCEPHALIZATION AND CORTICAL QUOTIENTS AND ITS RELATIONSHIPS WITH CORTICAL THINNING AND NEURODEGENERATION

PRIMARY PRESENTERS:

Samantha R. Rubi[1], Tokunbo J. Jose[2], Nimra Hameed[1], Sukhpreet Kaur[3],

Neena Matthew[3], Teddy Dacius[2], & Jalen R. Bonitto[2]

MENTOR: **Lorenz S. Neuwirth, Ph.D.[2-3]**

SUNY Old Westbury Department of Biology[1],
SUNY Old Westbury Department of Psychology[2],
SUNY Old Westbury Neuroscience Research Institute[3]

SUNY OLD WESTBURY

INTRODUCTION: HUMAN LEAD (PB) TOXICITY IN REVIEW

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

Year of CDC Revision	Number of Years Between CDC Revision	CDC BLL Listed as Threshold	CDC BLL Considered to be Safe /Actionable
1960	10	60µg/dL	≤59µg/dL
1970	10	40µg/dL	**≤39µg/dL**
1975	5	30µg/dL	≤29µg/dL
1985	10	25µg/dL	≤24µg/dL
1991	6	10µg/dL	≤9µg/dL
2017	26	5µg/dL	≤0µg/dL

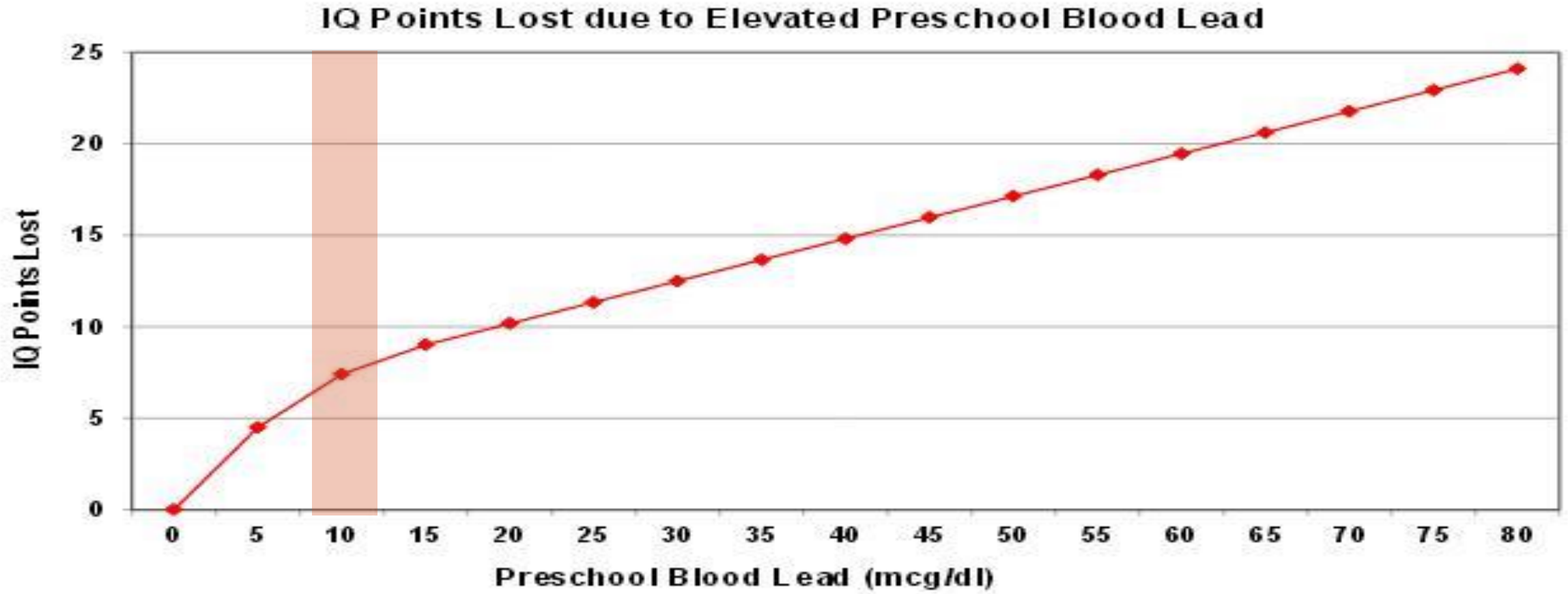
Today BLL's of 39 µg/dL or greater require immediate chelation therapy.

***BLL = Blood Lead Levels**

***CDC = Center for Disease Control**

CDC, 1991. Preventing lead poisoning in young children: A statement by the centers for disease control. Atlanta, GA: *Centers for Disease Control.*

Pb Effects on Child IQ & Life Time Predicted Outcomes

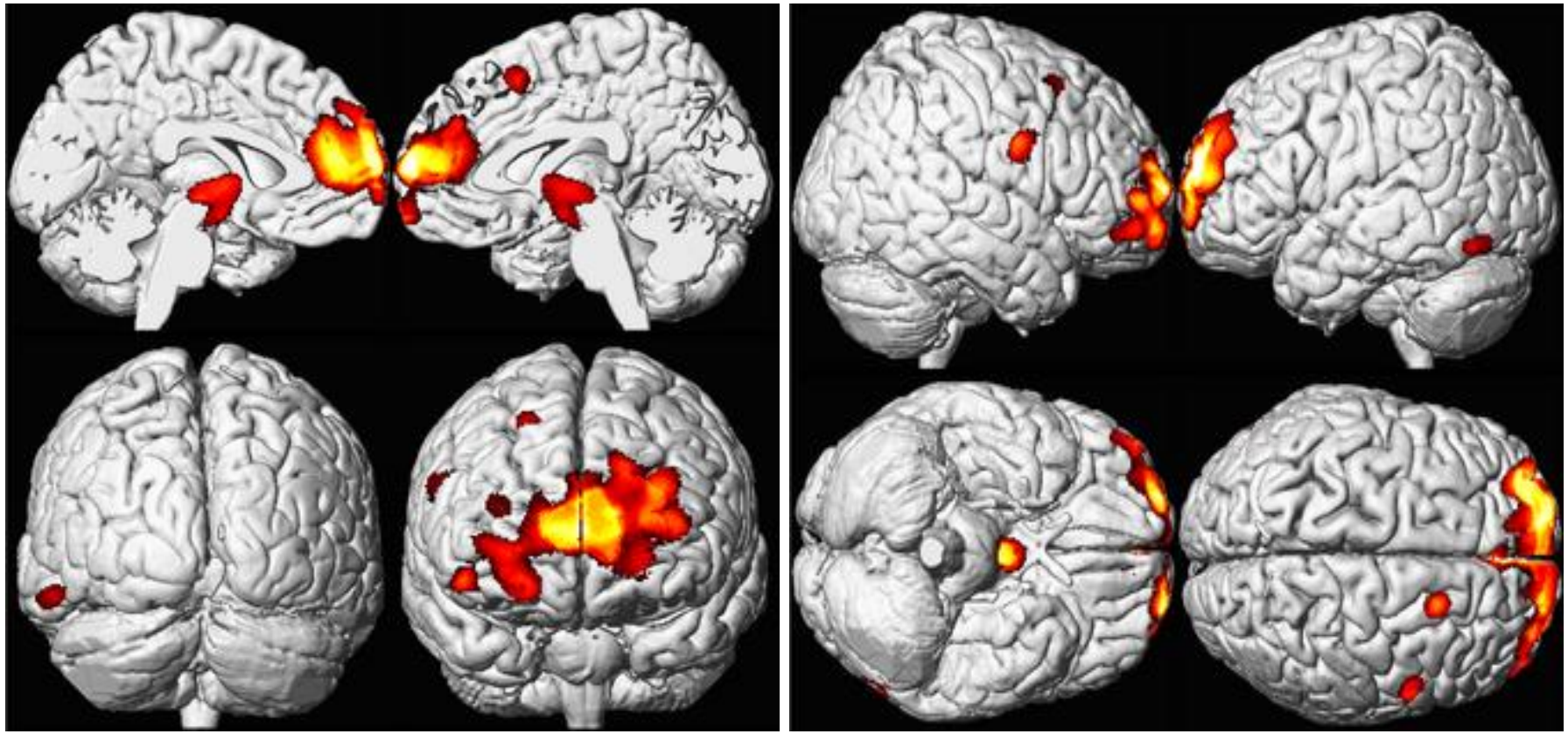


Pb produced consistent aberrant behaviors related to attention, visual-motor reasoning skills, social skills, mathematics and reading abilities at exposures of ~ 10µg/dL (Canfield et al., 2003; Lanphear et al., 2000; 2005; Wasserman et al., 1997)

Predicts for lifetime educational and emotional problems, delinquent and anti-social behaviors (Nevin, 2007).

Pb Induced Brain Volume Loss in Males

Left Medial Right Medial Right Lateral Left Lateral

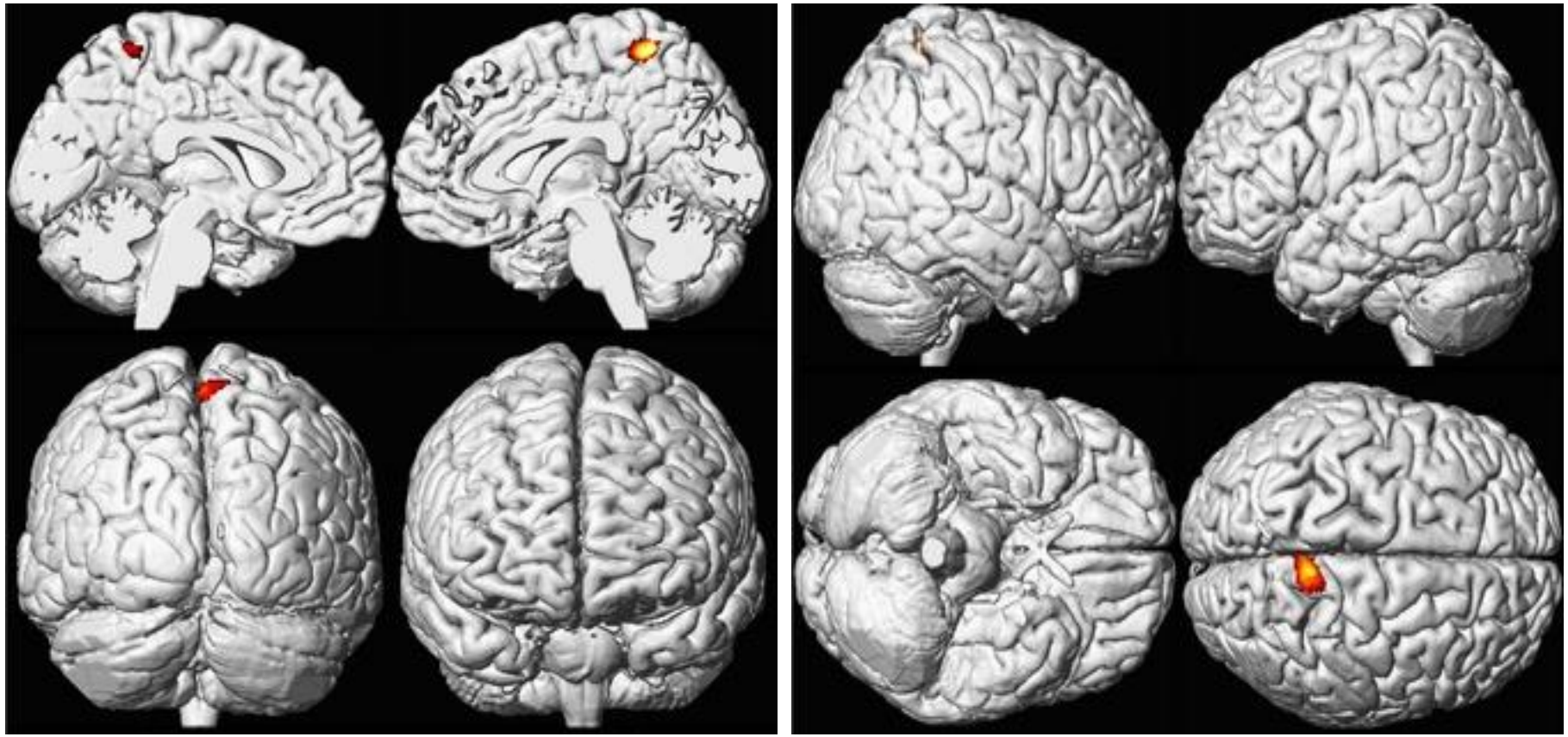


Posterior Anterior Inferior Superior

N = 85 Males ~ 5 years old BLL's ~ 13.5 µg/dL Brain Imaged 19-24 years old

Cecil et al., (2008). Decreased brain volume in adults with childhood lead exposure. PLoS Med 5: e112. doi:10.1371/journal.pmed.0050112.

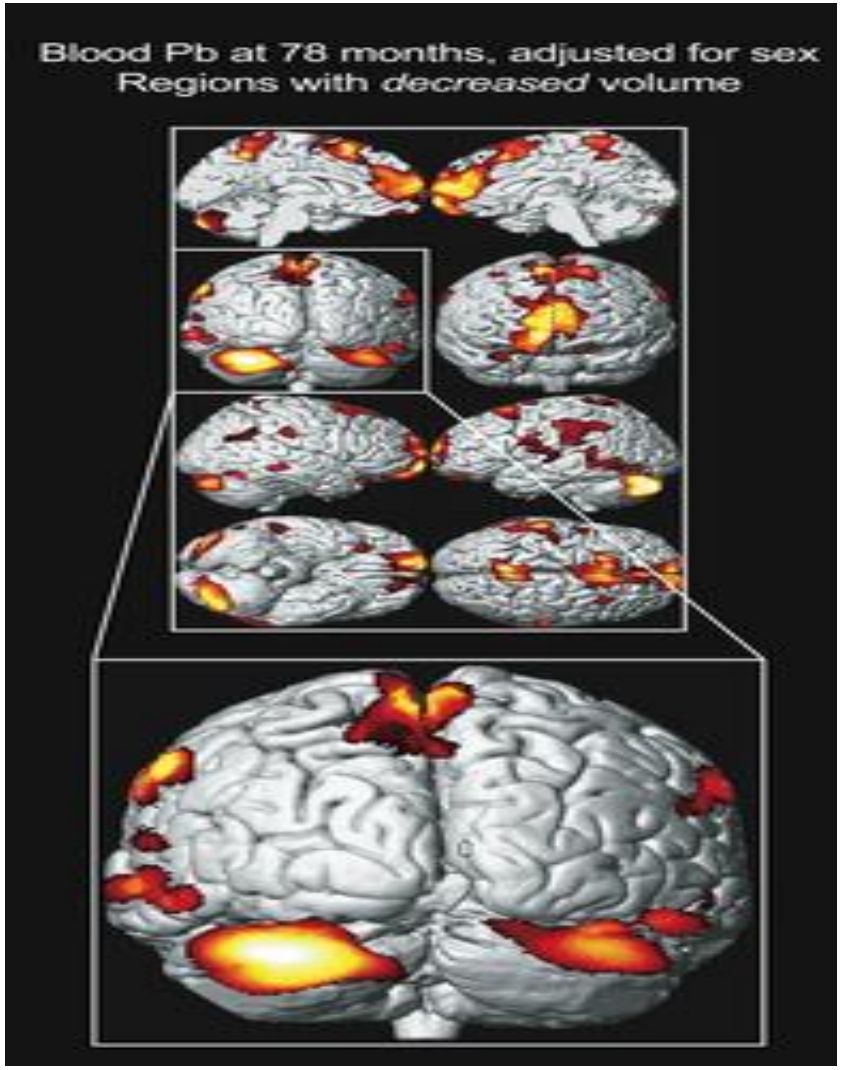
Pb Induced Brain Volume Loss in Females



N = 74 Females ~ 5 years old BLL's ~ 13.1 µg/dL Brain Imaged 19-24 years old

Cecil et al., (2008). Decreased brain volume in adults with childhood lead exposure. PLoS Med 5: e112. doi:10.1371/journal.pmed.0050112.

Figure 3. Childhood Lead Poisoning Structure-Function Relationships

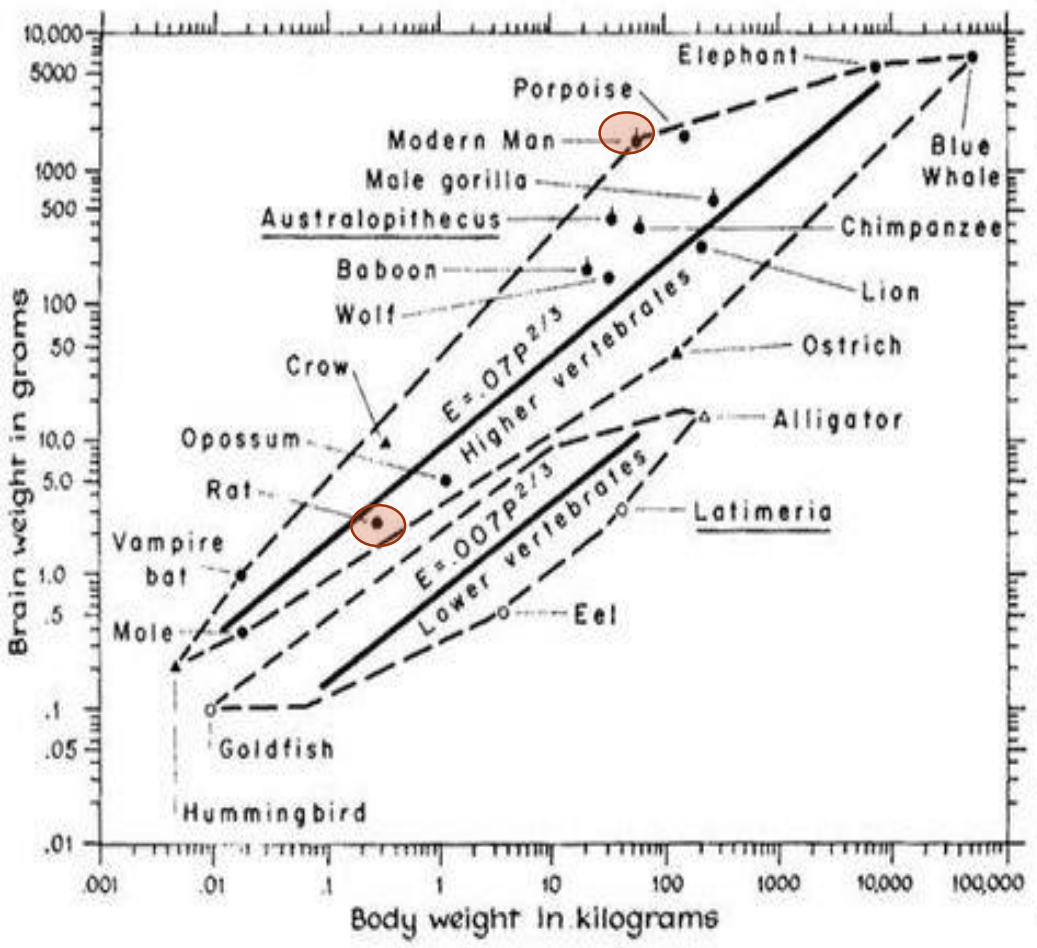


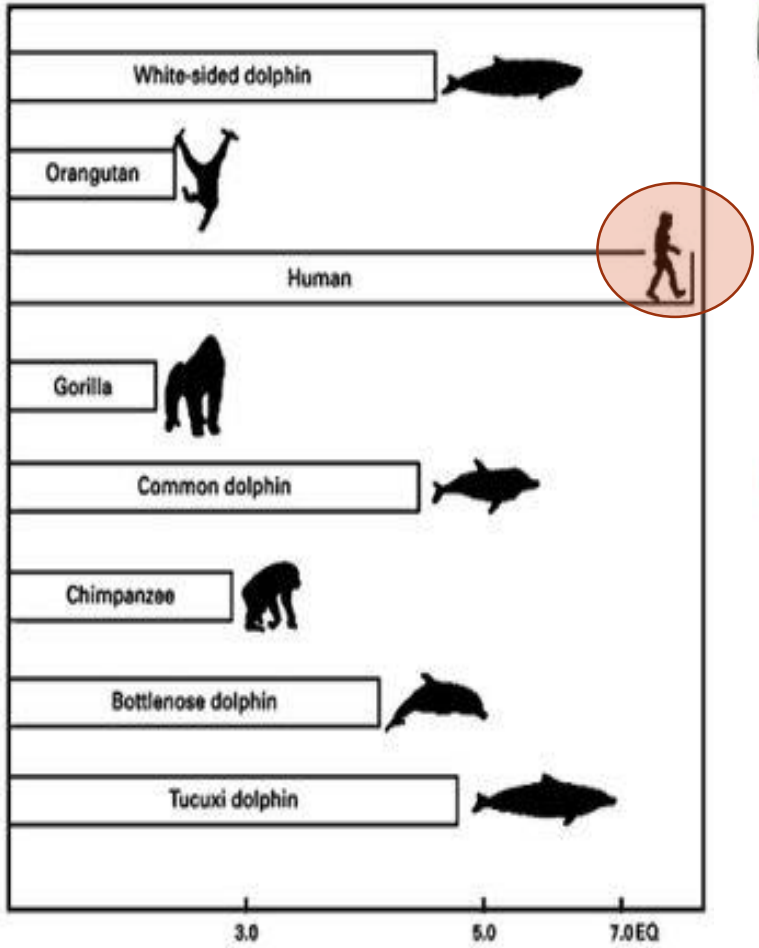
Cecil KM, Brubaker CJ, Adler CM, Dietrich KN, Altaye M, et al. (2008) Decreased Brain Volume in Adults with Childhood Lead Exposure. PLOS Medicine 5(5): e112. doi:10.1371/journal.pmed.0050112
http://journals.plos.org/plosmedicine/article?id=10.1371/journal.pmed.0050112

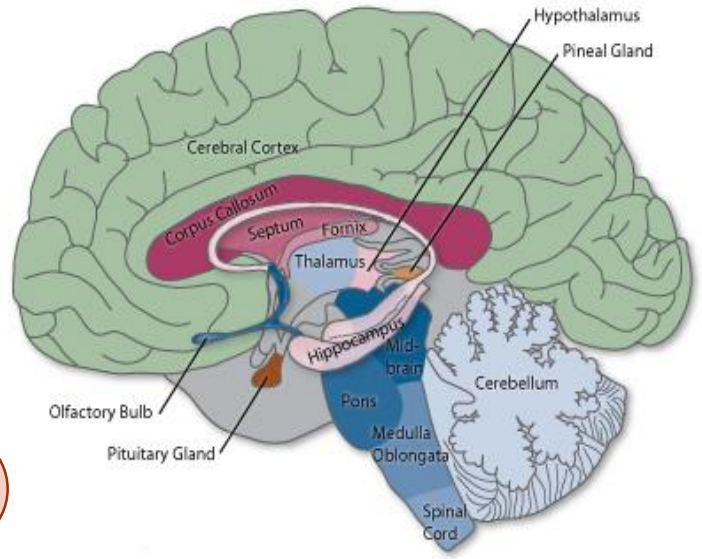
PLOS | MEDICINE

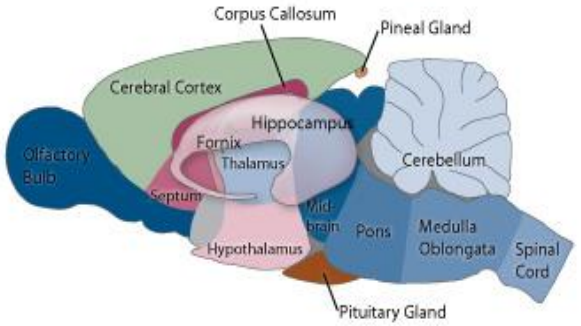
ENCEPHALIZATION QUOTIENTS

- Cross-specie cortical mass comparison calculation.





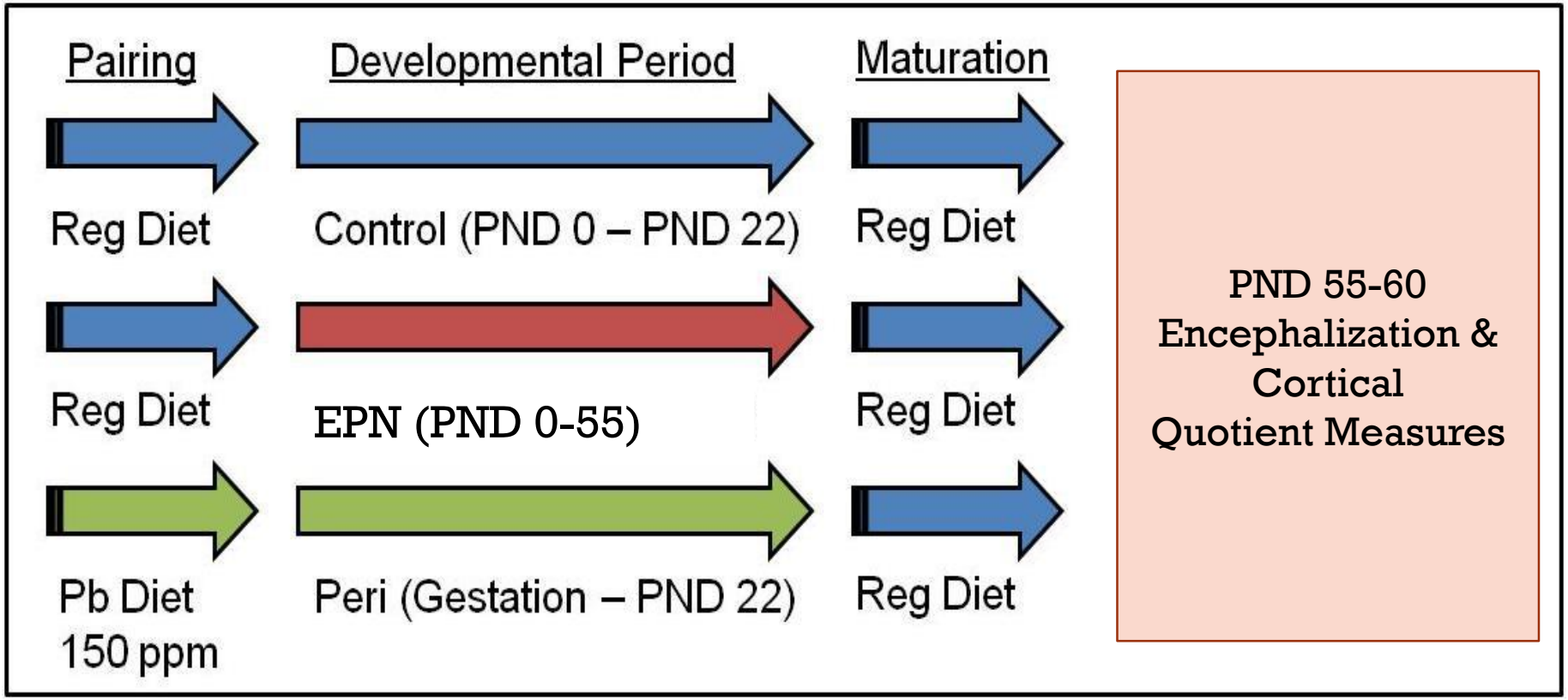




HYPOTHESES:

- Neurodevelopmental lead exposure would induce brain damage causing a reduced EQ and CQ?
- Gender would have differential EQ and CQ vulnerabilities to lead exposure?
- Neurodevelopmental lead exposure would cause different EQ and CQ outcomes based on the developmental time period of exposure?

DEVELOPMENTAL PB EXPOSURE PARADIGM



25 ppm Pb Acetate Food Produces The Following:
Early Post Natal (EPN) Rat BLLS ~ 1-3µg/dL
Perinatal (Peri) Rat BLLS ~ 2-6 µg/dL

METHODS CALCULATING ENCEPHALIZATION & CORTICAL QUOTIENTS EQ'S & CQ'S

***Encephalization and Cortical Quotients (EQ & CQ) Calculations*:**

Following obtaining rat body and brain weights the EQ and CQ were calculated for each rat using the equations below, averaged, and statistically compared as a function of sex and treatment groups using an *ANOVA*.

$$\text{Encephalization Quotient } \textit{(EQ)} = \frac{\textbf{Brain}\ \text{weight}}{0.12*(\text{Body weight}) - (\textbf{Brain}\ \text{weight})}$$

$$\text{Cortical Quotient } \textit{(CQ)} = \frac{\textbf{Cortex}\ \text{weight}}{0.12*(\text{Brain weight}) - (\textbf{Cortex}\ \text{weight})}$$

ANALYSIS METHODS & RESULTS:

- The following image will compare both Long Evans (LE) male and female, overall body weights (**Fig.1**), total brain weights (**Fig. 2**), and cortex weights (**Fig. 3**) The data are presented with the dependent variables weight measured in grams on the Y-Axis and the independent variables (*Gender* and *Treatment Conditions*) on the X-Axis.
- **Fig. 4** shows a different rate of EQ total brain volume loss, while **Fig. 5** shows a different rate of CQ cortex volume loss as a function of developmental time period of lead exposure.
- The data are presented with the dependent variables (EQ and CQ) on the Y-Axis and the independent variables (*Gender* and *Treatment Conditions*) on the X-Axis.
- All rats were tested at the same time of day under the same conditions to ensure consistent tissue processing and measurements across all subjects under study.

RESULTS:

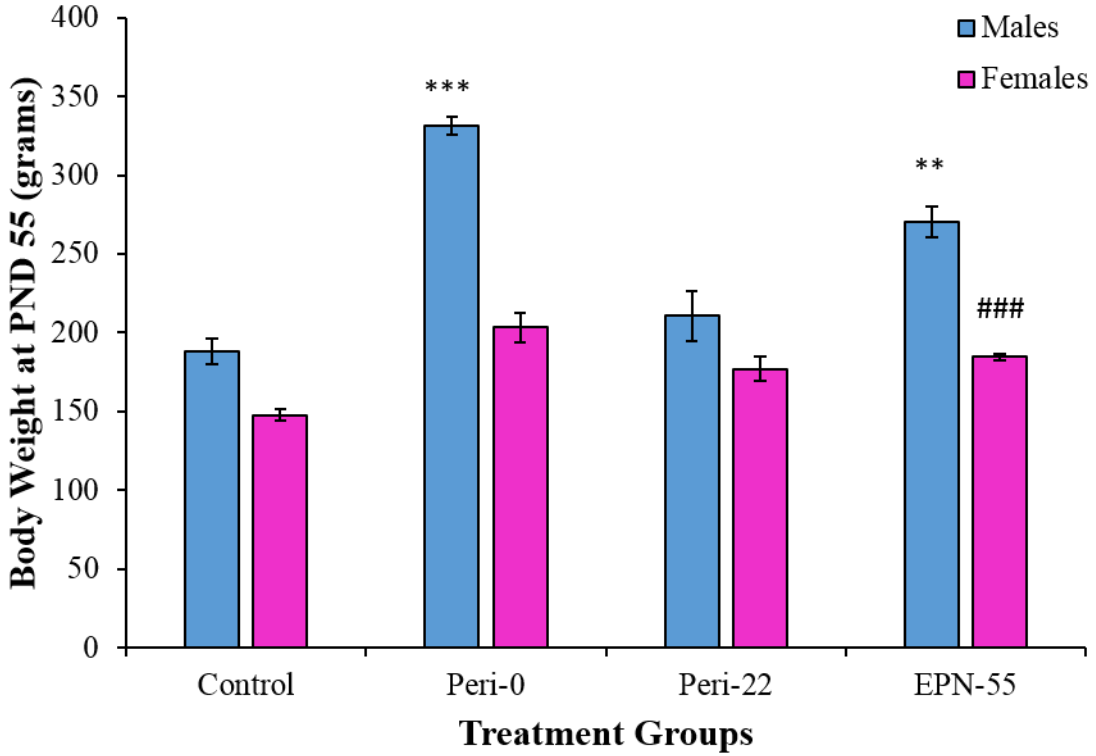
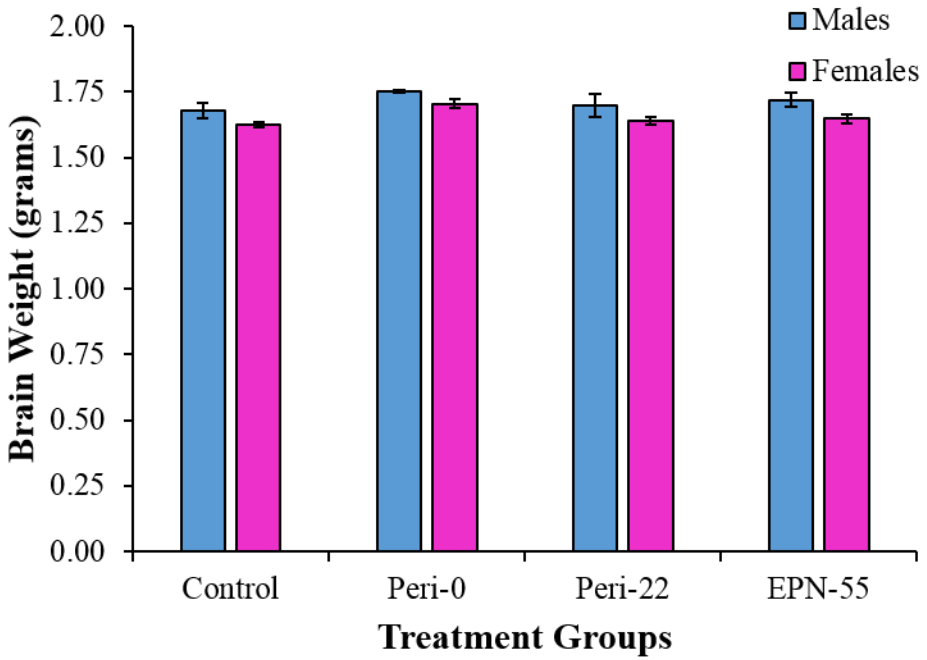


Fig. 1. Weight differences between males and females as a function of lead treatment and time period of exposure. The data revealed a significant effect of *Treatment* $F_{(3)}$=55.88, p = 0.001, *Sex* $F_{(1)}$=126.96, p = 0.001, and a *Treatment X Sex* interaction $F_{(3,1)}$=17.39, p = 0.001 (*** indicates male differences Compared to control, whereas ### indicates female differences compared to control).

RESULTS:



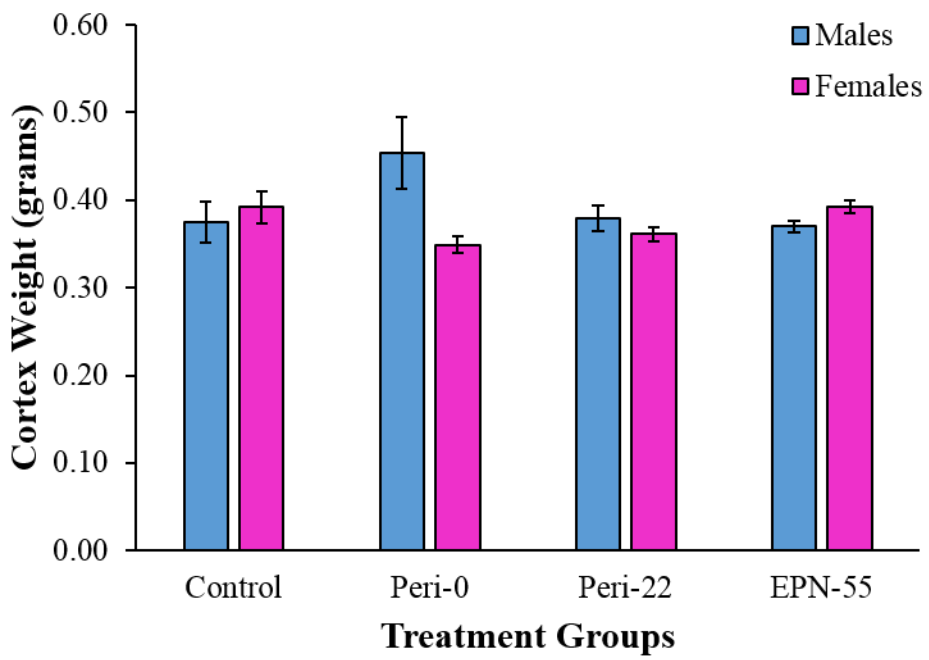


Fig. 2 Brain weight and **Fig.3** cortex weight differences between males and females as a function of lead treatment and time period of exposure. **Fig. 2.** The data revealed a significant effect of *Treatment* $F_{(3)}$=5.41, p = 0.003 and *Sex* $F_{(1)}$=13.30,p = 0.001. Fig. 3. The data revealed only a significant *Treatment X Sex* interaction $F_{(3,1)}$=3.45, p = 0.03 (*** indicates male differences compared to control, whereas ### indicates female differences compared to control).

RESULTS:

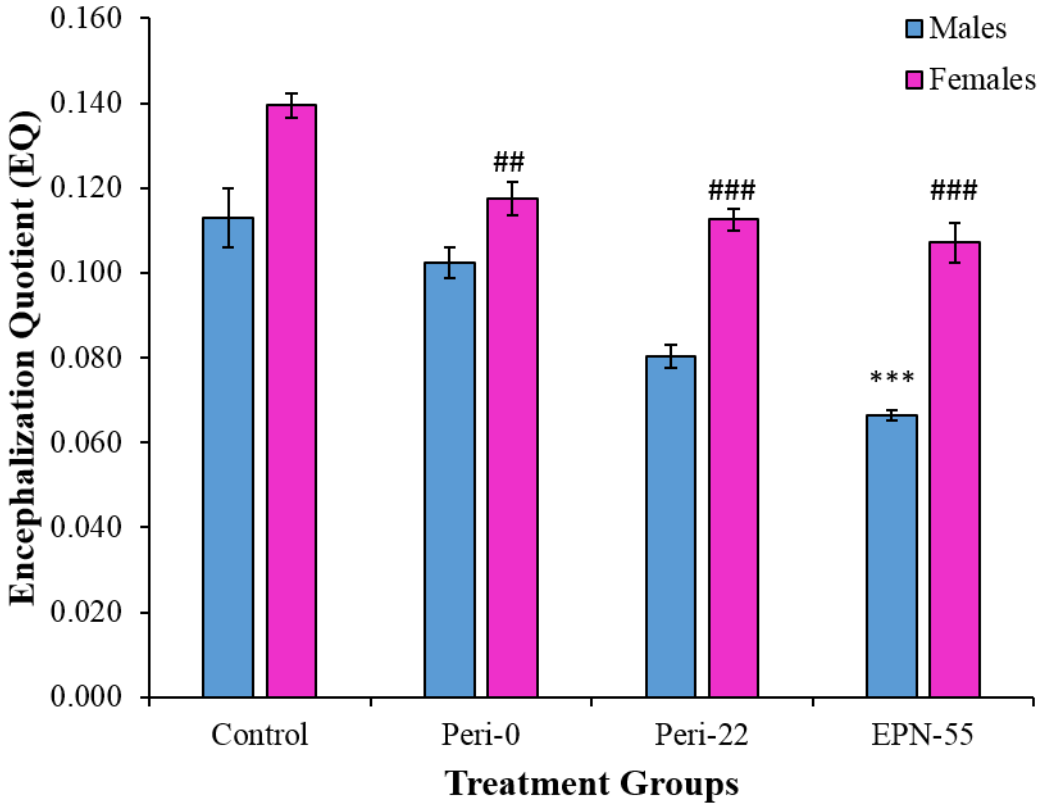


Fig. 4. Encephalization Quotient (EQ) differences between males and females as a function of lead treatment and time period of exposure. The data revealed a significant effect of *Treatment* $F_{(3)}$=27.15, p = 0.001, *Sex* $F_{(1)}$=71.23,p = 0.001, and a *Treatment X Sex* interaction $F_{(3,1)}$=4.10, p = 0.001 (*** indicates male differences compared to control, whereas ### indicates female differences compared to control).

RESULTS:

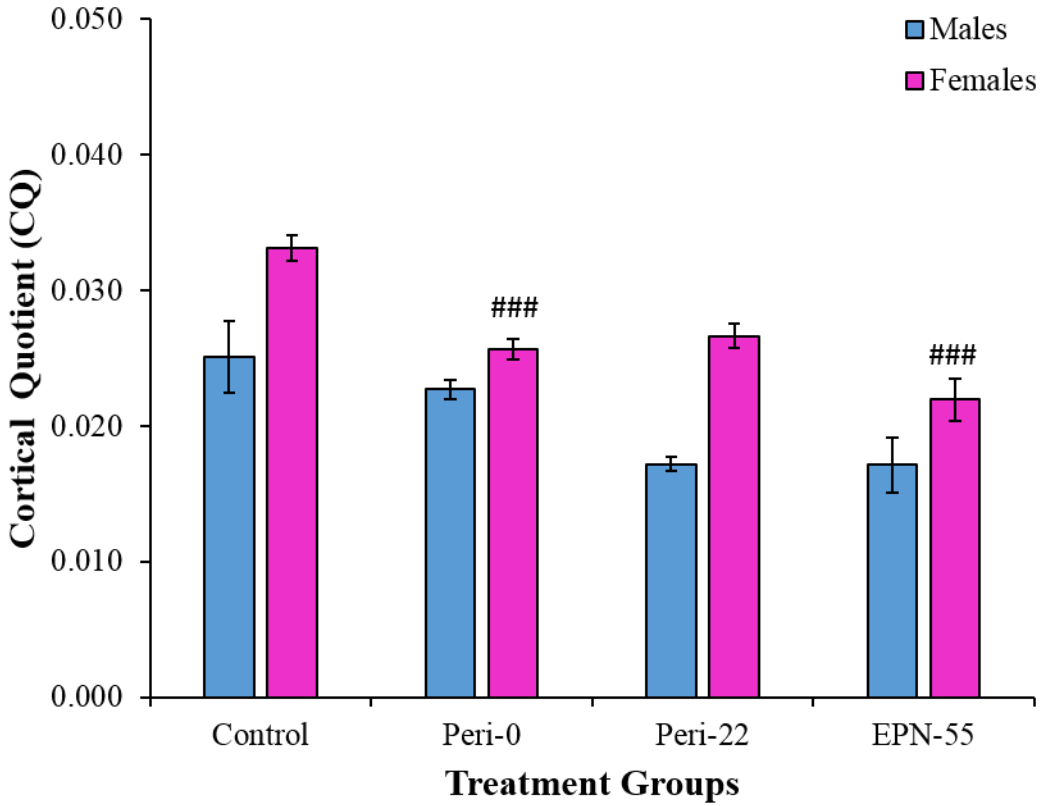


Fig. 5. Cortical Quotient (CQ) differences between males and females as a function of lead treatment and time period of exposure. The data revealed a significant effect of *Treatment* $F_{(3)}$=14.74, p = 0.001 and *Sex* $F_{(1)}$=34.80,p = 0.001(*** indicates male differences compared to control, whereas ### indicates female differences compared to control).

DISCUSSION:

- Lead treatment had a significant effect on body, brain, and cortical weights.
- Rats are a sensitive model to evidence how lead exposure shrinks brain and cortical volume using the EQ and CQ calculations.
- Such early and time dependent exposures to lead resulted in sex based differences in EQ and CQ.
- Such early brain and cortical volume loss is suggestive of accelerated cortical thinning and neurodegeneration. Thus, lead poisoning may predispose people to neurodegenerative disorders.

CONCLUSION & LIMITATIONS:

- Lead differentially effects both males and females rats in a gender specific manner.
- Moreover, lead effects rats differentially based upon the developmental time period of exposure (*i.e.,* EPN vs. Peri).
- Children may be best served clinically with fMRI brain volume studies following the detection of lead in their body.
- Combining such technology with relative old environmental diseases (i.e., lead poisoning) may perhaps help us to better serve these children across their lifespan.
- Our study was limited as we need to increase the number of control rats in all conditions to publish the results of our study.
- Future studies can look into higher levels of lead exposure to determine whether or not a larger amount of brain volume loss is detected or whether such a phenomenon is restricted to low lead level exposures.

ACKNOWLEDGEMENTS

- SUNY Old Westbury CSTEP Program: Dr. Henry Teoh & Ms. Monique Clark
- Dr. Lorenz S. Neuwirth, Department of Psychology (SUNY-OW FDG)
- CSTEP Statewide Student Conference Organizers and Faculty

REFERENCES:

- Canfield, R.L., Henderson Jr., C.R., Cory-Slechta, D.A., Cox, C., Jusko, T.A., & Lanphear, B.P. (2003). Intellectual impairment in children with blood lead concentrations below 10 microg per deciliter. *N Engl J Med,* 348, (16), 1517-1526.
- CDC, 1991. Preventing lead poisoning in young children: A statement by the centers for disease control. Atlanta, GA: *Centers for Disease Control.*
- Lanphear, B.P., Dietrich, K., Auinger, P., & Cox, C. (2000). Cognitive deficits associated with blood lead concentrations <10µg/dL in US children and adolescents. *Public Health Rep.* 115: 521-529.
- Lanphear, B.P., Hornung, R., Khoury, J., Yolton, K., Baghurst, P., Bellinger, D.C. et al. (2005). Low-level environmental lead exposure and children's intellectual function: An international pooled analysis. *Environ Health Perspect,* 113, 894-899.
- Mare, S., Luan Phan, K., & Liberzon, I. (2013). The contextual Brain: Implications for fear conditioning, extinction and psychopathology. Nature Reviews Neuroscience, 14: 417-428.
- Nevin, R. (2007).Understanding international crime trends: The legacy of preschool lead exposure. *Environmental Research,* 104, 315-336.
- Wasserman, G.A., Liu, X., Lolacono, N.J., Factor-Litvak, P., Kline, J.K., Popvac, D. et al. (1997). Lead exposure and intelligence in 7-year old children: The Yugoslavie prospective study. *Environ Health Perspect,* 105, 956-962.

THANK YOU!

Lead Free KIDS for a Healthy Future