Stress and the Developing Brain

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Presented at Nurturing Matters Conference
February 22 & 23, 2012 Brampton, Ontario Canada
Normal Brain Development

Video available on National Scientific Council on the Developing Child website
Social environment and health
Central Role of the Brain

Protective and Damaging Effects of Stress Mediators

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Social environment and health
Central Role of the Brain

Framework for interaction of biological embedding with cumulative change

Plasticity of brain is a key
Social environment and health

Stressors

- Environmental stressors (work, home, neighborhood)
- Major life events
- Trauma, abuse

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Types of Stress

Positive Stress
- Exhilaration from a challenge that has a satisfying outcome
- Sense of mastery and control
- Good self esteem

Tolerable Stress
- Adverse life events but good social and emotional support

Toxic Stress
- Exacerbated by chaos, abuse, neglect
- Poor social and emotional support
- *Unhealthy brain architecture*
Social environment and health
Allostasis and allostatic load

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Stress, allostasis and allostatic load

Many targets for cortisol

Acute - enhances immune, Memory, energy replenishment, Cardiovascular function

Chronic - suppresses immune, Memory, promotes bone Mineral loss, muscle wasting; Metabolic syndrome

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Social environment and health
Health-related behaviors
What we often mean by “stress” is being “stressed out”!

Feeling overwhelmed, out of control, exhausted, anxious, frustrated, angry

What happens to us?

Sleep deprivation

Eating too much of wrong things, alcohol excess, smoking

Neglecting regular, moderate exercise

All of these contribute to allostatic load
Psychosocial stress is a major factor

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Social environment and health
Central Role of the Brain

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The Human Brain Under Stress
Three Key Brain Areas Under Investigation

Prefrontal cortex
Decision making, working memory, self regulatory behaviors: mood, impulses
Helps shut off the stress response

Hippocampus
Memory of daily events; spatial memory; mood regulation
Helps shut off stress response

Amygdala
Anxiety, fear; aggression
Turns on stress hormones and increases heart rate

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Remodeling of neural architecture

- **Dendrites**: Shrink and expand
- **Synapses**: Disappear and are replaced
- **Neurogenesis**: Continues in some brain areas

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Stress causes neurons to shrink or grow
....but not necessarily to die

Control

Chronic stress

Prefrontal Cortex And Hippocampus

Control

Chronic stress

Amygdala
OFC

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Social environment and health
Central Role of the Brain

Reactive alleles

Epigenetic modifications – transgenerational

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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

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CASCADE OF CONSEQUENCES

Community

Family

Child

Cognitive and Intellectual

Social and Behavioral

Psychological and Emotional

Physical and Neurological

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Toxic stress effects and brain development

Video available on National Scientific Council on the Developing Child website

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### Adverse Childhood Experience – Health Consequences

carried out in Kaiser-Permanente Health System in California

**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>
</tbody>
</table>

#### Outcomes

- **Heart disease, smoking, obesity**
- **Drug abuse, high risk for AIDS**
- **Depression, anxiety, anger control**
- **Anti-social behavior**

Developmental Issues for Children
What Is Toxic Stress?

Chaos in home
- Helplessness and distress
- Poor self regulatory behavior
- Obesity, elevated blood pressure and cardiovascular reactivity
- Systemic inflammation

“Risky families” – cold and unsupportive
- Many same consequences, but not as extensively studied

Lack of verbal stimulation
- Poor language skills and executive function and other effects on learning ability

Abuse and neglect  
**CDC study – Kaiser-Permanente Health System in California**
- Impaired lifelong physical and mental health
- Shorter lifespan

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The Human Brain Under Stress: Developmental effects on hippocampus

Prefrontal cortex
Decision making, working memory,
Self regulatory behaviors: mood, impulses

Hippocampus
Contextual, episodic, spatial memory
Is smaller in
- Early life abuse
- Low self esteem
- Risk for PTSD

Amygdala
Emotion, fear, anxiety,
aggression

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Hippocampus: plasticity and vulnerability

Mossy fiber terminals release glutamate

CA3 neurons excite other CA3 neurons

CA3 vulnerable to damage.
CA3 dendrites shrink with stress

Neurogenesis Inhibited by stress

Entorhinal Cortex input

Subiculum

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Childhood maltreatment is associated with reduced volume in the hippocampal subfields CA3, dentate gyrus, and subiculum

Martin H. Teicher**, A., Carl M. Anderson**,**, and Ann Pollard**,**

**Developmental Psychopathology Research Program and Brain Imaging Center, MGH, Boston, MA; **Psychiatry, Harvard Medical School, Boston, MA 02115; **Department of Psychiatry, Harvard Medical School, Boston, MA 02115; and **School of Nursing, Northeastern University, Boston, MA 02115

6% lower volume in left CA2-3 and CA4-DG in subjects with high ACE scores

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Is there a neurobiology of self esteem?

Smaller hippocampus

Higher cortisol secretion

No habituation to repeated public speaking test (TSST)
Maternal support in early childhood predicts larger hippocampal volumes at school age

Joan L. Luby, Deanna M. Barch, Andy Belden, Michael S. Gaffrey, Rebeca Tillman, Casey Babb, Tomoyuki Nishino, Hideo Suzuki, and Kelly N. Botteron

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Fig. 2. Hippocampus volume by preschool depression severity and maternal support.
The Human Brain Under Stress:
Developmental effects on amygdala

Prefrontal cortex
Decision making, working memory,
Self regulatory behaviors: mood, impulses

Hippocampus
Contextual, episodic, spatial memory
Self-esteem

Amygdala
Emotion, fear, anxiety,
Aggression
Larger and more active in depression, anxiety disorders

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Larger amygdala but no change in hippocampal volume in 10-year-old children exposed to maternal depressive symptomatology since birth

Sonia J. Lupien\textsuperscript{a,b,c,1}, Sophie Parent\textsuperscript{d}, Alan C. Evans\textsuperscript{e}, Richard E. Tremblay\textsuperscript{c,f,g,h}, Philip David Zelazo\textsuperscript{i}, Vincent Corbo\textsuperscript{j}, Jens C. Pruessner\textsuperscript{k}, and Jean R. Séguin\textsuperscript{b,c}
The Human Brain Under Stress: Developmental effects on prefrontal cortex

Prefrontal cortex
- Decision making, working memory,
- Self regulatory behaviors: mood, impulses
- Chaos, early life abuse - poor development

Hippocampus
- Contextual, episodic, spatial memory
- Self-esteem

Amygdala
- Emotion, fear, anxiety, aggression

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Childhood poverty: Specific associations with neurocognitive development

Martha J. Farah\textsuperscript{a,}\textasteriskcentered, David M. Shera\textsuperscript{b}, Jessica H. Savage\textsuperscript{a}, Laura Betancourt\textsuperscript{a}, Joan M. Giannetta\textsuperscript{c}, Nancy L. Brodsky\textsuperscript{c}, Elsa K. Malmud\textsuperscript{c}, Hallam Hurt\textsuperscript{c}

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\textsuperscript{b}Division of Biostatistics and Epidemiology, Department of Pediatrics Children’s Hospital of Philadelphia and Department of Epidemiology and Biostatistics, University of Pennsylvania, USA
\textsuperscript{c}Division of Neonatology, Department of Pediatrics, University of Pennsylvania and Children’s Hospital of Philadelphia, USA

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Fig. 1 – Effect sizes, measured in standard deviations of separation between low and middle SES group performance, on the composite measures of the seven different neurocognitive systems assessed in this study. Black bars represent effect sizes for statistically significant effects; gray bars represent effect sizes for nonsignificant effects.

BRAIN RESEARCH 1110 (2006) 166–174
Perigenual anterior cingulate morphology covaries with perceived social standing

Peter J. Gianaros, Jeffrey A. Horenstein, Sheldon Cohen, Karen A. Matthews, Sarah M. Brown, Janine D. Flory, Hugo D. Critchley, Stephen B. Manuck, and Ahmad R. Hariri

1Departments of Psychiatry and Psychology, University of Pittsburgh, Pittsburgh, PA; 2Department of Psychology, Carnegie Mellon University; 3Department of Psychology, Queens College/City University of New York, NY, USA; 4Brighton and Sussex Medical School, Brighton, UK; and 5Department of Psychology, University of Pittsburgh, Pittsburgh, PA, USA

Fig. 1. Lower subjective social status, as reflected by a lower self-reported ranking on a 'social ladder', was associated with reduced gray matter volume in the perigenual area of the anterior cingulate cortex (pACC). (A) Illustration of 10-point social ladder scale used to assess subjective social status (instructions provided in the appendix). (B) Overlaid on a sagittal view of an anatomical template generated from the present sample is a statistical parametric map of color-scaled t-values which illustrate the pACC area where lower subjective social status was associated with reduced gray matter volume in a multiple regression analysis. The regression analysis controlled for conventional indicators of personal socioeconomic status (assessed by family income and education) and community socioeconomic status (assessed by census tract information reflecting social advantage), as well as age, sex and total gray matter volume. (C) Plotted along the y-axis is the standardized (z-score) gray matter volume from the peak pACC voxel within the cluster of voxels profiled in B. Plotted along the x-axis are social ladder rankings from the scale illustrated in A (1 = “Worst Off”, 10 = “Best Off”). *P < 0.001.
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

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The Poverty Clinic;

Can a stressful childhood make you a sick adult?

BYLINE: Paul Tough

SECTION: FACT; A Reporter At Large; Pg. 25 Vol. 87 No. 5

Story of Nadine Burke, Harvard trained inner city pediatrician working in the San Francisco Bay Area.

“Burke believes that regarding childhood trauma as a medical issue helps her to treat more effectively the symptoms of abused children. Moreover, she believes, this approach, when applied to a large population, might help alleviate the broader dysfunction that plagues poor neighborhoods.

In the view of Burke and the researchers she has been following, many of the problems that we think of as social issues-and therefore the province of economists and sociologists-might better be addressed on the molecular level, among neurons and cytokines and interleukins. ”

NOTE: AS SHOWN IN THE ACE STUDY, THE PROBLEMS OF ABUSE ARE NOT JUST PROBLEMS OF THE POOR!!
Looking to the Future

The adult brain shows plasticity and we are only beginning to recognize its potential!

Dendrites
Shrink and expand

Synapses
Disappear and are replaced

Neurogenesis
Continues in some brain areas

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Adult Disease Prevention Begins With Reducing Early Toxic Stress.

Early Childhood Programs Benefit Lifelong Health, Not Just Education.

Promoting physical health benefits the brain


- for example, the Nurse Family Partnership David Olds

- other programs that promote improved parent-child interactions and improve the home environment, along with external enrichment
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**: Crime-cost, special education & welfare savings, increased income taxes

**Break-Even Point**: $6.60


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