Putting the pieces together again: genes, child maltreatment and psychoanalysis

The 33rd Annual Daniel S. Prager Lecture
David Reiss, MD
Yale Child Study Center
May 1, 2014
Robert Plomin
Comparison of MZ (identical) and DZ (fraternal) twins: comparing heights within twin pairs (contrived data)
Summary of data from Plomin’s studies Twins reared together (T) and Apart (A)
MZ= monozygotic  DZ = dizygotic
Summary of Plomin’s data

Between-sibling differences:
- Nonshared environment + error

Between-family differences:
- Shared environment

Correlation coefficients

- MZT
- MZA
- DZT
- DZA
- Unrel sib
Summary of Plomin’s data

Correlation coefficients:
- MZT
- MZA
- DZT
- DZA
- Unrel sib

Shared family en: SES, Neighborhood decay, maternal depression
MIRROR IMAGE TWIN STUDIES: Adolescents-as-twins study (NEAD) vs parents-as-twins study (TOSS)

**Sib type (P-P) Genetic relatedness**
- 254 MZ moms 100%
- 284 DZ moms 50%
- 128 MZ dads 100%
- 183 DZ dads 50%

**Sib type (A-A) Genetic relatedness**
- 93 MZ 100%
- 99 DZ 50%
- 95 FS-non div 50%
- 182 FS-step 50%
- 109 HS-step 25%
- 130 Blended step 0%
MIRROR IMAGE TWIN STUDIES: Adolescents-as-twins study (NEAD) vs parents-as-twins study (TOSS)

Parent A

Spouse

Parent

Spouse

Sib type (P-P) Genetic relatedness
254 MZ moms 100%
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Sib type (A-A) Genetic relatedness
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# Adolescent antisocial behavior

<table>
<thead>
<tr>
<th>OBSERVER CODE</th>
<th>PARENT AND CHILD REPORT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Disruptive, rude, aggressive, coercive behavior</td>
<td>Trouble in school, skipped school mean, bully.</td>
</tr>
<tr>
<td>school behavior</td>
<td>Stole, lied, cheated</td>
</tr>
<tr>
<td>brief, in home video</td>
<td>home and neighborhood</td>
</tr>
</tbody>
</table>
Illustration of within sib pair correlations for estimating genetic influence on antisocial behavior

Sibling A

- A’s antisocial behavior

Sibling B

- B’s antisocial behavior

MZ

DZ
Antisocial behavior: Mother, father, child and observer reports
Numbers on vertical axis are intraclass correlations within sibships

Heritability = 67%
Environmentality: Shared = 12%    Nonshared = 21%
Parent-child negativity:

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<tr>
<td>Anger and rejection</td>
<td>Disagreement</td>
</tr>
<tr>
<td>Coercion</td>
<td>Punitiveness</td>
</tr>
<tr>
<td>Conflict</td>
<td>Yielding to coercion</td>
</tr>
<tr>
<td></td>
<td>Open conflict</td>
</tr>
<tr>
<td></td>
<td>Verbal aggression</td>
</tr>
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</table>
Illustration of within sibling correlations for detecting genetic influences on mother’s negativity

Sibling A

MZ

mother’s negativity to sib A

DZ

mother’s negativity to sib A

Sibling B

mother’s negativity to sib B

mother’s negativity to sib B
Mother’s negativity towards child: within sibship correlations across sibling types.
Numbers on vertical axis are intraclass correlations within sibships

Heritability = 59%
Environmentality: Shared = 15%  Nonshared = 26%
Illustration of cross-variable, within-sib pair correlations for detecting overlap of genetic influences

Sibling A
- mother’s negativity to sib A
- A’s anti-social behavior

Sibling B
- mother’s negativity to sib B
- B’s anti-social behavior
Overlapping genetic influences on mother’s negativity and adolescent antisocial behavior: comparing *cross variable*, within sib pair correlations

Phenotypic correlation = 0.59

- 68% of this corr. is attributable to G
- 27% of this corr. is attributable to SE
Evocative gene-environment correlations: null hypothesis, family effects and child effects versions

Mother-child negative interaction

parent influences

(heritable & evocative child characteristic)

Adolescent antisocial behavior

child evokes

FAMILY EFFECTS

CHILD EFFECTS

NULL HYPOTHESIS

Ga
Early Growth & Development Study
n=361 expanded to n = 561

BIRTH PARENTS
SUDs and related disorders

ADOPTED CHILDREN
Genetic Influences

ADOPTIVE PARENTS
Parenting in the context of depression, marital problems and economic worries

Environmental Influences

Externalizing and internalizing problems
Early Growth & Development Study

ADOPTED CHILDREN
Genetic Influences
Birth Parent
Adopted Child
Externalizing and internalizing problems

BIRTH PARENTS
SUDs and related disorders
Birth Mother
Birth Father

ADOPTIVE PARENTS
Parenting in the context of depression, marital problems and economic worries
Adoptive Mother
Adoptive Father

Environmental moderation
I can’t understand my baby
I can’t make my baby look at me
I don’t know what games and toys my baby likes
My kid struggles over bed time
Baby sitters are hard to find
Always cleaning up messes of toys and food
When my child misbehave I raise my voice and yell
When I am under stress I am picky and on my child’s back

*Items slightly paraphrased from D. S. Arnold (1993), KA Crnic (1990) and DM Teti (1991)*
Early Growth & Development Study

**BIRTH PARENTS: SUDs and related disorders**

**Evocative influences**

**ADOPTIVE PARENTS**
- Parenting in the context of depression, marital problems and economic worries

**ADOPTED CHILDREN**
- Internalizing and externalizing problems

- Genetic Influences
- Environmental Influences
Prospective adoption study

Adoptive Parents in ADVERSE CONTEXT

Adoptive Parents in FAVORABLE CONTEXT
Child' high and low genetic risk for externalizing disorders and adoptive parents' hostile parenting

Contrived data

BM high externalizing

BM low externalizing

adoptive parents' hostile parenting
Children high and low genetic risk for externalizing disorders and adoptive parents’ marital satisfaction (n = 561)

Source: P. Fearon, submitted
Birth mother externalizing

Marital distress

Adoptive mother vexation (9-27 mos.)

Child behavior Problems (27 mos.)

BM externalizing x Marital distress

0.03

0.23

0.42

0.16
David Barker  1938-2013
Low birth weight and hypertension

In their study of 77 men aged 28 Professor Gerhard Gennser and colleagues found a relation between increased diastolic blood pressure and low birth weight from a retrospective (28 May 1988).

D J P BARKER
C OSMOND

MRC Environmental Epidemiology Unit,
Southampton General Hospital,
Southampton SO9 4XY
Long term impact of restricted fetal growth: Standardized mortality ratios due to ischemic heart disease and chronic, obstructive pulmonary disease
7991 men born in Hertfordshire between 1911-1930
source: DJP Barker et al 1989

![Graph showing standardized mortality ratio vs birth weight for ischemic heart disease and obstructive lung disease.](image)
Critical evidence for programming: the added risk of “catch-up” growth for death from coronary artery disease. 3641 men born in Helsinki between 1924 and 1933.

Ponderal index (kg/m³) at birth

Body mass index (kg/m²) at 11 years

Hazard ratios (deaths/unit time compared to Finnish avg. for age and birth year)

Source: JG Erikson, 1999
Confirmation of the effects of fetal growth restriction in a rat model: birth weight and adult (12 week) systolic BP

source: MF Shreuder et al, 2006
Low birth weight and depression in teenage girls (n= 1420)
n=81 low birth weight (< 5.5 lbs)
Source: Great Smoky Mountain Study EJ Costello, 2007

(Post natal sexual abuse, physical abuse neglect, parental mental illness, stressful events)
Cumulative probability of coronary heart disease (MH, angina or other CHD): 1131 white, male Hopkins med students with annual follow-up (The Johns Hopkins Precursor Study Caroline Thomas original PI JHMS Classes of 1948-1961)

source MM Kittleson, 2006
Prospective study of childhood adversity before 11 and adult risk of illness at age 32: 972 in the Dunedin, NZ study

source A. Danese T Moffitt, 2009

Note: At least 3 of 1) overwt; 2)hi BP; 3)hi cholest.; 4) lo high density LP; 5)hi HbA1c; 6) low O2 consumption
Documented child abuse and neglect before age 11 and objective signs of illness risk at age 40

source: C Widom 2012

- Physical abuse (57)
- Sexual abuse (47)
- Neglect (275)

Controls:
- Age
- Gender
- Race
- Childhood SES
- Adult SES
- Smoking
- Substance abuse
- Depression/PTSD

- HbA1c > 6%
- Malnutrition (BMI/lymphocyte/albumin)

* p < .05  ** p < .01 in comparisons to 237 controls
Experimental assignment to rearing conditions: health outcomes
source: S. Suomi and colleagues (see Conti, G Suom S, Heckman J et al, 2012)

Timeline

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Nursery reared

Mother rearing continued

Group housing

Observations of impaired medical and behavioral health
Early childhood adversity and subsequent illness
source: Conti, G et al 2012

* Peer exposure 2 hr/d in first year
Accelerated telomere shortening in response to life stress

Elissa S. Epel*, Elizabeth H. Blackburn†, Jue Lin‡, Firdaus S. Dhabhar§, Nancy E. Adler*, Jason D. Morrow*, and Richard M. Cawthon∥

*Department of Psychiatry, University of California, 3333 California Street, Suite 465, San Francisco, CA 94143; †Department of Biochemistry and Biophysics, University of California, San Francisco, CA 94143; §Department of Oral Biology, College of Dentistry, and Department of Molecular Virology, Immunology, and Medical Genetics, College of Medicine, Ohio State University, Columbus, OH 43210; ∥Department of Medicine and Pharmacology, Vanderbilt University School of Medicine, Nashville, TN 37232; and ∥Department of Human Genetics, University of Utah, 15 North 2030 E Street, Room 2100, Salt Lake City, UT 84112

Contributed by Elizabeth H. Blackburn, September 28, 2004
39 care giving mothers     19 mothers of healthy children

Telomere length

Telomerase levels
Telomere length and adult reports of maltreatment “when I was growing up.”

Source: A Tryka, 2010
Genomic DNA

Primary transcript (RNA)

Mature transcript (RNA)

Protein
Experimental assignment to rearing conditions: health outcomes
source: S. Suomi and colleagues (see Conti, G Suom S, Heckman J et al, 2012)

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Nursery reared

Mother rearing continued

Group housing

Observations of impaired medical and behavioral health
Suomi

Early life social conditions

Mother reared

Peer reared

Inflammation

Cell growth/differentiation

Transcription control

Immunoglobulin production

Type I interferon antiviral response

Down regulated

Up regulated

Suomi

S.

Suomi

S.
Adolescent Twin Study
Robert Plomin, IOP (UK)
Mavis Hetherington, UVa
Jenae Neiderhiser, Penn State
Jody Ganiban, GWU

Adoption Study
Leslie Leve, U Oregon
Jenae Neiderhiser, Penn State
Danny Shaw, Pitt
Jody Ganiban, GWU
Pasco Fearon UCL (UK)

NIH/NIA Project on early adversity ("Reversibility")
Stephen Suomi, NICHD
Richard Suzman, NIA/BSR
Lisbeth Nielsen, NIA/BSR
Maternal negative and adolescent antisocial behavior: contemporaneous analysis at age 12.5

Maternal negativity

Adolescent antisocial behavior

A

C

.77

.52

.49

.32

a

c

e
Common genetic influence on association between prior parenting and subsequent antisocial behavior (controlling for stability, contemporaneous associations and adolescent asb -> maternal negativity)

Maternal negativity

Adolescent antisocial behavior

mean age of adolescent

11.5

14.5
The relationship between child temperament and maternal negativity and conflict

Source: J Ganiban, 2011

Variance of mn attributable to G (unstandardized)
Parental behavior and expression of genetic influence on antisocial behavior


These include the imperturbable parents.

Harsh parenting

Warm parenting
Parental behavior and expression of genetic influence on disinhibited behavior.

Source: J. Ulbricht, 2013
Evocative rGE on Child ADHD Symptoms

(G. Harold et al., JCPP in press)

Genetically Related

Biological Mother ADHD sx → Child Impulsivity/Activation

Adoptive Mother-to-Child Hostility

Adoptive Mother ADHD sx → Child ADHD sx (father report)

Genetically Unrelated

Child ADHD sx → Adoptive Mother ADHD sx

27 months 4.5 years 6 years
Child’s genetic risk for SUDs and mother’s depression/anxiety \( n = 361 \)

**Attention frustration task**

Source L. Leve, Child Develop. ‘10
Children at low and high risk for SUD (+) & adopted mothers structured parenting (n = 361)

Low Adoptive mother structured parenting*  High

BM low disinhibition + dep/anx
BM high disinhibition + dep/anx

* Coded videotape

Source: L Leve, JAACAP, 2009
Children at low and high risk for SUD (+) & adopted fathers structured parenting (n = 95)

Adoptive father structured parenting

Source: L Leve, JAACAP, 2009