Early origins of inflammation: An examination of prenatal and childhood social adversity in a prospective cohort study

Natalie Slopen, ScD
Assistant Professor
Department of Epidemiology & Biostatistics
School of Public Health
University of Maryland, College Park
nslopen@umd.edu
Collaborators:

E. Loucks, Brown University
A. Appleton, University at Albany
I. Kawachi, Harvard School of Public Health
L. Kubzansky, Harvard School of Public Health
A. Non, Vanderbilt University
S. Buka, Brown University
S. Gilman, Harvard School of Public Health, Massachusetts General Hospital (Senior Author)

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Inflammation

- Part of normal stress response
- Elevated levels adaptive in short term, maladaptive over time
- Physiological mechanism linking social environments to health over the life course?
Early adversity & adult inflammation

- Prenatal adversity
  - Childhood adversity
  - Inflammation (e.g., C-reactive protein)

- Entringer et al., Dev Psychobiol 2008
- Slopen et al, Psychosom Med 2010
- Danese et al, PNAS, 2007
- Pollitt et al., Eur J Epi, 2007
Research questions

1) Is social adversity during the prenatal period associated with inflammation in adulthood?

2) Independent of prenatal adversity, does adversity during childhood contribute additional risk for elevated inflammation in adulthood?

Hypothesis: Adversity during the prenatal and childhood periods have independent effects on inflammation in adulthood.
1) Pinpoint key stages for the development of stress response systems.

2) Identify periods when interventions to mitigate the long-term effects of adversity would be most effective.
Sample Origin

- National Collaborative Perinatal Project (NCPP) n~60,000
- NCPP – Boston and Providence n=17,921
- Pathways Linking Education and Health (EdHealth) Selected n=618
- EdHealth clinical assessment n=430
- Complete data n=355


- National Collaborative Perinatal Project (NCPP)
- Pathways Linking Education and Health (EdHealth)
- Complete data

- Sample Origin

- Sample Origin
# Measures of prenatal & childhood adversity

<table>
<thead>
<tr>
<th>Main exposures</th>
<th>Components</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prenatal adversity score</td>
<td>1. Family structure</td>
</tr>
<tr>
<td></td>
<td>2. Parental education</td>
</tr>
<tr>
<td></td>
<td>3. Parental occupation</td>
</tr>
<tr>
<td></td>
<td>4. Family income</td>
</tr>
<tr>
<td>Childhood adversity score</td>
<td>1. Family income, age 7</td>
</tr>
<tr>
<td></td>
<td>2. Parental occupation, age 7</td>
</tr>
<tr>
<td></td>
<td>3. Major environmental shifts, birth to age 7</td>
</tr>
<tr>
<td></td>
<td>4. Change in parental marital status, birth to age 7</td>
</tr>
<tr>
<td></td>
<td>5. Number of moves before age 7</td>
</tr>
<tr>
<td></td>
<td>6. Father unemployed in past year, age 7</td>
</tr>
<tr>
<td></td>
<td>7. Death of a sibling, birth to age 7</td>
</tr>
<tr>
<td></td>
<td>8. Housing density, age 7</td>
</tr>
</tbody>
</table>
### Outcome & Control Variables

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Inflammation in adulthood: C-reactive protein (CRP)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>• Continuous</td>
</tr>
<tr>
<td></td>
<td>• High risk threshold; &gt;3mg/L</td>
</tr>
<tr>
<td></td>
<td>• Excluded individuals with CRP &gt; 10 mg/L</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Potential Confounders</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>• Participant</td>
<td>• age, race, sex</td>
</tr>
<tr>
<td>• Mother</td>
<td>• age at child’s birth, health history during pregnancy (psychiatric, neurological, metabolic, cardiovascular, and pulmonary)</td>
</tr>
</tbody>
</table>
Statistical analysis

• Linear regression - continuous outcome
  Nested models to account for family clustering

• Sensitivity analyses
  Logistic regression for high risk CRP
### Sample characteristics (N=355)

<table>
<thead>
<tr>
<th></th>
<th>% or Mean (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex (% female)</td>
<td>57.8</td>
</tr>
<tr>
<td>Ethnicity (% non-white)</td>
<td>19.4</td>
</tr>
<tr>
<td>Age (mean)</td>
<td>42.1 (1.70)</td>
</tr>
<tr>
<td>CRP (mean)</td>
<td>1.7 (2.0)</td>
</tr>
<tr>
<td>CRP &gt; 3 mg/L (%)</td>
<td>16.6</td>
</tr>
</tbody>
</table>
Adversity categories

The bar chart shows the percentage of individuals with different levels of adversity scores, categorized as prenatal or childhood experiences.

- **Low Adversity Scores:**
  - Prenatal: 60%
  - Childhood: 48%

- **Medium Adversity Scores:**
  - Prenatal: 37%
  - Childhood: 40%

- **High Adversity Scores:**
  - Prenatal: 9%
  - Childhood: 7%

The chart indicates a higher percentage of prenatal adversity compared to childhood adversity in low and medium scores, with a notable drop in high adversity scores.
## Transitions across adversity categories

<table>
<thead>
<tr>
<th>Prenatal Adversity</th>
<th>Childhood Adversity</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Low</td>
</tr>
<tr>
<td>Low</td>
<td>59.7</td>
</tr>
<tr>
<td>Medium</td>
<td>18.3</td>
</tr>
<tr>
<td>High</td>
<td>14.3</td>
</tr>
</tbody>
</table>

Note: cell entries display the row percent.
Difference in CRP between high & medium prenatal adversity categories vs. low prenatal adversity.

Notes: Linear regression models, account for clustering within families. Demographic covariates: child’s age, sex, and race; mother’s age at child’s birth, pre-existing health conditions (psychiatric, neurological, cardiovascular, pulmonary, and metabolic)
Difference in CRP between high & medium childhood adversity categories vs. low childhood adversity.

Notes: Linear regression models, account for clustering within families. Demographic covariates: child’s age, sex, and race; mother’s age at child’s birth, and pre-existing health conditions (psychiatric, neurological, cardiovascular, pulmonary, and metabolic).
Odds of “high risk” CRP for high & medium prenatal adversity categories vs. low prenatal adversity.

Notes: Logistic regression models, account for clustering within families. Demographic covariates: child’s age, sex, and race; mother’s age at child’s birth and pre-existing health conditions (psychiatric, neurological, cardiovascular, pulmonary, and metabolic)
Odds of “high risk” CRP for high & medium childhood adversity categories vs. low childhood adversity.

Notes: Logistic regression models, account for clustering within families. Demographic covariates: child’s age, sex, and race; mother’s age at child’s birth and pre-existing health conditions (psychiatric, neurological, cardiovascular, pulmonary, and metabolic)
Difference in CRP for each component of the prenatal adversity score.

Notes: Linear models, account for clustering within families. Demographic covariates: child’s age, sex, and race; mother’s age at child’s birth and pre-existing health conditions.
• Prenatal and childhood adversity were associated with elevated CRP in adulthood in separate regression models.

• When prenatal and childhood adversity were analyzed together, only prenatal adversity was associated with elevated CRP.

• Prenatal adversity associated with 3-fold odds of CRP > 3 mg/L.

• Parental education and family structure show largest associations.
## Potential pathways across the life course

### Gestation

**Examples:**
- Maternal HPA axis activation
  - Elevated cortisol
- Obstetric complications
  - Epigenetic changes
  - Preterm birth
- Maternal health behaviors
  - Over/under nutrition
  - Nicotine, alcohol
- Environmental pollutants

### Childhood

**Examples:**
- Chronic HPA axis activation due to stress
- Emotional or behavioral problems
- Adiposity
- Poorer diet
- Less physical activity
- Academic difficulties

### Adulthood

**Examples**
- Chronic stressors
- Low socioeconomic status
- Psychological problems
- Physical health problems
- Poorer diet
- Less activity
- Nicotine use
- Alcohol consumption
Conclusions & Implications

Adversity during gestation may influence inflammatory processes in adulthood independent of experiences in early childhood.

Research Implications

1. Consideration of maternal social environment within studies of the developmental origins of disease.

2. Collection of detailed information on type and timing of prenatal experiences.

3. Identification of potential mechanisms for observed association.
In Press:


E-mail: nslopen@umd.edu

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