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Gene-Environment Interaction and Medical Sociology

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The boundaries between sociology and biology have long been sites of tension and contestation (Anderson 1967; Pescosolido 2006).[1] In part, these contestations emerge from a concern that biological accounts of the production of human difference pose a threat to sociology's defining focus on social and environmental causes of human health and social outcomes (Duster 2006). Medical sociologists have been at the vanguard of efforts to find productive modes of engagement between the social sciences and contemporary human genetics. Increasingly, these efforts center on gene-environment interaction. We consider here two domains of social scientific inquiry that address gene-environment interaction vis-à-vis health and illness. First, we discuss analyses of the social implications of research on gene-environment interaction, including studies of public understandings and beliefs about genetic and environmental causes of health and social outcomes. Second, we consider research that uses information about genetics and gene-environment interaction as a lever to reveal mechanisms of social and social psychological causation of health and illness. Taken together, this work points to the importance of moving past the assumption of an essential tension between genetic and social (or other environmental) explanations for health and illness toward more integrative analyses that can encompass multiple and simultaneous forms of causation, including the "looping effects" (Hacking 1995) of genetic categories and the enduring influence of fundamental causes of health and illness, especially as capacities for intervention change (Link and Phelan 1995; Freese and Lutfey, forthcoming).

Genes, Environments, and Health

At the turn of the century, gene-environment interaction emerged at the center of research funded by the National Institutes of Health (NIH) (Schwartz and Collins 2007), as well as in the human sciences more broadly (Rutter, Moffitt, and Caspi 2006).[2] As just one measure of its currency at the NIH, in 2006, health and human services secretary Mike Leavitt announced that the president's budget proposal for fiscal year 2007 would include $68 million for the Genes and Environment Initiative, an NIH research effort to combine genetic analysis and environmental technology development to understand how gene-environment interactions contribute to the etiology of common diseases.[3] The prominent role of the concept of gene-environment interaction in this initiative was highlighted in the press release that announced it: "Differences in our genetic makeup certainly influence our risks of developing various illnesses. . . . We only have to look at family medical histories

to know that is true. But whether a genetic predisposition actually makes a person sick depends on the *interaction between genes and the environment*" (NIEHS 2006 [emphasis added]).

In the United Kingdom, the UK Biobank represents a massive investment on the part of the Medical Research Council, the Wellcome Trust, and the Department of Health, with the goal of elucidating "the complex interplay of genetic and environmental factors involved in the aetiology of common diseases" (Tutton, Kaye, and Hoeyer 2004, 284). Gene-environment interaction is also of great interest in the private sector. In the United States, the GEI is to be "accelerated" by the efforts of a public-private partnership, the Genetic Association Information Network (GAIN), a joint venture between the NIH, Pfizer Pharmaceuticals, and the biotech company Affymetrix.

Social scientists also increasingly are taking up questions about gene-environment interaction. Indeed, one of the ironies of the success of the Human Genome Project is that it highlights the imperative for sophisticated conceptualizations and measures of the social environment, long the jurisdiction of sociology (Pescosolido 2006; Perrin and Lee 2007). While not explicitly focused on gene-environment interaction, the recent call for a "sociology of disease," which would incorporate biomarkers into studies of the experience of trajectories of illness, likewise points to the need for knowledge about the intersections of social and biological pathways (Timmermans and Haas 2008). With the inclusion of DNA and biomarker data in large-scale social science data sets (Weinstein, Vaupel, and Wachter 2008; Finch, Vaupel, and Kinsella 2000), the opportunities for sociologists to study gene-environment interaction will proliferate rapidly in the coming years. Likewise, sociologists already have given consideration to social implications of gene-environment interaction, pointing to many concerns and opportunities for the years ahead.

Social Implications of Research on Gene-Environment Interaction

Human genetics has been centrally concerned with understanding how genes work as causes of development and of disease and has turned only recently to studies of gene-environment interaction. As knowledge claims diffuse beyond the laboratory, they may serve as warrants for individual and collective action and transform social policies and institutions. Medical sociology offers at least three important vantage points on the social implications of genetic research—geneticization, biosociality, and public understanding of genetics.

Geneticization

As introduced by Lippman (1991, 19), geneticization refers to "an ongoing process by which differences between individuals are reduced to their DNA codes, with most disorders, behaviours, and physiological variations defined, at least in part, as genetic in origin." Geneticization is both "a way of thinking" about human differences, especially in the context of health and illness, and also "a way of doing," as genetic technologies are "applied to diagnose, treat, and categorize conditions previously identified in other ways" (Lippman 1998). Like many words that end in *-tion*, geneticization refers simultaneously to a social process and to its results (Hacking 1999, 36).

Much as with "medicalization" (Conrad 1992), there has been disagreement over whether the concept of geneticization is primarily "a heuristic tool" in a moral debate (ten Have 2001) or maintains sufficient neutrality to serve empirical research (Hedgecoe 1998).[4] Writing on geneticization often centers on a number of interlocking concerns about genetics as a "dominant discourse" (Lippman 1991, 18) with myriad potential negative social implications. These concerns include *genetic reductionism*, in which a complex understanding of the causes of human development is displaced by one in which genes are perceived as the "true cause" of difference (Sloan 2000, 17); *genetic determinism*, in which genes are taken as inevitably implying traits and behaviors (Lippman 1992; Nelkin and Lindee 2004; Rothman 2001); *genetic essentialism*, in which genetics becomes a dominant way to talk about fundamental life issues such as "guilt and responsibility, power and privilege, intellectual or emotional status"

(Nelkin and Lindee 2004, 16); and *genetic fatalism*, the belief that if a trait or behavior has a genetic etiology, then it is fixed and unchangeable (Alper and Beckwith 1993).[5]

In the context of health and illness, sociologists have been especially concerned about the possibility that such dynamics will contribute to the individualization of health and illness, with social, political, and economic etiological explanations relegated to secondary status or discredited altogether (Conrad 1999; Duster 2003, 2006; Hedgecoe 2001; Lippman 1991; Rothman 2001). Duster (2003) argues that extensive public sector investment in genetic research will disproportionately and negatively impact blacks by diverting attention and resources away from social environmental factors that contribute to increasing rates of lung cancer and cardiovascular disease in the African American population (see also Chaufan 2007). Related, social scientists have been leading critics of the potential of genetic information to reify social categories such as race, especially in the context of biomedical research (Duster 2005; Lee, Mountain, and Koenig 2001; Ossorio and Duster 2005). Recent work has considered also whether geneticization will result in increased stigmatization of people affected by mental illness or their relatives (Phelan 2005).

The consequences of scientists' emerging focus on gene-environment interaction for geneticization remains contingent upon how gene-environment interaction is conceptualized (Shostak 2003) and materialized in the lab (Hall 2005; Landecker, n.d.), articulated in biomedical texts (Hedgecoe 2001) and practices (Cunningham-Burley and Kerr 1999), and reported to the public (Horwitz 2005). At each of these sites, research highlights the multiplicity (Mol 2002) of the concept of gene-environment interaction and, concomitantly, the challenges of predicting its implications. For example, Shostak (2003) demonstrates that in the environmental health sciences, gene-environment interaction historically has been the focus of two very different lines of inquiry, one focused on how individual genetic susceptibilities predispose individuals to illness under specific environmental conditions, and the other focused on how environmental conditions affect genes and gene expression. Adding further complexity, how scientists in either line of research define "the environment" varies widely and may include the interior of a cell (as the environment of DNA) and the interior of a human body (as the environment of cells, organs, and organ systems), as well as the ambient environment (air, water, and soil) and the social environment (Shostak 2003). The complexities involved in defining, operationalizing, and measuring environmental influences on health may enhance "the allure of specificity" of genetic explanations (Conrad 1999).[6] Further, Hedgecoe (2001) describes a "narrative of enlightened geneticization" which accepts a role for environmental factors in disease etiology, while consistently prioritizing genetic causes, Such narratives of "enlightened geneticization" appear to be replicated in popular media coverage of research on gene-environment interaction, which selectively emphasizes genetic influences, while largely ignoring environmental causes (Horwitz 2005). This is concordant with the tendency toward "genetic optimism" which characterizes the reporting of genetics research, especially in the United States (Conrad 2001).[7]

At the same time, there is evidence that the social environment shapes understandings and uses of genetic information. Ethnographic and cross-national investigations have found that local knowledge (Rapp 1999), national contexts (Parthasarathy 2007; Prainsack and Siegal 2006; Remennick 2006), and everyday understandings of risk, kinship, and inheritance (Gibbon 2007; Richards and Ponder 1996) shape how people understand and make use of genetic information in daily life. Indeed, even in the context of prenatal genetics, arguably the clinical setting where genetic testing is most standardized and routinized, social factors shape both the use of genetic technologies and the interpretation of test results (Franklin and Roberts 2006; Lock et al. 2006; Markens, Browner, and Press 1999; Rapp 1999; Whitmarsh et al. 2007). Social scientists have highlighted also how the daily practices of diagnosis and disease management may mitigate geneticization, even for conditions with simple genetic etiologies such as hereditary polycystic kidney disease, a life-threatening, autosomal dominant trait for which genetic testing is available (Cox and Starzomski 2004). More broadly,

existing discourse, public opinion, and organizational arrangements may strongly condition the potential consequences of findings of genetic influence (Shostak, Conrad, and Horwitz 2008).

The expanding focus of the life sciences on complex biological systems (Fujimura 2005; Kitano 2002) and epigenetics (Feinberg 2008) can be expected to continue to challenge how social scientists think about gene-environment interaction and its social implications. Broadly speaking, epigenetics highlights processes by which cellular environments can modify genetic expression. The key insight of epigenetics is that gene expression can be altered by environmental exposures, even without changes in the actual sequence of DNA, and that these patterns of gene expression and regulation are heritable (Francis et al., 1999; Meaney 2001). Thus, scientists are increasingly focused on how social and historical factors can be seen as interacting directly with DNA, although how to operationalize such factors in laboratory settings (Landecker, n.d.) and how to connect social science data to such biologically fine-grained processes are major challenges. Meanwhile, the concept of biosociality raises questions about how genetic information may further blur boundaries between categories such as nature and culture, genes and environments.

Biosociality

In articulating the concept of "biosociality," anthropologist Paul Rabinow argued that advances in biological knowledge would yield new forms of collective identity and an increasingly efficacious orientation of individuals toward themselves as material entities. Consequently, "nature will be known and remade through technique and will finally become artificial, just as culture becomes natural" (1996, 99). In addition, Rabinow predicted, a variety of microlevel political practices and discourses embedding genetic information in social life would make the new genetics a potent force in reshaping society (98–99). In part, this is because the identification of genetic risks simultaneously will destabilize extant subjectivities and contribute to the emergence of new biosocial individual and group identities, which are defined not by traditional subject positions, but rather as sites defined by their relation to means, norms, and other measures of probabilistic risks (100).[8]

These new identities are expected to serve as the basis for innovative forms of social organization and interaction, as biosocial groups "will have medical specialists, laboratories, narratives, traditions, and a heavy panoply of pastoral keepers to help them experience, share, intervene in and 'understand' their fate" (Rabinow 1996, 102). Groups of persons at risk for illness or their family members and allies are reshaping and reorienting social movement organization and advocacy (Callon and Rabeharisoa 2003; Gibbon 2007), relationships between citizens and the state (Epstein 2007; Heath, Rapp, and Taussig 2004; Petryna 2002), and modes of capital production and economies, which increasingly rely on innovative relationships between disease advocacy groups and scientists (Heath, Rapp, and Taussig 2004; Novas 2007, 2008; Silverman 2008; Sunder Rajan 2006). Research on biosociality focuses also on how genetics fosters the reworking of extant identities, especially race and ethnicity (Abu El-Haj 2007; Atkinson, Glasner, and Greenslade 2007; Gibbon and Novas 2008; Hacking 2006; Nelson 2008; Reardon 2004).

In highlighting how genetic information enables new forms of human organization and agency, the concept of biosociality stands in stark contrast to the assumption of genetic fatalism and calls attention to how individuals make use of genetic information in specific environments. For example, Rose and colleagues (Novas and Rose 2000; Rose 2007) argue that genetic information creates new obligations to act on knowledge to protect health, maximize quality of life, and optimize life chances. In support of this argument, and reminiscent of Parsons's conceptualization of the sick role (1951), Condit and colleagues (2006) find that while laypeople do not hold individuals responsible for their genetic endowments, they still expect individuals to work to override negative genetic predispositions to whatever extent they are able. Thus, at least with respect to health, the rise of genetic science need not be coterminous with feelings of hopelessness or inefficacy. Rather, genetic research has secured enormous public funding precisely due to hopes

that understanding genetic causation will lead to the development of improved capacity for intervention, as seen especially today in the hope that genetics will yield a new era of personalized medicine (Novas 2007; Sunder Rajan 2006).

Thus, biosociality highlights the role of social relations in shaping social and material consequences of genetic variation. Indeed, for medical sociologists, a key insight of the literature on biosociality is that genetic causation of health and illness depends not just on the causality of genes or gene-environment interactions, but on the causality associated with social action based on scientific knowledge claims about genes. For example, increasingly, one response to diagnosis is to contribute to collective efforts to increase and improve the scientific study of one's illness; healthy individuals with genetic predispositions now lobby the state to fund scientists to discover knowledge that can be translated into new technologies that will intervene to prevent their genes from causing pathological consequences (Epstein 1996; Novas 2007; Petryna 2002; Silverman 2008). This trend points to the importance of research on how people understand genes and environments as causes of health and illness.

Public Understandings and Beliefs about Genetics, Environments, Health, and Illness

Assessing public perceptions and opinions provides an important means of understanding how people interpret social problems such as health inequalities, and how they respond to policy initiatives regarding health and illness (Schnittker, Freese, and Powell 2000). Traditionally, public opinion research has investigated attributions for health and social outcomes by considering genetics, environmental factors, and individual behavior as independent causes. Innovation in this area is clearly warranted to explore public understandings of gene-environment interaction and its implications for health and social policy.

Of course, there are many groups within "the public" with varying interests and perspectives regarding the causes of health and illness. Much of the early research on beliefs about genes as causes of health and illness focused on attitudes toward genetic testing for specific conditions. Such studies were largely clinically oriented and tended to draw on highly selected nonprobability samples of individuals from families affected by illnesses with genetic etiology (e.g., Lafayette et al. 1999; Lerman et al. 1994). While these studies provide important insights about how people in families affected by specific illnesses conceptualize genetic risk for those illnesses, they do not assess uses of genetic attributions more broadly.

Research on attitudes toward genetic testing also has been undertaken to assess racial/ethnic differences in use of genetic testing. This research indicates that African Americans and Latinos are more eager than are whites to avail themselves of both prenatal and adult genetic testing (Singer, Antonucci, and Hoewyk 2004, 41). One might infer that endorsement of genetic testing reflects underlying beliefs about genes as causes for these traits. Importantly, however, the study questions asserted the importance of genes for the disease outcome *as a premise to the question*, and therefore this work does not speak directly to beliefs about the importance of genes for individual health or social outcomes (33).

On the whole, surveys of representative samples of the U.S. population make plain that a strong majority of Americans regard genes as important determinants of health, illness, and other life outcomes. Over 90 percent of U.S. respondents report genetic makeup as at least somewhat important for physical illness, and almost two-thirds report the same for success in life (Shostak et al. 2009). Additionally, belief in the importance of genetics for particular outcomes may be increasing. For example, in 1979, 36 percent of respondents reported that heredity was more important than the environment in determining whether or not a person was overweight, while in 1995, 63 percent of respondents attributed "being substantially overweight" to genetics (Singer, Corning, and Lamias 1998, 637–38).[9] That said, it is unclear whether there has been any overall shift toward belief in genetics, as widespread notions of the importance of "breeding," "constitution," or "inborn character" predate the discovery of DNA (Kevles 1985).

Additionally, people appear to believe that the causal importance of genetics varies for dif-

ferent outcomes, in that the attribution of genetic influence does not rule out perception of the importance of other factors (Parrott, Silk, and Condit 2003), including both the environment and, especially, individual behavior (Condit et al. 2004, 260–61). For example, when asked to partition pie charts to represent the relative contribution of genes, the physical environment, the social environment, and personal action, participants assigned to "genes" 71 percent of etiologic responsibility for height, 41 percent for weight, 54 percent for breast and prostate cancer, 26 percent for talent, and 40 percent for mental abilities (Parrott, Silk, and Condit 2003). Additionally, when asked to compare the role of genes and individual behaviors in determining health outcomes, generally people assigned a greater role to personal behavior (Condit et al. 2004). Poll data similarly indicate that endorsement of genetics as an explanation for health and social outcomes varies by the outcome of interest and, possibly, perceptions of individual responsibility for specific outcomes. For example, in a 1995 Harris poll (n = 1005), 90 percent of respondents attributed success in life to learning and experience (vs. 8 percent to "genes you inherit"), while 63 percent of respondents attributed being substantially overweight to genetics (vs. 32 percent who chose learning and experience) (Singer, Corning, and Lamias 1998).

What outcomes are regarded as "more genetic" may be influenced by a cultural schema, at least in the United States, in which individual characteristics perceived as closer to the body are seen as more strongly caused by genetics. A recent study of genetic attributions for individual outcomes found that physical health is perceived as more strongly genetically influenced than is mental health; mental health is perceived as more strongly genetically influenced than is personality; and personality is seen as more strongly genetically influenced than is success in life (Shostak et al. 2009). Such a cultural schema may reflect the legacy of Cartesian dualism, which insists that the causes of bodily states, such as physical illness, are to be located in the body (Scheper-Hughes and Lock 1987). In addition, many people have a strong notion of individual will as a causal force independent from either genetics or environment, which could be seen as more important for social outcomes (Condit et al. 2004).

While research has considered the possibility of various sorts of social cleavages in beliefs about genes as causes of health and social outcomes, race/ethnic differences have received the most attention. This focus emerges in part from concerns about eugenics (Kevles 1985; Duster 2003) and the possibility that genetic information again could be used to reify racial classifications (Omi and Winant 1994; Duster 2005), undermine progressive policies, and promote discriminatory programs (for reviews, see Condit and Bates 2005; Condit et al. 2004). Reflecting on such abuses, social scientists have hypothesized that the historical use of biological claims to justify racial inequality will prompt minorities to be more skeptical of genetics. Using vignette data from the General Social Survey, Schnittker, Freese, and Powell (2000, 1109, 1112) found that blacks are less likely than whites to endorse genetic explanations of mental illness. In contrast, however, Shostak and colleagues find that blacks and Latinos rated genetic makeup on average as more important for a set of individual attributes than did whites. Black respondents were relatively more averse than whites to endorsing genetic makeup as important to individual differences in intelligence—the outcome for which historical abuse arguably has been most pervasive and invidious—but that was the only instance in their analysis in which a socially disadvantaged group evinced greater aversion to genetic explanation (Shostak et al. 2009). In an analysis of General Social Surveys since 1990, Hunt (2007) found that blacks were not less likely than whites to regard "innate ability" as important to explaining black-white differences in socioeconomic attainment (12.0 percent of whites and 12.2 percent of blacks).[10]

Despite the conventional wisdom that perceptions of the relative significance of genes and environments as causes of health and illness will be consequential for health and social policy, only a very few studies consider the relationship between beliefs about genetic causes and specific policy attitudes. Shostak and colleagues (2009) find that belief in the importance of genetics for individual differences in outcomes are associated with support for health policies predicated on

genetic causes being important, such as supporting human genetics research and genetic screening before marriage. Regarding beliefs in the genetic basis of group differences, Jayaratne and colleagues find that belief in the genetic basis of racial differences is associated with more negative attitudes toward blacks and less support for social policies to help blacks (Jayaratne et al. 2006; see also Keller 2005).[11] In contrast, genetic attributions for differences in sexual orientation are associated with greater tolerance toward gay men and lesbians, as measured by attitudes toward whether gays should marry, whether gay couples should adopt, and whether gay people should be allowed to teach elementary school (Jayaratne et al. 2006; see also Tygart 2000).

We have much to learn about how people make sense of theories and data about gene-environment interaction. As the social sciences increasingly are considering the relevance of gene-environment interaction to outcomes of longstanding sociological interest (Freese 2008), it is imperative that future research on public beliefs and opinions about genetics include questions on this broadening range of outcomes and their associations with orientations to specific health and social policies. Such policies will have a critical role in determining the consequences of knowledge about gene-environment interactions, as they shape the opportunities that people have both to make use of medical interventions and treatments developed using this knowledge and to avoid identified health risks (Link and Phelan 1995; Lutfey and Freese 2005).

Gene-Environment Interaction and Social Causation of Health and Illness

As noted previously, social environmental conditions have historically often been interpreted as competing with genetics in the explanation of disease. The notion that lung cancers were invariably genetically determined—and so any relationship between smoking and lung cancer had to reflect a common genetic cause—was the main alternative used to justify doubt that smoking causes cancer (Brandt 2007). Today, funding for research into the possibility that genetic differences may explain part of the observed racial disparities in health has been decried by some who believe this delays attention to the obviously fundamental role of socioeconomic differences, unequal treatment in the health-care system, and discrimination-related stressors (Sankar et al. 2004; Chaufan 2007). Sociological writing on the contingency and capriciousness of diagnostic processes may likewise be seen as contradictory to research attempting to document associations between genetic differences and diagnoses (Brown 1995; Zavestoski et al. 2004).

More recently, there has been stronger emphasis on constructive and integrative engagement between genetics and social science (Pescosolido 2006). This has been exemplified by the push for including "biomarkers" in social science data resources (Singer and Ryff 2001; Finch, Vaupel, and Kinsella 2000; Timmermans and Haas 2008; Weinstein, Vaupel, and Wachter 2008). For those who study disease, of course, biological measurement is already fundamental; if anything, it is remarkable how much epidemiology and social science have accomplished with self-report surveys. In thinking about how biomarkers may be incorporated into social research, a key distinction needs to be drawn between measures of genotype and measures of cortisol, immune response, allostatic load, or other of what Freese, Li, and Wade (2003) call "proximate" biomarkers. The latter are interesting to social scientists primarily for their role as mediating variables, that is, in elucidating the actual physiological process by which life circumstances get under the skin. Genotypic measures, by contrast, are quintessential *moderators*. While epigenetics provides ways in which external processes can influence the cellular expression of genes, the genotype itself is not influenced by life circumstances, even though the two interact in the production of health and other phenotypic outcomes.

Although discourse about genetic causes in much of social science is heavily freighted by a false moral equation of genetics with inevitability, this is much less the case in health research, which has always been premised on the possibility of salutary manipulation of the body. A favorite example for illustrating the pervasive interpenetration of genes and environments in dis-

ease etiology is phenylketonuria (PKU). Classic PKU is caused by an autosomal recessive genetic variant on chromosome 12, and those with PKU lack an enzyme needed to break down the amino acid phenylalanine. Consequently, phenylalanine accumulates in tissue and causes progressive, irreversible cognitive impairments, among other problems. PKU is thus a genetically determined disease for which severe negative health outcomes were once inevitable. For decades, it has been known that if someone with PKU adheres to a diet low in phenylalanine, the accumulation can be avoided and the negative consequences of the condition can be minimized. In other words, PKU is a genetically determined condition whose consequences medical science has transformed to being largely environmentally determined.

At the same time, MacDonald et al. (2008) find that, for children with PKU, lower maternal education is associated with higher child blood phenylalanine, apparently as a result of poorer adherence to a low phenylalanine diet (see also Russell, Mills, and Zucconi 1988). Consequently, while no one regrets our being able to treat PKU, this knowledge may have created an education-related disparity where none existed before. As science increases the possible leverage that humans have over their genes, socioeconomic factors may become relevant for understanding variation in the utilization of knowledge, technology, and ultimately outcomes.

With PKU, a drug to reduce blood phenylalanine levels was approved by the FDA in 2007 (sapropterin dihydrochloride; brand name Kuvan). Nothing is yet known about the consequences of this treatment for socioeconomic differences in children's blood phenylalanine levels. Thinking abstractly, however, one can imagine that such an innovation might reduce inequalities if it reduces the importance of dietary adherence and is widely utilized. On the other hand, it could increase inequalities if it is utilized primarily by advantaged individuals who are already most likely to have good adherence. Medical innovations that increase population health may increase or decrease disparities as they do so; what consequence innovations do have depends on the technology they supercede and on the barriers to utilizing the innovation. What will prove to be the key barriers for utilizing innovations from genetics research remains largely unknown, although a strong lesson from the existing literature on health disparities would be not to exaggerate the importance of financial resources per se (Mirowsky and Ross 2003; Cutler, Deaton, and Lleras-Muney 2006).

Another example of the fundamental interaction between genetics and social environment in disease is provided by diabetes. Diabetes is commonly divided into Types 1 and 2, with the former characterized by inability to produce insulin and the latter by relative deficiency or insulin resistance. Onset for Type 1 is typically in childhood, while onset of Type 2 is typically in adulthood and appears strongly linked to obesity. Rates of obesity have increased dramatically in recent decades, and of course this change cannot be attributed to underlying genetic changes in the population; it is rightly characterized as a social epidemic (Christakis and Fowler 2007; Martin 2008). At the same time, obesity is strongly heritable, with genetic differences implicated in level of caloric intake, physical activity, and the weight change of those with similar caloric intake and activity (Faith and Kral 2006). Consequently, concordance of identical twins for diabetes in U.S. society is higher for Type 2 diabetes than for Type 1 (Dean and McEntyre 2004). In societies where obesity is rare, Type 2 diabetes is rare. The environmental changes that have resulted in contemporary Western lifestyles have thereby created associations between genotypes and diabetes risk that did not exist before.

Over many years, the elevated blood sugar levels in diabetes lead to increased risk for a wide variety of vascular-related complications, and so the basic goal of diabetes treatment is typically to emulate normal blood sugar levels as closely as possible. Using ethnographic data, Lutfey and Freese (2005) compare two diabetes clinics serving very different SES populations and are able to articulate an array of possible reasons why lower SES diabetes patients may have more difficulty maintaining normal glucose levels. Others have suggested that psychological traits like cognitive ability and conscientiousness also may be important for managing chronic conditions with sustained and complex treatment regimens

(Goldman and Smith 2002). While few would dispute the importance of environments for understanding variation in either cognitive ability or conscientiousness, behavioral genetics has produced strong evidence that genetic differences are influential as well (Plomin and Caspi 1999; Plomin and Spinath 2002). If so, then as disease consequences become amenable to treatment by personal management, one may see a shift whereby the importance of genes related to the disease itself becomes less important for ultimate consequences, but genes related to the psychology of managing disease become more important (Freese 2006). In other words, the relevance of genetics for medical outcomes is not restricted to genetic effects on physiological processes, and, when disease risk and treatment depends strongly on individual behavior, understanding genetic differences in behavioral tendencies may be a vital part of developing interventions.

The conventional way of determining the overall contribution of genetic variation to population variation in a phenotypic characteristic has been to compare pairs of individuals with known genetic relatedness, especially monozygotic twins (MZ; identical) and dizygotic twins (DZ; fraternal). Given certain assumptions, the higher correlation of MZ twins is taken as evidence of genetic influence, with the estimated magnitude of genetic influence increasing as the difference in correlations increases (see Schaffner 2006 a, b for an especially lucid overview). When genes and environments interact, saying that some percentage of the outcome "is genetic" loses coherence, and heritability estimates seem instead best interpreted as an imperfect but informative indicator of genetic influence. In this respect, substantial heritability estimates have been observed not only for a wide range of health and psychological measures, but also for items of such longstanding sociological interest as educational attainment, earnings, divorce, and voting (Behrman et al. 1980; McGue and Lykken 1992; Fowler, Baker, and Dawes 2008). To be sure, criticism of twin studies exists, including debate among sociologists (Horwitz et al. 2003; Freese and Powell 2003). However, many have concluded that there is no evidence of problems severe enough that twin studies would pervasively produce evidence of substantial genetic influence when none existed (see detailed arguments in Kendler and Prescott 2006; Rutter 2006).

Studies of variation in estimated heritability across different populations—or in the same population at different times—can be used to provide broad information about gene-environment interactions. Boardman (2009) finds that more aggressive policies against cigarette use (e.g., higher taxes, stronger restrictions on advertising) are associated with lower heritability of daily smoking but not lower heritability of smoking onset. Given evidence of the success of aggressive policies in reducing onset overall, Boardman interprets this result as suggesting that existing antismoking policies may be most effective for those whose smoking initiation is least associated with underlying genetic causes. As a different example, Guo and Stearns (2002) find that the heritability of adolescent vocabulary score is higher in families with higher income (see also Turkheimer et al. 2003). Because genetic differences apparently matter more in wealthier families, Guo and Stearns speculate that richer environments better allow children to develop their differing genetic potential (cf. Perrin and Lee 2007).

While such findings are intriguing, comparing heritability estimates across groups is a rough tool for studying how genes moderate the effects of environments. Even when model assumptions are met, heritability estimates still measure only the proportion of overall variation resolved by genetic variability. Groups may differ in the heritability of an outcome because of differences in the effects of genes, but also because of differences in the overall level of genetic variation, environmental variation, or variation in measurement error. In the Guo and Stearns (2007) study, for example, the difference in heritability between the highest and lowest income groups was less than 0.1, and the heritability differences between the highest and lowest education groups were nearly this large in the opposite direction. In the end, the conclusions to be drawn from such indirect methods about the interaction of genes and social environments are likely quite limited.

For this reason, more enthusiasm currently surrounds the direct utilization of molecular genetic measures for studying gene-environment

interactions. The remarkably rapid drop in the cost of these measures has accelerated the effort to integrate them into existing social science data resources. To give one concrete example, in 2006 the Wisconsin Longitudinal Study planned an initiative to assay 4,500 cases for variants of a single gene (APOE) associated with Alzheimer's disease (Bertram and Tanzi 2008). Two years later, after all data were collected and the salivary samples were prepared to be submitted for assaying, the initiative had grown to include 6,800 participants and variants of more than ninety different single nucleotide polymorphisms (SNPs), and yet the estimated overall cost of assaying had declined slightly.[12] Sociologists interested in health will have vastly greater opportunities to incorporate molecular genetic data into their work.

As an example of a study of gene-environment interaction led by a medical sociologist, Pescosolido and colleagues (2008) found support for their hypothesis that the association between a variant of the gene GABRA2 and being diagnosed with alcoholism may be highest for individuals from disadvantaged backgrounds or low social support. Their results highlight the possibility that molecular genetic data may contribute to understanding the wide variation in the physical and mental health consequences of social adversity. Shanahan and colleagues (2008) have argued also that sociologists should be leaders in exploring how gene-environment interaction may require methods for assessing complex configurations of environmental characteristics (and, for that matter, configurations of genes). In other words, the consequences of genetic differences may be suppressed or accentuated less by particular environmental conditions than by the presence of multiple conditions that together provide special contexts of vulnerability or resilience.

Molecular genetic data may also be used to provide some leverage into famously difficult causal questions in social science research on health. In particular, as more becomes known about genetic determinants of health conditions, possibilities increase for being able to infer that the only reason some genetic variant would be associated with a social outcome like education and earnings is indirectly, via the effect of the genetic variant on health. In such a case, one could then use genotypic information as an instrumental variable to disentangle the causal effect of the genetically influenced health condition on socioeconomic outcomes from the effect of socioeconomic outcomes on health (Ding et al. 2009; see also Ebrahim and Davey Smith 2008). To cite an analogous example, a genetic variant that influences levels of c-reactive protein in blood was used to examine direction of causality issues in the association between c-reactive protein and insulin resistance (Lawlor et al. 2008). Roughly, because any influence of insulin resistance on c-reactive protein does not change the gene, any association between the gene and insulin resistance can instead be attributed to the influence of c-reactive protein on insulin resistance. Using full siblings who differ on the genes in question makes this an even stronger possible research design by eliminating the possibility of confounding the correlations among parent genes, child genes, and family environment (Fletcher and Lehrer 2008).

While molecular genetic data thus provides immense and exciting scientific opportunity for medical sociologists, the importance of caution in interpreting findings prior to replication must be emphasized. The extent of replication failure in medical genetics has been a source of regular lament (Ahsan and Rundle 2003; Taioli and Garte 2002). The particular reasons for such failures are many, but important among them is that having a large number of genetic measures and a large number of environmental measures yields a very large number of potential interactions that can be analyzed, especially when those analyses can be carried out for different subgroups and different outcomes. While methods of correcting for multiple significance tests exist, the number of tests underlying a presented result can be difficult for researchers to determine (and impossible for reviewers).

Given that statistical interactions are already notorious for replication problems when genes are not involved, reported gene-environment interactions should perhaps be approached even more gingerly than should reported main effects of genetic differences (Rutter 2006). Worse, many social science data resources are effectively unique with respect to some questions they can be used to address, making direct replication across samples far more difficult

than in many medical studies. Moffitt, Caspi, and Rutter (2005) provide an especially lucid guide to the proper theoretical justification motivating a search for a gene-environment interaction, and they caution strongly against "overreacting" to one study in advance of replication. When evidence for gene-environment interaction is appropriately adducted, researchers must also caution against unwarranted privileging of the "genetic" side of the interaction, and indeed often diseases described in the scientific literature as "complex genetic disorders" might just as easily be characterized as "complex environmental disorders."[13]

Conclusions

A longstanding strength of medical sociology is its theoretical and methodological diversity. Thus, it is no surprise to see medical sociologists at the forefront of widely varied approaches to the study of gene-environment interaction. Such efforts include historical excavations of the concept of gene-environment interaction, ethnographic studies of the operationalization of gene-environment interaction in specific laboratories, analyses of biomedical texts and newspaper reporting, surveys of public beliefs and attitudes about genes and environments as causes of health and social outcomes, and new forms of sociological research which directly incorporate genotypic data. Taken together, these inquiries underscore the importance of understanding health and illness as shaped by genes in interaction with multiple environments—social, economic, physical, biological. Genes and environments become embodied as health and illness in and through social processes that are conditioned by dimensions of social structure (Bearman, Martin, and Shostak 2008). Research about gene-environment interactions provides medical sociologists with another warrant—and another set of tools—for elucidating the complex causes of health and illness.

Notes

We thank Miranda Waggoner for providing research assistance.

1. This chapter draws on work that appeared originally in Freese and Shostak (2009).
2. A key word search using "gene-environment interaction" in PubMed generates 28 articles on the topic published from 1974 to 1989, 18 from 1990 to 1995, 85 from 1995 to 2000, and 243 from 2001 to 2005.
3. This represents a $40 million increase above the $28 million already planned for these efforts in the NIH budget, a significant allocation in relative scarcity at the NIH.
4. An alternative analytic frame is provided in writing on "molecularization," which refers to the reorientation of the life sciences to the submicroscopic level (de Chadarevian and Kamminga 1998; Kay 1993). Some authors prefer "molecularization" because it lacks the negative valence often associated with "geneticization" (Hedgecoe 1998), while others use it to describe how genes and environments both are increasingly known and governed at the molecular level (Shostak 2005).
5. For example, in an experimental investigation of the consequences of genetic information in a clinical context, participants presented with results for what was called a "genetic" test for heart disease perceived the disease to be less preventable than those assigned to the unspecified test condition (Senior, Marteau, and Weinman 2000).
6. This may occur even as scientists recognize that "there is no one single fact of the matter about what a gene is" (Keller 2001, 139)
7. The frame of genetic optimism consists of three components: (1) a gene for the disorder exists; (2) it will be found; and (3) this will be good (Conrad 2001).
8. Related, Clarke and colleagues use the concept of "technoscientific identities" to refer broadly to identities based in biomedical science and technology, including genomics (Clarke et al. 2003, 182–83).
9. Changes in the wording of the question and the structure of response options also may have contributed to this change (Singer, Corning, and Lamias 1998, 638).
10. Academic discussions of heritability regularly point out that evidence of the importance of genetics for explaining individual differences is not evidence of the importance of genetics for explaining group differences (e.g., Schaffner 2006a, b). To our knowledge, no published study has considered how the same people respond to questions about individual and group differences in the same trait.
11. The direction of causality here is unclear, and belief in genetic differences between oneself and an outgroup does not inevitably imply negative attitudes.
12. This information about the Wisconsin Longitudinal

Study was provided by personal communication with Robert M. Hauser and Taissa S. Hauser, January 2009.

13. We thank Peter Conrad for this point.

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