EDITORIAL

Genetics and Behavior

Nearly every other day it seems, a headline in our newspapers announces the discovery of yet another gene linked to some aspect of human biology, behavior, or disease. Perhaps most disturbing to our sense of being free individuals, capable to a large degree of shaping our character and minds, is the idea that our behavior, mental abilities, and mental health can be determined or destroyed by a segment of DNA. How much of our fate is in fact written in the DNA inside our cells? And how much freedom do we have to reach our full potential as human beings through our education and experiences?

These questions ultimately involve the enormously complex interaction between the genetic information that flows out from DNA into developing and mature brains and the experiential information that flows in through our nervous system as we perceive and act in the world. We are only beginning to understand the rudiments of each information pathway. Each cell in the brain, like all cells of the body, expresses only a subset of the genes present in its DNA. Studies have shown that many of the genes a nerve cell expresses can be regulated by environmental stimuli. Genes controlling embryonic development shape the structure of the infant brain; the infant's experience in the world then fine-tunes the pattern of neural connections underlying the brain's function. Such fine-tuning of the fabric of connections making up the brain must surely continue through adulthood.

Studies of the developing visual systems of mammals, for instance, have shown that the visual cortex is to a large extent wired up and ready to be used at birth. Yet if animals are deprived of early visual experience, dramatic changes in the structure of their visual cortex will occur. There is a critical period early in visual development in which both innate neural wiring and visual experience must interact in order to ensure proper development of the visual system. Throughout life, experience continues to modulate the fine pattern of cortical connections, allowing us to acquire new skills and knowledge.

Genetic studies of human disease have been highly successful in locating mutations in single genes that are directly responsible for the disease pathology. The recent identification of the mutations underlying Huntington's disease demonstrates that neurological disorders can also be caused by a single aberrant gene. But many other neurological diseases, such as schizophrenia and manic depression, are likely to have polygenic roots whose interaction with environmental factors will be highly complex.

It has long been known that schizophrenia clusters in families, and identical twin studies have supported the belief that the susceptibility to schizophrenia has a genetic component. Yet it is also important to recognize that the genes that predispose one toward schizophrenia may not be expressed except under special environmental circumstances; for instance, conditions of great stress. Indeed, understanding of how gene expression in brain cells is regulated by environmental experiences may serve as a foundation for the design of drugs or for preventive measures for better controlling gene expression patterns.

Perhaps the best reason for pursuing the genetic basis of such complex disorders as schizophrenia, manic depression, and Alzheimer's disease is that genetic studies often present the best entry point into the underlying biology of a disease. Michael Brown and Joseph Goldstein untangled the biology of cholesterol metabolism by studying the 5% of the population with the highest serum cholesterol levels. Yet the study of patients with a relatively rare genetic syndrome opened the door to understanding a biochemical pathway operating within the other 95% of the population suffering from elevated cholesterol. Genetic studies are likely to be an essential tool for unlocking the biochemical and cellular basis of neurological disorders as well, even in the subpopulation of patients whose disease is caused primarily by environmental factors. The operations of the brain result from a balance between inputs from heredity and environment—nature and nurture—and this balance should also be reflected in research into the biological basis of behavior.

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