# Weak Genetic Explanation 17 Years Later

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Oct 22, 2015

# Weak and Strong Genetic Explanation


## Heritability and Biological Explanation

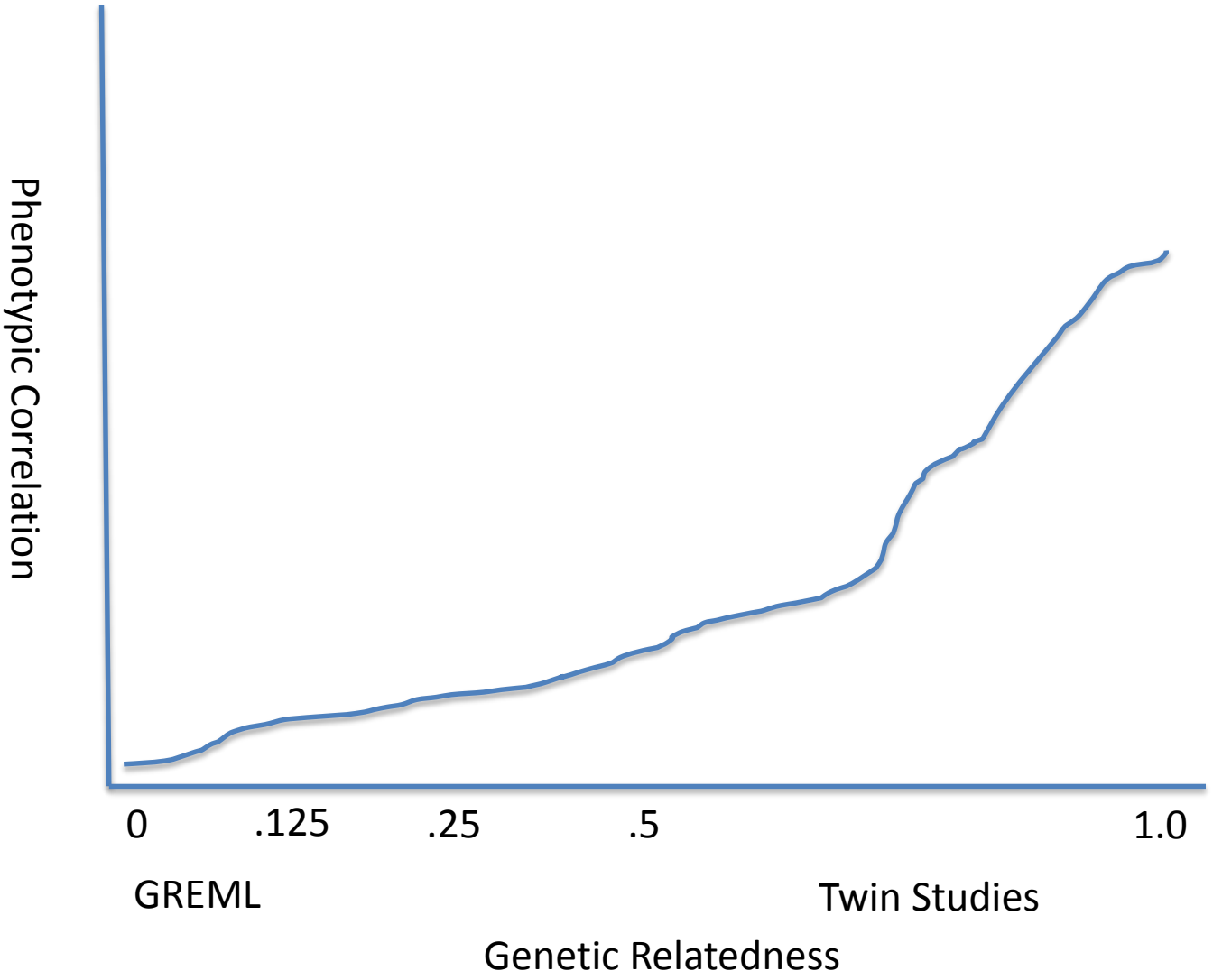
Eric Turkheimer ✉

AUTHOR AFFILIATIONS

# Weak Explanation

- Observation that there is a monotonic relation between genetic and phenotypic similarity
  - Removes “heritability” from the story
  - Strictly correlational
  - What Plomin calls “genetic influence”
  - Unites classical twin and family studies with modern GREML based approaches
  - Universally true

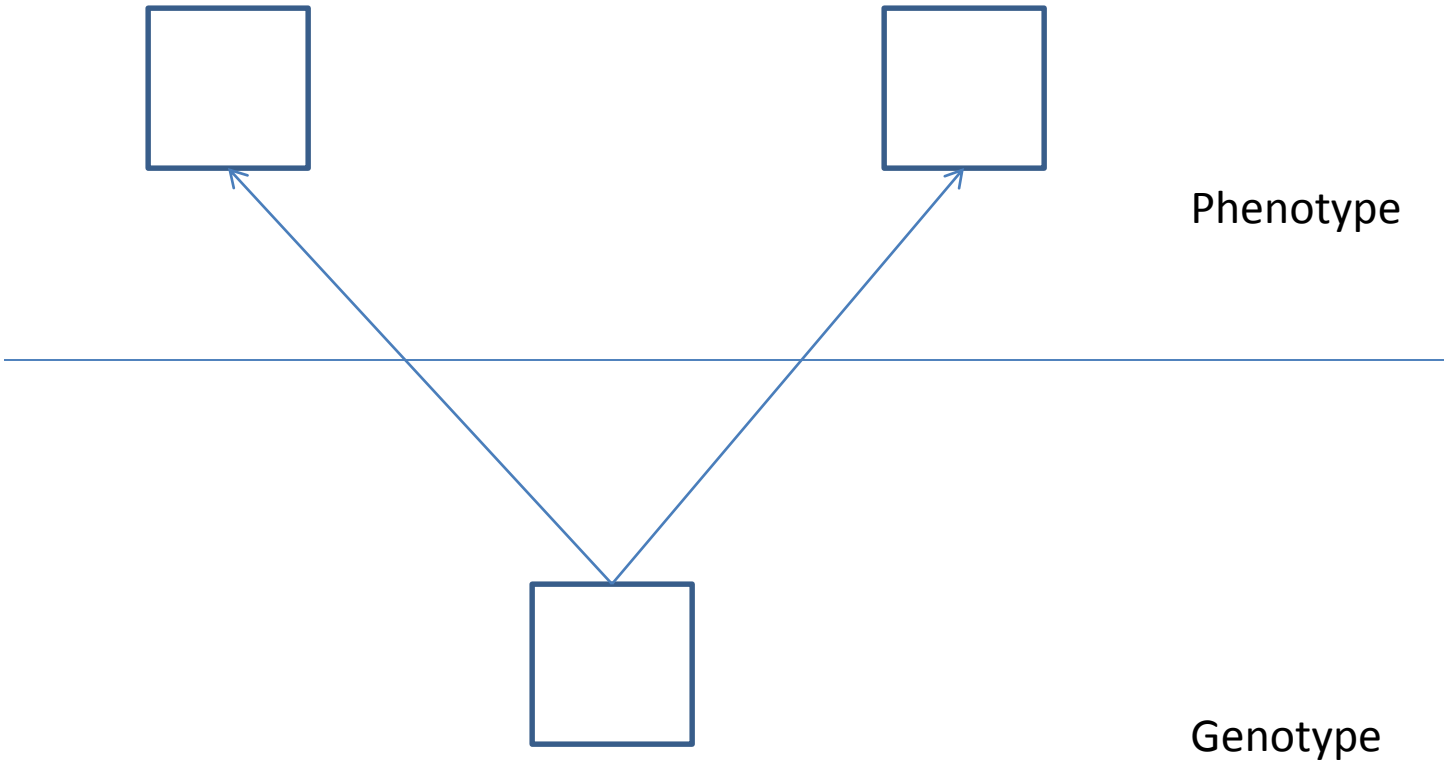
# Weak Explanation



# Weak Explanation Does Not Imply Mechanism

- “Explaining” crime rates in cities
- Imagine a large set of demo-geo-graphic variables on US cities.
  - Population density, latitude, income, etc
- Create similarity matrix among cities based on demographics
- Plot demographic similarity against similarity in crime
- If there is a relationship, say crime shows “demographic influence”
- Causal inference is even less than multiple regression because individual “causes” are not weighted

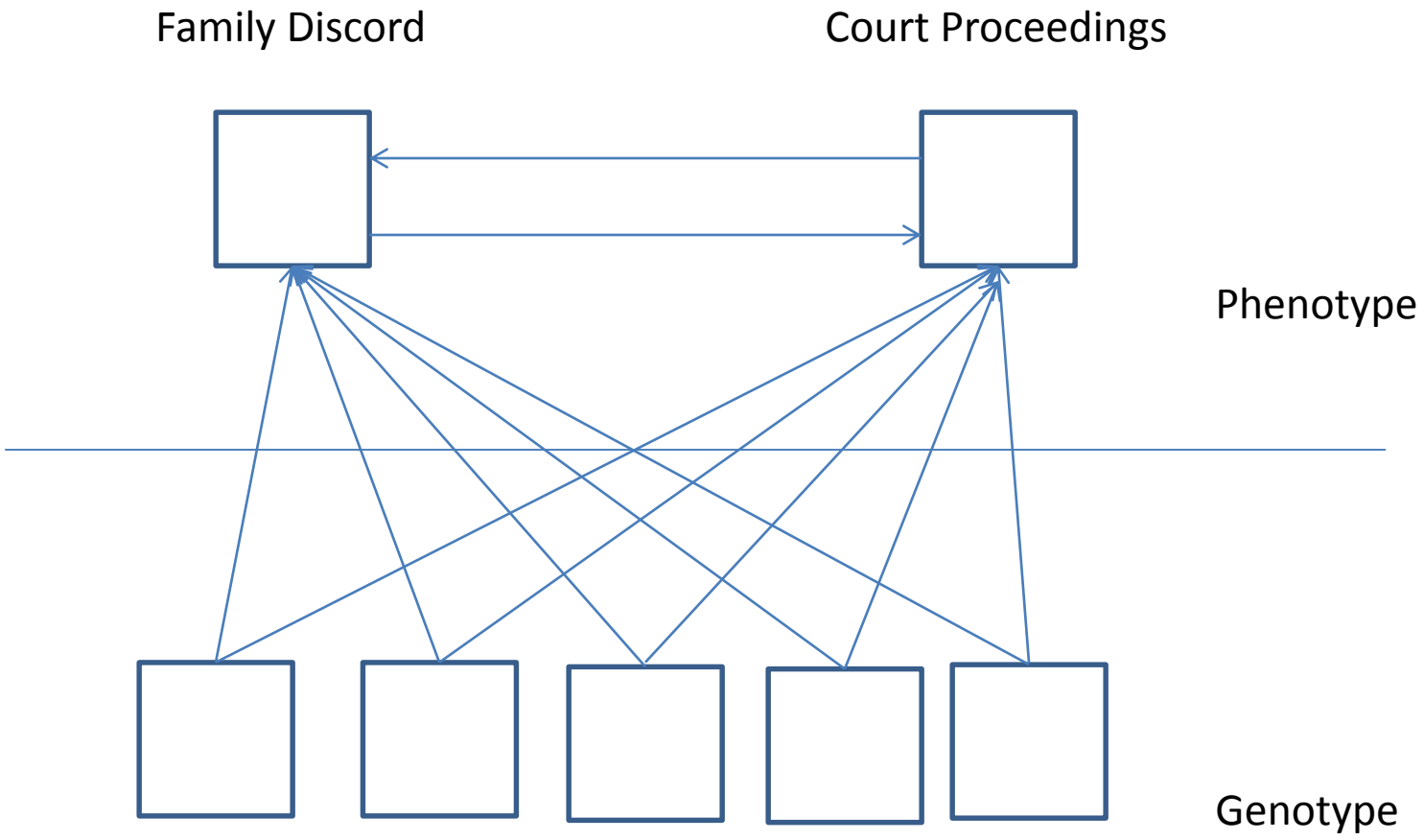
# Strong Genetic Explanation: Huntington's Disease



# Strong Genetic Explanation: Huntington's Disease

- Doesn't have to be single gene explanation
- But it's hard to think of good polygenic examples
  - Reduction of phenomena at higher level of analysis to specifiable mechanism at lower level
  - Known, specified biology
  - Relatively constant across high-level contexts

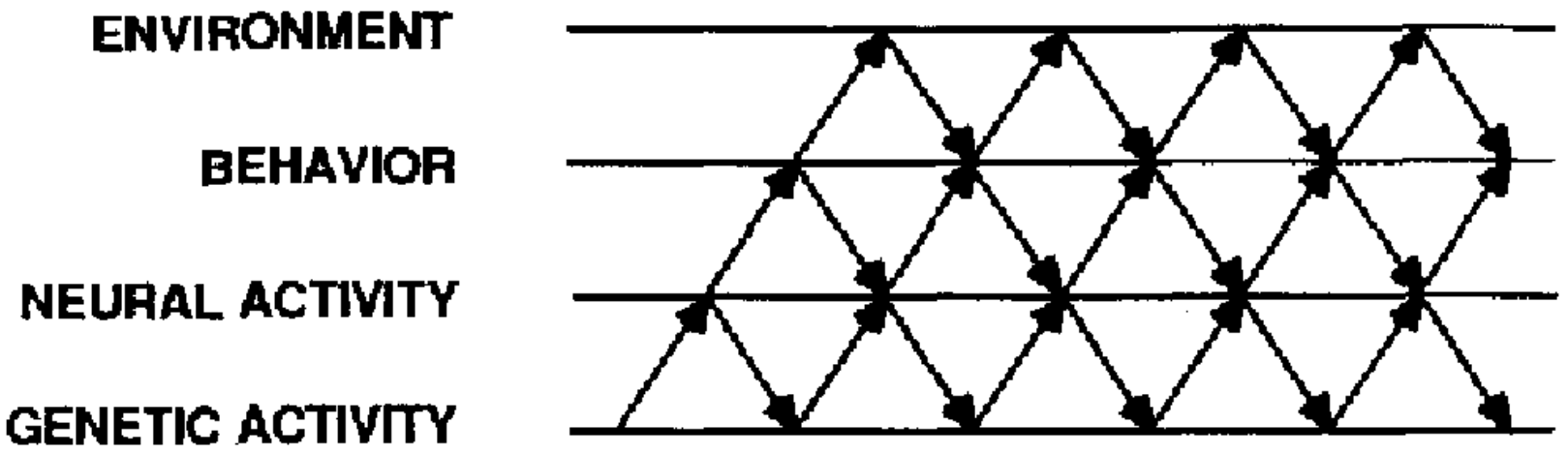
# Strong Genetic Explanation Not a Given: Divorce



# Strong Genetic Explanation Not a Given: Divorce

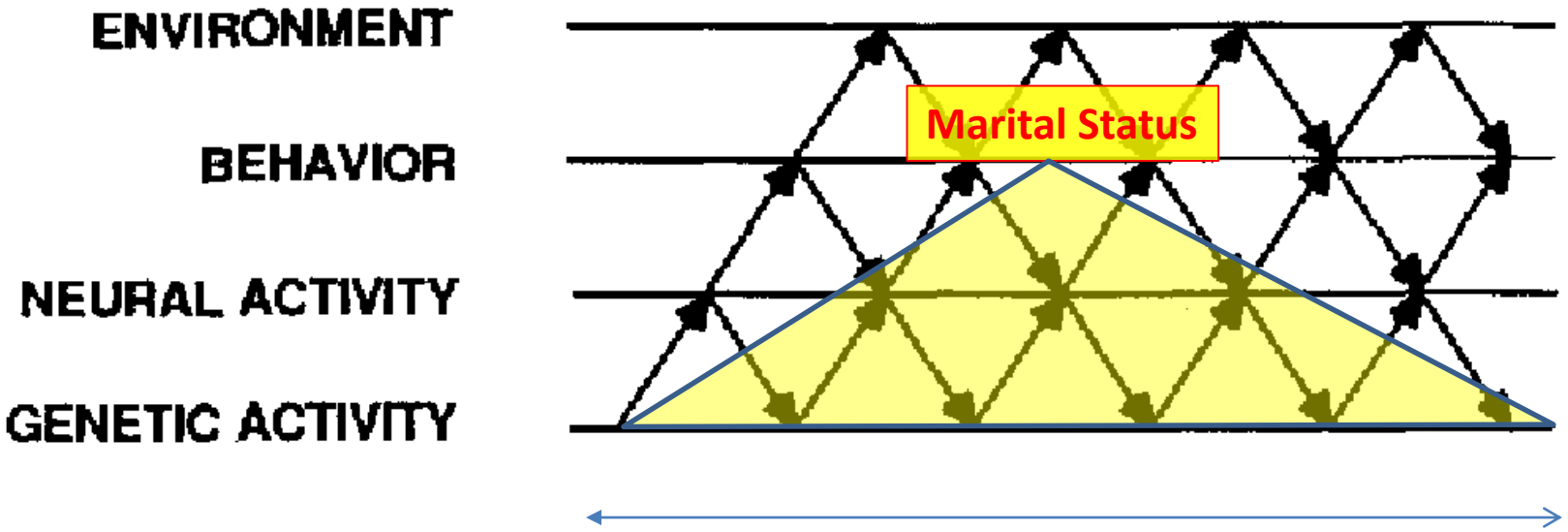
- Divorce is explained at a phenotypic level of analysis
  - Despite weak genetic associations with divorce
- Question is not genes vs environment
- It is whether phenomenon can be re-specified at a genetic level of analysis

# Levels of Analysis of Behavior



# Entities Exist at Levels

Defined at phenotypic level

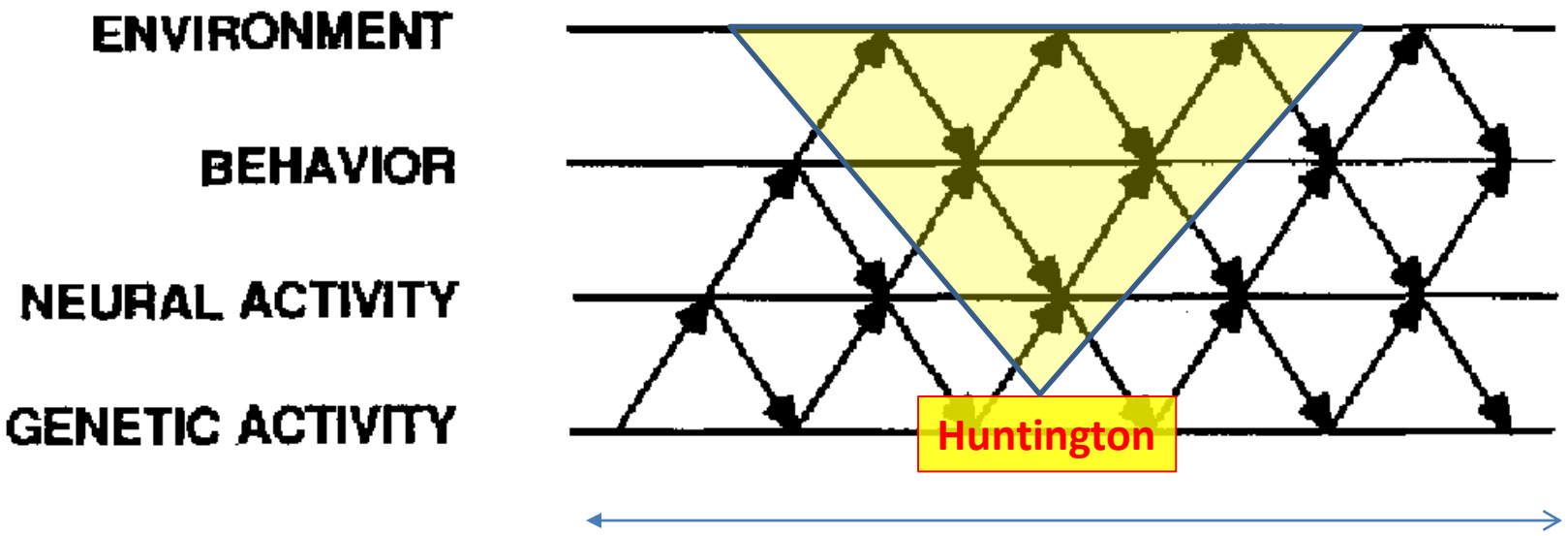



Spread out at genetic level

Weak Explanation

# Entities Exist at Levels

Spread out at phenotypic level




Defined at genetic level

Strong Explanation

# A Phenotypic Null Hypothesis of Behavior Genetics

Three Laws Revisited

# Three Laws of Behavior Genetics: All Twin Studies Come out the Same Way

1. Everything is heritable
2. Families contribute a relatively small portion of the variability in genetically informed studies
3. Most variability in human behavior cannot be predicted from genes or environment.

# Three Laws Revisited

- What are the Three Laws of Behavior Genetics?
  - They aren't really laws
  - They are null hypotheses

**Is $H^2 = 0$ a null hypothesis anymore?**

Eric Turkheimer and Irving I. Gottesman

A null hypothesis is a description of the simplest version of what we already know, a standard that has to be met before a finding can be considered interesting

# Once we knew it was heritable, what else was there to learn?

Differential Heritability

# Differential Heritability as a Basis For Molecular Genetics

…quantitative genetic studies are widely seen as a necessary preliminary to identifying heritable phenotypes that can be usefully examined at the molecular genetic level (Caspi et al.2005, citing Martin et al. 1997).

Data from twin studies for complex traits can be used to screen for "candidate traits" that can become the focus for connecting to candidate genes. The high heritabilities of traits such as general cognitive abilities and diseases such as schizophrenia tell researchers where to invest their efforts first, (Gottesman, 1997)

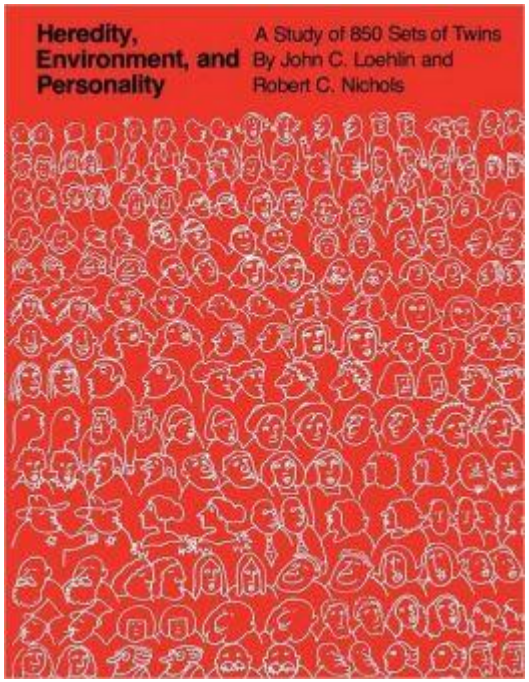
# Thompson and Wilde (1973)

– W. Robert Thompson was a founding member and President of BGA

**Table 11-11.** Consistency of $F = \sigma^2_{WDZ}/\sigma^2_{WDZ}$ Rankings of Personality Traits across Different Studies (expressed in rank-order correlation coefficients)

| | |
|---|---|
| (1) Cattell's HSPQ; 10 scales | |
| Cattell et al. (1955) vs. Vandenberg (1962) | = .45 |
| Cattell et al. (1955) vs. Gottesman (1963) | = −.45 |
| Vandenberg (1962) vs. Gottesman (1963) | = −.45 |
| Cattell vs. Vandenberg vs. Gottesman: | |
| Kendall's W = .26 (.70 > P > .50) | |
| (2) MMPI; 10 scales | |
| Gottesman (1963) vs. Gottesman (1965) | = .54 |
| Gottesman (1963) vs. Reznikoff et al. (1967) | = −.58 |
| Gottesman (1965) vs. Reznikoff et al. (1967) | = −.52 |
| Gottesman vs. Gottesman vs. Reznikoff et al.: | |
| Kendall's W = .20 (.90 > P > .80) | |
| (3) California Psychological Inventory; 20 scales | |
| Nichols (1966) vs. Gottesman (1966) | = −.22 (males) |
| | = −.24 (females) |

# Loehlin and Nichols (1976)




"In short, for personality and interests, as for abilities, the existing twin literature appears to agree with our own finding that while identical-twin pairs tend to be more similar than fraternal-twin pairs…. The difficulty is in showing that trait X is more heritable that trait Y."

"Identical twins correlate about .2 higher than fraternal twins, give or take some sampling fluctuation, and it doesn't matter much what you measure..."

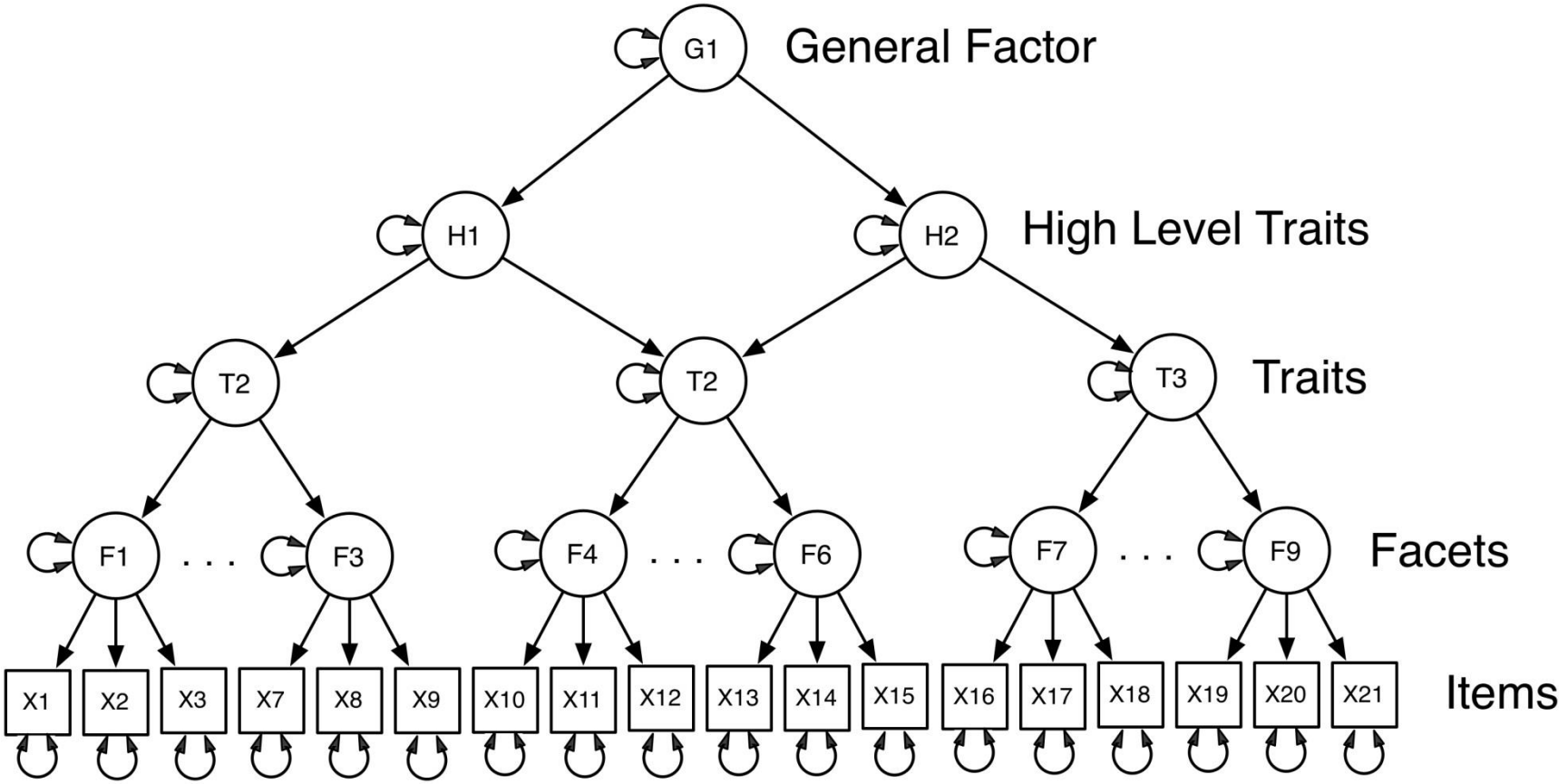
# Conclusion

- The heritability of personality is a broad, non-specific effect affecting all varieties of personality equally, albeit somewhat unsystematically.
- Statistically significant differences can be found with big enough samples, but they don’t add up to a theory across samples.

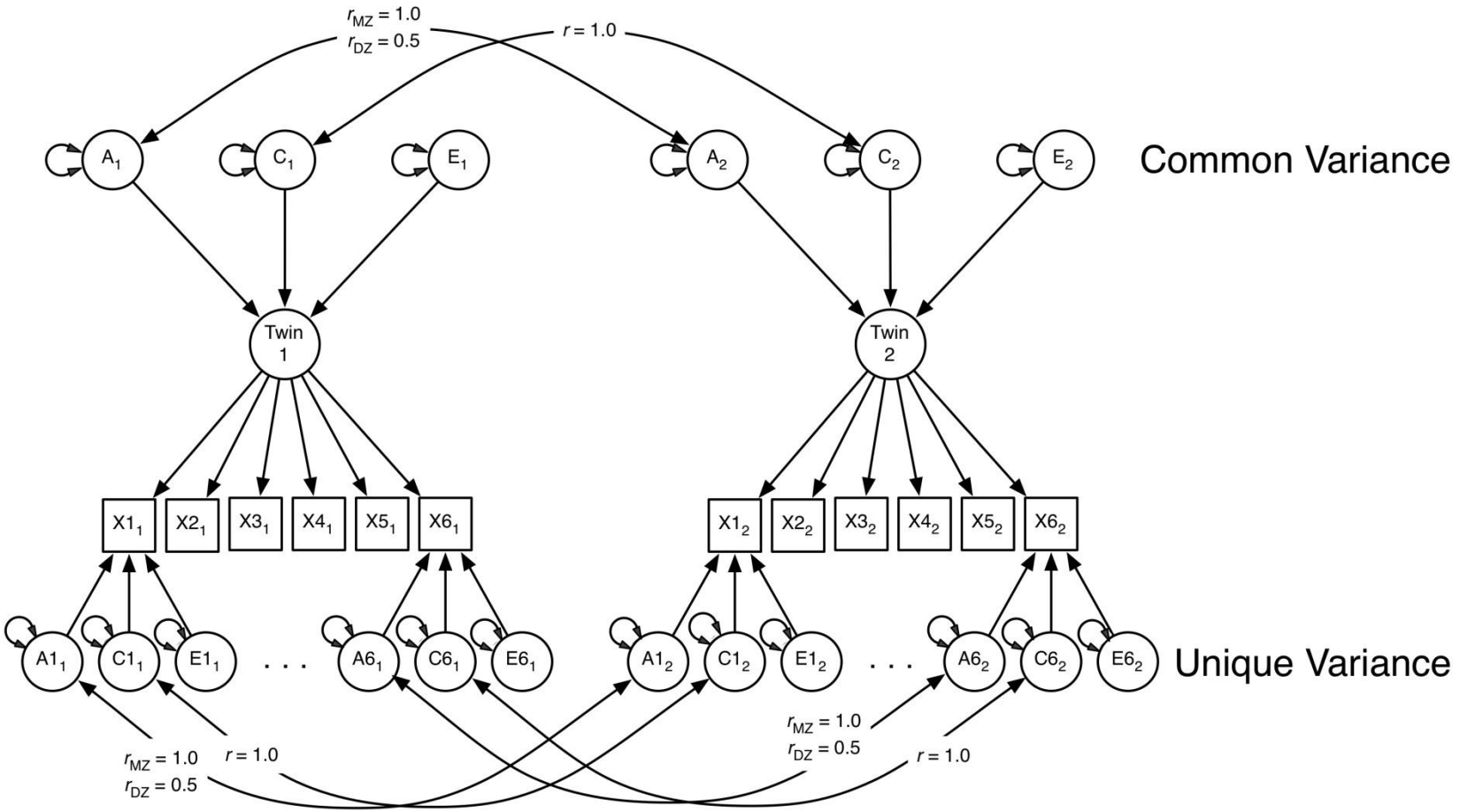
# Once we knew it was heritable, what else was there to learn?

2. The Structure of Personality

# Personality is Hierarchical

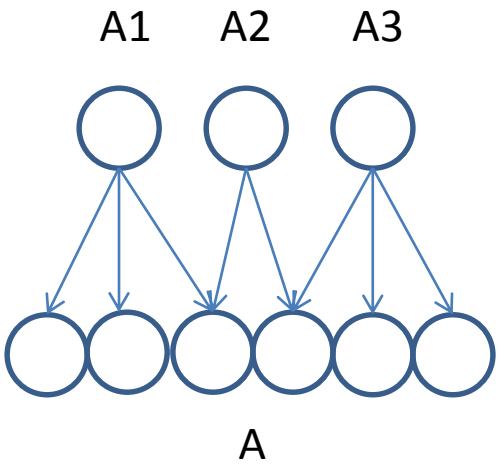


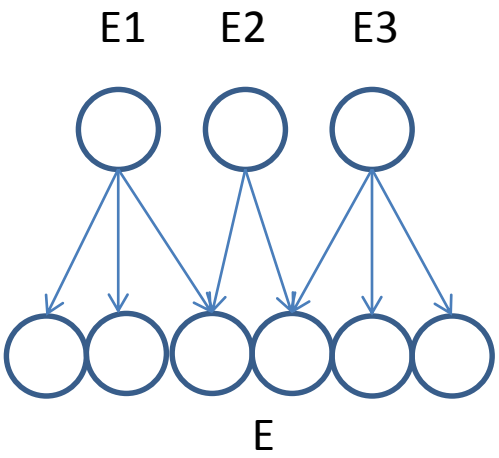
# Simplest Approach: Common Factor Model



# Structure of Personality in A and E Domains

- EFA of A and E covariance matrices
- Common and Independent Pathway Model
- Cloninger's Theory



# Loehlin (1987)

*Conclusions*

On the whole, then, one can say that the confirmatory analyses provide partial support for the findings of the original study. The presence of extraversion-introversion and emotional maladjustment factors in both the genetic and the unshared environmental covariation was clearly supported. In the cross-validation samples, these two factors also appeared to play some role in the shared environment as well. The family problems factor of the original study was confirmed to some degree in the adoptive sibling sample, but not in the Veterans twin sample; as suggested, the ages of the samples might be the important difference here.

# McCrae: The Puzzle of Parallel Structure

- Carey & DiLalla (1994)
  - "the loadings from the three [A, C and E] matrices are remarkably similar and, moreover, parallel the first three phenotypic factors of the CPI"
- Heath, Cloninger, and Martin (1994)
  - "The patterns of loadings ... were remarkably consistent for Genetic and Environmental Factors 1-4 and quite consistent with what would have been predicted from the observed phenotypic correlations"
- Krueger (2000)
  - Correlations between phenotypic and genetic components were all greater than .95, and correlations between phenotypic and nonshared environmental components were all at least .87.
- Yamagata et al. (2006)
  - These results suggest that… the phenotypic five-factor structure is reflective of not only genetic structure, but also environmental structure

# A Phenotypic Null Hypothesis of Behavior Genetics

- Loehlin and Martin (2013)
  - "*the structure of personality is inherent in the evolved phenotype, and is not the immediate consequence of either genetic or environmental organizing factors.*"
- Everything is heritable, and the multivariate genetic and environmental structures of behavior do not differ from the phenotypic structure of behavior.

# Lessons From the Nonshared Environment

Variance and Causation in Behavior

# Plomin and Daniels' Conjecture

...one implication of our conclusion concerning the importance of nonshared environment is that *environmental factors shared by both children in a family are unlikely to be important sources of environmental influence* [italics added]... (p. 9, Plomin & Daniels, 1987).

# Three step research program

(Plomin and Daniels)

1) Quantify Within Family Environment
2) Identify Specific Within Family Variables
3) Causal Associations between Within Family E and Behavior

Psychological Bulletin
2000, Vol. 126, No. 1, 78–108


0033-2909/00/$5.00 DOI: 10.1037//0033-2909.126.1.78

# Nonshared Environment: A Theoretical, Methodological, and Quantitative Review

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## Literature Search

- Computerized PsycLit and Medline searches with keywords: *bivariate, multivariate,* or *cholesky* and *genetic*
- Examination of reference lists of identified articles

## Inclusion Criteria

- Bivariate models only

## Identified Studies Meeting Criteria *N*=75 (345 models)

# Recorded Variables

Twin and Sibling Pair Characteristics

*N, zygosity, age of pairs*

Study Design

*Cross-sectional v.s. longitudinal*

Variables Examined

*e.g., biomedical, cognitive, personality and temperament, adjustment and psychopathology, and environmental characteristics*

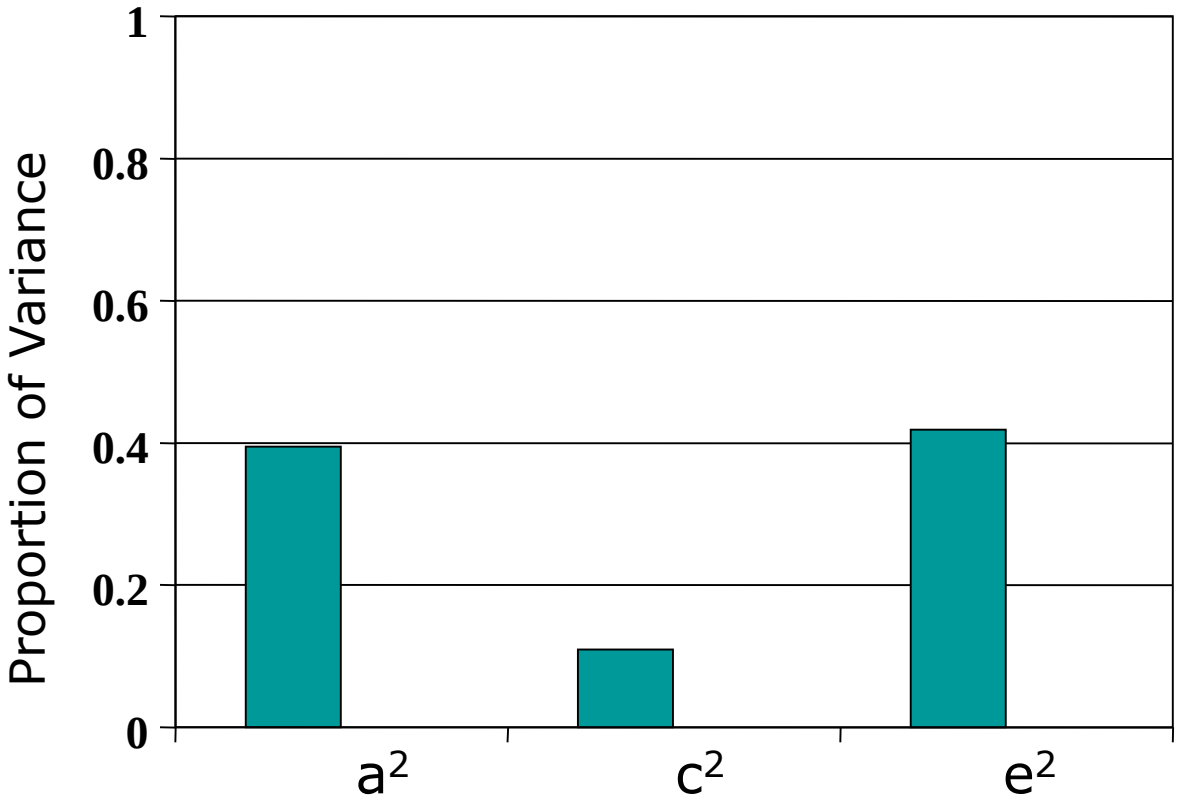
Effect Sizes

*Bivariate $a^2$, $c^2$ and $e^2$ and the average univariate $a^2$, $c^2$ and $e^2$ of the two variables examined*

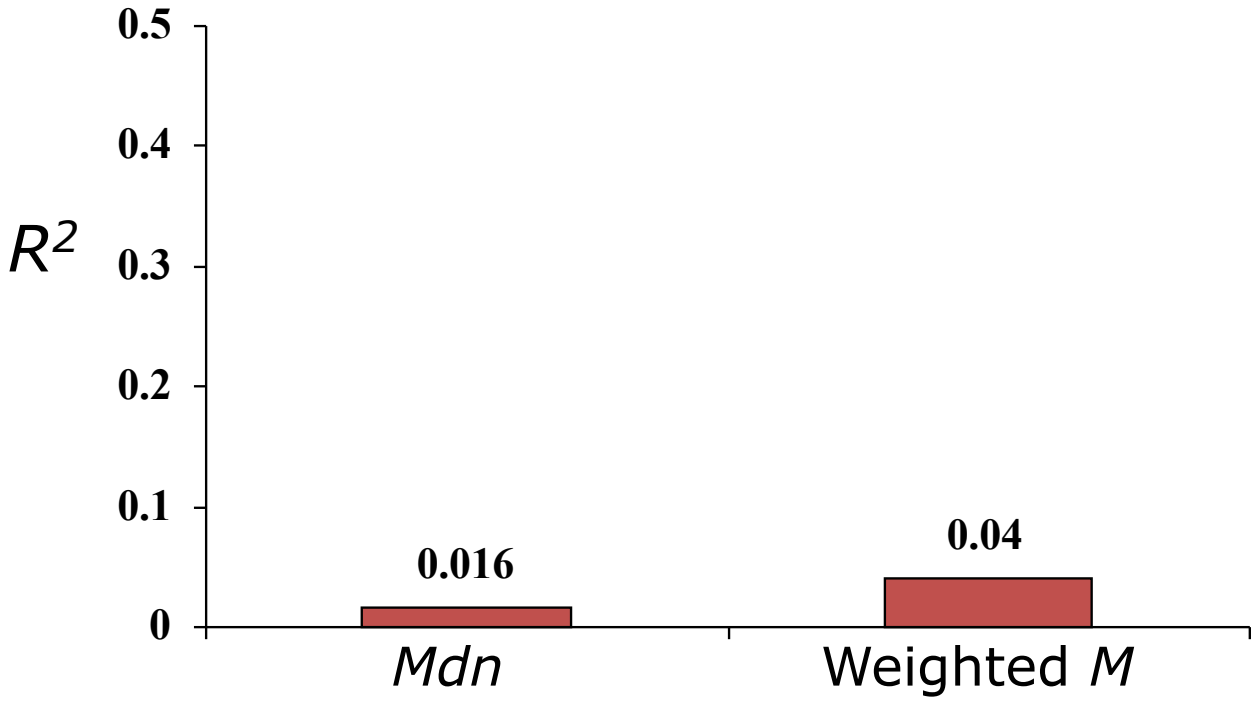
# Variance Components

## All Studies, *N*=75

(Turkheimer and Waldron, 2001)



# Measured Within Family Environment




Average $R^2$ for Studies Relating Sibling Differences in Measured Environment to Sibling Outcome (*N*=43)

# The Missing Environment Problem

Paradox:  Nonshared environment explains much of the *variation* in individual traits, but can't be broken down into meaningful environmental *mechanisms* for individual traits.

# The Gloomy Prospect

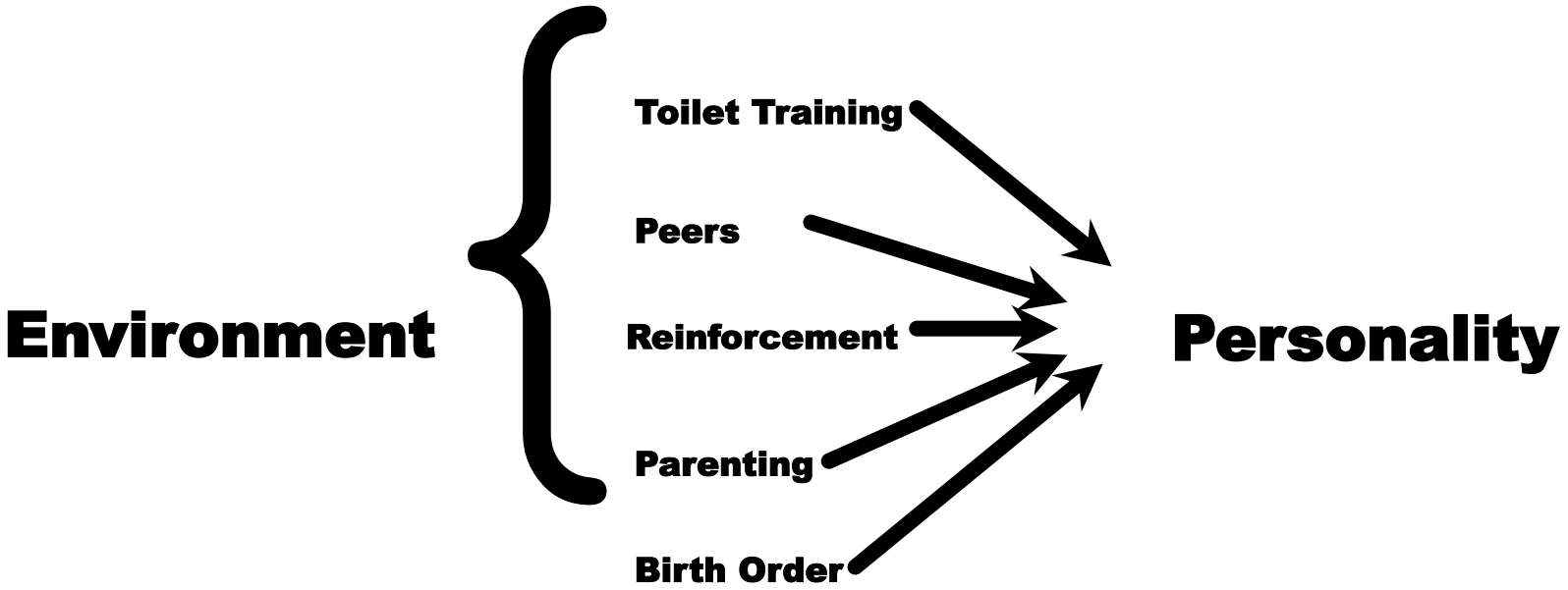
One gloomy prospect is that the salient environment might be unsystematic, idiosyncratic, or serendipitous events such as accidents, illnesses, or other traumas... Such capricious events, however, are likely to prove a dead end for research. More interesting heuristically are possible systematic sources of differences between families. (Plomin and Daniels, p. 8)

# How Environmental Causation Works

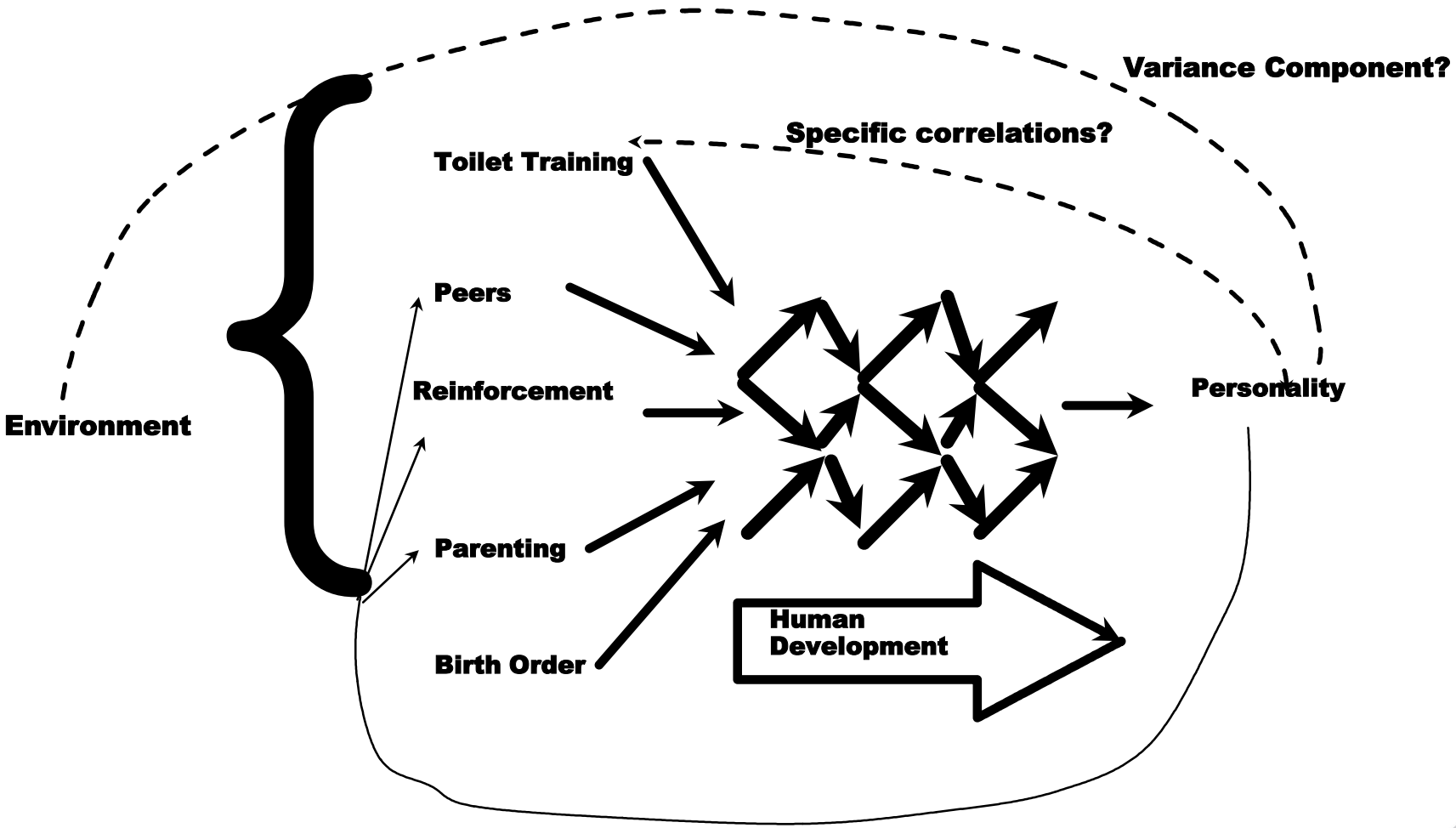
# Big Environmental Cause Model

**Toilet Training** → **Personality**

# Complex Environmental Causation Model



# *Complex Environmental Causation



# Spinach and Ice Cream (Bateson)

- A mother rewards a child for eating his spinach by giving him a bowl of ice cream.
- When child grows up, does he:
  - Love or hate spinach?
  - Love or hate ice-cream?
  - Love or hate mother?

# Behavior Genetics as Ordinary Social Science

A humbler paradigm

J Youth Adolescence (2007) 36:141–152
DOI 10.1007/s10964-006-9128-4

ORIGINAL PAPER

# Adolescent Sexual Debut and Later Delinquency

Stacy Armour · Dana L. Haynie

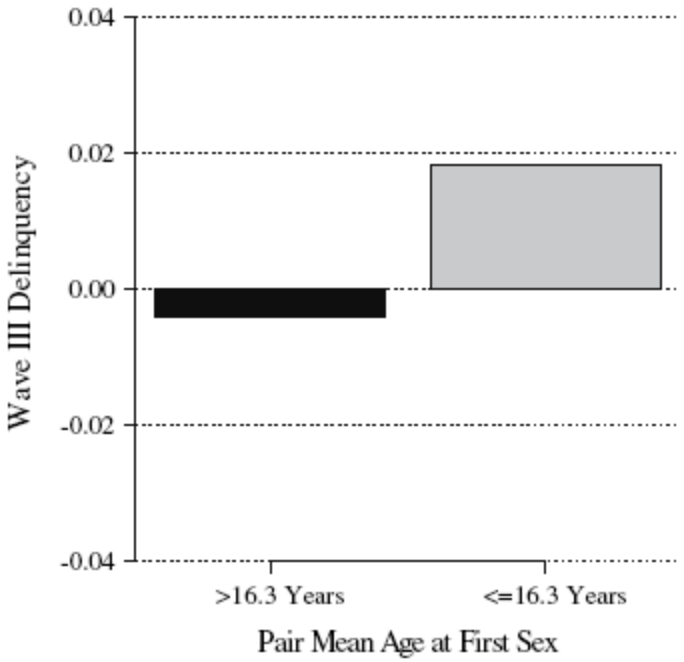
**Abstract** Does sexual debut (i.e., experiencing sexual intercourse for the first time) increase the risks of participating in later delinquent behavior? Does this risk increase if adolescents experience early sexual debut relative to the timing experienced by one's peers? Although many factors have been linked to sexual debut, little research has examined whether sexual initiation is linked to later behavioral outcomes. Using data on adolescents participating in three waves of the National Longitudinal Study of Adolescent Health ($N = 7{,}297$), we examine the interconnections between sexual debut and later delinquency. In addition, we pay particular attention to the role of timing of sexual debut. We find that experiencing sexual debut is associated with delinquency one year later. In addition, those adolescents who experience early sexual debut relative to their peers are at higher risk of experiencing delinquency compared to those who debut on-time; adolescents who experience late sexual debut are the least likely to participate in delinquency. Moreover, the protective effect of late sexual debut appears to persist for several years. Findings are interpreted by drawing on developmental theory and life course research.

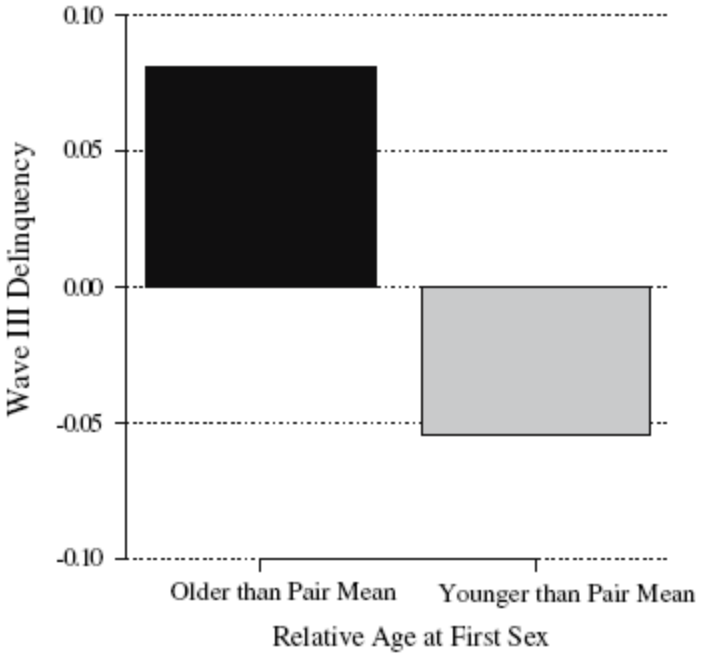
J Youth Adolescence
DOI 10.1007/s10964-007-9228-9

EMPIRICAL RESEARCH

# Rethinking Timing of First Sex and Delinquency

K. Paige Harden · Jane Mendle · Jennifer E. Hill ·
Eric Turkheimer · Robert E. Emery



# What Behavior Genetics Is Not

- A catalog of heritability coefficients
- A method for sorting out the Galtonian intuition one trait at a time
- A tool for figuring out “how genetic” things are
- A source of genetic or biological mechanisms of complex behaviors

# What Behavior Genetics Is

- A species of social scientific research methodology
- A reminder that correlations between biologically related family members can not be interpreted unambiguously or causally
- A *necessary* tonic for non-experimental social science
- A means of establishing quasi-experimental control in human domains where random assignment is impossible

# The Fourth Law

## AND WHAT IT MEANS

Why I Remain Skeptical About the Molecular Genetics of Very Complex Behavior

# Reason 1: The First Law

Remember, Heritability is Universal

# Turkheimer (2000)

The question is not whether there are correlations to be found between individual genes and complex behavior—of course there are—but instead whether there are domains of genetic causation in which the gloomy prospect does not prevail, allowing the little bits of correlational evidence to cohere into replicable and cumulative genetic models of development. My own prediction is that such domains will prove rare indeed, and that the likelihood of discovering them will be inversely related to the complexity of the behavior understudy.

# Reason 2: Spinach and Ice Cream in Genomics

The best scientific model for the molecular genetics of complex behavior comes from the non-shared environment

# Three step research program

1) Quantify Within Family Environment
2) Identify Specific Within Family Variables
3) Causal Associations between Within Family E and Behavior

# Three step research program

1) Quantify Heritability
2) Identify Specific Within Family Variables
3) Causal Associations between Within Family E and Behavior

# Three step research program

1) Quantify Heritability
2) Identify Specific QTLs
3) Causal Associations between Within Family E and Behavior

# Three step research program

1) Quantify Heritability
2) Identify Specific QTLs
3) Causal Associations between Within Family E and Behavior

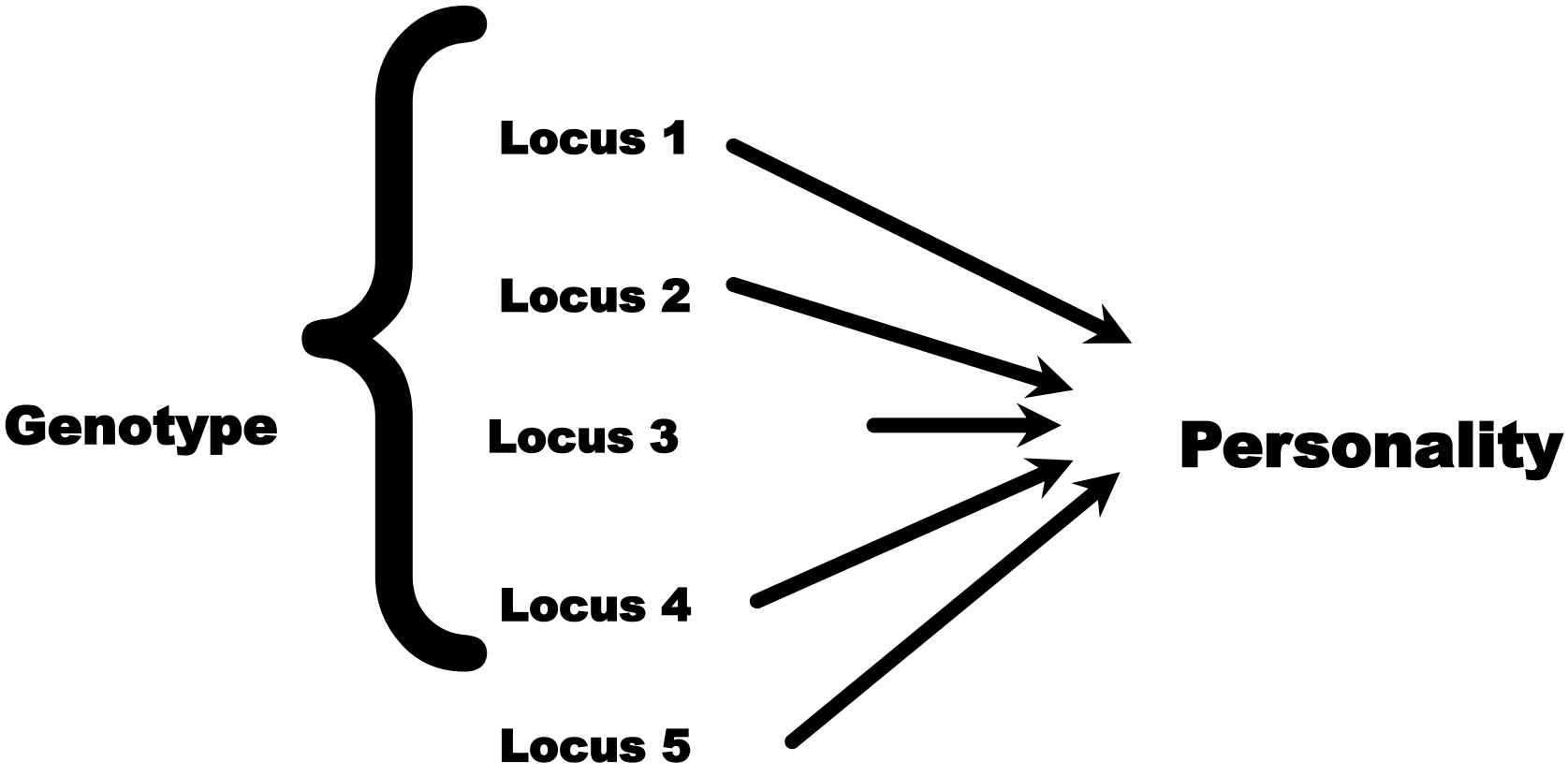
# The Human Genome Project

1) Quantify Heritability
2) Identify Specific QTLs
3) Causal Associations between QTLs and Behavior

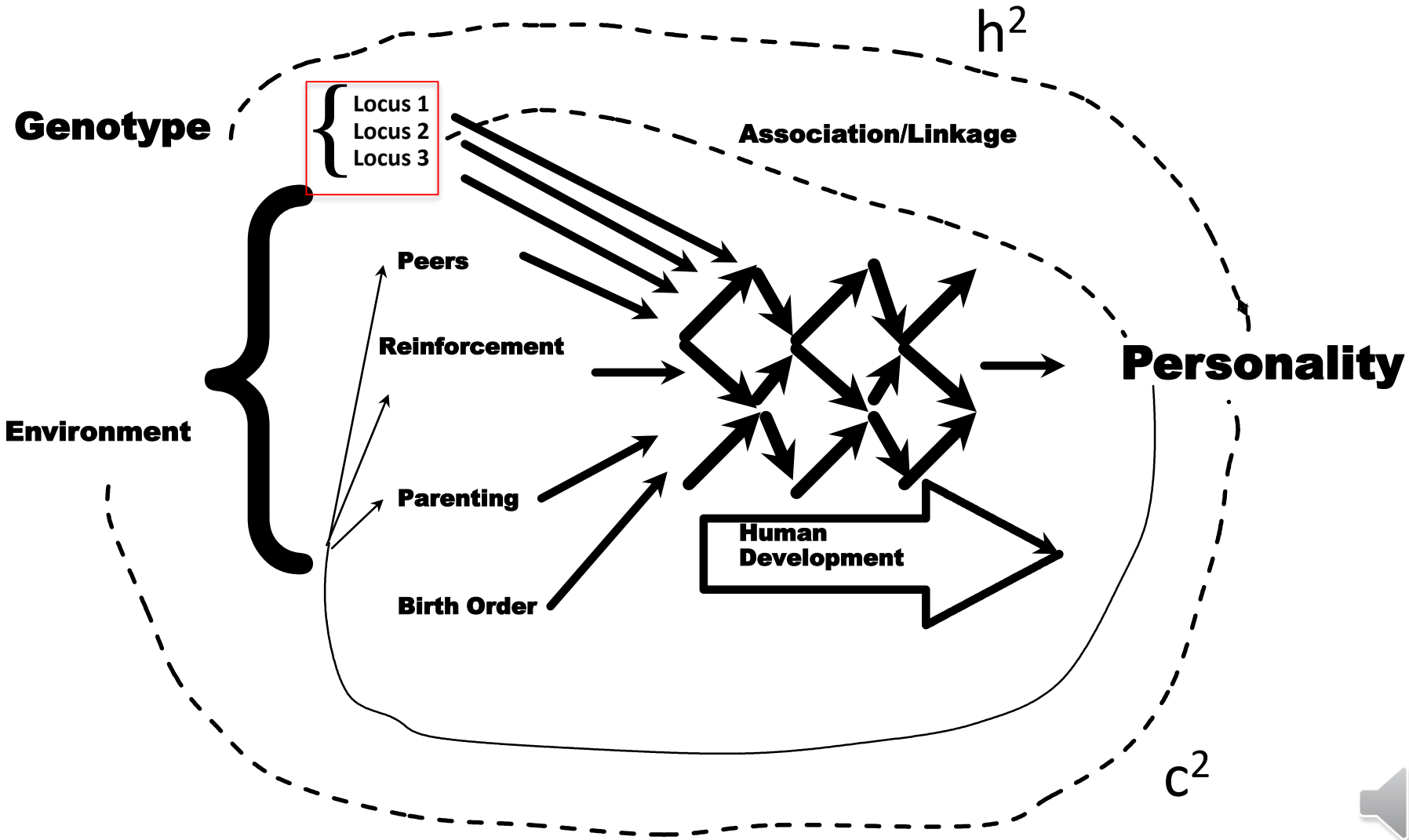
# One Gene One Disorder (OGOD) Model

**Single Major Locus** → **Personality**

# Complex Genetic Cause (QTL) Model



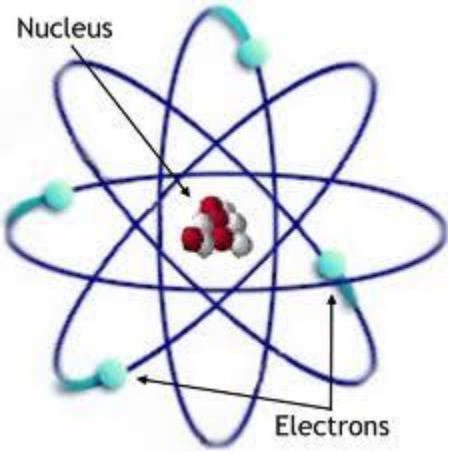
# *Complex Genetic Causation



# Reason 3: The Levels of Analysis Problem

# The Physics of Carpets

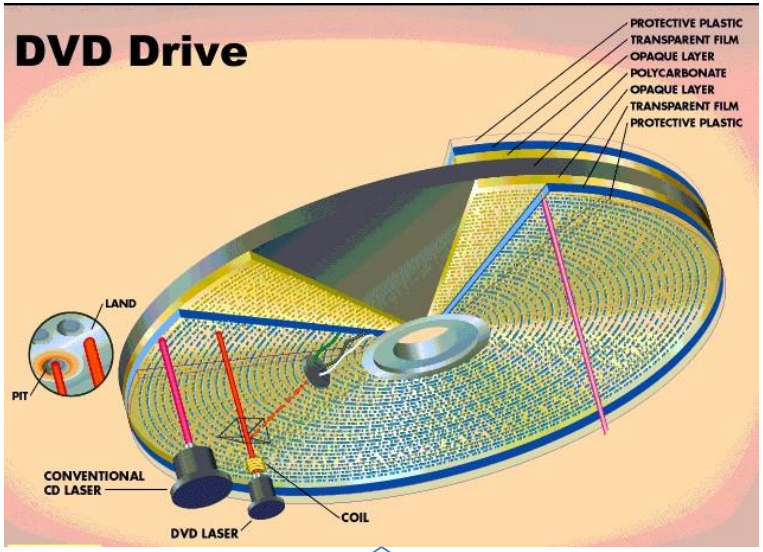
Harre, Clarke & DeCarlo, 1985

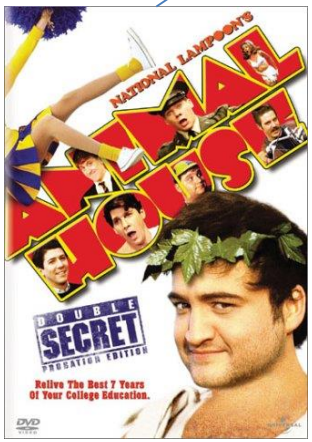



# Why is there no Physics of Carpets?

- It's not that carpets aren't physical objects.
  - It's not that people aren't genetically based organisms
  - This is what the first wave of behavior genetics established
- What makes something a carpet is not defined at the atomic level.
  - What makes someone a criminal is not defined at the the genetic level
- The problem is not that we are using an over simplified version of physics. No amount of physics will ever offer a good way to talk about carpets.
  - I have my doubts whether all the more sophisticated genetic technology at hand: sequencing, CNVs, gene expression, epigenomics, etc.

# DVDs




?


- DVDs are a thoroughly mechanistic, man-made device
- Suppose you are given a stack of DVDs and a microscope that allows you to visualise the individual dots read by the DVD laser
- Your job is to decide if the movie on the DVD is a drama or a comedy
- It isn't possible
- Not a matter of waiting until we understand DVDs better
- Not a matter of the inevitable progress of science
- It is in principle impossible
- But with enough DVDs, you will get "results"
- Drama doesn't exist as an entity at the level of the laser-readable units

# But actually, you can do it

# What is a DVD player?

- It is a system for decoding the pattern of dots on a DVD.
- What is the equivalent of a DVD player for a genome?
- It is a human life, human development
- The way to “predict” outcomes from DNA is to understand the DVD player of human development.
- That is what a MZ twin is:  A way to execute a genome, to “decode” it.
- So the problem of decoding the genome for behavior is the problem of human development itself.  GWAS is bad psychology.
- It would be very hard to reverse engineer a DVD player by looking at the linear sequence of dots.

# Reason 4: NHST

Weird Reliance on Outdated Methodology

# A Brief History of NHST in Psychology

- For many years, researchers relied blindly on $p<.05$ significance testing
  - It didn't work
- Now psychology faces a "replicability crisis" in which many significant findings can't be replicated
- Psychology realizes that misunderstanding and misuse of NHST is one of the main culprits

# p-Hacking

- p-hacking is the discredited practice of maintaining a lot of hypotheses, collecting data until one of them is significant, and reporting it
- Many top journals now forbid NHST of any kind
- There is a movement to pre-register hypotheses to prevent p-hacking

# Meanwhile, in Genomics

- Linkage and candidate-gene studies of behavior were a spectacular and embarrassing failure
- So a new technology was developed (GWAS), requiring hundreds of thousands of significance tests at very stringent p-levels
- Strategy is to test all of them at $p<10^{-8}$ and if that doesn't work, keep collecting data until something does
- GWAS is unapologetic high-tech p-hacking
- Someone explain to me why NHST is going to work better in genomics than it did in psychology

# Wait a Second

- Haven't we already identified lots of "hits"?
  - This was inevitable, and I said so 17 years ago
- Some of them have replicated!
  - Some will, some won't in various contexts, what they won't do is turn into a theory. Physics of carpets.
- Polygenic scores
  - Yes, but this is giving up on individual actions of genes. Also, beware the Phenotypic Null Hypothsesis.
- GREML
  - Gives up even further on individual actions of genes. In fact more like a twin study.

# What About Polygenic Risk Scores?

- They are an interesting new way to generate human traits
- Certainly no less valid than adding up responses on self-report checklists
- Maybe can do useful BG without twins
- Worth remembering what a scientific retreat they are
- Not an excuse to repeat every twin study that has ever been conducted
- The real standard is parental phenotype
- Extreme score arguments don’t help
- Beware the phenotypic null hypothesis

# Conclusion

Why Behavior Genetics Matters

# What is at Stake?

- No one cares anymore about genes and environment
- But the question of whether our complex behavior is actually a reflection of simpler genetic or neurological mechanisms has great importance
- The First Law means we have a choice: expect that all human behavior is ultimately explainable genetically, or accept that some heritable behavior must be explained psychologically
- The received modern view holds that it is just a matter of time – the inexorable progress of science– but I disagree.

# How Should We React?

- This is not a failure of the genetics of behavior
  - It is nature showing us that it works in a way that we didn't expect. *We should embrace it.*
- Ever-larger GWAS to find smaller and small effects at genome wide significance is not the answer.
  - It is an exercise on science at the wrong level of analysis
  - "Results" are theoretically necessary.
  - Give me one example from the history of science
- The only thing I want to hear about is the cumulative percentage explained by identified and replicated loci
  - Everything else is a just an indirect measure of sample size
- For complex human behavior, BG is a crucial quasi-experimental tool.
  - Doesn't depend on numerical heritability or mechanism.
- Winners and losers
  - Psychological explanation in a genetically instantiated world