Gene–Environment Interactions and Schizophrenia

A review of

The Origins of Schizophrenia

by Alan S. Brown and Paul H. Patterson (Eds.)


Reviewed by

Larry Davidson

This ambitiously titled volume, The Origins of Schizophrenia, edited by Alan Brown and Paul Patterson, presents up-to-date chapters on a range of factors that are increasingly being thought to contribute to the risk for, and eventual onset of, psychotic disorders in adolescence and young adulthood. Through the review of an elegant combination of clinical research and preclinical studies using animal models, the editors mount a persuasive case for there being a number of events (such as maternal infection or stress) and/or circumstances (such as obstetric complications or poor prenatal nutrition) that might help to create the vulnerability to psychosis proposed as one half of the diathesis–stress model first developed by Zubin and Spring (1977) in the 1970s.

What is perhaps surprising about the series of risk factors covered in this volume is that all of them—with the one exception of cannabis use—occur either prior to or during the
birth of what will become a psychosis-prone person. This fact poses the investigators pursuing this particular line of research with the challenge of explaining why and how the illness per se does not appear fully until 15–25 years later, and sometimes not for decades.

Given the research on the prevalence of adverse childhood experiences in the lives of persons later diagnosed with psychotic disorders—who are five to seven times more likely to have had such childhood experiences than are persons without psychosis (e.g., Schäfer & Fisher, 2011)—it is not a sufficient explanation to suggest that the “stress” component of the diathesis–stress model does not occur until later in life. In addition to whatever brains they are born with, persons with psychosis most often have had stressful experiences well prior to the onset of the disorder. There is little in this volume that I could find that helps to explain the 15- to 25-year gap between birth and onset.

According to Robert Freedman, who provided a foreword for the book, what is new, unexpected, and especially promising about the body of work presented in this volume is the emerging theory that underlies the selected studies. This theory suggests that it is not only the range of events and circumstances that befall the mother prior to and during the pregnancy and delivery of the psychosis-prone person, but it is also, and importantly, the reaction of the mother’s body, in particular of her immune system, that helps to account for the structural and functional changes in the developing baby’s brain that will eventually manifest as psychotic experiences. As Freedman writes: “All these factors can cause the mother to mount an immune response on the baby or at least its part of the placenta. The effects on fetal development, although subtle, can have ominous consequences” later in life (p. xi).

Putting aside the question of why these effects do not become manifest until the person begins to reach adulthood, it is encouraging to think that real breakthroughs are being made in a more sophisticated form of neuroscience that is grappling with discovering and understanding gene–environment interactions. Clearly, the answer to the puzzle of schizophrenia has not been provided by the sequencing of the human genome. Future models of psychosis will have to allow a significant role for life events, whether these occur following, or prior to, birth.

The research described in this volume takes on this challenge, and the authors seek to understand not only the genetic component of psychosis but also the various types of events and experiences that may have to interact with the person’s genetic inheritance in order to bring about psychosis. One hopes that this is a promising approach and that it will lead to more substantive advances in care than those made over the last 30 years of neurobiological research. However one gauges the degree of success made thus far, there is no doubt that a tremendous amount of human suffering and lost productivity continue to be associated with these conditions.

As a student of the history of psychiatry, though, I cannot help but point out some eerie parallels between certain findings reported in this volume and earlier efforts to discover the origins of schizophrenia. It was not so long ago, for example, that psychiatric researchers
were attributing the same characteristics of schizophrenia to a different form of maternal response, but at that time it was postnatal. The theory of the “schizophrenogenic mother” was, at its inception, no more of an attempt to “blame” mothers for their child’s psychosis (although it quickly became just that) than are the theories presented in this volume. It does not require a stretch of the imagination, however, to envision mothers being told in the future that the cause of their child’s psychosis was their not getting a flu shot, not managing the (inevitable) stresses of pregnancy well, or not taking in enough vitamin D.

I might not have brought up this ugly chapter in the history of psychiatry (which, unfortunately, has several ugly chapters) had it not been for the ambitious title of the book and for several of the authors of this volume (Waddington and colleagues) writing at length about what they describe as “craniofacial dysmorphology” (p. 8). By this term, they are referring to what they believe they have discovered about abnormalities of the face and head of persons with psychosis. I cannot read these passages without being reminded of what we now consider to be the pseudoscience of phrenology that was popular in the 19th century and that made its way into the best psychiatric textbooks of the time.

Even if they have yet to pin down the precise “origins of schizophrenia,” I hope the studies in this book do represent a substantive advance over phrenology in the light they shed on the causes of psychosis. But given the paucity of knowledge generated by the last 30 years of significant funding devoted to this type of research, there is at least one thing that is missing in this volume. Alongside all of the “hard” evidence (p. 8) that the investigators purport to have found (and Shakespeare might rightfully wonder why they “doth protest” so), what is lacking is an appropriate sense of humility in the face of this baffling and extremely disturbing condition.

References