The Urban Child Institute
Because We Care About Our Children
www.TheUrbanChildInstitute.org

Hank Herrod, MD
Optimizing Early Brain Development:
Can It Make a Difference in Memphis?
We Believe The Answer Is Yes!!
Why Is a Healthy Early Childhood So Important?

• The healthy development of children provides a strong foundation for healthy and competent adulthood, responsible citizenship, economic productivity, strong communities, and a sustainable society.
  Source: J. Shonkoff Harvard’s Center on the Developing Child

• Converging evidence from biology, economics, sociology, psychology, support the concept of the importance of brain development in early childhood as crucial to ultimate adult outcomes.
A BRIEF LIST OF ENDANGERED SPECIES

The Manatee
The Blue Whale
The Golden-Cheeked Warbler
The Spotted Owl
The Green Turtle
The Whooping Crane
The Urban Child
The Urban Child Institute: Mission

Our mission is to increase awareness of the importance of optimal brain development from conception to three years of age in Memphis and Shelby County.
TUCI Structure

• Emphasis on early brain development

• TUCI houses social scientists from UM, epidemiologists and bio-statisticians from UTHSC, employed staff

• Focus areas: Data ➔ Dissemination ➔ Policy

• Community-focused investments
  ✤ Neighborhood Christian Center
  ✤ Conditions affecting neurocognitive development and learning in early childhood (CANDLE) study
The Human Brain
The Brain from Conception to Birth
How Does the Mother’s Lifestyle Influence the Fetal Brain?

• Almost **anything** Mom does can affect the fetus both positively and negatively

• Examples
  - Environmental exposures
  - Substance abuse
  - Nutrition
  - **Stress**
Normal Brain (L) and Brain Exposed to Excessive Alcohol (R)
Maternal Nutrition: The Relationship Between Neural Tube Defects and Folic Acid
Status of the Brain at Birth

- 100 billion neurons present
- Each neuron can have up to 10,000 synapses
- The developing brain as an architectural project:
  Plans (blueprint – genes) and hardware (foundation, framing, exterior, interior – neurons, glial cells) are in place but connections (insulation, mechanics, making it work –synapses) not yet made
  - Quality building supplies (nutrition, nurturing, experiences)
  - Master carpenter (experiences)
- Use it or lose it
- Do it early – it’s too expensive and difficult to fix it later
The Developing Brain: From Birth to Adolescence
Both Nature (Genes) and Nurture (Environment) are important for optimal brain development.
The Developing Brain Has Periods of Exceptional Sensitivity to the Effects of Experience and Environment

- Maturing neural circuits are influenced by molecular events that are triggered by external factors e.g., vision, hearing, language, responses to social cues
- Sensitive periods occur at different ages for different parts of the brain
Neural Circuits are Wired in a Bottom-Up Sequence
(700 synapses formed per second in the early years)

- Sensory Pathways (Vision, Hearing)
- Language
- Higher Cognitive Function

Center on the Developing Child
HARVARD UNIVERSITY

http://www.theurbanchildinstitute.org
Pruning Effects, Neuron Density, and Synaptic Connections in Development: 
**Use It or Lose It**

3 mos  6 mos  14 yrs

Source: H.T. Chugani
Wayne State University
Critical Period for Visual Development in Kittens: The Influence of Visual Stimulus

After visual deprivation of one eye: Majority of brain cells are driven by the non-deprived eye (shift in ocular dominance).

Normal response properties of brain cells.

Source: NEUROSCIENCE, Third Edition, Figure 23.4 (Part 1) © 2004 Sereauer Associates, Inc.
Critical Periods for Language Development

Sensitive Periods in Language Acquisition
Age of Arrival in U.S. of Chinese and Korean Adults

- English Proficiency Score (mean)
- Age of Arrival in U.S. (years)

- Native
- 3-7
- 8-10
- 11-16
- 17-22
- 23-30
- 31-39
Expressive Language Scores for Hearing Impaired Children Identified Before and After 6 Months of Age

<table>
<thead>
<tr>
<th>Chronological Age in Months</th>
<th>Identified BEFORE 6 Months</th>
<th>Identified AFTER 6 Months</th>
</tr>
</thead>
<tbody>
<tr>
<td>13-18 Months (n=15/8)</td>
<td>10</td>
<td>15</td>
</tr>
<tr>
<td>19-24 Months (n=12/16)</td>
<td>15</td>
<td>20</td>
</tr>
<tr>
<td>25-30 Months (n=11/20)</td>
<td>30</td>
<td>25</td>
</tr>
<tr>
<td>31-36 Months (n=8/19)</td>
<td>35</td>
<td>30</td>
</tr>
</tbody>
</table>
The ACE Study

- The Adverse Childhood Experience (ACE) Study—A CDC, Kaiser Permanente Collaborative
- 17,000 Middle Class Enrollees average age 57 years
- 10 ACE: Abuse, Neglect, Household Dysfunction
Adverse Childhood Experiences (ACE Study)

- Three types of abuse
  - Sexual
  - Physical
  - Emotional

- Two types of neglect
  - Physical
  - Emotional

- Five types of family dysfunction
  - Having a mother who was treated violently
  - Household member who’s an alcoholic or drug user
  - Household member who’s been imprisoned
  - Household member who’s diagnosed with mental illness
  - Parents are separated or divorced
Negative Childhood Experiences Can Affect Adult Behavior

![Graph showing the adjusted odds ratio for different health outcomes (CHD, Diabetes, STD, Drugs, Suicide) based on the number of negative childhood experiences (0, 1, 2, 3, >=4).]
Adverse Childhood Experiences Can Last a Lifetime

Mechanisms by Which Adverse Childhood Experiences Influence health and Well-Being Throughout the Lifespan
Three Levels of Stress

**Positive**
Brief increases in heart rate, mild elevations in stress hormone levels.

**Tolerable**
Serious, temporary stress responses, buffered by supportive relationships.

**Toxic**
Prolonged activation of stress response systems in the absence of protective relationships.
Hypothesis:
SES-Associated Stresses Influence Brain Development

Low SES

↓ Poverty
↓ Poor Education
↓ Unstable Relationships

↑ Fear
↑ Food
↑ Shelter

Altered Neuroendocrine Status

↑ Cortisol
↑↓ Catecholamines

↓ Neuropeptides
↓ Other Hormones

Developing Brain

Altered Synapse Formation

↓ Vocabulary
↓ Strong Parental Interactions

Altered Brain Development

↓ Language
↓ Memory

Poor Academic Performance
Medial View of the Human Brain

- Cerebrum
- Hypothalamus
- Hippocampus
- Brainstem
- Cerebral Cortex
- Sulci
- Gyri
- Prefrontal Cortex
- Frontal
- Parietal
- Occipital
- Temporal
- Cerebellum
The Neuroscience of Stress

Toxic Stress Changes Brain Architecture

Normal

Toxic Stress

Prefrontal Cortex and Hippocampus

Typical neuron – many connections

Damaged neuron – fewer connections

Sources: Radley et al. (2004) Bock et al. (2005)

Center on the Developing Child
HARVARD UNIVERSITY

http://www.theurbanchildinstitute.org
Tying It All Together

- **Epigenetics** - Describes changes in gene function that are not the result of changes in the underlying DNA sequences.

- E.g. All cells in the human body have the same DNA but different cells do different things: neurons vs muscle.

- **Nature + Nurture** can result in modification of gene expression such that your DNA genome is not necessarily your destiny.

- In some situations changes in gene expression can be passed down at least one generation.

Effect of Maternal Care (Nurturing, Environment) on Gene Expression (Nature) in the Rat

On the left, a mother nurses her offspring without arching her back, which may lead to increased cytosine methylation (diagrammed on bottom left) in a glucocorticoid receptor gene promoter, which will decrease glucocorticoid receptor gene expression.

On right, a mother engages in arched-back nursing, which allows for greater movement and access to nipples and is associated with more demethylated cytosine (diagrammed on bottom right) and more glucocorticoid gene expression.

Maternal behavior changes expression of an important stress response gene through methylating a gene promoter.

Environmental Signals Can Remodel Epigenetic Marks that Regulate Gene Expression
(MJ Meaney, Child Psych, 2010)

- Low LG pups have enhanced HPA responsiveness when faced with stress
- Low LG pups have decreased hippocampal glucocorticoid receptors
- Effects of maternal care on hippocampal GCR expression are associated with an epigenetic modification of a neuron specific GCR promoter
- High LG pups have increased GCR expression in hippocampal tissue and a muted HPA response to stress
Epigenetic Regulation of GCR and Child Abuse
(McGowen et al. Nature Neuroscience 2009)

• 12 Accidental death controls

• 12 suicide victims who had a history of child abuse: decreased GCR in hippocampus, increased methylation of NR3C1 promoter

• 12 suicide victims without a history of child abuse: no significant difference from 12 acute accidental death controls.
Hippocampal GCR expression in humans

a) GR mRNA  b) GR receptor
Methylation of the NR3C1 Promoter in the Human Hippocampus
Toxic Stress.

Source: Bill Day, The Urban Child Institute, 2009
Optimizing a Baby’s Brain Development

- Family and friends
- Structured Interventions
  - Home Visitation
- Center Based Care
Language Experiences by SES Group

“Motherese”

Do I have to eat these?

Yeah.
Barriers to Educational Achievement Emerge at a Very Young Age

Effect of Oral Language on Reading Levels

High Oral Language in Kindergarten

Low Oral Language in Kindergarten

5.2 years difference
The Memphis Nurse Family Partnership Program
(Olds et al Peds 2007 e 832-e845.)

- Enrollment Characteristics-AA, unmarried, low income, <12 grade education, unemployed
- Control Group-515 enrollees. Prenatal visits and developmental screenings at 6, 12, 18 mos.
- Intervention Group-228 enrollees. As above plus home visits while pregnant and for first two years of child’s life
Effect of Memphis NFP on Mothers

• Increased interval between births of first and second children
• Longer period with same partner
• Decrease in number of months on food stamps and other welfare programs
• Fewer subsequent low birth weight babies
• Less substance use
Effect of Memphis NFP Program on Children Through First Nine Years

- During the first 2 years of life fewer hospitalizations for accidents and injuries
- By 9 years of age improved grade point averages - lowest resource children (LRC)
- Improved achievement test scores - LRC
- Deaths: Control group 10 deaths (4 SIDS, 2 firearm deaths) Intervention group 1 death (chromosomal abnormality)

Source: Olds et al Peds 2007 e 832-e845.
Model Preschool Programs May Have Lifetime Effects

Source: High/Scope Perry Preschool Study
Model Preschool Programs Have Large Return on Investment

Source: High/Scope Perry Preschool Study

Total return = $258,888; $17.07 per dollar invested; $12.90 to the public, $4.17 to participants
Preventive Intervention is More Efficient and Produces More Favorable Outcomes Than Later Remediation