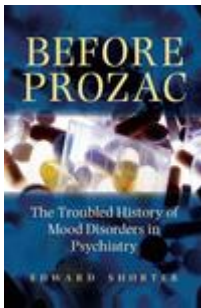


## Psychopharmacology and Depression

A review of



**Before Prozac: The Troubled History of Mood Disorders in Psychiatry**

by Edward Shorter

New York: Oxford University Press, 2009. 304 pp. ISBN

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Reviewed by

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Medical historian Edward Shorter notes that drugs are labeled for marketing and government regulation, not medical usefulness, and in *Before Prozac: The Troubled History of Mood Disorders in Psychiatry* he argues that this is why no progress has been made in psychiatric treatment since the 1950s. Shorter believes old drugs—amphetamines and barbiturates, tranquilizers such as Librium and Valium, antidepressants such as Marsilid, and antipsychotics such as Thorazine—were far more effective than anything available today.

So why did all those great drugs disappear? According to Shorter, some went off patent, thus becoming unprofitable and were no longer marketed, but many were regulated out of existence by the Food and Drug Administration (FDA), leaving, in his view, only drugs such as Prozac and other virtually useless antidepressants.

That is a radical thesis, to say the least. Does Shorter convince the reader? He convincingly describes the methods by which physicians are persuaded to use more

profitable but less effective drugs. He also gives a compelling history of numerous psychiatric drugs being removed from the market by the FDA when they were deemed dangerous. But is it true that, as a consequence, the psychiatric pharmacopeia today is useless? This is not supported by the facts.

Nevertheless, Shorter puts forth that non sequitur by narrowing the discussion from a general history of psychopharmacology to his idiosyncratic definition of depression as an organic condition best treated by electroconvulsive shock therapy (ECT), not drugs. He implies that all other mood disorders are suspect, defined only by the drugs designed to treat them. Thus, when drugs disappear, the disorders they treat also disappear (e.g., “nerves,” “melancholy”). When new drugs are produced (such as Prozac), new disorders are invented to fit the new medications (e.g., “major depression”). Shorter does not make this claim directly but suggests and implies it without clear logic.

## **How Drugs Rise and Fall**

Shorter claims that the marketing of psychiatric drugs has always been about profits, irrespective of whether the new drugs work better than those they replace. Psychiatrists are as susceptible as anyone to marketing, so new, less effective but more profitable drugs force out older drugs that may have been superior to the ones that replace them. Good drugs are also driven out by government regulation.

For example, the barbiturate phenobarbital was an anticonvulsant that was also used as a sleep aid and for the treatment of “nerves,” tension, and sometimes depression and mania. Barbiturate sedatives were overprescribed after 1945, despite their known tendency to enhance suicide risk, but Shorter says that the absolute number of suicides was low and was outweighed by the medical benefits that the drugs offered.

Shorter claims that the risk of addiction was also known, but it was lower than the risk of addiction to alcohol. In 1972 the U.S. Department of Justice classified barbiturates as Schedule II controlled substances, alongside narcotics, which removed them from the market. According to Shorter, this unnecessary action resulted in a serious loss to psychiatry and medicine; it was a politically motivated response to public hysteria about addiction and suicide and was not based on medical facts.

Shorter tells a similar story for amphetamines (Benzedrine, Dexedrine), meprobamate (Miltown), benzodiazepines (Xanax, Librium, Valium), monoamine oxidase inhibitors (MAOIs; Marsilid), chlorpromazine (Thorazine), and many other drugs. Repeatedly, a drug was found useful for several conditions, was discovered to have side effects, then was banned by regulators with little concern for scientific facts, clinical practice, or societal benefit. Although these drugs had side effects, this problem would have been better

addressed with risk–benefit analysis rather than with knee-jerk condemnation. It doesn't make sense to ban drugs, especially whole classes of drugs, on the basis of emotions.

This is a reasonable conclusion. Sunstein (2005), among others, has argued strongly for cost–benefit analysis over fear-based precautionary reactions in government policy, and Shorter's history illustrates that argument. Yet democratic governments must respond to people's fears, irrational or not; this is a fact that Shorter does not consider.

## **Imperial FDA**

Shorter is less convincing when he recounts the battle between the FDA and the pharmaceutical industry, describing the 1962 Congressional requirement that drug manufacturers prove that their products are both safe *and* effective, after which the FDA aggressively pursued the efficacy requirement. One can guess that the intent was to prevent drug companies from marketing miracle cure-alls, like the patent medicines of the 19th century. But Shorter uses opinion, innuendo, and ad hominem comments to argue that the motivation was bureaucratic self-aggrandizement—for example, FDA officials drunk with power set on humbling the pharmaceutical industry.

His accusations and claims are footnoted, but, upon reading the footnotes, one finds that the vast majority are unsubstantiated opinions. There are hardly any citations of published news stories, judicial rulings, legislative documents, or peer-reviewed scholarly sources.

## ***DSM Wars***

Shorter does a similar hatchet job on the academicians responsible for the third edition of the *Diagnostic and Statistical Manual of Mental Disorders*, released in 1980 (*DSM–III*; American Psychiatric Association, 1980). Psychiatrist Robert Spitzer headed a core group of physicians and scientists from Washington University and the New York Psychiatric Institute. Shorter says Spitzer “saw the clinicians at Wash U almost as special chums, soul mates to help him against the bad guys” (p. 156). Psychoanalysts were the bad guys. Shorter claims that Spitzer et al. were determined to eradicate the fanciful distinction between neurosis and psychosis and to eliminate unproven etiologies. But the psychoanalysts fought back. As a result, the *DSM–III* ended up being “a political artifact born of academic infighting” (p. 10).

Why does it matter? Because, Shorter says, if a diagnostic schema is based on politics rather than “nature,” then treatment is arbitrary. That would be true if the *DSM–III*

classifications, especially for mood disorders, were invalid, but Shorter does not provide substantial proof for such a claim.

The FDA's definitions are also arbitrary, he believes:

So keen was the FDA to limit the label of drugs to indications sanctioned by [government] panels, that the bureaucrats increasingly saw "depression" as the one indication that seemed solid amidst the tossing overboard of "nervousness," "hysteria," and the like. . . . Control of the label, in this case, turned out to mean control of the field, which increasingly became the "antidepressant" field. (p. 149)

Shorter does not make a connection between the government review panels and the *DSM-III*, but he concludes, "Bottom line: Major depression doesn't exist in Nature" (p. 165).

Shorter proposes instead two tiers of mood disorder that should be called *melancholic disorder* and *nonmelancholic disorder*; this terminology is based on the ancient theory of humors (melancholy being caused by an excess of black bile). He explains that melancholy is a biological disorder that is what used to be called endogenous depression, whereas nonmelancholic disorder is merely a situational (reactive) low mood (p. 14).

## The ECT Connection

Shorter takes the melancholia terminology from Max Fink, a prominent psychiatric researcher and author (p. 272, Footnote 2). A well-known advocate for ECT (Kaplan, 2005), Fink is the author of books and articles advocating ECT (e.g., Fink, 2002) and the founder of the *Journal of ECT*, in which Shorter occasionally publishes. Fink's private foundation, the Scion Natural Science Foundation, funded Shorter's earlier book on ECT that was written with David Healy, head of an ECT treatment unit at Cardiff University (Shorter & Healy, 2007), and also partially funded *Before Prozac* (p. 289). Fink also collaborated with Shorter on *Before Prozac* (p. 165).

The connection between Shorter, Fink, and advocacy for ECT is thus discoverable but not clearly identified in *Before Prozac*, although Shorter does state, "Electroconvulsive ('shock') therapy, originated in 1938, remains the most effective treatment of serious, melancholic depression" (p. 48). Enthusiasm for ECT connects Shorter's loosely related arguments.

He has a dim view of SSRI antidepressants and the FDA policies that—in his view—forced the pharmaceutical industry to produce them to the virtual exclusion of all else, even though they are ineffective in treating melancholia (p. 193), which calls for ECT, he says. A bias for ECT could also explain his theory that a cabal "invented" major

depression, causing that diagnosis to have “taken over virtually the entire practice of medicine” (p. 169) and making SSRIs the treatment of choice.

Shorter’s thesis seems to be that while melancholic depression is a particular biological disorder best treated by ECT, everyone has been deluded by the *DSM*, the FDA, and big pharma into thinking that depression is a diffuse category of disorders for which SSRIs are the best treatment, even though they are based on a false theory and are no more effective than placebos.


However, Shorter fails to make a convincing case that he is right and everybody else is wrong. A scattershot of bombastic arguments does not provide enough evidence for one to reject most contemporary theories about the efficacy of psychopharmacology. Another possible reason for the book’s lack of coherence is that it is a mere collocation of points already made elsewhere (e.g., Healy, 1999, 2004; Shorter, 1997; Shorter & Healy, 2007) and presents few new ideas.

That said, Shorter’s history of psychopharmacology in the United States since 1938 is engagingly written and informative. The reader should know a little about psychopharmacology to get the most out of the story, although the book does have a table listing the generic and trade names of each drug discussed and a glossary of biochemical, pharmacological, and diagnostic terms. Because *Before Prozac* is not an impartial history, I recommend it only to well-informed mental health professionals and for students only in the context of broader discussion.

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