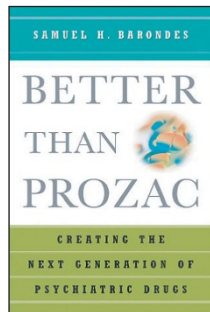


McKibben is right to worry about biotechnology. But as Tenner reveals, it is not at all obvious that a reliance on technology will be toxic to the meaning, purpose and dignity of human life. Nor has it always been the case that more technology has meant less contact with the 'natural' world. What is thought of as natural is always a

product of human interaction with an environment that includes various technologies. They are continuously shaping us as we struggle to make them conform to our will. That ongoing tension may well be a key component in what creates meaning for human beings.

The Prozac pipeline



Better Than Prozac: Creating the Next Generation of Psychiatric Drugs

by Samuel H. Barondes

Oxford University Press, 2003
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Reviewed by Herbert Y Meltzer

Those who have read about the side effects and limitations of psychotropic drugs in the *Wall Street Journal* and *New York Times* in the last year are likely to respond to this excellent popular account with a sigh of relief. The message of this new book on psychopharmacology is that drugs better than Prozac and other psychotropic drugs—the mainstay of psychiatric treatment in the last 50 years—are on the horizon.

The recent stories that would engender relief are many. For example, Prozac itself just missed being banned in Britain for fear it might cause suicide, while four other antidepressants that share the same mechanism of action (selective blockade of serotonin reuptake) were not so fortunate. Merck recently announced that the first drug in the class of NK1 receptor antagonists—described by Barondes as the leading candidate to be better than Prozac for treating depression—was indeed safer than Prozac but, alas, no more effective than placebo. That finding took five years of clinical testing and tens of millions of dollars to establish.

The so-called atypical antipsychotic drugs, such as Zyprexa and Risperdal, the main treatments for schizophrenia and the psychotic component of bipolar disorder, are now required by the US Food and Drug Administration (FDA) to include a warning that they increase the risks for diabetes mellitus and cardiovascular disease. Researchers from Yale recently reported that Zyprexa was no better than the conventional antipsychotic drug haloperidol, but was 30–50 times more expensive. Valproate, the highest-selling mood stabilizer in the United States, has received several challenges to its efficacy claims, most recently in an article in the *Journal of the American Medical Association* claiming that valproate was inferior to lithium, an inexpensive agent, in preventing suicide in bipolar disorder patients. On a more positive note, the FDA approved Clorazil (clozapine), another atypical antipsychotic drug, for reducing the risk of suicide, but there is no evidence that this evidence-based claim has had any influence on clinical practice. Are things really so bad in psychopharmacology?

Not according to Samuel Barondes. This eminent neurobiologist presents a decidedly positive picture from the patient's side of the prescription pad, a view that I am in accord with. Yet he is completely mindful of

the limitations and frequent side effects of the drugs available to treat the 10–15% of the population afflicted with psychiatric illnesses and dementias. Most of the bad news reported above represents, in fact, a series of bureaucratic and academic errors, and stems from a failure to take all available information into account and to understand specific features of the illnesses in question.

The drugs Barondes succinctly describes—detailing their development, mechanism of action and clinical effects—have indeed enabled the majority of patients to suffer less and to achieve substantial improvement to their quality of life, even as they leave patients considerably less than their best selves. In this, psychopharmacology at its best is not much different than, say, pharmacologic treatment for cardiovascular disease, and is far more effective than the drug treatments for neurologic diseases such as stroke and multiple sclerosis.

In *Better than Prozac*, Barondes has managed to lucidly present the essential information about antidepressants, drugs for psychosis and bipolar disorder, anxiety disorders, attention deficit disorder, Alzheimer disease and a few other less-common behavioral disturbances. He also provides many insights not usually found in the lay literature on psychopharmacology. These include sensitively written clinical vignettes, as well as salient information about the etiology and pathophysiology of the diseases psychotropic drugs are intended to treat. He offers frequent reminders that these drugs, to achieve optimal results, require caring and knowledgeable clinicians to tend to patients' psychological and medical needs. Finally, he describes the main strategies now used to identify targets for the next generation of drugs.

Barondes provides this information better than any other account I have read. Moreover, he does it in such a creative way that researchers and clinical practitioners will learn from and enjoy the material he has so skillfully assembled.

Barondes has an abiding faith that the enormous research effort to understand the nervous system, integrating genetic and environmental influences, will eventually produce truly novel agents that will be safer and more effective than current agents. This is a pretty safe bet, in the long run, but it is humbling to see how little has come thus far from at least one subset of basic research: the effort to identify genes whose expression is altered in disease populations or affected by current treatments. Although a number of genes have been identified by these methods, none has been translated into a drug that has started on the long road to approval for general use. This means that better agents from this approach could be a decade or more away. In a few areas, most notably that of antipsychotic drugs, variations on well-established themes, by classical pharmacologic means, may provide significantly better first-line drugs within a much shorter time. In addition, ideas for agents to improve components of schizophrenia not well treated by current drugs, such as cognition and deficits in reward and motivation, are emerging from basic research and are being tested in the clinic.

It will be difficult for any new psychotropic drug to have the societal impact of Prozac, which has strongly influenced public attitude toward psychiatric illness and the practice of mental health care. But it will happen, and none too soon. Readers of this excellent book will be in a better position to anticipate and appreciate those coveted breakthroughs when they are finally here.

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