# 3 Genetic and Environmental Influences on Antisocial Behaviors: Evidence from Behavioral–Genetic Research

**Terrie E. Moffitt**
Institute of Psychiatry, King's College London, SE5 8AF
United Kingdom and University of Wisconsin, Madison, Wisconsin 53706



*Advances in Genetics, Vol. 55*
0065-2660/05 $35.00

DOI: 10.1016/S0065-2660(05)55003-X

## ABSTRACT

This article reviews behavioral–genetic research into human antisocial behavior. The focus is on studies of antisocial behavior that have been leading the way in investigating environmental and genetic influences on human behavior. The first generation of studies, which provided quantitative estimates attesting that genes and environments each influence about half of the population's variation in antisocial behaviors is interpreted. Then how behavioral–genetic methods are being applied to test developmental theory and to detect environmental causes

of antisocial behavior is illustrated. Evidence for interactions between genes and the environment in the etiology of antisocial behavior is also examined. The article ends by envisioning future work on gene–environment interplay in the etiology of antisocial behavior. 

Despite many years of assiduous efforts to eliminate it, antisocial behavior is still a problem. Approximately 20% of people in the developed world experience victimization by perpetrators of violent and nonviolent illegal behavior each year (U.S. Bureau of Justice Statistics, 2002). The *World Report on Violence and Health* (WHO, 2002) tallies the staggering burden of mortality, disease, disability, and compromised well-being brought about by perpetrators of family violence and other violent crimes. Behavioral science needs to achieve a complete understanding of the causes of antisocial behavior to provide an evidence base for effectively controlling and preventing antisocial behavior. Research into genetic and environmental influences is making great strides toward uncovering the root causes of antisocial behavior. Studies are revealing which risk factors are causes, not just correlates. Studies are testing for effects of measured candidate genes. Studies are sorting out how our genotypes sway our susceptibility to environmental causes and how our environments rule the behavioral expression of our genotypes. Studies are refining the antisocial phenotype, uncovering a serious and persistently antisocial subgroup that appears to be more genetically influenced than ordinary antisocial behavior.

Journalists have drawn public attention to certain families that seem to contain far more than their share of criminal family members across several generations (Butterfield, 1996, 2002). This familial concentration of crime has been confirmed as a characteristic of the general population (Farrington *et al.*, 1996, 2001; Rowe and Farrington, 1997). In general, fewer than 10% of the families in any community account for more than 50% of that community's criminal offenses. The family concentration of antisocial behavior could be explained by a genetic influence on antisocial behavior, but it could just as easily be explained by nongenetic social transmission of antisocial behavior within families.

Behavioral–genetics research disentangles genetic from nongenetic aspects of familial transmission. Behavioral genetics also has methods to put genetic and nongenetic influences back together again in a systematic and controlled way, to work out how they jointly influence behavior. Behavioral genetics has been rapidly moving beyond the initial question of whether behavior is heritable (Dick and Rose, 2002; Kendler, 2001) to apply its methods to a broad array of causal questions about developmental processes influencing behavior. Given that virtually all behavior and certainly antisocial behavior must be the product of interplay between genes and environments, progress toward understanding cause–effect processes depends on studies not only to separate

genetic from nongenetic influences but also studies that can reunite them to observe their interplay. Here, interplay refers to processes in which genes and environments conferring risk for psychopathology co-occur (gene–environment correlation) and jointly influence the probability that psychopathology will develop (gene × environment interaction).

Section I of this article critiques the methodological quality of the behavioral–genetic research that has apportioned genetic versus environmental influences on antisocial behavior. How good is the evidence base? Section II summarizes the quantitative estimates of genetic and environmental influences on antisocial behavior resulting from this evidence base, and explains what the findings mean. Section III queries genetic findings with respect to sex differences, cohort effects, violence, the psychopath, antisocial behavior that co-occurs with mental disorders, and assortative mating. Section IV illustrates ways that behavioral–genetic designs are being applied to test developmental theory about antisocial behavior. Section V explains how behavioral–genetic designs are newly being used to distinguish risk factors for antisocial behavior that are bona fide environmental causes. Section VI examines interactions between genetic and environmental causes of antisocial behaviors. Section VII puts forward directions for future research.

## I. APPRAISING THE QUANTITATIVE BEHAVIORAL–GENETIC EVIDENCE BASE

Tables 3.1 to 3.3 bring together all quantitative behavioral–genetic studies of antisocial behaviors, inclusively defined, that were available as at 2004. Reviews up to the mid-1990s concluded that evidence was accumulating that genetic factors influence which individuals in the population exhibit antisocial behaviors (Carey, 1994; Carey and Goldman, 1997; Gottesman *et al.*, 1997; McGuffin and Thapar, 1998; Miles and Carey, 1997; Raine, 1993; Walters, 1992). The literature of published behavioral–genetic studies of antisocial behaviors has expanded dramatically since those reviews appeared, and there have been six notable improvements in the quality of research into the genetic and environmental architecture of antisocial behaviors.

### A. The number of studies has increased

To date, more than 100 quantitative genetic studies of antisocial behaviors have been published from more than 60 different genetically informative samples, totaling more than 77,000 families. The last columns of Tables 3.1 to 3.3 show that more than one-third of the studies have been published after 1994.

**Table 3.1.** Early Childhood: Estimates of Genetic and Environmental Influences on Population Variation in Antisocial Behavior, from Different Types of Behavioral–Genetic Studies of Young Children

| Heritability estimate | Environment estimates: Common | Environment estimates: Unique + error | Measure of antisocial behavior | Data source | Number of families | Age of probands | Nation/ sample | Authors | Year of publication |
|---|---|---|---|---|---|---|---|---|---|
| **Twins reared together design** | | | | | | | | | |
| 34% | 32% | 34% | CBCL Externalizing | Mother | 260 | 2–3 | USA, CO | Schmitz *et al.* | 1995 |
| 60% | 20% | 20% | CBCL Externalizing | Parents | 1358 | 3 | The Netherlands | van den Oord *et al.* | 1996 |
| 49–75% | 0–22% | 25–29% | CBCL Externalizing | Mother | 3620 | 2–3 | The Netherlands | van der Valk *et al.* | 1998 |
| 58% | 0% | 42% | Physical aggression | Mother | 4562 | 19 months | Canada, Quebec | Dionne *et al.* | 2003 |
| 82% | 0% | 18% | CBCL Externalizing/ opposition observations/ Berkeley Puppet Conduct Problems | Composite mother/teacher/ observer/self | 1116 | 5 | UK, E-risk | Arseneault *et al.* | 2003 |
| 69% | 0% | 31% | CBCL Externalizing | Mother | 1116 | 5 | UK, E-risk | Arseneault *et al.* | 2003 |
| 76% | 0% | 24% | CBCL Externalizing | Teacher | 1116 | 5 | UK, E-risk | Arseneault *et al.* | 2003 |
| 42% | 0% | 58% | Berkeley Puppet Conduct Problems | Self | 1116 | 5 | UK, E-risk | Arseneault *et al.* | 2003 |
| 61% | 0% | 39% | Oppositional behavior at home | Observer | 1116 | 5 | UK, E-risk | Arseneault *et al.* | 2003 |

(*Continues*)

**Table 3.1.** (*Continued*)

| Heritability estimate | Environment estimates: Common | Environment estimates: Unique + error | Measure of antisocial behavior | Data source | Number of families | Age of probands | Nation/ sample | Authors | Year of publication |
|---|---|---|---|---|---|---|---|---|---|
| 23% | 10% | 67% | Disruptive behaviors on videotape, blind observers | Observation in a game of SNAP! | 1116 | 5 | UK, E-risk | Hughes *et al.* | 2002 |
| **Adoptees design** | | | | | | | | | |
| No studies | | | | | | | | | |
| **Twins reared apart design** | | | | | | | | | |
| No studies | | | | | | | | | |

Note 1: Studies having fewer than 75 families are excluded from the table. We make an exception to this rule for studies having rare design features (twins reared apart or observational measurement).

Note 2: When variance estimates are presented as ranges (e.g., 45–65%), this is usually because the original publication provided estimates separately for males and females. In a few cases, ranges are estimates provided separately for successive waves of a longitudinal study, or for different subscales of a measure.

Note 3: Certain samples are represented on more than one row of the table, but each row presents data from a different cohort, a different age or a different measurement source or instrument.

**Table 3.2.** Middle Childhood to Adolescence: Estimates of Genetic and Environmental Influences on Population Variation in Antisocial Behavior, from Different Types of Behavioral–Genetic Studies of School-Aged Children and Adolescents

| Heritability estimate | Environment estimates | | Measure of antisocial behavior | Data source | Number of families | Age | Nation/sample | Authors | Year of publication |
|---|---|---|---|---|---|---|---|---|---|
| | Common | Unique + error | | | | | | | |
| **Twins reared together design** | | | | | | | | | |
| Very low in 7 studies | Not estimated | Not estimated | Delinquency | Official | 172 total | Adolescence | USA 2, Germany 1, Japan 3, UK 1 | DiLalla and Gottesman, 1989, Table 1; Raine, 1993, Table 5 | 1934–1977 |
| 0% | 45% | 35% | Hit Bobo doll | Observer | 85 | 5–11 | USA, CO | Plomin *et al.* | 1981 |
| 60% | 12% | 28% | Bullying | Adult | 87 | 7 | USA, CO | O'Connor *et al.* | 1980 |
| 0–42% | 19–69% | 31–39% | Rutter antisocial scale | Adult | 205 | 13 | UK, London children | Stevenson and Graham | 1988 |
| 57% | 22% | 21% | CBCL Externalizing | Adult | 399 | 4–18 | USA, CO | Schmitz *et al.* | 1995 |
| 51% | 28% | 21% | CBCL Externalizing | Adult | 181 | 7–15 | USA, Western Reserve | Edelbrock *et al.* | 1995 |
| 0% | 61% | 39% | Rutter antisocial scale | Adult | 198 | 8–16 | UK, Cardiff | Thapar and McGuffin | 1996 |
| 37–46% | 46–50% | 6–12% | CBCL Externalizing | Adult | 780 | 5–9 | Norway | Gjone and Stevenson | 1997 |
| 13–38% | 46–62% | 16–25% | CBCL Externalizing | Adult | 1264 | 8–16 | USA, VA | Silberg *et al.* | 1994 |
| 25–66% | 4–42% | 29–33% | Rutter antisocial scale | Adult | 1197 | 8–16 | USA, Virgnia | Silberg *et al.* | 1996 |
| 25–74% | 0–44% | 25–77% | Conduct disorder | Adult | 1412 | 8–16 | USA, VA | Eaves *et al.* | 1997 |
| 57–65% | 22–50% | 6–12% | CBCL Externalizing | Adult | 1048 | 12–15 | Norway | Gjone and Stevenson | 1997b |
| 60% | 30% | 10% | CBCL Externalizing | Adult | 720 | 9–18 | USA, NEAD | Deater-Deckard *et al.* | 1997 |

(*Continues*)

**Table 3.2.** (*Continued*)

| Heritability estimate | Environment estimates | | Measure of antisocial behavior | Data source | Number of families | Age | Nation/sample | Authors | Year of publication |
|---|---|---|---|---|---|---|---|---|---|
| | Common | Unique + error | | | | | | | |
| 62–77% | 4–12% | 18–27% | CBCL Aggression | Adult | 1022 | 7–9 | Sweden | Eley *et al.* | 1999 |
| 50–76% | 0–18% | 24–32% | CBCL Aggression | Adult | 501 | 8–16 | UK | Eley *et al.* | 1999 |
| 70–77% | 0% | 23–30% | CBCL Aggression | Adult | 492 | 8–12 | USA, Missouri | Hudziak *et al.* | 2000 |
| 29–69% | 0–27% | 31–44% | Conners' conduct probs | Adult | 125 | 7–11 | UK | Kuntsi *et al.* | 2000 |
| 50% | 18% | 32% | CBCL Externalizing | Mother | 1116 | 7 | UK, E-risk | Unpublished data from the author | 2003 |
| 70% | 1% | 28% | CBCL Externalizing | Teacher | 1116 | 7 | UK, E-risk | Unpublished data from the author | 2003 |
| 7% | 36% | 57% | Dominic-R DSM conduct problems | Self | 1116 | 7 | UK, E-risk | Arseneault *et al.* | 2005 |
| 63% | 29% | 8% | Olweus scale | Self/adult composite | 1412 | 8–16 | USA, VA | Simonoff *et al.* | 1995 |
| 61% | 14% | 25% | BPI antisocial | Self/adult composite | 405 | 10–18 | USA, NEAD | O'Connor *et al.* | 1998c |
| 52% | 14% | 34% | Conduct disorder symptoms | Self/adult composite | 1506 | 11 | USA, MN | Burt *et al.* | 2001 |
| 90% | 0% | 43% | Broad externalizing disorder spectrum | Self/adult composite | 524 | 17 | USA, MN | Krueger *et al.* | 2001 |
| 62% | 0% | 0% | Conduct problems scale | Self/adult composite | 1109 | 5–17 | CaStANET, Wales and North England | Scourfield *et al.* | 2004 |
| 80% | No report | No report | Broad externalizing disorder spectrum | Self/adult composite | 542 | 17 (plus parent) | USA, MN | Hicks *et al.* | 2004 |
| 42% | 6% | 52% | MMPI psychopathy | Self | 152 | 14–18 | USA,Boston | Gottesman | 1966 |

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| 14–74% | 0–41% | 26–45% | Socialization aggression | Self | 326 | 18 | USA, merit scholars | Loehlin and Nichols | 1976 |
| 70% | No report | No report | Delinquency | Self | 99 | 13–18 | USA, Ohio | Rowe | 1983 |
| 25–36% | 0–42% | 52–77% | Conduct disorder | Self | 1412 | 8–16 | USA, VA | Eaves *et al.* | 1997 |
| 81% | No report | No report | Conduct disorder items | Self | 81 | Adolescence | UK, Cardiff | McGuffin and Thapar | 1997 |
| 47–54% | 0–13% | 40–46% | Socialization | Self | 381 | 16–18 | USA, MN | Taylor *et al.* | 2000 |
| 18% | 26% | 56% | Delinquency | Self | 486 | 16–18 | USA, MN | Taylor *et al.* | 2000a |
| 35% | | | Conduct disorder items | Self | 334 | 12–18 | USA, CO | Young *et al.* | 2000 |
| 61% | 0% | 39% | Conduct disorder items | Self | 740 | 13–21 | USA, NLS Adolescent Health | Miles *et al.* | 2002 |
| 7% | 31% | 62% | Adults recall conduct symptoms | Self | 3226 | <15 | USA, Vietnam Era | Lyons *et al.* | 1995 |
| 23% | No report | No report | Adults recall conduct symptoms | Self | 3372 | <15 | USA, Vietnam Era | Slutske *et al.* | 2001 |
| 71% | 0% | 29% | Adults recall conduct symptoms | Self | 2682 | <15 | Australia | Slutske *et al.* | 1997 |
| 34% | 30% | 37% | Adults recall conduct symptoms | Self | 1075 | <18 | USA, VA | Jacobson *et al.* | 2000 |
| 38% | 0% | 61% | Adults recall conduct symptoms | Self | 558 | <15 | USA, VA | Goldstein *et al.* | 2001 |
| 31–36% | 10–17% | 52–54% | Antisocial to parent | Observer | 675 | 10–18 | USA, NEAD | O'Connor *et al.* | 1995 |
| **Sibhip design** | | | | | | | | | |
| 55% | 14% | 31% | BPI scale | Self | 822 | 5–12 | USA, NLSY | Rodgers *et al.* | 1994 |
| 32% | 5% | 63% | 4 physical violence items | Self | 1515 | Adolescence | USA, NLSY | Rowe *et al.* | 1999 |

(*Continues*)

**Table 3.2.** (*Continued*)

| Heritability estimate | Environment estimates | | Measure of antisocial behavior | Data source | Number of families | Age | Nation/sample | Authors | Year of publication |
|---|---|---|---|---|---|---|---|---|---|
| | Common | Unique + error | | | | | | | |
| 36% | 0% | 64% | 12 delinquent offences | Self | 2338 | 15–23 | USA, NLSY | Rodgers *et al.* | 2001 |
| **Adoptees design** | | | | | | | | | |
| Low | No report | No report | Antisocial symptoms | Adult | 513 | Adol. | USA, IA | Cadoret *et al.* | 1983 |
| 0% | No report | No report | Conflict | Observer | 124 | 3–11 | USA, CO Adoption Study | Rende *et al.* | 1992 |
| 17–49% | 0–27% | 42–70% | CBCL aggression, CBCL delinquency | Adult | 172 | 7–12 | USA, Colarado Adoption Study | Deater-Deckard and Plomin | 1999 |
| 60% | 20% | 20% | CBCL Externalizing | Adult | 332 | 10–15 | International, The Netherlands | van den Oord *et al.* | 1994 |
| 48–55% | 17–19% | 26–35% | CBCL Externalizing | Adult | 1816 | 12–15 | International, The Netherlands | van der Valk *et al.* | 1998 |
| Nil | No report | No report | Conduct disorder diagnosis | Adult | 162 | 10–17 | USA, IA | Cadoret | 1978 |
| No report | 0% | No report | CBL Externalizing | Self | 266 | 12–18 | USA, Midwest | McGue *et al.* | 1996 |
| **Twins reared apart design** | | | | | | | | | |
| 41% | No report | No report | Adults recall conduct symptoms | Self | 32 | <15 | USA, UK | Grove *et al.* | 1990 |

Note 1: Studies having fewer than 75 families are excluded from the table. We make an exception to this rule for studies having rare design features (twins reared apart or observational measurement).

Note 2: When variance estimates are presented as ranges (e.g., 45–65%), this is usually because the original publication provided estimates separately for males and females. In a few cases, ranges are estimates provided separately for successive waves of a longitudinal study, or for different subscales of a measure.

Note 3: Certain samples are represented on more than one row of the table, but each row presents data from a different cohort, a different age or a different measurement source or instrument.

**Table 3.3.** Adulthood: Estimates of Genetic and Environmental Influences on Population Variation in Antisocial Behavior from Different types of Behavioral–Genetic studies of Adults

| Heritability estimate | Environment estimates | | Measure of antisocial behavior | Data source | Number of families | Age | Nation/sample | Authors | Year of publication |
|---|---|---|---|---|---|---|---|---|---|
| | Common | Unique + error | | | | | | | |
| **Twins reared together design** | | | | | | | | | |
| Approximately 50%, 10 studies | Not estimated | Not estimated | Crime | Official | 607 | Adult | Denmark, Norway, UK, USA, Holland, Japan, Finland, Germany | Carey and Goldman, 1997, Table 23.1; DiLalla and Gottesman, 1989, Table 2 Raine, 1993, Tables 1 and 2 | 1929–1977 |
| 54% | 20% | 26% | Crime | Official | 8350 | Adult | Denmark | Cloninger and Gottesman | 1987 |
| 90% | No report | No report | Military dishonorable discharge | Official | 13,487 | 36 | USA, NAS-NRC | Centerwall *et al.* | 1989 |
| Nil | No report | No report | Crime | official | 201 | 20–80 | UK, Maudsley | Coid *et al.* | 1993 |
| 18% | 7% | 76% | Agression | Self | 503 | 28–37 | Finland | Partanen *et al.* | 1966 |
| 34% | 1% | 65% | MMPI psychopathy | Self | 133 | 20–25 | USA, IN | Pogue-Geile and Rose | 1985 |
| 70% | No report | No report | Buss-Durkee, verbal, indirect, anger scales | Self | 98 | 40–45 | USA, Midwest | Cates *et al.* | 1993 |
| 58% | 0% | 42% | MPQ aggression | Self | 331 | 19–41 | USA, MN | Tellegen *et al.* | 1988 |
| 0% | 53% | 47% | Conduct problems | Self | 175 | 16–71 | Canada, Vancouver | Livesley *et al.* | 1993 |
| 28–47% | Nil | 53–72% | Buss-Durkee aggression scales | Self | 300 | 36–54 | USA, Vietnam Era Study | Coccaro *et al.* | 1997 |
| 43% | 5% | 52% | Antisocial personality disorder | Self | 3226 | 36–55 | USA, Vietnam Era Study | Lyons *et al.* | 1995 |
| 0% | 37% | 62% | Antisocial personality disorder | Self | 558 | 38 | USA, VA | Goldstein *et al.* | 2001 |

(*Continues*)

**Table 3.3.** (*Continued*)

| Heritability estimate | Environment estimates | | Measure of antisocial behavior | Data source | Number of families | Age | Nation/sample | Authors | Year of publication |
|---|---|---|---|---|---|---|---|---|---|
| | Common | Unique + error | | | | | | | |
| 74% | 0% | 26% | Aggression | Self | 136 | 19–64 | UK, London | Rushton *et al.* | 1986 |
| 55% | 0% | 45% | Violence | Self | 274 | 19–64 | UK, London | Rushton | 1996 |
| 35–39% | 0% | 61–65% | MPQ aggression | Self | 1257 | 27–64 | USA, MN | Finkel and McGue | 1997 |
| 52% | 0% | 48% | Offending | Self | 397 | 33 | USA, MN | Krueger *et al.* | 2001 |
| 54% | 0% | 46% | Composite of 18 aggression questionnaires | Self | 247 | Adult | Ohio and British Columbia | Vernon *et al.* | 1999 |
| **Adoptees design** | | | | | | | | | |
| 20–78% in 5 studies | Not estimated | Not estimated | Offending | Official | 16,500 | Adult | Denmark, Sweden, USA | Carey and Goldman, 1997, Table 23.2; Raine, 1993, Table 4 | 1974–1989 |
| 50% | No report | No report | Socialization | Self | 253 | 14–76 | USA, TX | Loehlin *et al.* | 1985 |
| 50% | No report | No report | MMPI psychopathy | Self | 253 | 14–76 | USA, TX | Loehlin *et al.* | 1987 |
| **Twins reared apart design** | | | | | | | | | |
| 28% | No report | No report | ASPD symptoms | Self | 32 | 16–68 | USA–UK | Grove *et al.* | 1990 |
| 80% | 0% | 20% | MPQ agression | Self | 71 | 19–68 | USA, MN | Tellegen *et al.* | 1988 |
| 28% | 25% | 47% | Socialization | Self | 71 | 19–68 | USA, MN | Bouchard and McGue | 1990 |
| 60% | 40% | 0% | MMPI psychopathy | Self | 76 | 19–68 | USA, MN | DiLalla *et al.* | 1996 |
| 61% | 0% | 39% | MMPI psychopathy | Self | 119 | 18–77 | USA, MN | DiLalla *et al.* | 1996 |

Note 1: Studies having few than 75 families are excluded from the table. We make an exception to this rule for studies having rare design features (twins reared apart or observational measurement).

Note 2: When variance estimates are presented as ranges (e.g., 45–65%), this is usually because the original publication provided estimates separately for males and females. In a few cases, ranges are estimates provided separately for successive waves of a longitudinal study, or for different subscales of a measure.

Note 3: Certain samples are represented on more than one row of the table, but each row presents data from a different cohort or a different age or a different measurement instrument.

New behavioral–genetic reports on antisocial behaviors appear steadily from large, representative family samples examined by research teams around the world (Boomsma *et al.*, 2002; Martin, 2002).

## B. Techniques for statistical analysis are more sophisticated

Prior to the 1980s, researchers reported the percentages of MZ versus DZ twins concordant for a disorder, or chi-square tests of association between adoptees' and biological parents' diagnoses. At that time the research aim was merely to test for any evidence of heritable influence on behavior. Quantitative model-fitting approaches are now standard practice (Carey, 2003; Plomin *et al.*, 2001). These statistical procedures offer the advantage of comparing which of several different theoretically derived models to find out which fits a data-set best. In the course of estimating genetic influences, these data-analysis procedures also yield estimates of environmental influences on population variation in antisocial behavior. This advance reflects the field's growing interest in using genetically sensitive designs to study environmental effects. More information about statistical methods used in behavioral genetics can be found in Carey, 2003; http://psych.colorado.edu/hgss/; Neale and Cardon, 1992; Plomin *et al.*, 2001; Purcell http://statgen.iop.kcl.ac.uk/bgim/.

## C. More studies use large sample sizes

With the exception of reports from the very large Scandinavian twin and adoption registers reported during the 1980s (Bohman *et al.*, 1982; Cloninger and Gottesman, 1987; Mednick *et al.*, 1984), most studies of antisocial behaviors designed prior to 1995 examined 300 or fewer families. In contrast, most studies reported since 1995 examine a minimum of 1000 families, yielding more reliable estimates of genetic and environmental effects (Hopper, 1999; Martin *et al.*, 1978).

## D. More is known about how twins and adoptees represent the population

An important issue is whether the prevalence rates and distributions of antisocial behaviors among twins and adoptees represent antisocial behaviors among ordinary people (Rutter, 2002). This issue is relevant to the question of whether estimates of genetic and environmental influence from behavioral–genetic samples apply to the general population. Although this has been assumed more than it has been examined, the assumption is probably defensible for twin studies because twin-versus-singleton comparisons have not found differences in the prevalence rates of antisocial behavior or antisocial personality traits (Gjone and Novik, 1995; Johnson *et al.*, 2002; Levy *et al.*, 1996; Moilannen *et al.*, 1999; Simonoff *et al.*, 1997; van den Oord *et al.*, 1995; Van der Valk *et al.*,

1998a). Adoptees, on the other hand, tend to show elevated rates of antisocial outcomes, although the skewed distribution of these outcomes has the same shape within adoptee samples as in the general population (Hutchings and Mednick, 1973; Sharma *et al.*, 1998). Importantly, the effect sizes for *associations between* risk factors and psychopathology outcomes have been found to be similar across behavioral–genetic and nongenetic studies. For instance, in the Environmental Risk Longitudinal Twin Study (The E-risk Study) (Moffitt *et al.*, 2002), associations between children's antisocial behavior and maternal depression, exposure to domestic violence, maternal warmth and negativity, maternal smoking during pregnancy, socio-economic status, and neighborhood deprivation are all comparable to these associations in the wider literature.

## E. Behavioral–genetic studies have measured antisocial behaviors with different kinds of valid methods

Prior to 1980 most behavioral–genetic studies relied on official records of criminal conviction to measure antisocial behaviors. Since then, researchers have gathered self-reports of antisocial behaviors from research participants, reports from other informants, such as parents and teachers, and even observational measures (see Tables 3.1 to 3.3). Behavioral–genetic studies have assessed participants' antisocial behavior on a frequency continuum of acts, and also as formal psychiatric diagnostic categories of conduct disorder and antisocial personality disorder. This increased variety of measurements offers advantages for inference, because each measurement method's weaknesses are offset by the strengths of other methods. For example, court conviction records attest that antisocial behavior was serious enough to warrant official sanction by a judge or jury, but research participants' self-reports allow access to the majority of antisocial behaviors, which never come to the attention of the courts, or even the police. Contemporary behavioral genetics is surprisingly multidisciplinary. Four disciplines (i.e., psychopathologists, criminologists, personality psychologists, and child psychologists) conceptualize and measure antisocial behaviors somewhat differently, but all share a defining assumption about the construct—antisocial behaviors are behaviors that violate the rights and safety of others. Research from all four disciplines is included in Tables 3.1 to 3.3. Despite disciplinary differences in conceptualization and data-collection methods, research shows that genetic and environmental influences are more similar than different for clinical, legal, personality, and observational measures of antisocial behavior.

## F. Data are now available from many different types of behavior–genetic designs

Tables 3.1 to 3.3 show that antisocial behavior has been studied in twins reared together, adoptees, and twins reared apart. Because adoptions became unusual in the 1970s, most studies designed after 1990 feature twins. There are exceptions

(e.g., a Dutch study is examining international children adopted by Dutch parents) (Table 3.2.; van der Valk *et al.*, 1998b), and a new adoption study will be launched in California (Ge, 2002, personal communication). Behavior–genetics research is not limited to exotic samples; researchers also examine ordinary families whose members vary in genetic relatedness (e.g., full siblings, half-siblings, step-siblings, cousins, and unrelated children reared in the same family) (Rowe *et al.*, 1999). This variety of research designs offers a special advantage for inference because comparing their estimates tells us that the genetic and environmental effect sizes for antisocial behavior are robust across different designs; these estimates are not biased by the limitations and flaws peculiar to one design.

A number of potential flaws are unique to adoption studies. First, adoption agencies may attempt to maximize similarity between the adoptee's biological and adoptive families to increase the child's chance of fitting in with the new family (this is called "selective placement"). Relatedly, biological mothers who intend to give their baby away may neglect prenatal care and continue to abuse substances during pregnancy, and many unwanted babies experience institutionalization before they are adopted (Mednick *et al.*, 1986). If adoptive homes, prenatal care, and institutional care are selectively worse for the babies given up by antisocial biological mothers, this could bias estimates of heritability upward by adding the criminogenic influences of these three unmeasured nongenetic factors to any criminogenic influence of genes. Second, both adoptees and twins reared apart are likely to be reared in home environments that are unusually good for children because adoptive parents are carefully screened. The resulting restricted range of rearing environments could suppress estimates of environmental effects and thus bias heritability estimates upward (Fergusson *et al.*, 1995; Stoolmiller, 1999). However, this flaw of adoption studies is offset by studies of national twin registers (e.g., Cloninger and Gottesman, 1987) or stratified high-risk twin samples (e.g., Moffitt *et al.*, 2002) because such sampling frames represent the complete population range of environmental and genetic backgrounds.

Studies of twins avoid the potential flaws of adoption studies, but they suffer several potential flaws of their own. First, the logic of the twin design assumes that all of the greater similarity between MZ than DZ twins can safely be ascribed to MZ twins' greater genetic similarity. This "equal environments assumption" requires that MZ twins are not treated more alike than DZ twins on the causes of antisocial behavior (Kendler *et al.*, 1994). Because MZ twins look identical, in theory they might be treated more similarly than DZ twins in some way that promotes antisocial behavior, and as a result, estimates of heritability from studies of twins reared together could be biased upward relative to the correct population value (DiLalla, 2002). In fact, we found that young MZ twins receive somewhat more similar discipline than

DZ twins (Jaffee *et al.*, 2004a). However, studies of adoptees do not suffer this flaw, and neither do studies of twins reared apart because MZ twins reared apart do not share environments (unless their genetically influenced behaviors evoke similar reactions from care-givers in their separate rearing environments, which is a genetic effect). Second, in studies of twins, MZ twins differ more than DZ twins in prenatal factors affecting intrauterine growth (e.g., MZ twins sharing the same chorion appear to suffer more fetal competition for nutrients). These intrauterine factors also violate the assumption that environments are equal for MZ and DZ twins, but intrauterine differences tend to make MZ twins less alike than their genotypes and thus would bias heritability estimates downward (Rutter, 2002). Third, genomic factors that make some MZ twin pairs' genotypes less than perfectly identical (e.g., random inactivation of genes on one of each girl's two X chromosomes; Jorgensen *et al.*, 1992) could in theory affect twin-study heritability estimates, but no evidence shows that these processes influence antisocial behavior. Fourth, parental assortative mating can bias heritability estimates. Coupled partners are known to share similarly high or low levels of antisocial behaviors (Galbaud du Fort *et al.*, 2002; Krueger *et al.*, 1998). When parents of twins mate for similarity, this should increase the genetic similarity of DZ twins, but MZ twins' genetic similarity cannot increase beyond its original 100%, and as a result, heritability estimates will be biased downward relative to the correct population value. The implication of biological-parent assortative mating for adoption studies is the opposite, biological-parent similarity for antisocial behaviors would bias adoptees' heritability upward relative to the correct population value (because adoptee–biological-parent correlations would represent a double-dose of parental genes). Fifth, twin studies using adult reports to measure behavior sometimes suffer from rater artifacts (e.g., adults may mix up or conflate the behavior of MZ twins and they may exaggerate differences between DZ twins). Such a rater artifact does not afflict adoption studies (nor twin studies using the twins' self-reports, as twins do not confuse themselves).

Skeptics about twin research often comment that adoption studies show lower heritability estimates than twin studies, casting doubt about the twin method. However, where this discrepancy exists for a behavioral outcome, it is easy to explain. Adoption studies may show lower heritability estimates than twin studies because adoption breaks up the association between genetic and environmental risks naturally occurring in ordinary families by removing genetically at-risk children from damaging homes and placing them in salutary homes. As a result, interactions between environmental adversity and genetic vulnerability that enhance genetic influences on twins and ordinary children are suppressed among adoptees (Stoolmiller, 1999). Another reason for lower heritabilities in most adoption studies is that adoption studies must measure the behavioral phenotype for the family members being compared (parent versus

child) at different ages, in different cohorts, often using different instruments. In contrast, twin studies measure the phenotype for the family members being compared (two siblings) at the same age, in the same historical cohort, using the same instrument. As evidence that participants' age matters in this way, parent–child correlations are virtually always lower than sibling–sibling correlations, despite the fact that the genetic relatedness of these two pairs of relatives is the same, 50%. In our E-risk Longitudinal Twin Study, the father–son correlation for antisocial behavior is .28, whereas the brother–brother correlation for DZ twins is .45. Consistent with this analysis, a metaanalysis found that heritability estimates from traditional adoption studies of parent–child similarity were slightly different from heritability estimates from twin studies of twin–twin similarity, or from newer adoption studies comparing adopted versus natural siblings (Rhee and Waldman, 2002).

In any case, an eyeball comparison between designs on Tables 3.1 to 3.3 does not suggest that studies of twins reared together yield heritability estimates that are systematically higher, or lower, than estimates from studies of twins reared apart or of adoptees. On the one hand, this is because any bias arising from factors, such as selective adoptee placement, violations of the equal-environment assumption, intrauterine twin differences, or assortative mating, is only very small (Miles and Carey, 1997; Rutter, 2002). On the other hand, these factors bias heritability estimates upward as often as they bias them downward, canceling each other out.

## G. Looking for a sturdy finding

A fundamental assumption guiding this review is that sturdy inferences ought to be drawn from a cumulative body of studies whose methods differ as much as possible, but provide convergent findings about the same construct. As we have seen, each of the primary designs used by behavioral geneticists has its own Achilles heel(s), but fortunately, each design's idiosyncratic flaws are offset by compensatory strengths of the other designs. As a consequence, although particular studies and particular designs may be subject to critique, this does not invalidate inferences derived from the entire cumulative evidence base. The greatest confidence can be attained in science when studies deliberately employ different people, times, places, measurements, and research designs, but nonetheless converge on a similar finding (Robins, 1978). Tables 3.1 to 3.3 illustrate that behavioral–genetic studies of antisocial behaviors ranged in participants' age from 19 months to 70 years, covered the period from the Great Depression to the turn of the 2000 millennium, took place in numerous western nations, used a wide variety of measurement instruments and reporting sources, and comprised twins-together, adoption, twins-apart, and sibling designs. The next section asks: Have these studies converged on similar findings?

## II. ESTIMATING THE RELATIVE INFLUENCES OF GENES AND ENVIRONMENTS

This article does not adopt a metaanalytic approach. Rhee and Waldman (2002) already reported a valuable metaanalysis of 50 studies that clarifies the basic effect sizes for latent genetic and environmental influences on antisocial behavior. Instead, this review queries what the estimates of genetic and environmental influence are likely to mean.

Before going forward, it is worth acknowledging that coefficients estimating genetic and environmental influence are not immutable properties of nature; they are just statistical coefficients that indicate the balance between genetic and environmental sources of variation in a particular study sample (Hopper, 1998). Thus, it is true that every study's estimates of heritable and environmental influence on antisocial behavior can apply only to the specific balance of genetic and environmental variation in the time and place in which its participants grew up. Yet if there were no prospect of ever generalizing findings, there would be little reason to conduct any research. Further, the question of interest here concerns what relative influences on the population's antisocial behaviors can be expected under the balance of genome and environment during contemporary times and in places where we hope to reduce the burden of antisocial behaviors. After all, this is the setting to which all behavioral science hopes to generalize its findings. The field of behavioral genetics has accumulated enough data to address this question (Kendler, 2001).

### A. Genes influence approximately 50% of the population variation in antisocial behaviors

The basic logic used to make inferences about genetic influences is straightforward. In adoption studies, the correlation between adoptee and biological parent represents genetic transmission, whereas the correlation between adoptee and adoptive parent represents social (i.e., environmental) transmission. In twin studies, genetic influence is inferred if DZ twins' behavior is less similar than MZ twins' because DZ twins share on average only half of the genes on which humans can vary, whereas MZ twins share all their genes. In other words, if there were no genetic influence on a phenotype, zygosity should not matter. The more than 100 heritability estimates in Tables 3.1 to 3.3 form a distribution approximating a bell-shaped normal curve, as shown in Fig. 3.1, with its peak at 50%, and small tails to the left (0% heritability) and right (80% heritability). According to psychometric test theory, this distribution is to be expected from a sample of more than 100 imperfect estimates of a true effect that equals 50% in nature. Estimates below 20% or above 70% tend to emerge from studies with exceptional design features (e.g., observational measures, small sample sizes, very

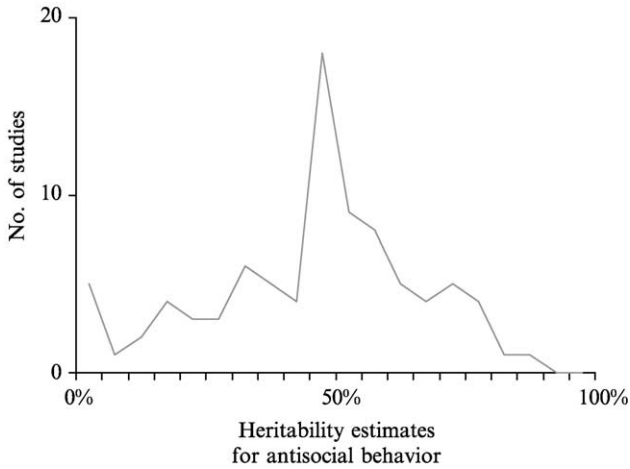


**Figure 3.1.** Heritability estimates for antisocial behavior.

wide age ranges, adults asked to retrospectively report childhood symptoms, and very young children). The most reliable estimates come from the contemporary studies in Australia, The Netherlands, Norway, Sweden, United Kingdom, and the United States, because these studies examined large, population-representative samples using quantitative modeling techniques. These studies' estimates tend to converge quite tightly around 50%.

Our summary of these studies is buttressed by complementary meta-analyses of twin and adoption studies. One metaanalysis reported a heritability estimate of 50% for 24 studies of measures of the personality trait, aggression (Miles and Carey, 1997). Another metaanalysis reported that the best fitting model to data from 51 studies of antisocial behaviors yielded a heritability estimate of 41% (Rhee and Waldman, 2002). Two differences between the studies in Tables 3.1 to 3.3 and those in Rhee and Waldman's metaanalysis may explain why our estimate is slightly higher than theirs. First, the metaanalysis allowed one heritability estimate per sample, whereas Tables 3.1 to 3.3 include more than one estimate per sample, if each estimate was for an independent measure. Because studies having better samples also tend to collect and report more measures, the metaanalysis ruled out much information from the most informative samples, which tend to generate heritability estimates near 50%. Second, the metaanalysis lacked information about three of the five early childhood studies shown on Table 3.1, and these studies of very young children tend to estimate higher heritabilities than studies of older children and adolescents.

## 1. Now that a heritable liability toward antisocial behaviors is known, what of it?

To answer this question, it is useful to revisit what heritability does not imply. First, evidence of genetic influence for antisocial behavior neither implies immutability nor resistance to intervention. Hair color, that most heritable of traits, is easily changed. The mean height of the population increased notably this century, whereas the amount of variation between individuals' heights attributable to genes remained the same. Second, evidence of genetic influence does imply that biological processes are involved in the etiology of antisocial behaviors, but biological etiology does not imply that change can only be brought about through biological intervention. A genetic liability to alcoholism is best treated through abstinence from the environmental agent, alcohol. Adoption studies have repeatedly illustrated that adoption into a good home can be an effective treatment for a genetic liability to antisocial behavior (Cadoret *et al.*, 1995; Mednick *et al.*, 1984). A third idea that the omnibus 50% estimate of genetic influence does not imply is that the influence of genes is the same for everyone. It could conceal important heterogeneity in genetic effects within subgroups, such as males versus females, older versus younger generations, or children versus adults (Slutske, 2001). Sections III and IV of this article will address this issue.

Fourth, a high heritability estimate does not imply confidence that research at the molecular level will easily find genes for antisocial behavior. This is amply illustrated by the chequered history of molecular research into highly heritable complex phenotypes, such as schizophrenia, autism, and intelligence (Risch, 2000). Nonetheless, if heritability were low, there would be less justification for pursuing molecular genetic research avenues in the first place (Martin *et al.*, 1997; McGuffin *et al.*, 2001), and a high heritability coefficient should be greeted with "healthy skepticism ... but not unhealthy cynicism" about finding genes functional in psychopathology (Insel and Collins, 2003, p. 618).

Fifth, evidence of high heritability does not imply that the causal role of nongenetic factors is trivial. To the contrary, it is now recognized that the heritability coefficient indexes not only the direct effects of genes but also the effects of interactions between genes and family-wide environments (Purcell, 2002; Rutter and Silberg, 2002). In such interactions the effect of an environmental risk may be even larger than previously reported, among the subgroup of individuals having a vulnerable genotype. This is likely to be the case for antisocial behaviors. Section VI of this article will address gene × environment interactions.

Perhaps the most pragmatic implication from evidence of genetic influence for antisocial behavior is that much of what we thought we knew about environmental causation could be wrong. It tells us that we can no longer

blindly assume environmental causation by risk factors that are known to predict antisocial outcomes. Rather, we must reexamine each putative environmental risk factor for antisocial behavior, one by one, while using research methods that are capable of applying explicit controls for genetic explanations of the connection between risk factor and antisocial outcome (Rutter *et al.*, 2001). Section V of this article presents research on controls for genetic influence when testing for environmental causation.

## B. Environmental factors shared by family members influence about 20% of population variation in antisocial behaviors

One useful feature of behavioral–genetic research designs is that they offer two powerful methods for documenting the importance of environmental effects (Plomin *et al.*, 2001). One of these methods of detecting environmental influence tests whether any of the family members in a study sample are more similar than can be explained by the proportion of genes they share. For instance, MZ twins' genetic similarity is twice that of DZ twins, and therefore, if nothing but genes influenced antisocial behavior, then MZ twins ought to be at least twice as similar as DZ twins. If not, then something environmental has influenced the twins and enhanced their similarity. For almost all human behavioral traits studied so far, environmental factors shared by family members (labeled as "family-wide," "shared," or "common" environment) have not been found to make family members similar. In other words, the estimated influence of common environment has been found to be almost nil for most human behavioral traits (Rowe, 1994). Antisocial behavior is a marked exception. A comparison of common environment effects across 10 psychiatric disorders revealed that such effects were stronger for antisocial personality and conduct disorder than for affective, anxiety, or substance disorders (Kendler *et al.*, 2003).

The estimates of common environment effects in the second columns on Tables 3.1 to 3.3 are highly variable across the studies. However, in general it is fair to say that these estimates cluster around 20%. This conclusion is consistent with the estimate from the aforementioned metaanalyses. One metaanalysis reported that a model omitting common environment effects made a poor fit to the data (Miles and Carey, 1997) and the other metaanalysis reported an estimate of 16% for the influence of common environments on antisocial behaviors (Rhee and Waldman, 2002). The small size of this common environment estimate should not be too surprising, because the twin-study coefficient indexing the common environment does not include environmental effects involved in gene–environment interactions. We can think of the common environment coefficient as the "residual" effects of common environments that remain, after controlling for the influence of gene–environment interactions on the phenotype. Most human behavior involves nature–nurture interplay,

and gene–environment interactions have been shown to play an important role in individual's differences in antisocial behavior in particular (see Section VI of this article). Therefore, it is remarkable that as much as 20% of the population variation in antisocial behavior can be attributed to direct environmental effects not conditional on genetic vulnerability.

## 1. Caveats

Three caveats qualify the conclusion that common environments account for 20% of population variation in antisocial behaviors. The first caveat is that a lot of statistical power is needed to estimate the common environment's effect. Although some studies are big enough, many have been underpowered to detect statistical significance for the quantitative effects of common environments (Hopper, 1999). Because it is customary to report coefficients from the most parsimonious model, after trimming away any nonsignificant parameters, many studies that obtained modest but non-significant common environment effects have trimmed them away and reported them as zero (see Tables 3.1 to 3.3). However, confidence intervals around non-significant common environment coefficients sometimes imply that the effect size of these coefficients could be small to moderate. The strategy of selecting the most parsimonious model with fewest significant parameters may have led smaller studies to conclude prematurely that the common environment makes no contribution to antisocial behavior. In keeping with this notion that limited power impedes finding common environment effects, Rhee and Waldman (2002) were able to detect a significant common environment effect for antisocial behavior because they reanalyzed prior studies' twin correlations to generate their own model parameters, with more than adequate power.

A second caveat is about the effects of sample composition on estimates of the common environment. Because selective enrolment and selective attrition are common occurrences in twin research, many twin studies have inadvertently restricted their range of participating families to mainly middle class families who are happy to volunteer for research. One consequence of failing to represent wider environmental variation may be underestimating the effects of common environment. A simulation study revealed that restricted range (i.e., censoring that results from selective sample recruitment–attrition) can lead to such biased parameter estimates in quantitative genetic models, and subsequent extension of the simulation exercise to real data (subsamples drawn with deliberate censoring from a twin registry) confirmed that censored samples underestimate common environment influences on behavioral phenotypes (Taylor, 2004).

A third caveat is that if the multiple genes influencing antisocial behavior interact (instead of summing), then common environment effects

will be underestimated in twin studies (but not adoption studies) (Miles and Carey, 1997). Rhee and Waldman (2002) were able to metaanalyze twin and adoption studies' data together, which allowed them to test for such nonadditive genetic effects. Their best-fitting model divided the genetic effect into additive (32%) and nonadditive (9%) parts, suggesting that some genes do interact in the etiology of antisocial behavior. Nonetheless, the common environment effect on antisocial behavior (16%) remained unchanged. In sum, limited statistical power, restricted sample composition, and gene–gene interactions may have lead to underestimates of the common environment component in behavioral–genetic studies of psychopathology.

## C. Environmental factors experienced uniquely by individuals influence about 20–30% of population variation in antisocial behaviors

The second method of detecting environmental influence is to test whether any family members are less similar than expected from the proportion of genes they share (Plomin and Daniels, 1987). For instance, if a pair of MZ twins is not perfectly identical in antisocial behavior, despite sharing all their genes, this indicates that experience has reduced their behavioral similarity. After estimates of the influences of heritability (50%) and common family environment (20%) on antisocial behavior are calculated, the remainder of population variation, 30%, is assumed to reflect environmental influences not shared by family members (labeled as "nonshared," "unique," or "person-specific" experiences). These experiences might include criminogenic experiences unique to the individual and not shared with his sibling, such as a head injury, being the unique target of sexual abuse, living with an antisocial spouse, or serving a prison sentence. Estimates of this effect are shown in the third column of Tables 3.1 to 3.3.

### 1. Caveats

Four important caveats to the conclusion that unique experiences account for 30% of population variation in antisocial behaviors should be considered. First, we should not underestimate the part of the so-called "unique environment" estimate that may arise from simple measurement error. Measurement error comes into the calculation because random mistakes in measuring behavior will result in scores that look different for twins in an MZ pair, and it is not easy to differentiate such faux MZ differences from true MZ differences caused by the twins' unique experiences. To ascertain a crude estimate of how much of the variance estimate might reflect real experience, as opposed to measurement error, we might focus on the estimates from studies that use structural factor modeling approaches to derive latent measures of the antisocial behavior

construct that are virtually free from measurement error. A handful of studies have constructed latent composites of twins' antisocial behaviors from multiple sources of data, using reports from the self, mothers, fathers, and teachers (Arseneault *et al.*, 2003; Burt *et al.*, 2001; O'Connor *et al.*, 1998a; Scourfield *et al.*, 2004, 1995). Their estimates of the unique environment effect were 18, 34, 25, 0, and 8%, respectively, averaging about 20%. This exercise suggests that as much as one-third of the 30% unique environment estimate from quantitative behavioral–genetic models may reflect error, and as such, the unique environment component may have been overemphasized somewhat.

The second caveat is that the coefficient for unique environmental effects indexes not only the direct effects of unique experiences but also the effects of interactions between unique environments and genes (Purcell, 2002; Rutter and Silberg, 2002). To the extent that an experience influences twin one more than co-twin two, and this greater influence depends on twin one's vulnerable genotype, this effect will be subsumed in the estimate of unique environment effects.

The third caveat is that a proposal has been made that this variance component reflecting unexpected dissimilarity among family members might not represent the influence of objective environmental experiences at all (Turkheimer and Waldron, 2000). The alternative put forward is that this variance component may arise from stochastic developmental events and idiosyncratic processes not accessible to empirical study. Debate about this is underway, resolution has not been achieved, and an in-depth treatment of the debate is beyond the scope of this article, but a couple of points are relevant to the study of antisocial behavior. First, Turkheimer and Waldron (2000) invoked stochastic causation in large part because they observed that studies measuring nonshared experiences so far (e.g., different child–peer interactions, different child–teacher interactions, birth order) report that such experiences have only small effects on behavioral differences among family members. However, it is not known whether these small effect sizes will also apply to antisocial behavior, because its main risk factors (e.g., child abuse and neglect, bonding with an antisocial partner, and drug addiction) have not yet been tested in studies of differential experience. Second, the reason for debate about interpretation of the unique-environment component in the first place was that, after common environment influences on most phenotypes were found to be nil, unique experience was put forward as the best if not only hope for finding environmental causes of psychopathology (Plomin and Daniels, 1987). However, with respect to antisocial behaviors, common and unique environment influences each explain about 20% of population variation in antisocial behavior and new studies of gene × environment interactions suggest the effects of individual experience can be large among subgroups at genetic risk. Thus, students of

antisocial behavior should be aware of the hypothesis that nonshared variance is stochastic variance but not overly discouraged by it.

The fourth caveat is that some longitudinal twin studies have suggested that whatever the actual experiences are that produce this unique component of variance; their effects on behavior are not lasting. For example, in a sample of twins assessed longitudinally, unique effects explained 24% of sample variation in antisocial behavior at age 7 and 24% again at age 14, but these unique effects explained only 6% of the stability of antisocial behavior across age. This means that although unique influences were important in many twins' lives at both ages, this influence was being shown by different twins at each age (Eley *et al.*, 2003). Common environment influences on antisocial behavior, in contrast, were very stable over time. This pattern has emerged in other studies, but it is not yet clear whether it will become a rule of thumb.

## D. Summary of quantitative genetic findings

Quantitative behavioral–genetic research reviewed in this section has revealed that genetic causal processes account for only about half of the population variation in antisocial behavior in any given research sample, thereby unequivocally proving that environmental influences account for the other half. This fact constitutes a remarkable contribution to the understanding of causation (Plomin, 1994). We need to know the sizes of omnibus genetic and environmental contributions for two reasons. First, if the genetic contribution is not zero, then it must be controlled in all further studies of alleged nongenetic causes of antisocial behavior. Without control for genetic variation, further risk-factor research is ambiguous if not uninformative. Second, if the environmental contribution is not zero, this affords more optimism about intervention. Of course, even if a disorder's origins were 100% genetic, this would not preclude intervention. This reassuring truism is often illustrated using the genetic disease phenylketonuria (PKU), which can be controlled by adhering lifelong to a strict diet. Hair color, like PKU, is 100% genetically determined. But it is easy to change brunette to blonde, again by using a targeted biological intervention. However, note that in the cases of hair color and PKU because knowledge of genetic influences has helped us to understand the causal processes, we know what environmental interventions to apply. Moreover, because we understand the causal processes, we know that intervention must be stringently maintained over the long term, lest the brunette color or the degenerative brain disease resurface. It would be highly unlikely that any behavior disorder is wholly determined by genes, but it is important to begin any program of research into causal processes by ascertaining what effect sizes we can expect for both genetic and environmental influences under natural conditions, in the absence of

intervention. For individual differences in antisocial behavior in the overall population, these effects are approximately 50:50 (keeping in mind all the previously-noted caveats).

## III. DO THE OMNIBUS ESTIMATES OF GENETIC AND ENVIRONMENTAL INFLUENCES ALWAYS APPLY, OR DO THESE INFLUENCES VARY UNDER DIFFERENT CONDITIONS?

Research reviewed here and elsewhere has suggested that genes account for about 50% of the population variation in antisocial behaviors. However, this omnibus estimate might conceal important heterogeneity in the genetic effects across subgroups. This section addresses genetic influence with regard to sex differences, cohort effects, violence, psychopathy, antisocial behavior that is comorbid with other disorders, and assortative mating between antisocial men and women.

### A. Is there a sex difference in the genetic influence on antisocial behaviors?

Sex differences in heritability of antisocial behaviors have been the target of extensive research. A sex difference may exist, but if it does it is very small (Eley *et al.*, 1999; Jacobson *et al.*, 2002; Silberg *et al.*, 1994; van der Valk *et al.*, 1998a). The estimates are not tabled by sex in this article because the evidence goes against any importance for sex differences.

There are several sources of confusion about sex differences in genetic influences on behavior. Rhee and Waldman (2002) point out that some of the unclarity arises because researchers have confused behavioral–genetic models (which ascertain the magnitude of genetic influences on individual differences within each sex) versus threshold models (which ascertain differences between the sexes in the degree of combined genetic and environmental liability required to express a disorder; Slutske *et al.*, 1997). The threshold model argues that because females experience gender-role socialization against antisocial acts, any female who becomes antisocial must be under very strong genetic influence. Elsewhere the empirical evidence is reviewed, the bulk of which suggests this model is not correct; the relatively few females who express antisocial behavior experience the same risk factors to the same extent as antisocial males (Moffitt *et al.*, 2001). Further confusion arises from studies that have observed that more antisocial children are produced by antisocial mothers versus antisocial fathers, and deduced from this that antisocial women must be transmitting

stronger genetic liability to their offspring (Baker *et al.*, 1989). However, as a natural consequence of the relative rarity of antisocial women, only one-third of antisocial men can mate with an antisocial woman, whereas fully two-thirds of antisocial women mate with an antisocial man (Cloninger *et al.*, 1978; Smith and Farrington, 2003). It follows that the children of an antisocial mother are twice as likely as children of an antisocial father to have two antisocial parents instead of one, and the children's greater likelihood of becoming antisocial probably stems from this two-parent risk, rather than from their mothers' female sex. Finally, a little-appreciated feature of sex-related chromosomal variation could produce an artifactual sex difference in heritability estimated from twins. Females have two X chromosomes, one of them is randomly subjected to inactivation, and this random inactivation could make female MZ twins less identical than male MZ twins on phenotypes associated with X-linked genes (Jorgensen *et al.*, 1992; Loat *et al.*, 2004). If antisocial behavior were associated with X-linked genes, we might expect somewhat lower heritability for female than male antisocial behavior.

On balance, the results of model tests in large samples indicate that heritability estimates sometimes appear to be slightly lower among females than males. However, formal tests of sex-specific models of heritability concur that sex-specific models are not justified (Eaves *et al.*, 1997; Finkle and McGue, 1997; Gjone and Stevenson, 1997a; Kendler *et al.*, 2003; Taylor *et al.*, 2000). The metaanalyses agree, and they had ample statistical power to detect a sex difference, if it had been there (Miles and Carey, 1997; Rhee and Waldman, 2002). Nonetheless, even if the genetic processes leading to antisocial behavior were exactly the same processes in males and females, this would not preclude the possibility that genetic differences between the sexes can explain the sex difference in antisocial behavior. This is because sex differences can be produced if the sexes experience the same cause but in different amounts (Moffitt *et al.*, 2001; Rowe *et al.*, 1995). This truism can apply to genes, raising the interesting possibility that further research into X-linked (and perhaps Y-linked) genotypes may help to explain part of the sex difference in antisocial behavior. To date, molecular genetic research has not been harnessed to the question of sex differences in antisocial behavior, but it may prove informative in the future (Rutter *et al.*, 2003).

## B. Are there historical cohort differences in the genetic influence on antisocial behaviors?

On the one hand, a historical increase in the amount of environmental variation relative to genetic variation might produce a downward shift in heritability estimates (e.g., if the genotype remains stable, but economic inequalities widen). On the other hand, a historic shift toward liberal social conditions that allow

people more freedom to express their genetic liability might produce an upward shift in heritability estimates (Dunne *et al.*, 1997). Two studies have compared birth cohorts from roughly 1900 to the 1970s (Jacobson *et al.*, 2000; Slutske, 2001). In both studies, the elder cohorts' recall of antisocial behavior was more remote, less reliable, and subject to more underreporting than the younger cohort's recall, which could have produced spurious cohort differences (Simon and VonKorff, 1995), but no differences were found. This null finding can be confirmed by thought experiment using Tables 3.2 and 3.3, to compare the 20 studies of adults published before 1989 or earlier (cohorts born between 1920 and 1960s) versus the 11 studies of young people published 1998 or later (cohorts born after the 1970s). The older-cohort studies used mainly official measures, whereas the younger-cohort studies used mainly parent reports, which again should bias toward spurious cohort differences. Nonetheless, no systematic pattern of cohort differences suggests itself.

## C. Is there a genetic influence on physical violence?

Public debates about the implications of heritability for criminal responsibility often focus on violent crime (Buchanan *et al.*, 2001; Glover, 1996; Rose, 2000; Ross and Shestowsky, 2003). To date, findings about genetic effects on violence are rare and inconsistent. Three studies report evidence of nil heritability for violence (Bohman *et al.*, 1982; Mednick *et al.*, 1984; Sigvardsson *et al.*, 1982), whereas three other studies report evidence that the genetic influence on violence is about the same as that for nonviolent antisocial behavior, 50% (50% in Cloninger and Gottesman, 1987; 32% in Rowe *et al.*, 1999; 55% in Rushton, 1996). The studies finding nil heritability used Scandinavian registers of conviction and low base rates compromised their power to detect effects (Carey, 1994). An area overlooked by behavioral–genetic research to date is partner violence; only one abstract has been reported, in which 1711 men in the Vietnam Era Twin Study were asked whether they ever hit or threw things at their female partners, yielding a heritability estimate of 38% for this question (Toomey *et al.*, 1997). Three behavioral–genetic studies have found moderate genetic influence on the MPQ Aggression scale (Table 3.3), which measures attitudes approving physical violence and has been shown to predict future conviction for violent crime (Moffitt *et al.*, 2000). A heritable liability toward violence remains a reasonable hypothesis.

## D. Is there a genetic influence on the psychopath?

Psychopathy is a clinical term applied to a subset of individuals considered to be qualitatively distinct from other offenders because their clinical presentation combines persistent and severe antisocial acts with a distinctive personality style

(callousness, lack of remorse, egocentricity, manipulativeness, and superficial charm; Hart and Hare, 1997) and distinguishing cognitive features (Blair, 1995). Behavioral–genetic studies report moderate heritability (22–67%) for scales assessing psychopathy-related traits in samples of children (Viding *et al.*, 2005), adolescents (Taylor *et al.*, 2003), and adults (Blonigen *et al.*, 2003; Lyons *et al.*, 1995). Raine (1993, pp. 76–78) concluded that no existing twin or adoption study had used a compelling diagnosis of true psychopathy, and this is still the case. The evidence base for psychopathy is not sufficient to support conclusions, but it seems reasonable to expect psychopathy to be heritable.

## E. Are genetic influences involved when antisocial behavior co-occurs with other forms of psychopathology, such as hyperactivity?

Epidemiological studies concur that more than 90% of individuals having conduct or antisocial personality disorder also meet diagnostic criteria for other disorders (Newman *et al.*, 1996; Robins and Regier, 1991), and conduct disorder has been shown to feature prominently in the developmental history of virtually every adult psychiatric disorder, including schizophrenia and eating disorders (Kim-Cohen *et al.*, 2003). A key hypothesis is that the co-occurrence of two disorders in one person arises from shared genetic causation. This hypothesis is tested in a "bivariate behavioral–genetic analysis" in which one twin's symptoms of conduct disorder are correlated with his co-twin's symptoms of the other disorder. If the resulting cross-trait cross-twin correlations are stronger for MZ than DZ pairs, this implies that twin A's genetic liability to conduct disorder influences twin B's genetic liability to the other disorder (i.e., the same genetic factors contribute to the two disorders) (Neale and Cardon, 1992; Waldman and Slutske, 2000). If two disorders are frequently comorbid and have substantial genetic influence and if most of their comorbidity arises from shared genetic influence, these circumstances stimulate important questions (Slutske *et al.*, in press). This directs (1) nosologists to question the two disorders' putative independence, (2) developmentalists to ask which disorder emerges earliest in ontology, (3) neuroscientists to investigate the two disorders' shared brain correlates, and (4) gene hunters to check whether genes associated with one disorder are also associated with the other.

There is frequent comorbid overlap between antisocial behaviors and hyperactive–impulsive–inattentive behaviors in the young population, and this comorbid presentation predicts poor prognosis into adulthood (Lynam, 1996; Waschbusch, 2002). Six studies have reported quantitative behavioral–genetic analyses of overlap between hyperactive–impulsive–inattentive and antisocial behaviors (Burt *et al.*, 2001; Nadder *et al.*, 2002; Silberg *et al.*, 1996; Thapar *et al.*, 2001; Waldman *et al.*, 2001; Young *et al.*, 2000). Taken together these

studies indicate that most if not all of the considerable overlap between hyperactive–impulsive–inattentive and antisocial behaviors can be ascribed to genetic influences they share, with several estimates reaching 90–100%. Other comorbid combinations are being investigated as well. There are reports about antisocial behavior and depression symptoms (e.g., Jaffee *et al.*, 2002; O'Connor *et al.*, 1998b), antisocial behavior and pathological gambling (e.g., Slutske *et al.*, 2001), and antisocial behavior and substance abuse (e.g., Hicks *et al.*, 2004; Jang *et al.*, 2000; Kendler *et al.*, 2003; Krueger *et al.*, 2002; Miles *et al.*, 2002; Slutske *et al.*, 1998; True *et al.*, 1999; Waldman and Slutske, 2000). In each pair of comorbid problem behaviors, so far genes explain roughly 40–90% of the overlap. The promiscuous way in which antisocial behavior co-occurs beyond chance with virtually all major mental disorders (Kim-Cohen *et al.*, 2003; Lambert *et al.*, 2001), coupled with initial evidence that much of this co-occurrence has genetic origins, suggests a hypothesis—the presence of marked antisocial symptoms might signal greater severity in an individuals' genetic liability toward any and all psychopathologies.

## F. Can antisocial experience influence genes?

This review has emphasized the way by which genes influence the distribution of antisocial behaviors in the population. A less-appreciated finding is that antisocial behaviors can influence how genes are distributed in the population. Men and women mate on the basis of similarity between the two partners' antisocial behavior (Farrington *et al.*, 1996, 2001; Galbaud du Fort *et al.*, 2002; Krueger *et al.*, 1998; Rowe and Farrington, 1997). Reported correlations between couple members are moderate to large in size (approximately .50). Although many dual-antisocial relationships do not last, the individuals in them tend to have more children than the norm (Krueger *et al.*, 1998). If parents mate assortatively for successive generations, genes relevant to antisocial behavior will become concentrated within families and entire families will increasingly differ from each other as a result of genetic and environmental modes of intergenerational transmission. Height provides a corollary; after generations of mild assortative mating for height, families are made up of people who are similar on height, and whole families tend to differ from other families on height. It is possible that assortative mating may in part account for a puzzling and unexplained fact about antisocial behavior. The prevalence of conduct problems among young people has been rising slightly during the 20th century (Collishaw *et al.*, 2004; Rutter and Smith, 1995). This increase is thought to be too rapid to be explained by a shift in the population genome, so it is presumed to be the result of worsening trends in the environmental causes of antisocial behaviors (Rutter and Smith, 1995). Nevertheless, if assortative mating for antisocial behavior increased over several successive generations and if antisocial individuals who mate assorta-

tively produced more children than average, then in combination these two processes could increase the population prevalence of antisocial behavior. It is likely that assortative mating for antisocial behavior has increased as a side effect of assortative mating for education. An enormous historical rise in assortative mating across the 20th century has been quantified for educational attainment (Mare, 1991). People tend to select a mate when they complete schooling. In the 1930s, when almost all Americans finished schooling in their mid-teens (e.g., 90% of women completed only 12 years of schooling), a variety of partners was available to choose from. But as demands for more education grew, people leaving school began to find their pool of prospective partners limited to those leaving school at the same age (in 1987, 50% of women had 12 years or fewer of schooling, 25% had 1–3 years of college, and 25% had 16 years or more of education). As women came to be breadwinners across the 20th century, men with good economic prospects increasingly competed for women with similarly good economic prospects. Antisocial behavior is a strong correlate of educational attainment (Harlow, 2003; Miech *et al.*, 1999; Moffitt *et al.*, 2002). Young people who engage in antisocial activities have high rates of school drop-out and school expulsion and restricted opportunities for higher education (Cairns and Cairns, 1994; Nagin *et al.*, 2003). As a result, their pool of potential mates may be limited to others also having little education; mates who are also statistically likely to engage in antisocial behavior. In this way, increasing assortative mating for education may inadvertently bring about an increase in the number of large families afflicted with coinciding genetic and environmental causes of antisocial behavior. Coinciding genetic and environmental risks often potentiate each other (Rutter and Silberg, 2002) and one consequence could be an increase in the prevalence of young people with conduct problems. This scenario remains speculative. It is included here to make the point that behavior can influence the gene pool and to provoke research. Uncovering reasons behind historic rises in prevalence can inform efforts to reduce prevalence.

## IV. TESTING DEVELOPMENTAL THEORY OF ANTISOCIAL BEHAVIOR

It is often said disparagingly that behavioral–genetics research is "a–developmental" and "a–theoretical". However, this is far from true, and behavioral–genetic methods are ideal for testing developmental theories about age-related changes in etiology (DiLalla, 2002). Think of the heritability statistic as an outcome variable. When the heritability coefficient changes with age, this suggests that the balance of genetic versus environmental causal processes in the population leading to antisocial behavior differs at successive developmental stages in the life course. For example, the heritability coefficient for IQ increases

from childhood to adulthood, and conversely the common environment coefficient for IQ decreases from childhood to adulthood (Cherney *et al.*, 1997; McGue *et al.*, 1993). A similar age-shift has been reported for bone mineral density (Hopper, 1999). These findings have been interpreted developmentally, suggesting that the effects of environmental factors shared by siblings dissipate once the siblings leave home and live apart. The study of antisocial behavior provides another compelling example of the application of behavioral genetics to testing developmental theory, but the pattern of developmental findings is rather different from that of IQ and bone mineral density.

## A. Stronger genetic liability may be associated with life-course-persistent than adolescence-limited antisocial behaviors

Research has provided support for a developmental taxonomy of antisocial behavior (Moffitt, 1993), which proposed two primary prototypes (i.e., life-course-persistent versus adolescence-limited antisocial individuals). Life-course-persistent offenders' antisocial behavior is thought to have its origins in neuro-developmental processes, and it begins in childhood and continues persistently thereafter. In contrast, adolescence-limited offenders' antisocial behavior is thought to have its origins in processes of social influence; it begins in adolescence and desists in young adulthood. Research has shown that adolescence-limited antisocials are common, relatively transient, and near normative, whereas life-course persistent antisocials are few, persistent, and pathological (for a review of research into this taxonomy since 1993, see Moffitt, 2003). If genetic etiological processes contribute more to life-course-persistent than adolescence-limited antisocial development, we would expect to find that heritability estimates are larger for antisocial behaviors committed by young children and adults than for antisocial behaviors committed by adolescents (Moffitt, 1993, p. 694).

DiLalla and Gottesman (1989) were the first to observe that adult crime seemed to be more heritable than adolescent juvenile delinquency. As it turns out, the lack of heritability among juveniles in their review probably resulted from low power and insensitive measurement; in 1989 the entire literature of behavioral–genetic studies of juvenile delinquency consisted of fewer than 200 twin pairs, and the measure of antisocial behaviors was conviction, a rare outcome for juveniles. Since then, a large number of better-designed behavioral–genetic studies have proven that juvenile antisocial behavior is at least somewhat heritable (see Tables 3.1 and 3.2). Nonetheless, among these studies, four groups of studies suggest that life-course-persistent antisocial behavior may have stronger heritable origins than its adolescence-limited counterpart.

The first group comprises four studies of large representative samples of very young twins (Table 3.1). Because life course persistent antisocial behavior

onsets early in life, if it is genetically influenced we would expect high heritability coefficients from studies of very young children. Dionne *et al.* (2003) report 58% heritability for aggression among 19-month olds. Van den Oord *et al.* (1996) report 69% heritability for aggression among 3-year olds. Van der Valk *et al.* (1998a) report 50% heritability for externalizing behaviors among 2–3-year-old boys and 75% for girls. Arseneault *et al.* (2003) report heritabilities of 61, 69, and 76 among 5-year-olds, for ratings of antisocial behaviors made by observers, mothers, and teachers, respectively. These high estimates for very young twins contrast against the lower estimate of 41% heritability from a metaanalysis of older samples (Rhee and Waldman, 2002).

A second group of studies has identified the two sub-types on the basis of the heterogeneity in the phenotype, often using the "Aggression" and "Delinquency" scales from the Child Behavior Checklist (CBCL) (Achenbach, 1991). The Aggression scale is thought to be associated with the life-course-persistent prototype because it measures antisocial personality and physical violence and its scores are stable across development, whereas the Delinquency scale is associated with the adolescence-limited prototype because it measures rule-breaking and its mean scores rise steeply during adolescence (Stanger *et al.*, 1997). In fact, both life-course-persistent and adolescence-limited young people engage in the behaviors on the Delinquency scale, but adolescence-limited young people are relatively more numerous and if they have less genetic risk, we would expect the Delinquency scale to yield lower heritability estimates than the Aggression scale. Twin and adoption studies of these scales report higher heritability for Aggression (around 60%), than Delinquency (around 30–40%), while the shared environment is significant only for the Delinquency scale (also around 30–40%) (e.g., Deater-Deckard and Plomin, 1999; Edelbrock *et al.*, 1995; Eley *et al.*, 1999; Schmitz *et al.*, 1995). The approach of contrasting two phenotypes within antisocial behavior was also taken by Viding *et al.* (2005), who reported that genes influenced 81% of the variation in antisocial behavior among callous, unemotional children, but only 30% of variation among the other children who engaged in ordinary antisocial behaviors. A different approach to contrasting two heterogeneous phenotypes was followed by Arseneault *et al.* (2003), who found that antisocial behavior that was pervasive across settings, was more heritable than antisocial behavior that was situational; heritability was 82% if a child's antisocial behavior was agreed on by four different reporters across settings at home and at school, but lower (28–51%) for antisocial behavior limited to one setting or one reporter. This finding has been replicated (Scourfield *et al.*, 2004).

A third group of studies has defined life-course-persistent antisocial behavior in terms of preadolescent onset, contrasting it against antisocial behavior that begins during the adolescent period. One study found early onset to be strongly familial and substantially heritable in contrast to adolescent onset,

which was less familial and largely influenced by environment (Taylor *et al.*, 2000b). In a Swedish twin study, 5-year continuity from childhood to adolescence in the CBCL Aggression scale was largely mediated by genetic influences, whereas continuity in the Delinquency scale was mediated both by the shared environment and genetic influences (Eley *et al.*, 2003).

A fourth group of studies has taken a developmental approach to the other end of the lifespan, defining life-course persistent antisocial behavior in terms of presence in adolescence combined with subsequent persistence to adulthood antisocial personality disorder. Two studies demonstrated that such persistent antisocial behavior was significantly more heritable than that limited to adolescence (Jacobson *et al.*, 2001; Lyons *et al.*, 1995). These longitudinal studies are supported by a metaanalysis containing adolescent and adult samples assessed with similar measures of aggression, in which adult samples generated significantly higher heritability estimates, on average, than adolescent samples (Miles and Carey, 1997). Rhee and Waldman's (2002) metaanalysis did not find higher heritability for adults than adolescents, because in the pool of studies they examined, age was wholly confounded with reporting source; adolescent studies used rating scales, whereas adult studies used official crime records.

Taken together, the four groups of existing studies suggest that the pattern of antisocial behavior that (1) begins early in life, (2) is pervasive across settings, (3) is characterized by aggressive personality traits, (4) includes physical aggression, and (5) persists into adulthood is associated with relatively more genetic influence than is the pattern of late onset, situational, and transient delinquency. What is missing from the evidence base are prospective-longitudinal twin studies that ascertain individual differences in trajectories derived from repeated measures of antisocial behaviors over meaningful developmental periods (Nagin *et al.*, 1995, 1999). The taxonomic theory would predict stronger MZ than DZ twin similarity for membership in a childhood-onset persistent trajectory and less MZ versus DZ difference in twin similarity for membership in an adolescent-onset transient trajectory.

## V. TESTING HYPOTHESES ABOUT ENVIRONMENTAL CAUSATION

During the 1990s, the assumption that "nurture" influences behavior came under fire. Traditional socialization studies of antisocial behavior that could not separate environmental influences from their correlated genes were challenged by four important empirical discoveries: (1) ostensible environmental measures are influenced by genetic factors (Plomin and Bergeman, 1991); (2) parents' heritable traits influence the environments they provide for their children (Kendler, 1996; Plomin, 1994); (3) people's genes influence the environments they encounter (Kendler, 1996; Plomin *et al.*, 1977); and (4) environmental

influences did not seem to account for the similarity among persons growing up in the same family (Rowe, 1994). It was said that although nonbehavioral–genetic studies might show that certain rearing experiences predict young people's antisocial outcomes, theories of causation based on findings from such designs were guilty of a fundamental logical error (i.e., mistaking correlation for causation) (Scarr, 1992). These challenges culminated in admonishments that so far the evidence for genetic influences outweighed the evidence for environmental influences within the family (Harris, 1998; Pinker, 2002; Rowe, 1994). Many social scientists responded to this claim, reasserting evidence for family environmental influences (Collins *et al.*, 2000; Reid *et al.*, 2002; Vandell, 2000). The best way forward to resolve the debate is to use genetically-sensitive designs that can provide leverage to test environmental causation.

To our knowledge, a study of antisocial behavior was the first ever in the behavioral sciences to apply behavioral–genetic methods to control for genetic confounds while testing an environmental hypothesis (VanDusen *et al.*, 1983). It was well established that low socioeconomic status is a risk factor for offending, but Mednick *et al.* were concerned that some dysfunctional genetic susceptibilities transmitted within families might account for the coincidence of fathers' low-status occupations with sons' antisocial activities. As such, they used the Danish Adoption Study data to disentangle the socioeconomic status that adoptees were conceived in (their biological father's occupational status) from the socioeconomic status in which they were reared (adoptive father's status). Results demonstrated that biological inheritance could not explain the majority of the class–crime connection; the social class in which people grow up had a direct causal environmental effect on their probability of criminal offending (VanDusen *et al.*, 1983).

A central barrier to interpreting an association between an alleged environmental risk factor and antisocial outcome as a cause–effect association is, of course, the old bugbear that correlation is not causation. Some unknown third variable may account for the association, and that third variable may well be heritable. For example, does the cycle of violence from abusive parent to aggressive child arise from environmental transmission, or genetic transmission (DiLalla and Gottesman, 1991)? This question is fundamental because studies of adoptions have documented the dispiriting fact that aggression emerges in adoptive children despite the fact that they were separated from their at-risk biological parents at birth and reared by skilled and loving adoptive parents. (For this result in a cross-fostering study of *Rhesus macaques*, see Maestripieri, 2003.) Because much research on the intergenerational transmission of antisocial behavior continues without genetic controls, this point cannot be made too often (Serbin and Karp, 2003).

A variable is called a risk factor if it has a documented capacity to statistically predict antisocial outcome. The causal status of most risk factors is

unknown, we know what predicts antisocial outcomes, but not how or why (Kraemer, 2003). Genetic influences can confound an environmental interpretation of the association between a risk factor and antisocial outcomes in two different ways. The first confound is termed a passive correlation between genotype and environment (rGE). A passive rGE confound occurs when a child's behavior and the environment his parents provide are correlated because they have the same origins in his parents' genotype (i.e., not because the bad family environment itself causes children's aggression). Parents may transmit to their child a genetic liability for aggression, and simultaneously provide an environment of violent and abusive maltreatment, which is symptomatic of the parent's own genetic liability for aggression. To the extent that parent-provided environments are under genetic influence, then the observed association between family environment and young peoples' antisocial outcomes could be a spurious artifact of a third variable causing both (i.e., genetic transmission).

The second confound is termed an "active" correlation between genotype and an environmental measure, and it is also abbreviated as "rGE" (Plomin *et al.*, 1977). Active rGE occurs when a person's behavior and the environment he receives are correlated because they have the same origins in his own genotype (i.e., not because the bad environment itself causes aggression). Active rGE occurs when people's genetically influenced behavior leads them to "(1) create, (2) seek, or (3) otherwise end up in environments that match their genotypes" (Rutter and Silberg, 2002, p. 473). Antisocial behavior "creates" social reactions from others when aggressive toddlers evoke harsh discipline, when bullies are rejected by peers and expelled from schools, when young shoplifters are convicted by courts, or when abusive husbands are divorced by their wives. Antisocial individuals "seek" environmental settings consonant with their proclivities when antisocial children gravitate toward a delinquent peer group, when antisocial young men and women mate assortatively, or when pedophiles seek volunteer work with children. People who have behaved antisocially selectively "end up in" criminogenic environments when misbehaving children are tracked into special classes for disturbed pupils, when troubled teenagers are recruited by gangs, when violent young men are imprisoned, or when parolees find nothing but unskilled jobs available to them. Like passive rGE, active rGE confounds interpretation of the association between risk factors and antisocial behavior. To the extent that criminogenic environments are elicited by a young person's genetically influenced behavior, then the observed association between environment and antisocial outcome could be a spurious artifact of a third variable that causes both (i.e., the young person's genotype).

Ordinary studies cannot test whether a risk factor is causal, and it would be unethical to assign children to experimental conditions expected to induce aggression. To rule out rGE to test causal hypotheses, researchers have three options. First, researchers can use the longitudinal method to show that an

environmental event coincides with the timing of within-individual behavior change (a natural experiment that rules out rGE by using participants as their own controls) (Cicchetti, 2003; Costello *et al.*, 2003). Second, researchers can test causation by implementing a randomized trial to show that altering the environment can reduce disordered behavior (a treatment experiment that rules out rGE by random assignment) (Howe *et al.*, 2002). Third, behavioral–genetic designs are a useful addition to a toolkit for testing environmental causation. It is somewhat counterintuitive to think about using behavioral–genetic designs to control for and rule out genetic influences while highlighting environmental influences in bas relief, but paradoxically, this is one of their strongest applications. The studies reviewed in a later section are not intended to be exhaustive, but are intended to illustrate the kinds of studies being done.

The new generation of behavioral–genetic research designs that can evaluate whether a risk factor has an environmentally mediated effect on children's aggression has three key features. First, the studies must employ a genetically sensitive design to control for the confounding effects of parents' genes (passive rGE) or children's genes (active rGE) on putative environmental measures. The second key feature is that designs must employ an observed measure of the construct alleged to have environmental effects on antisocial behavior. Traditional quantitative behavioral–genetic studies have reported latent environmental variance components, but not observed measures. The third key feature is that genetically informative samples must accurately represent the full range of families' environmental circumstances. Many behavioral–genetic samples suffer substantial biases in recruitment and attrition, inadvertently restricting their range of participating families to primarily the middle class. Contemporary theories of psychopathology implicate experiences outside the normal range, such as exposure to domestic violence or child maltreatment, which are generally concentrated in the poorest segment of the population, the segment not sampled by most behavioral–genetic studies. (Scandinavian national twin registers of psychiatric hospital and court records accurately represent variation in the population, but such register studies have been unable to measure children's environments directly.)

It is possible to incorporate a measured "environmental" risk factor into a study of twins to test if a shared experience makes twins more similar on antisocial behavior than could be predicted, based on their degree of genetic relationship. A basic approach is to conduct ordinary behavior–genetic modeling, which apportions genetic versus environmental effects on twins' behavior (ACE), and then add a measured putative environmental risk factor (M-ACE) to test if the twins' shared experience of that risk factor can account for any of the shared environmental variation in their behavioral phenotype. The first twin study to apply this approach to problem behavior reported that living in a deprived neighborhood explained a significant 5% of the shared environmental

variation in 2-year olds' behavior problems (Caspi *et al.*, 2000). Another study applied this approach to examine 5-year-old's exposure to their mothers' experience of domestic violence (Jaffee *et al.*, 2002). Exposure to domestic violence over the first 5 years of their lives was particularly relevant for children who developed both externalizing and internalizing problems simultaneously; such co-occurring problems are associated with poor prognosis. Domestic violence exposure explained a significant 13.5% of the shared environment variance in children's comorbid outcome. A caveat about this approach is in order. Inference of environmental causation is compromised if parent and child share genes that simultaneously influence both the measure of environment and the measure of child antisocial behavior.

Use of the basic twin design to test "environmental" risk factors has been improved upon by adding indicators of mothers' and fathers' behavioral phenotype to the usual indicators of twin behavior. This approach, called the "extended twin-family design" (Kendler, 1993), estimates the effect of the putative environmental risk factor on child behavior when controlling for genetic effects on both parents and children. An assumption of the design is that the parental phenotype measures carry genetic information parallel to that in the child phenotype measures. (Although this assumption is seldom fulfilled perfectly it seems not unreasonable for antisocial behavior, which has strong child-to-adult continuity.) The first twin study to apply this approach to parenting was reported from the Virginia Twin Study of Adolescent Behavioral Development (Meyer *et al.*, 2000). Antisocial conduct problems were assessed for adolescent twins and their parents in 1350 families. The measured parenting variables were called "marital discord" and "family adaptability". No effect was found for marital discord, but measured family adaptability accounted for 4% of the variance in adolescents' conduct problems.

Another approach is to use twin-specific measures of the "environmental" risk factor, which allows researchers to test whether an active rGE (i.e., a child effect evoking risk) accounts for the association between the risk factor and antisocial outcome. The Environmental Risk Longitudinal Twin Study used this approach to examine the effects of physical maltreatment on young children's aggression (Jaffee *et al.*, 2004b), using twin-specific reports of maltreatment. This study satisfied six conditions that together supported the hypothesis that physical maltreatment has an environmentally mediated causal influence on children's aggression: (1) children's maltreatment history prospectively predicted aggression, (2) the severity of maltreatment bore a dose–response relation to aggression, (3) the experience of maltreatment was followed by increases in aggression from prior levels, within individual children, (4) there was no child effect evoking maltreatment, (5) maltreatment predicted aggression while mothers and fathers' antisocial behavior were statistically controlled; and (6) modest but significant effects of maltreatment on aggression remained present

after controlling for genetic transmission of liability to aggression in the family. A similar analytic approach using twin-specific measures of risk was taken by the Minnesota Twin Family Study (Burt *et al.*, 2003), which studied 808 cases with 11-year-old twin pairs. Models revealed that measured parent–child conflict accounted for 12% of the variance in the externalizing syndrome of oppositional, conduct, and attention-deficit-hyperactivity disorders (23% of the common environment variation in this syndrome).

The Environmental Risk Longitudinal Twin Study also focused on MZ twins only to test if differences between siblings' exposure to differential parental treatment makes them different on antisocial behavior. The fact that MZ twins are not perfectly concordant for antisocial behavior opens a window of opportunity to uncover if a nongenetic cause specific to one twin has produced the behavioral difference. Comparing the experiences of discordant MZ twins allows the least ambiguous interpretation of results. Three studies have reported that MZ twin differences in parental treatment are correlated with MZ twin differences in antisocial behavior (Asbury *et al.*, 2003; Caspi *et al.*, 2004; Pike *et al.*, 1996).

The Environmental Risk Longitudinal Twin Study reported that within 600 MZ twin pairs, the twin who received relatively more maternal negativity and less maternal warmth developed more antisocial behavior problems (Caspi *et al.*, 2004). Negativity and warmth were measured by coding voice tone and speech content in mothers' audio taped speech about each of their twins separately, according to the "expressed emotion" paradigm. This study provided evidence that the effect of mothers' emotional treatment of children causes antisocial behavior, by ruling out five alternative explanations of the finding: (1) using MZ twin pairs ruled out the possibility that a genetically transmitted liability explained both the mother's emotion and her child's antisocial behavior; (2) using MZ twins also ruled out the possibility that a genetic child effect provoking maternal emotion accounted for the finding; (3) the study included a longitudinal natural experiment to rule out the possibility that any nongenetic child effect accounted for the finding, by controlling for prior child behavior that could have provoked maternal negative emotion; individual children whose mothers were negative toward them at age 5 evidenced a subsequent increase of antisocial behavior between age 5 and 7; (4) the study controlled for twin differences in birth weight in an effort to rule out the possibility that twins with neuro-developmental difficulties had more behavior problems that elicited more negative emotion from mothers; (5) the study measured the children's behavior using teacher reports to rule out the possibility that a mother's negativity toward a child led her to exaggerate her report of the child's behavior problems. These studies testing measured environmental variables were conducted very recently, illustrating that such testing is a new direction in behavior–genetic research (Dick and Rose, 2002; Kendler, 2001). So far, behavior–genetic designs

have been applied to test causation for only a handful of risk factors for antisocial behavior. We expect the list of risk factors studied with behavioral–genetic controls to grow to encompass environmental factors ranging from prenatal teratogens to prison sanctioning of adult offenders.

## VI. TESTING THE HYPOTHESIS OF INTERACTION BETWEEN GENES AND ENVIRONMENTS

The study of gene–environment interaction entails substantial methodological challenges. It requires measured environments that are truly environmental, measured genetic influence, some means of separating them from each other, and enough statistical power for a sensitive test of interaction (Rutter and Silberg, 2002). Despite the challenges, theory driven hypotheses of G × E interaction are well worth testing because where measured G × E are found to influence behavior disorders, both specific genes and specific environmental risks can conceivably have moderate-to-large effects. Specific genes revealed to be stronger in the presence of environmental risk would guide strategic research into those genes' expression, possibly leading to genetic diagnostics and improved pharmacological interventions (Evans and Relling, 1999). Specific environmental effects revealed to be stronger in the presence of genetic risk would prompt a new impetus for specific environmental prevention efforts, and would help to identify who needs the prevention programs most. The study of G × E is especially exciting in antisocial behavior research, where investigations have pioneered the way for all behavioral disorders. Studies of antisocial behavior were first to report evidence of interaction between latent genetic and latent environmental risks ascertained in adoption studies, and also first to report evidence of an interaction between a measured genetic polymorphism and a measured environmental risk.

### A. Adoption studies of latent G × E

The first evidence that genetic and environmental risks influence antisocial behavior together in a synergistic way came from adoption studies. Among the 6000 families of male adoptees in the Danish Adoption Study, 14% of adoptees were convicted of crime though neither their biological nor adoptive parents had been convicted, whereas 15% were convicted if their adoptive parent alone was convicted, 20% were convicted if their biological parent alone was convicted, and 25% were convicted if both biological and adoptive parents were convicted, although there were only 143 such cases (Mednick and Christiansen, 1977). This pattern of percentages did not represent a statistically significant cross-over interaction term, but it did illustrate clearly that the effects of genetic

and environmental risk acting together were greater than the effects of either factor acting alone. The finding was buttressed by two studies from American and Swedish adoption registers completed about the same time (Cadoret *et al.*, 1983; Cloninger *et al.*, 1982).

## B. Adoption studies of latent G × measured E

In a pool of 500 adoptees from the Iowa and Missouri adoption studies, adoptees had the most elevated antisocial behaviors when they experienced "adverse circumstances" in their adoptive homes as well as having birth mothers with antisocial personality problems or alcoholism (Cadoret *et al.*, 1983). This landmark study documented that the interaction was statistically significant, and replicated across two independent samples. This finding was replicated and extended in another Iowa adoption cohort of 200 families (Cadoret *et al.*, 1995). Adoptive parents' adversity was defined according to the presence of marital problems, legal problems, substance abuse, or mental disorder and it interacted significantly with biological parents' antisocial personality disorder to predict elevated rates of childhood aggression, adolescent aggression, and diagnosed conduct disorder in the adoptees. This Iowa adoption study was creatively analyzed to demonstrate that adversity in the adoptive home can moderate the genetic child-effect in which children's aggression provokes bad parenting (Riggins-Caspers *et al.*, 2003). Adoptees' genetic liability for antisocial behavior (defined as biological parents' psychopathology) provoked more harsh discipline from the adoptive parents in homes where the adoptive parents suffered adversity (marital, legal, substance, or psychopathology problems). The one problem in studying G × E in adoption designs is the adoption breaks up the naturally occurring processes of rGE that characterize the nonadopted majority population, thereby precluding the possibility of G × E (Stoolmiller, 1999). This separation allows the empirical study of G × E, but paradoxically, it probably results in an underestimate of the influence of G × E on antisocial outcomes. For this reason, adoption G × E studies should be complemented with twin studies.

## C. A twin study of latent G × measured E

Our E-risk twin study also yielded evidence that genetic and environmental risks interact (Jaffee *et al.*, 2005). Because we already knew that conduct problems were highly heritable in the E-risk twin sample at age 5 years (Arseneault *et al.*, 2003), we were able to estimate each child's personal genetic risk for conduct problems by considering whether his or her co-twin had already been diagnosed with conduct disorder, and whether he or she shared 100% versus 50% of genes with that diagnosed co-twin. This method's usefulness had been demonstrated previously in a landmark G × E study showing that the risk of depression

following life-event stress depends on genetic vulnerability (Kendler *et al.*, 1995). For example, an individual's genetic risk is highest if his or her co-twin sibling already has a diagnosis of disorder and the pair is monozygotic. Likewise, an individual's genetic risk is lowest if his or her co-twin has been free from disorder and the pair is monozygotic. Individuals in dizygotic twin pairs fall between the high and low genetic risk groups. In this study, an interaction was obtained so that the effect of maltreatment on conduct problem symptoms was significantly stronger among children at high genetic risk than among children at low genetic risk. (Because there was no genetic child effect provoking maltreatment, the genetic risk groups did not differ on concordance for maltreatment or the severity of maltreatment). In addition, the experience of maltreatment was associated with an increase of 24% in the probability of diagnosable conduct disorder among children at high genetic risk, but an increase of only 2% among children at low risk.

## D. Studies of measured G × measured E; testing a measured gene

The aforementioned adoption and twin studies established that genotype does interact with bad parenting in the etiological processes leading to antisocial behavior. However, the studies did not implicate any particular genes. One study was conducted to test the hypothesis of gene × environment interaction using a measured environmental risk, child maltreatment, and an identified gene, the MAOA polymorphism (Caspi *et al.*, 2002). We selected the MAOA gene as the candidate gene for our study for four reasons (*Caspi et al.*, 2002). First, the gene encodes the MAOA enzyme, which metabolizes the neurotransmitters linked to maltreatment victimization and aggressive behavior by previous research. Second, drugs inhibiting the action of the MAO enzyme have been shown to prevent animals from habituating to chronic stressors analogous to maltreatment, and to dispose animals toward hyperreactivity to threat. Third, in studies of mice having the MAOA gene deleted, increased levels of neurotransmitters and aggressive behavior were observed, and aggression was normalized by restoring MAOA gene expression. Fourth, an extremely rare mutation causing a null allele at the MAOA locus was associated with aggressive psychopathology among some men in a Dutch family pedigree, although no relation between MAOA genotype and aggression had been detected for people in the general population.

We selected maltreatment for this study for four reasons (Caspi *et al.*, 2002). First, childhood maltreatment is a known predictor of antisocial outcomes. Second, not all maltreated children become antisocial, suggesting that vulnerability to maltreatment is influenced by heretofore unstudied individual characteristics. Third, our abovementioned twin research had established that

maltreatment's effect on children's aggression is environmentally mediated (i.e., the association is neither an artifact of a genetic child-effect provoking maltreatment nor of transmission of aggression-prone genes from parents). As such, maltreatment can serve as the environmental variable in a test of gene × environment interaction. Fourth, animal and human studies suggest that maltreatment in early life alters neurotransmitter systems in ways that can persist into adulthood and can influence aggressive behavior.

Based on this logic to support our hypothesis of G × E, we measured childhood maltreatment history (8% severe, 28% probable, and 64% not maltreated) and MAOA genotype (37% low-activity risk allele and 63% high-activity allele) in the 442 Caucasian males of the longitudinal Dunedin Multidisciplinary Health and Development Study. We found that maltreatment history and genotype interacted to predict four different measures of antisocial outcome; an adolescent diagnosis of conduct disorder, an age-26 personality assessment of aggression, symptoms of adult antisocial personality disorder reported by informants who knew the study members well, and court conviction for violent crime up to age 26, the latest age of follow-up. Among boys having the combination of the low-MAOA-activity allele and severe maltreatment, 85% developed some form of antisocial outcome. Males having the combination of the low-activity allele and severe-to-probable maltreatment were only 12% of the male birth cohort, but they accounted for 44% of the cohort's violent convictions because they offended at a higher rate on average than other violent offenders in the cohort.

Replication of this study was of utmost importance, because the study reported the first instance of interaction between a measured gene and a measured environment in the behavioral sciences, and because reports of connections between measured genes and disorders are notorious for their poor replication record (Hamer, 2002). One initial positive replication, and extension, has emerged from the Virginia Twin Study for Adolescent Behavioral Development (Foley *et al.*, 2004). This team studied 514 Caucasian male twins and measured environmental risk using an adversity index comprised of parental neglect; interparental violence, and inconsistent discipline. MAOA genotype and adversity interacted significantly so that 15% of boys having adversity, but the high-MAOA-activity allele developed conduct disorder, in comparison to 35% of boys having adversity plus the low-activity allele. This study went a step further, controlling for maternal antisocial personality disorder to rule out the possibility that passive rGE might have resulted in the co-occurrence of environmental and genetic risk. This study thus replicated the original G × E between the MAOA polymorphism and maltreatment, extended it to other forms of parental treatment, and showed that it is not an artifact of passive rGE.

## E. Research implications of the nil main effect of the MAOA polymorphism on behavior

One important finding from these two studies of a measured gene was that, in contrast to the G × E interaction's marked effects on antisocial outcomes, the unique effects of MAOA genotype apart from its role in the G × E interaction were virtually nil. MAOA genotype was statistically unrelated to antisocial outcomes in the full cohorts, its effects were only revealed in the presence of maltreatment or adversity. Moreover, this pattern of a significant gene × environment interaction in the presence of an initial nil main effect of the measured gene has now emerged from a number of other G × E studies (Moffitt *et al.*, in press). This pattern of nil main effects for measured genes appears to be widespread, and if so, it has an implication for gene hunters. Gene-to-disorder connections may be diluted across all the individuals in a sample if the connection is apparent only among individuals exposed to specific environmental risks.

The expectation that simple direct paths will be found from gene to disease has not proven fruitful for complex psychiatric disorders—few linkage studies detect genes, many candidate gene association studies fail consistent replication, and genes that replicate account for little variation in the phenotype (Hamer, 2002). The MAOA G × E finding suggests four guiding hypotheses for future genetics research. First, a major source of error in linkage pedigrees, incomplete gene penetrance, could occur if a gene's effects are expressed only among family members exposed to environmental risk. Linkage studies should ascertain pedigree members' environmental risk exposure. Second, candidate gene studies will not replicate each other if G × E is operating and there are differences between research samples on risk exposure. Where possible candidate-gene association studies should measure and take into account subjects' environmental risk exposure. Third, most psychiatric genetics research, including genome-wide scans, aims to identify genes having main effects (i.e., to find genes that show associations with behavior irrespective of the environment), but this main-effects approach will not be efficient for detecting genes whose effects are conditional on environmental risk. (Interactions are independent of main effects, so main effects of risk factors are not a prerequisite for interactions between them.) Genome-wide scans might be more powerful if gene hunters deliberately recruit samples selected for known exposure to environmental risks for the disorder they wish to study. Finally, the two studies of the MAOA polymorphism showed that when G × E operates and risk exposure differs among participants within a sample, genes will account for little phenotypic variation and their effect sizes will be small to nil. To detect such small effects researchers have called for extremely large samples. Quantitative models of complex disorders having continuously distributed phenotypes have been interpreted to implicate many genes of small effect, but it is conceivable

that some of those "genes" might be environmental causes. In the Dunedin cohort, the G × E accounted for a sufficient proportion of psychiatric outcome to suggest a provocative hypothesis, that some multifactorial disorders, instead of resulting from many genes of small effect, might result from relatively fewer genes whose effect sizes are conditional on exposure to environmental risks. For revealing the effects of such conditional-effect genes, researchers will need to use strategic G × E research.

## F. Strategy for future G × E studies using measured genes

One can hope for careful, deliberate, and theory-guided G × E hypothesis testing of plausible triads of a candidate genetic polymorphism, a candidate environmental risk, and a behavioral phenotype. Elsewhere, we described in detail a research strategy to guide studies of measured gene–environment interaction (Moffitt *et al.*, 2005). What follows is a brief summary. Step 1 is to consult quantitative genetic models of the behavior in question derived from twin and adoption research. The estimate of genetic influence (i.e., the A term) in part represents gene–environment interplay, as does the estimate of unique environmental influence (i.e., the E term) (Purcell, 2002). When these quantitative estimates are moderate-to-large, this encourages constructing hypotheses about potential G × E interaction effects.

Step 2 is to identify candidate environmental risks for the behavior in question. It is necessary to glean from the literature the candidate environmental risk factors having the strongest predictive efficacy for each disorder. Fortunately, for the study of antisocial behavior, a large pool of candidate environmental risk factors is available (Loeber and Farrington, 1998). The best candidate environmental risks are those having evidence of a plausible effect on biological systems involved in psychopathology (e.g., maltreatment, DeBellis, 2001). Once candidate risks have been identified, it is important to go a step further to test whether each candidate risk factor has effects that are actually environmentally mediated. Why must G × E researchers prove environmental mediation? If an alleged environmental risk factor's association with psychopathology is wholly genetically mediated, then a putative G × E is really only an interaction between one specific gene and other unidentified genes. This article has described the several ways to test for environmental mediation.

Step 3 is to measure the environmental risk as well as possible. Measuring environmental risk exposure precisely and reliably can be costly, but simulations show that reliable risk measurement can hugely enhance power to detect G × E, thus reducing the need for large samples (Luan *et al.*, 2001; Wong *et al.*, 2003). Step 4 is to identify candidate susceptibility genes for a G × E hypothesis. The temptation to name candidate genes associated with antisocial behavior was resisted in this article because gene detection advances so rapidly that any

list made now will be shortly outdated; by the time the article comes to press a list would feature disappointing replication failures and omit newly found hot possibilities (Insel and Collins, 2003). However, one can propose the following guidelines for choosing candidate genes are best for a G × E hypothesis, as they emerge. First, seek empirical evidence that a gene has functional physiological significance in the brain (Tabor *et al.*, 2002). Second, good candidate genes for G × E will be those whose polymorphic variants are relatively common in the population. If a potentially damaging variant is maintained at a high prevalence rate, this might imply (but certainly does not guarantee) that natural selection has not eliminated the variant because it is only expressed under particular environmental conditions, or perhaps even because it confers advantage under particular conditions (Hill, 1999; Searle and Blackwell, 1999). From a more pragmatic point of view, common variants confer advantages of statistical power when testing interaction effects. As a third guideline for gene selection, if the gene has already been shown to have a replicated main-effect association with the psychiatric disorder, it will be an easy candidate choice. However, it is very important to appreciate that the endeavor cannot rely on such rare replicated main-effect associations because of the following paradox. Logically, if a gene's effects are conditional on the environment; this will have the natural consequence of diminishing researchers' capacity to detect a main effect!

As a final guideline for step 4, the most sound logical basis for selecting a candidate gene for G × E is evidence that the gene is related not to a disorder but rather to organisms' responses to environmental risk. This evidence is necessary to frame a biologically plausible hypothesis that the gene moderates responses to an environmental risk (i.e., G × E). As one example, the serotonin transporter polymorphism (5-HTTLPR) is a good candidate for G × E research into psychopathology because its two variants have been shown to affect physiological responsiveness to stressful environmental conditions in three experimental paradigms, including knockout mice (Murphy *et al.*, 2001), stress-reared *R. macaques* (Bennett *et al.*, 2002), and a human functional neuro-imaging paradigm (Hariri *et al.*, 2002). Most evidence of connections between genes and risk-responsiveness will emerge from studies of rodents and nonhuman primates having known human-relevant genotypes, because nonhuman animals can be subjected to environmental risk manipulations under experimental control (Crabbe, 2003; Flint, 2003; Francis *et al.*, 2003; Maxson, 2000; Meaney, 2001; Suomi, in press). A new wave of experimental investigations will ask if genotype influences human participants' responsiveness to emotion-eliciting stimuli or laboratory stress paradigms. These human studies will use psychophysiological phenotypes in G × E experimental designs, such as electrodermal reactivity, or reactivity of the brain as measured by the electroencephalograph and by functional neuro-imaging tools (Hariri *et al.*, 2002). The results of such studies will provide an evidence base to nominate gene candidates in G × E

hypotheses. Step 5 is to test for an interaction between the candidate gene and the environmental risk factor. The minimum design will begin with a pool of individuals exposed to environmental risk and hypothesize that genotype-risk individuals develop more psychopathology than genotype-controls (or the complement, beginning with individuals thought to be at genotypic risk and ascertaining whether individuals exposed to environmental risk develop more psychopathology than unexposed controls). The more informative design begins with a representative population-based cohort. For example, in the case of dichotomous genotypic and environmental variables, groups would include (1) low genotypic risk and environmental risk to establish the baseline level of psychopathology associated with factors apart from our hypothesis, (2) high genotypic but low environmental risk to ascertain any effect of the gene in isolation, (3) high environmental but low genotypic risk to ascertain any effect of risk environment in isolation, and (4) high genotypic and environmental risk to ascertain whether their joint association with psychopathology is additive or interactive (for more discussion of design issues and statistical approaches see Moffitt *et al.*, in press; Ottman, 1990; van Os and Sham, 2003; Yang and Khoury, 1997). Cohort designs allow us to report not only statistical significance but also to characterize the size of the G × E effect in the population, which is prerequisite for evaluating the potential clinical validity and utility of a finding.

Step 6 ensues if and only if the hypothesized G × E interaction is obtained. Step 6 is to evaluate whether the resulting associations show specificity to the initially hypothesized triad of gene, environmental risk factor, and disorder or extend beyond that triad. Work at this step systematically ascertains whether the interaction holds when the gene is replaced with other relevant candidate genes, when the environmental risk is replaced with the disorders' other risk factors, and when the disorder is replaced with other related disorder phenotypes. This step is exploratory. Whereas it is vital to frame a specific hypothesis of G × E prior to analyzing any data, once an initial hypothesis has been tested in the affirmative, it is also responsible scientific practice to ascertain how far beyond the original hypothesis the G × E may extend (Licinio, 2003).

Step 7 is replication, which is particularly vital because of the known difficulty of detecting interaction terms between any two factors, including genes.

Other kinds of research might also be stimulated by G × E findings. Knowledge that an environmental risk factor has stronger connections with a disorder ought to likewise kick-start new research into what brain mechanisms convert environmental experiences into the symptoms of psychopathology. Applied research might address the relevance of the G × E for clinical diagnostics and therapeutics. The 2002 report that maltreatment and the MAOA polymorphism interacted to predict antisocial outcomes stimulated

investigations in ethics, legal scholarship, and even theology (e.g., Nuffield Council on Bioethics, 2002; Peters, 2003; Ross and Shestowsky, 2003; Sankar, 2003; Stone, 2003).

## VII. THE WAY FORWARD

Behavioral–genetic research should be a priority because it has real world authenticity. Genetic and environmental risks for antisocial behavior often coincide in the same families, and these risks are concentrated together in the same small segment of the population. Because of this fundamental fact, developmental processes that originate where genetic and environmental risks coincide are the most relevant causal processes to study. "Bio-social" models of antisocial behavior made a good start at studying this co-occurrence (Raine *et al.*, 1997), but they did not tell the whole story because they did not disentangle environments from genes. Perhaps the most important point is that research that does not attack the co-occurrence of genetic and environmental risks will have only limited relevance for prevention. In contrast, findings from studies of the coincidence of genetic and environmental risks can be generalized to the real world circumstances where interventionists usually find their clients. As such, research into gene–environment interplay will continue to prove critical in the future of research into antisocial behavior. Some recommendations follow.

Behavior–genetic research into antisocial behavior should expand its focus beyond the current focus on young samples. If the aim is to explain the root etiology of serious and persistent antisocial behavior, then a research focus on childhood and the family environment is appropriate because that is when and where serious life-course-persistent antisocial behavior begins. However, there is far more to antisocial behavior that needs explaining. Gene–environment interplay research should embrace other risk factors, in other age periods, for example, the effects of peers on adolescents' delinquent offending and the effects of substance abuse on adults' domestic violence against partners. Behavioral–genetic research into the role of peers in antisocial behavior is well underway (e.g., Carey, 1992; Iervolino *et al.*, 2002; Plomin, 1994; Rose *et al.*, 2003; Rowe, 1985; Rowe and Osgood, 1984; Rowe *et al.*, 1992). To my knowledge there is no behavioral–genetic research into domestic violence outcomes.

Behavioral–genetic research into antisocial behavior should examine "endophenotypes." These are phenotypic traits or markers thought to represent biologic systems underlying a behavioral disorder, and therefore assumed to be under greater genetic influence than the disorder itself (Gottesman and Gould, 2003). For some disorders, such as schizophrenia, attention is shifting from the search for connections between genes and the disorder to the search for

connections between genes and endophenotypes, such as eye tracking or working memory. This shift offers advantages in statistical power because endophenotypes are generally better distributed than severe disorders, and they can be studied in nonpatients. However, the promise of endophenotypes must be tempered by cautions that each "underlying biological" variable is as likely to be a consequence as cause and may well be subject to the same gene–environment interplay processes as are disorders themselves (as opposed to representing a purer genetic etiology). That said, endophenotype studies will be very useful for explaining how genes increase the probability that people will commit antisocial acts. One edited volume suggests a starting list of endophenoytpes for antisocial behavior–sensation-seeking, over-activity, fearlessness, low self-control, negative emotionality, callous-unemotional style, weak verbal ability, poor memory, executive dysfunction, frontal lobe hypoarousal, serotonergic dysfunction, testosterone imbalance, and even large toddler body mass index (Lahey *et al.*, 2003). Bringing these traits into research in gene–environment interplay involves several steps. First, they can be examined in quantitative twin studies to ascertain if they are under genetic influence. Second, an endophenotype can be entered with antisocial behavior into a quantitative bivariate model, to ascertain how much of the correlation between endophenotype and disorder arises from genes predisposing to both. Third, traditional mediation models can ascertain whether the endophenotype mediates the pathway between measured genes and antisocial outcomes.

Behavioral–genetic research into antisocial behavior should be informed by findings from epigenetic studies. Although the DNA sequence is not itself altered by the environment, the science of epigenetic processes is revealing how environments can affect genes' capacity to influence phenotypes (Pray, 2004; Varmuza, 2003). Theorists are putting forward conceptualizations of genes as dependent variables that can be "switched on or off" by nongenetic influences (Johnston and Edwards, 2002; Ridley, 2003), or genes as mediating variables that carry out developmental processes initiated at the level of the environment (Belsky, 1997; Gottlieb, 2003). For example, compelling experiments show how variation in quality of parental care can alter gene expression and behavior in rat offspring (Cameron *et al.*, 2005; Meaney, 2001). This work has yet to be integrated into the study of antisocial behavior, but this is only a matter of time.

Behavioral–genetic research into antisocial behavior should benefit more from animal models. Nonhuman animal models of behavioral disorders offer undeniable scientific advantages, but the world of animal research has remained somewhat apart from the world of psychological research into human antisocial behavior, primarily as a result of skepticism about the validity of animal models for human behavior. The most often-used animal model in behavioral–genetic studies of aggression is the mouse intruder paradigm, in which the researcher introduces an intruder to the cage of the mouse subject

and measures the subject's latency to attack. The validity question applies to such animal models of aggression because the aggression is appropriate in the wild, biologically adaptive, and highly stylized (Sluyter *et al.*, 2003). Such animal behavior lacks strong parallels to the illegal behavior carried out by humans, which is considered inappropriate, is often maladaptive for the actor, and takes amazingly varied forms, involving force, but also fraud and theft committed by the same individual as part of an antisocial lifestyle. In contrast to this variation in the forms of human antisocial behavior, animals' aggression to defend territory has been so strongly selected that there is little variation within a species. Moreover, animal researchers must exert great efforts to artificially create individual differences by enforcing assortative mating to breed strains that differ on aggressive behavior (Cairns *et al.*, 1983). This stands in sharp contrast to the marked individual differences in aggression within the human population.

Luckily, animal models of disorders are not necessary for making a contribution to future GE research. Instead, there is huge potential for developing new animal models of environmental risk mechanisms, to clarify the nature of G × E interactions. Once an interaction between a gene and environmental risk is discovered in humans, uncovering the mechanisms behind it requires experimental inducement of environmental risk exposure, studies of the consequences for gene expression in brain tissue, and experimental manipulation of the genome. Such manipulations cannot be accomplished with human participants, but analogue methods are available, particularly in mice (Tecott and Wehner, 2001). The primary outcome measures in such research will be indicators of the animal's physiological and neurological reactivity to environmental risks, and indicators of gene expression in tissues of animals exposed to environmental risks. Animal models of environmental risk will prove to be invaluable tools for unpacking many elements of gene–environment interplay.

Behavioral–genetic research into antisocial behavior should incorporate treatment trials. Interventions are environments, and true randomized intervention trials are environments disentangled from any control by genetic influence. As such, harnessing interventions as environmental variables brings the power of experimental manipulation to the study of G × E interaction with human subjects. Note that this research is well under way in the field of pharmacogenetics, which explores genetic individuality in drug response to improve the efficacy and safety of prescribing (Evans and Relling, 1999; Wolf *et al.*, 2000). Given the known genetic influence on antisocial behavior, how far can interventions go to prevent the expression of genetic risk; just how powerful can the environment be when it is under our control? Integrating prevention research and behavioral–genetic research offers unprecedented opportunities to test etiological theories (Howe *et al.*, 2002).

Research into genetic and environmental influences is making great strides toward uncovering the root causes of antisocial behavior. This article has reviewed the large group of quantitative behavioral–genetic studies leading to the conclusion that environmental and genetic causes are equally important for antisocial outcomes. Newer findings are also emerging. Studies are revealing which risk factors are environmental causes not just correlates. Studies are testing for effects of measured candidate genes. Studies are sorting out how our genotypes sway our susceptibility to environmental causes, and how our environments rule the behavioral expression of our genotypes. The future of this work is exciting.

## Acknowledgments

Work on this review was supported by grants from the US National Institute of Mental Health (MH45070 and MH49414), the UK Medical Research Council (G9806489 and G0100527), and a Royal Society-Wolfson Research Merit Award. Helpful reviews of the article were provided by Louise Arseneault, Jay Belsky, Avshalom Caspi, Honalee Harrington, Julia Kim-Cohen, Robert Plomin, Michael Rutter, Kali Trzesniewski, Alan Taylor, and Essi Viding. Technical assistance was provided by Helena Kiernan.

## References

Achenbach, T. M. (1991). "Manual for the Child Behavior Checklist." University of Vermont Department of Psychiatry, Burlington, VT.

Arseneault, L., Kim-Cohen, J., Taylor, A., Caspi, A., and Moffitt, T. E. (2005). Psychometric evaluation of 5- and 7-year-old children's self-reports of conduct problems. *J. Abnorm. Child Psychol.* **33,** 537–550.

Arseneault, L., Moffitt, T. E., Caspi, A., Taylor, A., Rijsdijk, F. V., Jaffee, S., Ablow, J. C., and Measelle, J. R. (2003). Strong genetic effects on cross-situational antisocial behavior among 5-year-old children according to mothers, teachers, examiner-observers, and twins'self-reports. *J. Child Psychol. Psychiatry* **44,** 832–848.

Asbury, K., Dunn, J., Pike, A., and Plomin, R. (2003). Nonshared environmental influences on individual differences in early behavioral development: A monozygotic twin differences study. *Child Dev.* **74,** 933–943.

Baker, L. A., Mack, W., Moffitt, T. E., and Mednick, S. A. (1989). Etiology of sex differences in criminal convictions in a Danish adoption cohort. *Behav. Genet.* **19,** 355–370.

Belsky, J. (1997). Variation in susceptibility to environmental influence: An evolutionary argument. *Psychol. Inquiry* **8,** 230–235.

Bennett, A. J., Lesch, K. P., Heils, A., Long, J. C., Lorenz, J. G., Shoaf, S. E., Champoux, M., Suomi, S. J., Linnoila, M. V., and Higley, J. D. (2002). Early experience and serotonin transporter gene variation interact to influence primate CNS function. *Mol. Psychiatry* **7,** 188–122.

Blair, R. J. R. (1995). A cognitive developmental approach to morality : Investigating the psychopath. *Cognition* **57,** 1–29.

Blonigen, D. M., Carlson, S. R., Krueger, R. F., and Patrick, C. J. (2003). A twin study of self-reported psychopathic personality traits. *Pers. Individual Differences* **35,** 179–197.

Bohman, M., Cloninger, R., Sigvardsson, S., and von Knorring, A. L. (1982). Predisposition to petty criminality in Swedish adpotees. I. Genetic and environmental heterogeneity. *Arch. Gen. Psychiatry* **39,** 1233–1241.

Boomsma, D., Busjahn, A., and Peltonen, L. (2002). Classical twin studies and beyond. *Nat. Rev. Genet.* **3,** 872–882.

Bouchard, T. J., and McGue, M. (1990). Genetic and rearing environmental influences on adult personality: An analysis of adopted twins reared apart. *J. Pers.* **58,** 263–292.

Buchanan, A., Brock, D., Daniels, N., and Wikler, D. (2001). "From Chance to Choice: Genetics and Justice." Cambridge University Press, New York.

Burt, A. S., Krueger, R. F., McGue, M., and Iacono, W. (2003). Parent-child conflict and the comorbidity among childhood externalizing disorders. *Arch. Gen. Psychiatry* **60,** 505–513.

Burt, A. S., Krueger, R. F., McGue, M., and Iacono, W. G. (2001). Sources of covariation among attention deficit-hyperactivity disorder, oppositional defiant disorder, and conduct disorder: The importance of shared environment. *J. Abnorm. Psychol.* **110,** 516–525.

Butterfield, F. (1996). "All God's Children: The Bosket Family and the American Tradition of Violence." Avon, NY.

Butterfield, F. (2002). Father steals best: Crime in an American family. August 21. *The New York Times*, from *http://www.nytimes.com/2002/08/21/national/21FAMI.html*. Retrieved 1 September 2002.

Cadoret, R. J. (1978). Psychopathology in adopted-away offspring of biological parents with antisocial behavior. *Arch. Gen. Psychiatry* **35,** 176–184.

Cadoret, R. J., Cain, C. A., and Crowe, R. R. (1983). Evidence for gene-environment interaction in the development of adolescent antisocial behavior. *Behav. Genet.* **13,** 301–310.

Cadoret, R. J., Yates, W. R., Troughton, E., Woodworth, G, and Stewart, M. A. S. (1995). Genetic-environmental interaction in the genesis of aggressivity and conduct disorders. *Arch. Gen. Psychiatry* **52,** 916–924.

Cairns, R. B., and Cairns, B. D. (1994). "Lifelines and Risks: Pathways of Youth in Our Time." Cambridge University Press, Cambridge.

Cairns, R. B., MacCombie, D. J., and Hood, K. E. (1983). A developmental-genetic analysis of aggressive behavior in mice. I. Behavioral outcomes. *J. Comp. Psychol.* **97,** 69–89.

Cameron, N. M., Parent, C., Champagne, F. A. Fish, E. W., Ozaki-Kuroda, K., and Meaney, M. J. (2005). The programming of individual differences in defensive responses and reproductive strategies in the rat through variations in maternal care. *Neurosci. Biobehav. Rev.* **29,** 843–865.

Carey, G. (1992). Twin imitation for antisocial behavior. *J. Abnorm. Psychol.* **101,** 18–25.

Carey, G. (1994). Genetics and violence. *In* "Understanding and Preventing Violence: Vol. 2, Biobehavioral Influences" (A. J. Reiss Jr., K. A. Miczek, and J. A. Roth, eds.), pp. 21–58. National Academy Press, Washington, DC.

Carey, G. (2003). "Human Genetics for the Social Sciences." Sage Publications, Thousand Oaks, CA.

Carey, G., and Goldman, D. (1997). The genetics of antisocial behavior. *In* "Handbook of Antisocial Behavior" (D. M. Stoff, J. Breiling, and J. D. Maser, eds.), pp. 243–254. Wiley, New York.

Caspi, A, Taylor, A, Moffitt, T. E., and Plomin, R. (2000). Neighborhood deprivation affects children's mental health: Environmental risks identified using a genetic design. *Psychol. Sci.* **11,** 338–342.

Caspi, A., McClay, J, Moffitt, T. E., Mill, J., Martin, J., Craig, I., Taylor, A., and Poulton, R. (2002). Evidence that the cycle of violence in maltreated children depends on genotype. *Science* **297,** 851–854.

Caspi, A., Moffitt, T. E., Morgan, J., Rutter, M., Taylor, A., Arseneault, L., Tully, L., Jacobs, C., Kim-Cohen, J., and Polo-Tomas, M. (2004). Maternal expressed emotion predicts children's

antisocial behavior problems: Using MZ-twin differences to identify environmental effects on behavioral development. *Dev. Psychol.* **40,** 149–161.

Cates, D. S., Houston, B. K., Vavak, C. R., Crawford, M. H., and Uttley, M. (1993). Heritability of hostility-related emotions, attitudes, and behaviors. *J. Behav. Med.* **16,** 237–256.

Centerwall, B. S., and Robinette, D. (1989). Twin concordance for dishonourable discharge from the military: With a review of the genetics of antisocial behavior. *Comp. Psychiatry* **30,** 442–446.

Cherney, S. S., Fulker, D. W., and Hewitt, J. K. (1997). Cognitive development from infancy to middle childhood. *In* "Intelligence, Heredity, and Environment" (R. J. Sternberg and E. L. Grigorenko, eds.), pp. 463–482. Cambridge University Press, Cambridge.

Cicchetti, D. (2003). Experiments of nature: Contributions to developmental theory. *Dev. Psychopathol.* **15,** 833–835.

Cloninger, C. R., and Gottesman, I. I. (1987). Genetic and environmental factors in antisocial behavior disorders. *In* "The Causes of Crime: New biological Approaches" (S. A. Mednick, T. E. Moffitt, and S. A. Stack, eds.), pp. 92–109. Cambridge University Press, New York.

Cloninger, C. R., Christiansen, K. O., Reich, T., and Gottesman, I. I. (1978). Implications of sex differences in the prevalences of antisocial personality, alcoholism, and criminality for familial transmission. *Arch. Gen. Psychiatry* **35,** 941–951.

Cloninger, C. R., Sigvardsson, S., Bohman, M., and von Knorring, A. L. (1982). Predisposition to petty criminality in Swedish adoptees. II. Cross-fostering analysis of gene-environment interaction. *Arch. Gen. Psychiatry* **39,** 1242–1247.

Coccaro, E. F., Bergeman, C., Kavoussi, R. J., and Seroczynski, A. D. (1997). Heritability of aggression and irritability: A twin study of the Buss-Durkee Aggression Scales in adult male subjects. *Biol. Psychiatry* **41,** 273–284.

Coid, B., Lewis, S. W., and Reveley, A. M. (1993). A twin study of psychosis and criminality. *Br. J. Psychiatry* **162,** 87–92.

Collins, W. A., Maccoby, E. E., Steinberg, L., Hetherington, E. M., and Bornstein, M. H. (2000). Contemporary research on parenting. *Am. Psychol.* **55,** 218–232.

Collishaw, S., Maughan, B., Goodman, R., and Pickles, A. (2004). Time trends in adolescent mental health. *J. Child Psychol. Psychiatry* **45,** 1350–1362.

Costello, E. J., Compton, S. N., Keeler, G., and Angold, A. (2003). Relationships between poverty and psychopathology: A natural experiment. *JAMA* **290,** 2023–2029.

Crabbe, J. C. (2003). Finding genes for complex behaviors: Progress in mouse models of the addictions. *In* "Behavioral Genetics in the Postgenomic Era" (R. Plomin, J. C. DeFries, I. W. Craig, and P. McGuffin, eds.), pp. 291–308. American Psychological Association, Washington, DC.

Deater-Deckard, K., and Plomin, R. (1999). An adoption study of the etiology of teacher and parent reports of externalizing behavior problems in middle childhood. *Child Dev.* **70,** 144–154.

Deater-Deckard, K., Reiss, D., Heatherington, E. M., and Plomin, R. (1997). Dimensions and disorders of adolescent adjustment: A quantitative genetic analysis of unselected samples and selected extremes. *J. Child Psychiatry Psychol.* **38,** 515–525.

DeBellis, M. D. (2001). Developmental traumatology: The psychobiological development of maltreated children and its implications for research, treatment, and policy. *Dev. Psychopathol.* **13,** 539–564.

Dick, D. M., and Rose, R. J. (2002). Behavior Genetics. What's new? What's next? *Curr. Dir. Psychol. Sci.* **11,** 70–74.

Di Lalla, D.L, Gottesman, I. I., Carey, G., and Bouchard, T. J., Jr. (1996). Heritability of MMPI personality indicators of psychopathology in twins reared apart. *J. Abnorm. Psychol.* **105,** 491–499.

DiLalla, L. F. (2002). Behavior Genetics of aggression in children: Review and future directions. *Dev. Rev.* **22,** 593–622.

DiLalla, L. F., and Gottesman, I. I. (1989). Heterogeneity of causes for delinquency and criminality: Lifespan perspectives. *Dev. Psychopathol.* **1,** 339–349.

DiLalla, L. F., and Gottesman, I. I. (1991). Biological and genetic contributions to violence: Widom's untold tale. *Psychol. Bull.* **109,** 125–129.

Dionne, G., Tremblay, R., Boivin, M., Laplante, D., and Perusse, D. (2003). Physical aggression and expressive vocabulary in 19-month-old twins. *Dev. Psychol.* **39,** 261–273.

Dunne, M. P., Statham, D. J., Slutske, W. S., Dinwiddie, S. H., Bucholz, K. K., Madden, P. A. F, and Heath, A. C. (1997). Genetic and environmental contributions to variance in age at first sexual intercourse. *Psychol. Sci.* **8,** 211–216.

Eaves, L. J., Silberg, J. L., Meyer, J. M., Maes, H. H., Simonoff, E., Pickles, A., Rutter, M., Neale, M. C., Reynolds, C., Erickson, M. T., Heath, A. C., Loeber, R., Truett, K. R., and Hewitt, J. K. (1997). Genetics and developmental psychopathology: 2. The main effects of genes and environment on behavioral problems in the Virginia study of adolescent behavioral development. *J. Child Psychol. Psychiatry* **38,** 965–980.

Edelbrock, C., Rende, R., Plomin, R., and Thompson, L. A. (1995). A twin study of competence and problem behavior in childhood and early adolescence. *J. Child Psychol. Psychiatry* **36,** 775–785.

Eley, T. C., Lichtenstein, P., and Moffitt, T. E. (2003). A longitudinal analysis of the etiology of aggressive and non-aggressive antisocial behavior. *Dev. Psychopathol.* **15,** 383–402.

Eley, T. C., Lichtenstein, P., and Stevenson, J. (1999). Sex differences in the etiology of aggressive and non-aggressive antisocial behavior: Results from two twin studies. *Child Dev.* **70,** 155–168.

Evans, W. E., and Relling, M. V. (1999). Pharmacogenetics: Translating functional genomics into rational therapeutics. *Science* **286,** 487–491.

Farrington, D. P., Barnes, G. C., and Lambert, S. (1996). The concentration of offending in families. *Legal Criminol. Psychol.* **1,** 47–63.

Farrington, D. P., Jolliffe, D., Loeber, R., Stouthamer-Loeber, M., and Kalb, L. (2001). The concentration of offenders in families, and family criminality in the prediction of boys' delinquency. *J. Adolesc.* **24,** 579–596.

Fergusson, D. M., Lynskey, M., and Horwood, L. J. (1995). The adolescent outcomes of adoption: A 16-year longitudinal study. *J. Child Psychol. Psychiatry,* **36,** 597–615.

Finkel, D., and McGue, M. (1997). Sex differences and nonadditivity in the heritability on the Multidimensional Personality Questionnaire scales. *J. Pers. Soc. Psychol.* **72,** 929–938.

Flint, J. (2003). Animal models of anxiety. *In* "Behavioral Genetics in the Postgenomic Era" (R. Plomin, J. C. DeFries, I. W. Craig, and P. McGuffin, eds.), pp. 425–442. American Psychological Association, Washington, DC.

Foley, D, Wormley, B., Silberg, J., Maes, H., Hewitt, J., Eaves, L., and Riley, B. (2004). Childhood adversity, MAOA genotype, and risk for conduct disorder. *Arch. Gen. Psychiatry* **61,** 738–744.

Francis, D., Insel, T., Szegda, K., Campbell, G, and Martin, W. D. (2003). Epigenetic sources of behavioral differences in mice. *Nat. Neurosci.* **6,** 445–446.

Galbaud du Fort, G., Boothroyd, L. J., Bland, R. C., Newman, S. C., and Kakuma, R. (2002). Spouse similarity for antisocial behavior in the general population. *Psychol. Med.* **32,** 1407–1416.

Ge, X. (2002). Personal communication April.

Gjone, H., and Novik, T. S. (1995). Parental ratings of behavior problems: A twin and general population comparison. *J. Child Psychol. Psychiatry* **36,** 1213–1224.

Gjone, H., and Stevenson, J. (1997a). The association between internalizing and externalizing behavior in childhood and early adolescence: Genetic or environmental common influences? *J. Abnorm. Child Psychol.* **25,** 277–286.

Gjone, H., and Stevenson, J. (1997b). A longitudinal twin study of temperament and behavior problems: Common genetic or environmental influences? *J. Am. Acad. Child Adolesc. Psychiatry* **36,** 1448–1456.

Glover, J. (1996). The implications for responsibility of possible genetic factors in the explanation of violence. *In* "Symposium on Genetics of Criminal and Antisocial Behavior, Ciba Foundation 194" (G. R. Bock and J. A. Goode, eds.), pp. 237–247. Wiley, Chichester, UK.

Goldstein, R. B., Prescott, C. A., and Kendler, K. S. (2001). Genetic and environmental factors in conduct problems and adult antisocial behavior among adult female twins. *J. Nervous Mental Dis.* **189,** 201–209.

Gottesman, I. I. (1966). Genetic variance in adaptive personality traits. *J. Child Psychol. Psychiatry* **7,** 199–208.

Gottesman, I. I., and Gould, T. D. (2003). The endophenotype concept in psychiatry: Etymology and strategic intentions. *Am. J. Psychiatry* **160,** 636–645.

Gottesman, I. I., Goldsmith, H. H., and Carey, G. (1997). A developmental and a genetic perspective on aggression. *In* "Uniting psychology and Biology: Integrative Perspectives on Human Development" (N. L. Segal and G. E. Weisfeld, eds.), pp. 107–130. American Psychological Association, Washington, DC.

Gottlieb, G. (2003). On making behavioral genetics truly developmental. *Hum. Develop.* **46,** 337–355.

Grove, W. M., Eckert, E. D., Heston, L., and Bouchard, T. J. (1990). Heritability of substance abuse and antisocial behavior: A study of monozygotic twins reared apart. *Biol. Psychiatry* **27,** 1293–1304.

Hamer, D. (2002). Rethinking behavior genetics. *Science* **298,** 71–72.

Hariri, A. R., Mattay, V. S., Tessitore, A., Kolachana, B., Fera, F., Goldman, D., Egan, M. F., and Weinberger, D. R. (2002). Serotonin transporter genetic variation and the response of the human amygdala. *Science* **297,** 400–404.

Harlow, C. W. (2003). Education and corrections populations.. Bureau of Justice Statistics Special Report (NCJ 195670). U. S. Dept. of Justice, Washington, DC. Available at: *http://www.ojp.usdoj.gov/bjs/*

Harris, J. R. (1998). "The Nurture Assumption." Free Press, New York.

Hart, S. D., and Hare, R. D. (1997). Psychopathy: Assessment and association with criminal conduct. *In* "Handbook of Antisocial Behavior" (D. M. Stoff, J. Breiling, and J. D. Maser, eds.), pp. 22–35. Wiley, New York.

Hicks, B. M., Krueger, R. F., Iacono, W. G., McGue, M., and Patrick, C. J. (2004). Family transmission and heritability of externalizing disorders. *Arch. Gen. Psychiatry* **61,** 922–928.

Hill, A. V. S. (1999). Genetics and genomics of infectious disease susceptibility. *Br. Med. Bull.* **55,** 401–413.

Hopper, J. L. (1998). Heritability. *In* "The Encyclopedia of Biostatistics," Vol. 3, pp. 1905–1906. Wiley, New York.

Hopper, J. L. (1999). Why "common environmental affects" are so uncommon in the literature. *In* "Advances in Twin and Sib Pair Analysis" (T. Spector, H. Sneider, and A. MacGregor, eds.), pp. 152–165. Greenwich Medical Media, London.

Howe, G. W., Reiss, D., and Yuh, J. (2002). Can prevention trials test theories of etiology? *Dev. Psychopathol.* **14,** 673–694.

Hudziak, J. J., Rudiger, L. P., Neale, M. C., Heath, A. C., and Todd, R. D. (2000). A twin study of inattentive, aggressive, and anxious/depressed behaviors. *J. Am. Acad. Child Adolesc. Psychiatry* **39,** 469–476.

Hughes, C., Oksanen, H., Taylor, A., Jackson, J., Murray, L., Caspi, A., and Moffitt, T. E. (2002). "I'm gonna beat you, SNAP!" An observational paradigm for assessing disruptive behavior in young children. *J. Child Psychol. Psychiatry* **43,** 507–516.

Hutchings, B., and Mednick, S. A. (1973). Genetic and environmental influences on criminality in Denmark. *In* "International Collaboration in Mental Health" (B. S. Brown and E. F. Torrey, eds.), pp. 113–123. National Institute of Mental Health, Rockville, MD.

Iervolino, A. C., Pike, A., Manke, B., Reiss, D., Hetherington, E. M., and Plomin, R. (2002). Genetic and environmental influences in adolescent peer socialization: Evidence from two genetically sensitive designs. *Child Dev.* **73,** 162–174.

Insel, T. R., and Collins, F. S. (2003). Psychiatry in the genomics era. *Am. J. Psychiatry* **160,** 616–620.

Jacobson, K. C., Prescott, C. A., and Kendler, K. S. (2000). Genetic and environmental influences on juvenile antisocial behavior assessed on two occasions. *Psychol. Med.* **30,** 1315–1325.

Jacobson, K. C., Prescott, C. A., and Kendler, K. S. (2002). Sex differences in the genetic and environmental influences on the development of antisocial behavior. *Dev. Psychopathol.* **14,** 395–416.

Jacobson, K. C., Prescott, C. A., Neale, M. C., and Kendler, K. S. (2000). Cohort differences in genetic and environmental influences on retrospective reports of conduct disorder among adult male twins. *Psychol. Med.* **30,** 775–787.

Jacobson, K. C., Neale, M. C., Prescott, C. A., and Kendler, K. S. (submitted for publication). Behavioral genetic confirmation of a life-course perspective on antisocial behavior. Presentation at the 2001 Behavior Genetics Association, Cambridge. Available from jacobson@physio.vipbg.vcu.edu

Jaffee, S. R., Caspi, A., Moffitt, T. E., Polo-Tomas, M., Price, T. S., and Taylor, A. (2004a). The limits of child effects: Evidence for genetically-mediated child effects on corporal punishment, but not on maltreatment. *J. Dev. Psychol.* **40**(6), 1047–1058.

Jaffee, S. R., Caspi, A., Moffitt, T. E., and Taylor, A. (2004b). Physical maltreatment victim to antisocial child: Evidence of an environmentally-mediated process. *J. Abnorm. Psychol.* **113,** 44–55.

Jaffee, S. R., Moffitt, T. E., Caspi, A., Taylor, A., and Arseneault, L. (2002). The influence of adult domestic violence on children's internalizing and externalizing problems: An environmentally-informative twin study. *J. Am. Acad. Child Adolesc. Psychiatry* **41,** 1095–1103.

Jaffee, S. R., Caspi, A., Moffitt, T. E., Dodge, K., Rutter, M., and Taylor, A., Tully, L. (2005). Nature x Nurture: Genetic vulnerabilities interact with physical maltreatment to promote behavior problems. *Dev. Psychopathol.* **17,** 67–84.

Jang, K. L., Vernon, P. A., and Livesley, W. J. (2000). Personality disorder traits, family environment, and alcohol misuse: A multivariate behavioral genetic analysis. *Addiction* **95,** 873–888.

Johnson, W., Krueger, R. F., Bouchard, T. J., and McGue, M. (2002). The personalities of twins: Just ordinary folks. *Twin Res.* **5,** 125–131.

Johnston, T. D., and Edwards, L. (2002). Genes, interactions, and the development of behavior. *Psychol. Rev.* **109,** 26–34.

Jorgensen, A. L., Phillip, J., Raskind, W. H., Matsushita, M., Christensen, B., Dreyer, V., and Motulsky, A. A. (1992). Different patterns of X inactivation in MZ twins discordant for red-green color vision deficiency. *Am. J. Hum. Genet.* **51,** 291–298.

Kendler, K. S. (1993). Twin studies of psychiatric illness. *Arch. Gen. Psychiatry* **50,** 905–915.

Kendler, K. S. (1996). Parenting: A genetic epidemiologic perspective. *Am. J. Psychiatry* **153,** 11–20.

Kendler, K. S. (2001). Twin studies of psychiatric illness: An update. *Arch. Gen. Psychiatry* **58,** 1005–1014.

Kendler, K. S., Kessler, R. C., Walters, E. E., MacLean, C., Neale, M. C., Heath, A. C., and Eaves, L. J. (1995). Stressful life events, genetic liability and onset of an episode of major depression in women. *Am. J. Psychiatry* **152,** 833–842.

Kendler, K. S., Neale, M. C., Kessler, R. C., Heath, A. C., and Eaves, L. J. (1994). Parental treatment and the equal environments assumption in twin studies of psychiatric illness. *Psychol. Med.* **24,** 579–590.

Kendler, K. S., Prescott, C. A., Myers, J., and Neale, M. C. (2003). The structure of genetic and environmental risk factors for common psychiatric and substance use disorders in men and women. *Arch. Gen. Psychiatry* **60,** 929–937.

Kim-Cohen, J., Caspi, A., Moffitt, T. E., Harrington, H. L., Milne, B., and Poulton, R. (2003). Prior juvenile diagnoses in adults with mental disorder: Developmental follow-back of a prospective-longitudinal cohort. *Arch. Gen. Psychiatry* **60,** 709–717.

Kraemer, H. C. (2003). Current concepts of risk in psychiatric disorders. *Curr. Opin. Psychiatry* **16,** 421–430.

Krueger, R. F., Hicks, B. M., and McGue, M. (2001). Altruism and antisocial behavior: Independent tendencies, unique personality correlates, distinct etiologies. *Psychol. Sci.* **12,** 397–402.

Krueger, R. F., Hicks, B. M., Patrick, C. J., Carlson, S. R., Iacono, W. G., and McGue, M. (2002). Etiologic connections among substance dependence, antisocial behavior, and personality: Modeling the externalizing spectrum. *J. Abnorm. Psychol.* **111,** 411–424.

Krueger, R. F., Moffitt, T. E., Caspi, A., Bleske, A., and Silva, P. A. (1998). Assortative mating for antisocial behavior: Developmental and methodological implications. *Behav. Genet.* **28,** 173–186.

Kuntsi, J., Gayan, J., and Stevenson, J. (2000). Parents' and teachers' ratings of problem behaviors in children: Genetic and contrast effects. *Twin Res.* **3,** 251–258.

Lahey, B., Moffitt, T. E., and Caspi, A. (eds.) (2003). "Causes of Conduct Disorder and Juvenile Delinquency." Guilford Press, New York.

Lambert, E. W., Wahler, R. G., Andrade, A. R., and Bickman, L. (2001). Looking for the disorder in conduct disorder. *J. Abnorm. Psychol.* **110,** 110–123.

Levy, F., Hay, D., McLaughlin, M., Wood, C., and Waldman, I. (1996). Twin-sibling differences in parental reports of ADHD, speech, reading, and behavioral problems. *J. Child Psychol. Psychiatry* **37,** 569–578.

Licinio, J. (2003). Editorial. Molecular psychiatry: Moving away from one-polymorphism genetic association studies. *Mol. Psychiatry* **8,** 247.

Livesley, W. J., Jang, K. L., Jackson, D. N., and Vernon, P. A. (1993). Genetic and environmental contributions to dimensions of personality disorder. *Am. J. Psychiatry* **150,** 1826–1831.

Loat, C. S., Asbury, K., Galsworthy, M. J., Plomin, R., and Craig, I. W. (2004). X inactivation as a source of behavioral differences in monozygotic female twins. *Twin Res.* **7,** 54–61.

Loeber, R., and Farrington, D. (1998). "Serious and Violent Juvenile Offenders: Risk factors and successful Interventions." Sage Publications, Thousand Oaks, CA.

Loehlin, J. C., and Nichols, R. C. (1976). "Heredity, Environment, and Personality: A Study of 850 Sets of Twins." University of Texas Press, Austin.

Loehlin, J. C., Willerman, L., and Horn, J. (1985). Personality resemblances in adoptive families when the children are late-adolescent or adult. *J. Pers. Soc. Psychol.* **48,** 376–392.

Loehlin, J. C., Willerman, L., and Horn, J. (1987). Personality resemblance in adoptive families: A 10-year follow-up. *J. Pers. Soc. Psychol.* **53,** 961–969.

Luan, J. A., Wong, M. Y., Day, N. E., and Wareham, N. J. (2001). Sample size determination for studies of gene-environment interaction. *Int. J. Epidemiol.* **30,** 1035–1040.

Lynam, D. R. (1996). Early identification of chronic offenders: Who is the fledgling psychopath? *Psychol. Bull.* **120,** 209–234.

Lyons, M. J., True, W. R., Eisen, S. A., Goldberg, J., Meyer, J. M., Faraone, S. V., Eaves, L. J., and Tsuang, M. T. (1995). Differential heritability of adult and juvenile antisocial traits. *Arch. Gen. Psychiatry* **52,** 906–915.

Maestripieri, D. (2003). Similarities in affiliation and aggression between cross-fostered rhesus macaque females and their biological mothers. *Dev. Psychobiol.* **43,** 321–327.

Mare, R. D. (1991). Five decades of educational assortative mating. *Am. Sociol. Rev.* **56,** 15–32.

G.M.Martin (ed.) (2002). Twin registers across the globe [Special issue]. *Twin Res.* **5**(5).

Martin, N., Boomsma, D., and Machin, G. (1997). A twin-pronged attacked on complex traits. *Nat. Genet.* **17,** 387–392.

Martin, N. G., Eaves, L. J., Kearsey, M. J., and Davies, P. (1978). The power of the classical twin study. *Heredity* **40,** 97–116.

Maxson, S. C. (2000). Genetic influences on aggressive behavior. *In* "Genetic Influences on Neural Behavioral Functions" (D. W. Pfaff, W. H. Berrettini, H. J. Toh, and S. C. Maxson, eds.), pp. 405–415. CRC Press, New York.

McGue, M., Bouchard, T. J., Jr., Iacono, W. G., and Lykken, D. T. (1993). Behavioral genetics of cognitive ability: A life-span perspective. *In* "Nature, Nurture and Psychology" (R. Plomin and G. E. McClearn, eds.), pp. 59–76. American Psychological Association, Washington, DC.

McGue, M., Sharma, A., and Benson, P. (1996). The effect of common rearing on adolescent adjustment: Evidence from a U. S. adoption cohort. *Dev. Psychol.* **32,** 604–613.

McGuffin, P., and Thapar, A. (1997). The genetic basis of bad behavior in adolescents. *Lancet* **350,** 411–412.

McGuffin, P., and Thapar, A. (1998). Genetics and antisocial personality disorder. *In* "Psychopathy: Antisocial, Criminal and Violent Behavior" (T. Millon and E. Simonsen, eds.), pp. 215–230. Guilford Press, New York.

McGuffin, P., Riley, B., and Plomin, R. (2001). Toward behavioral genomics. *Science* **291,** 1232–1234.

Meaney, M. J. (2001). Maternal care, gene expression, and the transmission of individual differences in stress reactivity across generations. *Ann. Rev. Neurosci.* **24,** 1161–1192.

Mednick, S. A., and Christiansen, K. O. (1977). "Biosocial Bases of Criminal Behavior." Gardner Press, New York.

Mednick, S. A., Gabrielli, W. F., and Hutchings, B. (1984). Genetic factors in criminal behavior: Evidence from an adoption cohort. *Science* **224,** 891–893.

Mednick, S. A., Moffitt, T. E., Gabrielli, W. F., and Hutchings, B. (1986). Genetic factors in criminal behavior: A review. *In* "The Development of Antisocial and Prosocial Behavior" ( J. Block, D. Olweus, and M. R. Yarrow, eds.), pp. 33–50. Academic Press Inc., New York, NY.

Meyer, J. M., Rutter, M., Silberg, J. L., Maes, H., Simonoff, E., Shillady, L. L., Pickles, A., Hewitt, J. K., and Eaves, L. J. (2000). Familial aggregation for conduct disorder symptomatology: The role of genes, marital discord, and family adaptability. *Psychol. Med.* **30,** 759–774.

Miech, R. A., Caspi, A., Moffitt, T. E., Wright, B. E., and Silva, P. A. (1999). Low socio-economic status and mental disorders: A longitudinal study of causation and selection. *Am. J. Sociol.* **104,** 1096–1131.

Miles, D. R., and Carey, G. (1997). Genetic and environmental architecture of human aggression. *J. Pers. Soc. Psychol.* **72,** 207–217.

Miles, D. R., van den Bree, M. B. M., and Pickens, R. W. (2002). Sex differences in shared genetic and environmental influences between conduct disorder symptoms and marijuana use in adolescents. *Neuropsychiatric Genet.* **114,** 159–168.

Moffitt, T. E. (1993). "Life-course-persistent" and "adolescence-limited" antisocial behavior: A developmental taxonomy. *Psychol. Rev.* **100,** 674–701.

Moffitt, T. E. (2003). Life-course persistent and adolescence-limited antisocial behavior: A 10-year research review and a research agenda. *In* "The Causes of Conduct Disorder and Serious Juvenile Delinquency" (B. Lahey, T. E. Moffitt, and A. Caspi, eds.), pp. 49–75. Guilford, New York.

Moffitt, T. E., and the E-risk Study, Team (2002). Teen-aged mothers in contemporary Britain. *J. Child Psychol. Psychiatry* **43,** 1–16.

Moffitt, T. E., Caspi, A., and Rutter, M. (2005). Strategy for investigating interaction between measured genes and measured environments. *Arch. Gen. Psychiatry* **62,** 473–481.

Moffitt, T. E., Caspi, A., and Rutter, M. (in Press). Interaction between measured genes and measured environments in psychopathology: Concepts, methods, and implications for intervention, research, and public understanding of genetics. *Perspectives of Psychological Science*, in press.

Moffitt, T. E., Caspi, A., Harrington, H., and Milne, B. (2002). Males on the life-course persistent and adolescence-limited antisocial pathways: Follow-up at age 26. *Dev. Psychopathol.* **14,** 179–206.

Moffitt, T. E., Caspi, A., Rutter, M., and Silva, P. A. (2001). "Sex Differences in Antisocial Behavior: Conduct Disorder, Delinquency, and Violence in the Dunedin Longitudinal Study." Cambridge University Press, Cambridge, UK.

Moffitt, T. E., Krueger, R. F., Caspi, A., and Fagan, J. (2000). Partner abuse and general crime: How are they the same? How are they different? *Criminology* **38,** 201–235.

Moilannen, I., Linna, S. L., Ebeling, H., Kampulainen, K., Tamminen, T., Piha, J., and Almqvist, F. (1999). Are twins' behavioral/emotional problems different from singletons'? *Eur. Child Adolesc. Psychiatry* **8,** 62–67.

Murphy, D. L., Li, Q, Engel, S., Wichems, C., Andrews, A., Lesch, K. P., and Uhl, G. (2001). Genetic perspectives on the serotonin transporter. *Brain Res. Bull.* **56,** 487–494.

Nadder, T. S., Rutter, M., Silberg, J. L., Maes, H. H., and Eaves, L. J. (2002). Genetic effects on the variation and covariation of attention-deficit hyperactivity disorder (ADHD) and oppositional-defiant disorder/conduct disorder (ODD/CD) symptomatologies across informant and occasion of measurement. *Psychol. Med.* **32,** 39–53.

Nagin, D. S. (1999). Analyzing developmental trajectories: A semiparametric, group-based approach. *Psychol. Methods* **4,** 139–157.

Nagin, D. S., Farrington, D. P., and Moffitt, T. E. (1995). Life-course trajectories of different types of offenders. *Criminology* **33,** 111–139.

Nagin, D. S., Pagani, L., Tremblay, R. E., and Vitaro, F. (2003). Life course turning points: The effect of grade retention on physical aggression. *Dev. Psychopathol.* **15,** 343–361.

Neale, M. C., and Cardon, L. R. (1992). "Methodology for Genetic Studies of Twins and Families." Kluwer Academic Publishers, Dordrecht, The Netherlands.

Newman, D. L., Moffitt, T. E., Caspi, A., Magdol, L., and Silva, P. A. (1996). Psychiatric disorder in a birth cohort of young adults: Prevalence, co-morbidity, clinical significance, and new case incidence from age 11 to 21. *J. Consult. Clin. Psychol.* **64,** 552–562.

Nuffield, Council on Bioethics (2002). "Genetics and Human Behavior: The Ethical Context." Author, London. Report also available from www.nuffieldbioethics.org

O'Connor, M., Foch, T., Sherry, T., and Plomin, R. (1980). A twin study of specific behavioral problems of socialization as viewed by parents. *J. Abnorm. Child Psychol.* **8,** 189–199.

O'Connor, T. G., Deater-Deckard, K., Fulker, D., Rutter, M., and Plomin, R. (1998a). Genotype-environment correlations in late childhood and early adolescence: Antisocial behavioral problems in coercive parenting. *Dev. Psychol.* **34,** 970–981.

O'Connor, T. G., McGuire, S., Reiss, D., Hetherington, E. M., and Plomin, R. (1998b). Co-occurrence of depressive symptoms and antisocial behavior in adolescence: A common genetic liability. *J. Abnorm. Psychol.* **107,** 27–37.

O'Connor, T. G., Neiderhiser, J. M., Reiss, D., Hetherington, E. M., and Plomin, R. (1998c). Genetic contributions to continuity, change, and co-occurrence of antisocial and depressive symptoms in adolescence. *J. Child Psychol. Psychiatry* **39,** 323–336.

O'Connor, T. G., Heatherington, E. M., Reiss, D., and Plomin, R. (1995). A twin-sibling study of observed parent-adolescent relations. *Child Dev.* **66,** 812–829.

Ottman, R. (1990). An epidemiologic approach to gene-environment interaction. *Genet. Epidemiol.* **7,** 177–185.

Partanen, J., Bruun, K., and Markannen, T. (1966). "Inheritance of Drinking Behavior: A Study on Intelligence, Personality, and Use of Alcohol of Adult Twins." Keskuskirjapaino, Helsinki, Finland.
Peters, T. (2003). Holy Therapy: Can a drug do the work of the spirit? *Christian Century* **9,** August, 23–26.
Pike, A., Reiss, D., Hethington, E. M., and Plomin, R. (1996). Using MZ differences in the search for nonshared environmental effects. *J. Child Psychol. Psychiatry* **37,** 695–704.
Pinker, S. (2002). "The Blank Slate." Penguin, NY.
Plomin, R. (1994). "Genetics and Experience: The Interplay Between Nature and Nurture." Sage Publications, Thousand Oaks, CA.
Plomin, R., and Bergeman, C. S. (1991). The nature of nurture: Genetic influences on 'environmental' measures. *Behav. Brain Sci.* **14,** 373–427.
Plomin, R., and Daniels, D. (1987). Why are children in the same family so different from each other? *Behavioral and Brain Sci.* **10,** 1–16.
Plomin, R., DeFries, J. C., and Loehlin, J. C. (1977). Genotype-environment interaction and correlation in the analysis of human behavior. *Psychol. Bull.* **84,** 309–322.
Plomin, R., DeFries, J. C., McClearn, G. E., and McGuffin, P. (2001). "Behavioral Genetics," 4th ed. W.H. Freeman, New York.
Plomin, R., Foch, T. T., and Rowe, D. C. (1981). Bobo clown aggression in childhood: Environment not genes. *J. Res. Pers.* **15,** 331–342.
Pogue-Geile, M. F., and Rose, R. J. (1985). Developmental genetic studies of adult personality. *Dev. Psychol.* **21,** 547–557.
Pray, L. A. (2004). Epigenetics: Genome, meet your environment. *The Scientist* **18,** 5 July 2004.
Purcell, S. (2002). Variance components models for gene-environment interaction in twin analysis. *Twin Res.* **5,** 554–571.
Purcell, S. (n. d). Introduction to Quantitative Genetics. From Kings College London, Institute of Psychiatry web site: *http://www.statgen.iop.kcl.ac.uk/bgim/*
Raine, A. (1993). "The Psychopathology of Crime." Academic Press, New York.
Raine, A., Brennan, P. A., Farrington, D. P., and Mednick, S. A. (eds.) (1997). "Biosocial Bases of Violence." Plenum Press, NY.
Reid, J., Patterson, G. R., and Snyder, J. (2002). "Antisocial Behavior in Children and Adolescents." American Psychological Association, Washington DC.
Rende, R. D., Slomkowski, C. L., Stocker, C., Fulker, D. W., and Plomin, R. (1992). Genetic and environmental influences on maternal and sibling interaction in middle childhood: A sibling adoption study. *Dev. Psychol.* **28,** 484–490.
Rhee, S. H., and Waldman, I. D. (2002). Genetic and environmental influences on antisocial behavior: A meta-analysis of twin and adoption studies. *Psychol. Bull.* **128,** 490–529.
Ridley, M. (2003). "Nature via Nurture." Fourth Estate, London.
Riggins-Caspers, K. M., Cadoret, R. J., Knutson, J. F., and Langbehn, D. (2003). Biology-environment interaction and evocative biology-environment correlation: Contributions of harsh discipline and parental psychopathology to problem adolescent behaviors. *Behav. Genet.* **33,** 205–220.
Risch, N. (2000). Searching for genetic determinants in the new millennium. *Nature* **405,** 847–856.
Robins, L. N. (1978). Sturdy childhood predictors of antisocial behavior: Replications from longitudinal studies. *Psychol. Med.* **8,** 611–622.
Robins, L. N., and Regier, D. A. (1991). "Psychiatric Disorders in America: The Epidemiological Catchment Area Study." Free Press, NY.
Rodgers, J. L., Buster, M., and Rowe, D. C. (2001). Genetic and environmental influences on delinquency: DF analysis of NLSY kinship data. *J. Quantitative Criminol.* **17,** 145–168.
Rodgers, J. L., Rowe, D. C., and Li, C. (1994). Beyond nature versus nurture: DF analysis of nonshared influences on problem behaviors. *Dev. Psychol.* **30,** 374–384.

Rose, N. (2000). The biology of culpability: Pathological identity and crime control in a biological culture. *Theor. Criminol.* **4,** 5–34.
Rose, R. J., Viken, R. J., Dick, D. M., Bates, J. E., Pulkinnen, L., and Kaprio, J. (2003). It does take a village: Nonfamilial environments and children's behavior. *Psychol. Sci.* **14,** 273–277.
Ross, L., and Shestowsky, D. (2003). Contemporary psychology's challenges to legal theory and practice. *Northwestern University Law Review* **97,** 1081–1114.
Rowe, D. C. (1983). Biometrical genetic models of self-reported delinquent behavior: A twin study. *Behav. Genet.* **13,** 473–489.
Rowe, D. C. (1985). Sibling interaction and self-reported delinquent behavior: A study of 265 twin pairs. *Criminology* **23,** 223–240.
Rowe, D. C. (1994). "The Limits of Family Influence: Genes, Experience, and Behavior." Guilford Press, NY.
Rowe, D. C., and Farrington, D. P. (1997). The familial transmission of criminal convictions. *Criminology* **35,** 177–201.
Rowe, D. C., and Osgood, D. W. (1984). Heredity and sociological theories of delinquency: A reconsideration. *Am. Sociol. Rev.* **49,** 526–540.
Rowe, D. C., Almeida, D. M., and Jacobson, K. C. (1999). School context and genetic influences on aggression in adolescence. *Psychol. Sci.* **10,** 277–280.
Rowe, D. C., Rodgers, J. L., and Meseck-Bushey, S. (1992). Sibling delinquency and the family environment: Shared and unshared influences. *Child Dev.* **63,** 59–67.
Rowe, D. C., Vazsonyi, A. T., and Flannery, D. J. (1995). Sex difference in crime: Do means and within-sex variation have similar causes? *J. Res. Crime Delinquency* **32,** 84–101.
Rushton, J. P. (1996). Self-report delinquency and violence in adult twins. *Psychiatric Genet.* **6,** 87–89.
Rushton, J. P., Fulker, D. W., Neale, M. C., Nias, D. K. B., and Eysenck, H. J. (1986). Altruism and aggression: The heritability of individual differences. *J. Pers. Social Psychol.* **50,** 1192–1198.
Rutter, M. (2002). Nature, nurture, and development: From evangelism through science toward policy and practice. *Child Dev.* **73,** 1–21.
Rutter, M., and Silberg, J. (2002). Gene-environment interplay in relation to emotional and behavioral disturbance. *Ann. Rev. Psychol.* **53,** 463–490.
Rutter, M., and Smith, D. J. (1995). "Psychosocial Disorders in Young People: Time Trends and Their causes." Wiley, Chichester, UK.
Rutter, M., Caspi, A., and Moffitt, T. E. (2003). Using sex differences in psychopathology to study causal mechanisms: Unifying issues and research strategies. *J. Child Psychol. Psychiatry* **44,** 1092–1115.
Rutter, M., Pickles, A., Murray, R., and Eaves, L. (2001). Testing hypotheses on specific environmental causal effects on behavior. *Psychol. Bull.* **127,** 291–324.
Sankar, P. (2003). Genetic privacy. *Ann. Rev. Med.* **54,** 393–407.
Scarr, S. (1992). Developmental theories for the 1990's: Development and individual differences. *Child Dev.* **63,** 1–19.
Schmitz, S., Fulker, D. W., and Mrazek, D. A. (1995). Problem behavior in early and middle childhood: An initial behavior genetic analysis. *J. Child Psychol. Psychiatry* **36,** 1443–1458.
Scourfield, J., Van den Bree, M., Martin, N., and Mcguffin, P. (2004). Conduct problems in children and adolescents: A twin study. *Arch. Gen. Psychiatry* **61,** 489–496.
Searle, S., and Blackwell, J. M. (1999). Evidence for a functional repeat polymorphism in the promoter of the human NRAMP1 gene that correlates with autoimmune versus infectious disease susceptibility. *J. Med. Genet.* **36,** 295–299.
Serbin, L., and Karp, J. (2003). Intergenerational studies of parenting and the transfer of risk from parent to child. *Curr. Dir. Psychol. Sci.* **12,** 138–142.
Sharma, A. R., McGue, M. K., and Benson, P. L. (1998). The psychological adjustment of United States adopted adolescents and their nonadopted siblings. *Child Dev.* **69,** 791–802.

Sigvardsson, S., Cloninger, C. R., Bohman, M., and von Korring, A. (1982). Predisposition to petty criminality in Swedish adoptees. III. Sex differences and validation of the male typology. *Arch. Gen. Psychiatry* **39,** 1248–1253.

Silberg, J., Rutter, M., Meyer, J., Maes, H. H., Hewitt, J., Simonoff, E., Pickles, A., Loeber, R., and Eaves, L. (1996). Genetic and environmental influences on the covariation between hyperactivity and conduct disturbance in juvenile twins. *J. Child Psychol. Psychiatry* **37,** 803–816.

Silberg, J. L., Erickson, M. T., Meyer, J. M., Eaves, L. J., Rutter, M., and Hewitt, J. K. (1994). The application of structural equation modelling to maternal ratings of twins' behavioral and emotional problems. *J. Consult. Clin. Psychol.* **62,** 510–521.

Simon, G. E., and VonKorff, M. (1995). Recall of psychiatric history in cross-sectional surveys: Implications for epidemiologic research. *Epidemiologic Rev.* **17,** 221–227.

Simonoff, E., Pickles, A., Hewitt, J., Silberg, J., Rutter, M., Loeber, R., Meyer, J., Neale, M., and Eaves, L. (1995). Multiple raters of disruptive child behavior: Using a genetic strategy to examine shared views and bias. *Behav. Genet.* **25,** 311–326.

Simonoff, E., Pickles, A., Meyer, J. M., Silberg, J., Maes, H., Loeber, R., Rutter, M., Hewitt, J. K., and Eaves, L. J. (1997). The Virginia Twin Study of adolescent behavioral development. *Arch. Gen. Psychiatry* **54,** 801–808.

Slutske, W. S. (2001). The genetics of antisocial behavior. *Curr. Psychiatry Rep.* **3,** 158–162.

Slutske, W. S., Cronk, N. J., and Nabors-Oberg, R. E. (in press). Familial and genetic factors. *In* "Conduct and Oppositional Defiant Disorders: Epidemiology, Risk Factors, and Treatment" (C. Essau, ed.). Lawrence Erlbaum Assoc., New Jersey. Available from *SlutskeW@missouri.edu*

Slutske, W. S., Eisen, S. A., Xian, H., True, W. R., Lyons, M. J., Goldberg, J., and Tsuang, M. T. (2001). A twin study of the association between pathological gambling and antisocial personality disorder. *J. Abnorm. Psychology* **110,** 297–308.

Slutske, W. S., Heath, A. C., Dinwiddie, S. H., Madden, P. A. F., Bucholz, K. K., Dunne, M. P., Statham, D. J., and Martin, N. G. (1997). Modelling genetic and environmental influences in the etiology of conduct disorder: A study of 2682 adult twin pairs. *J. Abnorm. Psychol.* **106,** 266–279.

Slutske, W. S., Heath, A. C., Dinwiddie, S. H., Madden, P. A. F., Bucholz, K. K., Dunne, M. P., Statham, D. J., and Martin, N. G. (1998). Common genetic risk factors for conduct disorder and alcohol dependence. *J. Abnormal Psychol.* **107,** 363–374.

Sluyter, F., Arseneault, L., Moffitt, T. E., Veenema, A. H., de Boer, S., and Koolhas, J. (2003). Toward an animal model for antisocial behavior: Parallels between mice and humans. *Behav. Genet.* **33,** 563–574.

Smith, C. A., and Farrington, D. P. (2003). Continuities in antisocial behavior and parenting across three generations. *J. Child Psychol. Psychiatry* **44,** 1–18.

Stanger, C., Achenbach, T., and Verhulst, F. C. (1997). Accelerated longitudinal comparisons of aggressive versus delinquent syndromes. *Dev. Psychopathol.* **9,** 43–58.

Stevenson, J., and Graham, P. (1988). Behavioral deviance in 13-year twins: An item analysis. *J. Child Adolesc. Stud.* **27,** 791–797.

Stone, R. D. (2003). The cloudy crystal ball: Genetics, child abuse, and the perils of predicting behavior. *Vanderbilt Law Rev.* **56,** 1558–1588.

Stoolmiller, M. (1999). Implications of the restricted range of family environments for estimates of heritability and nonshared environment in behavior-genetic adoption studies. *Psychol. Bull.* **125,** 392–409.

Suomi, S. J. (in press). How gene-environment interactions can shape the development of socioemotional regulation in rhesus monkeys. *In* "Socioemotional Regulation: Dimensions, Developmental Trends, and Influences" (B. S. Zuckerman and A. F. Lieberman, eds.), Skillman, NJ.

Tabor, H. K., Risch, N. J., and Meyers, R. M. (2002). Candidate-gene approaches for studying complex genetic traits: Practical considerations. *Nat. Genet. Rev.* **3,** 1–7.

Taylor, A. (2004). The consequences of selective participation on behavioral-genetic findings: Evidence from simulated and real data. *Twin Res.* **7**(5), 485–504.

Taylor, J., McGue, M., and Iacono, W. G. (2000a). Sex differences, assortative mating, and cultural transmission effects on adolescent delinquency: A twin family study. *J. Child Psychiatry Psychol.* **41,** 433–440.

Taylor, J., Iacono, W. G., and McGue, M. (2000b). Evidence for a genetic etiology of early-onset delinquency. *J. Abnorm. Psychol.* **109,** 634–643.

Taylor, J., Loney, B. R., Bobadilla, L., Iacono, W., and McGue, M. (2003). Genetic and environmental influences on psychopathy trait dimensions in a community sample of male twins. *J. Abnorm. Child Psychol.* **31,** 633–645.

Taylor, J., McGue, M., Iacono, W. G., and Lykken, D. T. (2000). A behavioral genetic analysis of the relationship between the socialization scale and self-reported delinquency. *J. Pers.* **68,** 29–50.

Tecott, L. H., and Wehner, J. M. (2001). Mouse molecular genetic technologies: Promise for psychiatric research. *Arch. Gen. Psychiatry* **58,** 995–1004.

Tellegen, A., Lykken, D. T., Bouchard, T. J., Wilcox, K. J., Segal, N. L., and Rich, S. (1988). Personality similarity in twins reared apart and together. *J. Pers. Soc. Psychol.* **6,** 1031–1039.

Thapar, A., and McGuffin, P. (1996). A twin study of antisocial and neurotic symptoms in childhood. *Psychol. Med.* **26,** 1111–1118.

Thapar, A., Harrington, R., and McGuffin, P. (2001). Examining the comorbidity of ADHD-related behaviors and conduct problems using a twin study design. *Br. J. Psychiatry* **179,** 224–229.

Toomey, R., Lyons, M. J., Eisen, S. A., True, W., Goldberg, J., and Tsuang, M. T. (1997). Abstract: A twin study of domestic violence. *Am. J. Med. Genet. (Neuropsychiatric Genet.)* **74.**

True, W. R., Heath, A. C., Scherrer, J. F., Xian, H., Lin, N., Eisen, S. A., Lyons, M. J., Goldberg, J., and Tsuang, M. T. (1999). Interrelationship of genetic and environmental influences on conduct disorder and alcohol and marijuana dependence symptoms. *Am. J. Medical Genet.(Neuropsychiatric Genet.)* **88,** 391–397.

Turkheimer, E., and Waldron, M. (2000). Nonshared environment: A theoretical, methodological, and quantitative review. *Psychol. Bull.* **126b,** 78–108.

U. S. Bureau of Justice Statistics (2002). *Criminal Victimization 2001.* (NCJ Report 194610). U. S. Department of Justice, Washington, DC. Available at http://www.ojp.usdof.gov/bjs

van den Oord, E. J. C. G., Boomsma, D. I., and Verhulst, F. C. (1994). A study of problem behavior in 10- to 15-year-old biologically related and unrelated international adoptees. *Behav. Genet.* **24,** 193–205.

van den Oord, E. J. C. G., Koot, H. M., Boomsma, D. I., Verhulst, F. C., and Orlebeke, J. F. (1995). A twin-singleton comparison of problem behavior in 2–3 year olds. *J. Child Psychol. Psychiatry* **36,** 449–458.

van den Oord, E. J. C. G., Verhulst, F. C., and Boomsma, D. I. (1996). A genetic study of maternal and paternal ratings of problem behaviors in 3-year-old twins. *J. Abnorm. Psychol.* **105,** 349–357.

van der Valk, J. C., Verhulst, F. C., Stroet, T. M., and Boomsma, D. I. (1998a). Quantitative genetic analysis of internalising and externalizing problems in a large sample of 3-year-old twins. *Twin Res.* **1b,** 25–33.

van der Valk, J. C., Verhulst, F. C., Neale, M. C., and Boomsma, D. I. (1998b). Longitudinal genetic analysis of problem behaviors in biologically related and unrelated adoptees. *Behav. Genet.* **28,** 365–380.

van Os, J., and Sham, P. (2003). Gene-environment interaction and correlation in schizophrenia. *In* "The Epidemiology of Schizophrenia" (R. Murray, P. B. Jones, E. Susser, J. van Os, and M. Cannon, eds.), pp. 235–253. Cambridge University Press, Cambridge, UK.

Vandell, D. L. (2000). Parents, peer groups, and other socializing influences. *Dev. Psychol.* **36,** 699–710.

VanDusen, K., Mednick, S. A., Gabrielli, W. F., and Hutchings, B. (1983). Social class and crime in an adoption cohort. *J. Criminal Law Criminol.* **74,** 249–269.

Varmuza, S. (2003). Epigenetics and the renaissance of heresy. *Genome* **46,** 963–967.

Vernon, P. A., McCarthy, J. M., Johnson, A. M., Jang, K. L., and Harris, J. A. (1999). Individual differences in multiple dimensions of aggression: A univariate and multivariate genetic analysis. *Twin Res.* **2,** 16–21.

Viding, E., Blair, J. R., Moffitt, T. E., and Plomin, R. (2005). Psychopathic syndrome indexes strong genetic risk for antisocial behavior in 7-year-olds. *J. Child Psychol. Psychiatry* **46,** 592–597.

Waldman, I. D., and Slutske, W. S. (2000). Antisocial behavior and alcoholism: A behavioral genetic perspective on comorbidity. *Clin. Psychol. Rev.* **20,** 255–287.

Waldman, I. D., Rhee, S. H., Levy, F., and Hay, D. A. (2001). Causes of the overlap among symptoms of attention deficit hyperactivity disorder, oppositional defiant disorder, and conduct disorder. *In* "Attention, genes, and ADHD" (F. Levy and D. A. Hay, eds.), pp. 115–138. Taylor &Francis, Philadelphia, PA.

Walters, G. D. (1992). A meta-analysis of the gene-crime relationship. *Criminology* **30,** 595–613.

Waschbusch, D. A. (2002). A meta-analytic examination of comorbid hyperactive-impulsive-inattention problems and conduct problems. *Psychol. Bull.* **128,** 118–150.

Wolf, C. R., Smith, G., and Smith, R. L. (2000). Science, medicine and the future: Pharmacogenetics. *BMJ* **320,** 987–990.

Wong, M. Y., Day, N. E., Luan, J. A., and Wareham, N. J. (2003). The detection of gene-environment interaction for continuous traits: Should we deal with measurement error by bigger studies or better measurement? *Int. J. Epidemiol.* **32,** 51–57.

World Health Organization (2002). "World Report on Violence and health." Author, Geneva.

Yang, Q., and Khoury, M. J. (1997). Evolving methods in genetic epidemiology. III. Gene-environment interaction in epidemiological research. *Epidemiol. Rev.* **19,** 33–43.

Young, S. E., Stallings, M. C., Corley, R. P., Krauter, K. S., and Hewitt, J. K. (2000). Genetic and environmental influences on behavioral disinhibition. *Am. J. Med. Genet.* **96,** 684–695.