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The Epidemic of Mental Illness: Why?

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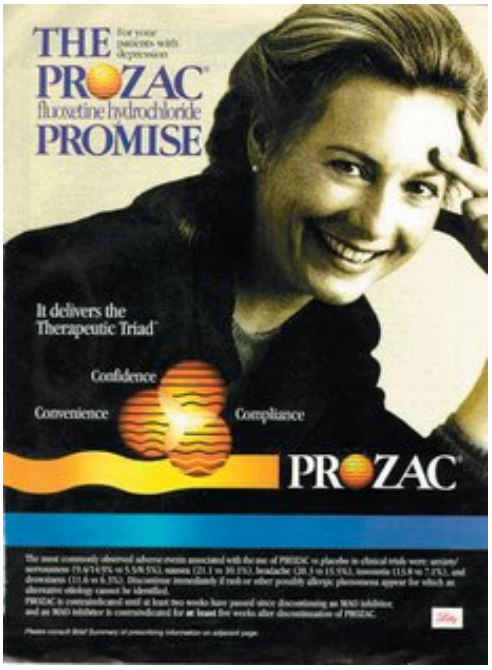
The Emperor's New Drugs: Exploding the Antidepressant Myth
by Irving Kirsch
Basic Books, 226 pp., $15.99 (paper)

Anatomy of an Epidemic: Magic Bullets, Psychiatric Drugs, and the Astonishing Rise of Mental Illness in America
by Robert Whitaker
Crown, 404 pp., $26.00

Unhinged: The Trouble With Psychiatry—A Doctor's Revelations About a Profession in Crisis
by Daniel Carlat
Free Press, 256 pp., $25.00

It seems that Americans are in the midst of a raging epidemic of mental illness, at least as judged by the increase in the numbers treated for it. The tally of those who are so disabled by mental disorders that they qualify for Supplemental Security Income (SSI) or Social Security Disability Insurance (SSDI) increased nearly two and a half times between 1987 and 2007—from one in 184 Americans to one in seventy-six. For children, the rise is even more startling—a thirty-five-fold increase in the same two decades. Mental illness is now the leading cause of disability in children, well ahead of physical disabilities like cerebral palsy or Down syndrome, for which the federal programs were created.



An advertisement for Prozac, from The American Journal of Psychiatry*, 1995*

A large survey of randomly selected adults, sponsored by the National Institute of Mental Health (NIMH) and conducted between 2001 and 2003, found that an

astonishing 46 percent met criteria established by the American Psychiatric Association (APA) for having had at least one mental illness within four broad categories at some time in their lives. The categories were "anxiety disorders," including, among other subcategories, phobias and post-traumatic stress disorder (PTSD); "mood disorders," including major depression and bipolar disorders; "impulse-control disorders," including various behavioral problems and attention-deficit/hyperactivity disorder (ADHD); and "substance use disorders," including alcohol and drug abuse. Most met criteria for more than one diagnosis. Of a subgroup affected within the previous year, a third were under treatment—up from a fifth in a similar survey ten years earlier.

Nowadays treatment by medical doctors nearly always means psychoactive drugs, that is, drugs that affect the mental state. In fact, most psychiatrists treat only with drugs, and refer patients to psychologists or social workers if they believe psychotherapy is also warranted. The shift from "talk therapy" to drugs as the dominant mode of treatment coincides with the emergence over the past four decades of the theory that mental illness is caused primarily by chemical imbalances in the brain that can be corrected by specific drugs. That theory became broadly accepted, by the media and the public as well as by the medical profession, after Prozac came to market in 1987 and was intensively promoted as a corrective for a deficiency of serotonin in the brain. The number of people treated for depression tripled in the following ten years, and about 10 percent of Americans over age six now take antidepressants. The increased use of drugs to treat psychosis is even more dramatic. The new generation of antipsychotics, such as Risperdal, Zyprexa, and Seroquel, has replaced cholesterol-lowering agents as the top-selling class of drugs in the US.

What is going on here? Is the prevalence of mental illness really that high and still climbing? Particularly if these disorders are biologically determined and not a result of environmental influences, is it plausible to suppose that such an increase is real? Or are we learning to recognize and diagnose mental disorders that were always there? On the other hand, are we simply expanding the criteria for mental illness so that nearly everyone has one? And what about the drugs that are now the mainstay of treatment? Do they work? If they do, shouldn't we expect the prevalence of mental illness to be declining, not rising?

These are the questions, among others, that concern the authors of the three provocative books under review here. They come at the questions from different backgrounds—Irving Kirsch is a psychologist at the University of Hull in the UK, Robert Whitaker a journalist and previously the author of a history of the treatment of mental illness called *Mad in America* (2001), and Daniel Carlat a psychiatrist who practices in a Boston suburb and publishes a newsletter and blog about his profession.

The authors emphasize different aspects of the epidemic of mental illness. Kirsch is concerned with whether antidepressants work. Whitaker, who has written an angrier book, takes on the entire spectrum of mental illness and asks whether psychoactive drugs create worse problems than they solve. Carlat, who writes more in sorrow than in anger, looks mainly at how his profession has allied itself with, and is manipulated by, the pharmaceutical industry. But despite their differences, all three are in remarkable agreement on some important matters, and they have documented their views well.

First, they agree on the disturbing extent to which the companies that sell psychoactive drugs—through various forms of marketing, both legal and illegal, and what many people would describe as bribery—have come to determine what constitutes a mental illness and how the disorders should be diagnosed and treated. This is a subject to which I'll return.

Second, none of the three authors subscribes to the popular theory that mental illness is caused by a chemical imbalance in the brain. As Whitaker tells the story, that theory had its genesis shortly after psychoactive drugs were introduced in the 1950s. The first was Thorazine (chlorpromazine), which was launched in 1954 as a "major tranquilizer" and quickly found widespread use in mental hospitals to calm psychotic patients, mainly those with schizophrenia. Thorazine was followed the next year by Miltown (meprobamate), sold as a "minor tranquilizer" to treat anxiety in outpatients. And in 1957, Marsilid (iproniazid) came on the market as a "psychic energizer" to treat depression.

In the space of three short years, then, drugs had become available to treat what at that time were regarded as the three major categories of mental illness—psychosis, anxiety, and depression—and the face of psychiatry was totally transformed. These drugs, however, had not initially been developed to treat mental illness. They had been derived from drugs meant to treat infections, and were found only serendipitously to alter the mental state. At first, no one had any idea how they worked. They simply blunted disturbing mental symptoms. But over the next decade, researchers found that these drugs, and the newer psychoactive drugs that quickly followed, affected the levels of certain chemicals in the brain.

Some brief—and necessarily quite simplified—background: the brain contains billions of nerve cells, called neurons, arrayed in immensely complicated networks and communicating with one another constantly. The typical neuron has multiple filamentous extensions, one called an axon and the others called dendrites, through which it sends and receives signals from other neurons. For one neuron to communicate with another, however, the signal must be transmitted across the tiny space separating them, called a synapse. To accomplish that, the axon of the sending neuron releases a chemical, called a

neurotransmitter, into the synapse. The neurotransmitter crosses the synapse and attaches to receptors on the second neuron, often a dendrite, thereby activating or inhibiting the receiving cell. Axons have multiple terminals, so each neuron has multiple synapses. Afterward, the neurotransmitter is either reabsorbed by the first neuron or metabolized by enzymes so that the status quo ante is restored. There are exceptions and variations to this story, but that is the usual way neurons communicate with one another.

When it was found that psychoactive drugs affect neurotransmitter levels in the brain, as evidenced mainly by the levels of their breakdown products in the spinal fluid, the theory arose that the cause of mental illness is an abnormality in the brain's concentration of these chemicals that is specifically countered by the appropriate drug. For example, because Thorazine was found to lower dopamine levels in the brain, it was postulated that psychoses like schizophrenia are caused by too much dopamine. Or later, because certain antidepressants increase levels of the neurotransmitter serotonin in the brain, it was postulated that depression is caused by too little serotonin. (These antidepressants, like Prozac or Celexa, are called selective serotonin reuptake inhibitors (SSRIs) because they prevent the reabsorption of serotonin by the neurons that release it, so that more remains in the synapses to activate other neurons.) Thus, instead of developing a drug to treat an abnormality, an abnormality was postulated to fit a drug.

That was a great leap in logic, as all three authors point out. It was entirely possible that drugs that affected neurotransmitter levels could relieve symptoms even if neurotransmitters had nothing to do with the illness in the first place (and even possible that they relieved symptoms through some other mode of action entirely). As Carlat puts it, "By this same logic one could argue that the cause of all pain conditions is a deficiency of opiates, since narcotic pain medications activate opiate receptors in the brain." Or similarly, one could argue that fevers are caused by too little aspirin.

But the main problem with the theory is that after decades of trying to prove it, researchers have still come up empty-handed. All three authors document the failure of scientists to find good evidence in its favor. Neurotransmitter function seems to be normal in people with mental illness before treatment. In Whitaker's words:

> Prior to treatment, patients diagnosed with schizophrenia, depression, and other psychiatric disorders do not suffer from any known "chemical imbalance." However, once a person is put on a psychiatric medication, which, in one manner or another, throws a wrench into the usual mechanics of a neuronal pathway, his or her brain begins to function…*abnormally*.

Carlat refers to the chemical imbalance theory as a "myth" (which he calls "convenient"

because it destigmatizes mental illness), and Kirsch, whose book focuses on depression, sums up this way: “It now seems beyond question that the traditional account of depression as a chemical imbalance in the brain is simply wrong.” Why the theory persists despite the lack of evidence is a subject I’ll come to.

Do the drugs work? After all, regardless of the theory, that is the practical question. In his spare, remarkably engrossing book, *The Emperor’s New Drugs*, Kirsch describes his fifteen-year scientific quest to answer that question about antidepressants. When he began his work in 1995, his main interest was in the effects of placebos. To study them, he and a colleague reviewed thirty-eight published clinical trials that compared various treatments for depression with placebos, or compared psychotherapy with no treatment. Most such trials last for six to eight weeks, and during that time, patients tend to improve somewhat even without any treatment. But Kirsch found that placebos were three times as effective as no treatment. That didn’t particularly surprise him. What did surprise him was the fact that antidepressants were only marginally better than placebos. As judged by scales used to measure depression, placebos were 75 percent as effective as antidepressants. Kirsch then decided to repeat his study by examining a more complete and standardized data set.

The data he used were obtained from the US Food and Drug Administration (FDA) instead of the published literature. When drug companies seek approval from the FDA to market a new drug, they must submit to the agency all clinical trials they have sponsored. The trials are usually double-blind and placebo-controlled, that is, the participating patients are randomly assigned to either drug or placebo, and neither they nor their doctors know which they have been assigned. The patients are told only that they will receive an active drug or a placebo, and they are also told of any side effects they might experience. If two trials show that the drug is more effective than a placebo, the drug is generally approved. But companies may sponsor as many trials as they like, most of which could be negative—that is, fail to show effectiveness. All they need is two positive ones. (The results of trials of the same drug can differ for many reasons, including the way the trial is designed and conducted, its size, and the types of patients studied.)