BIOMARKERS OF STRESS
.....are we there yet?

SIREN 2019
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SOCIO-ECOLOGICAL MODEL OF HEALTH

- Socio-economic, Cultural, and Environmental Conditions
- Living and Working Conditions
- Social and Community Networks
- Individual Level Factors
- Host Level Factors

Dahlgren and Whitehead 1991
Number of Stressors for Poor vs. NonPoor Children

![Bar chart showing the percentage of children exposed to different numbers of stressors. The chart compares nonpoor (gray bars) and poor (white bars) children. The x-axis represents the number of stressors, ranging from 0 to 5, and the y-axis represents the percentage of children exposed, ranging from 0 to 60. The chart shows a higher percentage of nonpoor children exposed to stressors compared to poor children, especially for 1 stressor.]
LONG TERM EFFECTS OF SOCIAL AND ENVIRONMENTAL STRESS

Socio-economic, Cultural, and Environmental Conditions
- Living and Working Conditions
- Social and Community Networks
- Individual Level Factors
- Host Level Factors

Cumulative Effects Over Time
- Biology-Environment Interactions
- Physiological Adaptation and/or Disruption
- Disease Risk

DISEASE
- Susceptibility and Morbidity

Biological Embedding

Thakur Race and Ethnicity in Respiratory Health Disparities (Ed. Celedon) 2016, Adapted from Halon et al Life Course Health Development Model and from the biodevelopmental framework.
TYPES OF BIOLOGICAL RESPONSE

Neuro-hormonal and Inflammatory
- Allostatic Load

Genetic
- GxE
- Epigenetic
- Microbiome

Neuroplasticity
- Poverty Shrinks Brain Networks
Primary Outcome
“Fight or Flight Response”
- Catecholamines
- HPA (cortisol)

Secondary Outcome
- Tissue/Organ specific
- e.g. blood pressure, lipid metabolism, and inflammation

Adapted from Matteri, Carroll & Dyer, 2000
ALLOSTATIC LOAD

Cumulative Effect over time leads to new set point.

Adapted from Matteri, Carroll & Dyer, 2000
ALLOSTATIC LOAD AND SOCIOECONOMIC STATUS

- Cardiovascular
- Metabolic
- Immune Response
- HPA Axis
- Respiratory
- Parasympathetic Nervous System
+ Kidney/Liver Function

Allostatic Load Index

Gustafsson J Epidemiology Health 2011, Johnson Social Science & Medicine 2017
<table>
<thead>
<tr>
<th>System</th>
<th>Physiologic</th>
<th>Biomarker</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiovascular</td>
<td>Blood pressure, heart rate, ankle-brachial index</td>
<td>Myeloperoxidase, endothelin-1, VEGF-A</td>
</tr>
<tr>
<td>Metabolic</td>
<td>Waist-hip circumference/BMI</td>
<td>Lipids, HbA1C, insulin, leptin</td>
</tr>
<tr>
<td>Immune System</td>
<td>CRP, fibrinogen, cytokines (IL-6, TNF-a), white count</td>
<td></td>
</tr>
<tr>
<td>HPA Axis</td>
<td>hair cortisol, DHEA-S, epinephrine, norepinephrine</td>
<td></td>
</tr>
<tr>
<td>Respiratory</td>
<td>Spirometry, bronchodilator response</td>
<td></td>
</tr>
<tr>
<td>Parasympathetic</td>
<td>Heart beat variation</td>
<td>Creatinine</td>
</tr>
<tr>
<td>Nervous System</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Kidney/Liver Function</td>
<td></td>
<td>Creatinine</td>
</tr>
</tbody>
</table>
Hair Cortisol consistently associated with low SES

Change in levels seen with interventions targeted at:

- Intense parenting interventions
- Nutrition focused
- Time frame: Months

Vliegenthart Psychoneuroendocrinology 2016
CHANGE WITH INTERVENTION?

STRONG AFRICAN AMERICAN FAMILY

SAAF Program

Parenting

• Decrease drug use
• Decrease alcohol use
• Postpone sexual involvement

Youth protective factors

Fig. 1. Youth whose families participated in SAAF had less inflammation than did controls. The endpoint is a composite indicator of inflammation, formed by summing each subject’s z-scored values for interleukins-1β, 6, 8, and 10, plus tumor necrosis factor-α and IFN-γ. Dots represent individual data points. Within each group, the wide horizontal bar is the mean composite score, and the error bars reflect 95% confidence intervals.

Not ready for PRIME time

Brody Pediatrics 2012, Miller PNAS 2014
GENETICS: EPIGENETIC CHANGES

- Telomere Length
- DNA Methylation

https://www.whatisepigenetics.com/fundamentals/
Strong evidence with perceived stress....
Building evidence with education, less evidence with other measures of socioeconomic status

Robertson Epidemiologic Reviews 2012
Change seen with interventions targeted at ‘stress’
- Meditation
- Exercise
- Lifestyle change
- Timeframe: months to 1 year

Difficult to extrapolate
Biomarkers are helpful at establishing baseline effects
- Candidate biomarkers: Allostatic Load, Hair Cortisol, Telomere Length

More Research Needed
- Do biomarkers change with intervention?
- Does the change in biomarkers equate change in the health outcome of interest?
TAKE HOME

Lasting thought:

- Can biomarkers be used to identify individuals at high risk for poor outcomes?
- If elevated at baseline, would these individuals benefit the most from intervention?
  - Help with allocating resources in low-resource settings
  - Help reduce negative studies
QUESTIONS?
**Positive stress**
*Brief* increases in heart rate
*Mild* elevations in stress hormones

**Tolerable stress**
Serious, *temporary* stress responses
*Buffered* by supportive relationships

**Toxic stress**
*Prolonged* stress response activation
*Absence* of protective relationships

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J Shonkoff Harvard University Center on the Developing Child
**Stressors**
Trauma, Access, Demographics
Violence, Neighborhood deprivation, Air pollution

**Nature of stressor**

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How stressor is perceived

Individual Characteristics
Sex, genes, development, experience, behavior

Ability to cope

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**Biologic Response**
- Neuro-endocrine and humoral response, epigenetics, GxE interaction, microbiome

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