

# Introduction

## General Considerations

As with any new and provocative theory, this book is a work in progress, and some of the ideas presented are sure to change over time as research scientists like myself delve deeper into the brain, applying tools and methods not yet devised. I believe it nonetheless represents a significant and perhaps massive step forward for the field of psychiatry, both in a theoretical and a practical sense. In attempting to understand general principles of brain function that characterize different types of mental illness, including my own bipolar illness, I may have not only stumbled upon important principles for treating these illnesses but also uncovered basic brain characteristics that drastically affect our experience of the world. I have a Ph.D. in neuroscience from Johns Hopkins University, I am currently performing brain mapping studies at the Krieger Mind/Brain Institute of Johns Hopkins, and in my free time I have done extensive research on mental illness and the effects of psychiatric drugs.

The field of drug-based, biological psychiatry—the focus of this book—is really still in its infancy, as most of the commonly used drugs are no more than fifty years old, and even Prozac is less than twenty years old. Therefore, it is not surprising that there is a good deal of disagreement regarding which drug regimen—including even which class of drugs—to use on a given mentally ill individual. Moreover, many people with overt mental illnesses, even when given what are thought to be the best drugs, are not able to function normally and remain occupationally impaired even after years of tinkering with their drugs and dosages. However, some people do get dramatically better with drug treatment—psychiatrist Peter Kramer has argued that some people can even be made ‘better than well’ by Prozac, for example—and I am living proof that other drugs can also make one better than well (see Chapter 2). The existing pharmaceutical drugs are very powerful and potentially extremely effective *when used properly*, though in the field of psychiatry today there is no such consensus on how to use these drugs. Moreover, some of the more widely believed tenets of the field, such as that the most effective drugs for treating schizophrenia are the antipsychotics, may simply be wrong. So because of all this confusion, I have written this book in an effort to provide a coherent, unified framework for understanding the various mental illnesses, with the hope that such a framework will lead to much more effective drug treatment and higher quality of life for a large number of people. Indeed, this is a very exciting time for psychiatry, as it may now come much closer to reaching its full potential, with very positive consequences for society and humanity in general.

Actually, I like to think this is more than just a book about psychiatric drug treatment of the mentally ill. It also has at least two other major points of interest: one is that it provides a greater description of how the brain works and what it means to experience the world as a human being, and the other is that it indicates that psychiatry is no longer just of interest to very sick persons but also may help many so-called normal people have a much better life and live up to their full potential. Regarding the first point: I think people tend to think that others experience the world in a very similar manner to themselves, and perhaps that minor differences in temperament and major differences in life history explain the diversity of human behavior. I think my book explains that this is

not the case. On the second point: The Adjustment theory, which involves adjusting two or three brain neurotransmitter systems in a particular way with drugs, should make life better both for the mentally ill and also for perhaps nearly everyone else. And if The Adjustment is very potent with the existing pharmaceutical drugs, and we pursue such treatment on an international scale, then the world may indeed become a much better place, partly because both human behavior and society might change to make it such a place. So we may be living at a very exciting time!

### **Nuts and Bolts of a Theory**

Any theory reflects the biases and limited knowledge of the theorist; no one is truly a master of all the disciplines relevant to understanding and treating mental illness. I come from a systems neuroscience background—which means I study the functioning of general brain systems, such as the circuits responsible for the sense of touch—and I have no formal training in psychiatric medicine, pharmacology, or psychological brain science, and only a limited knowledge of molecular neuroscience. Nonetheless, the current theory (note: by ‘current theory’, I mean the set of theories contained in this book) is consistent with the general principles of these disciplines.

This book represents a synthesis of a large amount of information into a working theory of brain function that is relevant to treating mental illness. What are the origins of the theory? Some aspects come from my laboratory research, some from the scientific literature, some from the popular literature, some from my observations of many people over the years, and some from my experiences during the treatment of my own illness, bipolar disorder. I believe a reasonable theory with testable hypotheses is better than no theory at all for at least two reasons: 1) it affirms or eliminates one of the hypotheses, and 2) it stimulates discussion that may lead to improvement of the field of psychiatry. I want the reader to feel that he or she can make a contribution to this discussion also, by using common sense reasoning to analyze what I’ve written and thereby try to improve the theory.

The foundation of the current theory is that the brain chemicals serotonin (**ser**), norepinephrine (**nore**), and dopamine (**dop**)—the ‘Big Three’—as well as the neural circuits they affect, provide the basis for not only understanding what causes most types of mental illness and how to treat those illnesses, but also for understanding basic human characteristics, personality traits, and our very perception of the world. A fundamental premise of the current theory is that the ‘strengths’—by which I mean the chemical levels plus the sensitivity of the relevant brain circuits they affect—of these three chemical systems vary from individual to individual, mainly as a result of genetics, and that understanding approximately what the strengths are in a given individual is critical for treating mental illness and understanding mental health. Furthermore, it is assumed that the strengths or at least functioning of the three systems can be altered by environmental stimuli, such as stressors, and can be adjusted with psychiatric drugs and possibly talk therapy.

Part of the current theory is a rehashing of ideas that many researchers already had in the 1950s and 1960s, when many new types of psychiatric drugs were being synthesized and tested. In some respects it is a more general version of the chemical imbalance theories of depression and mania from the 1960s, which state that low brain

levels of ser, nore, and dop cause depression, and that high levels cause mania, though many of the ideas are, to my knowledge, new. It is not meant to provide exhaustive information about any particular mental illness, but rather to examine some properties that prominent mental illnesses share.

### **Pop Philosophy**

The current theory concerns both differences and similarities between people, particularly how different aspects of brain function affect our conscious experience of the world. In examining these issues, we are faced with popular philosophical problems, such as that language and all other forms of communication are limited in their ability to describe subjective conscious states, and this problem is additionally confounded by the possibility that a given individual may never experience a given state. For example, most people would say that we can't conceive of colors other than those we have experienced, and we can never know if others perceive those known colors in the same way that we do.

To return to the subject of mental illness, how will we know, for example, if one person is mildly depressed and another is not? And how will we know, for example, if the subjective experience produced by taking a psychiatric drug, such as Prozac, is similar among different people? Moreover, comparing this drug induced experience to our imagined effect of the drug prior to taking it, or trying to explain the effect to someone who has never tried it or even to someone who has, is certainly not straightforward and may not even be possible.

One objective source of information that we can use to address these problems is behavior. For understanding mental illness, this primarily includes both people's reports of their own experiences—including perceptual experiences—as well as our observations of those people. If behavior is similar among different people, we may infer not only what a given conscious experience is but also that the experience is similar among different people, though these inferences may not always be correct. Much of the current theory is, out of necessity, based on such inferences.

We can also address these philosophical problems by studying brain function. We can ask the question: to what extent can the brain be idealized to be the same, or at least very similar, among different people—or among all mammals, for example? If, for example, brain dysfunction is physiologically similar across individuals with the same (or similar) mental illness, then those different people may be experiencing similar conscious states. Most researchers would acknowledge that while each brain is unique in its exact structure and function, much of scientific research and medical practice, including psychiatry, assumes that there are common properties to the brain across individuals. For example, the diagnosis of a discrete number of mental illnesses (syndromes, such as schizophrenia) relies on some degree of commonality across individuals. I take the stance in this book that there are brain structural and functional commonalities that, while not being exactly the same across individuals, are similar enough that they produce similar conscious states that can be modulated, for example, by a given drug in similar ways.

### **Personality Differences**

When there are significant, normal differences in the brain across individuals, I believe such differences evolved, by natural selection, to produce different personality traits, and that these differences are not frequently unique, but rather exist in clusters of other similar individuals. Given that there are significant and sometimes drastic differences in both personality and behavior between individuals, what accounts for the differences? The current theory's answer: variations in perception, originating from basic differences in brain function, form the basis of personality differences. If we could perceive the world the way others do, I think these differences would be obvious and profound. Indeed, philosophers and psychologists have long wondered whether we all perceive the world in a similar if not identical manner. The current theory indicates that people's perceptions—including their sensory perceptions—are, in fact, not identical.

The advent of widespread treatment of mental illness with drugs in the 1950s caused a revolution in psychiatry that continues today. As the eminent psychiatrist and author Peter Kramer has stated, one can 'listen to' the effect of a drug, assuming the validity of a particular brain mechanism of action for that drug (such as Prozac boosting ser), and from that action infer brain function both in the mentally ill brain and in the normal brain. Using this reasoning, part of the origin of the current theory lies with listening to the likely mechanisms of the drugs that are currently used to treat mental illness (pharmaceuticals), as well as drugs of abuse. Similarly, I have listened to personality across many people, because from it we can also infer brain function that, as I will describe in Chapter 12, may be directly related to Big Three function.

### **The *DSM-IV-TR***

The *Diagnostic and Statistical Manual of Mental Disorders* (current version: *DSM-IV-TR*), the standard diagnostic text of the American Psychiatric Association, probably represents the most widely read theoretical description of mental illness, though it is not very biological. I'm not trying to replace it with the current theory, but rather to supplement it. Nonetheless, that book is a caricature of the truth, even though it has probably identified the major forms of mental illness, and to an approximation, their clusters of symptoms.

In defense of the *Diagnostic and Statistical Manual*: it has represented important stages in our understanding of mental illness, namely that there are syndromes with constellations of symptoms, an idea which originated with eminent psychiatric researcher Emil Kraepelin. This idea is essentially correct, but the actual descriptions of particular illnesses in the current version are not completely correct; if they were then why do the authors keep changing the book? I believe there are almost certainly mental illnesses that have not been identified and accurately described, based solely on the incredible complexity of the brain. Moreover, some of the illnesses in the *Diagnostic and Statistical Manual* may have unidentified subtypes—such as atypical and typical bipolar disorder, which I describe in Chapter 10—and the lists of symptoms or characteristics will also probably change (possibly be expanded) somewhat as we come to understand these illnesses better. Nonetheless, abnormalities of the Big Three systems probably explain a significant number of the actual mental illnesses.

### **Origins of the Theory**

The current theory originates from multiple sources of information: eminent psychiatric researcher C. Robert Cloninger's tri-dimensional (Big Three) personality model; ideas of my mentors, including Vernon Mountcastle and the late Kenneth Johnson, at the Johns Hopkins University Mind/Brain Institute on sensorimotor transformation and pattern recognition; Michael Norden's observation of ser strengthening drugs, such as Prozac, treating so many conditions and other ideas described in *Beyond Prozac*; Peter Kramer's observations of presumably weak ser/strong nore patients described in the epic *Listening to Prozac*, especially the observation that some patients can be made 'better than well' by Prozac; John Ratey's and Catherine Johnson's description of ubiquitous mild mental illness in *Shadow Syndromes*; Kay Jamison's observation of bipolar disorder being overrepresented among artists and other information about bipolar disorder in her books, *An Unquiet Mind*, *Touched with Fire*, and *Manic-Depressive Illness* (the latter book was co-authored by Frederick Goodwin); Samuel Barondes' various observations on the state of psychiatry in *Better than Prozac*; Raymond DePaulo's detailed information about depression and bipolar disorder in *Understanding Depression*, including the description of assortative mating; the Enneagram personality model, most informatively described by Don Riso; my own experiences with bipolar disorder, including the effects of drugs on me; my observations of normal and overtly mentally ill people throughout my life; and the scientific literature, including animal studies.

Regarding the scientific literature, there are often conflicting data on a single issue, partly because of the sheer number of studies that have been conducted, including studies of rodents and occasionally non-human primates. Indeed, the advanced studies of the brain in rodents and monkeys, primarily carried out in the last fifty years, are probably the most relevant to the current theory. I have avoided getting into he said, she said debates.