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Topic 2. The Interface of Biological and Experiential Conditions in Health Inequalities

Media Portrayals and Health Inequalities: A Case Study of Characterizations of Gene \times Environment Interactions

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Objectives. This article examines how genetic and environmental interactions associated with health inequalities are constructed and framed in the presentation of scientific research.

Methods. It uses the example of a major article about depression in a longitudinal study of young adults that appeared in *Science* in 2003.

Results. This portrayal of findings related to health inequalities uses a genetic lens that privileges genetic influences and diminishes environmental ones.

Discussion. The emphasis on the genetic side of gene \times environment interactions can serve to deflect attention away from the important impact of social inequalities on health.

HEALTH inequalities across the life course often begin at early ages (McLeod & Shanahan, 1996). Socioeconomic differences in rates of depression, for example, commonly arise in young adulthood (Turner, 2003). More precarious positions in the social structure expose young adults to more acute life events and chronic strains but endow them with fewer resources they can use to mediate or moderate the effects of stressors. Young people from poor socioeconomic backgrounds face more of the kinds of stressful experiences, including financial difficulty, job instability, and housing problems, that are associated with depression. These mental health disadvantages that begin in earlier stages of the life course often cumulate across the life course to exacerbate socioeconomic differences in mental health statuses of adults (Ross & Wu, 1996).

Although unequal structural positions are strongly related to the kinds of events that cause depression over the life course, not all people who are exposed to stressful events and strains become depressed. Socioeconomic status has a consistent, but moderate, relationship with rates of depression (Eaton & Mutaner, 1999). The examination of variations in genetic vulnerabilities and strengths can help specify those individuals whose social positions expose them to stressors will or will not become depressed. To this end, some behavioral geneticists now use a model that views environmental and genetic perspectives as complementary rather than contradictory (Plomin, DeFries, McClearn, & McGuffin, 2001). This model stresses how genetic vulnerabilities become manifest only under certain environmental circumstances. One version of the diathesis-stress theory, for example, predicts that genetic vulnerabilities are latent under conditions of low stress but

appear only under very stressful conditions (Monroe & Simons, 1991). Studies of health inequalities can potentially benefit from knowledge of genes, environments, and their interactions.

This article examines one aspect of gene and environmental interactions in health inequalities: the way such interactions are constructed and framed in the presentation of scientific research. The results of scientific studies do not speak for themselves. The media are very selective in which studies they attend to, how they characterize the findings of these studies, and what solutions they think that research implies (Tuchman, 1978). Conrad (1997) suggests that the construction of scientific findings about mental illness privileges genetic effects and diminishes environmental effects. If so, then reporting about gene \times environment interactions will selectively focus on the genetic side of this interaction while largely ignoring the environmental aspect. To the extent that this is true, reporting about the impact of health inequalities and genes will minimize the strength of these inequalities and maximize the power of genetic influences.

This article provides a case study that examines whether the social construction of gene \times environment interactions overemphasizes the influence of genes and underemphasizes environmental effects. It examines a single article, "Influence of Life Stress on Depression: Moderation by a Polymorphism in the 5-HTT Gene," by Avshalom Caspi and 10 co-authors that appeared in the July 18, 2003, issue of *Science*. This article's influence on the general scientific community may be greater than any other life course study that has ever been conducted. *Science* magazine named it the second most important scientific breakthrough of 2003 (after only an article

about newfound insights into the nature of the cosmos). The National Institute of Mental Health's (NIMH) Web site cites the study as one of the great accomplishments of this agency's focus on the biological basis of mental illness. Thomas Insel, the director of the NIMH, claimed: "What they have done is going to change the paradigm for how we think about genes and psychiatric disorders" (Vedantam, 2003). Another NIMH psychiatrist called the study "the biggest fish yet netted for psychiatry" (Holden, 2003). The study's findings were broadly disseminated and featured both in the United States and worldwide. The *New York Times*, for example, featured it in two stories, the first an article, "Gene Is Linked to Susceptibility to Depression," and the second an op-ed piece by the psychiatrist Peter Kramer, "Tapping the Mood Gene." The study's prominence provides a good opportunity to examine portrayals of gene \times environment interactions and the consequences of these portrayals for the dissemination of research about health inequalities.

FINDINGS ABOUT GENE \times ENVIRONMENT INTERACTIONS

The research stems from a longitudinal study of a birth cohort of 847 Caucasians in New Zealand born in the early 1970s and followed from birth into young adulthood. The article's central concern is to examine the association between stressful life events, depression, and the 5-HTT gene when cohort members were 26 years old. The 5-HTT gene was chosen for study because serotonin has been the focus of much genetic research on depression, and this gene controls the way that serotonin passes messages through brain cells. Previous research suggested that the gene is associated with reactions to stressful stimuli in mice, monkeys, and people undergoing brain imaging, although no prior studies had found a direct link between the gene and depression.

The 5-HTT gene has three genotypes: Seventeen percent of the sample had two copies of the short (s) allele, 31% two copies of the long (l) allele, and 51% had one s and one l allele. The study measures stressful events through an additive index of 14 life events including employment, financial, housing, health, and relationship stressors that participants experienced between ages 21 and 26. The major measure of depression uses the Diagnostic Interview Schedule (DIS) to determine whether or not participants experienced an episode of major depression over the last year (17% report major depression during this time period). The study also reports the number of depressive symptoms, suicidal ideation, and informant reports of depression. Its central hypothesis is that people who have the short version of the 5-HTT gene might be especially vulnerable to highly stressful environments, whereas those with the long version might be more resistant to adverse environmental stressors.

The study has three major findings. First, it finds no association between the 5-HTT gene and who becomes depressed. There is, in other words, no direct genetic effect on depression: People with two s alleles, two l alleles, or one of each allele have equivalent chances of becoming depressed. For example, the 69% of the population with at least one s allele account for approximately 74% of depressive episodes, a difference that does not nearly reach statistical significance. In addition, the study finds no relationship between the 5-HTT genotype groups and the number of stressful life events that

participants experienced, so that the genotype should not account for differential exposure to stressors. Therefore, it is unlikely that the gene exerts a selection effect on the number of life events that the study group report.

Second, the study finds a strong positive relationship between experiencing more stressful life events and developing depression. As the number of life stressors increases from zero to four or more, rates of depression increase from 10% to 13%, 15%, 20%, and 33%. Put another way, people who experience four or more life events are about three and a half times more likely to develop depression than those who do not experience any stressful events.

The study's third major finding regards a significant gene \times environment interaction. Among the 15% of the sample that experiences four or more stressful life events, those who have one or two copies of the short allele on the 5-HTT gene are significantly more likely to have each of the depression outcomes than those with two copies of the long allele. In the group that faced four or more stressful life events, 33% of individuals with an s allele became depressed compared with 17% of those with two long alleles who did.

In summary, the study does not find a direct effect of the 5-HTT gene on depression. It does find a fairly strong relationship of stressful life events with depression so that people who experience more stressful events have a greater chance of becoming depressed. Finally, although there is no direct association between the 5-HTT gene and depression, this gene interacts with the number of life events to predict depression. How were these findings interpreted and what implications were drawn from them?

SOCIAL CONSTRUCTION OF GENE \times ENVIRONMENT INTERACTIONS

The findings from the study of Caspi and colleagues (2003) presumably support the central themes of research about health inequalities. A majority of the 14 life events it measures, including long-term unemployment, being made redundant, being fired from a job, debt problems, not having enough money to pay for basic expenses, lacking money for medical expenses, difficulty paying bills, and homelessness, are strongly, or even tautologically, related to low socioeconomic status. Others, including multiple residential changes, disabling physical illnesses, disabling injuries, and being involved in physically violent relationships, also are associated with lower social class status. Indeed, the only indicators of stress that the study uses that are arguably not associated with lower social class position are losing a job because the company moved and the break-up of a cohabiting, intimate relationship. Although this study does not report the association of social class with these life events, other studies of similar age groups find strong relationships between low socioeconomic status and the number of major life events that young adults experience (Turner, 2003). The Caspi and colleagues study seemingly reinforces the thrust of past work on health inequalities that shows how people with limited economic resources are exposed to the kinds of life events and chronic stressors that are associated with depression (Pearlin, 1989).

Despite the absence of a direct genetic relationship and the presence of a strong environmental relationship, media reports of the study's results are particularly striking. Typical headlines

read: “Scientists Find Depression Gene” (BBC News), “Variation in One Gene Linked to Depression” (*Washington Post*), “Gene Length Predicts Depression Risk” (*Nature Science Update*), and “Tapping the Mood Gene” (*New York Times*). The contents of the articles, although they mention the gene \times environment interaction, also focus on genetic effects. The *Times*, for example, features a quote from one of the study’s collaborators: “No matter how many stressful events they had in a five-year period, [people with a long allele] were no more likely to become depressed than people who had no stressful events at all” (Duenwald, 2003). The lead sentence of the BBC News story runs: “A study has shown that the likelihood of becoming depressed is partly determined by which version of a specific gene a person has” (BBC News, 2003). Peter Kramer’s op-ed piece concludes: “Depression has a firm basis in harm to the brain” (2003).

These media reports reflect the press releases from the NIMH and sponsoring institutions of the research (NIMH, 2003; University of Otago, 2003). The NIMH press release, reflecting the agency’s focus on genetic influences on mental illness, emphasizes the genetic findings and downplays the influence of the social environment. It characterizes the environment through stressors “such as loss of a job, breaking up with a partner, death of a loved one, or a prolonged illness,” which are mostly generic life stressors that most people can identify with. Many news stories quoted verbatim this description of life events. Yet, the study did not, in fact, measure “a death in the family,” and most of the (unmentioned) stressors it did measure were intrinsically connected to socioeconomic status. The press releases fail to mention both the lack of a direct genetic effect and the presence of a direct environmental effect. Researchers who focus on health inequalities operate in a climate where genetic and environmental influences are not placed on an equal footing. Media presentations, heavily influenced by the way that the NIMH frames the findings of research, use a genetic lens that amplifies the importance of genetics and diminishes that of the environment (Conrad, 2001). This emphasis deflects attention from social inequalities in health and is particularly striking when a study finds that these inequalities exert a more important influence than genetic effects.

In contrast to media reports, the article itself is clear that the genetic effect operates only in highly stressful environments. Yet, the text of the article still fails to mention the direct relationship between social stressors and becoming depressed; this information is found only by reading the detailed statistical information that accompanies the tables in the article. The study’s emphasis on the gene \times environment interaction comes at the expense of a focus on the direct environmental effect. Moreover, the article uses terms including “stressful life events,” “life stress,” and “environmental stress” to characterize the nature of stressful environments. These generic terms can give the misleading impression that exposure to the kinds of stressful life events the study measures is random rather than structured by social inequalities. A general emphasis on “stress” replaces the role of structured social inequalities in leading to differential exposure to stressors. The “environment” in the gene \times environment interaction is not one where social inequalities lead to unequal exposure to life events and to ongoing chronic stressors but is one where anyone might encounter stressful experiences.

The study also raises the question of how to interpret the gene \times environment interaction it finds. The authors interpret their finding as confirming the diathesis–stress theory of depression, which predicts experiences of higher levels of stressful events will elevate the vulnerability of depression among people who are at high genetic risk and diminish this vulnerability among those at low genetic risk. The short allele on the 5-HTT gene presumably makes people more sensitive to stress, whereas the l allele protects them from the impact of stress. The interpretation that the s allele is a vulnerability gene is open to question. Most theories of depression predict that a genetic vulnerability to depression would be more likely to have an influence under conditions of low than of high stress [e.g., Post, 1992]. Indeed, an early attempt at replicating the Caspi et al. (2003) results shows that high levels of stress were associated with increasing rates of major depression among all genotypes, while low levels of stress were associated with increased risk only among individuals with the ss genotype (Kendler et al., 2005).

Another problem with the authors’ interpretation is that it does not deal with the question of the quality of the life events that participants experienced. The study counts the number of life events participants report over the last 5 years and assumes that experiencing a greater compared with a lesser number of life events leads to more stress. Yet, the quality of events can have a powerful effect on the amount of stress that people experience. For example, George Brown’s research indicates that severely threatening events that involve important losses of relationships or roles account for most depression. He concludes: “It is the impact of just one event or difficulty of a sufficient severity that appears to be critical” (Brown & Harris, 1978, p. 138). To the extent that Brown and Harris’s findings hold more generally, many of the participants who experienced one or two life events might face more stress than those who experienced a greater number of more trivial events. If so, it would call into question the finding that people with an s allele are more sensitive to stress.

Other stress researchers, particularly Leonard Pearlin, emphasize how stressors are not isolated but are interconnected so that some primary stressors might lead to additional stressors, although others might not (Pearlin, 1989). For example, the loss of an important romantic relationship for a young adult might be a very powerful stressor but might not lead to additional stressors. In contrast, the loss of a job can lead to additional stressors such as financial and housing losses. If so, there could be an interaction between the number of life events and the quality of life events so that young adults in the four and more category would not just be experiencing more life events but life events of a different quality than those experiencing fewer events. This study, in particular, lends itself to this interpretation because so many of the events it measures, such as problems with debt, not having money for food and household expenses, lacking money for medical expenses, and difficulty paying bills, are intrinsically interconnected. A particularly interesting question is whether people with the s allele are more sensitive to particular types of stressors rather than to additive levels of stress. We would need to know more detail about the particular quality of the life events and chronic stressors involved and the relationship between experiencing each type before we could speculate about whether either allele is the genotype that confers

vulnerability or protection. One intriguing path for future research would be to examine the qualities of events and chronic strains that participants experienced to see whether or not this would shed light on the gene \times environment interaction.

A final question regards the practical implications of the study. The framing of problems influences what solutions to the problem seem to be possible (Conrad, 1997). The NIMH press release, media reports, and the study itself mention two possible implications: for the prevention of depression and for the treatment of cases of already depressed people. The authors themselves are somewhat skeptical about the study's preventive implications, noting that the short allele is "too prevalent for discriminatory screening." They do, however, note that "a microarray of genes might eventually identify those needing prophylaxis against life's stressful events." The NIMH news release accompanying the story does focus on preventive possibilities, stating that eventually diagnostic tests for the short allele can be used to discover "genes that predispose for depression in a 'gene array' test that could help to identify candidates for preventive interventions" (NIMH, 2003). Some of the experts quoted in news stories are even more optimistic, one psychiatrist claiming: "This can help us identify vulnerable populations even before they become depressed after a life stressor" (Doheny, 2003). These preventive interventions, however, seem thoroughly impractical. Slightly over two thirds of the population has at least one *s* allele. There would be no way of knowing in advance which of these people will experience four more stressful events. Screening all 581 persons with an *s* allele would yield 33 people who will also experience four or more life events and 548 who will experience fewer than four events. The number of false positives such screening would yield would far exceed the number of true future cases. The usefulness of these findings for preventive purposes seems negligible.

The second possible use of these findings that has been raised regards improving the treatment of depressed people. The article notes that "more knowledge about the functional properties of the 5-HTT gene may lead to better pharmacological treatments for those already depressed" (Caspi et al., 2003, p. 389). Yet, this emphasis on developing differential genetic interventions based on the 5-HTT genome also seems misplaced because the gene influences only people who face intense environmental stressors. The relevant group for differential intervention would be the 15% of participants who have experienced four or more recent stressful life events. Successful interventions with this group seemingly would have to focus on changing their intensely stressful situations. It is not clear, however, what differential medication treatment would follow for people with the *s* or the *l* allele, given that they are all under intense social stress. Paradoxically, in light of the emphasis on developing better pharmacological treatments, a plausible implication of the findings is that people with an *l* allele facing four or more stressful events should not be medicated because medication might hamper their presumably strong coping abilities. At the least, no clear practical implications stem from the gene \times environment interaction that would not already follow from the (unreported) direct effect of the social environment on depression.

What is striking about the consequences that are drawn about the study's findings is that neither the article nor the reports about it even mention the possibility of interventions that would

reduce social inequalities. Its findings about the impact of life events on depression seem to imply optimizing the psychological well-being of the sample members through social policies that emphasize the provision of adequate and satisfying employment, finances, housing, and the like. Focusing on genes, however, even when the focus is on a gene \times environment interaction, shifts attention from efforts to change environments toward efforts to alter presumably defective genotypes. The reactions to this study focus on developing better ways to change vulnerable genomes, which can help perpetuate the inequalities that seem primarily responsible for why people become depressed as long as these inequalities are ignored.

Conclusion

Researchers on health inequalities must be aware of the way that findings are constructed and disseminated to the public. Even when research focuses on gene \times environment interactions, discourse focuses on internal qualities and attributes undue causal power to genetic effects. The case study used here shows that experiencing four or more stressful life events is a necessary condition for the emergence of a genetic effect on depression. Likewise, the genetic vulnerability works only in the presence of highly stressful environments. The stressful events that it measures are strongly related to social inequalities and might actually be better measures of ongoing and chronic circumstances than of transient and acute events. Conrad (1997, p. 151) raises the following question: "How will the location of small genetic differences shape the reconstruction of large social problems?" The disquieting answers that the reception of this study provides to this question are that social inequalities that lead to mental health disparities are likely to be framed as genetic effects that should be medicated or, optimally, prevented through genetic screening.

Researchers who study health inequalities can fruitfully use genetic studies to explore variations in individual responses to the consequences of structural social hierarchies. However, they should be aware that even when social environments have presumably stronger impacts than genes on outcomes, discourse will feature genetic, rather than social, influences. The sociologist C. Wright Mills famously asserted that the core mission of sociology was to show how personal problems actually reflect public issues. Genetic studies, conversely, reduce social problems to individual deficits. While we should applaud the efforts of behavioral geneticists to enhance our knowledge about the way that genes and social environments interact, we should remain vigilant about the ways that this knowledge will be interpreted and used. Even the best life course studies of genetic and environmental interactions are open to questions about the uses to which their findings will be put.

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