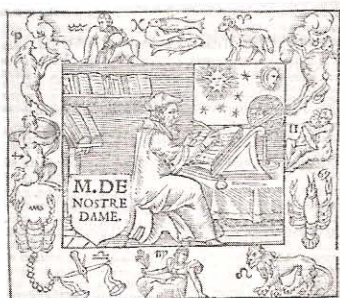


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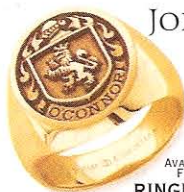
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## MEDICAL DISPATCH

**WHAT'S NORMAL?***The difficulty of diagnosing bipolar disorder in children.*

BY JEROME GROOPMAN

In April, 2000, Steven Hyman, a psychiatrist who at the time was the director of the National Institute of Mental Health, convened a meeting of nineteen prominent psychiatrists and psychologists in order to discuss bipolar disorder in children. The disorder has long been recognized as a serious psychiatric illness in adults, characterized by recurring episodes of mania and depression. (It is sometimes called manic depression.) People with bipolar disorder are often unable to hold down jobs; require lifelong treatment with powerful medications, many of which have severe side effects; and have high suicide rates. The disorder is thought to afflict between one and four per cent of Americans and tends to run in families, although no genes for it have been identified. At the time of the meeting, few children had been given a diagnosis of the illness, and it was considered to begin, typically, in adolescence or early adulthood.

In the late nineteen-nineties, however, there was an increase in awareness of bipolar disorder in children, first in medical journals and then in places like BPParents, a Listserv founded by the mother of an eight-year-old boy who had been diagnosed with the disorder. Hyman himself had been consulted by parents of children who, he told me, were "really suffering and extremely disruptive, having violent outbursts at school and at home, and hard to contain under any circumstances." Many of the parents told Hyman that they believed their child had bipolar disorder, and they cited a book called "The Bipolar Child: The Definitive and Reassuring Guide to Childhood's Most Misunderstood Disorder." The book, which was written by Demetri Papolos, a psychiatrist affiliated with the Albert Einstein College of Medicine, in New York City, and his wife, Janice, the author of several how-to manuals, had been published in 1999. (It has sold more than 200,000 copies, and a third edition came out last sum-

mer.) "The first parents who visited me came with the Papolos book in hand," Hyman said.

The Papoloses argued that bipolar disorder was often overlooked in children. In 1998, according to "The Bipolar Child," nearly four million children were given Ritalin or other stimulants for hyperactivity; of that number, the Papoloses contended, more than a million would eventually receive a bipolar diagnosis. They also cited researchers' estimates that anywhere from a third to half of the 3.4 million children thought to suffer from depression were actually experiencing the early onset of bipolar disorder. The book detailed the negative effects of bipolar disorder on patients (disruptive behavior, drug abuse, suicide attempts) but also prominently featured what might be described as its paradoxical benefits:

This illness is as old as humankind, and has probably been conserved in the human genome because it confers great energy and originality of thought. People who have had it have literally changed the course of human history: Manic-depression has afflicted (and probably fueled the brilliance of) people like Isaac Newton, Abraham Lincoln, Winston Churchill, Theodore Roosevelt, Johann Goethe, Honoré de Balzac, George Frederic Handel, Ludwig von Beethoven, Robert Schumann, Leo Tolstoy, Charles Dickens, Virginia Woolf, Ernest Hemingway, Robert Lowell, and Anne Sexton.

(These claims are similar to those made about other serious psychiatric disorders, particularly depression.)

The Papoloses' research was based on responses to questionnaires that they distributed through BPParents, whose several hundred members are parents who suspect that their children have the disorder. "These children seem to burst into life and are on a different time schedule from the rest of the world right from the beginning," the Papoloses wrote. "Many are extremely precocious and bright—doing everything early and with gusto. They seem like magical children, their creativity can be astound-



ing, and the parents speak about them with real respect, and sometimes even awe." The book included some parents' observations:

She was always ahead of her time. She started talking at eight months with the words "kitty cat." She walked at nine months and was speaking in complete sentences by a year. She was writing small novels in the second grade. She acted and danced and sang way beyond her years.

At eighteen months he climbed out of the baby bed in the middle of the night, opened the fridge, got out three dozen eggs (it was Easter time), and proceeded to sit in his booster chair and crack three dozen eggs onto our hardwood floors. (He wanted to bake a real cake—he didn't like the toy mixing bowl I had given him to play with.) After the insurance company quit laughing they did pay to refinish our floors.

During the meeting at the N.I.M.H., the psychiatrists and psychologists argued about whether bipolar disorder existed in children, and, if it did, how it could be distinguished from other syndromes affecting mood and behavior, such as attention-deficit hyperactivity disorder (A.D.H.D.) and autism. One psychiatrist, Barbara Geller, a professor at Washington University, in St. Louis, had published articles about children whose moods often fluctuated rapidly. In the course of a single day, the children were extremely sad, even suicidal, and then, suddenly, they became elated and "grandiose"—a term that psychiatrists use to mean an inflated sense of one's abilities. Geller believed that some of these children who matched several specific and narrow criteria had bipolar disorder. Joseph Biederman, a child psychiatrist at Massachusetts General Hospital, in Boston, who also attended the meeting, had treated children suffering from extreme symptoms of irritability and aggressive behavior and, often with a colleague, Janet Wozniak, had published several articles in medical journals asserting that these children met the criteria for bipolar disorder described in the *Diagnostic and Statistical Manual of Mental Dis-*

*orders (D.S.M.-IV)*, the reference book for psychiatric illnesses. Hyman encouraged the group to arrive at a consensus, in part to create a uniform set of criteria that could be used to enroll children in studies of the disorder.

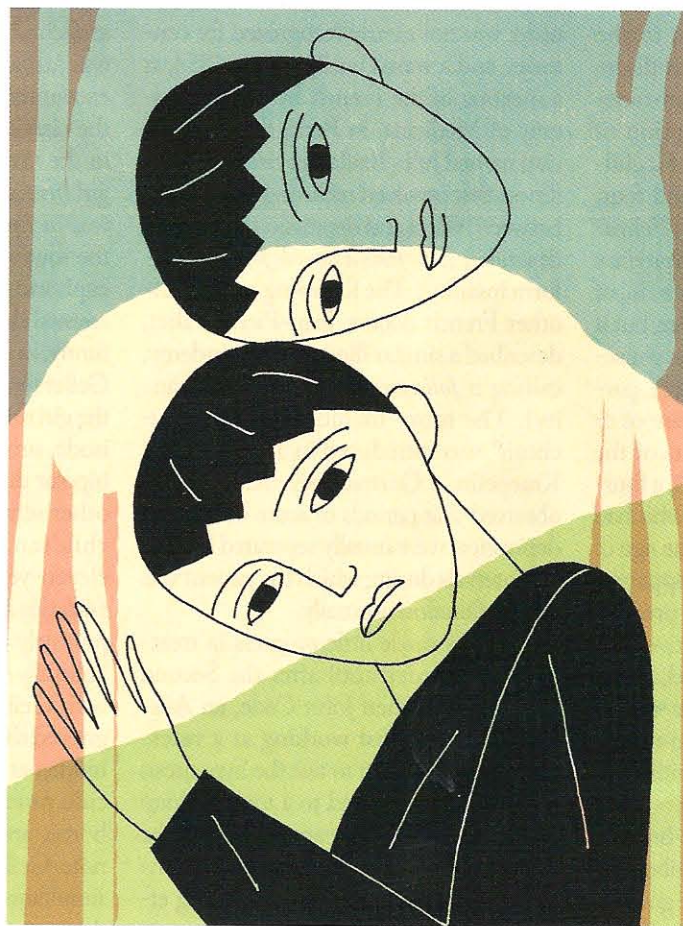
In August, 2001, the results of the meeting were published in the *Journal of the American Academy of Child and Adoles-*

of behaviors—adapted from the Papoloses' book—that was intended to help parents "recognize some warning signs" of the disorder. Among those were "poor handwriting," "complaints of being bored," "is very intuitive or very creative," "excessively distressed when separated from family," "has difficulty arising in the A.M.," "elated or silly, giddy mood states," "curses viciously in anger," and "intolerant of delays." The magazine also published a sidebar listing prominent writers and musicians who may have suffered from bipolar disorder, including Lord Byron, Edgar Allan Poe, and Kurt Cobain. Although the article cited external factors such as stress and drug use, it also noted that the disorder is "hugely familial," as one doctor put it. (One mother, who was afflicted with bipolar disorder, claimed that she knew before her son was born that he would be bipolar, because he was restless even in the womb.)

Not long after the article came out, a research team at Massachusetts General Hospital, led by Biederman and Wozniak, began an eight-week comparative study of the antipsychotic drugs olanzapine (marketed under the name Zyprexa) and risperidone (Risperdal) for thirty-one children between the ages of four and six who had been given a di-

agnosis of bipolar disorder based on *D.S.M.* criteria. During the trial, the children gained an average of six pounds and experienced sharp increases in prolactin, a pituitary hormone, which, when elevated, might interfere with sexual development. But their symptoms of severe irritability and aggression were markedly muted by the treatment, and the researchers, while noting the adverse effects, concluded that the drugs could be beneficial to bipolar children.

There are few reliable statistics on the incidence of pediatric bipolar disorder, but according to a national study of community-hospital discharge records, led by Brady Case, a research assistant professor of psychiatry at New York University and



*Is it possible to make a bipolar diagnosis before adolescence?*

*cent Psychiatry*, and it was concluded that "bipolar disorder exists and can be diagnosed in prepubertal children," though the article went on to say that not all children who appeared to have the disorder satisfied the *D.S.M.* criteria. The vagueness of the definition offered few guidelines for practical diagnosis.

Meanwhile, articles inspired by the Papoloses' book had begun appearing in newspapers and magazines, promoting the idea that there was a new diagnosis for troubled children. In August, 2002, *Time* published a cover story titled "Young and Bipolar," with the tagline "Once Called Manic Depression, the Disorder Afflicted Adults. Now It's Striking Kids. Why?" The article featured a list



a child-psychiatry fellow at Bradley Hospital, in Providence, the percentage of mentally ill children under eighteen who have been given a diagnosis of the disorder increased more than fourfold between 1990 and 2000. Many doctors fear that the media, in drawing attention to bipolar disorder, may have exaggerated its prevalence in children and presented a misleading picture of the disorder. The situation has some similarities to the overdiagnosis of attention-deficit disorder in the first half of the nineteen-nineties, during which the prescription of stimulants such as Ritalin tripled for children between the ages of two and four, according to a study published in February, 2000, in the *Journal of the American Medical Association*. Some children do, of course, suffer from bipolar disorder, but it is important to recognize that the consequences of its treatment can be dire, particularly when parents are unaware of or ignore the dangerous side effects of the medications. In December, 2006, a four-year-old girl in Massachusetts, who had received a bipolar diagnosis at the age of two and a half, died from an apparent overdose of Clonidine, a blood-pressure medicine used to sedate hyperactive children. She was also taking Seroquel, an antipsychotic, and Depakote, an anti-seizure medication that helps regulate mood. (Her parents have been charged with murder and have pleaded not guilty.)

"The diagnosis has spread too broadly, so that powerful drugs are prescribed too widely," Hyman told me. "We are going to have hell to pay in terms of side effects."

One of the earliest accounts of bipolar disorder comes from Aretaeus the Cappadocian, a Greek physician who was believed to have practiced in Alexandria and Rome in the second century

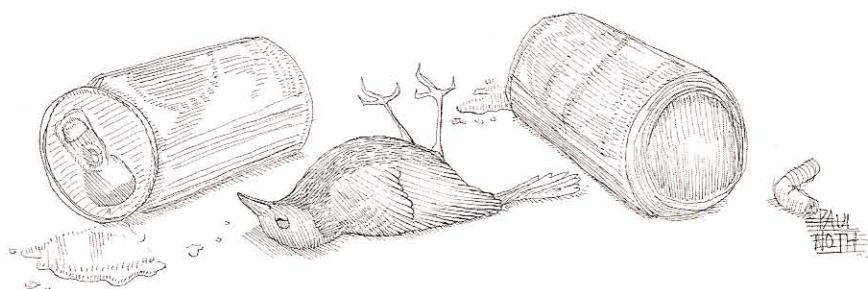
A.D. He wrote of the afflicted, "They are prone to change their mind readily; to become base, mean-spirited, illiberal, and in a little time, perhaps, simple, extravagant, munificent, not from any virtue of the soul, but from the changeableness of the disease. But if the illness becomes more urgent, hatred, avoidance of the haunts of men, vain lamentations; they complain of life, and desire to die." However, the disorder was not clearly recognized for centuries, and it wasn't until January, 1854, at a meeting of the French Imperial Academy of Medicine, in Paris, that a physician named Jules Baillarger cited a mental illness that involved recurring oscillations between mania and depression. Baillarger described it as *folie à double forme* (dual-form insanity). The following month, another French doctor, Jean-Pierre Falret, described a similar illness to the academy, calling it *folie circulaire* (circular insanity). The term "manic-depressive psychosis" was introduced in 1896 by Emil Kraepelin, a German psychiatrist, who observed that periods of acute mania and depression were usually separated by longer intervals during which the patient was able to function normally.

Doctors made little progress in treating the disorder until after the Second World War, when John Cade, an Australian psychiatrist working at a veterans' hospital, set out to test the hypothesis that mania was related to a toxic buildup of urea in the bloodstream. By chance, he discovered that the lithium urate he injected into guinea pigs had a calming effect. After testing lithium carbonate on himself, he began administering it to his manic patients. It became the first successful drug therapy for a psychiatric disorder. (Lithium remained the only treatment for bipolar disorder for decades, and is still the most prevalent, but in re-

cent years anticonvulsants and some antipsychotics have also proved effective.) In 1980, the term "bipolar disorder" replaced "manic-depressive disorder" as a diagnostic term in the *D.S.M.*, but it was applied only to teen-agers and adults.

"Until about ten years ago, it was considered quackery to talk about bipolar disorder in children," Barbara Geller told me. "The overwhelming number of adult and child psychiatrists believed that this was just a hyperactive child." Geller first encountered a child she believed exhibited the classic symptoms of bipolar disorder in the early nineties, a thirteen-year-old girl from a white middle-class family who was in the juvenile-correction system in the southern United States. The girl was euphoric despite her incarceration. "She seemed elated, grandiose, and infectiously funny, in spite of being in reform school," Geller recalled. Geller wondered whether the girl might be experiencing a manic episode, similar to those seen in adults with bipolar disorder. She began to interview other school-age and young adolescent children, seeking similar cases. One eleven-year-old girl harbored romantic fantasies about her teacher that led her to routinely disrupt class. She was also "delightfully euphoric" in an interview session with Geller, but as the questioning progressed she said that she had a loaded gun hidden at home, and had prepared a suicide note. Her parents searched their home, and found both the gun and the note. Geller was struck by the young girl's simultaneous grandiosity and depression; the two states are hallmarks of adult bipolar disorder, but they are rarely seen in such quick succession.

Geller found that the manner in which symptoms appeared in children with bipolar disorder was significantly different from that of most adults who had the illness. The episodes of mania and depression in most adults tend to subside after a few weeks or several months; children's episodes generally last longer, and cycle on a daily basis through a more extreme set of moods. "We have these kids who look so sad it hurts to watch them. And a moment later it looks like they've had a snort of coke," Geller said. "For four hours, they will be high: they are giggling, they are laughing, they are hypersexual, they want to touch the teacher, they want to undress in church, they talk too much, they sleep too little, and they think they are in charge



THE FIRST ROBIN OF SPRING BREAK



of things. Then they switch. In the same day, they can suddenly become suicidal and depressed."

In 1995, with a grant from the N.I.M.H., Geller began a longitudinal study of three groups of children: those she had diagnosed as having bipolar disorder, using more precise categorical criteria than those specified in the *D.S.M.*; those with attention-deficit hyperactivity disorder; and a control group of children who had no known behavioral disorders. There were about ninety subjects in each group, and the average age was ten. Based on interviews with their parents and close relatives, Geller and her colleagues found that adult bipolar disorder was relatively common in the family members of the children who suffered from the disorder but not in those who had A.D.H.D., or those in the control group. Geller concluded that there is a strong genetic basis for bipolar disorder in children, and that, among those diagnosed as having the disorder, more than eighty per cent might also have A.D.H.D.

Experts now agree that bipolar disorder can occur in children, but there is disagreement about which symptoms clearly indicate a diagnosis. Geller maintains that inappropriate euphoria and grandiose behavior must accompany symptoms of irritability or depression. Biederman and Wozniak contend that extreme irritability, including aggression, should compel a clinician to consider a diagnosis of pediatric bipolar disorder, in keeping with *D.S.M.* criteria. However, Ellen Leibenluft, who heads the pediatric bipolar-disorder research program at the N.I.M.H., told me that there is no certain way to classify even severe irritability as normal versus aberrant, particularly as children develop. Geller uses the analogy of sore throats: "Strep infection causes sore throat, but only five per cent of all sore throats are due to strep, and ninety-five per cent are due to viruses. Irritability is akin to the symptom of a sore throat: children with bipolar disorder are extremely irritable, but they comprise only a small subset of all irritable children."

Despite these differences, most researchers use the *D.S.M.* criteria as a guideline. Demetri Papolos, however, argues against applying these categorical

criteria, saying that their vagueness can cause confusion. "The diagnostic category in and of itself doesn't really capture the condition," he said. He prefers to make a diagnosis based on whether a patient's behavior matches the "core phenotype" he has developed, which includes mania and depression, among several other symptoms. "Once you see what this"—pediatric bipolar disorder—"looks like, you can't

mistake it," he told me. "They call it the View. If you have the View, you get it. It's not apocalyptic, it's a very clear picture." Papolos, who is not a child psychiatrist, said that he has had children referred to him from all over the country, as many as two a week in the past seven years. He could not immediately recall any child in this group who did not have a bipolar diagnosis, because, he said, "the people who come to see me have read the book."

The need to establish diagnostic criteria is particularly urgent because many of the drugs given to bipolar children are relatively new and have not been tested extensively, especially in children. Depakote, the most common brand name for valproate, is an anti-seizure medication for adults and children over the age of ten, which is also used to treat acute mania in adults; it can cause obesity and diabetes and has been associated with polycystic ovarian disease. The antipsychotic drug Risperdal can result in involuntary distorted movements, or "tardive dyskinesia." Lithium can cause decreased thyroid function and kidney failure. "Most important, we don't understand their long-term effects on the developing brain," Geller said. Failing to correctly diagnose pediatric bipolar disorder has its own dangers, since treating a bipolar patient with a selective serotonin reuptake inhibitor like Paxil or Zoloft, as if he were simply depressed, or with a stimulant like Ritalin, as if he had A.D.H.D., might worsen his symptoms. Like other serious psychiatric illnesses, bipolar disorder is diagnosed largely by observing the patient's behavior. There is no blood test, or other clinical diagnostic tool, for the disorder; although brain scans have been performed on children who have been given the diagnosis, none have shown a definitive pattern.

Some books and articles on bipolar



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disorder in children and adolescents have suggested that a positive response to a drug like Risperdal, which can be effective in adults with manic bipolar disorder, indicates that the child is bipolar. In fact, the drugs typically given to bipolar children are what doctors call "nonspecific," which means that their apparent efficacy is not diagnostic of the syndrome. "All the medicines that work in bipolar cases also work in kids who are just aggressive," Geller said. "Children with mental retardation who acted aggressively were treated with drugs like lithium, and it helped to mute their behavior. But it also made them very thirsty, so they started drinking from toilet bowls and engaging in other kinds of unsuitable behavior. The contention that treatment with these drugs 'makes' the diagnosis is frightening—and completely untrue."

In January, 2007, the American Academy of Child and Adolescent Psychiatry published a paper to guide clinicians in their assessment and treatment of children and adolescents with bipolar disorder. The paper cited a survey of members of the Illinois-based Child & Adolescent Bipolar Foundation, in which twenty-four per cent of the children from eight hundred and fifty-four families who had been given a diagnosis of bipolar disorder were between the ages of zero and eight. (A more recent survey conducted by the foundation puts the number at fifteen per cent.) "The validity of diagnosing bipolar disorder in preschool children has not been established," the academy's paper noted. "Until the validity of the diagnosis is established in preschoolers, caution should be taken before making the diagnosis in anyone younger than age six. The evidence is not yet sufficient to conclude that most presentations of juvenile mania are continuous with the classic adult disorder." Biederman and Wozniak have given the diagnosis to preschool children and have included them in drug trials. But other experts, Geller and Leibenluft among them, contend that bipolar disorder cannot yet be accurately diagnosed in a child younger than six, because there is currently no consensus on what constitutes aberrant behavior at that age. In addition, they say, symptoms of manic behavior must be elicited through an interview not only with the parents but also with the children themselves; those

younger than six may lack the language to describe what they are experiencing.

In the early nineties, in an effort to insure that children were receiving the correct diagnosis, Geller established a second-opinion clinic for bipolar disorder at Washington University. "Following the publication of the Papoloses' book, we began to have a greater influx of people into the clinic," she said. The positive effect of the book, she added, was that "parents realized it was O.K. to take their kids to a child psychiatrist." At the same time, the book could lead to false diagnoses. Geller went on, "In the clinic, the first question we have learned to ask of parents is 'Have you read the Papoloses' book?' And 'What in the book resembles your child?' And we will get answers like 'My child is irritable and he likes sweets.'" Geller's team developed stringent criteria to characterize mania as abnormal elation and grandiosity—such as inappropriate bouts of extreme giddiness, or hyperbolic statements of one's importance or ability—so that irritability alone was not adequate to establish a diagnosis of bipolar disorder. Many parents, she said, cling to a bipolar diagnosis when, in fact, the child is suffering from an autistic developmental disorder: "Wouldn't you rather have

your child grow up to be Ted Turner," who has bipolar disorder, "than Rain Man?"

April Prewitt, a child psychologist who trained at Harvard and practices in Lexington, Massachusetts, also spends a good deal of time "undiagnosing" children who have been told they are bipolar. In the past three years, Prewitt says, she has seen thirty children and adolescents diagnosed as having bipolar disorder. In her opinion, only two had the malady. "It has become a diagnosis du jour, as A.D.H.D. was five years ago," Prewitt told me. "Not only is the diagnosis being made incorrectly but it's being made in younger and younger children." She said that parents routinely arrive at her office with the Papolos book, and with lists of behaviors like the one featured in *Time*. "Each one of these could be behaviors due to something completely different," she said. "I could score twenty on this list on a bad day."

Prewitt recalled a seven-and-a-half-year-old boy she saw, who lived in an affluent Boston suburb. Max (a pseudonym) had trouble concentrating and was refusing to go to school. His pediatrician had diagnosed bipolar disorder and begun treating him with Risperdal and Seroquel. "It turned out that the diagnosis was 'a divorce situation,'" Prewitt said. Max's par-

## LINCOLN'S DREAM

It is impossible to state just how in love I am  
with my own body, the white snows of me,  
the sudden involutions and crevasses of me,  
my muscles tensed or slack in anger or fear.

This is why, wherever I go, I am in Lincoln's dream.  
A sentry stands by, the stairway is eerily lit,  
light is a little milk splash on people's faces,  
the faces of my Cabinet, grotesque and funny masks.

*Who is dead in the White House?* I demand. *Who's not?*  
answers a soldier, pointing to a shrouded head  
on my own body, encased like a gangly insect  
on the catafalque, and the loud sobs wake me up.

Reader, when you caress yourself in the morning,  
amazed that you are made the way you are,  
sure that yours is the finest body of all,  
remember, you are Lincoln having Lincoln's dream.

—Dan Chiasson



ents had separated and were undergoing bitter divorce negotiations. "Max had put on twenty pounds because of the medication, while he was being shuttled back and forth, one week with mom and one week with dad." Prewitt believed that the parents' feuding was causing Max to oscillate between being sullen and withdrawn and aggressive and hyperactive. She recommended that Max be evaluated by a neuropsychologist, who found that he had only some minor attention deficits. During the following six months, his parents went into mediation in an effort to settle their divorce more amicably, and Max was weaned off his medications.

Prewitt maintains that it may not be possible to diagnose bipolar disorder with certainty in a preadolescent child. "After all these years, I am not sure of the diagnosis of bipolar disorder until a child is well into adolescence," she told me. "I've never seen a seven- or eight-year-old that I would be comfortable definitively diagnosing with bipolar disorder. The changes that children undergo, both in the biology of their development and in the need to adapt to changes in environment at home and at school—interactions with parents, siblings, and other children—all can trigger behaviors with rapid and wild swings of mood."

Phillip Blumberg, a psychotherapist in Manhattan, told me, "Psychological diagnosis is, in essence, a story. If you have a mood disorder, there is the fear, the shame, and the confusion—the stigma—associated with it, so you want to grab on to the most concrete and clear story you can. There is something about the clarity of bipolar disease, particularly its biological basis, which is incredibly soothing and seductive."

Blumberg, who for two years was a vice-president at ABC Motion Pictures, believes that advertising by pharmaceutical companies has influenced the public's view of bipolar disorder. (Eli Lilly, in particular, has come under fire for its marketing practices. The drug company is currently the subject of lawsuits that claim that the company attempted to hide Zyprexa's side effects, and promoted the drug for off-label uses. Lilly has denied the accusations.) Blumberg described recent ads, for drugs like Zyprexa, that include a list of symptoms characteristic of the disorder. "But, of course, we all have

these symptoms," he said. "Sometimes we're irritable. Sometimes we're excited and elated, and we don't know why. With every form of advertising, the first goal is to make people feel insecure. Usually, they are made to feel insecure about their smell or their looks. Now we are beginning to see this in psychiatric advertising. The advertisements make frenetic, driven parents feel insecure about the behavior of their children."

Blumberg noted that he had seen instances of the disorder in some children, and that it was a real and serious diagnosis. But he also cited the mounting pressure on children, particularly in the middle and upper classes, to succeed, first at private or selective public schools, and then at exclusive colleges and universities. "These kids become very well turned-out products," he said. "They live to have résumés. They don't have résumés because they live." Parents may fear that children who behave in an eccentric way are at a disadvantage, and in turn pressure the pediatrician or the psychiatrist to come up with a diagnosis and offer a treatment. "Then an industry grows up around it. This, then, enters as truth in the popular imagination."

The debate over pediatric bipolar disorder will likely extend to the next edition of the *Diagnostic and Statistical Manual of Mental Disorders*. "D.S.M. always has an out in its definitions, a category called N.O.S.—'not otherwise specified,'" Steven Hyman said. "The problem with describing a kid who is up-and-down and irritable and sullen and wild and then grandiose is that he could indeed be rapidly cycling between mania and depression, but it could be an awful lot of other things, too. Bipolar disorder in children represents the intersection of two great extremes of ignorance: how to best treat bipolar disorder and how to treat children for anything. It's really important that we define the kids with bipolar disorder and treat them, but it's also important that we not begin to diagnose kids with excess exuberance or moodiness as having the disease. We have to realize that we are risking treating children who could turn into obese diabetics with involuntary movements. There is something very real about the kids with devastating and disruptive symptoms, but the question is still the boundaries. You can do more harm than good if you treat the wrong kid." ♦

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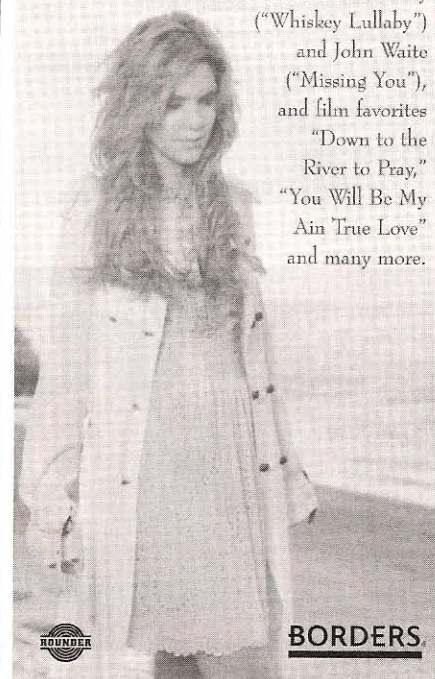
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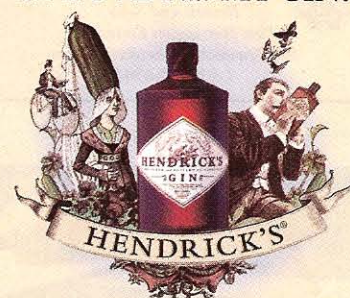
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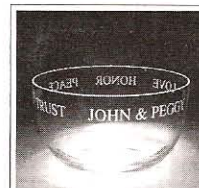
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