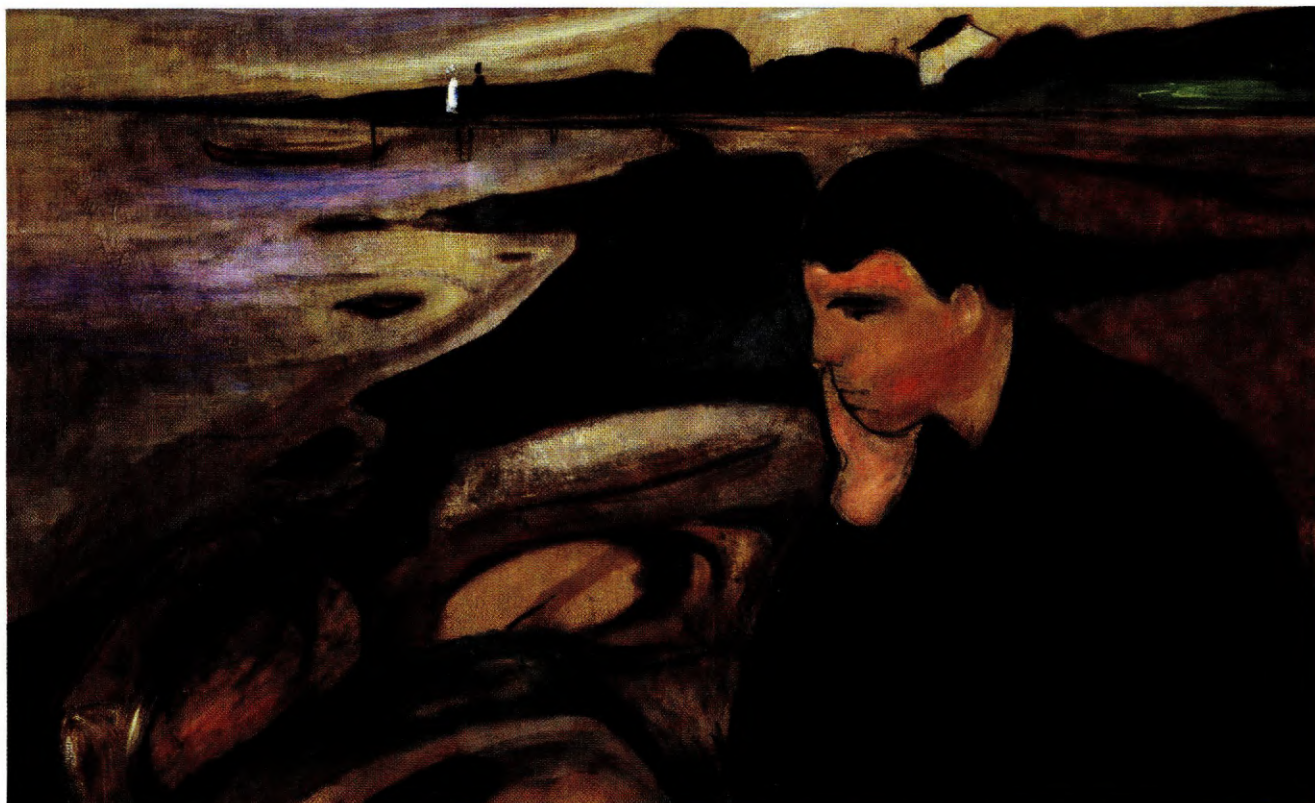


JOANNA BOURKE ON THE INVENTION OF HUMAN RIGHTS

HARPER'S

HARPER'S MAGAZINE/MAY 2007



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MANUFACTURING DEPRESSION

A journey into the economy of melancholy
By Gary Greenberg

Doctor George Papakostas has some bad news for me. For the last half hour, he's been guiding me through a catalogue of my discontent—the stalled writing projects and the weedy garden, the dwindling bank accounts and the difficulties of parenthood, the wife I see mostly in the moments before sleep or on our separate ways out the door, the typical plaint and worry and disappointment of a middle-aged, middle-class American life, which you wouldn't bore your friends with, which you wouldn't bore yourself with if you could avoid it and if this sweet man with his solicitous tone hadn't asked. He's been circling numbers and ticking boxes, occasionally writing a word or two in the fat three-ring binder on his desk, and now he has stopped the interview to flip the pages and add up some numbers. His brown eyes go soft behind his glasses. He looks apologetic, nearly embarrassed.

"I'm sorry, Greg," he says. "I don't think you're going to qualify for the study. You just don't meet the criteria for Minor Depression."

Even if my confessor had gotten my name right, I would still be a little humiliated. I had come to his office at the Depression Clinical and Research Program of the Massachusetts General Hospital, insisting that I would qualify. I had told him that

I figured anyone paying sufficient attention was bound to show the two symptoms out of the nine

listed in the *Diagnostic and Statistical Manual (DSM-IV)* of the American Psychiatric Association—sadness, diminished pleasure, weight loss or gain, trouble sleeping, fatigue or malaise, guilt, diminished concentration, and recurrent thoughts of death—that are required for the diagnosis.¹ To explain my certainty and my interest in his study, I had told Papakostas that these days my native pessimism was feasting on a surfeit of bad news—my country taken over by thugs, the calamity



of capitalism more apparent every day, environmental cataclysm edging from the wings to center stage, the brute facts of life brought home by the illnesses and deaths of people I love and by my own creeping decrepitude. I told him that I had more or less resigned myself to my dourness, that it struck me as reasonable, realistic even, and no more or less mutable than my short stature, my

¹ Minor Depression is a provisional diagnosis, listed at the back of the DSM-IV, where it awaits further study. Research that uses this diagnosis thus has a twofold aim: to provide another FDA-approved indication for a particular drug and to give Minor Depression medicine's most lucrative imprimatur—the five-digit code that allows doctors to bill insurance companies for treatment.

Gary Greenberg is a psychotherapist and a freelance writer. He is working on a book about the misuses of medical diagnoses.

constitutional laziness, my thinning hair, my modest musical talents, the quirks of my personality that drive away some people and attract others. I told him that, as a therapist, I lean toward talk therapies for psychic distress, but I am not at all opposed to better living through chemistry. If the drugs offered by his clinical trial—Celexa, Forest Laboratories' blockbuster antidepressant, and Saint-John's-wort, an herb with a reputation as a tonic for melancholy—did what they promised, I might like that, and if I did not, at least I'd know what I was turning down. And, finally, I had told him that I was going to write about whatever hap-

pened, which meant that either way, I wouldn't come away empty-handed.

THIS IS WHERE MEDICINE IS
INFUSED WITH THE MIRACLES OF
SCIENCE, AND I'VE COME TO SEE
HOW IT'S DONE

Unless I didn't meet the criteria.

But before I can get too upset, Papakostas has more news. "What you

have is Major Depression." He looks over the notebook again. "It's mild, but it's not minor. Nope. Definitely major depressive disorder, atypical features, chronic." Which means, he seems pleased to tell me, that I meet the criteria for at least four other studies that Mass General is running. I can take Celexa or Mirapex or Lexapro or something called s-adenosyl-l-methionine. I can climb into an MRI, get hooked up to an EEG, take home a device to monitor my pulse and breathing. I can get paid as much as \$360 for my trouble. I can go back to the waiting area, read over the consent forms that spell out in great detail—down to the final disposition of the two tablespoons of blood that they will take—what will happen to me, what is expected of me, what my rights are, how I can bail out if I want to, and then I can make my decision.

I'm a quick shopper, and when Papakostas returns, I have already signed the papers for research study 1-RO1-MH74085-01A1, agreeing to return to Mass General next week and then every other week for the next two months, so that they can evaluate the alleged antidepressant properties of omega-3 fatty acids—in other words, fish oil.²

Which is why Julie and Caitlin—tall and attractive and polished bright, like all the research

² According to the World Health Organization, the countries with the highest consumption of fish have the lowest rates of depression. And it happens that omega-3s make cell membranes, such as the receptors in your brain that absorb serotonin and other neurotransmitters, more permeable. To a psychiatrist already convinced that depression is the result of deficiencies in serotonin transmission, the significance of this correlation outweighs any of the other possible explanations for why someone in fish-deprived France might be more prone to depression than someone in Korea or Japan.

assistants here—are soon hovering over me in a tiny exam room that contains a metal table and a scale and a phlebotomist's chair, tweezing tentatively through the thatch on my chest and worrying out loud that they are hurting me. They finally clear the spots for the EKG electrodes and run the scan. They take my pulse and blood pressure, weigh and measure me, and draw my blood into a vial. Fair-skinned Caitlin is blushing a little as she hands me the brown paper bag with a cup for my urine specimen. I can see how cowed these young women are by this forced intimacy, and I try to tell them they needn't be so shy. But they know I have just been declared mentally ill, and I wonder if reassurance from the likes of me just makes things worse.

But I haven't come here to minister to them or, for that matter, to maintain my dignity. In this nondescript office building beside the towers and pavilions of Massachusetts General Hospital in Boston, these dedicated people do the research that determines whether drugs work—which is to say, whether drugs will come to market as government-sanctioned cures. In the process, they turn complaint into symptom, symptom into illness, and illness into diagnosis, the secret knowledge of what really ails us, what we must do to cure it, and who we will be when we get better. This is the heart of the magic factory, the place where medicine is infused with the miracles of science, and I've come to see how it's done.

I never used the term "magic factory"—you wouldn't want to seem paranoid in a place like this—but I told Papakostas about my suspicions of the drug industry and even referred him to what I had already written about it. If he caught a whiff of bad faith here, if he thought me a blue-stocking on an evidence-gathering excursion to the porn shop, or if he worried that I would lie to him just to get a story (he knew I was a therapist, that I was intimately acquainted with that checklist of symptoms), he was too good-natured to say so.³ But then again, he is a doctor and has to believe that if depression is the medical illness that the antidepressant industry is built on—if it is, as the drug company ads say and as doctors tell their depressed patients, a chemical problem with a chemical solution—then my intentions shouldn't matter. Diseases don't care whether you believe in them. What matters is the evidence, how much insulin is in the blood or how much sugar is in the urine and all the other ways nature has of telling you something is wrong.

But there is no lab to send my bodily fluids to

³ Or too hard up for subjects. The investigators expect that it will take five years to enroll the three hundred subjects needed to complete the study.

in order to assay my level of depression. Instead, there are tests like the Hamilton Depression Rating Scale. The HAM-D was invented in the late 1950s by a British doctor, Max Hamilton. He was trying to find a way to measure the effects of the antidepressants that the drug companies were just bringing to market. To figure out what to test for, he observed his depressed patients and distilled their common characteristics into seventeen items, such as insomnia and guilt. Patients could get as many as four points per item, and a total of eighteen of the fifty-two possible points is now considered the threshold for depression. Ten of the seventeen items were about neurovegetative signs like sleep and appetite, the kind most likely to respond to antidepressants—something Hamilton knew because he'd worked with the drugs. Not surprisingly, this drug-friendly test quickly became a favorite of drug companies. In fact, it remains the gatekeeper to the antidepressant industry, used by the Food and Drug Administration to evaluate candidate drugs.

Because the people from whom Hamilton derived the items were determined already to be sick, the HAM-D cannot be used to *diagnose* depression. So psychiatrists have developed the Structured Clinical Interview for DSM-IV (SCID), which is tied to the DSM-IV's catalogue of the 270 afflictions that cause people sufficient "psychic distress" to be considered diagnosable mental illnesses (the second edition of the *DSM*, published in 1968, lists a mere 168 diagnoses). The DSM-IV's fifty-one possible mood disorders take up 74 of its 886 pages, which list criteria and specifiers that a clinician assembles into such diagnoses as Major Depressive Disorder with Melancholic Features, Chronic with Seasonal Pattern.

There is no magic to the SCID. To determine whether you meet the DSM-IV criterion of "depressed mood most of the day, every day," it asks, "In the last month, has there been a period of time when you were feeling depressed or down most of the day nearly every day?" To find out whether you have a "diminished ability to think or concentrate," it asks, "Did you have trouble thinking or concentrating?" And so on with the lists of symptoms, until, based on your answers, you get shunted, like coins in a sorter, from one chute to another, and you drop into the drawer with all the other pennies.

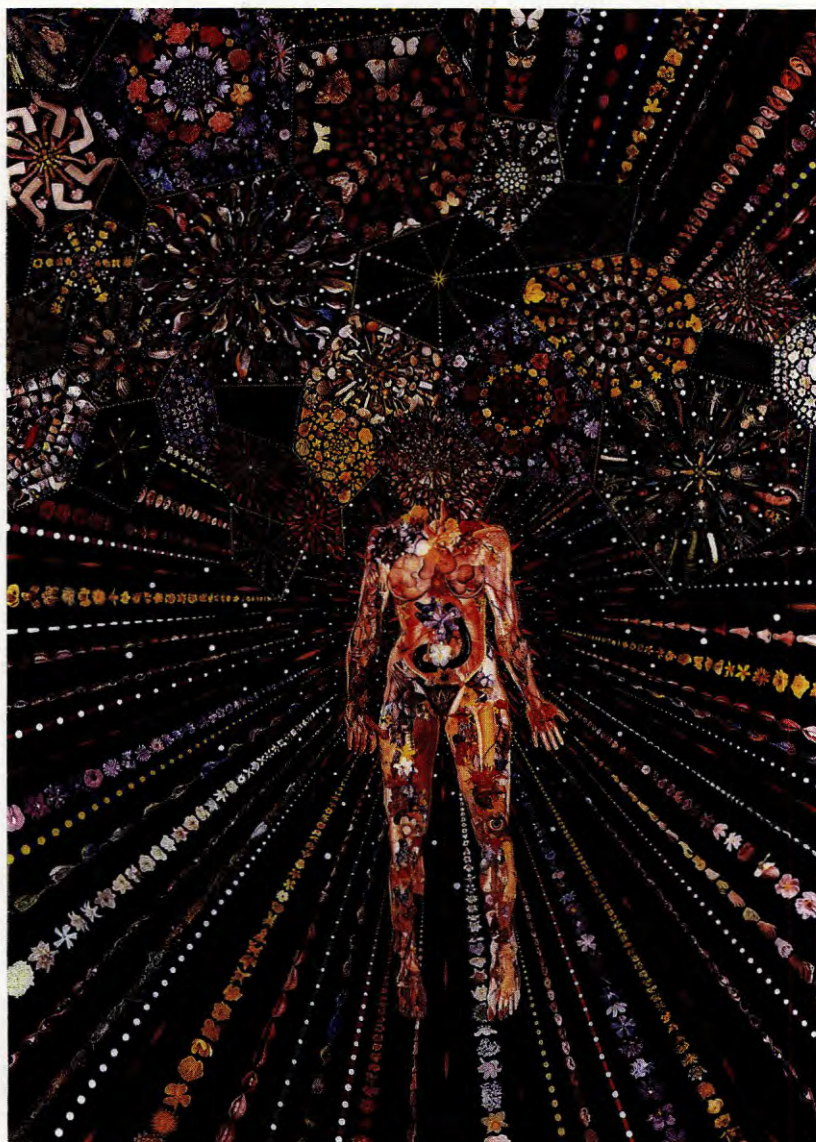
I never saw the scoring from my SCID, so I'm not sure how I ended up with my diagnosis. (I was relieved, however, that it would not be entered into my medical dossier, where it might wreak havoc on future attempts to get life or health insurance or to run for president.) I do know that I told Papakostas the truth, at least to the extent that I could figure out how to answer his questions about my psychic life. And I also know that in the course of a quarter-century as a practicing therapist, I have met people who are hammered flat, unable to get out of bed or find solace in any quarter, who are nearly insensate to anything other than their abject misery, who can



think of little other than dying—who, in short, meet the criteria for Major Depression in my own private *DSM*. There have been a handful of them, maybe ten or twenty out of the seven hundred or so patients I've seen. Whatever my score on the SCID, it was hard to believe that Papakostas really thought I had Major Depression. I wasn't tearful with him, and although I whined about the things that the SCID invited me to whine about, I was alert and smiling, joking, more effusive—perhaps out of nervousness—than I normally am.

I didn't say this to Papakostas, didn't protest that my aches and complaints were not really Major Depression. Just as well: Item 17 ("Insight") on the HAM-D awards two points to anyone who "denies being ill at all."

Julie greets me when I arrive the next week. I'm eavesdropping on the receptionist, who is reassuring someone on the phone that many of the doctors at the Depression Clinical and Research Program teach at Harvard. I get my



medicine today, assuming that my EKG checked out, that my blood and urine were clean of illicit drugs and indication of disease. Julie hands me a clipboard with three questionnaires and a pen. The Quick Inventory of Depressive Symptomatology (Self-Report)—the

QIDS-SR—comprises sixteen multiple-choice questions. Here is number 11:

View of Myself

0. I see myself as equally worthwhile and deserving as other people
1. I am more self-blaming than usual
2. I largely believe that I cause problems for others
3. I think almost constantly about major and minor defects in myself

The Q-LES-Q-SF, the Quality of Life Enjoyment and Satisfaction Questionnaire (Short Form), wants me to circle the numbers from 1 (Very Poor) to 5 (Very Good) that describe how satisfied I've been during the past week with sixteen aspects of my life, from my economic status to my sex drive, interest, and/or performance. And on the Ryff Well-Being Scale, I can express—by filling in the little bubbles, like on the SAT—one of six degrees of agreement with fifty-four statements about my attitude toward life, such as, "For me, life has been a continuous process of learning, changing, and growth," or, "My daily activities often seem trivial and unimportant."⁴

The tests in the women's magazines dotting the waiting-room tables aren't much different from these, save for one thing: social scientists have stamped their approval on the official questionnaires after subjecting them to various statistical challenges and worrying over such considerations as the fact that people will answer according to how they want to look to the tester. But aside from a passing frisson over telling Julie, however elliptically, about my *very good* sexual performance, I am not thinking about impressing her. I am thinking about how little I seem to know of myself. I didn't know, for instance, that wondering if "life is empty" or "if it's worth living," which I do at least once a week, is, as the QIDS insists, a Thought of Suicide or Death. I think I march to my own drummer just as much as the next guy, but when the Well-Being Scale asks me to rate how difficult it is "for me to voice my own opinions on controversial matters," I think of how often I disagree with myself over what my opinion is, how the closer I get to fifty the less sure I feel of anything, even of the answer to this question, and I cannot find a place to bubble in

⁴ The way that researchers decide whether these tests can accurately indicate depression is by correlating responses on them to responses on tests already known to measure depression—a good idea, unless there is no anchor at the end of the chain, in which case you may well have created a self-validating semiotic monster.

that uncertainty. I wonder what it means that I hesitate so long over these questions, whether I should circle the QIDS item that says, "My thinking is slowed down."

I haven't finished with the Well-Being Scale when Papakostas comes to fetch me. I tell him I'm confused about a consent form Julie just handed me; she explained that the one Papakostas and I signed last week was "outdated." But, I tell him, this new form seems to be for a different study, one that requires me to take two different pills at the same time. He looks perplexed, excuses himself, and returns with Julie. Together they explain that the study I signed up for last week was full, so they reassigned me. He looks mortified. Julie, who told me she was fresh out of Amherst, looks worried. They're explaining, apologizing, reassuring, as if they were waiters in a restaurant who have just delivered the wrong meal to a valued customer.

But we all know what has happened here. They have broken the code, the Nuremberg Code, the one that says that they cannot conduct experimentation on a human unless the human in question knows exactly what he's getting himself into, of which it is their responsibility to inform me. Not only that—and this is bad enough, since the U.S. government is paying for this research,⁵ and the funding is contingent on scrupulous attention to such matters—but for a moment they have laid bare the thing that all this scrupulous attention to my autonomy is supposed to obscure: that they are using me, that my Well-Being, my Life Satisfaction, my blood, my piss, will all get rendered into raw data for these doctors and their sponsors. They have moved me around like a pork belly, and for a split second the bald fact of the commerce we are conducting is right in front of our faces.

I reassure them that I am satisfied with their disclosures, that I just wanted to make sure we were all on the same page. Julie leaves the room with a last apology, and Papakostas hands me my copy of the form, countersigned by him. He opens the binder again and asks me how my week was. Papakostas has a way of making the HAM-D into a reasonable facsimile of an actual conversation. So when he asks me for an example of what I feel self-critical about (Item 2), I open the spigot a little, telling him I worry that my insistence on working at my therapy practice part-time, my giving up a plum teaching job, my indulgence in writing and other less savory vices, my seemingly endless desire for free time—that these reflect a hedonism and irresponsibility that have led me to squander my gifts. Papakostas waits a beat, then nods

and says, "In the past week, Greg, have you had any thoughts that life is not worth living?" It's time for Item 3.

Papakostas is so unfailingly kind—and I want him to *care*, I want him to tell me that I am not really feckless—that I cannot be mad at him for sticking to the script, let alone correct him about my name. He's not doing it because he's a bad man, or a disingenuous one, or a shill for the drug companies. On the contrary. He does it because he wants to help me, because he thinks I am suffering, and because he is a doctor and this is what he knows how to do: to find the targets and send in the bullets, then to ask the questions and circle the numbers and decide if those bullets really are doing their job. We're not here to talk about *me*, at least not about the homunculus we call

a *self*. We're trying instead to figure out what's going on in my head—in the gray, primordial ooze where thought and feeling, according to the latest psychiatric fashion, arise.

Back on the street, blinking in the noon-day sun, I peek into the brown paper bag they have given me. The "study medicine" comes in a pair of plastic bottles stuffed with two weeks' worth of glistening amber gel caps. They look just like regular prescription drugs but for the sticker that says, DRUG LIMITED BY FEDERAL LAW TO INVESTIGATIONAL USE. That seems a little dramatic for something I can get at any health-food store or by eating however much salmon it would take to provide two grams of omega-3s per day. But under the agreement we've made—that they are doctors, that I am sick, that I must turn myself over to them so they can cure me—the medicine must be treated with the reverence due a communion wafer.

Not that anyone at Mass General would say so. In fact, they've designed this study to minimize the possibility that something as unscientific as faith or credulity or the mystifications of power could be at work here. The trial is a so-called three-armed study. I have been randomly assigned to one of three groups. One group gets placebos in both bottles. Another group gets eicosapentanoic acid and a placebo, and the third group gets docosahexaenoic acid and a placebo. Only the anonymous pharmacist laboring in the bowels of Mass General, armed with a random number generator and sworn to secrecy, knows which group I'm in. The study will then be able to show which of the two omega-3s has more ef-

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⁵ About \$2.5 million over five years.

fect, and whether either one is more powerful than a placebo.

This method is known as the “double-blind, placebo-controlled design,” and it provides a way to deal with something that the drug industry would rather forget: that in any given clinical trial, especially one for a psychiatric drug, people are very likely to respond to the fact that they are being given a pill—any pill, even one containing nothing but sugar. Which is why the FDA requires all candidate drugs to be tested against place-

bos—to try to separate the medicine from the magic, to see what the drug does when no one is looking. But, like a pain-in-the-ass brother-in-law, the placebo effect keeps showing up, curing

people at a rate alarming to both regulators and industry executives. In fact, in more than half the clinical trials used to approve the six leading antidepressants, the drugs failed to outperform the placebos, and when it came time to decide on Celexa, an FDA bureaucrat wondered on paper whether the results were too weak to be clinically significant, only to be reminded that all the other antidepressants had been approved on equally weak evidence.⁶

Despite the fact that the placebo effect is the indirect subject of virtually every clinical trial, no one really understands how it works. Science, designed to break things down to their particulars, cannot detect something so ineffable, so diffused throughout the encounter between physician and patient. Until there is money to be made in sugar pills—at which point the drug companies are sure to investigate them thoroughly⁷—about the best we can say is that the placebo effect has something to do with the convergence between the doctor’s authority and the patient’s desire to be well. But this relative ignorance doesn’t stop doctors, wittingly or not, from using their power as a healing device.

⁶ The advantage of antidepressants over placebos in those trials was an average of two points on the HAM-D, a result that could be achieved if the patient ate and slept better. The average improvement in antidepressant clinical trials is just over ten points, which means, according to Irving Kirsch, a University of Connecticut psychologist, that nearly 80 percent of the drug effect is actually a placebo effect.

⁷ In 2002, researchers observing the EEGs of patients in an antidepressant-versus-placebo trial stumbled on a pattern of brain activity common to those subjects who respond to placebos. Drug companies were very interested in this discovery, not because it allowed them to study the placebo effect but because it might allow them to identify those placebo responders and bounce them out of a trial before it starts.

For instance, they can reshape you in a way that makes you a good fit for the drugs. That’s what these questionnaires, with their peculiar way of inventorying personhood, do; they alert you to what it is in yourself that is diseased—casting your introspection as “excessive self-criticism,” your suspicions of your own base motives as “low self-esteem,” your wish to nap in the afternoon as “excessive daytime sleepiness,” your rooting hunger late at night as “increased appetite”—and they prepare you for the cure by letting you know how you will feel better.

Just before I got my pills, Papakostas asked me how long it had been since I had felt good for any appreciable time. Good? I asked him.

“Symptom-free,” he said, as if we had agreed that my feelings were symptoms.

“For how long?”

“Thirty days. Or more. At least a month.”

I wanted to tell him that I was a writer, that I counted myself lucky to feel good from the beginning of a sentence to the period. I wanted to ask him if he had ever heard of betrayal, of disappointment, of mortality. Instead, I laughed—derisively, I suppose (was this the “irritability” of Item 10?)—and said I had no idea what a month of feeling good would feel like.

Of course, this only confirmed his diagnosis.

But *thirty days* is ringing in my ears as I head back to my car. I make a sudden decision: to duck into a restaurant, to order a glass of water with my meal, to start the trial not tomorrow morning but right now. I cannot resist the wish, the temptation, to lay down my pessimism at this altar, to put myself in the hands of these doctors, to take their investigational drug and let them cure me of myself. I gulp down my six golden pills.

Drugs do work. By themselves, I mean, even without the benefit of the placebo effect. Just ask the tuberculosis patients at Sea View Hospital in New York who, in 1952, took a derivative of hydrazine, a chemical that Germany used in the waning days of World War II to power its V-2s. The drug, called Marsilid, worked not only on their lungs but also on their heads; enough of them reported feeling euphoric—there was even a rumor they were dancing in the wards—that doctors started prescribing it for their melancholic patients.

In a society famously ambivalent about pleasure and the use of intoxicants to achieve it, however, it isn’t enough to take drugs to feel better. It’s preferable, especially for a drug company, if you have an actual illness to treat. When it was discovered that Marsilid prevented the brain from manufacturing an enzyme that broke down serotonin, an intriguing chemical that had just been found in the brain, scientists had their disease. De-

IN OVER HALF THE TRIALS USED TO APPROVE THE SIX LEADING ANTIDEPRESSANTS, THE DRUGS FAILED TO OUTPERFORM THE PLACEBOS

WHAT WOULD HAPPEN TO THE
CONSUMER ECONOMY IF WE BEGAN
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HAPPINESS IS ENOUGH?

pression, the new theory went, was not a psychological or existential condition but a brain disease caused by a "serotonin deficiency" or some other "chemical imbalance." Drug companies spread this gospel aggressively. In the early 1960s, for example, Merck bought 50,000 copies of *Recognizing the Depressed Person*, a book by a doctor who had pioneered the serotonin theory and the use of drugs to treat it, in order to distribute the book to doctors who might not yet have heard that depression was the disease for which the new drugs were the cure.

But the evidence for the serotonin theory was circumstantial to begin with, and it has remained so for the last half-century. Although scientists have mapped the jungle of nerve fiber through

which serotonin makes its way from brain stem to synapse, analyzing the biochemistry of that journey and inventing drugs that inhibit or encourage it along the way, they have never

proved that a serotonin deficiency actually exists in depressed people or, for that matter, figured out how much serotonin we ought to have in our brains in the first place. Nor have they explained certain inconvenient facts: that reserpine, for instance, a drug that *decreases* serotonin concentrations, also has antidepressant effects, or that so many people fail to respond to antidepressants—which, if antidepressants were really arrows aimed at a molecular bad guy, simply shouldn't be the case.⁸ In the face of these dismal results, many scientists have begun to move on to theories about neurogenesis and cellular damage and other brain events of which serotonin may be only a marker, the finger pointing to the mood.

None of this stops doctors from continuing to manipulate serotonin in order to relieve depression. The omega-3s I'm taking are thought to render neurons more supple, allowing them to make the most efficient use of whatever serotonin is available. So far, however, the pills don't seem to be having an effect. Indeed, as I end my second week, I notice only one change. When I wake up early in the morning, when I crave my afternoon nap, when I find myself frustrated by my shortcomings or deflated by the seeming impossibility of getting done what I want to get done, when I read the newspaper and, like Ivan Karamazov with his catalogue of

⁸ Neither have they shown that in identifying the brain chemistry of a given mood or experience they have found the cause rather than the correlates; that is, they could have found the ways the brain provides, but doesn't originate, that mood or experience.

atrocities, want to return my ticket, when I feel sorry for all of us, I wonder if indeed I've been suffering from an illness all along.

But I am still thinking about those thirty days, preoccupied with the idea that there are others right now in the midst of that month of resilience to setback and hardship who are not simply luckier (or, as I think in my self-flattering moments, *shallower*) but *healthier* than I, that they have dodged a bullet that has caught me; that I can don some armor and make up for what nature has, so these doctors say, denied me.

The third visit, the first one after I started the drugs, is shorter, more perfunctory than the first two. Papakostas moves briskly from one question to the next and looks at his watch if we digress. But the protocol calls for him to ask whether I have any questions. So I tell him I wasn't sure I had understood him in our last meeting. How long was it that he thought I should be feeling good?

"For at least a month," he says

I ask him why he wanted to know.

"People, when they're depressed, they get a sort of recall bias," he says. "They tend to feel that their past is *all* depressed."

Which would suggest, I want to point out, that depression is more like an ideology than an illness, more false consciousness than disease.

This isn't the first impertinence I've stifled today. Earlier he asked, "Are you content with the amount of happiness that you get doing things that you like or being with people that you like?"

"I'm not big on contentment," I said. *Is anyone?* I wondered. Is anyone ever convinced that his or her pursuit of happiness has reached its goal? And what would happen to the consumer economy if we began to believe that any amount of happiness is enough? "I'm sorry to seem dense," I explained, "but it's not how I usually think about things."

Papakostas was reassuring. "You know, this question condenses a lot of areas of life into just a number. It doesn't work well," he said. "Some questions we just don't like."

Well, if these are dumb questions, I wanted to shout, *then why are you asking them?* Why are we pretending that these answers mean anything? Indeed, if I'm just the middleman here, the guy you've got to go through to get to the molecular essence of my troubles, then why ask me any questions at all?

Later, when he asked how many days there were in the last week that I had napped for more than thirty minutes, and I told him four, he said, "See, some of the questions are really nice in terms of being objective," before putting me down for two points on that item.

"I suppose it would be easier if there were biochemical markers," I offered. "Otherwise, you're just stuck with language."

"Hey, we're psychiatrists," Papakostas said. "Language is good."

Now I was really confused. Hadn't we just spent the last half hour circumventing language's approximations? If language is good, then why wasn't he taping this visit, taking down my words instead of translating them into the tests' pale simulacrum of language? For the same reason, I suppose, that he doesn't seem to think that consciousness itself, in all its insuperable indeterminacy, matters very much, as I discover when we meet two weeks later. I ask Papakostas about a promising new experimental treatment for depression, one that uses an anesthetic drug called ketamine. A government psychiatrist was trying to bring ketamine in from the cold, from the psychiatric underground where LSD and psilocybin are used for transformative purposes⁹ and where ketamine has a reputation for delivering a powerful and salutary (if terrifying) experience of being disembodied and dislocated—not unlike a near-death encounter. To Papakostas—who is not familiar with this unofficial research, discredited since the excesses of the sixties grew like an adipose layer over the therapeutic promise of psychedelic drugs—I'm explaining the idea that a single whack upside the head, one glimpse into the cosmos and all its glory and indifference, can set you straight for a long time. I am getting to the part about how inconvenient the economics of a one-time-only drug are for an industry addicted to One-A-Days, when he interrupts me.

"Sort of like ECT," he says, using the new and improved name for electroshock therapy. "The way it's supposed to reset your neurotransmitters. But we know that theory doesn't work, because ECT patients relapse."

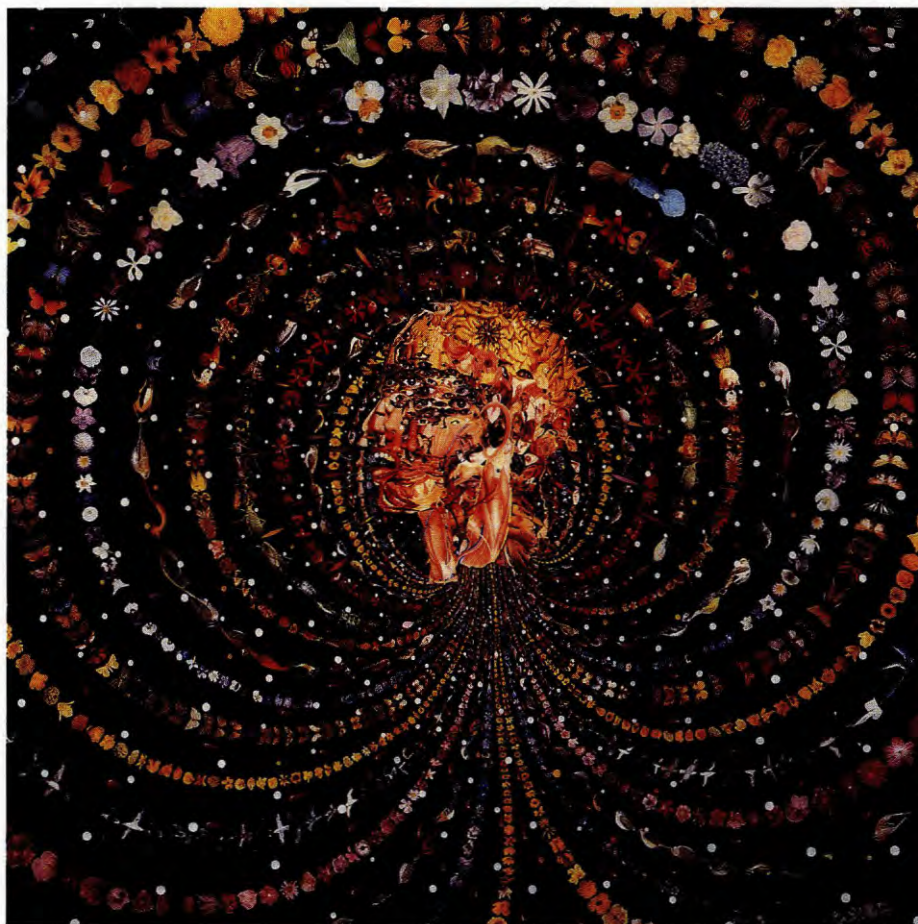
⁹ As it happens, these are also drugs that affect serotonin. The concept of "serotonin deficiency" was invented in 1954 by two Rockefeller University scientists. In a short notice in the back of *Science*, they noted that LSD, whose profound effects on consciousness were well known, contained within itself a copy of the serotonin molecule, and that serotonin had recently been discovered in the brain. They speculated that a lack of serotonin, whose role in neurotransmission was still not accepted, must have something to do with mental illness.

"But isn't there a difference between ECT and ketamine?"

"Well, of course ketamine works mostly on glutamate pathways..."

"No. I mean that you're conscious when you take ketamine and unconscious when you get ECT."

The distinction seems lost on Papakostas, or maybe he just doesn't have time for a discussion on the nature of consciousness. Either way, you cannot help but admire the purity of his devotion to the material, the way he has pared down psychic life to its bare bones. His is a spare and unrelenting pursuit, and his single-mindedness right now seems nearly ascetic.



Papakostas may be circumscribing my subjectivity in order to make it work for the drugs, but he's also renouncing his own subjectivity, putting aside whatever curiosity he might have about the shape of the self, the objects of consciousness, the raw nature of our encounter, in order to make good his claim to possess the instruments of science. Armed with them, he can take my emotional measure and report my depression with the dispassion and confidence of an astronomer reporting the distance to a star. The truth thus de-

rived, decontaminated of aspiration and expectation, is better, truer somehow, than the one we know through our credulous senses and fickle sensibilities. Maybe that's why I don't argue with him when he adds up my numbers and tells me that in the world behind the world, the one in which I am officially depressed, the survey says I'm getting better.

Which is news to me. I hadn't been keeping track of my HAM-Ds and Q-LES-Qs, but apparently my numbers were trending steadily toward health. I'm discomfited, disturbed, maybe even a little depressed at this, at my apparent inability to know my own inner state—not to mention the possibility that I will have to relinquish my own idea of happiness and settle for “symptom-free” living instead.

I arrive at my next visit resolved to get the dazzle out of my eyes and to make my psychiatrist take account of the seams I think I'm seeing in the Matrix. But as I'm finishing up with the tests on my clipboard, a petite woman with short hair and large eyes comes into the waiting room. She's not quite looking at me as she introduces herself quickly, beckons me to follow her, and, before I can tell her that there must be some mistake, that I am Dr. Papakostas's patient, she turns her back and briskly leads the way into the warren of offices beyond the waiting room.

Papakostas must be away on vacation, I think. It is August, after all. But when we pass his office, there he is at his desk, leaning into his computer screen. He doesn't see me. I imagine that he has tired of my questions or that his colleagues have caught wind of our extracurricular discussions, all that *language*, decided it's time to remind me who is asking the questions around here, and pulled him off the case. Whatever the explanation, it is hard not to take this personally—which, of course, is exactly how a depressed person, whose disease makes him “rejection-sensitive,” would take it.

In fact, I can't seem to escape the gravitational field of my diagnosis today. When I tell the new psychiatrist I didn't catch her name, she repeats it carefully and slowly, as if to account for my “psychic retardation.” When I explain why I am going to record our session (she asked, something Papakostas never did), she says, “Oh... in-ter-est-ing,” filling the spaces between syllables with professional smarm. I suspect that she's running the numbers in her head and wondering whether this will be the “difficult” interview that's worth three points on Item 8.

If the purpose of the switch was to make things more businesslike, then Christina Dording was the perfect choice. She is cold and unflappable, her lines well rehearsed, her inflected concern perfectly pitched. When she asks me if I think my depres-

sion is a punishment for something that I've done (Item 2), and I try joking—“It's an entertaining thought, but I haven't had that one”—she seems not to notice. When I confess that I'm baffled, even after all this time, by the HAM-D's questions—“This past week, have you been feeling excessively self-critical?”—that require me to parse words like “excessively” and “normally” and “especially” (something that Papakostas has dealt with affably by letting me ramble on until I say something that allows him to circle a number), she answers with such crisp condescension—“If there's a comparator implied, it's always to when you're not depressed”—that I wonder whether I'm the one asking silly questions. Maybe I'm the only person who wonders whether “excessive” means more than I think others do or more than I think I ought to. Maybe her answer isn't as circular as it sounds, maybe it means more than saying it's a problem when it's a problem and not when it's not, maybe it isn't yet another denial of the basic assumption here—that they are the experts about my mental health, that depression isn't something I'm equipped to detect in myself, because if I was, I'd be in the other study, the one for the Minor Depression I thought I had in the first place. Or maybe all these maybes, and my resulting inability just to blurt out a yes or a no, are just another example of my “excessive self-criticism.”

Dr. Dording and I are not off to a good start. Which makes it a little easier to interrupt the interview to ask her whether she really thinks self-criticism is pathological.

“Pathological?” she asks, as if such a thing had never occurred to her. “I don't know if I'd call it pathological.”

“Symptomatic, then,” I offer.

“Well, it's certainly not optimal.”

“Optimal,” I say, deploying the therapist's repeat-and-pause tactic, hoping she'll tell me exactly how much self-criticism is optimal, and how she knows.

“Certainly not optimal.” She does her own pause.

“But being self-critical is something that helps people succeed, isn't it?”

“Sometimes yes, sometimes no. I don't think being *excessively* self-critical is ever a great thing. No.” She starts turning pages again, resumes the interview.

But I don't want to let it drop. I've come to pull back the curtain, and, the numbers aside, I want to know, colleague-to-colleague, just between us pros, do I really seem depressed to her? *Majorly* depressed? I ask her to tell me what she thinks the difference is between Major Depression and Dysthymia, a DSM-IV mood disorder that, if I have to be diagnosed, comes closest to capturing my melancholy.

“You're getting into close quarters here,” she says.

In another world, one in which psychiatrists actually liked language, we might explore this slip—for she really means to say that I'm getting into fine diagnostic distinctions here—and its revelation of discomfort at my intrusion into her professional space. But she seems unaware of what she has just said as she explains: "Dysthymia is more low-level chronic. Minor Depression may or may not be long term, but it typically has less criteria than Major Depression."

And before I can ask her how any of this compares with what she actually sees, she closes the notebook and walks me out.

George Papakostas is a few paces in front of me as I round the corner of the reception desk. He's headed for the men's room. I decide to spare him strained pleasantries at adjoining urinals. But I dawdle to the elevator, and he shows up just as it arrives. We ride down and walk out of the building together. I tell him how fascinating I find this process, and how many questions I still have. I'm working toward asking him if we can extend our next meeting somehow, maybe go out for lunch or something, so that I can debrief him. But he tells me he is going to Greece to visit his ailing father, and he won't be back in time. We shake hands goodbye.

I imagine that he is relieved to be done with me. I know how this looks to him, the patient challenging the boundaries of the professional relationship, the *What About Bob?* nightmare. Or I think I do. Maybe I don't know anything about this. Maybe what he really sees as we stand on the threshold of his concrete fortress is a conversation orchestrated by ion channels and neural pathways and axonal projections, two people deep in the grips of their chemicals, one of them still clinging (because of those chemicals, no doubt) to his old-fashioned idea that he is more than the sum of his electromolecular outputs, that a conversation like this one, not to mention recalcitrant unhappiness, might be complex and mysterious and meaningful.

I am already deflated when I arrive for my last interview. Of course, there's no place in the HAM-D to express this, to talk about the immeasurable loss that I think we all suffer as science turns to scientism, as bright and ambitious people devote their lives to erasing selfhood in order to cure it of its discontents. The HAM-D questions, Dording's unconvincing solicitude, the banality of this exercise, the tyranny of the brain—they all seem as unassailable, solid, and impenetrable as the office building itself. I'm downright unpleasant when Dording asks me if I've been feeling guilty or self-critical. "A constant feature of my life," I say. She ignores me.

But then she does something strange. She skips the Insight item, the one where she's supposed to

ask whether I think I'm suffering from an illness and to give me points if I don't think I am. I ask her why. "You typically don't ask," she replies. "It's atypical that a person is something other than a zero. Clearly psychotic people could have a two. There are occasions when you can get a one, like if a person thinks their lack of interest or energy doesn't have anything to do with being depressed. But typically people who are in here are a zero."

"So you would have to be either psychotic or believe that your symptoms are the result of some other conditions?"

"Yeah."

"As opposed to just saying, 'Well, you know, this is just how I am.'"

"That's a good question. I think that an answer like that would require an explanation. You would need to talk a little more about an answer like that." And I'm thinking that we should have this discussion, right now, because I am that patient, and I don't think I'm psychotic.

But that isn't going to happen. Instead, Dording is going to give me a physical. She goes to find out if the exam room is available, returns to tell me that it is not, that I can wait or do it on my next visit.

"Next visit?" I ask. According to the protocol, this is my last.

"You're not coming in for the follow-up?" She looks as surprised as I am, as if no one would pass up that opportunity. I ask whether it would be any different from what we've been doing. It wouldn't, she says. So I tell her I'll skip the follow-up and wait for my exam.

Julie is also gone for vacation, so Caitlin takes my vitals and draws my blood. Then Dr. Dording comes in. She taps my knees, looks in my mouth, listens to my heart and lungs. When she asks me to follow her finger with my eyes, she puts her hand on my bare knee. The touch of her fingertips is firm and cool and impersonal, my knee just a prop to hold her up.

She repeats her offer of follow-up, then elaborates on something she mentioned at the end of our interview. "Give me one second here," she had said as she flipped the pages of my binder. "Look at your scores. Nice response." Now she says, in case I didn't get it the first time, "I think you've done very well, you're *much improved*." She doesn't ask whether I agree, nor does she explain why if I'm better I would need *follow-up*, why I would need to do more than buy some fish oil at the Whole Foods next door.

If, that is, I have been taking fish oil for the last eight weeks.

NUMBERS ASIDE, I WANT TO
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MAJORLY DEPRESSED?

I ask her if I was on placebo or drug. She's befuddled for a moment. "I don't think we unblind the study," she says. She deliberates over my paperwork. "No, not in this one. No unblinding."

I protest. "I don't get to find out?" It's as if she's never been asked, as if no one in the whole history of clinical trials had ever wanted to know which side he had been a witness for.

"No," she says. "But you had a good response."¹⁰ She's chipper now, like she's trying to convince me that I ought to take my improvement and go home happy, another satisfied customer. And really, it doesn't matter. Because the point here is not to teach me anything about myself, or for them to learn anything from me. It's not even to prove whether or not omega-3s work. It's to strengthen the idea that this is what we are: machines fueled by neurotransmitters at the mercy of our own rene-gade molecules.

Once upon a time, the scientific explanation for depression sounded something like this:

If one listens patiently to a melancholiac's many and various self-accusations, one cannot in the end avoid the impression that often the most violent of them are hardly at all applicable to the patient himself, but that with insignificant modifications they do fit someone else, someone whom the patient loves, has loved or should love.... So we find the key to the clinical picture: we perceive that the self-reproaches are reproaches against a loved object which have been shifted away from it on to the patient's ego.

For a modernist like Freud, who wrote *Mourning and Melancholia* in 1917, depression was embedded in history, personal and cultural, and untangling that history, rescuing it from the oblivion of the unconscious by turning it into a coherent story, was the key to a cure. A fascinating and tragic notion—that we carry within us an other whom we can never fully know, but whom we must try to know—is headed for the dustbin of history. Freud, with his extravagant hermeneutics, his because-I-said-so epistemology, his unfalsifiable claims—not to mention the sheer inefficiency of psychoanalysis—has given way to the Dordings and Papakostases of the world, with their inventories and brain scans and pills. They have replaced Freud's unconscious, the repository of that which is too much to bear and which

¹⁰ All of which raises the question of how the doctors know what kind of follow-up to provide, whether to give a drug or not. Later, the lead investigator on the study, David Mischoulon, told me that they "take their best guess" about whether the subject was on drug or placebo. The reason for not disclosing my experimental condition, he explained, was so that doctors wouldn't detect a pattern in the responses and thus "break the blind." He added that I could indeed find out when the study is completed—about five years from now, he estimated.

will only stop tormenting us to the extent that we give it language, with an unconscious populated by carbon and hydrogen and nitrogen and oxygen, the basic building blocks of the material world, essential but forever dumb.

Still, I'm not exactly pining for Freud as I leave Mass General for the last time. He got too much wrong, some of it inexcusably so. Indeed, as I drive through the lunch-hour scurry on the hospital-zone streets, the doctors in blue scrubs hurrying between buildings, wan patients wheeling IV stands down the sidewalks, ambulances and private cars delivering a legion of the sick to this city of hope shimmering in the late summer heat, I am once again struck by temptation—to believe, as I hurtle down Storrow Drive having these thoughts, passing all these other I's having their own thoughts, convinced that we are driving ourselves just as surely as we are driving our cars, that I am wrong about who I am, that we are all wrong. That scientists peering into the darkness in our skulls will eventually illuminate it entirely and show us that such thoughts and the conviction with which they are held are only accidental: spandrels of our cerebral architecture that can be rearranged with surgical precision. And just as we once were playthings for the gods or sinners poised over a fiery pit or enlightened rationalists cogitating our way to the truth of ourselves, we will become the people who needn't take ourselves too seriously, who will stop mistaking the vicissitudes of personal history for the vagaries of personal biochemistry, who will give up the ghost for the machine.

Because irresistible ideas about who we are only come along every so often, and here at Mass General they've gotten hold of a big one. They have figured out how to use the gigantic apparatus of modern medicine to restore our hope: by unburdening us of self-contradiction and uncertainty, by replacing pessimism with "optimization," by inventing us as the people who seek Life Enjoyment and Satisfaction, who will buy from the pharmacy what we need to forge ahead toward Well-Being unhindered by Depressive Symptomatology, to pursue antidepressant if not happiness. Who can resist this idea that our unhappiness is a deficiency that is in us but not of us, that it is visited upon us by dumb luck, that it can be sent packing with a dab of lubricant applied to a cell membrane?

The epiphany makes me wonder whether I've been unduly churlish to Christina Dording; maybe I should take her word for it, accept that I am better now, and thank her. But remorse lasts only as long as it takes to get the results from the lab to which, out of curiosity, I sent my pills. There wasn't a drop of fish oil among them; I was on the placebo. ■