

# INTRODUCTION

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American psychiatry is said to have changed from blaming the mother to blaming the brain. It was not so very long ago that the cause of mental disorders was thought to be rooted in early experiences within the family, but now it is widely believed by most authorities and the public alike that the cause is a chemical imbalance in the brain. Today, schizophrenia is commonly claimed to be caused by an excess of the neurotransmitter dopamine and depression by a deficiency of serotonin, while anxiety and other mental disorders are attributed to other neurotransmitter abnormalities. Brain chemistry is believed to be not only the cause of mental disorders, but also the explanation of the normal variations in personality and behavior. How did these radical changes occur within the span of a few decades and does the evidence really support these new theories? Whose interests are served by promoting drug treatment and biochemical explanations and how are these interests advanced? What are the long-range implications of the biochemical theory of mental disorders and the growing reliance on drugs to treat all psychological and behavioral problems? This book attempts to answer these questions and to provide a long-overdue examination of the assumptions fundamental to current biochemical theories.

From about 1945 through 1960, most people had very different ideas about the cause of mental disorders. Although orthodox psychoanalytic therapy was practiced by only a small percentage of mental health professionals, psychoanalytic explanations of the causes of different mental disorders and the best way to treat them dominated the field. In 1950, it was rare that someone not committed to psychoanalytic theory would head a major psychiatry department.<sup>1</sup> Psychotherapists in private practice often spent years trying to discover the repressed causes of their patients' mental disorders. The value of this approach and the theory underlying it is now widely questioned, if not totally rejected, by most mental health professionals. Today, the disturbed thoughts and behavior of mental patients are believed to be caused by a biochemically defective brain, and symptoms are not "analyzed," but used mainly as the means of arriving at the diagnosis that will determine the appropriate medication to prescribe. Almost all current chairmen and the majority of the staffs of psychiatry departments are committed to a biochemical approach to mental illness.

How radically our ideas have changed is indicated by the fact that most psychiatric residents no longer receive any instruction in intensive psychotherapy, and many complete their training without meeting regularly with a single patient in psychotherapy sessions.<sup>2</sup> During the 1950s, any research on schizophrenia was considered unethical if it included a control group given drugs without complementary psychotherapy. By 1970, however, the situation had reversed, and it was considered unethical to have a group that received only psychotherapy and no drugs.<sup>3</sup>

These changes started in the 1950s, following the accidental discoveries of several drugs capable of altering mood and mental states. When tested on mental patients, these drugs alleviated some symptoms of mental illness. Many patients became calmer and less of a problem for those responsible for their care. Initially, psychiatrists in private practice were highly skeptical of drug treatment, but in the large institutions, where there was a pressing need to reduce costs, drugs were widely adopted. By 1965, over 50 million prescriptions had been written for Thorazine (chlorpromazine), the first of the new psychotherapeutic drugs to be marketed for schizophrenia, and there were many other drugs available for treating depression and anxiety as well. At first, psychiatrists in private practice were willing to try these drugs only as an adjunct to psychotherapy, but gradually they began to rely more on drugs and less on intensive psychotherapy. Today, it is not uncommon for a psychiatrist to rely almost exclusively on drug treatment, and the annual sales of quite a few psychotherapeutic drugs are in the billions of dollars.

The many recent books on the so-called “pharmacological revolution in psychiatry” are another indication of how much our prevailing notions of mental illness have changed. These popularly written books use such phrases as “molecules of the mind” and “chemistry of mood” to convey the idea that all the important aspects of mental life are determined by brain chemistry. Chemical imbalances are believed to be the cause not only of depression, schizophrenia, anxiety, and obsessive-compulsive disorders, but also of much maladaptive behavior, such as eating disorders, violence, alcoholism, excessive gambling, and compulsive shopping. Moreover, personality traits ranging from shyness to assertiveness, from passiveness to aggressiveness, from risk aversion to sensation seeking, and from the capacity to delay gratification to requiring immediate satisfaction all are claimed to be caused by abnormal activity of only a couple of brain neurotransmitters, or even only one. Brain serotonin level, for example, is claimed to underlie self-confidence, and all pleasurable experiences are said to depend on brain dopamine activity.

Many recent books exaggerate and distort the connection between brain chemistry and psychological states. A University of Washington psychiatrist recently described a “world-wide epidemic of depression” caused

by the “serotonin depleting times” we are living in.<sup>4</sup> Actually, there is not a shred of evidence of any worldwide decrease in brain serotonin. In another book, a Pulitzer Prize-winning science writer describes the “revolutionary” finding that major personality and behavioral traits are regulated by the balance between norepinephrine and serotonin.<sup>5</sup> There is really no convincing evidence supporting this view, but by describing some weak trends as established facts and by failing adequately to acknowledge contradictory evidence, many popular writers make it appear that complex personality variables are completely dependent on the balance between two neurotransmitters. It is not surprising that so many people now believe that drugs are able to produce “cosmetic” changes in personality. We have almost reached the point where there will be no limits to what people will believe brain chemistry can explain and where the slogan “Better living through chemistry” could well be changed to “Better lives through chemistry.”

Today, physicians are routinely informing patients with mental disorders that their condition is caused by a biochemical imbalance that can be corrected by drugs in the same way that insulin treats diabetes. While many physicians are apparently convinced that this is true and that it has been firmly established by scientific investigation, others may not be completely convinced, but they have found the insulin analogy useful in overcoming the reluctance of some patients to take psychotropic drugs. Pharmaceutical companies have an enormous influence in promoting this message both to physicians and to potential consumers of drugs. Patient advocate groups also play a prominent role in this area. In order to encourage people in need to seek professional help for a psychological problem, various support groups, often funded by large grants from the pharmaceutical industry, exaggerate and sometimes distort the effectiveness of drug treatment and what is known about the relationship of brain chemistry to mental illness. Patients with psychological problems and their family members are usually more than willing to believe that the problem is biochemical, as this interpretation does not convey the stigma of mental illness that is unfortunately commonly associated with many traditional psychological theories.

Throughout this book I will argue that the evidence and arguments supporting all these claims about the relationship of brain chemistry to psychological problems and personality and behavioral traits are far from compelling and are most likely wrong. The claim that psychotherapeutic drugs correct a biochemical imbalance that is the root cause of most psychological problems also rests on a very shaky scientific foundation. These ideas are simply an unproven hypothesis, but for reasons that will be explored, they are heavily promoted as a well-substantiated explanatory theory. Because these ideas have enormous implications, there is a great need to examine the evidence and basic assumptions much more critically than has been done up to now.

It may surprise you to learn that there is no convincing evidence that most mental patients have any chemical imbalance. Yet many physicians tell their patients that they are suffering from a chemical imbalance, despite the reality that there are no tests available for assessing the chemical status of a living person's brain. While there are some reports of finding evidence of an excess or deficiency in the activity of a particular neurotransmitter system in the brains of deceased mental patients, these claims are controversial, as other investigators cannot find any such relationship. At best, such claims are trends that result from averaging the data from many patients. As the brain chemistry of many patients in these studies was found to be perfectly normal, it is hard to argue that their mental problems were caused by a chemical imbalance.

Moreover, the brains of some "normals"—people with no history of any mental disorder—may show signs of some excessive or deficient neurotransmitter activity. It needs to be recognized that even if a chemical abnormality were eventually found to be highly correlated with the incidence of a particular mental illness, it would not be clear how such a finding should be interpreted. It might well be that the chemical "abnormality" was caused by the stress or some behavioral peculiarity commonly associated with a particular mental illness, rather than having been the cause of that illness. It is also well known that psychotherapeutic drugs can be the cause of chemical abnormalities. The "cause" and the "effect" of a mental illness are routinely confused.

When the first psychotherapeutic drugs were accidentally discovered we knew so little about brain chemistry that it was not possible to even propose a biochemical theory of mental illness or to offer any explanation of how drugs were acting on the brain. Our initial chemical theories of mental disorders emerged after it was realized that the first drugs introduced seemed to be acting on the few neurotransmitters then known to exist in the brain. It is now estimated, however, that the number of substances that act as brain neurotransmitters may be over one hundred, and we have learned that most psychotherapeutic drugs affect many more neurotransmitters than initially suspected.<sup>6</sup> Yet the theories have changed very little over the years despite much evidence that they cannot possibly be correct. The theories are held on to not only because there is nothing else to take their place, but also because they are useful in promoting drug treatment.

There is a tendency to confuse the giant strides that have been made in our knowledge of brain chemistry and neuropharmacology with our still primitive understanding of the causes of mental illness and knowledge of how drugs can produce psychological changes. Stimulated to a great extent by the discovery of psychotropic drugs, the advances in our knowledge of brain chemistry and neuropharmacology have truly been remarkable. We now know not only that there are a great many more neurotransmitters in

the brain than were suspected, but also where in the brain these different “chemical communicators” are located. We have learned how a neuron can use enzymes to make neurotransmitters from chemical precursors and how the different neurotransmitters act on their respective targets (“receptors”). We also know how the action of the different neurotransmitters is normally terminated and how, under certain conditions, the action may be prolonged. The science of neuropharmacology has contributed enormously to our understanding of the ways that drugs can modify all of these neuronal processes. However, all of this new knowledge has revealed critical exceptions to *every* chemical theory that has been proposed to explain mental illness, and the task of integrating all this new information and relating it to mental states grows more, rather than less, formidable.

Scientists, clinicians, and pharmaceutical companies have predicted that our new knowledge of brain chemistry and neuropharmacology will make it possible to develop drugs capable of acting like “smart missiles” that can correct the precise biochemical error responsible for each mental illness without any of the adverse side effects commonly seen with the drugs now marketed. The history of the neurotransmitter serotonin illustrates why we should maintain a healthy skepticism about these predictions of pharmacological “magic bullets” for treating mental illness. When serotonin was first discovered in the brain, it was thought that it acted on only one receptor target. We now know that there are at least fifteen different serotonin receptors. While technical advances may soon make it possible to develop drugs that act on only one of those receptors, we have little idea what these receptors do or how they may be related to any psychological state. There are good reasons for believing that every psychological state is influenced by different neurotransmitters and by brain circuits distributed widely throughout the brain that undoubtedly involve a number of different neurotransmitters. Furthermore, all information available should lead us to conclude that every neurotransmitter and every receptor target plays a role in different behavioral and psychological phenomena. There is no good reason to believe that there will be a simple and unitary relationship between a particular neurotransmitter or receptor target and any psychological state.

Most proponents of drug therapy use the fact that certain classes of drugs seem to be most effective in alleviating a particular mental illness as a strong argument for a biochemical cause. However, the relationship between the cause of an illness and the claimed effectiveness of a treatment can be quite misleading. The history of medicine is rife with examples of treatments that alleviated the symptoms of an illness without addressing its cause. Prefrontal lobotomy, insulin coma, and other treatments that are now totally rejected were claimed, in their time, to be just as effective in treating mental illnesses as it is now claimed that drug treatment is. Many

current studies also have shown that electroconvulsive treatment (ECT) of depression may be more effective than drugs and there is good evidence that several of the briefer psychotherapies are at least as successful as drugs in treating some mental disorders. The tenuous relationship between what is judged to be effective in treating an illness and what has caused that illness in the first place is discussed in later chapters. Also discussed is how the judgment of improvement is made and how political and economic factors can influence that judgment. The success that is claimed for drug treatment is often exaggerated, while adverse side effects are commonly minimized.

Contrary to what some readers may conclude, I did not write this book because I am opposed to using drugs to treat mental illness. I believe that drugs are often useful in treating mental disorders. I should also make clear that I do not treat patients and have no reason to be for or against drug therapy, psychotherapy, or behavior therapy or to take any side in any disagreement between nonmedical therapists and psychiatrists. Furthermore, I am definitely not opposed to biological explanations of mind and behavior. In fact, I have spent over forty years working as a biopsychologist studying how the brain and other biological factors such as hormones and drugs influence behavior. I am certain as a scientist that biological factors have an important influence on behavior. In short, my motivation for writing this book was not that I was for or against anything. The book had a completely different origin.

I am convinced that biological factors may predispose some individuals toward developing a mental illness, but there is more to biology than neurotransmitters and brain chemistry. While I believe in the importance of biological factors, I am equally convinced that the way all biological factors are expressed in behavior and mental states depends equally on social and psychological variables. There is nothing startling about this statement, and there are probably very few who would not agree that biological and environmental factors interact to produce their effects. However, in their everyday practice physicians are increasingly being pressured to neglect everything but drugs and chemical explanations in treating patients with mental disorders, and therein lies a great danger.

For a number of years, I have been interested in how scientific ideas and explanations arise and change. My plan when I started this book was to trace the accidental discoveries of psychotherapeutic drugs that led to the revolutionary changes in how we think about mental disorders. Today, mental disorders are so widely believed to be caused by chemical deficiencies or excesses in the brain that even some psychotherapists are jumping on this biochemical bandwagon by suggesting that the "talking cure" works because it changes brain chemistry.<sup>7</sup> While it may be true that every mental change must be accompanied by some change in the brain, the claim has little substance behind it, as almost nothing is known about what brain

changes take place during psychotherapy or how they may relate to any improvement in a patient's condition.

I was aware at the outset that this would not be a simple story of scientific progress. When the first psychotherapeutic drugs were introduced there were groups that opposed them, while other groups had a considerable interest in promoting their use and a different way to think about mental disorders. At the time that chlorpromazine and the other early drugs used to treat mental illness were discovered, little was known about brain chemistry or neuropharmacology. In the early 1950s, the field of psychopharmacology did not really exist. The discipline developed and matured together with the increased use of drugs to treat many different mental disorders. All of this background had convinced me that there was a fascinating story to be told about how serendipity, science, and psychosocial and economic factors interacted to bring about the changes in how mental disorders are conceptualized.

Starting with the discovery of the first psychotherapeutic drugs, I let the literature lead me backward and forward in time, learning more about early theories of mental disorders, brain physiology and chemistry, and how these changed over the years. I chose not to work from an outline, because I wanted the conclusions to emerge from the literature rather than the other way around. This made my progress much slower, but it had the advantage of leading me to some literature that I knew little about when I began. Besides, when working closely from an outline it is all work, without the joy of discovery. As I read more of the experimental and clinical literature and examined the social and intellectual context in which much of the evidence and theories was embedded, the purpose of the book gradually changed. Although I still wanted to describe the history of how all these changes took place, I decided that it was equally important to evaluate the evidence and arguments that are claimed to justify the biochemical theory. My own views were not well formed when I started the book, but as they became firmer I wanted to state them as clearly as possible so that others could challenge them in a way that I hoped might start a long-overdue dialogue about what is being claimed and what we really know about drugs and mental disorders.

Chapter 2 describes the fascinating story of how the major classes of psychotherapeutic drugs were discovered. This history provides the intellectual and social context that is necessary for understanding how drug treatment became widely accepted and how the effects of drugs revolutionized our theories about the causes of mental illness. Chapter 3 discusses the emergence of chemical theories proposed to explain how the drugs worked and what could be inferred about the causes of the different mental disorders. The evidence and arguments for the biochemical theories that emerged are presented as clearly and as convincingly as possible in this

chapter to make it clear why so many came to accept these theories as having a sound scientific foundation. Chapter 4 examines the evidence and arguments for the chemical theories much more critically. This chapter documents the fact that much of the evidence that was described as convincing and compelling was often difficult to replicate, based on a very limited knowledge of brain chemistry and neuropharmacology, and often subject to other interpretations than the one offered.

Chapter 5 raises issues and arguments that go beyond an examination of the reliability of the empirical evidence. Included in this chapter are discussions of such topics as the confusion of the cause and the effect of a mental illness and, in general, what can be inferred about the origin of an illness from the effects of a treatment. Also discussed in Chapter 5 are the limits of reductionism, how much of psychology and behavior can be explained by genetics, whether drugs act as specifically on different mental disorders as claimed, and the role that science and politics have played in the classification of mental disorders. Chapter 6 and 7 examine the various ways that economic and psychosocial factors and special interest groups have promoted the "biochemical theory of mental disorders." These chapters discuss the enormous influence of the pharmaceutical industry in promoting drugs and the many different ways this influence has been exerted. The chapters also discuss how psychiatrists, medical insurers, and patient support groups promote drug treatment and the chemical theories of mental illness. The conflict between medical and nonmedical mental health professionals in interpreting the effectiveness of various treatments is also discussed in these chapters. Chapter 8 reviews the major arguments presented throughout the book that are believed to justify the conclusions reached. This chapter also attempts to anticipate and answer some of the criticisms likely to be raised and discusses some of the implications of the path we are now following.

So much for introduction. It is time to begin at the beginning with the discoveries that set the stage for all that followed.