How SES Gets Under the Skin: Inflammation

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What is inflammation?

- **Biological process**
  - Important for host defense
  - Maladaptive if not contained in space and time
- **Blood-borne proteins**
  - Pro-inflammatory cytokines
    - Interleukin-6 (IL-6)
  - Acute phase proteins
    - C-reactive protein (CRP)
  - Clotting factors
    - Fibrinogen
- **Health implications**
  - Linked to morbidity and mortality
    - Increased risk of later cardiac events in healthy individuals
    - Increased risk of cardiac mortality in patients with CVD
    - Limited screening for CRP currently recommended
  - Sensitive to sociodemographic and psychosocial factors
Sources of some inflammatory proteins

- Immune cells
- Fibroblasts
- Smooth muscle
- Visceral fat
- Endothelial cells

Liver

IL-6

CRP

Fibrinogen
Outline

- Links between SES and inflammation
- Links between inflammation and psychological factors
  - Focus on psychological well-being
- Interactions between SES and well-being in predicting inflammation
- Intervention to improve psychological well-being
SES and inflammation

- Income and education
  - NHANES\(^1\); MESA\(^2\); Framingham offspring\(^3\); Heart and Soul Study\(^4\); Health, Aging, and Body Composition Study\(^5\); CARDIA\(^6\)

- Occupational status\(^7\)

- Community SES\(^8\)
  - Composite of income and education

- Subjective social status\(^9\)
  - Hypothesized by Adler et al, 2000

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\(^1\)Alley et al., 2005; \(^2\)Ranjit et al., 2007; \(^3\)Loucks et al., 2006; \(^4\)Lubbock et al., 2005; \(^5\)Koster et al., 2006; \(^6\)Gruenewald et al., 2009; \(^7\)Owen et al., 2003; \(^8\)Petersen et al., 2008; \(^9\)Demakakos et al., Soc Sci Med, 2008
Education and inflammation in Framingham offspring

Loucks et al., Am J. Epidemiol., 2006
SES and inflammation

- Research questions
  - Are SES indicators independently linked to inflammation?
  - Are associations explained by health status and health behaviors?
The MIDUS study

Survey of MidLife Development in the United States (MIDUS)
- Longitudinal study of health and well-being of adults
  - Wave 1 1994-1996
  - Wave 2 2004-2006

Subsamples
- National probability random digit dial sample
- National sample of twins
- Oversample of African Americans living in Milwaukee County

Data collection
- Telephone interviews and self-administered questionnaires (SAQ)
- Laboratory sub-sample
  - Overnight stay at General Clinical Research Center (GCRC)
  - Fasting blood samples for inflammatory proteins

Demographic and psychosocial data: N = 3,741
Biomarker data: N = 1,255
MIDUS – Descriptive statistics

- Biomarker sample (N = 1,255)
  - Mean age 57.3 yrs
  - Female 56.8%
  - Married 62.9%
  - Caucasian 78.5%
  - Median income $38,727.70
- Education
  - HS grad, GED, or less 35.4%
  - Some college 30.1%
  - College degree 34.5%
## Income and IL-6

Dependent measure: IL-6

<table>
<thead>
<tr>
<th>Variables</th>
<th>Model 1(β)</th>
<th>Model 2(β)</th>
<th>Model 3(β)</th>
<th>Model 4(β)</th>
<th>Model 5(β)</th>
<th>Model 6(β)</th>
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</thead>
<tbody>
<tr>
<td>Educational attainment</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;High School</td>
<td>0.12**</td>
<td>0.03</td>
<td>0.02</td>
<td>0.01</td>
<td>0.01</td>
<td></td>
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<tr>
<td>HS grad or GED</td>
<td>0.12**</td>
<td>0.05</td>
<td>0.05</td>
<td>0.03</td>
<td>0.02</td>
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<tr>
<td>Pre-tax income (quintiles)</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Q1 (lowest)</td>
<td>0.36****</td>
<td>0.34****</td>
<td>0.27****</td>
<td>0.23****</td>
<td>0.21****</td>
<td></td>
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<tr>
<td>Q2</td>
<td>0.16****</td>
<td>0.15**</td>
<td>0.10*</td>
<td>0.08</td>
<td>0.07</td>
<td></td>
</tr>
<tr>
<td>Q3</td>
<td>0.10*</td>
<td>0.09</td>
<td>0.07</td>
<td>0.04</td>
<td>0.03</td>
<td></td>
</tr>
<tr>
<td>Q4</td>
<td>0.11*</td>
<td>0.10*</td>
<td>0.08</td>
<td>0.07</td>
<td>0.05</td>
<td></td>
</tr>
<tr>
<td>Adjusted R² for model</td>
<td>0.01***</td>
<td>0.06***</td>
<td>0.06***</td>
<td>0.11***</td>
<td>0.24***</td>
<td>0.26***</td>
</tr>
</tbody>
</table>

Models 1-3: Unadjusted
Model 4: Adjusted for age, gender, race, marital status
Model 4: Model 3 plus chronic conditions, BMI, medications
Model 6: Model 5 plus smoking, alcohol, caffeine, and exercise

*P<.05; **P<.01; ***P<.001

Friedman & Herd, (2010)
Income and IL-6

Friedman & Herd (2010), *Psychosomatic Medicine*, 73: 290-300
Childhood SES predicts inflammation

- **Miller & Chen (2007)**
  - 13-19 year-old women in Vancouver, BC (N = 136)
  - Age when parents purchased first home
  - Not owning home increased risk of pro-inflammatory profiles of gene expression
    - Critical period: ages 2-3

- **Danese et al (2009)**
  - Prospective birth cohort from Dunedin, NZ (N = 1,037)
  - Parent’s occupational status before age 15
  - Low status predicted higher levels of CRP at age 32

- **Miller et al (2009)**
  - 25-40 year-old adults in Vancouver, BC (N = 103)
  - Parent’s occupation in first 5 years of life
  - Low status predicted pro-inflammatory profiles of gene regulation
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IL-6 – psychosocial links

- Higher levels associated with
  - Clinical depression\(^1\) and depressive symptoms\(^2\)
  - Stress of caregiving\(^3\)
    - Rate of accumulation higher in caregivers\(^4\)
  - Job dissatisfaction\(^5\)
- Higher stress-induced responses associated with
  - Early life adversity\(^6\)
- Lower levels associated with
  - Religious participation\(^7\)
  - Social attachments in women with gynecologic cancer\(^8\)
  - Positive affect\(^9\) and psychological well-being\(^10\)
- Lower stress-induced levels associated with
  - Meditation\(^11\)

\(^{1}\)Penninx et al, 2003; \(^{2}\)Christian et al., 2009; \(^{3}\)Lutgendorf et al., 1999; \(^{4}\)Amati et al., 2010; \(^{5}\)Kiecolt-Glaser et al., 2003; \(^{6}\)Carpenter et al., 2010; \(^{7}\)Lutgendorf et al., 2003; \(^{8}\)Costanzo et al., 2005; \(^{9}\)Steptoe et al., 2008; \(^{10}\)Friedman et al., 2007; \(^{11}\)Pace et al, 2009
Psychological well-being

- **Hedonic well-being**
  - Pleasure; absence of distress; life satisfaction
  - Positive and negative affect scales

- **Eudaimonic well-being**
  - Pursuit of personal excellence rather than pleasure
    - From Aristotelian ideal of the “good life” (“eudaimonia”)
  - Ryff (1989) Psychological Well-Being (PWB) scales
    - Autonomy, Positive relations with others, Self-acceptance, Purpose in life, Environmental mastery, Personal growth
Well-being and IL-6

MIDUS 2 Biomarker Sample (N = 1,157)

Regression coefficients are from models adjusted for age, sex, race, educational attainment.
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SES, inflammation, and psychological well-being

- Rationale
  - Psychological factors, such as social support, buffer against the effects of stress on biological processes related to health

- Research question
  - Will psychological well-being moderate the association of SES and inflammation?

- Hypothesis
  - Among low SES adults, inflammation will be lower in those with higher levels of well-being than in those with lower levels of well-being
Education and IL-6

Serum IL-6 (ln-transformed)

Educational Attainment

- HS grad, GED, or less
- Some college
- College grad or more

* Indicates a statistically significant difference between educational attainment levels.
PWB moderates the association of education and IL-6

Figure 2. Several aspects of well-being moderated the effect of education on IL-6. Lines represent simple effects of positive affect on IL-6 for categories according to educational attainment, controlling for age, gender, smoking status, alcohol consumption, caffeine consumption, physical activity, medication usage, BMI, WHR, and chronic health conditions. In all panels, the inverse relationship between IL-6 and well-being for individuals with a high school education or less is significant, with the exception of the simple effect of positive relations with others on IL-6, which was marginally significant. The positive relationship between positive affect and IL-6 for individuals with a college degree or higher was also significant. Figure 2a. With education interpreted as a continuous variable, the simple effect of positive affect at one standard deviation below the mean on education was not significant. Figure 2b. With education interpreted as a continuous variable, the simple effect of environmental mastery at one standard deviation below the mean on education was marginally significant. Figure 2c. With education interpreted as a continuous variable, the simple effect of positive relations with others at one standard deviation below the mean on education was not significant.
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Well-being therapy

- Pioneered by psychiatrist Giovanni Fava
- Based on Cognitive Behavioral Therapy
  - Emphasis on promoting well-being rather than reducing ill-being
- Has been shown to prevent relapse in recurrent depression, treating generalized anxiety disorder\(^1\), and PTSD\(^2\)
- Application to adolescents?

\(^1\) Fava et al., 2005; \(^2\) Belaise et al., 2005
Well-being therapy (WBT)

- Ruini et al (2009) – WBT intervention in Italian high school
  - 9th and 10th grade students
    - N = 227  Mean age = 14.4  61% female
  - Random assignment
    - 5 classes – WBT
    - 4 classes – Placebo intervention
  - 6-week protocol
    - Six sessions
      - 2 hrs per session
      - Once per week
  - Outcomes
    - PWB (Ryff scales) – 6 subscales
    - Distress (Kellner’s Symptom Questionnaire) – 8 subscales
    - Anxiety (Revised Children’s Manifest Anxiety Scale) – 4 subscales
    - Measured at 3 times: pre- and post-intervention; 6-month follow-up
Well-being therapy

- **WBT condition**
  - Week 1 – emotion recognition
  - Week 2 – thoughts and emotions
  - Week 3 – cognitive restructuring
  - Weeks 4-6
    - Focus on positive social relations, purpose in life, self-acceptance
    - Recognition of positive characteristics in self and others
    - Recognition of positive life experiences and daily moments

- **Goal**: promote well-being

- **Placebo condition**
  - Week 1 – emotion recognition
  - Week 2 – thoughts and emotions
  - Week 3 – cognitive restructuring
  - Weeks 4-6
    - Focus on improving communication, conflict resolution, sharing feared situations
    - Relaxation techniques

- **Goal**: reduce ill-being
Well-being therapy
Ruini et al, 2009

**PWB**

- Pre-intervention
- Post-intervention
- 6 month follow-up

**SQ Somatization**

- Pre-intervention
- Post-intervention
- 6 month follow-up
Well-being therapy
Ruini et al (2009) – Results

- Compared to the Placebo group, the WBT group had:
  - Modest increases in total PWB and improvements in physical well-being
  - Modest decreases in anxiety and physiological symptoms (both SQ and RCMAS scales)
Conclusions

- Low SES predicts higher levels of inflammation
- Low SES alters genetic regulation of inflammation
- This association begins to take hold as early as 2-3 years of age and appears to be last into adulthood
- Psychological well-being in adults may buffer against the relationship between low SES and inflammation
- Well-being therapy reduces depression in adults and anxiety in adolescents
  - Effects on inflammation?
With gratitude

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