Once called manic depression, the disorder afflicted adults. Now it's striking kids. Why?

It wasn't every day that Patricia Torres raced down the streets of Miami at 70 m.p.h. But then it wasn't every day that her daughter Nicole Cabezas hallucinated wildly, trying to jump out of the car, pulling off her clothes and ranting that people were following her, so this seemed like a pretty good time to hurry. Nicole, 16, had been having problems for a while now--ever since she was 14 and began closeting herself in her bedroom, incapable of socializing or doing her schoolwork, and contemplating suicide.

The past few months had been different, though, with the depression lifting and an odd state of high energy taking its place. Nicole's thoughts raced; her speech was fragmented. She went without sleep for days at a time and felt none the worse for it. She began to suspect that her friends were using her, but that was understandable, she guessed, since they no doubt envied her profound gifts. "I was the center of the universe," she says quietly today. "I was the chosen one."

Finally, when the chosen one was struck by violent delusions--the belief that she had telekinetic powers, that she could change the colors of objects at will--Torres decided it was time to take Nicole to the hospital. Emergency-room doctors took one look at the thrashing teenager, strapped her to a gurney and began administering sedatives. She spent two weeks in the hospital as the doctors monitored her shifting moods, adjusted her meds and talked to her and her parents about her descent into madness. Finally, she was released with a therapy plan and a cocktail of drugs. Six months later, doctors at last reached a diagnosis: she was suffering from bipolar disorder.

While emotional turmoil is part of being a teenager, Nicole Cabezas is among a growing cohort of kids whose unsteady psyches do not simply rise and fall now and then but whipsaw violently from one extreme to another. Bipolar disorder--once known as manic depression, always known as a ferocious mental illness--seems to be showing up in children at an increasing rate, and that has taken a lot of mental-health professionals by surprise. The illness until recently was thought of as the
rare province of luckless adults--the overachieving businessman given to sullen lows and impulsive highs; the underachieving uncle with the mysterious moods and the drinking problem; the tireless supermom who suddenly takes to her room, pulls the shades and weeps in shadows for months at a time.

But bipolar disorder isn't nearly so selective. As doctors look deeper into the condition and begin to understand its underlying causes, they are coming to the unsettling conclusion that large numbers of teens and children are suffering from it as well. The National Depressive and Manic-Depressive Association gathered in Orlando, Fla., last week for its annual meeting, as doctors and therapists face a daunting task. Although the official tally of Americans suffering from bipolar disorder seems to be holding steady--at about 2.3 million, striking men and women equally--the average age of onset has fallen in a single generation from the early 30s to the late teens.

And that number doesn't include kids under 18. Diagnosing the condition at very young ages is new and controversial, but experts estimate that an additional 1 million preteens and children in the U.S. may suffer from the early stages of bipolar disorder. Moreover, when adult bipolars are interviewed, nearly half report that their first manic episode occurred before age 21; 1 in 5 says it occurred in childhood. "We don't have the exact numbers yet," says Dr. Robert Hirschfeld, head of the psychiatry department at the University of Texas in Galveston, "except we know it's there, and it's underdiagnosed."

If he's right, it's an important warning sign for parents and doctors, since bipolar disorder is not an illness that can be allowed to go untreated. Victims have an alcoholism and drug-abuse rate triple that of the rest of the population and a suicide rate that may approach 20%. They often suffer for a decade before their condition is diagnosed, and for years more before it is properly treated. "If you don't catch it early on," says Dr. Demitri Papolos, research director of the Juvenile Bipolar Research Foundation and co-author of The Bipolar Child (Broadway Books, 1999), "It gets worse, like a tumor." Heaping this torment on an adult is bad enough; loading it on a child is tragic.

Determining why the age-of-onset figures are in free fall is attracting a lot of research attention. Some experts believe that kids are being tipped into bipolar disorder by family and school stress, recreational-drug use and perhaps even a collection of genes that express themselves more aggressively in each generation. Others argue that the actual number of sick kids hasn't changed at all; instead, we've just got better at diagnosing the illness. If that's the case, it's still significant, because it means that those children have gone for years without receiving treatment for their illness, or worse, have been medicated for the wrong illness. Regardless of the cause, plenty of kids are suffering needlessly. "At least half the people who have this disorder don't get treated," says Dr. Terrence Ketter, director of the bipolar disorder clinic at Stanford University.

Yet scientists are making progress against the disease. Genetic researchers are combing through gene after gene on chromosomes that appear to be related to the condition and may offer targets for drug development. Pharmacologists are perfecting combinations of new drugs that are increasingly capable of leveling the manic peaks and lifting the disabling lows. Behavioral and cognitive psychologists are developing new therapies and family-based programs that get the derailed brain back on track and keep it there. "We did a good job for a long time of putting a lid on [the disorder]," says Dr. Paul Keck, vice chairman of research at the University of Cincinnati College of Medicine. "Now the goal is to completely eradicate the symptoms."

For Lynne Broman, 37, of Los Angeles, just taming the disorder would be more than enough. A single mom, she is raising three children, two of whom--Kyle, 5, and Mary Emily, 2--are bipolar. At the moment it's Kyle who is causing the most trouble. He has been expelled from six preschools and two day-care centers in his short academic career and has made a shambles of their once tidy home. Kyle was hospitalized for violent outbursts at age 4 and still has periods when he goes almost completely feral. He once threw a butcher knife at his mother, nearly striking her before she ducked out of the way. "That day started out fine," Broman says, "but he turned on me like a rabid dog."
Until quite recently, a child who behaved like this would have been presumed to have either attention-deficit/hyperactivity disorder (ADHD) or oppositional defiant disorder. Bipolar would not even have been considered. And with good reason: the classic bipolar profile, at least as it appears in adults, is almost never seen in kids.

Most bipolar adults move back and forth between depressions and highs in cycles that can stretch over months. During the depressive phase, they experience hopelessness, loss of interest in work and family, and loss of libido—the same symptoms as in major (or unipolar) depression, with which bipolar is often confused. The depressive curtain can descend with no apparent cause or can be triggered by a traumatic event such as an accident, illness or the loss of a job.

But in bipolar disorder, there is also a manic phase. It usually begins with a sort of caffeinated, can-do buzz. "Sometimes the patients find the highs pleasant," says Dr. Joseph Calabrese, director of the mood-disorders program at Case Western University in Cleveland. As the emotional engine revs higher, however, that energy can become too much. Bipolars quickly grow aggressive and impulsive. They become grandiose, picking fights, driving too fast, engaging in indiscriminate sex, spending money wildly. They may ultimately become delusionally mad.

With kids, things aren't nearly so clear. Most children with the condition are ultra-rapid cyclers, flitting back and forth among mood states several times a day. Papolos, who co-wrote The Bipolar Child, studied 300 bipolar kids ages 4 through 18, and he believes he has spotted a characteristic pattern. In the morning, bipolar children are more difficult to rouse than the average child. They resist getting up, getting dressed, heading to school. They are either irritable, with a tendency to snap and gripe, or sullen and withdrawn.

By midday, the darkness lifts, and bipolar children enjoy a few clear hours, enabling them to focus and take part in school. But by 3 or 4 p.m., Papolos warns, "the rocket thrusters go off," and the kids become wild, wired, euphoric in a giddy and strained way. They laugh too loudly when they find something funny and go on long after the joke is over. Their play has a flailing, aggressive quality to it. They may make up stories or insist they have superhuman abilities. They resist all efforts to settle them and throw tantrums if their needs are denied. Such wildness often continues deep into the night—which accounts in part for the difficulty they have waking up in the morning. "They're like Dr. Jekyll and Mr. Hyde," says Papolos, "which is how their parents describe them."

Preverbal toddlers and infants cannot manifest the disorder so clearly, and there is no agreement about whether they exhibit any symptoms at all. However, many parents of a bipolar say they noticed something off about their baby almost from birth, reporting that he or she was unusually fidgety or difficult to soothe. Broman insists she knew her son Kyle was bipolar even when he was in the womb. "This child never slept inside," she says. "He was active 24 hours a day."

For Broman, making that diagnosis may not have been hard since the condition, as Ketter puts it, "is hugely familial." Broman herself is bipolar, though her illness was not diagnosed until adulthood. Children with one bipolar parent have a 10% to 30% chance of developing the condition; a bipolar sibling means a 20% risk; if both parents are bipolar, the danger rises as high as 75%. About 90% of bipolars have at least one close relative with a mood disorder.

For all that, when the disorder does appear in a child, the diagnosis is often wrong. ADHD is the likeliest first call, if only because some of the manic symptoms fit. The treatment of choice for ADHD is Ritalin, a stimulant that has the paradoxical ability to calm overactive kids. But giving Ritalin to a bipolar child can deepen an existing cycle or trigger one anew. Brandon Kent, a 9-year-old from La Vernia, Texas, in whom ADHD was diagnosed in kindergarten (they did not yet know he was bipolar), took Ritalin and paid the price. "It sent him into depression," says his mother Debbie Kent. "Within a couple of months, he was flat on the couch and wouldn't move." By some estimates, up to 15% of children thought to have ADHD may actually be bipolar.

Similar misdiagnoses are made when parents and doctors observe symptoms of the low phase of
the bipolar cycle and conclude that a kid is suffering from simple depression. Treat such a child with antidepressants like Prozac, however, and the rejiggering of brain chemistry may trigger mania. Some researchers believe that nearly half of all children thought to be depressed may really be bipolar.

For most kids, the consequences of not identifying the illness can be severe, since the bipolar steamroller gets worse as children get older. Though they tend to be verbally skilled and are often creative, bipolars find school difficult because the background noise of the disorder makes it hard for them to master such executive functions as organizing, planning and thinking problems through. The most serious symptoms may appear when kids reach age 8, just when the academic challenge of grade school starts to be felt. "They're being asked to do things that they're very poor at," Papolos says, "and it's a blow to their self-esteem." If school doesn't kick the disorder into overdrive, puberty often does, with its rush of hormones that rattle even the steadiest preteen mind.

Still, all these natural stressors and the new awareness of the disorder may not be enough to account for the explosion of juvenile bipolar cases. Some scientists fear that there may be something in the environment or in modern lifestyles that is driving into a bipolar state children and teens who might otherwise escape the condition.

One of the biggest risk factors is drugs. People with a genetic predisposition to bipolar disorders live on an unstable emotional fault line. Jar things too much with a lot of recreational chemistry, and the whole foundation can break away, especially when the drugs of choice are cocaine, amphetamines or other stimulants. "We do think that use of stimulating drugs is playing a part in lowering the age of onset," says Hirschfeld.

Stress too can light the bipolar fuse. Many latent emotional disorders, from depression to alcoholism to anxiety conditions, are precipitated by life events such as divorce or death or even a happy rite of passage like starting college. And bipolar disorder can also be set off this way. "Most of us do not think environmental stress causes the disorder," says Dr. Michael Gitlin, head of the mood-disorders clinic at UCLA. "But it can trigger it in people who are already vulnerable."

A decidedly more complicated explanation may be gene penetrance; not every generation of a family susceptible to an illness develops it in the same way. Often, later generations suffer worse than earlier ones because of a genetic mechanism known as trinucleotide repeat expansion. Defective sequences of genes may grow longer each time they are inherited, making it likelier that descendants will come down with the illness. This phenomenon plays a role in Huntington's disease and could be involved in bipolar. "There's a stepwise genetic dose that can increase the risk," theorizes Ketter.

The first part of determining how those genes work is figuring out where they are hiding, and the National Institute of Mental Health is looking hard. Investigators at eight research centers around the country, working under an NIMH grant, are studying the genomes of 500 families with a bipolar history to see what genetic quirks they share. So far, at least 10 of the 46 human chromosomes have shown irregularities that may be linked with the condition. The most interesting is chromosome 22, which has been implicated not only in bipolar disorder but also in schizophrenia and a little-known condition called velo-cardio-facial syndrome, which has schizophrenia links as well. The seeming relatedness of disorders that so prominently feature delusions has not been lost on researchers, though with so much still unknown about chromosome 22--to say nothing of the other nine tentatively linked with bipolar--no one is ready to draw any conclusions. "There are probably genetic variants that cut across multiple systems in the brain," says Dr. John Kelsoe, psychiatric geneticist at the University of California, San Diego.

While this wealth of chromosomal clues makes fascinating work for geneticists, it promises little for bipolar sufferers, at least for the moment. What they want is relief--and fast. Thanks to rapid advances in pharmacology, they are finally getting it. In fact, children on a properly balanced drug regimen supplemented with the right kind of therapy can probably go on to lead normal lives.
For decades, the only drug for bipolar patients--and one that is still an important part of the pharmacological arsenal--was lithium. It works by regulating a number of neurotransmitters, including dopamine and norepinephrine, as well as protein kinase C, a family of chemicals that help determine the neurotransmitter amounts that nerve cells release. With its hands on so many of the brain's chemical levers, lithium can help bring bipolars back to equilibrium. For 30% of sufferers, however, it has no effect at all; for others, the side effects are intolerable. "It's still a miraculous drug," says Keck. "But some people simply don't respond to it enough."

New drugs are stepping into the breach. Rather than rely on the imprecise relief that a single drug like lithium provides, contemporary chemists are investigating a battery of other medications. Depakote, an anticonvulsant developed to calm the storms of epilepsy, was found to have a similarly soothing effect on bipolar cycling, and it was approved in 1995 to treat that condition too. The success of one anticonvulsant prompted researchers to look at others, and in the past five years, several--including Lamictal, Tegretol, Trileptal and Topamax--have been put to use.

Anticonvulsants are not the only drugs being reformulated. Also showing promise are the atypical antipsychotics. The best-known antipsychotic, Thorazine, is a comparatively crude preparation that controls delusions by blocking dopamine receptors. In the process, it also causes weight gain, mood flattening and other side effects. Atypical antipsychotics work more precisely, manipulating both dopamine and serotonin and suppressing symptoms without causing so many associated problems. There are numerous atypical antipsychotics out there, including Zyprexa, Risperdal and Haldol, and many are being used to good effect on bipolar patients.

For any bipolar, the sheer number of drug options is a real boon, as what works for one patient will not necessarily work for another. When Brandon Kent, the 9-year-old Texas boy, started taking Depakote and Risperdal, his body began to swell. Then he switched to Topamax, which made him lethargic. Eventually he was put on a mix of Tegretol and Risperdal, which have stabilized him with few side effects. Kyle Broman in Los Angeles is having a harder time but has grown calmer on a combination of Risperdal and Celexa, an antidepressant that for now at least does not appear to be flipping him into mania.

But drugs go only so far. Just as important is what comes after medication: therapies and home regimens designed to help patients and their families cope with the disorder. Early last year the National Institute of Mental Health launched a five-year, $22 million study, the Systematic Treatment Enhancement Program for Bipolar Disorder (STEP-BD) to refine bipolar therapies. Some 2,300 volunteers are participating in the program, and enrollment is expected to reach 5,000. Of all the treatments the STEP-BD doctors are studying, the most basic and perhaps the most important one for children and teens involves lifestyle management.

From infancy, kids can easily be unsettled by disruptions in their circadian cycles, as parents of newborns and toddlers learn whenever they try to change nap times. Bipolars, regardless of age, are also reactive to fluctuating schedules; many things can destabilize patients, but Keck believes that sleep deprivation and time-zone changes are the most upsetting.

For this reason, parents of bipolar kids are urged to enforce sleep schedules firmly and consistently. Bedtime must mean bedtime, and morning must mean morning. While that can be hard when an actively manic child is still throwing a tantrum two hours after lights-out, a combination of mood-stabilizing drugs and an enforced routine may even bring some of the most symptomatic kids into line. Teens, who are expected to do a lot more self-policing than younger children, must take more of this responsibility on themselves, even if that means a no-excuses adherence to a no-exceptions curfew.

Also important is diet. Caffeine can be a mania trigger for bipolars, so teens are advised to stay away from coffee and tea. Bipolar kids of all ages must also be careful with less conspicuously caffeinated foods such as sodas and chocolate. And for adolescents and teens, staying free of alcohol and drugs
is critical. Not only is the risk of addiction high, but treatment of the underlying bipolar problem is much more difficult if the patient's mind is clouded by recreational chemicals.

For children old enough to benefit, the second leg of treatment is individual therapy, which includes social-rhythms work—learning to balance meals, sleep, studies and recreation. If a triggering incident such as a divorce or death kicked the condition off, the doctor can help the child process that too.

The last, perhaps hardest element of treatment is family therapy. Bipolar disorder, like schizophrenia, depression and certain anxiety conditions, is powerfully influenced by surroundings. When an identical twin suffers from bipolar, the other twin has only a 65% chance of developing it too. Conversely, adopted children with no genetic legacy for bipolar have a 2% chance of coming down with the condition if they are raised in a home with one nonbiological bipolar parent. Clearly, something is in play besides mere genes, and that something is environment. Raise a child in a steady and stable home, and you reduce the odds that the illness will gain a toehold, which is why counselors work hard to teach parents and kids how to minimize family discord.

One strategy is to avoid too much negatively expressed emotion. Tough love, for example, is a good idea in principle, but in some situations it can do more harm than good, especially if it makes kids who can't control their behavior feel worse about themselves. When family arguments do break out, they need to be conducted in a controlled way. Psychology professor David Miklowitz of the University of Colorado encourages families to avoid what he calls the "three volley," a provocation followed by a rejoinder, then a rebuttal. Hold the volleys to just one or two, and you'll avoid some domestic breakdowns.

The most important thing parents and siblings can do is simply to serve as the eyes and ears of the bipolar child. A teen in a depression can't see the hope beyond the gloom. A child in a manic cycle can't see the quiet reality behind the giddiness. It's up to people whose compasses are more reliably functioning to step in and point the way. Says Dr. Gary Sachs, director of the Bipolar Treatment Center at Boston's Massachusetts General Hospital and principal investigator for the STEP-BD project: "Treatment is modeled on Homer's Odyssey. When Odysseus gets blown off course, he asks the help of his crew."

In the future, kids should be getting yet more assistance as they sail. At the Stanley Research Center, in Massachusetts General Hospital, investigators are beginning a yearlong study of at least 10 bipolar drugs, comparing the merits of each and the ways they can best be combined. Others are looking at such unconventional treatments as omega-3 fatty acids, found in fish oil, which may inhibit the same brain receptors that lithium affects. Elsewhere, researchers are running brain scans to determine which lobes and regions are involved in bipolar disorder and how to target them more accurately with drugs. Investigators also hope to develop a blood test that will allow bipolar disorder to be spotted as simply as, say, high cholesterol, eliminating years of incorrect diagnoses and misguided treatments.

Getting all this work done right—and getting the treatments to the kids who need it—is one of the newest and most challenging goals of the mental-health community. Doctors who recognize bipolar disorder and know how to handle it are in critically short supply. Growing up is hard enough for children who are bipolar. The last thing they need is a misdiagnosis and treatment for something they don't have.

For more information, visit these websites: time.com/bipolar, bpkids.org (Child & Adolescent Bipolar Foundation) and jbrf.org (Juvenile Bipolar Research Foundation)

Natalie Bible, 18

HOMETOWN Knoxville, Tenn.

BIO At 15, Bible was misdiagnosed with ADHD and a year later had her first manic episode. She
decided to drive to a religious revival in Florida but left town without telling anyone. "I had this feeling that if I didn't get in the car and drive, I was going to explode," Bible says. Bipolar disorder was diagnosed, and now she takes an anticonvulsant drug to keep symptoms in check. A recent high school grad whose favorite spot to sit and think is a nearby cemetery, Bible plans to take a year off before going to college to study theater.

Keith Trautner, 21

HOMETOWN McAllen, Texas

BIO Homeless since last year, Trautner will have a place to sleep for the next six months--the Hidalgo County Jail, where he's doing time for criminal trespass. Then it's back to the streets. His illness diagnosed at 10, he tried a buffet of meds but couldn't stay with them. "I've lost faith in the drugs and the doctors," he says.

Ian Palmer, 9

HOMETOWN Wayland, Mass.

BIO He started showing aggression at age 3. When doctors put him on Prozac and Ritalin, he spun out of control. Now well medicated, Ian has gone back to the mainstream classroom. But even playing with Dad, above, can lead to anger and tears.

Brandon Kent, 9

HOMETOWN La Vernia, Texas

BIO An A student in first grade, Brandon was pulling Fs by second. He would rant and trip other students; at home he would rock and cry. After a few false starts with the wrong meds, he's on a combination that helps. Now his sister Cheyenne, 4, is showing early signs of the disorder.

THE MOOD SPECTRUM

Not all bipolar states are alike. The three major forms of the disorder—bipolar I, bipolar II and cyclothymia—cover different parts of the mood arc. Other conditions, such as dysthymia or depression, are sometimes confused with bipolar but stay fixed in one emotional state.

SEVERE DEPRESSION

SYMPTOMS: At least two weeks of hopelessness, apathy, decreased appetite, insomnia

MILD/MODERATE DEPRESSION

SYMPTOMS: Similar to severe depression but not as long lasting or debilitating

NORMAL

Moods may change from day to day but not in a way that interferes with life.
HYPOMANIA

SYMPTOMS: Four days of unusually elevated mood, less need for sleep, distractability, inflated self-esteem

MANIA OR MIXED MANIA

SYMPTOMS: At least a week of even greater mania; mixed states show signs of both mania and depression

IS YOUR CHILD BIPOLAR?

There is no standard test for bipolar disorder, but this checklist, adapted from The Bipolar Child, may help you recognize some warning signs. Place a check next to each behavior your child currently exhibits or has exhibited in the past. If you mark more than 20 boxes, you should have your child evaluated by a professional

1. Is excessively distressed when separated from family
2. Exhibits excessive anxiety or worry
3. Has difficulty arising in the a.m.
4. Is hyperactive and excitable in the p.m.
5. Sleeps fitfully or has difficulty getting to sleep
6. Has night terrors or frequently wakes in the middle of the night
7. Is unable to concentrate at school
8. Has poor handwriting
9. Has difficulty organizing tasks
10. Has difficulty making transitions
11. Complains of being bored
12. Has many ideas at once
13. Is very intuitive or very creative
14. Is easily distracted by extraneous stimuli
15. Has periods of excessive, rapid speech
16. Is willful and refuses to be subordinated
17. Displays periods of extreme hyperactivity
18. Displays abrupt, rapid mood swings
19. Has irritable mood states
20. Has elated or silly, giddy mood states
21. Has exaggerated ideas about self or abilities
22. Exhibits inappropriate sexual behavior
23. Feels easily criticized or rejected
24. Has decreased initiative
25. Has periods of low energy or withdraws or isolates self
27. Is intolerant of delays
28. Relentlessly pursues own needs
29. Argues with adults or bosses others
30. Defies or refuses to comply with rules
31. Blames others for his or her mistakes
32. Is easily angered when people set limits
33. Lies to avoid consequences of actions
34. Has protracted, explosive temper tantrums or rages
35. Has destroyed property intentionally
36. Curses viciously in anger
37. Makes moderate threats against others or self
38. Has made clear threats of suicide
39. Is fascinated with blood and gore
40. Has seen or heard hallucinations

IF SO...

Treating bipolar disorder in kids is not easy, but these days it's at least possible. The first step is usually drugs. After that come individual therapy, family therapy and lifestyle changes.

LITHIUM The old standby; eases symptoms by regulating several neurotransmitters, but doesn't work for everyone.

ANTICONVULSANT DRUGS First used for epilepsy, such medications as Depakote and Lamictal calm manic storms.

ATYPICAL ANTIPSYCHOTICS Drugs designed to help schizophrenics battle delusions, including Zyprexa and Risperdal, can do the same for bipolars.

ANTIDEPRESSANTS Risky, since they can trigger bipolar cycling, but drugs such as Prozac may be part of the mix.

LIFESTYLE Schedules are key, with fixed bed and wake-up times. Foods with caffeine should be limited. Teens should avoid drugs and alcohol.

INDIVIDUAL THERAPY Kids need counseling to help them balance sleep, meals, work and play. They also must talk about problems at home and resolve crises that can trigger the disorder.

FAMILY THERAPY Parents must learn when to give in to a child--this is critical early in treatment--and when to stay firm. Family bickering should be kept to a minimum. Siblings can serve as trusted eyes and ears for a child whose perceptions are out of whack.

PHOTO (COLOR): MISUNDERSTOOD: At 14, Cabezas suffered a breakdown that finally led to a diagnosis.

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By Jeffrey Kluger; Sora Song, Reported by; Dan Cray; Jeffrey Ressner, Los Angeles; Jeanne DeQuine, Miami; Melissa Sattley, Texas; Cristina Scalet, New York and Maggie Sieger, Chicago

INSIDE THE BIPOLAR BRAIN
Scientists can’t point to one lobe that makes a person bipolar, but they have identified several areas that are involved in ways they are just beginning to understand.

**VENTRAL STRIATUM**

**WHAT IT DOES:** Helps the brain process rewards

**WHAT HAS GONE WRONG:** Studies show overactivity and a 30% loss in gray matter in this region, causing people to lose judgment about how certain behaviors, such as overspending or being sexually indiscriminate, will affect their lives.

**PREFRONTAL CORTEX**

**WHAT IT DOES:** Parts of the prefrontal cortex regulate emotion and are instrumental in processing rewards and motivation.

**WHAT HAS GONE WRONG:** Studies show a 20% to 40% reduction in gray matter—the result of a loss of the branches that connect neurons.

**AMYGDALA**

**WHAT IT DOES:** One of the brain’s emotional centers; helps in the recognition of facial expressions and tones of voice. Neural transmissions increase in response to emotional stimuli. Normally, repeated exposure to the same experiences or images leads to habituation, or reduced response.

**WHAT HAS GONE WRONG:** Habituates slowly to some stimuli, remaining reactive beyond the usual response time.

**HIPPOCAMPUS**

**WHAT IT DOES:** One of the brain’s memory centers. One layer of the hippocampus, the subiculum, helps recognize contexts that represent danger or reward.

**WHAT HAS GONE WRONG:** Loss of branches that connect neurons may lead to a constant state of anxiety because the person can no longer identify safe situations.

**BRAIN STEM**

**WHAT IT DOES:** The raphe nucleus in the brain stem is home to serotonin cell bodies, which create and disperse the neurotransmitter to different parts of the brain.

**WHAT HAS GONE WRONG:** Bipolar patients have a 40% loss of the serotonin 1a receptor in the raphe, which may contribute to atrophy of neurons and depression.

**SOURCE:** Wayne Drevets, M.D., National Institute of Mental Health

**PHOTO (COLOR)**

**MANIC GENIUS**

In Touched with Fire, psychologist Kay Redfield Jamison explores bipolar disorder’s link with artistic temperament.

**LORD BYRON**
The poet was "a young man of tumultuous passions," said his tutor. Byron described his mental state as "a chaos of the mind"

EDGAR ALLAN POE

Alcoholism is common in bipolars, and Poe fit the profile. "What made Poe write was what made Poe drink," said a biographer

ROBERT SCHUMANN

The son of a bipolar author, the German composer wrote 130 songs in one year. He died in an asylum

VINCENT VAN GOGH

He once wrote of his illness, "The weakness increases from generation to generation." Geneticists now suspect that's true

VIRGINIA WOOLF

She filled her pockets with stones and drowned herself. "I have a feeling I shall go mad," she wrote. "I cannot go on longer..."

ERNEST HEMINGWAY

Born into a family plagued by suicide, the writer--haunted by manic enthusiasms and depressions--shot himself

CURT COBAIN

Seattle grunge rocker took his band Nirvana to the pinnacle with Nevermind (one song: Lithium) but took his life at 27

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