Peering Inside the Black Box: Understanding the Biology of Childhood Adversity and Resilience

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Disclosures

- I do **NOT** intend to discuss any unapproved or investigational uses for commercial products or devices

- I do **NOT** have any financial relationships with any commercial entities to disclose
Learning Objectives

• Explain the significance of recent advances in the **basic science of development**

• Describe the advantages of an **EcoBioDevelopmental** framework

• Reframe vague concepts like “**adversity**” and “**resilience**” within the context of the **physiologic stress response**
Critical Concept #1

Life-Course Science

Experiences in childhood (both affiliative and adverse) are strongly associated with behaviors, health and economic productivity ... ... DECADES LATER!
Linking **Childhood Experiences** and **Adult Outcomes**

**Childhood Experience**
- Parent Engagement
- Quality Childcare
- Play

**ACEs**
- Poverty
- Violence

**Adult Outcomes**
- Healthy Lifestyles
- Academic Success
- Economic Stability
- Poor Health
- Academic Failure
- Economic Hardship
ACEs Impact Multiple Outcomes

**ACEs**
- Smoking
- Alcoholism
- Promiscuity
- High Perceived Risk of HIV
- Poor Perceived Health
- Multiple Somatic Symptoms
- Sexually Transmitted Diseases

**Risk Factors for Common Diseases**
- Illicit Drugs
- IV Drugs
- Obesity

**Prevalent Diseases**
- Cancer
- Skeletal Fractures
- Chronic Lung Disease
- Ischemic Heart Disease

**General Health and Social Functioning**
- Marriage to an Alcoholic
- Difficulty in job performance
- High perceived stress
- Relationship Problems

**Sexual Health**
- Teen Paternity
- Teen Pregnancy
- Sexual Dissatisfaction

**Mental Health**
- Depression
- Anxiety
- Panic Reactions
- Poor Anger Control

**Poverty**
- Poor Self-Rated Health
- Hallucinations
- Sleep Disturbances
- Memory Disturbances
- Early Age of First Intercourse
Developing a Model of Human Disease and Wellness

Early childhood **ecology** strongly associates with lifelong developmental outcomes.

**How do you begin to define or measure** the ecology?

**What are the mechanisms** underlying these well-established associations?
Defining **Adversity or Stress**

- How do you define/measure adversity?

- Huge **Individual variability**
  - Perception of adversity or stress (subjective)
  - Reaction to adversity or stress (objective)

- National Scientific Council on the Developing Child (Dr. Jack Shonkoff and colleagues)
  - **Positive** Stress
  - **Tolerable** Stress
  - **Toxic** Stress

Based on the **REACTION** (objective physiologic responses)
Neuroscience of the Body’s Stress Response

- Amygdala
- Hypothalamus
  - CRH
  - Anterior Pituitary
    - ACTH
    - Adrenal Cortex
      - CORTISOL
    - Adrenal Medulla
      - SYMPATHETIC INNERVATION
        - EPINEPHRINE
        - NOREPINEPHRINE
  - Posterior Pituitary
    - OXYTOCIN

Associated Behaviors:
- FREEZE
- FLIGHT or FIGHT
- AFFILIATE
The Regulators

Prefrontal Cortex -> Amygdala -> Hypothalamus

Hippocampus -> Amygdala -> Hypothalamus

Vagus Nerve

CRH -> Pituitary

ACTH -> Adrenal Cortex

CRH

Pituitary

Adrenal Cortex

Adrenal Medulla

EPINEPHRINE, NOREPINEPHRINE

Sympathetic Innervation

PARASYMPATHETIC INNERRVATION

Adrenal Medulla -> Vagus Nerve

End Organs

The Regulators

Prefrontal Cortex

Hippocampus

Amygdala

Hypothalamus

Pituitary

Adrenal Cortex

Adrenal Medulla

EPINEPHRINE, NOREPINEPHRINE

Vagus Nerve

CRH

ACTH

CORTISOL
Defining Adversity or Stress

- **Positive** Stress Response
  - Brief, infrequent, mild to moderate intensity
  - Most normative childhood stress
    - Inability of the 15 month old to express their desires
    - The 2 year old who stumbles while running
    - Beginning school or childcare
    - The big project in middle school
  - Safe, Stable, Nurturing Relationships*** allow a return to baseline
    (responding to non-verbal clues, consolation, reassurance, planning assistance)
  - Builds motivation, confidence and RESILIENCE IN THE FUTURE!!
  - “Positive Stress” is NOT the ABSENCE of stress
Defining Adversity or Stress

- **Toxic** Stress Response
  - Long lasting, frequent, or strong intensity
  - More extreme precipitants of childhood stress (ACEs)
    - Physical, sexual, emotional abuse
    - Physical, emotional neglect
    - Household dysfunction

- **Insufficient social-emotional buffering (SSNR deficiency!)**
  (Deficient levels of emotion coaching, re-processing, reassurance/support)

- Chronic exposure to the physiologic mediators of stress (cortisol, epi) leads to **potentially permanent changes** and long-term effects
  - **Epigenetics** (there are life long / intergenerational changes in how the genetic program is turned **ON** or **OFF**)
  - **Brain architecture** (the mediators of stress impact upon the mechanisms of brain development / **connectivity**

Epigenetics
Critical Concept #2

EPIGENETICS

• “Above the genome”
• Change in gene expression/no change in DNA sequence
• Larger revolution in genomic science
  • OLD VIEW = STATIC; NEW VIEW = PLASTIC (responsive to environ. Input)
• Complex set of SWITCHES
  • Some are: Master; Dynamic; Programmed Early and Stable

“Genes load the gun; the environment pulls the trigger”

“Epigenetics: NOT your parents’ genome!”
Impact of Early Stress

MATERNAL STRESS

↑ NEWBORN HPA reactivity and salivary cortisol levels

↑ methylation of the FETAL glucocorticoid (GC) receptor gene

↓ brain expression of the GC receptor

NEWBORN HPA reactivity and salivary cortisol levels

methylation of the FETAL glucocorticoid (GC) receptor gene

brain expression of the GC receptor
Through epigenetic mechanisms, the early childhood ecology becomes biologically embedded, influencing how/which genes are used.
Critical Concept #3
Developmental Neuroscience

• **Brain Architecture** is experience dependent (individual connections or “synapses” and complex circuits of connections or “pathways” are both dependent upon activity)

• **Ecology** (environment/experience) influences how brain architecture is formed and remodeled (plasticity)

• **Diminishing cellular plasticity** limits remediation

• Differential Maturation + Significant Adversity -----------------> Vicious Cycle of Stress

• **Early Experiences** create potentially permanent alterations in brain architecture and functioning
Who is “in charge?”

The PFC and Hippocampus promote reflective / adaptive behaviors, but they are inhibited by the amygdala.

The amygdala promotes impulsive / aggressive behaviors, but it is inhibited by the PFC and Hippocampus.

In the absence of SSNRs or when in “survival mode,” the amygdala is “in charge,” and behaviors tend to be more impulsive and aggressive.

In the presence of SSNRs or when in “relational mode,” the PFC and Hippocampus are “in charge,” and behaviors tend to be more reflective and adaptive.
Impact of Early Stress

**CHILDHOOD STRESS**

Hyper-responsive stress response; calm/coping

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Chronic “fight or flight;” ↑ cortisol / norepinephrine

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Changes in Brain Architecture
Declining plasticity in the developing brain results in potentially permanent alterations in brain functioning and development.
Critical Concept #4

Toxic Stress: Many End-Organs

- **Genome** – changes in telomeres, base-pair mismatch repair, etc.
- **Brain** – changes in the structure/function of the PFC, hippocampus, and amygdala, etc.
- **Endocrine** – changes in acute “stress reactivity” & chronic “basal levels;” altered metabolism, etc.
- **Immune system** – changes in immune regulation & surveillance (associations with asthma, dementia, diabetes, cancer, rheumatologic disease, etc.)
- **Cardiovascular system** - changes in risk AFTER adjusting for standard risks and “behavioral allostasis”
Eco-Bio-Developmental Model of Human Disease & Wellness

NOT: “What’s WRONG with you?

BUT: “What’s HAPPENED to you?

Ecology Becomes biology, development
And together they drive development across the lifespan
The critical challenge now is to translate game-changing advances in developmental science into effective policies and practices for families with children to improve education, health, and lifelong productivity.
“You never change things by fighting the existing reality.

To change something, **build a new model** that makes the existing model obsolete.”

- R. Buckminster Fuller
I. **Biomedical Model of Disease**

- mid 19th century
- embraced biological reductionism
  (disease is due to a single, organic etiology)
- embraced mind-body dualism
  (psychosocial vs. organic etiologies)
  (‘problems of living’ versus ‘problems of life’)
- the practice of medicine demands a knowledge of human biology and the physical sciences
- health is simply the absence of disease
II. **Biopsychosocial Model of Health**

- 1977

- grounded in social-cognitive theory; refuted mind-body dualism; embraced a broader vision of health

- the practice of medicine demands an understanding of the nexus between human biology, psychology and sociology

- health is the product of many factors and more than the absence of an objective disease state
III. **Ecobiodevelopmental Model of Disease & Wellness**

- 2012
- driven by advances in basic developmental science, replaces mind/body dualism with adaptive vs maladaptive responses to experience, and acknowledges the developmental origins of both disease and wellness
- the practice of medicine demands an understanding of how the ecology (e.g., the physical, nutritional and psychosocial milieu) and biology (e.g., the genome, the brain) interact in a dynamic and cumulative manner over time
- health is a dynamic continuum between disease & wellness, and early experiences play a pivotal role because the foundations for both disease and wellness are built over time
A Few Implications:

- Need to get the ecology right (biological advocacy)
- No artificial distinction between physical/mental wellness (changes due to ecol)
- Most NCDs (due to the BIG FIVE) are adult manifest diseases with early childhood origins
- Ground vague terms like adversity and resilience in biology
Redefining Adversity/Resilience

- **Adversity** leads to physiologic stress responses
  - Positive Responses (if buffered by SSNRs)
  - Toxic Responses (if unmitigated by SSNRs)

- **Resilience** is the ability to handle adversity in a healthy manner
  - In the absence of SSNRs, toxic stress leads to maladaptive responses (chronic stress, behavioral allostasis, BIG 5)
  - In the presence of SSNRs, positive stress builds motivation and adaptive responses (resilience) in the future
  - It’s all about “relational health” and the development of SSNRs
Yin / Yang of EBCD

YIN = Build New Skills
Long Standing *Educational* Model
Vygotsky’s Zone of Proximal Development.
“Step on the Gas”

YANG = Protect the Brain
Emerging *Medical* Model
Prevent Toxic Stress Responses
“Release the Brake”

Early childhood experiences & relationships
determine which way this coin spins

Releasing the brake on development is not
a new idea! Montessori and Maslow!!
# Deficiency Needs Inhibit Development

## Models

<table>
<thead>
<tr>
<th>Needs</th>
<th>Maslow’s Hierarchy of Needs (Theoretical - 1943)</th>
<th>America’s Promise Alliance (Evidence-based)</th>
<th>ASCD’s Whole Child Education (Implementation)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Self-Actualization</td>
<td>Need to know, explore and understand</td>
<td>An effective education</td>
<td>Each student is actively engaged in learning</td>
</tr>
<tr>
<td>Esteem</td>
<td>Need to achieve and be recognized</td>
<td>Opportunities to contribute</td>
<td>Each student has numerous opportunities to demonstrate achievement</td>
</tr>
<tr>
<td>Love/Belonging</td>
<td>Need for friends</td>
<td>Caring adults and family</td>
<td>Each student has access to qualified, caring adults</td>
</tr>
<tr>
<td>Safety/Security</td>
<td>Need to feel secure and safe from danger</td>
<td>Safe places</td>
<td>Each student learns in a physically and emotionally safe environment</td>
</tr>
<tr>
<td>Physiological</td>
<td>Need to satisfy hunger, thirst, sleep</td>
<td>A healthy start</td>
<td>Each student enters school healthy</td>
</tr>
</tbody>
</table>

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Release the **BRAKE** before stepping on the **GAS**!!
Modifiable Resilience Factors

Per literature review by Traub and Boynton-Jarret (May, 2017 Pediatrics):

1) Building cognitive skills – positive appraisal style and executive functions (cognitive flexibility & inhibitory control)
2) Promoting parental competence and relationship quality (responsive, caring, positive in regard)
3) Treating maternal mental health problems (maternal depression - increases injury risk and decreases sensitivity)
4) Promoting self-care skills (healthy coping styles) and household routines (more predictability)
5) Enhancing trauma understanding (seeing maladaptive behaviors as opportunities to learn new skills)
**Critical Concept #6**

**SAFE:**
- Prevent toxic stress responses (protect brain) and promote self-actualization (build skills) by meeting Maslow’s level 1 (biological) and level 2 (safety) deficiency needs

**STABLE:**
- Prevent toxic stress responses and promote self-actualization by meeting Maslow’s level 2 (sense of safety due to predictable interactions) and level 3 (sense of connection) deficiency needs

**NURTURING:**
- Prevent toxic stress responses and promote self-actualization by meeting Maslow’s level 3 (sense of connection) and level 4 (sense of competency) deficiency needs

**SSNRs are the ANTI-DOTE to Toxic Stress and ACEs!!**
Childhood Experience

**Safe, Stable and Nurturing Relationships**

- Social-Emotional Learning
- Healthy Adaptations

**Toxic Stress**

- Epigenetic Modifications
- Disruptions in Brain Architecture
- Behavioral Allostasis

Parent Engagement
Quality Childcare
Play

ACEs
Poverty
Violence

Healthy Lifestyles
Academic Success
Economic Stability

Adult Outcomes

Poor Health
Academic Failure
Economic Hardship

To Sum
The **BIG** Questions are...

Since **TOXIC STRESS** mediates the association between **ACE exposure** and **poor adult outcomes**, it raises the following **BIG** questions:

- Are there ways to:
  - Treat,
  - Mitigate, and/or
  - Prevent toxic stress?

But the corollary is ...
The **BIG** Questions are...

Since **Relational Health / SSNRs** are the antidotes to **toxic stress**, it raises the following big questions:

- Are there ways to:
  - **Repair**,  
  - **Eliminate barriers to**, and/or  
  - **Promote** relational health?

- If so:
  - Why are we not actually **DOING** them?!
**PH Approach to Toxic Stress / Relational Health**

**Treating TS / Repairing RH**

- Consequences are **Biological Mal-adaptations** ("what’s wrong with you," vs "what’s happened to you")
- **PCIT, CPP, and ABC** are evidence-based therapies (RH!)
- Efficacy linked to age / chronicity (brain plasticity)
- **REACTIVE** – mal-adaptations are already happening!
- **ACCESS** – interventions must be local
  - More providers / better reimbursement / advocacy
  - Need a universal but local platform (Medical homes? Schools?)
    - Better Identification
    - Better coordination / communication between HC/ED/SS
Mitigating TS / Reducing RH barriers

- Focused, targeted interventions for those deemed to be “at high” or the “highest risk”
- Home Visiting Programs (NFP, PAT, Child First, etc.)
- Parenting Programs (PPP, Nurturing Parenting, Legacy)
- Still issues with stigma, numbers of/access to providers/programs
- Who is “at high risk?” Requires screening (e.g., SWYC, SEEK, ACEs?)
  - No screen is perfect! No ‘OMNI-screen! Might risks also vary by locale?
  - Screening the Child or the Family? For Dysfunction or for Risk Factors?
  - What to do with a + screen? Or can screening itself be an intervention?
PH Approach to Toxic Stress / Relational Health

- **Preventing TS / Promoting RH**
  - Proactive, universal preventions to make stress positive, or tolerable instead of toxic
  - Acknowledges that preventing all childhood adversity is impossible and even undesirable (build skills not bubbles!)
  - **SSNRs / Relational Health** allow the physiologic stress response to return to baseline
    - **Parenting/Caregiving** skills for younger children (2GEN; AAPLeads?)
    - **SEL (www.casel.org)** for older kids (modeled/taught/practiced/learned)
Public Health Approach to Building Resilience:
Layers of Toxic Stress Prevention and SSNR Promotion

Universal Primary Preventions
AG+ (ROR/VIP/PN/PFR/BF Grid)
Consistent messaging (CTC/PPP)
No identification
No stigma
Ceiling effects => Limited evidence base

Targeted Interventions
(for those “at risk”)
Address SDoH (SEEK, HealthLeads)
Home visiting (NFP/PAT); CHWs
Parenting programs (Center; Legacy)
Less ceiling => More evidence
Requires screening
Potential issues with stigma

Evidence-Based Treatments
(for the symptomatic)
ABC/CPP/PCIT
Treatment works!
Screening / stigma / access

ALL are necessary – NONE are sufficient!
Since there are known, established ways to treat, mitigate & prevent toxic stress / to repair, eliminate barriers to & promote relational health,

**WHY ARE WE NOT DOING THEM?!**

- “They cost too much” or “TS is not my concern”

  When kids don’t fulfill their potential, we ALL lose

- “Defensiveness” (“It’s not MY fault” or “It’s THEM!”)

  Toxic stress is not restricted by race, wealth, zip code

- “Too complicated”

  The biology suggests that it is all about RELATIONAL HEALTH!

- “Too hard”

  1) understand the science, 2) advocate for a public health approach, 3) develop a shared language/vision across sectors
SUMMARY

Advances in **Developmental Sciences:**

- Allow us to "peer inside the black box"
- Allow us to redefine **adversity** and **resilience**
- Demonstrate how ACEs may lead to changes at the **molecular**, **cellular** and **behavioral** levels that can be maladaptive (over time or in different contexts)
- Demonstrate the importance of **relational health**, as **SSNRs** are the antidote to toxic stress responses
- Support an **EBD Model of Disease and Wellness**
EBD Model of Disease & Wellness:

- Suggests investments in the early childhood ecology are the right thing to do \textbf{BIOLOGICALLY}

- Suggests that the NCDs that result from unhealthy lifestyles (BIG 5) are \textbf{adult manifest diseases}

- Suggests that a vertically + horizontally integrated \textbf{public health approach} is needed to effectively change the ecology and to improve life course trajectories
What can we do about all of this?

- **EDUCATION** – for providers, trainees, families, the general public and business/philanthropic communities (re: science, TS, EBD, SSNRs)

- **MESSAGING** – be a “convener” (ala CTC); develop a shared “vision” locally to support a public health approach that decreases TS and increases SSNRs

- **ADVOCACY** – investments in the early childhood ecology are the right thing to do biologically; “think developmentally” to improve life course trajectories

- **RESEARCH** – basic (non-invasive biomarkers for TS, personalized medicine), clinical (standardized screens – not just for the child, but the family; not just for dysfunction, but those at risk), and translational (medical homes, schools, communities are integrated both vertically and horizontally into PH approach)

- **PRACTICE TRANSFORMATION** – promote wellness (in addition to chronic/acute care), support families in fostering SSNRs, develop QI/MOC Learning Collaboratives and Communities, form partnerships to incentivize change!!
CONCLUSION:
It is easier to build strong children than to repair broken men.

Frederick Douglass
REFERENCES


