Incorporating evidence from gene-environment studies into health disparities research in the United States

Jason D. Boardman
University of Colorado at Boulder
Department of Sociology and Institute of Behavioral Science

1. Limited perspective of gene-environment interaction typology
2. Very limited understanding of the “environment”

Both of these issues are critical to health disparities research.
Pushing for a testable typology

Defining the Environment in Gene—Environment Research: Lessons From Social Epidemiology

Jason D. Boardman, PhD, Jonathan Daw, PhD, and Jeremy Freese, PhD

In this article, we make the case that social epidemiology provides a useful framework to define the environment within gene–environment (G×E) research. We describe the environment in a multilevel, multidomain, longitudinal framework that accounts for upstream processes influencing health outcomes. We then illustrate the utility of this approach by describing how intermediate levels of social organization, such as neighborhoods or schools, are key environmental components of G×E research. We discuss different models of G×E research and encourage public health researchers to consider the value of including genetic information from their study participants. We also encourage researchers interested in G×E interplay to consider the merits of the social epidemiology model when defining the environment. (Am J Public Health. Published online ahead of print August 8, 2013: e1–e9. doi:10.2105/AJPH.2013.301355)
Note. The dashed line corresponds to the presence of “risk” (or responsive in the case of differential susceptibility) allele.

FIGURE 1—Diathesis-stress model of gene-environment interaction differentiated by (a) heritability-by-environment specifications and (b) allele-by-environment specifications.
Note. The dashed line corresponds to the presence of “risk” (or responsive in the case of differential susceptibility) allele.

FIGURE 2—Differential susceptibility model of gene–environment interaction differentiated by (a) heritability-by-environment specifications and (b) allele-by-environment specifications.
FIGURE 3—Social distinction model of gene–environment interaction differentiated by (a) heritability-by-environment specifications and (b) allele-by-environment specifications.
FIGURE 4—Social push model of gene-environment interaction differentiated by (a) heritability-by-environment specifications and (b) allele-by-environment specifications.

Note. The dashed line corresponds to the presence of “risk” (or responsive in the case of differential susceptibility) allele.
Health disparities and GxE research: how we characterize the environment

- Multilevel (schools, neighborhoods, areas, etc.)
- Multidimensional (institutional, built, social)
- Longitudinal (historical periods and individuals)
  - All of these are very different for different racial and ethnic groups in the US now and over time.
What is the environment: a need to emphasize social factors

Genetic Sensitivity to Peer Behaviors: 5HTTLPR, Smoking, and Alcohol Consumption

Jonathan Daw¹, Michael Shanahan², Kathleen Mullan Harris², Andrew Smolen¹, Brett Haberstick¹, and Jason D. Boardman

School Drinking Decile

Alcohol Consumed, 12 Months

L'/L' ---- S'/S'
The heritability of smoking is the highest in schools with pro-smoking norms. But there are different associations between prevalence and norms across predominately white or black schools.
Consider differences in the ‘environment’ as historical periods.

Understanding the genetic influences on health behaviors requires understanding the location of specific behaviors as related to trends.

Think of this same story with respect to obesity. Consider what the factors are for different groups in the US.
Consider differences in the ‘environment’ as norms about body size

• Understanding the genetic influences on health behaviors requires understanding the specific health norms of a particular population, in a particular place, at a particular time.
Social distinction: an emphasis on neighborhoods

• Genes have little to nothing to do with cognitive decline in the most disorganized neighborhoods.
• It is a social phenomena.
• As such, the etiology of the disease is different for whites and blacks for social reasons.
How social and genetic factors predict friendship networks

Jason D. Boardman\textsuperscript{a,b,1}, Benjamin W. Domingue\textsuperscript{b}, and Jason M. Fletcher\textsuperscript{c,d}

\textsuperscript{a}Department of Sociology, University of Colorado, Boulder, CO 80309-0327; \textsuperscript{b}Population Program, Institute of Behavioral Science, University of Colorado, Boulder, CO 80309-0483; \textsuperscript{c}School of Public Health, Yale University, New Haven, CT 06520-8034; and \textsuperscript{d}Robert Wood Johnson Health and Society Scholars Program, Columbia University, New York, NY 10027

Edited by Kenneth Wachter. University of California. Berkeley, CA. and approved September 10, 2012 (received for review June 1, 2012)

www.pnas.org/cgi/doi/10.1073/pnas.1208975109

PNAS | October 23, 2012 | vol. 109 | no. 43 | 17377–17381

![Graph showing relationships between DRD2 and Alpha/Gini scores in friendship networks](image-url)
Race differences in cumulative risk by family risk
Summary of typology and importance to health disparities research

• Causal models
  – Stress diathesis
    • Exacerbates risk; for some associations, the genetic association may appear stronger because of elevated levels of stress
  – Differential susceptibility
    • Perhaps the most important because it suggest that the same environmentally sensitive individuals will have very different health lifestyles if placed in different environments.

• Non causal models
  – Social push and social distinction
    • Inherent theme of “fairness” in that latent genetic factors for salutary outcomes do not manifest for those who live in the most disorganized environments.
The importance of genome wide data

- Small allele frequency differences across the genome align with self-identified racial classifications with social origins.
Ethnicity, Body Mass, and Genome-Wide Data

JASON D. BOARDMAN,1 CASEY L. BLALOCK,1 ROBIN P. CORLEY,2 MICHAEL C. STALLINGS,2 BENJAMIN W. DOMINGUE,3 MATTHEW B. McQUEEN,2 THOMAS J. CROWLEY,4 JOHN K. HEWITT,1 YING LU,5 AND SAMUEL H. FIELD6

<table>
<thead>
<tr>
<th></th>
<th>Variance explained</th>
<th>PC-BMI association</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Unique</td>
<td>Cumulative</td>
</tr>
<tr>
<td>PC1</td>
<td>0.030</td>
<td>0.030</td>
</tr>
<tr>
<td>PC2</td>
<td>0.014</td>
<td>0.044</td>
</tr>
<tr>
<td>PC3</td>
<td>0.013</td>
<td>0.057</td>
</tr>
<tr>
<td>PC4</td>
<td>0.013</td>
<td>0.070</td>
</tr>
<tr>
<td>PC5</td>
<td>0.012</td>
<td>0.083</td>
</tr>
<tr>
<td>PC6</td>
<td>0.012</td>
<td>0.095</td>
</tr>
<tr>
<td>PC7</td>
<td>0.012</td>
<td>0.106</td>
</tr>
<tr>
<td>PC8</td>
<td>0.012</td>
<td>0.118</td>
</tr>
<tr>
<td>PC9</td>
<td>0.011</td>
<td>0.129</td>
</tr>
<tr>
<td>PC10</td>
<td>0.011</td>
<td>0.141</td>
</tr>
</tbody>
</table>
Relationship models using genome wide data

- Univariate and bivariate heritability models (GCTA)

\[
A_{jk} = \frac{1}{N} \sum_i A_{ijk} = \begin{cases} 
\frac{1}{N} \sum_i \frac{(x_{ij} - 2p_i)(x_{ik} - 2p_i)}{2p_i(1-p_i)}, & j \neq k \\
1 + \frac{1}{N} \sum_i \frac{x_{ij}^2 - (1 + 2p_i)x_{ij} + 2p_i^2}{2p_i(1-p_i)}, & j = k
\end{cases}
\]

<table>
<thead>
<tr>
<th>BMI-HRS</th>
<th></th>
<th>Educ-HRS</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Source</td>
<td></td>
<td>Source</td>
<td></td>
</tr>
<tr>
<td>V(G)</td>
<td>9.578172</td>
<td>Variance</td>
<td>2.766574</td>
</tr>
<tr>
<td>V(e)</td>
<td>17.849174</td>
<td>SE</td>
<td>0.469424</td>
</tr>
<tr>
<td>Vp</td>
<td>27.427346</td>
<td>1.834859</td>
<td>4.056518</td>
</tr>
<tr>
<td>V(G)/Vp</td>
<td>0.349220</td>
<td>0.072933</td>
<td>6.823093</td>
</tr>
<tr>
<td>logL</td>
<td>-12724.303</td>
<td>-8548.751</td>
<td>-8583.039</td>
</tr>
<tr>
<td>logL0</td>
<td>-12736.698</td>
<td>-8583.039</td>
<td>-8583.039</td>
</tr>
<tr>
<td>LRT</td>
<td>24.790</td>
<td>68.577</td>
<td>6e-17</td>
</tr>
<tr>
<td>df</td>
<td>1</td>
<td>1</td>
<td>5967</td>
</tr>
<tr>
<td>Pval</td>
<td>3e-07</td>
<td>6e-17</td>
<td>5967</td>
</tr>
<tr>
<td>n</td>
<td>5967</td>
<td>5967</td>
<td>5967</td>
</tr>
</tbody>
</table>
Relationship models and population stratification (it matters)
Further evidence of assortative mating

Genetic and educational assortative mating among US adults

Benjamin W Domingue a*, Jason Fletcher b, Dalton Conley c, Jason D Boardman a, d

a. Institute of Behavioral Science, University of Colorado Boulder; 1440 15th St., Boulder, CO 80309; b. La Follette School of Public Affairs, University of Wisconsin-Madison; 1225 Observatory Drive, Madison, WI 53706; c. Center for Genomics and Systems Biology, New York University; 12 Waverly Place, New York, NY 10003; d. Department of Sociology, University of Colorado Boulder; UCB 327 Ketchum 219, Boulder, CO 80309
It gets more complicated: bivariate models

- The genetic covariance indicates if the two traits are correlated for common genetic reasons.

Consider what thesis means for health disparities
Implications of bivariate models and health disparities: period effects

- Education and health: their social and genetic factors as well as rG may change across social contexts and over historical time.
Summary

• Most health behaviors in health disparities research show a considerable influence of additive genetic factors.
• These genetic effects vary in magnitude as a function of the social environment.
• Differences in the social environment drive the observed differences in heritability estimates across racial and ethnic groups.
• Small differences in allele frequencies across the genome complicate this work but the opportunities to advance social scientific perspective