Prescriptions for the Mind

A Critical View of Contemporary Psychiatry

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Introduction

Two Visions of Psychiatry

Psychiatrists are experts on the mind and its maladies. But no one is quite sure anymore what it is they do.

It is not surprising that the public has difficulty understanding the field. Psychiatrists themselves are confused about how they should practice.

The discipline remains divided between two visions, and there is a continuing struggle within psychiatry about its future role. Should psychiatrists be more like neurologists—examining patients, making diagnoses, and prescribing drugs? Or should they be more like psychologists—probing the inner workings of the mind and providing expert psychotherapy?

These contrasting visions are not new. In a book published fifty years ago, a sociologist, August Hollingshead, and a psychiatrist, Fritz Redlich, described two types of psychiatrists (Hollingshead and Redlich, 1958). One wore white coats and treated patients in hospitals; the other wore sports jackets and treated patients with psychotherapy in offices. Twenty

years later, when I studied psychiatry, my teachers could easily be separated into these two camps.

A seminal article in the *British Journal of Psychiatry* in 1986 by the Harvard psychiatrist Leon Eisenberg, entitled "Mindlessness and Brainlessness in Psychiatry," followed by other publications, critically examined both approaches (Eisenberg, 1986, 1995, 2000). Eisenberg labeled the psychiatry of the past—one that relied on the speculative theory of psychoanalysis—"brainless" because it did not give any serious attention to neuroscience. He was equally critical of a psychiatry that simply saw mental illness as disorders of the brain; a view he labeled "mindless."[1]

In short, both visions are too narrow. Mental illness cannot be understood without taking both biology and psychology into account. In that way, psychiatrists are unique. They are almost the only practitioners who regularly treat patients with combinations of biological and psychological interventions.

Unfortunately, the complexity of the real world runs counter to the preference of the human mind for simplicity. Most people find it easier to think that diseases have single causes. Yet direct and linear relationships between risk factors and actual illness are very rare. One of the themes of this book is that to carry out its mission, psychiatry must embrace complexity.

The Public Image of Psychiatry

Every month, scientific findings in the field of psychiatry appear in top journals and are summarized and discussed in leading newspapers and magazines. Many educated people are familiar with the latest research in the field. In recent years, the media have highlighted biological findings in psychiatry, and one gets the impression that the neurosciences are about to solve the mystery of mental illness. Psychiatrists also seem to believe this. They have become much more biological in their thinking and their practice, and their encounters with patients have come to focus more and more on drug prescriptions.

As psychiatry has changed, so has its public image. Even today, some people see psychiatrists as psychotherapists and are unsure how they differ from psychologists. To counter this confusion, psychiatry has defined itself firmly as a medical specialty. As we will see, this choice of identity has had vast implications.

The Couch and the Prescription Pad

For many years the most familiar symbol of psychiatry was the analytic couch. Readers of *New Yorker* cartoons can attest that the stereotype remains alive and well. But few psychiatrists today are psychoanalysts, and only some psychoanalysts are psychiatrists. Those who practice talk therapies see patients in an armchair, face-to-face. Many psychiatrists, however, never practice formal psychotherapy. Like other physicians, their primary tool is a prescription pad.

As the biological model of mental illness triumphed, talk therapies were marginalized. In a previous book, I examined the decline of psychoanalysis and its dramatic fall from grace within academic psychiatry (Paris, 2005a). With psychoanalysis a fallen icon, what role was left for talk therapies? Unfortunately, a healthy baby was thrown out with the bathwater. As this book will show, psychotherapy has as strong a base in scientific evidence as any drug on the market. Newer forms of treatment, such as cognitive-behavioral therapy, have a solid base in science, but are most often provided by psychologists.

The force driving psychiatry today is its wish to be accepted as a medical specialty. To gain acceptance, psychiatry adopted a new paradigm paralleling the worldview of internal medicine, in which practice is based on systematic diagnosis, laboratory tests, and drug prescriptions. This change was overdue and was in most ways positive. But since our knowledge base remains sadly undeveloped, the idea that a new psychiatry can be built entirely on neuroscience is a dangerous illusion. In spite of all its advances, brain research has thus far taken only baby steps. It will be many decades before the complexity of the brain is unraveled and the true causes of mental disorders are known.

In reality, psychiatrists are treating conditions that they barely understand. Our diagnoses are, at best, rough and ready, and do not deserve the status of categories in other specialties. We have no laboratory tests that can reliably identify any mental disorder, and the measures we use are entirely based on clinical observations. Although our drugs can be powerful and effective (when used properly), we are over-prescribing them and offering them to patients who do not need them.

This book will challenge the myth of the expert who cures mental illnesses by adjusting and adding medications. Psychiatrists could help more people by spending less time with prescription pads and more time

listening and talking to their patients. But this does not mean we should return to the analytic couch. It means, at least in part, that psychiatrists have to be interested in patients' lives and understand how events influence symptoms. They also need to acknowledge what they know and what they do not know so they can treat patients more intelligently and more effectively.

The Best of Both Worlds

This book will focus on the cost of psychiatry's shift in orientation. The choice of a narrowly medical identity that focuses exclusively on biological research and treatments has led to an impoverished practice. Biology is a necessary part of the theory and practice of psychiatry but does not provide a complete explanation of disease or a comprehensive guide to treatment. Psychiatrists diagnose patients from a manual and convince themselves that they are describing illnesses as specific as stroke or breast cancer. Even more seriously, some psychiatrists have forgotten how to talk to people. Many prescribe medication and do little else.

This critique should not in any way be seen as devaluing biological research or biological treatments. The conditions psychiatrists treat affect the brain. But this does not mean that the *source* of mental problems always lies at the level of neurons. Our psychological and social environment can make us anxious or depressed, leading in turn to changes in brain function. A discipline devoted to mental illness cannot ignore the mind.

The biological paradigm that dominates psychiatry today can be understood as a reaction *against* the past, when theories were spun out of thin air and patients were offered unscientific methods of treatment. But this book is not intended in any way to be an attack on psychiatry itself. We have had too much of that sort of thing. Starting with Thomas Szasz, "anti-psychiatrists" have refused to accept the biological basis of mental illness, and some even seem to think that psychiatrists should stop prescribing drugs (Breggin, 1994; Szasz, 1974). The very real benefits of pharmacological treatment would be lost if we were to adopt such backward-looking and misguided ideas. Psychiatrists must resist an either/or attitude when it comes to the study and treatment of mental illness.

Who This Book Is for and What It Is About

I have written this book for several audiences. Health professionals and trainees, inside or outside psychiatry, will want to know where the field is going and how much science is behind it. Moreover, since this book emphasizes the importance of scientific practice, I will be quoting data to support most of what I have to say. Of course, there are many controversies in psychiatry, and I do not have enough space to go into all of them in depth. And however much I am committed to evidence-based psychiatry, there are many important issues about which we have very limited data. But wherever I express a clinical opinion based on my own experience, I will make that clear.

I also hope that nonprofessionals will find this book enlightening. In an era of open information, psychiatric patients (and their families) need to understand the concepts behind our specialty. The educated public, which has long had a special interest in the field, needs to be updated on the vast changes occurring in psychiatry.

In summary, this book aims to provide an overview of contemporary psychiatry—how we got there, where we are now, and what is likely to happen in the future. As an academic, a researcher, and a teacher, I examine the discipline from the perspective of an insider. And as a practitioner who has always been committed to a psychiatry rooted in biology and psychology, I have written a book that aims to provide a balanced point of view, taking into account the strengths and weaknesses of both perspectives.

1

Neuroscience and Psychiatry

Almost every day, one can read media reports on the latest developments in neuroscience. Scientific journals are packed with exciting new findings. As a result, we have never known so much about the human brain as we do now, and psychiatrists and their patients could eventually be among the beneficiaries of this research. New research has, for example, raised hope that the causes of mental illness will be explained by brain abnormalities. It has also spurred investigations into genetics and specifically prompted a search for genes that may be associated with mental disorders. Meanwhile, a large body of research has examined the role of neurotransmitters in these disorders. Part of what has made this extraordinary brain science possible involves new imaging techniques that, by producing dramatic pictures of the brain, seem to unlock its secrets. A large body of research has examined how neurotransmitters are involved in mental disorders. Even more exciting is the prospect that research in neuroscience may lead to new and more effective methods of treatment.

The advances in neuroscience in recent years have, without doubt, been scientifically impressive. But how do they affect medical practice? Will the psychiatrist of tomorrow prescribe more powerful drugs guided

by gene profiles and brain scans? Will future psychiatrists become high-tech practitioners, differing little from specialists in internal medicine?

Research leaders in psychiatry have little doubt that the field is headed precisely in that direction. They believe that most mental disorders are due to abnormal biology. Many psychiatrists have accepted this idea, and for them the primacy of neuroscience has become almost a dogma.

Is Psychiatry Different from Neurology?

In a 2005 article, "Psychiatry as a Clinical Neuroscience Discipline," published in the *Journal of the American Medical Association,* Thomas Insel (director of the National Institute of Mental Health) and Rémi Quirion (director of the Canadian Institute of Psychiatry and Neurosciences) argued that mental illnesses are complex genetic disorders in which abnormalities in brain chemistry and circuitry lead to behavioral symptoms (Insel & Quirion, 2005; for a similar view, see Martin, 2002). Insel, a psychiatrist best known for research on how brain hormones influence mating behavior in rodents, and Quirion, a PhD neuroscientist who studies brain chemistry, are influential administrators directing the future of psychiatric research. They acknowledge that mental disorders emerge from interactions between genetic predispositions and environmental stressors but recommend that psychiatry redefine itself as a form of "applied neuroscience."

This is a point of view that has captured psychiatry and that has critical implications for practice. If psychiatry is applied neuroscience, then drugs to restore normal brain chemistry would be the primary tool for the treatment of mental illness. Significantly, the words "psychology" and "psychotherapy" are not to be found anywhere in this article.

Insel and Quirion also suggested that the division between psychiatry and neurology, which goes back to the 19th century, is artificial and unnecessary. They recommended that because both medical specialties treat diseases of the brain, they should be reunited into one discipline.

But why did psychiatry become separated from neurology in the first place? One reason is that mental disorders produce changes in thinking, emotion, and behavior; neurological disorders, although they can produce mental effects similar to those seen in diseases treated by psychiatrists, primarily concern physical symptoms (such as paralysis, abnormal movements, or loss of sensation).

Another reason for the separation was that neurological diseases (like strokes or multiple sclerosis) cause visible damage to the brain. Neurologists can explain symptoms on the basis of which structures of the brain are affected. In the past, no one was able to locate any form of brain damage in diseases of the mind (like schizophrenia).

Recent research has challenged this division. More subtle effects on brain anatomy and physiology can now be measured, and imaging studies show that specific regions can "light up" differently in specific mental disorders. In the past, when an organic cause was found for diseases formerly seen as "psychiatric" (such as tertiary syphilis), the diseases were transferred to neurology (Shorter, 1997). The argument can be made that the same process will happen with schizophrenia and mood disorders once their effects on the brain are properly mapped. In this context, one might readily imagine a future in which all brain diseases are treated by one specialty.

A few of the more severe disorders psychiatrists treat, including schizophrenia, melancholic depression, and bipolar disorder, may not actually be different from neurological conditions. These are disorders in which the evidence for brain abnormalities is strong, and in which the environment plays a relatively minor role. These are the diseases in which biological therapies are the most useful.

However, most of the disorders that psychiatrists see do not fit into this model. To reduce most cases of depression, anxiety, eating disorders, or personality disorder to brain damage would be rather simplistic. As later chapters in this book will show, understanding these conditions requires a model that takes life circumstances into account, even for the so-called biologically caused mental illnesses like schizophrenia.

A narrowly biological view to treatment runs counter to the approach that has characterized psychiatry for decades. A *biopsychosocial* model of mental illness, in which disorders are seen as arising from interactions between biological, psychological, and social factors, was proposed by the American psychiatrist George Engel (Engel, 1980). This model has been highly influential and emphasizes interfaces between psychiatry and other disciplines—not only neuroscience but psychology and other social sciences as well. Psychiatrists who use a broad theory are more likely to offer a broad range of treatments, including psychotherapy and social interventions.

Turning psychiatry into applied neuroscience would strip psychiatry of much of what makes it unique. It would also support a style of practice

in which the main thing that psychiatrists do is prescribe drugs. If psychiatry becomes "mindless" and consists of nothing more than the clinical application of neuroscience, patient care will suffer.

To adapt a famous quotation from the Vietnam War, Insel and Quirion seem to believe it is necessary to destroy psychiatry in order to save it. They propose a model in which the main skill of psychiatrists is knowing how to repair twisted molecules. But psychiatry is a humanistic medical discipline, not a branch of chemistry. Moreover, recombining psychiatry and neurology into one specialty would not make sense as long as psychiatrists continue to see patients with psychological problems. And finally, after a hundred years of separation, each specialty has its own traditions and its own culture. Neurology, for example, has always taken pride in its ability to explain disease by precise effects on sites in the brain (or in peripheral nerves). Its patients are treated with drugs or surgery. Most of its practitioners know little about depression, do not recognize it or find it interesting, and hardly ever treat it. If they do recognize symptoms of a mental health condition in their patients with, say, Parkinson's disease or multiple sclerosis, they are likely to consult a psychiatrist about the ideal treatment for those symptoms.

Causes and Risk Factors

What causes mental illness? By and large, advances in neuroscience notwithstanding, we still don't know. But as human beings, psychiatrists are not immune to the temptation to believe that in fact they have the answers to these unanswered questions. And as practitioners who are trained to heal and who daily face enormous human suffering, they are not the type of people who can afford to be paralyzed by doubt.

The problem is that there is no one answer to the question of what causes mental illness. Most illnesses do not have simple or single causes. With the exception of a few genetic diseases, pathology arises from the interaction of many factors (Paris, 1999). Some are hereditary, whereas others are environmental. Each factor, by itself, contributes to the overall risk. But no single risk is the cause of any one disease. What best predicts illness is the total weight of all risk factors. This model is called *stress-diathesis theory* (Monroe & Simons, 1991). The idea behind the model is that people do not fall ill from stress unless they are vulnerable (i.e., have a diathesis), and those who have a diathesis will not fall ill unless they are

stressed. Only when the weight of risk factors exceeds the threshold of the patient's vulnerability does overt illness emerge.

Failure to consider this complexity can lead to wrong conclusions. Thus, when research demonstrates a statistical relationship between a risk and a disease, we may be tempted to conclude that one is the cause of the other. Yet even when a strong relationship is found, causality is not proven. For example, data may show that risk and disease are correlated in a large number of cases, but the confluence may occur only in a minority. Thus, most people with the disease will not have the risk, and most people with the risk will not develop the disease.

This mistake has also afflicted past psychological theories of mental illness. For example, a number of mental disorders are associated with childhood trauma and family dysfunction (Paris, 1999). However, it does not follow that all our patients must have had an unhappy childhood. Many will have had a childhood no worse than anyone else's. Statistical relationships arise because some patients (and not all) are particularly sensitive to stressful events because of their temperamental vulnerabilities.

What research has demonstrated (but not everyone knows) is that most people who suffer childhood trauma and family dysfunction function normally as adults (Paris, 2000a). A large degree of resilience has been repeatedly shown in community surveys of people exposed to adverse events (Rutter & Rutter, 1993). In the face of trauma, even the worst kind, the vast majority of people never develop posttraumatic stress disorder (McFarlane, 1989; McNally, 1999). Most people are resilient to stress. If they were not, the human species would have gone extinct long ago.

Neuroscientists who account for mental disorders entirely through biological correlates are making a mistake similar to that of their psychotherapeutic predecessors. Again, one can see strong associations between a biological marker, such as a gene or a change in a brain structure, and a mental illness. But this need not mean that every case of the disease will be associated with the marker—research usually shows that most are not. Nor does it mean that everyone who has the marker will get the disease—most will not.

One can identify several reasons for the discrepancy. First, with a few exceptions, no single biological risk factor leads predictably to disease. Thus, even in mental disorders with strong genetic components,

such as schizophrenia or bipolar illness, no *single* gene is associated with illness (Braff, Freedman, Schork, & Gottesman, 2007a). Instead, one sees a pattern of *complex inheritance* in which many genes in combination (we are not sure exactly how many) produce vulnerability (van den Bree & Owen, 2003; Prathikanti & Weinberger, 2005). It requires a complex genetic mix to produce susceptibility to mental disorders.

Second, genes associated with illness may never be expressed unless the individual is placed in a specific environment. A new science of *epigenetics* (the study of heritable traits that do not involve changes to the underlying DNA sequence) examines how genes can be "turned on" or "turned off" by the environment (Petronis et al., 2000). Genetic variations can be positive, negative, or neutral, depending on environmental context. A large body of research shows that people are most likely to develop mental disorders when they are genetically vulnerable *and* exposed to a stressful life situation (Caspi et al., 2002, 2003).

Third, the diseases psychiatrists treat are not well defined. Scientists refer to this as "the phenotype problem," where one cannot identify genetic vulnerability (*genotype*) associated with disease without first establishing how they are expressed in thought, emotion, and behavior (*phenotype*) (Flint & Munafo, 2007). Moreover, visible phenotypes reflect underlying biological processes referred to as *endophenotypes*. As we will see, some of the categories of illness used in psychiatry are so broad and fuzzy that studying their biological markers with any specificity is an almost hopeless task. If we were to break larger categories down into more specific entities, they might have more specific correlates.

One of the great mysteries of psychiatry is the fact that many people with severe mental disorders are fairly normal up to the age when they fall ill. Quite a few mental disorders begin in adolescence after a normal childhood—some young people who develop schizophrenia have functioned reasonably well until a few years before the illness starts (van Nimwegen, de Haan, van Beveren, van den Brink, & Linszen, 2005). This observation points to the importance of brain development and the role of environmental stressors in precipitating illness. We are all born with vulnerabilities, yet most of us never become ill.

Genes and biological markers are linked to variations in temperament (Nigg, 2006; Rutter, Moffit, & Caspi, 2006). *Temperament* refers to individual differences in behavior that are present at birth. But temperamental differences do not produce mental illness. Simply put, we are all

different. Some of us are shy, others bold. Some are emotional, others stoic. These characteristics all have a biological component and can, under certain conditions, be associated with a risk for a mental disorder. However, all these temperamental patterns are compatible with normality.

In summary, there is no direct cause-and-effect relationship between either biological or psychological factors and mental disorders. The overall risk for disorder is cumulative (Rutter & Rutter, 1993). People become ill only when they suffer from temperamental vulnerability *and* are exposed to environmental stressors. This is why no theory exclusively based on biology (or psychology) can explain why people develop mental illness.

How Well Does Neuroscience Explain Mental Illness?

A careful look at the relevance of neuroscience for psychiatry uncovers a more humbling picture than is often drawn in current scientific literature. Research in neuroscience is still in its infancy. In spite of recent triumphs, we still know little about how the brain works. Future generations could think of contemporary neuroscience the way we see Columbus's voyages to America—he made a courageous exploration but lacked a good map.

The problem might be understood by comparing the brain to the heart or kidney. Instead of a muscular pump or filtration system, we are looking at a network of billions of neurons, capable of producing consciousness, free will, and highly complex behaviors. It took many decades to understand hearts and kidneys. For the brain, the time line will be much longer. It will be longer still before our knowledge of the brain translates into a deeper understanding of the mind and of all that can go wrong with it, as in mental illness.

Later in this chapter, we will consider what genes, imaging, and neurochemistry tell us about mental illness now. Broadly speaking, we live in an era where DNA has become an icon of science. Yet genes lack consistent associations with major mental illnesses. Positron emission tomography (PET) scans and magnetic resonance imaging (MRI) produce beautiful pictures. Everyone has seen them—they show areas of the brain "lighting up," as if we were visualizing the very chemistry of thought. (Actually, the brilliant colors of brain scans are added artificially.) Yet while imaging suggests that disorders affect specific parts of the

brain, they have explained little about the *causes* of most forms of mental illness. Finally, research on communication through neurotransmitters, and on chemical processes within neurons, is impressive. But these findings have also not shed great light on the causes of mental illness.

Psychiatrists are hoping that breakthroughs in neuroscience will lead to improved treatment for patients. Paradoxically, the great breakthroughs in psychopharmacology occurred decades ago, before any of the mechanisms by which drugs worked had even been discovered. If psychiatrists were to prescribe in much the same way they did a generation ago, their patients might not notice a great difference.

Fifty years ago, when I was an undergraduate student, little was known about the brain. No neurotransmitters had been definitively identified. The only form of imaging available was a skull X-ray. The brain was a kind of "black box," most of whose regions appeared to have no specific function.

While neuroscience has greatly advanced since then, progress should not blind us to our still vast ignorance about the human brain. As Isaac Newton once remarked about his own discoveries, "I feel like a child who while playing by the seashore has found a few bright colored shells and a few pebbles while the whole vast ocean of truth stretches out almost untouched and unruffled before my eager fingers."[1] The same can be said about our limited knowledge of the brain. An extremely complex structure, it has billions of cells that can be connected in billions of ways. Each of these cells is—to shift to a different metaphor now—a factory producing proteins under the guidance of half of all the genes in the human genome (Andreasen, 2001). A great deal can and does go awry in this system, and in ways that we largely do not yet understand.

Reductionism and Emergence

The question of whether neuroscience can be the primary basis of psychiatry should be seen in the context of two larger questions. The *mind-brain problem* concerns whether the mind and its thought are equivalent to (and determined by) activity in the brain (Schimmel, 2001a, 2001b). This is a philosophical issue, and most psychiatrists do not usually get involved in philosophy (even the philosophy of science). Nonetheless, what one believes about the question has a vast impact on clinical practice and on the direction of psychiatry.

The mind-brain problem might conceivably be resolved through empirical data. For now, many philosophers and neuroscientists have weighed in on the question. Whereas some claim that mental processes and human consciousness are ultimately an illusion and that the only reality is the physics, chemistry, and biology of neurons (Churchland, 1995), others insist that thought and consciousness exist in their own right and that the mind can determine (through its capacity for "free will") what happens in the brain (Searle, 2004).

A broader question concerns whether larger-scale phenomena in nature can be explained by small-scale phenomena. This approach, called *reductionism,* has been applied to the study of the mind, explaining complex phenomena like the human brain through simpler mechanisms, "reducing" mind to the actions of neurons, chemical transmitters, and specific proteins (Jones, 2000). This approach leads to the idea that illnesses with behavioral symptoms can be explained entirely through brain mechanisms. In other words, behind every twisted thought must be a twisted molecule.

Reductionism is a strategy with a long history of success. Over the centuries, science has triumphed by reducing the large to the small, and the complex to the simple. Different levels of science can be linked in this way. Physics studies matter by breaking it down into atoms, and nuclear physics has broken down the atom—first into particles, then into quarks. Chemistry was linked to physics through Mendeleev's periodic table, which showed that all molecules are combinations of only 92 natural elements. Biology has been linked to chemistry through the discovery that living organisms make use of molecules to perform many functions. And psychology has been linked to biology by research showing that changes in the brain can influence behavior.

Although many scientific advances have resulted from reductionism, the approach has definite limits (Jones, 2000). Some observations are illuminated by mechanisms at a simpler level, but not everything is explained. The whole is usually more than the sum of its parts, and larger-scale phenomena usually need to be studied in their own right. For example, the reality of a table cannot be accounted for by atoms and quarks. The properties of hydrogen and oxygen do not explain the molecular characteristics of water. Biological organisms are not robots driven by chemistry and physiology. And even though molecules are necessary for consciousness, they do not explain it.

Psychiatry, which treats and studies the mind, faces a more complex reality than do other specialties. Medicine may have gone mad over molecules, but livers, brains, and kidneys have no will of their own.

One does not have to be a dualist (or believe in a soul) to consider the mind a subject of independent study (Jones, 2000). Mental processes cannot exist without a functioning brain. But it is a logical error to conclude that all pathways of causation must go "upward," from neurons to mental processes. Causation can also go "downward," from cellular structures to genes and proteins (Noble, 2006), as well as from thought to behavior (i.e., the existence of "free will").

Needless to say, not everyone agrees with this point of view. It has been argued repeatedly that consciousness and free will are illusions (Dennett, 1991). But even if they were, we would still need to study the mind on its own terms. To prove that reductionism works, one would have to show that complex forms of behavior can be predicted from biology alone. Neuroscience is nowhere near such a goal. It is replete with associations, and short on predictions.

Mental processes are influenced by multiple factors, only some of which can be understood at the level of molecules. The mind, with its crucial (although still unexplained) property of consciousness, operates at a different level. This idea is not "holistic" mush but follows directly from the nature of complex phenomena. Although mind cannot exist without brain, it represents another level of analysis—one with features that cannot be fully explained at the level of neurons.

Models of complexity, such as "general systems theory," suggest that systems have *emergent* properties that cannot be explained by their components (von Bertalanffy, 1968). Emergence is defined as a process in which complex *patterns* arise from simpler components and in which higher-level patterns are unpredictable from phenomena at a lower level (Beckermann, Flohr, & Kim, 1992).

A good example in modern science is the relationship between the structure of DNA and the development of organisms. DNA does not determine how the body develops. It is a recipe, not a blueprint. Just as making a cake from a recipe will not always produce the same result because of varying circumstances, the environment (which turns genes on and off) makes everyone different. (This is why even identical twins do not have the same traits.) The new science of epigenetics, focusing on the

interactions between genes and environment, may help us understand these complexities (Meaney & Szyf, 2005).

Consider the following example. The conscious mind arises from the interactions of billions of neurons in the human brain. Yet no single neuron is capable of thought. That is what is meant by emergence.

When we study complex phenomena such as human behavior, we have to reverse the process of reductionism and practice integration, that is, study complex phenomena on their own terms while not ignoring links to other levels of analyses. Reductionism is a powerful tool that should not be discarded and will continue to play a role in psychiatric research. (In fact, Chapter 3 suggests that psychiatric diagnoses will never be valid without using biological markers that have proved so valuable in other areas of medicine.) Knowledge of brain mechanisms could also allow pharmacologists to develop new and more effective drugs.

Even so, psychiatrists should not set their sights on a utopian future in which neuroscience will solve most clinical problems. The science behind psychiatry needs a broader and more comprehensive framework. Clinical symptoms such as pain are features of consciousness. In the same way, depression is an emergent property of the mind.

I recently attended a conference in which basic neuroscientists described how their skills might be applied to mental disorders. One researcher working on neural growth suggested that he might be able to solve the problem of schizophrenia if someone could define an abnormal protein that would be a phenotype for the illness. But that is just what psychiatry cannot do!

Nonetheless, the best research has the capacity to establish a link between the complex and the simple. Cognitive neuroscience differs from classical neuroscience in that it concerns thought and not just neurotransmitter activity (Pinker, 1997). This new and productive field examines relationships between various types of thinking processes and activity in specific brain structures. It takes the mind seriously, and although cognitive scientists are deeply interested in the brain mechanisms behind thought, they study mental processes on their own terms.

In summary, reductionism is a philosophical principle but is not "just philosophy." This is a point of view that underlies the current impoverishment of the practice of psychiatry. If you believe that depression consists of nothing but disordered neurotransmitters and that life

circumstances affecting mood are not particularly relevant, you do not really need to learn how to talk to people. You just need to reach for your prescription pad and correct the chemistry.

Genetics

That psychiatrists have learned a great deal about the brain from research in neuroscience is clear. (For a brief review of the principles of psychiatric genetics, see Prathikanti & Weinberger, 2005.) And the future of medicine as a whole will be influenced by what we know about genes. However, it is important to take a closer look at genetics to determine what it does and does not tell us now about disease.

The discovery of DNA was followed by the deciphering of the genetic code, showing how this molecule guides the construction of proteins—the building blocks of all organisms. More recently, the sequencing of the human genome revealed a surprise—we manage with only 20,000-plus genes—not much more than many less intelligent creatures. Thus the complexity of the human body is not built on the total number of genes but how they are used. About half are involved in building the brain. Given that the absolute number of neurons in the human brain is about one trillion and that neurons are widely interconnected, their potential combinations could number more than all the stars in the universe.

Physicians, scientists, and the educated public are awaiting the therapeutic breakthroughs expected to follow inevitably from genetic discoveries. At a minimum, patients in the future could have their genomes scanned to find out which disease they are most susceptible to. At a maximum, gene therapy could be used to reverse the course of diseases.

Yet the hard facts are that we are nowhere near any of these goals. To understand why, consider how genes actually work. First, genes make proteins, not diseases. Even if we were able to identify all human genes, we would still need to know what proteins they make. The emerging science of "proteomics" aims to do just that—to reduce all biological processes to protein synthesis. (For a review of proteomics, see Twyman, 2004.) But it will take decades to accomplish this.

Second, when genes do affect susceptibility to disease, complex inheritance is the rule, not the exception. For this reason, there is no such thing as a gene "for" most of the diseases in medicine, and it is rare for

single genes to be associated with specific diagnoses (Kendler, 2006). A Mendelian scenario (named after Gregor Mendel, the founder of scientific genetics) occurs only in a few rare conditions. Most of the illnesses that physicians treat do not develop in this way. In the most common human diseases (such as arteriosclerosis and cancer), associations with single genes that have been identified account for more than a small percentage of the total variance. Disease susceptibility could be associated with variations in as many as 20 or 30 genes in various combinations.

Third, genes are "turned off" most of the time (Meaney & Szyf, 2005). To become active, they must interact with the environment. (A genetic susceptibility to lung cancer, for example, may never show itself clinically unless the patient also smokes.)

Fourth, even when genes associated with disease can be identified, applying this knowledge in a practical way is not easy. A decade after a gene strongly associated with cystic fibrosis was discovered, for example, patients suffering from this terrible disease have not yet benefited (Rosenhecker, Huth, & Rudolph, 2006).

In short, although genetic knowledge will *eventually* benefit psychiatry, we are decades away from practical application. Moreover, since mental disorders are based on complex genetic dispositions subject to environmental influences, the study of single genes will probably not help psychiatrists treat patients. This is not to say that genetics is not of importance to psychiatry—it could turn out to have supreme importance. But genes are only one piece of a much more complex puzzle.

Imaging

Specialists in other areas of medicine have long been able to "see" the organs in which disease occurs, by feeling them through the skin, observing them during surgical operations, or using advanced radiological techniques. One of the great frustrations for psychiatrists has been that they cannot observe the brains of people with mental disorders but instead must rely on observable or self-reported signs and symptoms in order to assess what their patients are experiencing. With the arrival of new imaging technology, however, psychiatrists now have several methods for "seeing" inside the brain and observing its activity (Morihisa, 2001).

In the 1970s, computerized tomography (CT) scans began to replace X-rays as a way to visualize the brain. These impressive machines yielded unparalleled pictures that looked like slices of the brain, with a readily visible and detailed structure. Although these images told us little about function, CT scans were striking enough to be used in court cases in which the presence of mental illness was an issue (as happened in the case of John Hinckley, discussed in Chapter 12).

Magnetic resonance imaging (MRI) provided even better pictures of brain slices, and the development of functional imaging was even more of a breakthrough. Functional MRI (fMRI) allows researchers to examine patients' brains while the patients are performing tasks or experiencing emotions. This technique is easier to administer and gives a more precise image. In positive emission tomography (PET), the patient is injected with a radioactive isotope that resembles chemicals used in specific areas of the brain and not in others. The beauty of the pictures produced by these scans is that one can see brain areas "lighting up" in association with a specific function. As a result, we now have much more information about which brain regions do what.

These methods have greatly illuminated research in neuroscience. Seeing what parts of the brain become active in relation to thought, emotion, and behavior is of enormous significance. However, localized brain activity is just as likely to be a result of mental activity as it is to be a cause of it. Thus far, imaging has had few clinical applications to diseases like schizophrenia or mood disorders (Nemeroff, Kilts, & Berns, 1999). That situation could change in the future, but at this point practical use of imaging to guide treatment remains only a hope.

Neurotransmitters

Fifty years ago we knew little about how neurons communicate with each other. It was thought that electric sparks jumped the gap between the end of one neuron and the beginning of another. Today, we know that neurotransmission, while partly electrical, mainly depends on a large number of chemical messengers, many of which are simple molecules (others are proteins). Neurons have different receptors for these chemicals, so the same transmitters produce different effects at different sites. All these events take place at the junction between one neuron and another—the synapse.

Molecules derived from the amino acids in our diet do much of the work. One is glutamate, the most widely distributed of all neurotransmitters, which excites neurons beyond the synapse. Another is gamma-amino butyric acid (GABA), an amino acid that functions as the main inhibitory transmitter in the brain.

The most studied group of neurotransmitters for psychiatry is the *monoamines,* a group of molecules derived from amino acids that are produced in older, deeper structures of the brain. These chemicals mainly act to modulate the effect of other transmitters higher up in the brain (Nestler, Hyman, & Malenka, 2001).

One monoamine is dopamine, a substance thought to be particularly important for addictions because it is concentrated in brain systems involved in pleasure or emotional reward (Schultz, 2006). Because some antipsychotic drugs block the action of dopamine, a long-standing theory in psychiatry has proposed that schizophrenia results from abnormalities in receptors for this transmitter. This theory was, in the end, not supported by sufficient evidence, and current research on schizophrenia focuses more on glutamate (Coyle, 2006).

Norepinephrine, a neurotransmitter associated with stress responses, activates many brain systems and the sympathetic nervous system. Several antidepressant drugs increase the activity of this transmitter through their effects on receptors at synapses. However, this theory of antidepressant action, once dominant in psychiatry, turned out to be too simple (Iversen, 2006).

Serotonin has been the most important of all neurotransmitters in psychiatric research. This substance has very broad effects on the brain and is particularly important for its relationship to depression, anxiety, and impulsivity (Carver & Miller, 2006). The theory that serotonin is deficient in many mental disorders has long been current, although research has failed to find any consistent deficiency of this kind (Valenstein, 1998). However, antidepressants cause neurons to keep serotonin around longer at the synapse, which has been hypothesized to be one of the mechanisms of their effect.

Unlike genes and neuroimaging, research on neurotransmitters has had practical applications in the treatment of mental disorders. For example, SSRIs were developed as "designer drugs" for increasing serotonin activity at the synapse (Kramer, 1993). Yet for many of the drugs that

psychiatrists prescribe, the reasons for their effectiveness remain unknown. After fifty years, psychiatrists still do not understand why antipsychotic drugs help patients with schizophrenia, how lithium and other mood stabilizers help control bipolar disorder, or what precise effects antidepressants have on neurotransmitters.

One reason for this uncertainty is that drugs affect several chemical systems, not just one (see Schatzberg & Nemeroff, 2004). Another major unsolved mystery concerns why antidepressants take several weeks to be fully effective in many patients. One possibility is that they encourage neurons to grow new connections, which takes time.

In summary, although research on neurotransmitters has had a strong relationship to drug development, we are left with more questions than answers. These chemicals have different effects in different parts of the brain, which is not just a "soup" of chemicals but a complex organ with a structure and a physiology.

Neural Networks

The brain operates through connections among billions of neurons. But for a long time the function of large areas of the brain remained a mystery. We have long known the location of sensory and motor areas in the brain, but much of the cerebral cortex (the part that thinks) was unmapped.

Imaging studies have helped unlock this mystery (Mandzia & Black, 2001). For example, we now know that the prefrontal and orbital cortexes, regions of the brain that lie at the front of the head and behind the eyes, have a special role in decision making and controlling impulsivity. We can also distinguish among parts of the cortex that affect specific aspects of thought. For example, the anterior cingulate gyrus, a structure lying deeper in the brain, has roles in decision making, attention, and memory. Deep inside the temporal lobe of the brain are the hippocampus, the main center for short-term memory, and the amygdala, a region governing responses associated with fear and unexpected events.

These discoveries have led to research—much of it using PET and fMRI—in which brain structures are examined to see whether they function differently in mental disorders. In many cases, they do. Yet again, such observations do not tell us why. Are we looking at causes or effects? This growing area of neuroscience is still in its infancy.

Conclusion

For all that it has accomplished, neuroscience has not yet delivered a convincing understanding of the causes of mental disorders. One can hardly compare our knowledge of the brain to what we know about the heart or the kidney and their diseases. But to dismiss the dramatic advances in neuroscience would be foolish. Every year our knowledge of the brain grows by leaps and bounds. And what has been discovered so far is only the beginning.

One might say that neuroscience is still awaiting its Newton—that is, someone who can produce a theory that will make sense out of complexity. It might take fifty to a hundred years for that to happen. In the meantime, one can practice psychiatry and help most of one's patients without knowing precisely how the brain works.

But there is a more immediate issue. In principle, nothing in neuroscience prevents clinicians from being empathic and interested in the lives of their patients and from trying to understand their difficulties in the context of their total experience. This is the essence of the biopsychosocial perspective, and the best psychiatrists, whatever their orientation, do try to bring this perspective into their work. However, we need only to look around us to see the clinical results of the current obsession with the neurobiology of mental illness—and the many psychiatrists giving out prescriptions without taking the time to understand the specific problems that affect patients. Even if a working knowledge of neuroscience is an essential part of psychiatric practice, it does not fully explain the mind—or provide the whole answer to treating mental illness.