

in a cold, bare, rented room, disheartened further by your journey to it, depending upon people you can no longer trust, yet with your head nevertheless about to burst with announcements that need posting, there is no other weapon against despair—forsaken by your own skepticism, seduced by visions of what might be, and betrayed by opportunity and your own soul—than one loud *ja-sagend* after another. But this is acceptance driven like a truck toward a checkpoint.

**B**ack in the world of chronic pain, depressing news, and bad weather, Nietzsche is quarreling with former friends and future enemies, and grows closer in his own frayed mind to “the crucified one” than to his Zoroastrian namesake (he will soon sign letters *Der Gekreuzigte* or sometimes *Dionysos*); yet despite the insidious depredations of syphilis, which was probably the undiagnosed cause of many of his torments, he produces some of his most esteemed books, principally *Beyond Good and Evil* (1886) and *On the Genealogy of Morals* (1887). Nietzsche’s behavior grew more and more uninhibited, as if, with an irony too bitter to be borne, the frenzied god had taken his body hostage, so it pranced and sang, with unthinking fingers played wild riffs on the piano, embraced strangers, or compelled him to turn on those closest to him in unrestrained fury, howling, sobbing while subsiding with weariness, then displaying a hunger for food that had not even an animal’s limits. He was placed in an asylum. Later a patron, Meta von Salis, purchased a vacant villa above Weimar where Nietzsche and his sister (presently his nurse and guardian) could live. Nietzsche was oblivious to the century’s turn, now nearly a sofa’d corpse that visitors were allowed to view, a little like Lenin would be laid out later, although Lenin would be immune from the flu that slipped into Nietzsche’s lungs, where, immobile as he was, it was soon a pneumonia that prospered until a heart attack ensued.

At the funeral services, they played Brahms. ■

## MISERY’S FOGS

Is depression a diagnosis or a distraction?

By Gary Greenberg

Discussed in this essay:

*Against Depression*, by Peter D. Kramer. Viking, 2005. 337 pages. \$25.95.



**T**wenty-five hundred years before anyone understood how the brain worked, Hippocrates speculated that an excess of “black bile” or “melancholy”—one of the four humors believed to be coursing through the body—was the culprit for the condition we know as depression. Five hundred years later, Galen of Pergamon added to Hippocrates’ theory, describing, in an image that will resonate with any modern-day depressive, how melancholy causes suffering “when its

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darkness throws a shadow over the area of thought.”

But what sort of pathology is this inner darkness? Keeping with the Hippocratic notion that each humor gives rise to a different temperament, Aristotle decided that an abundance of black bile was not necessarily an illness, and that melancholy might even be a gift: “all men who have become outstanding in philosophy, statesmanship, poetry or the arts are melancholic.” At the same time, however, early physicians understood melancholy as a sickness to be remedied. Galen, for instance, treated the

melancholic emperor Marcus Aurelius with theriac, a concoction of sixty-odd ingredients, chief among them the pulverized flesh of a viper—that is to say, snake oil. The uncertainty over whether melancholy is disease or disposition persisted through the millennia, and, as a result, melancholy has acquired a dual reputation: scourge and blessing, symptom of illness and sign of refinement, suffering to be treated and insight into the real and infinite sadness of human existence.

When medieval anatomists began cracking open bodies, they managed to find approximations of three of the four ancient humors: yellow bile in

the liver, blood in the veins, and phlegm in the mucosa. Black bile, however, was nowhere to be found, and indeed the causes of the melancholic condition—or at least the observable, biological causes that are the gold standard of modern medicine—have, until recently, remained elusive, leaving us with an account of depression as something other than pure, physical illness. As Susan Sontag noted in *Illness as Metaphor* (1978), the stories that arise when we cannot explain illness as something gone awry in our natural states can lead us to overlook the physical suffering in favor of the metaphysical or psychological. Even more than tuberculosis and cancer, which were Sontag's subjects, depression tempts us to sentimentality and abstraction—not only because scientific explanations have been hard to come by or even because depression is so amenable to metaphor but also because enduring, recalcitrant unhappiness is an affront to a society devoted to the pursuit of its opposite.

For those dissatisfied with metaphorical explanations, the last half-century has been full of good news. Armed with PET scans and MRIs, scientists have mounted an expedition into our interior landscapes and concluded that thought and feeling and mood—indeed the entire range of human experience, once thought to be the province of spirit—are ultimately indebted to neurotransmitters: molecules made of nothing more exotic than carbon, oxygen, hydrogen, and nitrogen. Since the early 1950s, when neurotransmitters were first discovered in the brain, doctors increasingly looked to them for explanations of pathological mental states. In particular, they surmised that insufficiencies or other imbalances in neurotransmitters, especially in serotonin, are the causes of depression. With this new theory, melancholy acquired the unique biochemical signature that qualified it as a genuine disease.

If any doctors noticed how this explanation resembled the speculations of Hippocrates and Galen, with serotonin standing in for black bile, they didn't mention it. Discoveries in neuroscience quickly became the bailiwick of the pharmaceutical industry, and depres-

sion, a common malady, was of particular interest. By the late 1950s, the antidepressant era had begun, with neuroscientific advances begetting successive generations of neurotransmitter-targeted drugs while statistical refinement was creating the means by which depression could be quantified and the drugs could be tested. Not all of this work was conducted at the lab bench, however; particularly since the introduction of selective serotonin reuptake inhibitors (SSRIs) such as Prozac in the late 1980s, drug companies have also been promoting the idea that depression is an illness, plain and simple—and one for which, of course, they claim to have the cure.

This hasn't been an especially hard sell, which is a little curious when you consider that SSRIs, like their progenitors, seem upon analysis to be much more like Galen's theriac than their makers would like to admit: a 2002 article in *Prevention & Treatment* found that of the forty-seven trials submitted to the Food and Drug Administration for the six most widely prescribed antidepressants (Prozac, Paxil, Zoloft, Effexor, Serzone, and Celexa), only twenty trials showed any significant advantage of the drugs over the placebos. But SSRIs do, on some level, make people feel better, and they have been wildly successful before the only jury that counts: the marketplace. In this sense, the drugs do work, and if their salutary effect has resisted explanation by statisticians, it has been clearly elucidated by at least one expert: Peter Kramer, a psychiatrist whose 1993 best-seller, *Listening to Prozac*, details the transformation of personality that the drugs famously bring about—even if they don't actually "cure" depression.\*

Eli Lilly himself could not have fash-

\* In clinical trials the effectiveness of antidepressants is measured by their ability to bring about improved scores in the Hamilton Depression Rating Scale, a checklist of behaviors and feelings. The Hamilton Scale is skewed toward the physical signs of depression—such as insomnia and palpitations—the very symptoms that the drugs are likely to affect (drowsiness, for example, is a common side effect of SSRIs). But even then, the Hamilton Scale cannot assess whether a person feels less sensitive to rejection or whether he or she feels more resilient over the long haul—precisely the kinds of ineffable, immeasurable improvements that Kramer reports are widely noted in people taking SSRIs.

ioned so effective an advertising campaign, for each of Kramer's clinical vignettes serves as an encomium to better living through chemistry, and the praise he bestows on the pharmaceutical industry, despite the blatant product placement in the book's title, comes wrapped in disavowals of partisanship. Kramer's earnest inquiry into the implications of the widespread use of Prozac for our sense of what it means to be human is balanced enough to be disarming, and when he finally comes down on the side of antidepressants that can make us "better than well," it's hard to disagree. Whatever cavils he has—he worries, for instance, that Prozac can rob our moral sensibilities of their emotional capacity—aren't sufficient, he says, to reject the drug's ability to help us. And regardless, resistance may well be futile:

Is Prozac a good thing? By now, asking about the virtue of Prozac... may seem like asking whether it was a good thing for Freud to have discovered the unconscious. Once we are aware of the unconscious, once we have witnessed the effects of Prozac, it is impossible to imagine the modern world without them.... In time, I suspect we will come to discover that modern psychopharmacology has become, like Freud in his day, a whole climate of opinion under which we conduct our different lives.

To judge from his latest book, Kramer believes that this "whole climate of opinion" is not yet fully upon us. He claims that we have not listened carefully enough to psychopharmacologists about depression. Even if "the results [of SSRIs] have been disappointing" and "serotonin... play[s] at best [a] supporting [role] in the biology of mood" (facts that he mentions in passing, as if everyone already knew all of this), the course set in the 1950s from the discovery of serotonin toward the development of silver-bullet cures has taken us to a decisive moment: now we can assert that depression is a disease like any other. Depression has an onset and a course, it runs in families, it occurs throughout culture and history, it inflicts pain and impairment—and, according to the latest evidence gleaned from brain scans and other advanced diagnostic techniques, depression has a unique biochemical signature.

Specifically, depression seems to

result from a corrosive cycle, one in which the brain's natural and recently discovered tendency to grow new neurons, especially in the hippocampus (an area implicated in mood and learning), is impaired, and the resulting stress causes even greater suppression of neurogenesis and hippocampal erosion: a downward spiral of neurologically induced, brain-damaging unhappiness that Kramer likens to a stuck switch. Something—the loss of a loved one, perhaps—turns on that switch, and then, in the unlucky individual who is predisposed to the illness, depression is kindled. Untreated, the vulnerable suffer until the switch turns itself off, but as time goes on the episodes get longer and more intense. "Symptoms signal ongoing injury. Recovery is urgent," Kramer declares. "The time to interrupt the illness is yesterday."

"I have written a polemic," Kramer announces at the outset of *Against Depression*. He is too polite a writer to be properly polemical, but he is nevertheless at pains to persuade us that we have at once made too much and too little of depression: too little because we don't think of it as a disease like any other, and too much because we embrace it instead as an indispensable and even valuable aspect of human life. Kramer illustrates how easy it is to make this mistake with a case history of Margaret, a depressed patient whom he treated successfully with drugs and therapy. After she felt better, she complained that he pushed her too hard to explore the worries and regrets she confessed to him while in the throes of her suffering. A psychotherapist would usually interpret this kind of objection as an attempt to avoid meaningful, albeit uncomfortable, topics, but Kramer argues that Margaret's accusation was a legitimate indictment of his technique. "The dark, mixed feelings . . . those were illness. . . . She wanted to know why, in our discussions, I had granted an impostor—the depression—such standing. I had been negotiating with an occupying government, of Margaret's mind, while the legitimate ruler was in exile."

This story explains why we have been so slow to recognize and treat depression as a disease. Depression has so thoroughly colonized our con-

sciousness that when we are confronted with it, we are like "fish judging the ocean." Indeed, "the cultural history of depression is the history of the culture," and Kramer takes us on a whirlwind tour of Western civilization to show us how the *faute de mieux* notion that depression is a privileged, if not desirable, state of mind—what he calls "heroic melancholy"—took root. From Hamlet's dithering, Poe's horror, Kierkegaard's resignation, and Van Gogh's self-torture, to the post-Prozac spate of "autopathographies" (as Kramer calls them) by the likes of William Styron, the romantic notion that melancholy bestows a special insight prevails. We have come to accept that depression is "a divine gift that confers consciousness of surface and depth." Like Sontag, however, Kramer believes that depression is best shorn of its metaphorical and metaphysical sentimentality, unmasked as an illness, nothing more.

*Against Depression* is, in part, a memoir of Kramer's "immers[ion] in depression," when the round of lectures and readings he gave for *Listening to Prozac* taught him just how tightly depression holds us in its thrall. At every stop on the tour, someone asked him "the van Gogh question": What would have happened if the great artist had taken Prozac? Implied was that a cured Van Gogh would have been a mediocre artist, and Kramer reads the question as evidence of how deeply depression has insinuated itself into our attitudes toward art and artistic genius:

The denigration of art that arises from joy and contentment merely—the insistence on grief as depth—struck me as a cultural equivalent to . . . the conviction . . . that the psychologically resilient must subscribe to a distorted—Pollyannaish—view of reality.

This is not merely a point of aesthetics. Melancholy's dominion has expanded "to encompass the human condition. When we are in touch with ourselves, we are all melancholics. . . . This is the grand hypothesis of melancholy—not that it creates art, but that it describes our place in the universe."

Depression, in other words, has done more than subject people to unnecessary suffering; it has also infected us

all with a "contempt for the sanguine," with "ideas of civics, beauty, wisdom, religion, and morality . . . shape[d] around theories of mood and mood disorder." This is Kramer's most sweeping assertion, his most polemical argument: that the misunderstanding of depression has led to a terrible misunderstanding of our place in the universe, one that we need to reconsider in light of scientific discovery. "If the unacknowledged legislators of mankind . . . are depressives," he contends, "then we might want to examine the source of our value judgments when it comes to pessimistic views of the human condition." Pessimism, then, is not ontological but pathological. And it can be cured: now that we know how depressive brains are diseased, it's only a matter of time before some technique—most likely pharmaceuticals or genetically engineered "neuro-protectants"—can interrupt the progress of depression, turn off the stuck switch so that "in due course . . . your stress hormones will abate." These techniques will be surgically precise, winnowing the unnecessary suffering from the necessary. They won't, as Prozac does, "ask us to change who we are, in a fundamental way, in order to fend off a particular disease"; they will bring about their own climate of opinion, one that frees us from the misguided notion that "melancholy is the depth of modernity" and confronts pessimism for the treatable disease that it is.

This is an audacious claim, and Kramer anticipates, even encourages, the controversy it might provoke. Just as he invited readers of *Listening to Prozac* to wonder if we should really engage in "cosmetic psychopharmacology" (only to answer, "Why, yes—of course we should!"), in *Against Depression* he raises the question of whether it's really a good idea to rid the earth of melancholy: "Isn't all this talk about pathology really a foot in the door for the great American campaign of self-improvement, consumerism, and bland happiness?" Isn't he really seeking to diagnose away alienation, to treat "resistance to the seductions of bourgeois satisfactions" as a disease? Won't politics and culture be compromised, not to say impoverished, with the end of depression?

Kramer tries to settle these questions in part with a brief and awkward memoir that reaches its climax with what is perhaps the book's strongest (and most embarrassing) rhetoric: "Don't talk to me about alienation," he declares. "I lived where it flourished, at Harvard in the sixties, and even there I was a brooding outsider." Kramer wants us to know that he is no enemy of alienation; he only "demand[s] that it prove its bona fides, as a state that is separate from depression." The disease, he insists, can be safely hived off from the critical stance of the alienated intellectual, so we needn't fear that the cured patient will turn into Pollyanna, or the newly sanguine world into Stepford: "The opposite of depression is not indifference to the human condition. The opposite of depression is a resilient mind, sustained by a resilient brain and body." When "nerve cells stand far from the verge of destruction, and new connections grow and sprout, allowing for new learning and further vigor in the face of future stressors," their lucky owners are able to "face threats and persevere," to suffer in proportion to circumstances and then move on.

How much comfort you take from this apologia depends largely on how well you trust the doctors who will be making this distinction and the drug companies whose products they will be recommending in the event that your alienation does not pass diagnostic muster. With more than two decades of clinical practice under my belt, I am not sure I want the job of deciding whose suffering is inherently meaningful and whose is merely electrochemical static. Nor would I recommend that you give it to me, for the dustbin of history is littered with deservedly discredited notions of human nature, of how happy we ought to be and what we can do to get there. But undoubtedly there are doctors, perhaps charmed by the prospect of eliminating gloominess with surgical precision, who will be happy to decide if you are more despondent than your alienation really warrants, and one result of the kerfuffle that Kramer raises in *Against Depression* is to make it seem that the experts have carefully considered the Big Questions and, con-

sequently, declared it safe to rid humanity of the scourge of melancholy. An age of resilience, in which benign, bourgeois comfort is restored to respectability, will be a golden age. Aesthetics will be transformed as people demand "poetry with a wide sweep of subjects and story lines" and art that reflects a diversity of temperament. Freed from the shackles of melancholy, we will enter an era of cultural and political plenty: "How much more art there would be, how much more of every creation we value, if not for depression," Kramer promises. "How much freer we would be to live life knowing ourselves to be reliably resilient."

Indeed, how much? Like all the questions that give *Against Depression* its apparent gravitas—such as whether pessimism is really pathology, or whether we should take drugs to cure our pain, or whether you really have to suffer if you want to sing the blues—this one is entirely unanswerable. Or, more accurately, it is like those questions about feeding tubes and steroids and late-term abortions, questions whose answers depend on (and can be predicted from) which side of the abyss that has opened up in American cultural life—the discursive divide across which red and blue, secular and religious, Luddite and technocrat holler pointlessly at one another—you prefer. If you already believe that human agency is an epiphenomenon of biochemical processes, or that scientific progress leads inexorably into a sunny future, you will be primed to join Kramer's campaign against pessimism. If, on the other hand, you think that human agency is something substantial whose purposes are merely served by biochemistry, or that science and technology are no match for the shocks that flesh is heir to, then the coming neuroprotectant era is as troubling as the current antidepressant era. Of course, in the unfalsifiable scenario Kramer has created here—wherein insisting that there might be something worth getting despondent over is evidence of illness—maybe that's just your depression talking.

But it doesn't really matter what you think. Drug companies have driven neuroscientific research since its earliest days, using their knowledge of our inner workings for profit, and they're

not about to stop anytime soon. And they can only afford to foster certain states of mind. There is no greater American campaign than the effort to get the citizenry to withstand whatever execrations its leaders throw its way without missing a day on the job or a night at the mall—to convince them that happiness is just one lottery ticket, one good consumer choice, one positive thought, one little pill away. Not that there is anything wrong with better living through chemistry (for who could begrudge anyone's comfort!), but there are many versions of "better" and many ways to achieve them, and the drug companies will always favor the ones that work best for themselves. That's why we don't know (and probably never will) whether Saint-John's-wort, an herb that can't be patented, is really effective for depression. Or whether rhythmic exercise of large muscle groups would help to relieve depression, as Barry Jacobs, a Princeton professor of psychology, has suggested. Or what effect marijuana has—another unpatentable drug whose proponents claim as an antidepressant but whose political baggage is sure to set off a stockholder revolt. Or if MDMA, also known as Ecstasy, which is not only illegal but is designed to be used just a few times in the course of a lifetime—hardly enough to recoup the half-billion dollars the industry says it costs to develop a drug—has the long-term effects on depression that some research suggests. None of these interventions is good for the bottom line, so research into them, or into the neurochemistry behind them, is unlikely to command many resources.

Launching great unanswerables into a polarized society, like all good marketing devices, is a devastatingly effective distraction. In the case of *Against Depression*, Kramer's musings distract us from the fact that the biochemical secrets of our interior lives have been rendered into raw material for the pharmaceutical industry. Seemingly oblivious to the implications of this entanglement, Kramer is unable to tell us how the climate of opinion about our psychic suffering has been manufactured for us and, in turn, what that means for the future he promises.

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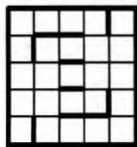
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## REVIEWS

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There's nothing really controversial in saying that depression originates in the brain—after all, where else does it come from?—or that it's a disease (especially if you agree with philosopher Peter Sedgwick that to call something a disease is not so much to make a claim about nature as to demand social resources); or even that people deserve equal access to happiness in a society dedicated to its pursuit, so long as all it requires is a trip to the pharmacy rather than some inconvenient redistribution of goods. There is surely nothing controversial about being "against depression." But to propose that we turn over our minds to a new empire, one ruled by stockholders and accountants? Now, there's a prospect worth some controversy, or at the very least worth getting depressed about. ■

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