

Chapter 2. My Case Study

Background

What follows is a summary of the events surrounding my successful drug treatment for bipolar disorder, including some of the amazing effects those drugs had on me. I'm including this case study for three primary reasons: 1) it illustrates a long journey similar to that which many people with mental illness must endure before eventually getting effective treatment; 2) some of my experiences provide the basis for parts of the current theory; and 3) it illustrates some useful principles for treating bipolar disorder and other mental illnesses, including a common sense problem solving approach that I believe should be applied by medical practitioners and their patients when treating mental illness.

The Case

One day in the summer of 1999, about four years into neuroscience graduate school at Johns Hopkins University in Baltimore, Maryland, I consulted a psychiatrist because I thought I might be suffering from clinical depression. The psychiatrist and I went over my list of symptoms, which included: depressed mood, persistent negative thinking, loss of appetite, and difficulty sleeping, with early morning awakenings. He concluded that I was indeed suffering from a bout of depression and decided to put me on Prozac. I faithfully took the proper dose every day, but after a month passed I still didn't feel any better, so my doctor decided to try Remeron, a newer antidepressant. I was on that drug for about six months, though it didn't do much to lift the depression, so I stopped taking it.

I went home to West Lafayette, Indiana for Christmas (1999) vacation, and soon realized that I probably shouldn't return to the lab in Baltimore until I was feeling better. I found a local psychiatrist who put me on Effexor, which like Remeron was a fairly new antidepressant at the time. After a month on Effexor, I still had no response and decided to get a new doctor, partly because I was again starting to feel desperate to escape from the unrelentingly miserable depression. The new doctor decided to try Zoloft, which is a ser boosting drug like Prozac. After about two weeks on Zoloft, I began sleeping and feeling better, and soon I returned to Baltimore.

Though I had improved quite a bit (April 2000), I was still only sleeping six hours a night instead of my usual nine hours, and my personality seemed to have changed somewhat, as now I had a great interest in buying and selling things, couldn't sit still for very long, was filled with grand ideas and plans, was hyperactive and somewhat agitated, and couldn't seem to stop talking. I also noticed some clearly unpleasant side effects: my senses, especially my hearing, were less acute, and I seemed less emotionally sensitive. My new doctor in Baltimore concluded that I was exhibiting symptoms of hypomania, which is a mild form of mania, and therefore I had bipolar disorder, also known as manic-depressive illness. He suggested that I should be put on a mood stabilizing drug, such as lithium, but first decided to gradually reduce and then eliminate the Zoloft, and also added a small dose of the new mood stabilizing drug, Zyprexa, which deactivates dop and ser brain receptors. The hypomania soon subsided and then, after several weeks of feeling somewhat slowed down, I crashed into a depression that was just as severe as ever.

I then decided to check myself into the Johns Hopkins Hospital (October 2000). The doctors there confirmed the diagnosis of bipolar disorder and put me back on Zoloft to bring me out of the depression, and also added the mood stabilizing drug Depakote to prevent me from becoming hypomanic. After a few weeks on Depakote, I decided I didn't like the stuff because it felt like I had been hit over the head with a hammer, so I gradually stopped taking it. I also reduced the Zoloft to a very small dose, hoping this would prevent me from becoming hypomanic. It did not because soon I was exhibiting the same hypomanic symptoms as the first time on Zoloft.

Around this time I came up with the theory that I had a super high genetic level of ser, the brain chemical that Zoloft boosts, based both on my reaction to Zoloft and information I had gleaned from Peter Kramer's classic book, *Listening to Prozac*. I reasoned that Zoloft was making me hypomanic because it was making this chemical imbalance even more extreme, and that if I instead took an antidepressant that boosts nore, a brain chemical of which I thought I had a super low genetic level, then the hypomania would not be triggered. Moreover, I reasoned that a nore boosting antidepressant, such as desipramine or nortriptyline, would not only *not* trigger hypomania, but also terminate Zoloft induced hypomania through reduction of the level of ser by nore (feedback inhibition). I ran this theory by my doctor who, though he didn't seem to believe it, was willing to let me test the theory by prescribing a small dose of nortriptyline to replace the Zoloft. Unfortunately, after several weeks on the nortriptyline it was apparent that the theory was incorrect, as I remained at least as hypomanic as on the Zoloft, though my senses seemed sharper. With this setback, I decided to follow the doctor's advice and try a low dose of the mood stabilizer lithium. Around this time, I also decided to leave graduate school with a Master's Degree and head back to Indiana.

I actually did feel a little better after the move (February 2001), though I was still somewhat hypomanic. Thinking that I might recover completely after some time in the new environment, I stopped taking the nortriptyline as well as the lithium. My new doctor prescribed a small dose of Zyprexa to quell the continuing mild hypomania, and this time on Zyprexa I noticed something new—like nortriptyline, it sharpened my senses, in contrast to the sensory deadening that Zoloft produced. However, by the middle of summer I crashed into another severe depression, much like I had after the first prolonged hypomanic episode on Zoloft in the summer of 2000. I checked myself into a hospital in Lafayette and asked the doctor to put me on a super high dose of Zyprexa, which I reasoned wouldn't make me hypomanic and may boost my low level of nore by inhibiting my high level of ser. The doctor agreed to try the massive dose, also adding Wellbutrin, which is an unusual antidepressant in that it usually does not induce hypomania.

Soon I was released from the hospital (summer 2001) even though I was still in pretty bad shape. I limped along for a few months on this pair of drugs, but the depression only lifted slightly. My doctor wanted to put me back on Zoloft, but I vetoed this in favor of the nore boosting antidepressant desipramine. I still didn't believe that I was truly bipolar, instead maintaining the theory that I had a super high level of ser and a low level of nore, and that boosting nore alone would cause the depression to lift and not make me hypomanic. Five weeks after starting on a low dose of desipramine, I weaned myself of the Wellbutrin and the massive dose of Zyprexa, viewing these drugs as no longer necessary; the depression had now lifted and I thought I was cured. Unfortunately,

after a few more weeks on desipramine I realized that the depression had given way to an unpleasant hypomania. Now, for the first time realizing that maybe I really was bipolar, I consulted the doctor and he put me back on a moderate dose of Zyprexa and kept me on the low dose of desipramine, and within a few days I was much less hypomaniac.

I spent the next year (early 2002 to early 2003) tweaking the doses of both desipramine and Zyprexa. Too much desipramine made me feel like a zombie (which I call the ‘zombie effect’) and also induced rapid, unpleasant mood cycling; too much Zyprexa caused a multi-year depression-like effect that I call the ‘brain freeze’, from which I’m still recovering. It took only a slightly higher dose of Zyprexa than I’m currently on to produce the brain freeze, and it’s possible that other drugs besides Zyprexa can cause a similar brain freeze. I was only on the higher dose of Zyprexa for three weeks, during which time I had a headache and felt tired most of the time, which I now realize were signs of the developing brain freeze, but at the time I thought these were just normal side effects of the higher dose of the drug that would soon go away. The main symptoms of the brain freeze that I first noticed were that my ability to think, remember things, and express myself were greatly impaired.

In summer 2003, I went back to graduate school at Johns Hopkins to finish my Ph.D., a testament to the partial success of my treatment. During this first year of the brain freeze, I didn’t recognize that my low energy, poor appetite, headache, and general malaise had been caused by the high dose of Zyprexa—I instead thought I was suffering from a prolonged illness of some kind. Accordingly, I visited a general practitioner (April 2004) and obtained a prescription for a potent antibiotic, Zithromax, which I took over the course of five days. Unfortunately, the Zithromax appeared to interfere with the breakdown of desipramine, because I soon became both markedly hypomaniac and ‘zombified’. The hypomania lasted about a week and then I crashed back into a significant depression, which lasted about a month. After that, something amazing happened: I got slightly hypomaniac again, but this time the characteristics of the hypomania were different and glorious. My perception of the world was altered such that everything seemed like a colored cartoon (as in Andy Behrman’s book, *Electroboy*) in which just about everything seemed thrillingly interesting and women, especially their faces, seemed much more attractive, with pretty ones looking like goddesses (I mean their actual physical appearance was different)—effects that can’t be described as merely sensory sharpening, but rather as perceptual changes. This strange and wonderful bout of hypomania, which made the whole year worth living, only lasted a few days, and then the usual, milder depressions and hypomanias returned, though I also noticed that the hypomanias now tended to be accompanied by arrhythmia (irregular heartbeat).

As summer (2004) continued, I gradually started feeling worse and then identified the cause: I had been using old desipramine that was apparently losing its potency, so I switched back to new desipramine in September. Then, once again, something amazing happened: whereas before the world seemed stale, flat, and unprofitable, it now seemed full of life and color. Once again, women looked extraordinarily beautiful, and everything else seemed inviting and extremely interesting—even though I wasn’t necessarily very hypomaniac. In other words, it was as if this is the way the world seems *all the time* to someone who isn’t depressed (or, as I’ll describe in Chapter 11, ‘expanded dysthymic’), particularly since the brain freeze was subsiding.

This wonderful effect lasted until early October, at which point I crashed into another mild depression and started sleeping a lot—at first I thought that I was sick again. But after the depression lasted a few more months, I realized that this might be a wintertime, seasonal depression, superimposed upon mood cycling. So I decided to try bright light therapy—the standard treatment for seasonal affective disorder (SAD)—with a fluorescent light box. I also remained on my previous doses of Zyprexa and desipramine. The light box produced a few unpleasant side effects: cold and shaky hands, and an upset gut—consistent with it boosting ser in the brain and throughout the rest of the body, though I didn't think so at the time—but after a few weeks of sitting in front of it for thirty minutes every morning, I began feeling better. I continued using the light box throughout the winter, and by the beginning of April (2005), my brain seemed to begin undergoing a transitional state out of the wintertime depression. By the start of May, the arrhythmia returned, which had been absent throughout the winter, accompanied by marked and unpleasant hypomania—it actually seemed more like a mixed state (which is a mixture of hypomania and depression), with mood cycling every few days. At this point I realized that the light box was probably just boosting ser, since the hypomania wasn't that much different than the Zoloft induced hypomanias of several years before, so I quit the light box cold turkey, gradually recovering over the next few months from a state of mild depression, and that gets us up to the present day (July 2005).

Typically now I'm slightly hypomanic for a day or two, slightly depressed for the next day or two, and the cycle then repeats. I've reached the conclusion that I'm on the optimal doses of both Zyprexa and desipramine, both of which have essentially no side effects, other than mild arrhythmia presumably caused by desipramine, though I expect mild mood cycling will always be present. Both during hypomanias and depressions, this combination of drugs now clearly produces sensory sharpening, increases my level of interest in most things, heightens my emotions, and affects perceptual phenomena such as women seeming more beautiful or music sounding altered in a more interesting manner—effects that I definitely perceive as positive. Just how dramatic these changes will become, particularly after the brain freeze subsides completely, remains to be seen. Even if things don't get any better, in some ways I seem to have come to life for the first time, and the Big Three drugs if used properly may essentially do the same for many other people.

Conclusions that can be drawn from this case study (in chronological order):

- 1) A person may seem to have unipolar depression rather than bipolar disorder until an antidepressant induces mania or hypomania, 'unmasking' the bipolar disorder. In retrospect, the person may realize that he had mild hypomanias, as well as depressions, before taking antidepressants, especially in the case of bipolar II disorder.
- 2) A person may have no response or a partial response to several antidepressants, while having a robust response to others. Moreover, a person can respond to one drug within a class (say, SRIs—the serotonin reuptake inhibitors, such as Prozac and Zoloft, that boost the level of ser) and not to another drug in the same class.

- 3) Just because a particular antidepressant makes a bipolar depressed person hypomanic, doesn't mean it's the right one for him (or that he should be on an antidepressant at all). Moreover, a drug that is excellent for one person may be terrible or useless for someone else.
- 4) A newer drug is not necessarily better than an older drug, both in its average effect on many people and also for a given individual.
- 5) Changing the strengths of ser or nore with drugs can alter personality traits.
- 6) In some individuals, drugs that strengthen ser may deaden the senses and emotions, whereas drugs that strengthen nore may heighten the senses and emotions. Moreover, drugs that weaken ser (such as Zyprexa) may also heighten the senses and emotions. These effects may occur most prominently when the individual has genetically strong ser and weak nore—as in my case—with the drugs serving to counteract this chemical imbalance.
- 7) Periods of hypomania or mania are typically followed by a crash into depression, with the magnitude of the depression proportional to the magnitude of the preceding hypomania or mania. So perhaps the best strategy when treating bipolar disorder with an antidepressant and a mood stabilizer is to maximize the dose of the mood stabilizer and minimize the dose of the antidepressant, in an effort to avoid pronounced hypomanias that are followed by pronounced depressions.
- 8) Very low doses of a drug can still be effective for a given person, and too high a dose of a drug can be a bad thing, since there seems to be a limit to the extent to which the brain can adjust to changes in Big Three strengths. Moreover, the effect of being on two drugs—in my case, Zyprexa and desipramine—at the same time can be different both in character and in magnitude than the effect of either drug alone. In other words, the net effect is different than the sum of the parts—what an engineer might call a 'nonlinearity'.
- 9) Adjusting the strengths of ser and nore with drugs in bipolar persons may affect the characteristics of hypomanias and depressions. Moreover, bringing the strengths of ser and nore closer to optimal, mid-range values (i.e., The Adjustment) may make the hypomanias more pleasant and depressions less unpleasant.
- 10) Without taking drugs or even while taking the existing drugs, bipolar (especially bipolar II) persons may always experience mood cycling. The best treatment strategy may be to use the existing drugs to minimize the magnitude—though not necessarily the frequency—of the hypomanias and depressions.
- 11) Mania/hypomania and perhaps depression, whether influenced by drugs or not, may produce perceptual changes, such as altering the physical appearance of other people.

12) Heart pain or arrhythmia may be indicative of systemic nore changes; gut malfunctioning—and possibly cold hands, given the effect of ser on smooth muscle tissue such as that which lines blood vessels—may be indicative of systemic ser changes.

13) A change of scenery, activities, friends, even significant other, probably won't stop overt mental illness—these things may help coping, however.

14) Zyprexa may be anti-Zoloft in that these drugs may have opposing effects; more generally, atypical antipsychotics such as Zyprexa may be anti-SRI.

15) The 'brain freeze' may have been specific to ser, nore, or dop, or some combination of the three, including adjusting ser and nore in opposite strength directions with drugs.

16) If bright light therapy boosted nore and the nore strength had not dropped during the wintertime, it should have produced a zombie effect in me, but it did not. Moreover, I had no arrhythmia during the wintertime. Both of these observations are consistent with my wintertime depression being caused by a decrease in nore strength.

17) It was as if the brain freeze, or more generally depression itself, affects a number of perceptual traits simultaneously, such as sensory perception, rate and subject matter of thought, emotion, mood, drive states such as hunger and thirst, memory, and sexual potency—integrated in the brain in some as yet undiscovered manner (in other words, a 'neural integrator'). The basis for the neural integrator could be common input from the Big Three transmitters to multiple brain areas, or a single brain area interconnected with many other areas. More generally, the neural integrator may exist in every brain, whether the person suffers from overt mental illness or not.

18) It's possible for a given individual to become much better than well by adjusting ser and nore closer to mid-range, optimal strengths (i.e., The Adjustment).