This volume represents a burgeoning perspective on the origins of psychopathology, one that focuses on the development of the human central nervous system. The contemporary neurodevelopmental perspective assumes that mental disorders result from etiologic factors that alter the normal course of brain development. Defined here in its broadest sense, neurodevelopment is a process that begins at conception and extends throughout the lifespan. We now know that it is a complex process and that its course can be altered by a host of factors, ranging from inherited genetic liabilities to psychosocial stressors.

This book features the very best, cutting-edge thinking in the converging fields of developmental neuroscience and developmental psychopathology. The developmental window represented is broad, extending from the prenatal period through adulthood, and the authors cover a broad range of etiologic factors and a spectrum of clinical disorders. Moreover, the contributors do not hesitate to use the opportunity to hypothesize about underlying mechanisms and to speculate on future research directions.

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Neurodevelopmental Mechanisms in Psychopathology

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Preface

This volume represents a burgeoning perspective on the origins of psychopathology, one that focuses on the development of the human central nervous system (CNS). The contemporary neurodevelopmental perspective assumes that mental disorders result from etiologic factors that alter the normal course of brain development. Defined here in its broadest sense, neurodevelopment is a process that begins at conception and extends throughout the lifespan. We now know that it is a complex process and that its course can be altered by a host of factors, ranging from inherited genetic liabilities to psychosocial stressors. This knowledge has challenged clinical researchers to devise novel methodologies aimed at identifying links in this chain of events that can lead to psychopathology.

Neurodevelopmental perspectives on psychopathology have become increasingly dominant as a consequence of major advances in both basic animal research and clinical investigations of human populations. Basic research efforts have succeeded in elucidating amazing facets of brain development that extend from the molecular to the behavioral levels of analysis. For example, using animal models, basic scientists have documented the long-term effects of prenatal and postnatal events on brain structure and function and have shown how these effects vary as a function of hereditary factors. They also have demonstrated that there are significant behavioral sequelae of aberrant neurodevelopment. At the same time, clinical research has yielded extensive evidence that prenatal and early childhood factors are associated with subsequent risk for psychopathology. For example, within the past two decades, there have been numerous reports of correlations between prenatal complications and psychological functioning in adulthood. There are obvious points of convergence between the findings yielded by these basic and clinical research endeavors, and the result has been an increasing focus on the neurodevelopmental origins of psychopathology.

Inspired by this plethora of new theories and empirical findings, the editors of this volume organized a conference on neurodevelopmental aspects of psychopathology. The plan was to assemble a group of investigators who shared a primary interest in the field, including basic researchers who employ animal models to shed light on neurodevelopment and clinical researchers who study developmental factors in human psychopathology. The chief goals were to examine cutting-edge findings and to chart the directions for future research efforts. The meeting took place at Emory University in
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1999. Generous financial support was provided by the Essel Foundation, the William T. Grant Foundation, the Janssen Research Foundation, and the Spunk Fund. In addition, invaluable guidance was provided by Constance and Stephen Lieber, two philanthropic leaders in the field of mental health research.

What began as a relatively modest plan to assemble a small group of investigators quickly blossomed into a conference that was attended by more than eighty scientists. More than twenty distinguished investigators, representing those at the forefront of their fields, presented their most recent work. They were encouraged to stretch their imaginations and to share their speculations on the evolution of the field. They did so, and in the process we believe they set the stage for the next decade of research on neurodevelopmental aspects of psychopathology.

This volume presents a collection of chapters that evolved from presentations at the conference. The chapters feature the very best thinking in the converging fields of developmental neuroscience and developmental psychopathology. The developmental window represented in the chapters is broad, extending from the prenatal period through adulthood, and the authors cover a broad range of etiologic factors and a spectrum of clinical disorders. Moreover, it is obvious that the contributors did not hesitate to use the opportunity to hypothesize about underlying mechanisms and to speculate on future research directions.

The first chapters, written by Mayes and Ward and by Nosarti, Rifkin, and Murray, address basic mechanisms in the prenatal and neonatal development of the human nervous system and the implications for subsequent behavioral development across the lifespan. The authors of these chapters have heightened our understanding of the intricate processes involved in fetal and neonatal brain development. Further, their work sheds light on the myriad factors that can perturb the early development of brain structures that are known to play a role in human emotion and cognition. The chapter by Spear takes us into a later period associated with significant neuromaturational change – adolescence. It is clear that the postpubertal brain is undergoing pervasive changes that result in a new pattern of cortical circuitry. Although advances in cognitive function emanate from these changes, they may also set the stage for heightened vulnerability for certain forms of mental disorder.

Chapters by Brown and Susser, Rosso and Cannon, and Shiffman, Mednick, Machón, Huttenen, Thomas, and Levine, present recent empirical findings on the associations of prenatal and perinatal events with adult psychiatric disorders. Through careful longitudinal research, these investigators have demonstrated relations between early insults to the developing CNS and mental health in adulthood. They show us how latent congenital vulnerabilities can lay dormant until later developmental events trigger their expression.

In the next section, the focus shifts to animal models. In chapters authored by Schneider, Moore, and Kraemer and by Maestripieri and Wallen the investigators describe the results of experimental research programs that are helping to clarify the mechanisms involved in the genesis of psychopathology. By manipulating exposure to nonoptimal environmental influences, the authors are able to provide strong support for the importance of early experience for later psychological functioning. In the final chapter in this section, Bachevalier and Loveland present experimental evidence derived from brain-lesioned monkeys and propose a developmental model of autism based on this animal work.
The next group of chapters focus on general models of the nature of genetic and environmental influences on the developmental course of psychopathology. Todd and Constantino suggest new approaches to conceptualizing genetic influences on development and psychopathology. In his chapter, Waldman explicates a number of behavioral and molecular genetic research strategies that may aid in our understanding of the neurodevelopmental contributors to psychopathology. Granger, Dreschel, and Shirtcliff explore the immune system and its impact on brain function, and they describe the myriad of ways in which viral and bacterial agents might give rise to aberrations in neurodevelopment that could lead to behavioral disorders. In his chapter, Keshavan draws our attention to adolescence as a sensitive neurodevelopmental period. He offers a convincing argument for the pivotal nature of adolescence in the genesis of major mental illnesses. In her chapter, Benes discusses the interaction of several neurotransmitter systems during childhood and adolescence and describes how stress can influence an individual's vulnerability for the development of psychopathology. In their chapter, McBurnett, King, and Scarpia describe research on neuroendocrine functioning and the emergence of conduct disorder and substance abuse disorders. Relatedly, Cicchetti illustrates how child maltreatment, a chronic social stressor, affects neuroendocrine functioning and the emergence of psychopathology.

In the final section of chapters, the authors address the developmental course of some specific mental disorders: personality disorders, schizophrenia, depression, bipolar illness, and posttraumatic stress disorder. The neural underpinnings of diverse personality disorders, which are often the developmental prelude to Axis I mental disorders, are discussed by Siever, Koenigsberg, and Reynolds. In chapters by Goodman, by Kaufman and Charney, by Post, Leverich, Weiss, Zhang, Xing, Li, and Smith, and by Walker and Walder we see how different syndromes of psychopathology can arise from interactions between specific constitutional liabilities and environmental factors that impinge on the individual.

The nature of the theoretical shift this volume represents is brought into clearer focus when we examine key theoretical papers published prior to 1980. These landmark theoretical models foreshadowed contemporary developments in the field. In 1973, Hagop Akiskal and William McKinney published a seminal paper in *Science* entitled, “Depressive disorders: Toward a unified hypothesis.” In this paper, the authors began by briefly reviewing the major theoretical perspectives of the time: psychoanalytic, interpersonal, object relations, learning, and “biogenic amine” theories. They proceeded to argue that each of these theories deals with a different level of analysis and that there are important interactions among the various levels. They criticized the notion of a single initial cause for depression, and emphasized the importance of bidirectional interrelations among brain, behavior, and experience. Along the same lines, in 1977, Joseph Zubin and Bonnie Spring published a paper entitled, “Vulnerability: A new view of schizophrenia.” They argued that schizophrenia is best understood as a disorder that arises from the dynamic interaction between constitutional vulnerabilities and stressful experiences. In support of this, they presented evidence that both biological and environmental factors contribute to schizophrenia, apparently interacting at multiple levels. Both of these papers were widely cited, stimulating a great deal of discussion in the field. The arguments were intuitively appealing. Yet, in the 1970s, there was very little empirical evidence for neural mechanisms that might subserve interactional influences. It had been demonstrated that biological factors (genetics and...
neurotransmitters) were correlated with behavior, but the details were unclear. Even less clear were the processes mediating the effects of experience on brain function.

Now, at the turn of the century, the picture is very different. Neuroscientists have clearly documented the neural events that mediate the relation between experience and behavioral phenomena. Clinical researchers are currently using this knowledge base to inform their investigative strategies. We believe that the publication of this volume highlights the importance of scientific progress that has been made in our understanding of the neurodevelopmental origins of psychopathology. This book presents the work and ideas of some of the most talented researchers in the field. The chapters illustrate the interactional processes that characterize the genesis and maturation of the brain. They demonstrate how constitutional vulnerability to mental disorder can arise from the interplay of multiple factors, some specific and some nonspecific. Moreover, the authors have offered us some invaluable leads on promising directions for future research. We hope that their insights will inspire other investigators to take up the challenge.

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REFERENCES

