Editorial

Genes, Environment, and Mental Health Wellness

In this issue, Kendler and colleagues raise an intriguing question: How do genes and environment contribute to the mental health of women? This is a creative research strategy that has seen little use in psychiatric genetics, which traditionally has focused on specific mental illnesses and their concomitant neurobiological and behavioral features (1). We know from past psychiatric genetic studies that the etiology of most psychiatric disorders is complex, requiring the action and, perhaps, interaction of many genes and environmental risk factors. In contrast to the many genetic studies of psychiatric disorders, little is known about the inheritance of mental health wellness.

We can, of course, assume that mental health wellness is fostered by the absence of the genes that cause specific disorders. But Kendler et al. reach further than this. They seek to know whether there are genes and environmental risk factors that might be considered health inducing. The discovery of health-inducing genes or environments would be a major contribution to the empirical and theoretical foundations of psychiatry. Indeed, it could motivate a paradigm shift by which studies of wellness become as important as studies of illness.

To understand the implications of the study by Kendler et al., we must first consider how they defined wellness, the phenotype used in their genetic analyses. Recognizing the complexity of this construct, these authors included measures in several domains: self-perceived physical health, nonconflictual interpersonal relationships, social support, self-esteem, low levels of anxiety and depression, and low levels of substance use. The authors acknowledge that this is a limited sampling of the wellness construct. So future work should examine other features of wellness, such as quality of life and occupational functioning.

The genetic modeling analyses partitioned the causes of mental health into genetic, shared environmental, and individual-specific environmental influences. Each of these three factors contributed equally to low substance use, but individual-specific influences were the most important factors for the other measures of wellness. There was a smaller, yet significant role for genes and the shared family environment. What does this mean?

The individual-specific environment comprises factors that differentially influence siblings in the same family. For example, one sibling may be exposed to drugs through peers, whereas another may not. The twin study contrasts these with shared environmental influences—those that are shared by siblings. For example, if both siblings are exposed to a drug-abusing parent, drug exposure is a shared environmental factor. One weakness of the twin method is that, although it shows us that broadly defined features of the environment influence wellness, it cannot tell us exactly what these features are. Another obstacle to interpretation is that errors of measurement will inflate the apparent effect of the individual-specific environment. Nevertheless, it is worthwhile to speculate as to what aspects of the individual-specific and shared environments might be targeted for further study.

Information about relevant features of the individual-specific environment can be gleaned from research in child psychopathology that has attempted to define factors that protect children from illness (see, for instance, references 2 and 3). This work

has led to the concept of "resilience" or "invulnerability," which applies to children who become reasonably well-adjusted adults despite being exposed to risk factors for mental illness (see, for example, references 4 and 5).

Resilience is a multidimensional construct, including constitutional strengths in domains such as temperament and personality along with specific skills and abilities that help people cope with the stresses and constitutional vulnerabilities that lead to psychopathology in less resilient peers (6, 7). Garmezy's studies of stress-resistant children (2, 3) provide a view of some features of resilience. Resilient children are autonomous, have high self-esteem, and get along well with others. Their families are cohesive and free from frequent conflicts among family members. Resilient children also have access to social support both within and outside the family that helps them cope with stress.

Although the constructs of resilience and wellness both apply to mentally healthy people, they differ in one important respect. Wellness is purely descriptive. It assesses a person's absolute level of healthy functioning without regard to either the person's constitutional vulnerability to mental illness or his or her exposure to environmental risk factors. In contrast, by definition, resilience refers to the achievement of healthy levels of functioning despite the presence of constitutional or environmental risk factors (7). For example, a well-adjusted person who has mentally ill parents or has been exposed to poverty and family conflict can be described as resilient. But the term "resilience" does not apply to a well-adjusted person who has not been exposed to risk factors. In the latter case, the resilience of the person is unknown.

Thus, Kendler et al. did not study resilience, because they did not assess wellness in the context of exposure to risk factors. Nevertheless, by definition, all resilient people are mentally healthy, so we can infer that some of the mentally healthy subjects of Kendler et al. must also be resilient. It is therefore possible that the mechanisms that mediate resilience might be candidates for the three causal domains assessed by the twin methodology. It is also possible that genetic studies of resilience would implicate a mix of genes, shared environment, and individual-specific environment different from the one Kendler et al. implicate for wellness.

Because genes also appear to influence wellness, we must consider whether the findings of Kendler et al. suggest that searching for mental health genes might be a useful endeavor for psychiatric genetics. From table 3 in the article by Kendler et al. we see that the influence of genes on wellness is relatively low (ranging from 0.16 to 0.49 on a scale of 0 to 1) compared to the known influence of genes on most psychiatric disorders (which often exceeds 0.70 [1, 8–10]). The relatively low level of genetic influence on wellness suggests that finding genes for mental health will be difficult.

Yet, despite this cautionary note, there is already one report of a potential chromosomal locus for mental health. Ginns et al. (11) conducted a genetic linkage study to identify genes that prevented or reduced the risk of bipolar disorder in multigenerational families having many affected members. They defined mental health wellness as the absence of any psychiatric disorder and found strong evidence for its linkage to a locus on chromosome 4p and suggestive evidence for linkage to a locus on chromosome 4q. Their findings support the idea that certain genes may prevent the clinical expression of bipolar disorder.

Studies of the forces that mold wellness and resilience will have substantial clinical implications. Most important, they will provide new directions for efforts to develop preventive interventions. Future studies of wellness should use a broader range of highly reliable measures. High reliability, or the use of repeated measures, will help disentangle apparent effects of the individual-specific environment from measurement error. Future work also needs to determine whether the findings of Kendler et al. in women will generalize to men.

Studies of shared and unique environmental factors can identify features of the environment that can be manipulated to promote wellness. Molecular genetic studies

may eventually discover biological reasons why some people remain mentally healthy in the face of adversity. If so, that could lead to pharmacologic strategies to protect children at risk from mental illness.

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MING T. TSUANG, M.D., PH.D., D.SC., F.R.C.PSYCH.

Address reprint requests to Dr. Tsuang, Harvard Medical School Department of Psychiatry at the Massachusetts Mental Health Center, 74 Fenwood Rd., Boston, MA 02115; ming_tsuang@hms.harvard.edu (e-mail). *Supported in part by NIMH grants MH-41879 and MH-43518.*