

TOXIC STRESS IN CHILDREN: BEYOND ACES AND INTO RELATIONAL HEALTH

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DISCLOSURE

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ADDITIONAL DISCLOSURE:

This lecture involves discussing child maltreatment with some graphic photographs which can be disturbing to some participants

The child and family featured in this talk have signed a legal release allowing them to be represented.

LEARNING OBJECTIVES

- Identify key factors of toxic stress in children
- Detect biological impacts toxic stress has on a child's developing body
- Develop a plan for treating toxic stress in children

PROFESSIONAL PRACTICE GAP

Addressing the need for awareness and appropriate treatment strategies related to toxic stress beyond being aware of adverse childhood experiences.

EARLY LIFE ADVERSITY

- Adverse Childhood Experiences
 - 1995-1997 study
 - Two Waves
 - 1st wave: looked at abuse & household dysfunction
 - 2nd wave: neglect items added

EARLY LIFE ADVERSITY

- Adverse Childhood Experiences
 - Abuse
 - Psychological
 - Physical
 - Sexual
 - Neglect
 - Emotional
 - Physical

EARLY LIFE ADVERSITY

- Adverse Childhood Experiences
 - Household dysfunction
 - Divorce or separation
 - Intimate partner violence
 - Substance use
 - Mental illness
 - Criminal behavior

EARLY LIFE ADVERSITY

- Adverse Childhood Experiences
 - Around 63% of adults have at least 1 ACE
 - 12% have 4 or more ACEs
- Behavioral Risk Factor Surveillance
 - Found similar data to ACE study
- Study of children show similar data

EARLY LIFE ADVERSITY

- Adverse Childhood Experiences
 - Health outcomes
 - Dose response theory
 - Increase risk of leading causes of death
- Additional research shows similar risk across populations
 - Including pediatric patients
- Risk of death increases

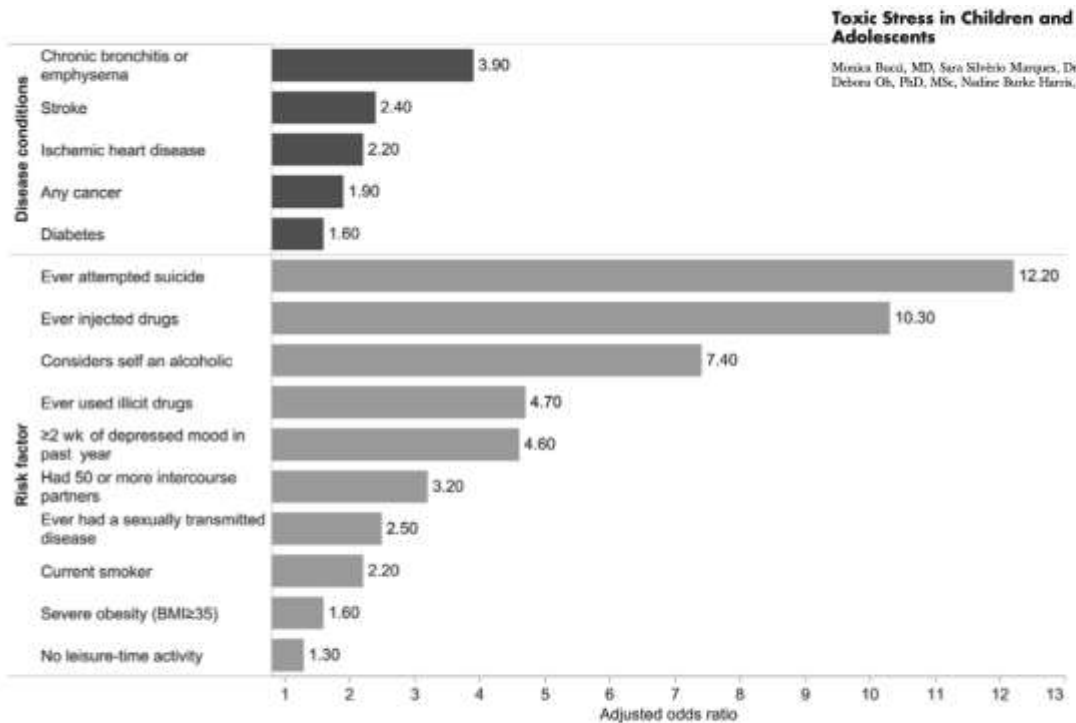


Fig. 1. Odds of outcomes among individuals experiencing 4 or more ACEs. ACEs, adverse childhood experiences; BMI, body mass index. Adjusted for age, gender, race and educational attainment. Referent group 0 ACEs. Data from [9]

EARLY LIFE ADVERSITY

- There are additional traumatic & stressful events
 - Community violence
 - Bullying
 - Experiencing houseless-ness
 - Parental stress
 - Economic hardship
 - Racism
 - Historical trauma
 - Discrimination



TOXIC STRESS



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S T R E S S R E S P O N S E

POSITIVE

Physiological response to mild or moderate stressor

Brief activation of stress response elevates heart rate, blood pressure, and hormonal levels

Homeostasis recovers quickly through body's natural coping mechanisms

Tough test at school, playoff game

TOLERABLE

Adaptive response to time-limited stressor

Time-limited activation of stress response results in short-term systemic changes

Homeostasis recovers through buffering effect of caring adult or other interventions

Immigration, natural disaster

TOXIC

Maladaptive response to intense and sustained stressor

Prolonged activation of stress response in children disrupts brain architecture and increases risk of health disorders

Prolonged allostasis establishes a chronic stress response

Abuse, neglect, household dysfunction

Fig. 2. Spectrum of the stress response: positive, tolerable, and toxic.



MEET JOY



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TYPES OF STRESS

Positive



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TYPES OF STRESS

Tolerable



TYPES OF STRESS

Toxic Stress











STRESS RESPONSE: BIOLOGY

- The Stress Response
 - Central Nervous System
 - Amygdala
 - Hypothalamus
 - Hippocampus
 - Prefrontal cortex
 - Brainstem
 - Locus coeruleus
 - Medulla oblongata

STRESS RESPONSE: BIOLOGY

- The Stress Response
 - Peripheral Nervous System
 - Sympatho-adrenomedullary (SAM)
 - Hypothalamic-pituitary-adrenal
 - Adrenal medulla
 - Adrenal cortex
 - Peripheral changes

STRESS RESPONSE: BIOLOGY

Hypothalamus		Corticotropin-releasing hormone
Hypothalamus/Pituitary gland		Arginine vasopressin
Pituitary gland		Adrenocorticotropin hormone
Medulla and locus coeruleus		Norepinephrine
Adrenal medulla		Epinephrine
Adrenal cortex		Glucocorticoids

HPA axis

The HPA axis controls the body's response to stress and is a complex interplay of direct interactions. The HPA axis is composed of:

1. The **hypothalamus** which releases AVP and CRH to the pituitary gland
2. The **pituitary gland** which secretes ACTH when stimulated by AVP and CRH
3. The **adrenal cortex** which secretes glucocorticoids (cortisol) when stimulated by ACTH

SAM axis

The SAM axis mediates a rapid response to stress through interconnected neurons and regulates autonomic functions in multiple organ systems. The SAM axis is composed of:

1. The **sympathetic neurons** which release epinephrine and norepinephrine and activate the body's "fight or flight" response
2. The **parasympathetic neurons** which withdraw the activity of the sympathetic neurons and promote the body's "rest and digest" response
3. The **adrenal medulla** which when triggered by the sympathetic neurons secretes circulating epinephrine and activate the body's "fight or flight" response

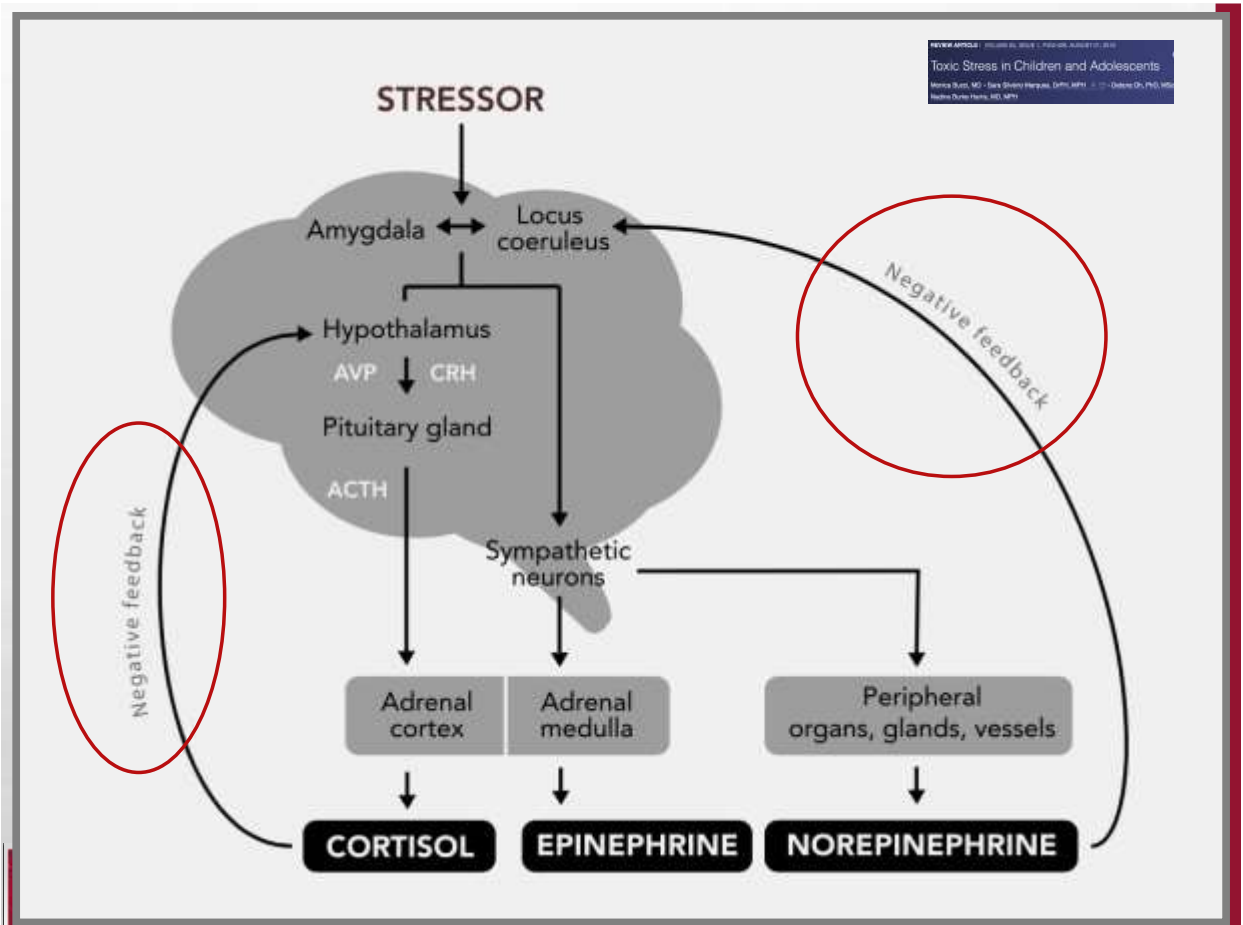
Fig. 3. Stress response pathway. HPA axis, hypothalamic-pituitary-adrenal axis; SAM axis, sympathoadrenomedullary axis; AVP, arginine vasopressin; CRH, corticotropin-releasing hormone; ACTH, adrenocorticotropin hormone.

STRESS RESPONSE: EFFECTS

- Classic Flight-or-Fight-or-Freeze
 - Blood circulation
 - Respiration
 - Metabolism

STRESS RESPONSE: EFFECTS

- Behavioral Changes
 - Increased arousal
 - Improved cognition
 - Euphoria
 - Decreased pain perception
 - Rise in body temperature





TOXIC STRESS: DYSREGULATION

- Loss of homeostasis of the system
 - Prolonged exposure disrupts these mechanism
 - Decrease ability to regulate SAM and HPA
 - Prolong activation leads to:
 - Alteration in stress hormones
 - Initially excessive
 - Eventually deficient

TOXIC STRESS: DYSREGULATION

- Biological alterations
 - Nervous
 - Endocrine
 - Immune

TOXIC STRESS: CLINICAL OUTCOMES

- Systemic alterations
 - Neurological
 - Psychiatric
 - Behavioral
 - Endocrine
 - Metabolic

TOXIC STRESS: CLINICAL OUTCOMES

- Systemic alterations
 - Cardiac
 - Reproductive
 - Immune
 - Inflammatory
 - Genetic

REVIEW ARTICLE | PEDIATRICS | 134(8) | AUGUST 2015
Toxic Stress in Children and Adolescents
Honora Blythe, MD · Sara Shalizi Marquez, DrPH, MPH · — · Debra O'Leary, PhD, MSW ·
Rachna Datta-Hartig, MD, MPH



EARLY LIFE ADVERSITY

Protective factors^a →



← Predisposed vulnerability^a



CLINICAL IMPLICATIONS

Epigenetic		
Endocrine Metabolic Reproductive	Neurologic Psychiatric Behavioral	Immune Inflammatory Cardiovascular



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“Approaches to minimizing toxic stress that only look at measures of adversity, such as ACE scores or biomarkers, will miss out on opportunities to support the relational health that promotes flourishing despite adversity.”

- AAP Preventing Childhood Toxic Stress: Partnering with Families and Communities to Promote Relational Health



TOXIC STRESS VS RELATIONAL HEALTH

Toxic Stress: defines the problem.

“Toxic stress explains how many of our society’s most intractable problems (disparities in health, education, and economic stability) are rooted in our shared biology but divergent experiences and opportunities.”

Relational Health: defines the solution.

“Relational health explains how the individual, family, and community capacities that support the development and maintenance of SSNRs also buffer adversity and build resilience across the life course.”

TOXIC STRESS VS RELATIONAL HEALTH

- Relational Health
 - Definition
 - Contribution
 - Clinical care
 - Prevention
 - Primary
 - Secondary
 - Tertiary

Public Health Level	Types of Prevention	Approaches to Toxic Stress	Examples	Approaches to Relational Health
3	Tertiary	<u>Indicated treatments</u> for toxic stress related diagnoses (e.g, anxiety depression, PTSD)	ABC PCIT CPP TF-CBT	<u>Repair</u> strained or compromised relationships
2	Secondary	<u>Targeted interventions</u> for those at higher risk for toxic stress responses	Parent/Child ACEs SDoH BStC	<u>Identify and address</u> potential barriers to SSNRs
1	Primary	<u>Universal preventions</u> for all	Positive parenting ROR Play Consistent messaging	<u>Promote</u> SSNRs by building 2-generational skills

APPLICATIONS TO PRACTICE

- Applications to Practice
 - Promote Safe Stable Nurturing Relationships (SSNRs)
 - Core focus of Family Center Pediatric Medical Homes
 - Reduce Sources of Stress within Families
 - Core Life Skills

FUTURE APPLICATIONS

- Population-Level Changes
 - Training program
 - System-wide changes in appointments
 - Coordination across systems
 - Focus on Social Determinants of Health
 - Racism
 - Historical trauma
 - Poverty
 - Demographic risk factors



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REFERENCES

- Shonkoff JP, Boyce WT, Levitt P, et al. Leveraging the Biology of Adversity and Resilience to Transform Pediatric Practice. *Pediatrics*. 2021;147(2):e20193845
- Shonkoff, JP, Garner, AS, & THE COMMITTEE ON PSYCHOSOCIAL ASPECTS OF CHILD AND FAMILY HEALTH, COMMITTEE ON EARLY CHILDHOOD, ADOPTION, AND DEPENDENT CARE, AND SECTION ON DEVELOPMENTAL AND BEHAVIORAL PEDIATRICS *Pediatrics* 2012;129:e232–e246 www.pediatrics.org/cgi/doi/10.1542/peds.2011-2663
doi:10.1542/peds.2011-2663
PEDIATRICS
- Oral, R. et. al. Adverse childhood experiences and trauma informed care: the future of health care. *Pediatric Research* Vol 79 No1 January 2016
- Garner A, Yogman M, COMMITTEE ON PSYCHOSOCIAL ASPECTS OF CHILD AND FAMILY HEALTH, SECTION ON DEVELOPMENTAL AND BEHAVIORAL PEDIATRICS, COUNCIL ON EARLY CHILDHOOD. Preventing Childhood Toxic Stress: Partnering With Families and Communities to Promote Relational Health. *Pediatrics*. 2021;148(2):e2021052582
- Franke, HA "Toxic Stress: Effects, Prevention, and Treatment" *Children* 2014, 1, 390-402
- Bucci, M. et. al. "Toxic Stress in Children and Adolescents" *Advances in Pediatrics* 63 (2016) 403-428
- Boyce WT, Levitt P, Martinez FD, et al. Genes, Environments, and Time: The Biology of Adversity and Resilience. *Pediatrics*. 2021;147(2): e20201651



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OPPORTUNITIES TO IMPROVE: AAP POLICY STATEMENT

- “Expand Toolbox of Effective Strategies for Strengthening the Foundations of Healthy Development in the Face of Adversity”
 - AAP projects show how we can enact change
 - Immunizations
 - Back to Sleep
 - Car Seats
 - The “Next Great Projects”
 - Relationship between childhood experiences and adult disease
 - Biology, Physical, and Social Environments
 - Reducing Global Poverty

OPPORTUNITIES TO IMPROVE: AAP POLICY STATEMENT

- “Compelling Need to Revisit the Criteria Used to Designate an Intervention as Evidence Base and to Strengthen Measurement Capacity in the Early Childhood Period”
 - Challenging Federal Guidelines on outcome measurements
 - Improving measurement capacity

OPPORTUNITIES TO IMPROVE: AAP POLICY STATEMENT

- “The Potential Benefits of 2 Complementary Pathways Toward Greater Impact on the Health and Development of Young Children and Families Facing Adversity.”
 - Pathway 1
 - Pathway 2

GENE ENVIRONMENT TIME FRAMEWORK

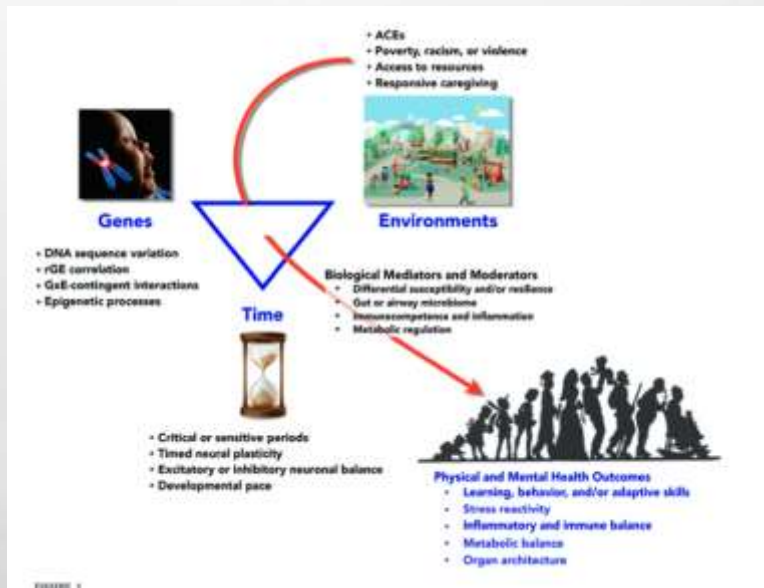


FIGURE 1

TOXIC STRESS: GENES

Gene-environment
correlation (rGE)



Genetic variation &
environmental exposures are
correlated, but not casually
interactive

Specific environmental
conditions (GxE)



Variations happen only in
specific environmental
exposures

Epigenetic gene-regulatory
processes (eGEs)



Environmental exposures
regulate or calibrate level of
gene expression

TOXIC STRESS: GENES

TABLE 1 Three Forms of GxE Interplay, With Mechanisms and Examples

Forms of GxE Interplay	Mechanisms	Examples
1. rGE	Individuals with certain genetic variants choose, alter, or create their environments.	Children with particular genotypes may evoke specific parenting behaviors, such as harsh discipline.
2. GxE	Environmental influences are apparent only among individuals carrying a particular gene variant.	Lack of early endotoxin exposure predisposes children to asthma, but only among children with a genetic variant in the <i>CD14</i> gene.
3. eGE	Environmental exposures regulate or calibrate gene expression through epigenetic processes.	Methylation of cytosine nucleotides within certain sets of genes is associated with increased sympathetic reactivity to stressors.

TOXIC STRESS: ENVIRONMENTS

- Environmental Stressors
 - Trigger adaptive mechanisms
 - Increase inflammation
 - Systemic stressors
 - Recessions
 - Poor parenting
 - Microbiome
 - Buffers

TOXIC STRESS: TIME

- Critical periods in brain development
- Cells build capacity to change
- Differential plasticity over time
- Timing of experiences