

Psychiatric Genetics and Forensic Psychiatry: A Review

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Research in psychiatric genetics has been revolutionized by the development of new and powerful molecular genetic techniques. Family, twin, and adoption studies of antisocial personality disorder (ASPD) and criminality are reviewed, and ramifications of new research methods for the study of antisocial behavior are considered. Implications of these developments for forensic psychiatry are discussed.

Recent advances in molecular genetic techniques and psychiatric genetics hold the promise that heritable factors associated with increased liability for psychiatric illness as well as those influencing normal personality variation may be identified, ultimately leading to characterization of their structure and function at the molecular level. Such analysis may ultimately allow researchers the opportunity more fully to understand how inborn, heritable traits and postnatal environment interact in the development of psychopathology. The purpose of this article is therefore to review recent developments in psychiatric genetics, with particular emphasis on studies of criminality and Antisocial Personality Disorder (ASPD).

Family Studies

The familial nature of many psychiatric illnesses has long been recognized.

Over time the list of familial psychiatric illnesses has grown to include alcoholism,¹ other substance abuse,² schizophrenia,³ unipolar depression and manic-depressive illness,^{4, 6} Briquet's syndrome,^{7, 8} obsessive-compulsive disorder,⁹ and anxiety states,^{10, 11} among others.

The inheritance of criminal behavior has likewise been studied for decades.^{12, 13} Such studies generally take one of two approaches: Either studying the transmissibility of criminality between generations, or investigating the familiarity of ASPD. It should be kept in mind, however, that while there is considerable overlap, ASPD is not equivalent to criminality, and both may differ in important respects from antisocial behavior, which does not necessarily imply either early onset or arrest.¹⁴⁻¹⁶ Moreover, from the standpoint of genetic studies, even ASPD, a reliable and validated diagnostic category, appears to be a heterogeneous grouping.^{17, 18}

Early family studies of criminality and

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antisocial behavior, although consistent with the hypothesis that liability to such behavior had a heritable component, generally share a number of methodologic weaknesses such as biased ascertainment of cases, confounding of criminality with the effects of alcoholism, imprecise or inadequate classification of criminality, and inadequate assessment of environmental factors.^{12, 14} More recent studies, however, are also consistent with the presence of a familial component of antisocial behavior and ASPD.

In one of the first studies to diagnose psychiatric disorders systematically among first-degree relatives of convicted felons, Guze and coworkers^{19, 20} found elevated rates of hysteria (Briquet's syndrome), sociopathy, alcoholism, and drug addiction, but not other psychiatric disorders. Subsequently, Cloninger, Reich, and Guze²¹ evaluated 86 felon probands and 387 of their biological first-degree relatives. Blind to the proband's diagnosis and using explicit diagnostic criteria, they found the rate of ASPD to be 17 percent among male relatives of male felons and four percent among female relatives of male felons. Among relatives of female felons, the rate was higher for both men (36%) and women (19%). For both male and female relatives, the rates were substantially higher than in the general population, indicative that the disorder was familial. They concluded that the data best fit a model of multifactorial transmission; that is, either multiple genes of relatively small individual effect, or a combination of genetic and environmental etiologic factors. The finding that

fewer women in the general population were diagnosed with ASPD, combined with the fact that women with ASPD tended to have a higher proportion of affected relatives, also indicated that the sexes differed in threshold for expression of the trait, i.e., that affected women tended to be more deviant (from the population mean) in liability for the disorder.

A subsequent family study using felon probands²² reported similar findings, revealing a phenotypic correlation between relatives for ASPD of 0.425. They further found that the familial factors (environmental and genetic) relevant to the development of ASPD appeared to be the same for men and women, with little evidence for sex-specific causes.

It should be kept in mind that the finding of familiarity does not mean that all cases (or even the majority of cases) of an illness must be familial; it merely means that the illness is more prevalent among relatives of a proband with the illness than among the general population. Family studies, moreover, are not without limitations or pitfalls. Bias in ascertainment of probands for family studies can lead to substantial over- or underestimation of prevalence of familial illness; similarly, excessively restrictive or lenient definitions of illness or "caseness" can lead to spurious or ungeneralizable results. Unsystematic assessment of subjects or evaluation of family members by investigators not blind to the proband's diagnosis can further distort conclusions. Probability of consenting to interview or being available to be interviewed may be affected

by disease status; for example, if the disorder is associated with premature death, incarceration, and so forth. Assortative mating can inflate the estimated heritability of a disorder, whereas reliance on family history (as opposed to direct interview) data is known to underestimate prevalence of affected subjects.²³ Estimates of familial rates may be confounded by secular trends in disease prevalence or its transmissibility.²⁴ Familiality of illness could be due wholly or in part to a familial aggregation of risk factors for the illness, rather than to the specific inheritance of the illness or liability to it.^{25, 26}

Finally, familiality does not necessarily imply a genetic basis for inheritance. As Goodwin²⁷ has pointed out, the ability to speak French runs in families, but one need not invoke a genetic cause of French speaking. Other techniques, therefore, are necessary in order to separate cultural from biological inheritance.

Adoption Studies in Criminality and ASPD

In theory, adoption studies isolate constitutional from acquired traits because the infant is raised by parents to whom he or she is not genetically related. A correlation between presence of a psychiatric illness in the biological, but not adoptive, parents and in the child would be evidence in favor of a biologically inherited, presumably genetic liability factor, whereas excess concordance with the adoptive parents would favor familial, but not genetic, transmission.

Adoption studies in general may be biased by factors such as selective or delayed placement of adoptees, and some biological effects on the infant (such as prenatal exposure to alcohol or other drugs) may persist indefinitely after placement in an adoptive home. Interpretation of results of older adoption studies of antisocial behavior is difficult, also, because of the same problems noted for family studies, e.g., differences in assessing ASPD, other psychopathology, and criminality, or failure to account for the possible effects of substance abuse. Nonetheless, substantial evidence for heritable factors in adoptees has been found in Danish adoptees by Schulsinger²⁸ and in US samples by Crowe²⁹⁻³¹ and Cadoret.³²

In contrast, Bohman,³³ studying criminal records and registrations for alcoholism of 2324 adoptees in Sweden, found evidence for inheritance of alcoholism, but not criminal behavior. In that study, a subsample matched for a number of parental characteristics; and contrasting the biological parents with and without criminal records was used, with no differences seen in rates of criminality among either adopted men or women.

Subsequently, however, Bohman, Cloninger, and Sigvardsson³⁴ reanalyzed data on 862 Swedish male adoptees of known paternity placed before the age of three years. In this sample, they identified a form of criminality (commission of property offenses) that appeared to be inherited separately from alcohol abuse. Although this trait conveyed no protection against alcohol abuse, it appeared

distinct from alcohol-related criminality, characterized by repetitive commission of antisocial acts that were more often violent in nature.

Further analyses^{35, 36} indicated substantial gene-environment interaction in the production of this behavior; 40 percent of those from high-risk prenatal backgrounds reared in high-risk homes became petty criminals, as compared to 2.9 percent of those from neither high-risk biological nor environmental backgrounds. Exposure to an exacerbating environment in the absence of a high-risk biological background was associated with a 6.7 percent rate of petty criminality, whereas presence of high-risk biological background without placement in a high-risk environment was associated with a rate of 12.1 percent.

Consistent with these findings, in a study examining court convictions of 14,427 Danish adoptees as well as their biological and adoptive parents, Mednick, Gabrielli, and Hutchings³⁷ found a strong association in convictions for property offenses, but not violent crimes, between biological parents and adoptive sons. Higher numbers of convictions were associated with higher rates of offending in the sons; moreover, the proportion of repeated offenders among adoptees increased with the amount of crime seen in the biological parents.³⁸ Criminality in the adoptive parents, by contrast, was not associated with criminality in the sons.

Subsequent analyses of this large data set have expanded these findings considerably. Moffitt³⁹ found that “antisocial

disorders” (treatment for substance abuse or personality disorder) in the biological parents were associated with conviction for property crimes in the child. Baker⁴⁰ was able to estimate the relative contributions of genetic and environmental factors to these observed phenotypic correlations, finding that in addition to high correlations for genetic factors, the relationship appeared to be strongly mediated by correlated environmental factors. Finally, Baker et al.⁴¹ found that, although genetic and environmental influences apparently contribute equally to liability for being a property criminal, women convicted of property crime tend to have a greater degree of genetic predisposition, a finding consistent with that of Cloninger et al.²¹

Cadoret, O’Gorman, Troughton, and Heywood⁴² directly interviewed 127 male and 87 female adoptees and their adoptive parents; information on psychiatric disorders among biological relatives was obtained from agency records. In their analysis, antisocial behavior in first-degree biological relatives increased the odds of diagnosis of ASPD in male adoptees by a factor of 3.7. Among female adoptees, the odds were increased by a factor of 1.9, but the relationship was not statistically significant. A biological background of alcoholism, by contrast, did not increase the risk of ASPD among adoptees, although it did increase the odds for alcoholism among both men and women. Finally, none of the environmental factors studied was associated with increased odds for ASPD. A replication study by the same investiga-

tors using a different sample of adoptees⁴³ yielded very similar results, though in the latter study, problems in the adoptive family such as antisocial behavior, substance abuse, or other psychiatric difficulty were also found to be related to the development of ASPD. Subsequent analyses⁴⁴ also found evidence for gene-environment interaction, with lower socioeconomic status associated with increased risk for ASPD in those with an antisocial biological background.

Twin Studies

Thus, adoption studies on balance support the hypothesis that some of the factors contributing to liability for ASPD or criminality are heritable. Another line of evidence supporting the existence of heritable factors comes from twin studies. In the most commonly employed design, the difference in concordance rates for illness in monozygotic (MZ) versus same-sex dizygotic (DZ) twins is studied, the assumption being that environmental factors should be comparable between twins, whereas genetic factors would differ, since MZ twins share the same genome, and DZ twins share on average 50 percent of their genes. Thus, excess concordance for a disorder among MZ twins would be evidence for genetic influence on the development of illness. As with adoption studies, twin studies have provided support for the hypothesis of genetic liability factors in schizophrenia and affective illness³ as well as substance abuse.⁴⁵

Early twin studies of criminality appeared to support the role of genetic factors,¹² but are difficult to interpret

because of variations in ascertainment, zygosity determination, and classification of criminality. A later twin study by Christiansen²² found substantially higher concordance for criminality (51% of 338 MZ pairs versus 26.2% of 637 DZ male pairs); phenotypic correlation was estimated at .600 for MZ twins and .407 for DZ pairs.

By contrast, Dalgard and Kringlen,⁴⁶ studying 138 Norwegian twin pairs, found concordance rates of 25.8 percent and 14.9 percent in MZ and DZ twins, respectively. However, after controlling for similarities in environment, they found that MZ-DZ differences in concordance were so reduced that they concluded that "hereditary factors are of no significant importance in the etiology of common crime."

Later studies, however, cast doubt on that conclusion. Rowe,⁴⁷ ascertaining 168 MZ and 97 same-sex DZ twin pairs through high schools, used an anonymous survey form to determine zygosity and antisocial behavior. By fitting various biometric models to the data, Rowe concluded that a purely environmental model (ignoring genetic effects) could not sufficiently account for twin similarities, whereas models accounting for genetic effects and specific environmental (i.e., factors not shared by both twins) factors, with or without a factor accounting for environmental influences common to both twins (common environment), satisfactorily explained twin similarities.

Rowe and Osgood⁴⁸ extended the analysis on this sample to correlations between self-reported antisocial behav-

ior and association with delinquent peers, commonly felt to be a contributing factor to antisocial behavior in adolescents. Partitioning the relationship into genetic, common environmental, and specific environmental components, they found that most of the phenotypic resemblance between the two traits could be explained by genetic factors, (61%) with common environmental factors and environmental factors specific to one co-twin less important, accounting for 23 percent and 16 percent of the observed correlations between male twins, respectively. For female twin pairs, estimates were very similar (64%, 17%, and 19%).

However, Carey⁴⁹ has suggested that most twin studies of criminality do not adequately account for reciprocal interactions between twins, i.e., the possibility that co-twins may influence each other's likelihood of engaging in antisocial behavior. Using the Danish twin sample, it was shown that such effects could not be ignored without causing the importance of genetic factors to be substantially overestimated.

As with family and adoption studies, twin studies also have methodologic pitfalls. Twins are a select population, tending to have higher rates of obstetric complications, infant mortality, and older mothers, whereas the assumption that MZ and DZ twins are treated similarly or that environmental influences (even intrauterine environment) are identical may be questioned.⁵⁰

Physiologic Markers of Criminality and ASPD

Another line of evidence suggesting the role of biological susceptibility fac-

tors in antisocial behavior comes from study of physiologic parameters in antisocial individuals. It has long been known that group differences between criminals and controls exist on a number of measures, such as electrodermal responses, resting heart rate, and orienting responses to various stimuli, as well as showing EEG evidence of cortical underarousal.^{51, 52} These factors may in turn be related to a repeated finding that criminals demonstrate impairment on a variety of neuropsychological tasks,⁵³ particularly those that require passive avoidance or inhibition of punished behavior.^{54, 55}

Numerous biochemical differences between criminals and noncriminals have also been suggested.⁵⁶ A number of studies have suggested a correlation between low serotonin (as measured by cerebrospinal fluid assay) and violence or impulsivity,⁵⁷⁻⁶⁰ although since low central levels of serotonin have also been found in suicide victims,⁵⁸⁻⁶¹ the relationship appears nonspecific.

Many of these psychophysiological differences appear to be at least partially under genetic control.^{51, 54, 56, 62} Thus, a more complete understanding of the genetic basis of antisocial behavior may require studies of the inheritance of specific aspects of the ASPD phenotype, rather than ASPD *per se*, analogous to studies currently underway of the phenotypes of alcoholism, schizophrenia, and bipolar illness.⁶³

Heritability of Personality Traits

Thus, evidence from family, twin, and adoption studies, combined with find-

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ings of population differences on a variety of physiologic markers gives strong support to the overall conclusion that, like most psychiatric illnesses, ASPD and criminality have a biologically heritable component; and from these studies several conclusions may be drawn. First, heritable factors associated with criminal behavior and ASPD can be differentiated from those predisposing to substance abuse. Although the two syndromes are frequently confounded, they appear to have different genetic components (at least for property crimes), though coexistent substance abuse appears to substantially exacerbate the course of criminal behavior.

Secondly, genetic factors are insufficient by themselves to fully explain antisocial behavior. Thus, attention is more properly focused not on establishing the cause of illness as nature versus nurture, but on characterizing and quantifying the role of genotype-environment interaction in the genesis of psychiatric illness.

Finally, there is little evidence that single genes of major effect play a significant role in the inheritance and development of antisocial behavior in most cases. Rather, the genetic influence appears best explained by polygenic effects, i.e., a number of genes, each of relatively modest power acting together.

These conclusions are little different from what was known of the inheritance of antisocial behavior two or three decades ago. However, several recent conceptual and technical advances now enable researchers to go from these classical techniques to more fundamental

descriptions of the specific genetic factors which may be involved in antisocial behavior. But in order to assess their implications, it is necessary first to review recent thinking about the heritability of personality traits in general, and then to review the fundamentals of current molecular genetics.

Unlike psychiatric illness, which is typically seen as a threshold phenomenon (i.e., expression of the disorder is seen as exceeding the threshold of an unmeasured underlying, normally distributed continuum of liability, so that clinical description is dichotomous, either affected or unaffected), personality traits are generally conceptualized as continuous variables, approximately normally distributed in the population. Although a tremendous number of personality assessment scales have been proposed, most appear to measure roughly the same underlying factors, and most differences in personality can be explained fairly well in terms of variation along three independent axes.⁶⁴

It is unlikely that single loci that commonly play a major role in determination of personality will be found.^{65, 66} Rather, it appears that a number of genes, each of relatively small individual importance, influence personality traits, with the overall heritability of these traits estimated to be between 30 percent and 50 percent. Even relatively modest genetic contributors may be relevant to the study of the inheritance of antisocial behavior. For example, measuring the effect of specific environmental factors in the setting of a twin study design has enormously increased statistical power

when applied to other disorders, e.g., depression,⁶⁷ and could appropriately be used in studies of antisocial behavior, as well. Another potentially valuable method is quantitative trait loci (QTL) analysis, a technique whereby it may be possible to establish linkage to loci that individually account for small amounts of the variance of a given trait.⁶⁸

Genetic Linkage Studies in Psychiatric Illness

Up to this point, much has been made of the inheritance of personality traits or liability characteristics, but mode of inheritance has been neglected. By modeling parameters such as population frequency of alleles, their degrees of penetrance and dominance, and applying these models to known pedigrees (segregation analysis), multiple hypotheses about mode of inheritance (single major locus or polygenic effect, primarily genetic or multifactorial influences, etc.) may be tested, thus significantly narrowing the field of possible ways susceptibility to illness might be inherited. If models are constrained to remain within bounds suggested by available data regarding these parameters, the technique may be of significant value in supporting some possible modes of inheritance and eliminating others—although, of course, as with any model-fitting exercise, construction of a model that cannot be rejected is not identical to confirming a given mode of inheritance. Information about likely inheritance patterns may be of great use, however, especially if genetic linkage studies are to be undertaken.

At the present time, genetic linkage studies⁶⁹ may hold the most promise for elucidating the genetics of psychiatric illness. The rationale for linkage studies rests on the fact that the normal human has 23 pairs of chromosomes, 22 autosomes, and two sex chromosomes. These can be thought of as strings of genes, and while the actual DNA sequence may differ between individuals (or even between homologous chromosomes in the same individual) at a given point or locus, the ordering of the loci is the same for everyone, barring chromosomal translocations. Since the normal situation is that everyone has two copies of each chromosome (one inherited from each parent), particular DNA sequences at a given locus in principle can be traced from parent to child. (Obviously, in practice the sequences must differ at that locus in the parents in order to be fully informative.)

The various DNA sequences that can occur at that locus are referred to as alleles; there may be few or many such variants to be found at a given locus. The *genotype* of the individual at that locus is determined by the allele actually found at that site on each of the two chromosomes. The *phenotype* of the individual is the observable expression of the genotype that often therefore must be inferred rather than directly observed. Perhaps the best understood example is the classical Mendelian situation where two alleles (one dominant, one recessive) exist for a given locus. In this case, the observable characteristic (or phenotype) will vary depending on the genotype at that locus: two recessive alleles (homo-

zygous recessive), two dominant alleles (homozygous dominant), or one of each (heterozygous). Assuming complete dominance, the latter two conditions will express the same phenotype.

This scenario is frequently an oversimplification, however. Most such characteristics are not clearly dominant or recessive, so that the heterozygous condition may show intermediate characteristics; moreover, at many loci, a large number of alleles exist, resulting in a wide range of possible phenotypic expression. Furthermore, as far as is currently known in psychiatric genetics, phenotypic characteristics of interest rarely (if ever) depend only on gene expression at one locus.

When two characters are consistently cotransmitted within a pedigree, they are considered linked. Given the above discussion, it would seem that any two characters found on the same chromosome would always be inherited together; the fact that this is not so is due to the phenomenon of crossing over.

During meiosis, the paired chromosomes become closely approximated, and indeed overlap. Breaks in the chromosomal material occur at these junctures and as the breaks are repaired homologous portions of DNA are exchanged. It is this altered chromosome that is passed on in the gamete.

Thus, the greater the distance between two loci on the same chromosome, the greater the "recombination fraction" (θ), i.e., the chance that the two characters will be independently transmitted. As the distance between loci on the same chromosome increases, the probability

that the characters will be transmitted together approximates the probability of cotransmission of characters on different chromosomes, i.e., 0.5. Similarly, crossings over between two loci become less and less likely as the distance separating the loci decreases. Thus, the null hypothesis of no linkage means that $\theta = 0.5$; a value of θ significantly lower is evidence for linkage. Generally, rather than directly comparing odds of observed values to odds under the null hypothesis, researchers use the logarithm of these odds, or *lod score*, generally accepting a lod score of 3 or greater as evidence in favor of linkage, and a score of less than -2 as evidence against it.⁷⁰⁻⁷²

Until relatively recently, linkage studies were severely hampered by a lack of useable genetic markers. With the widespread use of endonucleases (enzymes that cleave DNA at specific points), however, numerous heritable differences have been found in sequences of DNA that could be cleaved. These *restriction-fragment-length polymorphisms* (RFLPs) are easily separated based on electrophoretic mobility and have been used with great success as genetic markers. Unfortunately, not all such markers are informative (90% of polymorphic markers have a heterozygosity of less than 50%); however, techniques focusing on highly informative regions such as sites with variable numbers of tandem repeats, or VNTRs (stretches of DNA with repeated C-A base sequences) have substantially improved informativeness.^{73, 74} Other new approaches, such as application of polymerase chain reaction (PCR) technology to expand the amount of

genetic information available to researchers, or large-scale cloning of segments of the human genome via yeast artificial chromosomes (YACs) may also improve researchers' abilities to identify specific genetic factors in a variety of psychiatric disorders.⁷⁵ By use of these and other markers, the technology has, in fact, advanced to the point of making a high-resolution map of the human genome an attainable goal.⁷⁶

Once a putative disease locus has been demonstrated to be linked to a genetic marker, it can be precisely located, e.g., through "walking the chromosome" starting from the marker locus by use of cloned, overlapping DNA fragments, until the DNA sequence of interest is characterized. This should lead to identification of the gene product or function and thus to better understanding of disease pathophysiology at the molecular level.^{77, 78}

This technology has proven most useful for diseases inherited in a classical Mendelian fashion, e.g., Huntington's disease or Duchenne muscular dystrophy.⁷⁹ However, for common, complex disorders which are strongly genetically influenced, such as certain cancers, atherosclerotic cardiovascular disease, and many psychiatric disorders, the precise mode of genetic inheritance is not known. This means that researchers must make a variety of assumptions regarding transmission, chief among them that a single locus of major effect that can be linked to a marker exists, though it may be modified by presence of other genes or a variety of environmental factors, such as secular trends in illness as

well as exposure to putative environmental risk factors.

Other technical difficulties in psychiatric genetic linkage studies include errors or diagnostic instability in assessment (since there are no diagnostic laboratory tests), variable penetrance of the character of interest, variable age-of-onset of illness, and phenotypic variance. Moreover, major psychiatric illnesses are thought to be etiologically heterogeneous; that is, similar illness presentations may be caused in a variety of ways, including more than one genetic mechanism.⁸⁰

It is therefore understandable that, while researchers have reported evidence for linkage in several psychiatric disorders, confirmation so far has proven elusive. Currently, a number of techniques are being developed to address these difficulties. It may prove more practical, for example, to evaluate linkage with a specific phenotypic character of the illness, rather than the entire syndrome. Use of large, extended pedigrees with multiple affected relatives for linkage studies should minimize the problem of etiologic heterogeneity (since affected family members are more likely to have the same form of illness); statistical methods are being developed to assign probabilities of "caseness" rather than classify in an all-or-none fashion, methods of multilocus linkage analysis have been proposed, as have ways of accounting for environmental influences on risk for development of psychiatric illness.^{81, 82} While these techniques have not yet been applied to criminality or ASPD, such linkage efforts are currently

underway in studies of schizophrenia, manic-depressive illness, alcoholism, and Alzheimer's disease.

Gene-environment Interaction

Given the evidence supporting the role of environmental factors in the genesis of criminality and ASPD, it is likely that further advances will come not just from refinements in molecular genetic techniques, but from the study of gene-environment interactions: The disparate effects specific genes have under different conditions. It is well understood that gene effects may manifest differently with changes in the environment; for example, someone heterozygous for sickle cell anemia will be asymptomatic at sea level, but may develop sickling at high altitudes. Similarly, children with phenylketonuria, if exposed to normal levels of dietary phenylalanine, develop mental retardation that may be minimized or prevented by environmental manipulation, i.e., restricting phenylalanine intake.

Although it is a long jump from such simple Mendelian disorders to the complex, polygenic factors that interact with environmental influences to determine personality or psychiatric illness, the logic remains the same. By classifying individuals based on both biological and environmental risk factors, behavioral genetic techniques should be able to identify increasingly homogeneous groups, leading to increased accuracy of behavioral prediction and perhaps ultimately to the clinical ability to quantify risk of certain behaviors, and thus the ability to stratify the population into

low and high-risk groups. Indeed, for some forms of criminality this process has begun, as researchers have attempted to identify more homogeneous forms.^{35-37, 39, 83} Furthermore, as is beginning to occur for other psychiatric disorders such as depression, by controlling for genetic factors (e.g., in twin study designs), use of behavioral genetic techniques should allow researchers to identify environmental risk factors and characterize their influences on different genotypes with a high degree of precision.⁸⁴⁻⁸⁶

Forensic Implications

Promising as these research developments are, the moderate degree of heritability of antisocial behavior suggests that if genetic markers can be identified, they will likely prove to be of limited discriminatory power. Because antisocial behavior appears to be associated with a number of factors (including environmental and experiential influences), one may predict that many cases would be genetic "false-negatives" (i.e., would be individuals without the putative genetic risk factors or risk indicators who nonetheless commit antisocial acts). Conversely, it is doubtful that genetic factors would by themselves be either necessary or sufficient causes of most antisocial behavior; thus, a number of genetic "false-positive" cases (those with genetic liability factors who do not commit antisocial acts) would also exist. In fact, in any population with a low base rate of antisocial behavior, reliance on genetic predictors would simultaneously miss most predisposed individuals

while overpredicting those at risk for such behavior—the same situation, in other words, that exists now with clinical ability to predict violence.^{87, 88} Nonetheless, the prospect of a simple, “scientific” test for liability to future antisocial behavior might prove attractive to those charged with protecting society, e.g., prosecutors faced with dispositional questions such as whether to grant or revoke parole or probation, whether to try a violent offender as a juvenile or an adult, whether to seek the death penalty, or similar issues that might hinge on a prediction of future criminal activity. Should specific genetic associations with violent or otherwise antisocial behavior be discovered, the forensic clinician may be the only resource available to the court able to assess critically the implications of such research, including the potential errors of classification that may occur when applying the results of such tests to individuals ascertained through the legal system.

Another question that could be influenced by deeper understanding of the role of genetic factors in antisocial behavior is the issue of the insanity defense. Should such factors become better characterized, the question of whether and to what extent such factors “caused” the unlawful behavior or permitted it to occur will undoubtedly be debated in the legal setting. Similar questions about biological determinants of behavior have already been raised when experts have been asked to relate the relevance of abnormal findings from neuropsychological or neuroimaging studies to the defendant’s ability to refrain from

wrongful conduct.^{89, 90} As other biological factors influencing (or potentially influencing) the occurrence of socially proscribed behaviors become better described, it is likely that they will be invoked in the courtroom as causative of the wrongful behavior, and hence exculpatory. Once again, the forensic clinician may be uniquely equipped to weigh the scientific evidence, avoiding such oversimplification, and apply it to the legal and moral issue of criminal responsibility.

More generally, the prospect of genetic testing for liability to antisocial behavior raises a number of questions regarding issues of privacy and freedom of choice.⁹¹ If a group with elevated propensity to crime becomes identifiable through such testing, to what extent (if any) should individual rights give way to efforts aimed at protecting society? Does widespread testing make sense if no preventative intervention is known to work (or is cost-effective)? If effective interventions became available, would that justify testing on a voluntary basis? Given the cost to society of antisocial behavior, could it justify involuntary testing or forcing those at risk to accept treatment? As the biological underpinnings of repetitive antisocial behavior are more precisely characterized, such issues will assume greater importance.

Conclusions

ASPD, depending on the criteria used to diagnose it, occurs in approximately 2 percent to 7 percent of men and 0.5 percent to 1 percent of women on a lifetime basis.^{15, 21} Likewise, criminal be-

havior is not evenly distributed among the general population; it has been estimated that six percent of offenders are responsible for more than half of police contacts.⁹² Thus, from a standpoint of public policy, it seems appropriate to study such persistent offenders so that the causes of antisocial behavior can be better understood.

Such study, using a variety of methods, has demonstrated the existence of associated familial, heritable factors.¹³ A variety of neurochemical and physiological markers associated with antisocial behavior have also been identified. Thus, as for other complex, common syndromes, converging lines of evidence indicate the presence of biological factors relevant to the development of the phenotype of antisocial behavior, factors that may themselves be under substantial genetic control.

Behavioral genetic studies not only demonstrate the presence of heritable factors, however; they are also necessary in order to understand the role of environmental factors (particularly those not shared by siblings) in the genesis of psychopathology and antisocial behavior.⁹³

Further advances in our understanding of antisocial behavior are likely to come from a more detailed understanding at the level of molecular genetics of the processes mediating learning and temperament, as well as how such learning styles themselves might influence later behavior. Much remains to be learned as well about how expression of inborn factors is influenced by specific postnatal experiences, and in what way genetic factors may influence later ex-

posure to environmental risk factors. From a research perspective, such advances hold great promise in early identification, and ultimately perhaps even prevention or treatment of behaviors that heretofore have proven to be quite resistant to intervention.

However, such advances in knowledge have already begun to present ethical issues that will continue to grow in significance as more is learned. Oversimplification of complex gene-environment interactions may lead to inaccurate labeling of individuals as prone to criminal or violent behavior; even if accurate, the harm to those so identified may outweigh any potential good to society. Conversely, evidence of genetic markers indicative of heightened liability to antisocial behavior may be preferred as an excuse for wrongful behavior. As more is learned of genetic influences on antisocial behavior, the need for informed clinicians able to relate these research findings to forensic issues will continue to grow.

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