IRON DEFICIENCY: IMPACT ON NEURODEVELOPMENT

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EARLY CHILDHOOD MENTAL HEALTH PROGRAM
GLOBAL PEDIATRICS

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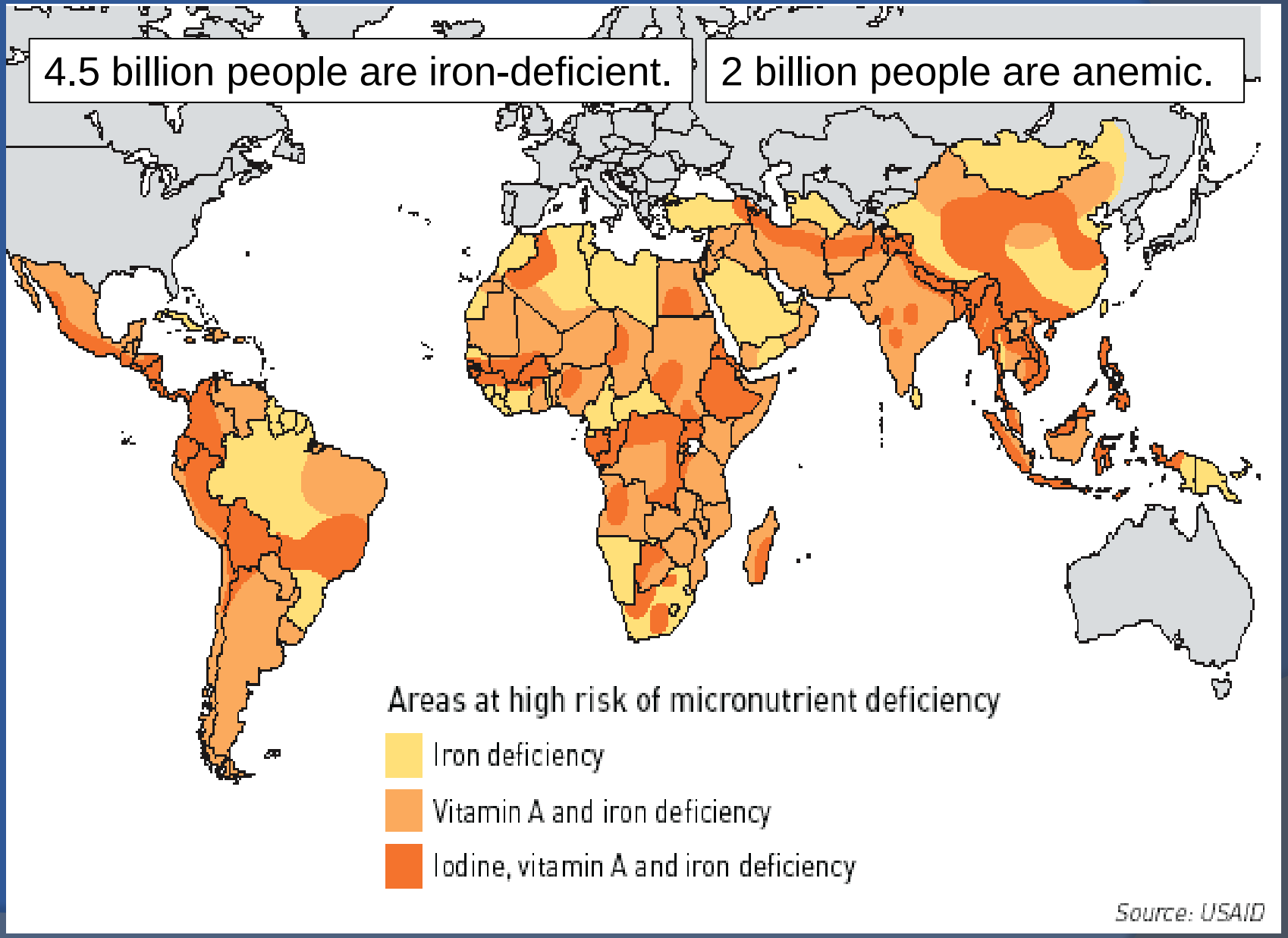
Plan

- Overview of iron deficiency and why young children are vulnerable
- Effects of iron deficiency on developing brain
- Ongoing research projects in the Division of Global Pediatrics assessing neurodevelopment as an outcome of iron intervention studies.

Dietary Causes of Iron Deficiency

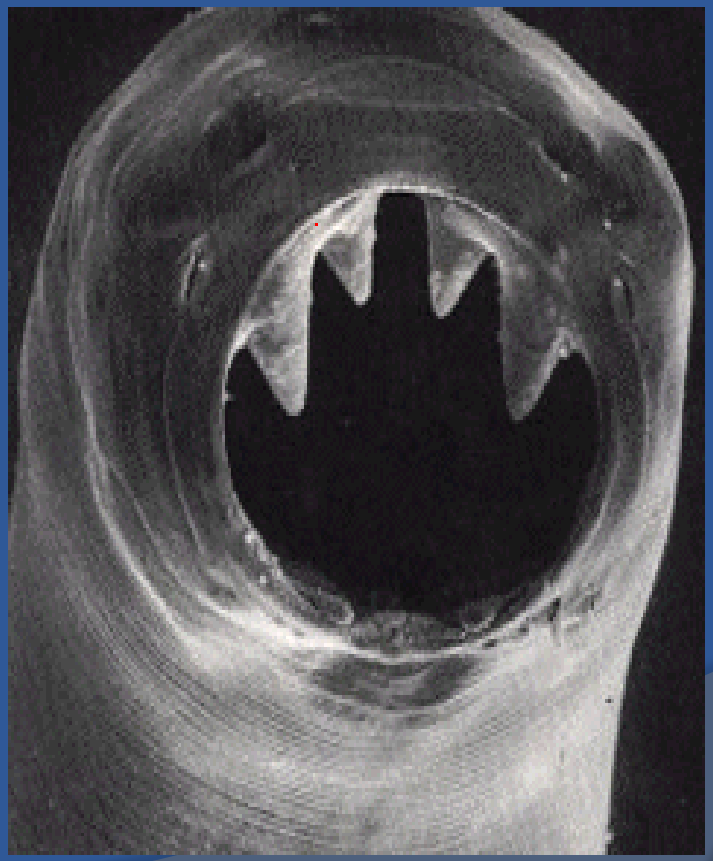
- Insufficient iron intake relative to requirements (infancy, adolescence, pregnancy)
- Low bioavailability of dietary iron (low meat and vitamin C intake; high phytate diets)

Global burden of iron deficiency



Iron deficiency due to infection and malabsorption

- Hookworm, H. pylori, schistosomiasis
- Other conditions that impair iron absorption and/or utilization
- Chronic and/or repeated diarrhea, malabsorption syndromes



Iron deficiency in the United States

- Prevalent in high-risk populations, e.g., low-income preschool-aged children
- 10-20% have iron deficiency

- 5-10% have iron deficiency anemia

Consequences of iron deficiency in children

- Anemia
- Poor growth
- Weakened immune system
- Impaired neurobehavioral development

May not be fully reversible with treatment!

Iron Deficiency and Neurodevelopment

Negative neurodevelopmental outcomes:

- Speed of process
- Recognition memory
- Attention
- Higher-order cognition (frontal lobe-based)
- Social-emotional domain

Iron Deficiency and Neurodevelopment

- Timing of exposure
- Degree (IDA, ID)
- Timing of intervention
- Timing of assessment post-exposure and post-intervention

Developing Brain

sensitive periods

- Last trimester of gestation

  Myelin, striatum, hippocampus

- 6 months to 3 years of life

Myelin, frontal cortex, basal ganglia

ID May not be fully reversible with treatment!

Iron Deficiency and Neurodevelopment

During the critical developmental periods negatively impacts:

- Myelination
- Hippocampal and striatal development
- Dopamine neurotransmitter system

Prenatal Iron Deficiency

- The prenatal brain is much more vulnerable to disruption of substrates critical for normal brain development
- impact on:
  - *recognition memory*
  - *slower speed processing*
  - *difficult temperament*

Postnatal Iron Deficiency

Infancy

- Effects on myelination

Early Childhood

- Social-emotional behaviors

Iron Deficiency and Neurodevelopment

Emotional functioning

Dopamine related behaviors:

- Positive responsively
- Reward responsiveness
- Sensitivity to novelty

Lozoff et al., 2014

Iron Deficiency and Neurodevelopment

Emotional functioning

<u>More chronic IDA or later treatment:</u>

- Fearfulness
- Wariness
- Hesitance
- Other internalized behavioral problems

Lozoff et al., 2014

Functional Isolation Hypothesis

Undernutrient- micronutrient deficiency (ID)

Altered socio-emotional behavior

Negative effects on caregiving environment

Poorer developmental outcomes

Early Childhood Mental Health Program:
Global Pediatrics

Focus on:

1. Identification of early risk factors for neurodevelopment and mental health (children <5y)

2. Effective Early Interventions
   - Psychosocial interventions
   - Nutritional interventions

Mental Health Program:
Global Pediatrics

International Adopted Children

- Initial assessment of nutritional status and neurodevelopment

Other high-risk populations

Mental Health Program:
Global Pediatrics

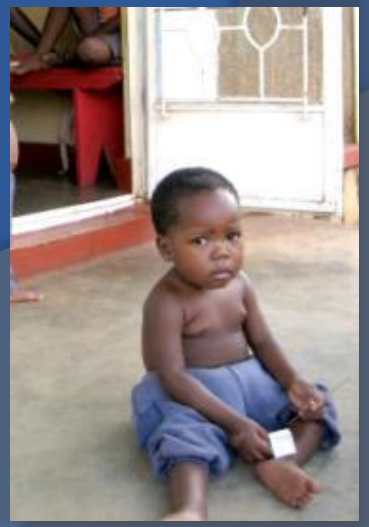
International work

- Children in Institutional Care:

  Kazakhstan, Russia, Spoon Foundation work

- Iron Deficiency (ID) intervention:

  in children with malaria, Uganda

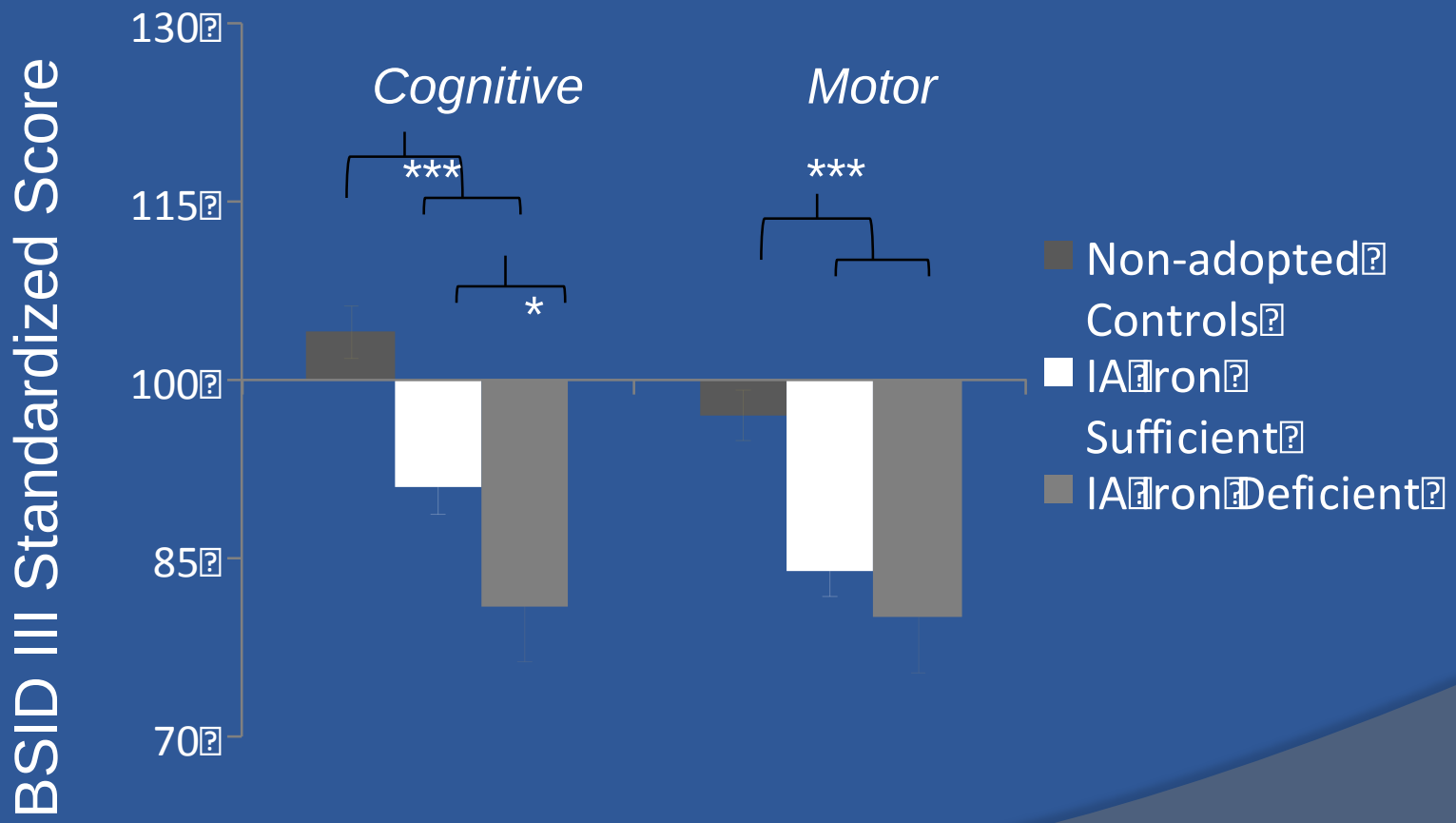


International Adoption Study

- 58 children internationally adopted (IA) from:
- Eastern Europe (n=15) Ethiopia (n=26) China (n=17)
- ages 8-18 months at arrival
- within one month of arrival and a follow-up assessment six months later.

Biological Risk Factors

Iron Status and Bayley Scales



Fuglestad et al under submission

Behavioral Coding

Child's behavior was coded during standardized developmental assessement

- Time: baseline, 6 months post
- 5 point scales
- >80% agreement

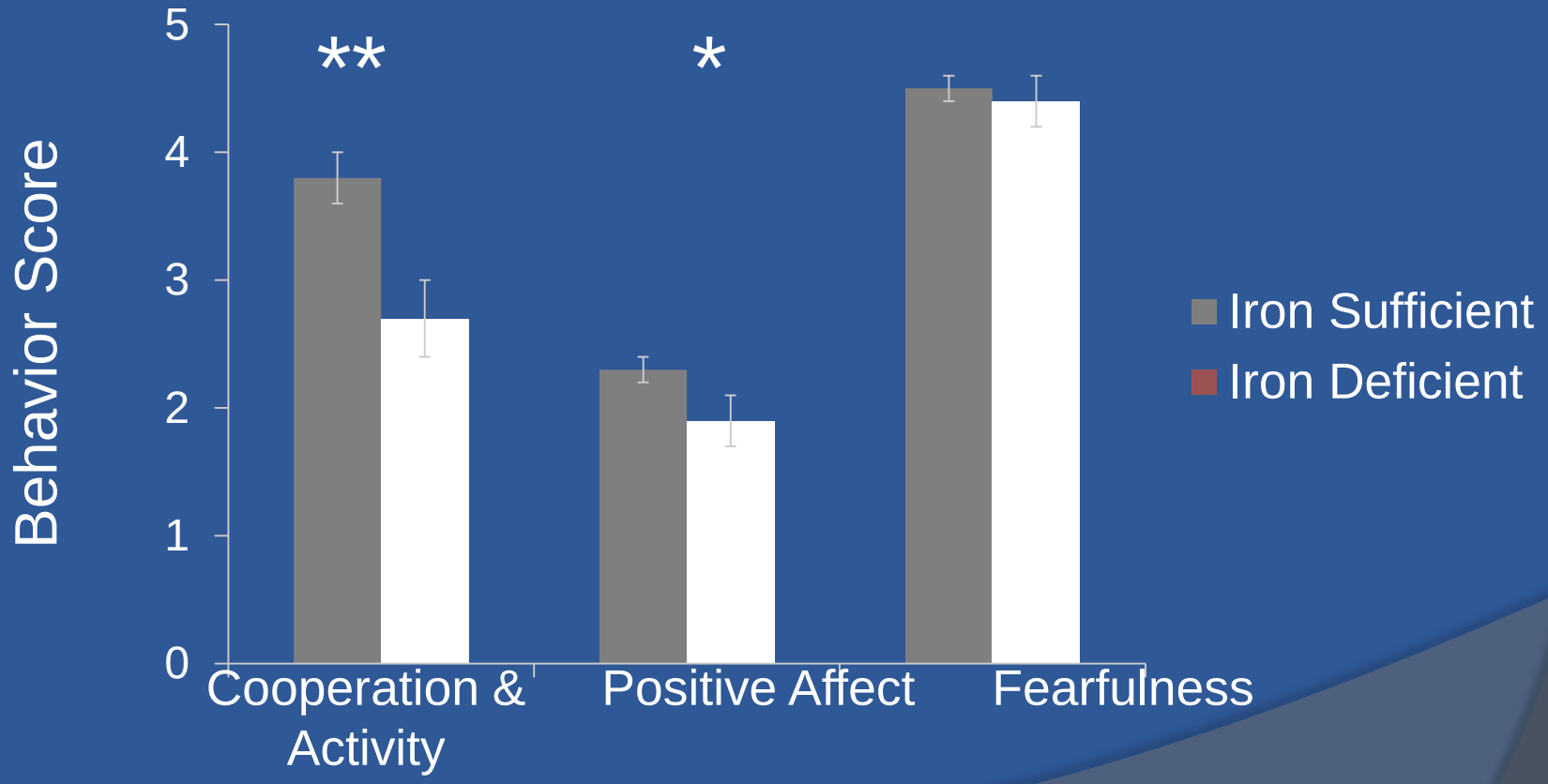
- Categories:
- Positive and negative emotions
- Interest and exploration
- Social interactions and social responsiveness

- Fearfulness, wariness, hesitance

- Hyperactivity

Iron Deficiency: Risk for Emotional and Behavioral Problems

6 months post-arrival



Fuglestad et al 2012

ID Long Term Behavioral and Neurodevelopment Outcomes

1.ID anemia was associated with poorer cognitive functioning 12 months postadoption (*Doom et al., 2014).*

2. IA children had greater ADHD symptomology and lower IQ at 5 years of age.

Within the IA group, children with more severe ID at adoption had greater ADHD symptomology and lower IQ (*Doom et al., 2014)*.

Kampala, Uganda iron study, 2009-present

Acute vs. delayed iron therapy:
Effect on anemia, iron status and cognition (U01)

Malaria and Neurodevelopment

In children < 5 years, negative long-term outcomes

Malaria

- General cognitive development
- Attention
- Memory

Bangirana et al., 2014

Is iron deficiency part of the problem?

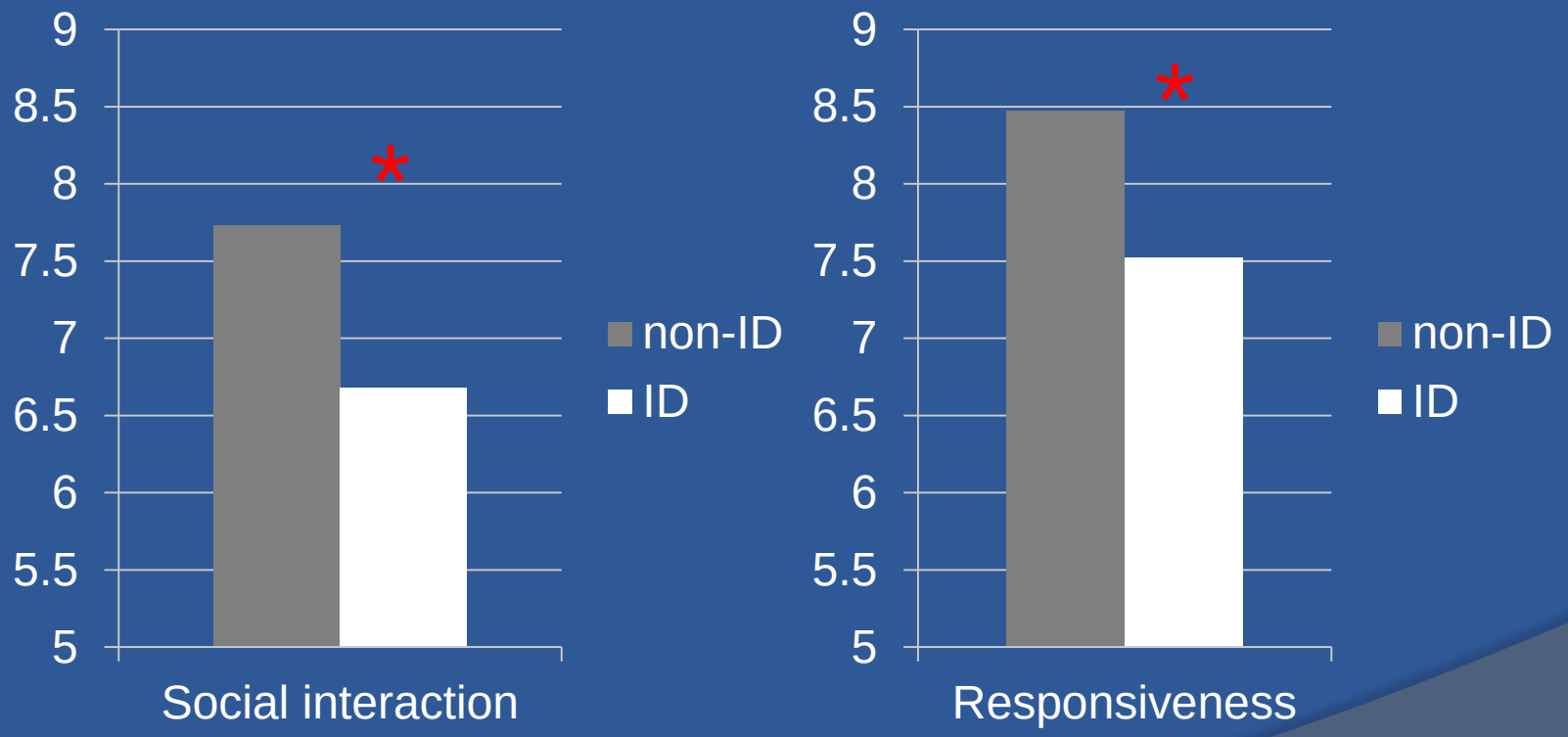
- Prevalence of iron deficiency among Ugandan children 6 mo- 5 yr = ~60% (WHO)
- Iron deficiency also has established harmful effects on brain development.
- Does iron deficiency play a role in the neurodevelopmental impairment observed in children with severe malaria?

Hypothesis

- Social-emotional behaviors assessed at the baseline would be associated with ID (defined as zinc protoporphyrin, ZPP>=80) and other ID-related parameters

Differences Based on ID groups

- All children (*N* = 160)



* $p < .05$

Preliminary Results and Next Step

- ID relates to less social competence including responsiveness and initiation
- Impact of timing of ID intervention on child's neurodevelopmental status

Implications for Clinical Work

- Early screening
- Designing multinational biological and psychosocial interventions
- Timing of intervention: sensitive periods

Our team

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- *Sarah Cusik*
- *Dana Johnson and IAC team*

- *Bob Opoka, Paul Bangirana and Uganda team*

Coding Team

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