A biology of misfortune
How stratification, sensitivity and stress diminish early health and development

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Three arguments

• Maladaptive consequences of social stratification in early childhood anticipate, parallel and amplify the effects of inequalities in adult societies.

• These effects operate through neurobiological circuits that are responsive to stress and adversity.

• The extensive variation in stress responsivity reveals a subgroup of children with heightened susceptibility to both aversive and protective social conditions.
Half of the world’s childhood population live in poverty.

10 million children die each year, most of them in impoverished countries.

Poor children sustain substantially higher rates of acute and chronic, often disabling diseases.
SES: Active environmental ingredients?

- Conventional accounts
  - Medical care
  - Diet, childhood nutrition
  - Social support
  - Health behavior (e.g., smoking, exercise, etc.)

- Odds of heart disease among British civil servants, after controlling for all presumed mediators

- The majority of SES effect persists

Adjusted for:
- Age
- Height
- Social support
- Smoking, cholesterol, BMI, BP, exercise

* p < .05
Socioeconomic partitioning of stressors and adversities

Evans & English, 2002

Density
Housing problems
Noise
Family turmoil
Violence

Poverty
Middle Income
Differences in the everyday lives of children
(Hart & Risley, 1995)

- 42 Kansas families over 3 years
- Children in professional families heard 11 million words in a year, vs. 6 million in working class, and 3 million in families on welfare
- By kindergarten, children from welfare families had heard 32 million fewer words
Subjective social status

- English Longitudinal Study of Aging
- MacArthur ladder: “Think of this ladder as representing where people stand in our society…”
- Significant associations with subjective social status, even after adjustment for education, occupation, and wealth

Might the health effects of SES be related to the subjective, non-material dimensions of social position?
• African cichlid fish maintain severe hierarchical organization in which only dominant males have reproductive access to females

• Rats in subordination paradigm show pro-inflammatory shifts in cytokine signaling pathways

• Primate species form stable, linearly transitive social hierarchies

• Subordinate positions: upregulated adrenocortical function, impaired immune competence, decreased resistance to disease

• Young children form social orders within weeks of entering new social groups

• Are subordinate positions in early peer hierarchies associated with greater stress, exaggerated reactivity, and excessive, stress-related morbidity?
Naturalistic measures of dominance/subordination behavior

- Social dominance: a pattern of repeated encounters in which the outcome consistently favors the same dyad member
- Dominance observations: critical event and scan sampling over 3-5 weeks
- Behaviors: physical attack, imitation, directing, threat, relational aggression
Dominance/subordination behavior in 3-5 year old children
Subordinate social positions are associated with more depression and inattention, poorer peer relationships, and less prosocial behavior.

Boys > girls
Subordinate social rank diminishes prosocial behavior in low SES children and increases it in high SES children.

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Influence of subordination on depression moderated by classroom ‘climate’: level of learner-centered practices (LCPs)

- With few LCPs, steep depression gradient by social position
- At highest level of classroom LCPs, almost no relation between social position and depression
- Girls > boys (not shown)
Experimental measures of dominance/subordination behavior
In both naturalistic and experimental settings, kindergarten children order themselves into hierarchical social groups. Children in subordinate positions had more presyndromal psychopathology, fewer prosocial and learning-directed behaviors, and higher biological reactivity to challenge. These associations were augmented by low SES and diminished by teachers’ use of learner-centered pedagogical practices.
Why the homology between the health effects of societal-level SES and classroom-level social position? Why does social position covary with health in both? Might there be health effects of subordination *per se*?
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1. Corticotropin releasing hormone (CRH) system
2. Locus coeruleus-norepinephrine (LC-NE) system
SES and the activation of stress-responsive pathways

- Basal salivary cortisol levels among Quebec children
  
  Lupien et al, 2000

- NKC reactivity to mental stressors in Whitehall II study participants

- Increased basal adrenocortical activation and immune reactivity among low SES subsample
  
  Owen et al, 2003
• Dental caries: the single most common chronic disease of childhood
• U.S. treatment cost $4.5 billion annually
• Strong SES and racial disparities
• Associated inflammatory changes may be related long-term to chronic disease in adulthood
• Related to lead exposure, tobacco smoke, diet, access to fluoridated water, but these are only partial accounts
• Oral bacteria *Strep mutans* and *Lactobacillus acidophilus*
• Leading account of disparities: neglect of children’s dental hygiene by low SES parents
Deciduous teeth as a stress biomarker in young children?
• 96 5-year-old children from PAWS Project

• Nearly half had a filling or decay in at least one primary or secondary tooth

• Lower SES significantly associated with increased financial stress, cariogenic bacteria and caries
- Counts of cariogenic bacteria and diurnal salivary cortisol secretion were independently and interactively associated with dental caries.
- Highest rates among children with the combination of high cariogenic bacteria and high salivary cortisol.

- Cortisol reactivity and SES interactively were associated with differences in dental microanatomy.
- Lowest enamel thickness among children with high cortisol reactivity and low household SES.

**Graphs:**
- Upper graph: Oral cariogenic bacteria vs. decayed, missing or filled dental surfaces.
- Lower graph: Household education level vs. enamel thickness (mm).
Sociobiological effects on childhood dental caries
(Boyce et al, 2010)

Oral health disparities related to two interacting pathways:
• Earlier and more intensive exposure to an agent of disease among low SES children
• More family adversity resulting in greater HPA activation, cortisol secretion, and microanatomic vulnerability
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Variability in SES-development associations: Socioeconomic status and reading/literacy scores in Canadian children
(D Willms, 2006)
Differential susceptibility to environmental influence

• Measures of autonomic (LC-NE) and adrenocortical (CRH) reactivity to highly standardized laboratory stressors
  - Impedance cardiography
  - Salivary cortisol
• Broad and reliable individual variability in magnitude and patterns of response

Individual differences in biological reactivity to psychological challenge

Boyce et al, 1995
Psychobiological reactivity and health among children and macaques
(Boyce WT, et al., 1994-2010)

- Internalizing Behavior Problems
- Respiratory Illnesses
- Injuries in Children
- Violent Injuries in Rhesus Macaques
- Memory for Stressful Events

Supportive - Stressful

High Reactivity
Low Reactivity
Pubertal development by parental warmth and sympathetic nervous system reactivity
Ellis, Shirtcliff, Boyce, Deardorff & Essex, 2011

- Low warmth, low SNS reactivity
- Low warmth, high SNS reactivity
- High warmth, low SNS reactivity
- High warmth, high SNS reactivity
Neurobiological sensitivity to social context

Maskrosbarn (Sw): dandelion child

Orkidebarn: orchid child
• Same species of buckeye butterfly
• Polyphenism driven by temperature and length of daylight
• A conditional adaptation involving differential epigenetic regulation of genes determining wing coloration and pattern
A CpG site

Chromatin → Nucleosome → DNA methylation

Histone modifications

B

Gene “switched on”
- Active (open) chromatin
- Unmethylated cytosines (white circles)
- Acetylated histones

Gene “switched off”
- Silent (condensed) chromatin
- Methylated cytosines (red circles)
- Deacetylated histones

Transcription possible

Transcription impeded
Coals to Newcastle
Wisconsin Study of Families and Work
Essex, Boyce, Hertzman & Kobor, 2011

N = 570

Stress:
• depression symptoms
• expressed anger
• parenting stress
• role overload
• financial stress

Infancy
Preschool

N = 109

Epigenetic profiling:
• Buccal epithelial cells
• Illumina microarray
• ~28,000 CpG sites in 
~14,000 gene promoters
Epigenetic vestiges of early developmental adversity

- Differential methylation of multiple CpG sites by parental stress in infancy and preschool
- Mothers’ stressors in infancy more related to differences in methylation for both girls and boys
- Fathers’ stressors in preschool associated with demethylation differences, primarily for girls
- All associations substantial in magnitude, with rho’s in the range of -.60 to .60
A physical *nexus* of gene-environment interplay?
Adult societies and childhood groups self-organize into hierarchical social structures, generating early exposures to subordination, coercion and scapegoating, in addition to poverty, hunger and material injustices.

These exposures—sustained pervasively in early life—establish a developmental biology of misfortune, involving neurobiologic and epigenetic processes and setting life course trajectories toward diminished health, unrealized developmental potential, and early mortality.

Is it not therefore an ethical, moral task of human societies to foster, on behalf of children, developmental settings of early life that are more egalitarian, more protected, more supportive and generous?
The world breaks everyone, and afterward many are strong in the broken places.

—Ernest Hemingway

A Farewell to Arms
Nancy Adler, Abbey Alkon, Loïc Belingard, Pam Den Besten, Nicki Bush, Nicole Catherine, Bruce Ellis, Tanya Erb, Marilyn Essex, John Featherstone, Clyde Hertzman, Young Shin Kim, Mark Kishiyama, Mike Kobor, Stephanie Lam, Amani Nuru-Jeter, Tim Oberlander, Doug Jutte, Amani Nuru-Jeter, Jelena Obradović, Khaled Sarsour, Margaret Sheridan, Juliet Stamper, Anat Zaidman, the MacArthur Foundation Research Network on Psychopathology and Development, the National Institute of Mental Health, the National Institute of Child Health and Human Development, the WT Grant Foundation, the Robert Wood Johnson Foundation Health & Society Scholars Program, the University of British Columbia, the UBC Human Early Learning Partnership, and the Experience-Based Brain and Biological Development Program of the Canadian Institute for Advanced Research