The Impact of Early Life Adversity – and How to Break the Cycle

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Lipsitt-Duchin Lecture
Brown University & Rhode Island Kids Count
May 4, 2017
The Lifelong Impact of Early Life Adversity—and How to Break the Cycle

born anxious

Daniel P. Keating

St. Martin’s Press, April 2017
The Cycle

- Early Life Adversity/Stress
- Bio-embedding Epigenetic/Brain
- Stress Dysregulation (SDR)
- Lifelong Harm to Developmental Health
- Social Inequality and the Stress Epidemic
- Stress Contagion: Harsh Social Environments
Social Epidemiology of Adverse Childhood Experiences

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Developmental Origins of Health and Disease (DOHaD): The Social Environment

- “Barker hypothesis” linking suboptimal intra-uterine growth to midlife cardiovascular disease (~1990)
- Marmot’s work linking lower social status (in UK civil service) to increased health problems across many kinds of diseases
- Hertzman and Power’s work with 1958 UK birth cohort linking family of origin socioeconomic status (SES) to developmental health outcomes into adulthood
- Felitti’s Adverse Childhood Experiences (ACE) retrospective questionnaire linking U.S. population health outcomes to cumulative risk factors in early life
Developmental Health (DH) Outcomes

• What are the outcomes whose distribution reveals disparities by social position (SES) and/or by race/ethnicity?
  o Virtually all do, with similar social patterning:
    ▪ Physical Health
    ▪ Educational achievement
    ▪ Career trajectories
    ▪ Mental health conditions and diagnosis differentials
    ▪ Justice system involvement
    ▪ In other words: the full range of developmental health

Social Epidemiology of Adverse Childhood Experiences

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Developmental Mediators of Social Disparities

**Experience-Based Mediators**
- Social interactions (e.g., parent-child)
- Physical Exposures (e.g., neurotoxins)
- Material Resources (e.g., nutrition)

**Child Mediators**
- Genetic/epigenetic
- Brain/biology (e.g., neural, neuroendocrine, neuroimmune)
- Behavior, cognition, emotion (e.g., regulation)

**Social Circumstances Predictors**
- Demographic (e.g., gender, ethnicity)
- Socioeconomic (e.g., income, education)
- Residential (e.g., segregation, exposures)

**Social Disparities in Developmental Health Outcomes**
- Physical Health
- Mental Health
- Cognitive/Academic
- Social Competence

_Figure 1_
Causal Model of Social Disparities in Developmental Health
Mortality Rates (per 100,000 people, aged 30-74) in Three Countries, at Different Levels of SES

Understanding How Early Adversity Works: What Needs to be Accounted For?

• The effects are *pervasive*
  o Childhood problems in development and behavior
  o Adolescent achievement and health
  o Adult diseases of many types
  o Longevity

• The effects are *portable*
  o Can persist across changing contexts

• The effects are *lifelong*
Key Reviews


The Cycle

“Getting under the skin”

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Multiple Pathways for “Getting Under the Skin”

• To explain how both adolescent achievement and adult heart disease (and many other DH outcomes) are affected by early adversity, we need to understand how it “gets under the skin”

• Brains “listen to the environment”:
  o neural sculpting/synaptic pruning, with early foundations especially important with life course consequences
  o Adolescence is a second critical period for brain development

• Genes also “listen to the environment”: epigenetic modification of gene expression
  o also an early life effects bias, with life course consequences
  o and a strong potential for transgenerational transmission via biological inheritance – an enduring population burden
Key Reviews

Figure 1. Role of promoter region DNA methylation on gene expression. Upper panel depicts a gene promoter with unmethylated cytosine-phosphate-guanine (CpG) dinucleotides (open circles), allowing access to transcription binding sites and the opportunity for gene expression. Lower panel depicts methylated CpG dinucleotides (filled circles), which would block transcription factor binding and thus repress gene expression.
“Supernurturing” an SDR Infant

• For multiple reasons, infants may have the SDR pattern
  - High stress pregnancy
  - Epigenetic inheritance
  - Genetic vulnerability
  - High stress in early infancy

• Sustained and persistent positive interactions can create resilience
  - Suomi’s work with peer-reared and/or genetically vulnerable infant monkeys shows the benefit, and even turn-around
Challenges and Approaches for “Supernurturing”

• Parents (who themselves may have high stress and/or SDR) will not be getting the positive reinforcement of being able to soothe their baby in a regular fashion – including less of the positive neurochemical oxytocin response

• Supports for parents to provide respite/ help
  o Co-parenting when available
  o “Alloparenting” (Hrdy’s term) from extended family or others
  o Programs to provide support through high quality child care, home visiting, Early Head Start, or others
The Cycle

Focus: NR3C1 methylation
Why Focus on This Gene?

- Stress response is highly complex, why focus on this specific candidate gene?
- Central to glucocorticoid feedback loop, key to controlling a return to baseline “calm” after stress system response
- Earliest and most frequently studied
- Evidence from animal and human work, and from multiple cell types
- Links to epidemiological evidence on the lifelong effects of dysregulated stress system response
Stress Dysregulation (SDR)

• Stress system essential for survival, highly preserved across many species

• Excess or “toxic” stress levels during pregnancy or during an infant’s first year of life can trigger this epigenetic change

• An environmental “signal” that it’s a dangerous environment, so vigilance is advised:
  o “Live fast, live hard, as you are likely to die young!”
Pathways to Resilience

• Social connection
  o Support and nurturance
  o Biological counteragents (oxytocin, serotonin)
  o Note: Harder for SDR individuals to achieve

• Mindfulness based stress reduction
  o Focus on present, not rumination nor fear of future
  o Observed brain changes

• Physical exercise

• Avoidance of unhealthy habits that do reduce cortisol and/or provide temporary relief (“comfort foods”, alcohol, other drugs)
No Magic Bullets

• Resilience after early adversity remains a minority percentage, even with interventions
• Pathways are harder for those with SDR, at any age
• No evidence the stress physiology changes, rather mitigation and work-arounds
• Points toward the need for systemic change that interrupts the cycle at the start
The Cycle

Affects behavior and health over time
SDR Consequences

- Internal feelings of anxiety, stress, agitation, being overwhelmed
- Expression varies across development
- Can be expressed as fight or flight, acting out or withdrawing, or both in rapid succession
- Associated with externalizing and internalizing symptomatology and diagnosis
- Can affect learning and cognitive development, via attention and emotion regulation pathways
Stress Related Diseases and Disorders

• “Allostatic load” over a lifetime leads to multiple health problems

• SES or ACE are the stress patterns most often studied, but the *social gradient* indicates that this stress can occur at any level of SES (though with decreasing probability)
The Cycle

Social Inequality in DH Effects

Stress Contagion: Harsh Social Environments

Early Life Adversity/Stress

Bio-embedding --- Epigenetic/Brain

Social Inequality and the Stress Epidemic

Lifelong Harm to Developmental Health

Stress Dysregulation (SDR)
Mortality Rates (per 100,000 people, aged 30-74) in Three Countries, at Different Levels of SES

A Stress Epidemic?

- CDC data on increases from about 1980 to recently in stress-related disorders and diseases (metabolic, obesity, diabetes, sleep) in the 20% to 25% range
- Self-reported health shows a related pattern, but increasingly for younger cohorts
Stress Load

• Effects are seen not only in expressed diseases and self-reported health

• But also as changes in physiological “stress load index” over the same time period

• Similar inequality in this stress load index
Figure 5.

Stress Load by Income

Source: NHANES II; NHANES 2009–14

Note: Sample restricted to non-Hispanic blacks and whites ages 25 to 74 with nonmissing values for age, race, and income. Stress indicators are levels of albumin, creatinine, cholesterol, triglycerides, and blood pressure. Income is measured as tertiles of reported family income. The stress load index is weighted by the coefficients of the biomarkers in a logistic regression with “fair” or “poor” self-reported health as the dependent variable. Data for 1976–80 are reweighted to mirror the age, race, and gender distribution of the 2009–14 sample.
Population Developmental Health
International Comparisons

- Social gradients are a consistent pattern across (WEIRD) societies on all DH outcomes

- But steepness of social gradients does not reflect inevitability: population developmental health differences by country*
  - This pattern tells us that it is possible to do better (see next Figure)
  - Measured achievement for adolescent DH outcomes, but similar patterns observed for health and social participation
  - And makes it clear that we should all care, because it affects all of us: it is better at a population level (not just a threshold, poverty issue)
  - The same basic pattern for multiple outcomes, with social “resilience” at the country level across them

$Y = -0.03 - 0.57X;\$
$p=0.002$, $r$-square $= 0.32$
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Why Do Nations Differ?

- **Note**: these patterns of inequality linked to population DH outcomes are persistent over time and across outcomes
- Income Inequality
- Human Development Investment
- “Collective Imaginary”
  - “Rights” versus charity/free riding (Justice)
  - “Investment” versus unearned/undeserved benefits (Utilitarian)
The Cycle

High Ambient Stress > Parental Challenges to Nurturing
Stress Affects Nurturing

- Workplace stress increases, in part because it is physiologically contagious
- Work stress is carried into family stress via contagion
- Steep inequality increases stress
  - At lower end, resource concerns re housing, food, employment
  - At middle and higher end, worries about “losing” what one has, and/or children’s future prospects
  - Exacerbated in a fearful political climate (health insurance, deportation, etc.)
  - “Status” inequality as “loss”: Case & Deaton observations on white working class increased mortality
Policies to Support Parents

- Workplace flexibility for expectant mothers
- Workplace civility approaches that help everyone
- Parental leave policies that protect income and career
- Home visiting and other supports for all, but especially for at-risk parents
- Supports from primary care providers, an existing institutional point of contact in infancy
The Cycle

Completing the Cycle: Multiple Pathways

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“All Hands on Deck”

• A cycle like this is a dynamic system, which tend to be highly stable, pulled back to the central dynamic by multiple, linked forces
• Interrupting the cycle and moving to a more virtuous cycle thus requires pressing strongly on all available connection points identified as “control parameters”
• Especially helpful is when there is coordination and integration across the various groups who have responsibilities for different sectors
• Including the non-profit sectors (like the Y or other groups aiming to support healthy development)
But Not Hopeless

• Contemporary international comparisons show that steep inequality, and its consequences for population developmental health, are not inevitable – “high resilience” countries

• Work by Pinker *The Better Angels of Our Nature*) and others shows considerable progress over long historical time (decreased violence, increased likelihood of dying from natural causes, etc.)

• But progress is also not guaranteed – regression is also possible