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Nature and Nurture: The Far-reaching Implications of Behavioral Genetics Research

Science is inching toward answers in the longstanding nature vs. nurture debate: How do genes and environment independently influence human behavior, and how do they interact to exert an effect? With the emergence of suggestive data, more questions arise: How predictive of behavior are such findings, and how might they be applied to the potential benefit, or harm, of individuals and society? This Issue Brief reviews the broad implications of ethical, medical, legal, and policy questions that were raised during a seminar on genetics and human behavior sponsored by the Center for Strategic and International Studies (CSIS) in Washington, D.C., on December 12, 2002. The seminar served as a forum for discussion of Genetics and Human Behaviour: The Ethical Context, *a recently published report from the London-based Nuffield Council on Bioethics.*

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Speakers

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Eugenics, free will, gene therapy, prenatal selection. These are among the topics considered in a new report entitled *Genetics and Human Behaviour: The Ethical Context* from the Nuffield Council on Bioethics, an independent research group established in London in 1991. The report examines the ethical, legal, and social issues related to research on the genetics of human behavior within the normal range. (The full text of the report is available online at http://www.nuffieldbioethics.org/behaviouralgenetics/index.)

The CSIS seminar convened to discuss this report followed a three-part format: (1) two presentations about the report's findings and recommendations; (2) two critiques of its strengths and weaknesses; and (3) a response and discussion session.

GENES AND THE NORMAL RANGE OF HUMAN BEHAVIOR: AN OVERVIEW OF THE REPORT

What is "normal" behavior? Sidestepping the moral judgments inherent in that question, the report's multidisciplinary working group defined normal as an extent of variation that is distinct from disease. In statistical terms, this definition covers some 95 percent of the population.

The following behavioral traits were considered in the report—measures displayed, to a greater or lesser extent, by each individual that are not generally seen as disorders:

- Intelligence
- Personality: anxiety, novelty-seeking, shyness, agreeableness, trustworthiness
- Antisocial behavior: violation of the rights and safety of others
- Sexual orientation

The report also included a historical survey of relevant research, including eugenics. As Sandra Thomas, director of the Nuffield Council, explained, "It is important to understand the past as we embark on similarly sensitive research now."

From its investigation of more current behavioral work in quantitative genetics, molecular genetics, and research involving animals, the report's working group noted difficulties in:

- Isolating the gene-environment correlation and interaction. For example, environment may reinforce the genetic contribution.
- Identifying the size of the effect. Genes that have a small effect may work in concert with others to influence behavior. (Even for conditions like Huntington's disease, where the genetic contribution is less complex, it is clear that someone who carries the culprit gene will manifest the disease, but it cannot be predicted when.)
- Understanding developmental processes. This is another complicated strand that affects the science.

The working group ultimately agreed that there are no current applications for behavioral genetic research, genes do not determine human behavior, and phrases such as "a gene for intelligence" and "the gay gene" are highly misleading.

The report did cite genetic variants associated with behavior outside defined norms. For example, certain monoamine A (MAOA) genotypes have been linked to greater likelihood of violence in adult men, but only if they were abused in childhood (see box on New Zealand Findings), and variants in dopamine D4 receptor (DRD4) have been tied to impulsive and compulsive behaviors, substance abuse, and attention deficit hyperactivity disorder (ADHD), but their role remains equivocal. Although genetic tests are likely to have poor predictive reliability, because they may show a predisposition or susceptibility to certain behaviors, "It's not too early to discuss the ethical issues," Thomas noted. "What was unforeseeable in the past, such as *in vitro* fertilization, has become possible. We must find ways to discuss such possibilities without frightening people."

The New Zealand Findings on MAOA and Antisocial Behavior

A paper published in August 2002 presents intriguing data on monoamine A levels, abusive childhood environments, and antisocial behavior.[1] Researchers followed 442 boys in New Zealand from childhood to age 26. Of this cohort, 154 were maltreated in their home environment, and 33 were severely maltreated. The genotypes of some subjects allowed production of high levels of MAOA; others had low-MAOA genotypes. Over time, 85 percent of the severely maltreated subjects with low levels of MAOA developed antisocial behavior. Despite abusive environments, few subjects with high levels of MAOA developed antisocial behavior. The data suggest that high levels of MAOA somehow protected the subjects from the ravages of an abusive upbringing. The fact that it was a longitudinal study designed by social scientists "enhances the credibility of the findings," in David Wasserman's opinion.

1. Caspi A, McClay J, Moffitt T, et al. Role of genotype in the cycle of violence in maltreated children. *Science* 2002;297:851-854.

> ***"Research in behavioral genetics has the potential to advance our understanding of human behavior; however, it raises important ethical issues and generates public concern."*** **Genetics and Human Behaviour: The Ethical Context**

From Pathology to Premiums

The report identified red flags for concern in areas of medical practice, employment, insurance, and education.

The Medicalization of Behavior Traits. As research in behavioral genetics produces more suggestive data, traits now viewed as normal (e.g., some levels of anxiety) may come to be seen as disorders that require treatment. This trend, in turn, raises concerns that (1) tolerance for different behavior traits may decline, (2) medical and genetic solutions may be tried routinely in preference to other options (e.g., Paxil for shyness), and (3) diagnostic categories may be expanded in an unhelpful way that encourages the use of medication.

> **Recommendation:** Health service providers should charge a named agency with monitoring and, if necessary, controlling this means of the deliberate medicalization of normal populations.

Preimplantation Genetic Diagnosis (PGD). This technique enables embryos created by *in vitro* fertilization to be tested for genetic disorders before they are implanted. Alexander McCall Smith, a member of the report's working group, said that in the controversial area of PGD, the United Kingdom is facing growing demands for its application in the name of parental rights. The government currently licenses clinics through its Human Fertilisation and Embryology Authority, which is conducting a public inquiry into gender selection. The working group had a strong consensus that "procreative autonomy" stops far short of the use of PGD to select embryos for traits within the normal range.

> **Recommendation:** The use of PGD should not be extended to include behavioral traits in the normal range, such as intelligence, sexual orientation, and personality traits.

Employment. A survey conducted by the Human Genetics Commission found that in the United Kingdom, genetic discrimination in the workplace was one of the areas of greatest concern stemming from genetics research. The Nuffield Council report states that employers should be held accountable for providing an environment safe from such discrimination—a principle emphasized in the European Convention Biomedicine and Human Rights (also known as the Oviedo Convention), which has a growing number of signatory states in Western Europe. Additionally, a genetics protocol to that convention is being negotiated.

> **Recommendation:** Employers should not demand a genetic test as a condition of employment, and any inquiry into the use of genetic tests in the workplace should examine the use of other purportedly scientific methods (e.g., psychometric tests).

Insurance. The use of genetic information for insurance purposes is a topic of intense public concern on both sides of the Atlantic. In the United Kingdom, it falls within the purview of an existing five-year moratorium on the use of genetics test information for insurance purposes, as recommended by the Human Genetics Commission. McCall Smith pointed out that insurance companies are allowed to use family histories, which can provide powerful genetic information, but this subject generates far less heated discussion than the direct use of DNA test results.

> **Recommendation:** Genetic information about behavior traits in the normal range should fall within the scope of that moratorium and should not be used by insurance companies in setting premiums.

Education. The implications of behavioral genetics for education have not received adequate attention and merit further research.

> **Recommendation:** Dialogue between researchers and educators should be promoted. Until this has been achieved, genetic information about traits in the normal range should not be used in the context of education.

"Genetic variants within the normal range cannot absolve individuals from responsibility for their actions." **Genetics and Human Behaviour: The Ethical Context**

Personal Behavior and Criminal Law

The working group spent significant time considering legal implications, particularly within the framework of how behavioral genetics might affect society's concept of individual responsibility. Its members concluded that a greater understanding of genetic influences on behavior does not undermine human dignity, and that research in behavioral genetics does not pose a fundamental challenge to our notions of responsibility. From these premises, the following recommendations were developed:

Exculpation. Genetic variants within the normal range cannot absolve individuals from responsibility for their actions. The roots of the debate about behavioral genetics and criminal behavior go back to the 19th century (e.g., phrenology), and the same concerns remain today. McCall Smith cited a "fairly crude form of reductionism" that seeks a biological basis for criminal behavior. People come to a position of biological determinism for different reasons, he noted, which are not necessarily prompted by a desire to devise better methods of social control.

The public is concerned that behavioral genetics may destabilize notions of personal responsibility, McCall Smith said. This concern is exemplified by the following excerpt from the Sunday *Times* on October 2002:

> *Personal responsibility is a quasi-religious idea, an article of irrational faith on which everything we value depends. Without this belief, there can be no guilt, and therefore no innocence or virtue. Without it there can be no accountability or justice as we now understand them. Without it, our moral universe is reduced to pathology. Tradition, convention, and community depend on our belief in personal responsibility and so above all do our ideals of equality and freedom. Civilization involves a great deal of pretending and the pretense of personal autonomy is one of the best and most generous of all. And perhaps we're genetically predestined to believe in it anyway.*

Sentencing. Criminal law should be receptive to whatever psychiatric and behavioral evidence is available. In this regard, credible and convincing evidence of influence and a robust test for a genetic variation would be essential, and judges would determine the weight such information should be accorded.

Although the working group felt that it could not allow behavioral genetics to serve as an excuse for criminal behavior, its members did see a role for insights from the genetic and behavioral sciences as potential mitigating factors in the sentencing process. McCall Smith speculated that the generally unfavorable press response to this point might have resulted from confusion between the notions of accountability and punishment. He further expressed the hope that a genetic predisposition toward violent crime in a person who commits violent acts would, like alcohol abuse, be used to promote sensitivity to medical interventions as part of sentencing.

Prediction. For those who haven't exhibited antisocial behavior, genetic information about behavior in the normal range should not be used in isolation to predict behavior. If the aim is to benefit the individual, however, it may be justified to use such information in conjunction with information about environmental factors that increase the chance of antisocial behavior. Finally, detaining an individual who has not committed a crime on the basis of predictions of behavior—whether they're based on information about genetic or nongenetic behavioral influences—is not justified.

In the United Kingdom, "psychopaths are in the limelight," McCall Smith said. Politicians have picked up on public pressure to deal with people who are socially dangerous because of a mental disorder, and psychiatrists are threatening to resign in the face of the government's position that it should be able to detain psychopaths preventively. The working group concluded that it would be inappropriate to use genetic information to predict anything related to behavior. Nevertheless, "Psychogenetics may well become more important, especially if pressed to produce harder scientific predictions for use in social protection provisions of mental health legislation," according to McCall Smith, "and that raises very serious ethical and human rights issues."

TWO CRITIQUES OF THE REPORT

Facts and Speculative Fantasies: Dealing with Modest Data

"Boring truths are hard to sell, but hype is easy," observed Erik Parens of The Hasting Center, explaining the media tendency to overstate research results. For example, a paper in *Nature*, describing an apparent boost in IQ of a genetically modified mouse dubbed "Doogie," concluded by suggesting that enhancement of mammalian intelligence may be possible. This conservative speculation came to the attention of an enterprising reporter, who asked a bioethicist to accept the premise and ponder the ramifications. The result was a *Time* magazine cover featuring a human infant and a tantalizing headline: "The IQ Gene?"

The challenge is to find a balance between contemplating the future and helping to defuse cultural fantasies about where the science actually is, said Parens. He rated the Nuffield Council report an outstanding overview of the fields involved in behavioral genetics—careful, clear, and accessible to anyone with a college education—which "steers away from hype in an admirable way." Its greatest contribution, he said, is its clear account of how modest the scientific results actually are so far.

"Boring truths are hard to sell, but hype is easy," Parens observed

From the report, he gleaned "three deeply important boring truths":

- Heritability estimates alone are of little value. Knowing that intelligence is 40-80 percent heritable and homosexuality is 40-60 percent heritable is of very little value. Such data do, however, provide justification for molecular studies.
- Molecular genetics has produced very few confirmed and replicated findings.
- At this point, this research has no practical applications.

Given the last fact, should the Council have speculated about future applications? Concurring with Sandra Thomas, Parens argued that yes, we should think about such issues now, in case applications become more feasible. He faulted the report not for addressing potential applications but for how this was done, particularly in the discussion of genetic enhancement, prenatal diagnosis and selective abortion, and preimplantation genetic diagnosis. These are large topics, he said, and the report tried to cover far too much bioethical ground here too quickly.

Specifically, in Parens' opinion, the report paid too little attention to the expressivist argument—the position articulated most clearly by the disability community, which holds that by using prenatal diagnosis to test against disabling traits, we're sending a strong discriminatory message against people who have those traits. Additionally, he thought that the authors relied too heavily on a simplistic and too-narrow distinction between liberal endorsers and conservative critics in the discussion of prenatal selection.

Finally, Parens noted that the generally cautious tenor of the report was not reflected in the Council's media release about the publication. The first line of the release stated: "Embryos should not be selected for behavioural traits such as intelligence on the basis of genetic information." Following this lead, the *Daily Telegraph* began its story: "The selection of babies with genes linked to high IQ should be banned, along with the abortion of embryos predicted to have below average intelligence." The newspaper overinterpreted the report's recommendation; however, both leads obscured the important fact that scientists cannot yet select for IQ, even if they wished to do so.

Conceding that exciting pronouncements will always draw attention away from boring truths, Parens said that "we need to work harder to figure out how to tell the deeply important, 'boring' truths of this superb report."

Where Statistical Concepts of "Normality" Fall Short

David Wasserman's main complaint: despite its richness, "it is not comprehensive enough in a critical way," in part because earlier Nuffield Council work examined conditions outside the norm, for example, mental disorders. In this report, the authors limited their investigation to a statistically defined range of normal behavior (i.e., ± 2 SD, or 95 percent distribution in a population).

One problem with this approach is the large number of conceptions of normality, Wasserman said. A statistical definition overlooks (1) moral, normative, and social conceptions that examine what is normal-acceptable/appropriate vs. abnormal-unacceptable/inappropriate and (2) a biological function conception that deems certain traits normal or abnormal, regardless of their population distribution and the acceptance or disapproval they elicit. A complex relationship exists among these conceptions. Further, normal and abnormal can be described in at least three terms:

- Behavior (which itself has different measure, e.g., conduct, which involves intention; movements and twitchings)
- Mental states or conditions
- Genes or genetic variations (alleles)

“Fascinating and incredibly rich, with a level of argument unusual in a report that elicits such a wide range of opinions and involves diverse groups of specialists”, Wasserman commented.

Wasserman sees great potential for confusion in allowing the frequency of a genetic variation and association with behavior to “categorically determine whether it should be exculpatory.” To support this view, he offered a “fanciful example.” Suppose we found that 25 percent of the U.S. population had a genetic variant that contributed to nonviolent impulsivity that made it extraordinarily difficult for a person to resist the allure of designer apparel seductively arrayed in a Beverly Hills store. In circumstances of modest prosperity, this allele doesn’t manifest because the person is not exposed to this type of array. Only in the extreme abnormal environment of Beverly Hills does this genetic difference start to show.

A woman with such a statistically “normal” genetic variant should be able to argue that she is not criminally responsible for shoplifting, given the constant gauntlet of temptation she would have to run in her “normal” environment, Wasserman suggested. “Implications for moral and legal judgments for statistical distributions are going to be less clear than implications of ‘normal’ and ‘abnormal’ defined evaluatively, or even biologically.”

The statistical approach to normality imposes other limitations, Wasserman said. In the domain of prenatal testing, for example, it “precludes critical comparison of the very permissive policy for what is called ‘clinical selection’ now in place and the more restrictive policy suggested for nonclinical selection.” In the United States and Britain, it is considered acceptable to screen for genes associated with serious abnormalities and impairments but unacceptable to screen for variations within the normal range (or above the normal range, e.g., a blue-eye child with high IQ). As Wasserman sees it, a discussion of policy toward prenatal testing must include the full range of human variations—both normal and abnormal.

Wasserman concurred with Parens on the handling of the expressivist argument about stigmatizing impairments and the use of prenatal diagnosis: “The expressivists’ view can’t get a fair hearing in this report because of its self-imposed limitations,” he said. He also agreed with Parens that the report mischaracterized natural humility as "conservative" but thought it dealt well with the threat posed to this concept by prenatal selection. Many critics of prenatal selection against disability argue that natural humility should make parents willing to accept not just ordinary attributes but significant impairments. The concept of natural humility recognizes the inevitability of pain and suffering in human life, and "cultural blindness" to that fact keeps many parents from seeing the problems with prenatal selection, Wasserman said. He found it "frustrating" that the report could not extend this argument to clinical selection because the subject was outside its purview.

Wasserman concluded that "the report could have been richer and stronger if it had been able to address the full range of behavioral, psychiatric, and genetic variations and had not had to confine itself to a difficult and slippery definition of 'normal' behavioral characteristics."

RESPONSE AND DISCUSSION

"Genes may help villains escape jail." "Crime may be all in the genes." "Criminal gene 'should mean lighter sentence.'" Thomas said that these actual headlines misstate research results, to the detriment of the public's understanding. Noting the media tendency to condense complex science into misleading headlines and oversimplified sound bites, she stated the Nuffield Council's position: Researchers and those who report research have a duty to communicate findings in a responsible manner, and initiatives in the area of communicating science should be strongly encouraged. Regarding comments about its media release for the behavioral genetics report, Thomas said that after producing a cautious report, the Council should have given less prominence in the release to one controversial recommendation.

Thomas agreed with comments about the difficulties of defining "normal" and some resulting limitations of the report. In fact, the Council commissioned an evidence review on addiction, considering it to be "on the edge of normal/abnormal," but ultimately excluded it as being a pathological set of conditions. It was tempting to have broadened the report's scope, Thomas said, particularly with regard to disabilities and prenatal testing, but the Council accepted the limitations of its focus on the normal range.

It would be interesting to consider the earlier report's recommendations about prenatal diagnosis in relation to mental disorders, such as schizophrenia and depression, in parallel with this report's recommendations, Thomas said. Parens pointed out that the report gave no reasons for opposing the use of prenatal testing to select for traits within the normal range. "There seems to be a consensus for this view, but we don't have the kind of ready-made public policy arguments that we want," he said. "This is precisely the kind of difficulty we should be getting on the table, not waving it away." Thomas noted that the working group struggled a long time with reasons to recommend that people should not be allowed to select embryos for some traits, which came as a surprise to the Council.

McCall Smith explained that in the United Kingdom, regulation restricts prenatal testing and selection for "serious conditions" but uses no tighter definition. In a prenatal context, genetic counselors want more specific guidelines, he said. Guidelines developed by the Human Genetics Commission encountered great difficulties, especially with the disability lobby. The Commission also faces corporate pressure to give the public direct access to over-the-counter genetic tests and must advise the government on this issue by February 2003. The difficult considerations involved in this issue include autonomy—the right to learn about one's individual genome.

Religious convictions are a potent force for restrictions on prenatal testing and PGD, Wasserman noted, but the separation of church and state might, by excluding religious references, also exclude some of the most powerful reasons behind strongly held positions. Parens found the secular/religious distinction unhelpful but considered the concept of "natural humility" worth pursuing with advocates of both positions.

Clearly, further development of this discussion is warranted, Thomas said, and McCall Smith suggested that international declarations, conventions, and statements of values be consulted, especially the European Council's Convention on Biomedicine and Human Rights. UNESCO also is developing a universal declaration of the human genome. People turn to these when they can't turn to religious sources because we live in too pluralistic a society, he said: "I think that's a promising source of moral values in a morally confused age when we don't have those old religious certainties."

"We must engage in speculation but keep one foot on the ground," said McCall Smith.

This Issue Brief was written by The Stein Group.