What We Have Learned: Physical and Mental Health

Stress and the Central Role of the Brain

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Levels of stressful experiences:
Their causes, consequences and why we experience them!

**Positive Stress**
- A personal challenge that has a satisfying outcome
  - Result: Sense of mastery and control

**Tolerable Stress**
- Adverse life events buffered by supportive relationships
  - Result: Coping and recovery

**Toxic Stress**
- Unbuffered adverse events of greater duration and magnitude
  - Result: Poor coping and compromised recovery
  - Result: Increased life-long risk for physical and mental disorders
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      --COMPROMISED BRAIN ARCHITECTURE
      - Dysregulated physiological systems
Behavioral responses ("lifestyle") as well as stressful experiences

CRH

AVP

ACTH

Cortisol

Many targets for cortisol

ACUTE:
- Enhances immune
- Memory
- Energy replenishment
- Cardiovascular function

CHRONIC:
- Suppresses immune
- Memory
- Promotes bone mineral loss
- Muscle wasting
- Metabolic syndrome

... and so what about stress?
Mediators of stress and adaptation

NETWORK OF ALLOSTASIS

CNS function

Cardiovascular function

Metabolism

Immune function

Dysregulation by
-unhealthy lifestyle, poor sleep, toxic chemicals
-feed into network of allostasis
(eg elevated inflammation, cortisol)

Biphasic and non-linear
Examples of diseases
that are exacerbated via network of allostasis

Cardiovascular disease

Depression

Diabetes

Alzheimer’s disease

Arthritis

Cancer
Structural plasticity in the adult brain is modulated by experience and hormones.
Stress causes neurons to shrink or grow
....but not necessarily to die

Control

Chronic stress

Prefrontal Cortex And Hippocampus

Control

Chronic stress

Amygdala Orbitofronal Ctx
Brain Under Stress:
Role in cognitive function, emotion, neuroendocrine and autonomic regulation

**Medial prefrontal cortex**
Decision making, working memory, top down control of impulsive behavior and mood
Autonomic and cortisol regulation

**Hippocampus**
Contextual, episodic, spatial memory
Shut off of cortisol

**Amygdala**
Emotion, fear, anxiety, Aggression
Turns on cortisol and autonomic response
Hypertrophy
Neuroscience, Molecular Biology, and the Childhood Roots of Health Disparities
Building a New Framework for Health Promotion and Disease Prevention

Jack P. Shonkoff, MD
W. Thomas Boyce, MD
Bruce S. McEwen, PhD

A scientific consensus is emerging that the origins of adult disease are often found among developmental and biological disruptions occurring during the early years of life. These early experiences can affect adult health in 2 ways—either by cumulative damage over time or by the biological embedding of adversities during sensitive developmental periods. In both cases, there can be a lag of many years, even decades, before early adverse experiences are expressed in the form of disease. From both basic research and policy perspectives, confronting the origins of disparities in physical and mental health early in life may produce greater effects than attempting to modify health-related behaviors or improve access to health care in adulthood.

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www.jama.com

Cumulative damage; biological embedding
Developmental Issues for Children

Low socioeconomic status
Poor language skills and executive function
and other effects on learning ability
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Low socioeconomic status
Poor language skills and executive function
and other effects on learning ability

Chaos in home
- Greater helplessness and distress, poor self regulatory behavior
- Obesity, elevated blood pressure and cardiovascular reactivity
  - Systemic inflammation and poor dental health
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Abuse and neglect
- Physical and mental health
  - Shorter lifespan

ACE – adverse childhood experiences study
Robert Anda, Vincent Felitti  CDS
PREVALENCE OF TYPES OF MALTREATMENT IN USA

CASCADE OF CONSEQUENCES

Community

Family

Child

Cognitive and Intellectual

Social and Behavioral

Psychological and Emotional

Physical and Neurological
### Table 1. Health and social problems and the ACE score

<table>
<thead>
<tr>
<th>Problems from the baseline data</th>
<th>Outcomes associated with the ACE score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prevalent diseases</td>
<td>Ischemic heart disease, cancer, chronic lung disease, skeletal fractures, sexually transmitted diseases, liver disease</td>
</tr>
<tr>
<td>Risk factors for common diseases/poor health</td>
<td>Smoking, alcohol abuse, promiscuity, obesity, illicit drug use, injection drug use, multiple somatic symptoms, poor self-rated health, high perceived risk of AIDS</td>
</tr>
<tr>
<td>Mental health</td>
<td>Depressive disorders, anxiety, hallucinations, panic reactions, sleep disturbances, memory disturbances, poor anger control</td>
</tr>
<tr>
<td>Sexual and reproductive health</td>
<td>Early age at first intercourse, sexual dissatisfaction, teen pregnancy, unintended pregnancy, teen paternity, fetal death</td>
</tr>
<tr>
<td>General health and social problems</td>
<td>High perceived stress, impaired job performance, relationship problems, marriage to an alcoholic, risk of perpetrating or being a victim of domestic violence, premature mortality in family members</td>
</tr>
</tbody>
</table>

Insights from research on animal models.

- Prenatal stress – retards development of hippocampus

- Maternal care - quality and frequency but also consistency

- Benefits of novel experiences with background of good care

- Undeveloped amygdala - attachment in spite of abuse

- Maternal anxiety transmitted to offspring

- Intrauterine environment - metabolism, obesity

- Biological embedding at level of gene regulation
Epigenetics
Biological Embedding

“above the genome”

Refers to the gene-environment interactions that bring about the phenotype of an individual.

- Modifications of histones - unfolding/folding of chromatin to expose or hide genes
- Binding of transcription regulators to DNA response elements on genes
- Methylation of cytosine bases in DNA without changing genetic code
- MicroRNA’s – regulate mRNA survival and translation

Effects can extend to next generation
Examples: obesity; parental behavior
http://www.pbs.org/wgbh/nova/sciencenow/3411/02.html
How Early Experience Gets Into the Body: A Biodevelopmental Framework

Foundations of Healthy Development and Sources of Early Adversity

- Environment of Relationships
- Physical, Chemical & Built Environments
- Nutrition

Gene-Environment Interaction

Physiological Adaptations & Disruptions

Cumulative Effects Over Time

Biological Embedding During Sensitive Periods

Lifelong Outcomes

- Health-Related Behaviors
- Educational Achievement & Economic Productivity
- Physical & Mental Health

Center on the Developing Child

Harvard University
Cost/Benefit Analyses Show Positive Returns

Early Childhood Programs Demonstrate Range of Benefits to Society

- **Abecedarian Project (through age 21)**: $4.10
- **Nurse Family Partnership (High Risk Group)**: $5.70
- **Perry Preschool (through age 40)**: $9.20

**Total Return per $1 Invested**
- To Individuals: Increased earnings
- To the Public: Lower crime-cost, savings on special education & welfare, increased income tax revenues

**Break-Even Point**