# Neuromotor Effects of Manganese Exposure in Adolescents Entering Workforce

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## Outline

- Background
- Hypothesis & Specific Aims
- Study Design
- Results
- Future Directions

# Paradox of Manganese (Mn) Essential & Neurotoxin






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# Local Mn Point Source


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# Effects on Neuromotor Function

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**Effect of chronic low level manganese exposure on postural balance: A pilot study of residents in southwest Ohio**

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**Childhood exposure to manganese and postural instability in children living near a ferromanganese refinery in Southeastern Ohio**

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*However, no longitudinal studies of Mn exposed children have evaluated the long term impact on gross motor function.*

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# Hypothesis & Specific Aims

*We hypothesize biomarkers of Mn exposure in childhood (ages 7-9) will exhibit a negative association with motor function in adolescence (ages 13-17).*

Specific Aim 1: Determine the extent of exposure to Mn, as measured by internal dose biomarkers of Mn exposure in hair and blood

Specific Aim 2: Evaluate the effect of Mn exposure on adolescent neuromotor function, as measured by postural balance and gait

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# Communities Actively Researching Exposures Study (CARES) Study Design

Marietta, OH

**Recruitment Criteria**
Mother resided in community since 16th week pregnancy, continued participation in CARES study, continued residence in catchment area

**Exclusion Criteria**
Uncorrected vision problems, any health issues affecting balance

**Exposure Biomarkers Collected In Childhood (Ages 7-9)**
Blood Mn, Pb; Hair Mn; Serum cotinine

**Neuromotor Measurements in Adolescence (Ages 13-17)**
Postural Balance, Gait

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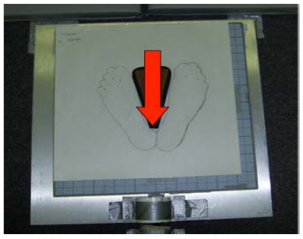
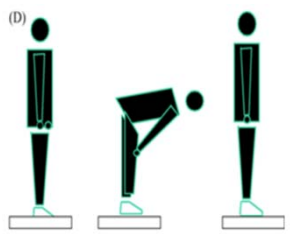
# Postural Balance

| Test Condition | Sensory Afferents | |
|---|---|---|
| | Challenged | Dependent |
| Eyes Open (EO) | | Visual |
| | | Proprioceptive |
| | | Vestibular |
| Eyes Closed (EC) | Visual | Proprioceptive |
| | | Vestibular |
| Standing on Foam, Eyes Open (FO) | Proprioceptive | Visual |
| | | Vestibular |
| Standing on Foam, Eyes Closed (FC) | Visual | Vestibular |
| | Proprioceptive | |
| Bending, Eyes Open (BO) | Vestibular | Visual |
| | | Proprioceptive |
| Bending, Eyes Closed (BC) | Visual | Proprioceptive |
| | Vestibular | |

*Rugless et al. Neurotox and Terat. 2013*



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# Gait

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# Results

**CARES Cohort Demographics & Characteristics, n=124**

| CARES Cohort Demographics n=124 | |
|---|---|
| Female | 54% |
| Caucasian | 98% |

| Characteristics | Median | IQR | Range |
|---|---|---|---|
| Age at visit (years) | 16 | 15, 17 | 13 to 17 |
| Height Weight Ratio | 0.47 | 0.36, 0.52 | 0.22 to 1.91 |
| Total Foot area ($cm^2$) | 233 | 209, 260 | 171 to 313 |
| Parent Education | 15.50 | 14, 17 | 10 to 19.5 |
| Parent IQ | 109 | 100.5, 116 | 65 to 132 |

**Childhood Biological Measures, n=108-119**

| Biological Measures* | Median | IQR | Range |
|---|---|---|---|
| Hair Mn ng/g | 380.16 | 201.35, 801.7 | 63.19 to 7379.09 |
| Blood Mn (µg/L) | 9.80 | 8, 11.50 | 5.3 to 18.8 |
| Blood Pb (µg/dL) | 0.76 | 0.6, 1.01 | 0.36 to 2.71 |
| Serum Cotinine (µg/L) | 0.03 | 0.01-0.08 | 0 to 6.08 |

*Natural log transformed

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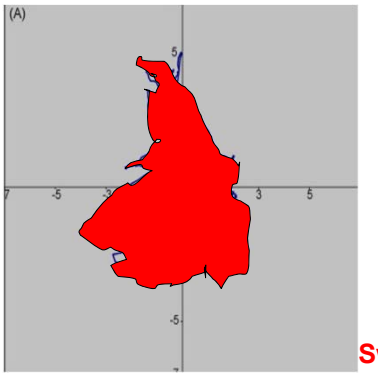


Sway Area (SA)

**Descriptive Statistics – Sway Area, Test Condition D (eyes closed, on foam)**

| | Median | IQR | Range |
|---|---|---|---|
| *Total Sway Area D ($cm^2$) | 3.8 | 2.6, 5.3 | 0.7 to 20 |

*Average of 2 trials

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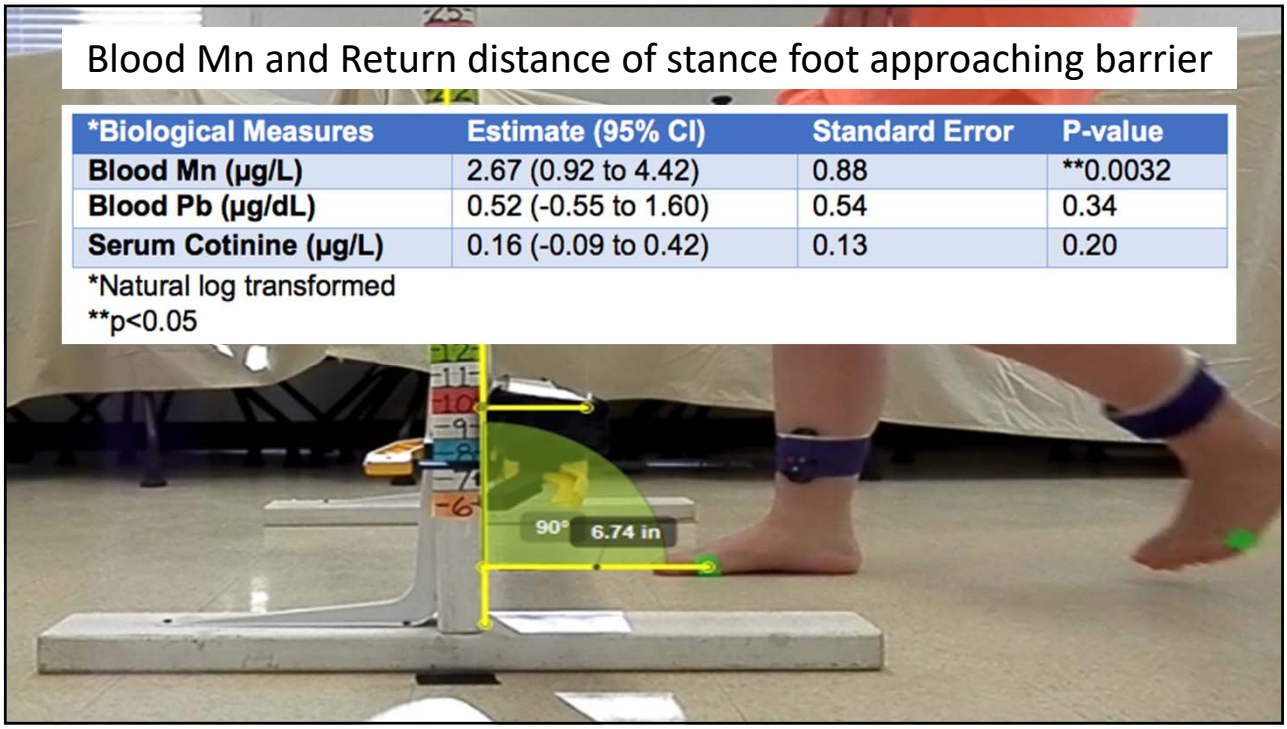
## Blood Mn and Return distance of stance foot approaching barrier

| *Biological Measures | Estimate (95% CI) | Standard Error | P-value |
|---|---|---|---|
| **Blood Mn (µg/L)** | 2.67 (0.92 to 4.42) | 0.88 | **0.0032 |
| **Blood Pb (µg/dL)** | 0.52 (-0.55 to 1.60) | 0.54 | 0.34 |
| **Serum Cotinine (µg/L)** | 0.16 (-0.09 to 0.42) | 0.13 | 0.20 |

*Natural log transformed
**p<0.05




## Hair Mn and Return clearance of foot in swing phase above barrier


| *Biological Measures | Estimate (95% CI) | Standard Error | P-value |
|---|---|---|---|
| **Hair Mn (µg/L)** | 0.19 (-0.80 to 0.46) | 0.13 | 0.16 |
| **Blood Pb (µg/dL)** | -0.67 (-1.30 to -0.05) | 0.31 | **0.03 |
| **Serum Cotinine (µg/L)** | 0.02 (-0.13 to 0.17) | 0.07 | 0.78 |

*Natural log transformed
**p<0.05

# Relevance to NORA sector: manufacturing

Objective 1: Reduce the burden of **acute and chronic occupational illnesses, injuries and fatalities** in **manufacturing** by a) enhancing knowledge of occupational safety and health hazards and their effects, and b) developing effective interventions to reduce exposure to known occupational safety and health hazards

Objective 1.3: Contribute to the reduction of occupational **musculoskeletal disorders** in manufacturing.

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# Scientific Impact and R2P

*Evidence from recent epidemiological studies suggests childhood Mn exposure causes subclinical developmental neurotoxicity. However there is limited knowledge on the longitudinal impact of childhood Mn exposure. This is the first longitudinal study of Mn exposed children to evaluate the long-term impact on gross motor function. Findings from this epidemiological longitudinal cohort study confirm childhood Mn exposure may manifest subclinical developmental neurotoxicity, seen in adolescent . Findings suggest Mn-exposed children as at risk for occupational slips, trips, and fall. This study has implications regarding the research needs identified at the 2016 international Mn conference to revise NIOSH standards for more adequate protection of workers' health and strategies for prevention of Mn toxicity*

R2P: Study results identify Mn-exposed children living near a ferromanganese refinery as an at risk population for occupational safety problems. To improve future occupational safety, exposed children should undergo interventions such as balance training to mitigate risk of falls, slips and trips in the workplace.

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# Future Directions

- Investigate sex differences
- Examine postural balance in childhood & adolescence
- Additional dissertation analyses
- Future funding potential – CARES 3

# The Power of a Team!

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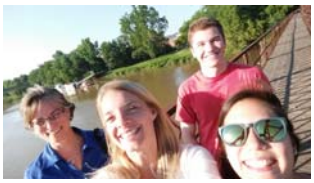
# Thank you. Questions?



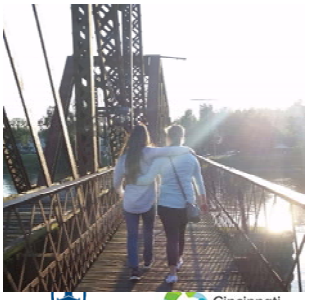


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**Table 6. Descriptive Statistics Gait Obstacle Variables, n=122**

| Measurement (in) | Median | IQR | Range |
|---|---|---|---|
| 1 | 7.92 | 6.9, 9.1 | 4.2 to 12.1 |
| 2 | 3.8 | 3.2, 4.5 | 1.4 to 6.6 |
| 3 | 11.3 | 10.2, 12.9 | 7.5 to 14.7 |
| 4 | 9.4 | 8, 11 | 4 to 15.3 |
| 5 | 4 | 3.2, 4.8 | 1.9 to 7.1 |
| 6 | 10.1 | 9, 11.4 | 7.2 to 14 |

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# University of Cincinnati
# 20th Annual
# Pilot Research Project
# Symposium
# October 10-11, 2019

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