

Bipolar Disorder

Bipolar disorder means the brain's mood-control circuits swing wildly between dangerously high energy (so high you can't sleep, you take huge risks, and you may lose touch with reality) and dangerously low energy (so low you can't feel joy, can barely move, and may think about ending your life)—all because dopamine, serotonin, and norepinephrine levels surge and crash instead of staying steady.

THE ONE-LINE TRUTH

Bipolar disorder causes repeating cycles of sky-high energy and mood (mania or hypomania) and crushing low mood (major depression), all driven by broken control of dopamine, serotonin, and norepinephrine (brain chemical messengers) in the circuits that manage emotion and drive.

The chain — how it unfolds

1. Genetic vulnerability and early-life stress prime mood circuits for instability. — why: You inherit variants in genes controlling dopamine receptors (DRD2, DRD4), serotonin transporter (5-HTTLPR short allele, which reduces serotonin signaling), calcium channels (CACNA1C, which control how neurons fire), and circadian rhythm proteins (CLOCK and ARNTL, which regulate daily sleep-wake cycles), which make prefrontal-limbic-striatal circuits hypersensitive to stress, sleep loss, and seasonal light changes. Childhood trauma, abuse, or chronic stress further remodels these circuits by raising baseline cortisol (the body's main stress hormone, made by the adrenal glands) and lowering the threshold for mood swings, so by adolescence or early adulthood, the system is primed to break with even moderate triggers.

2. A trigger—stress, sleep deprivation, substance use, or sometimes no clear cause—destabilizes the mood thermostat. — why: Sleep loss (even one or two nights of less than six hours) disrupts circadian rhythm genes in the suprachiasmatic nucleus (the brain's master clock, located in the hypothalamus), which directly controls dopamine and serotonin release. Chronic stress floods the brain with cortisol, which damages hippocampal neurons (memory and emotion-regulation cells) and dysregulates the hypothalamic-pituitary-adrenal (HPA) axis (the body's main stress-response system). Stimulants (cocaine, methamphetamine, even prescription amphetamines) dump dopamine into the striatum. Alcohol disrupts GABA (the brain's main calming messenger) and glutamate (the main excitatory messenger) balance. Antidepressants raise serotonin but can overshoot and trigger mania if no mood stabilizer is on board. Any of these pushes the unstable system past its breaking point.
3. Dopamine and norepinephrine surge in the striatum, thalamus, and prefrontal cortex, launching mania or hypomania. — why: Dopamine floods the nucleus accumbens (reward center in the ventral striatum), making everything feel intensely pleasurable and meaningful—so starting ten projects at once, spending your entire paycheck in one night, or having sex with a stranger all feel like brilliant ideas. Excess dopamine in the dorsal striatum (movement and habit center) speeds up movement and speech (you talk so fast others cannot get a word in). Norepinephrine overwhelms the locus coeruleus (alertness center in the brainstem), so you feel wide awake and energized after only two or three hours of sleep. Racing thoughts (flight of ideas) happen because the prefrontal cortex, flooded with dopamine and norepinephrine, jumps from idea to idea faster than you can speak, and every idea feels urgent and profound.
4. The ventromedial and dorsolateral prefrontal cortex shut down, erasing impulse control and judgment. — why: Extremely high dopamine silences the prefrontal regions that normally put the brakes on risky behavior, foresee consequences, and keep you socially appropriate. You lose insight (anosognosia)—you cannot see that anything is wrong—so when loved ones worry, you feel angry or misunderstood. You make decisions you would never make when stable: draining your savings, driving 100 mph, quitting your job without a plan, having unprotected sex, using dangerous drugs. If dopamine climbs even higher in the mesolimbic pathway (running from the ventral tegmental area in the midbrain to the limbic system), delusions form—believing you have superpowers, are destined for greatness, or are receiving special messages from God or the universe—and sometimes hallucinations (hearing voices, seeing things) appear, identical to schizophrenia but driven by mood instability.

5. Sleep architecture collapses during mania, fueling the upward spiral. — why: Hyperactive orexin (also called hypocretin, a wakefulness chemical) neurons in the lateral hypothalamus (sleep-wake control center) and suppressed melatonin (the sleep hormone from the pineal gland) block deep NREM (non-REM, or slow-wave) sleep, the stage that restores the body and stabilizes mood. You feel fully rested after two or three hours because high norepinephrine creates a false sense of alertness, but your brain never gets the deep sleep it needs to reset dopamine and serotonin systems—so the mania accelerates. Each night of lost sleep makes the next day worse, creating a self-reinforcing upward spiral until you crash, are hospitalized, or the episode burns out after days to weeks.
6. Dopamine, serotonin, and norepinephrine collapse, flipping the brain into major depression. — why: After days or weeks of mania (or sometimes without any preceding mania, especially in Bipolar II), the same circuits that surged now crash. Dopamine drops far below normal in the nucleus accumbens, so nothing brings pleasure—food tastes like cardboard, music sounds flat, being with loved ones feels empty (anhedonia). Serotonin drops in the raphe nuclei (brainstem serotonin factory) and limbic system, causing overwhelming sadness, guilt, worthlessness, hopelessness, and suicidal thoughts. Norepinephrine drops in the locus coeruleus and prefrontal cortex, causing crushing fatigue, psychomotor retardation (thinking and moving in slow motion), inability to concentrate, and early-morning awakening (waking at 3 or 4 a.m. and unable to fall back asleep). You may sleep ten or twelve hours and still wake up exhausted because REM (rapid eye movement) sleep is fragmented and non-restorative.
7. Mixed episodes combine high motor activity with depressive cognition—the most lethal state. — why: Sometimes dopamine and norepinephrine stay partially elevated—enough to cause agitation, racing thoughts, pressured speech, and motor restlessness—while serotonin stays low, so you feel hopeless, irritable, worthless, and suicidal at the same time. You have the despair and suicidal thoughts of depression plus the energy and impulsivity to act on them, which is why mixed episodes have the highest rate of suicide attempts and completions of any bipolar state, far higher than pure mania or pure depression. This state is agonizing—you feel trapped in your own revved-up, miserable mind—and it is often missed or mistaken for severe depression or agitated depression, delaying the right treatment.

8. Without mood stabilizers, each episode remodels the brain, shortening cycles and worsening outcomes (kindling effect). — why: Every manic or depressive episode causes measurable changes in brain structure: hippocampal volume shrinks (the memory center, which also regulates the HPA stress axis), prefrontal cortex gray matter thins (worsening impulse control and planning), and synaptic connections between neurons are pruned or strengthened in ways that make the next episode easier to trigger and harder to stop. This is called kindling (borrowed from epilepsy research): just as repeated small electrical stimuli can eventually cause a seizure, repeated mood episodes lower the threshold for future episodes, so over time smaller stressors—or no stressor at all—can launch full mania or depression. Early, continuous treatment with lithium or other mood stabilizers prevents kindling, protects brain structure, and dramatically improves long-term outcomes.

Spot it — what you see, and why

- Mania: sky-high mood or explosive anger lasting at least one week, bad enough to wreck work or land you in the hospital: Too much dopamine (a brain chemical that drives pleasure and action) floods the limbic system (the brain's emotion center) and weakens the prefrontal cortex (the front part that normally pumps the brakes on big feelings), making the person feel unstoppable happy or furiously angry when things don't go their way.
- Hypomania: noticeably higher mood and energy lasting at least four days—people see the change but you can still function: A moderate bump in dopamine and norepinephrine (a brain chemical that revs up alertness and drive) boosts energy, confidence, and get-up-and-go without destroying judgment—this marks Bipolar II, not Bipolar I.
- Barely needing sleep—feeling fully rested after only two or three hours: High norepinephrine keeps the locus coeruleus (the brain's wake-up alarm in the brainstem) firing nonstop, blocking the normal signal that says it's time to sleep.
- Pressured speech: talking fast, loud, and nonstop so it's almost impossible to interrupt: Too much dopamine speeds up how fast thoughts form—faster than the mouth can keep up—and the loss of prefrontal cortex brakes removes the normal social filter on talking.
- Flight of ideas or racing thoughts—your mind jumps from topic to topic without finishing any one idea: Dopamine overactivity in the thinking centers fires connections between ideas too fast, so thoughts leap from one thing to another before finishing the first.
- Grandiosity: blown-up self-esteem, believing you have special powers, are famous, or can do impossible things: Dopamine flooding the reward pathways (the ventral striatum and nucleus accumbens, deep brain circuits that tag things as important or pleasurable) creates false confidence and a distorted self-view, sometimes reaching delusional intensity—a fixed false belief that cannot be shaken even by proof.

Red flags — act now

- Suicidal thoughts or behavior, especially during mixed episodes or in the first weeks of starting an antidepressant
- Psychotic symptoms—delusions or hallucinations—during mania
- Severe insomnia (no sleep for three or more days) or complete loss of insight (the person cannot recognize they are sick)
- Lithium toxicity signs: coarse hand tremor, confusion, slurred speech, muscle twitching, or seizures
- Rapid cycling—four or more mood episodes in one year—signaling treatment resistance and worse long-term outcome

Treat it — in this order

1. Lithium started as mood stabilizer for acute mania or maintenance treatment to prevent future episodes → Lithium enters brain cells and changes the signaling pathways that control how excitable neurons are. Specifically, it blocks enzymes called inositol monophosphatase and glycogen synthase kinase-3 (GSK-3), which stabilizes the circuits that swing between mania and depression. By blocking GSK-3, lithium strengthens connections between brain cells (neurons) and protects them from stress damage. Over weeks to months, lithium prevents extreme mood swings in both directions. It also reduces suicide risk more than any other mood stabilizer — studies show up to 80% reduction in suicide attempts. Think of lithium as resetting the brain's thermostat so it does not overheat (mania) or freeze (depression).
2. Valproate (divalproex) started as mood stabilizer for acute mania or maintenance treatment → Valproate increases the amount of GABA (gamma-aminobutyric acid, the brain's main calming chemical) by blocking the enzyme GABA transaminase (which breaks GABA down) and by increasing the enzyme glutamic acid decarboxylase (which makes GABA). More GABA means the overactive circuits in mania are calmed. Valproate works faster than lithium for acute mania (within 1 to 2 weeks). It is especially effective for mixed episodes (depression plus mania at the same time) and rapid cycling (four or more episodes per year), which lithium may not control as well.

3. Second-generation antipsychotic (such as quetiapine, lurasidone, olanzapine, aripiprazole, or cariprazine) for acute mania or bipolar depression → These medications block dopamine D2 receptors in the mesolimbic pathway (the brain's reward circuit), which reduces the euphoria, grandiosity, impulsivity, and racing thoughts of mania by turning down excess dopamine signaling. Some (quetiapine, lurasidone) also block serotonin 5-HT_{2A} receptors, which improves depressive symptoms by rebalancing serotonin (a brain messenger that steadies mood). They work fast — within days to a week — so they are used to calm acute agitation, psychotic features (delusions like believing you have special powers, hallucinations like hearing voices), and severe mania. Think of antipsychotics as turning down the volume on an overloaded circuit.
4. Fixed sleep-wake schedule (same bedtime and wake time every day, including weekends; dark, quiet sleep environment; no screens 1 hour before bed; no daytime naps) → The suprachiasmatic nucleus (a tiny cluster of nerve cells in the hypothalamus) is the brain's master clock that controls circadian rhythms — the 24-hour cycles that regulate sleep, body temperature, hormone release (like cortisol, the stress hormone), and mood. In bipolar disorder, this clock is unstable. A fixed sleep schedule resets the clock by giving it consistent time cues (light in the morning, darkness at night). This stabilizes the hypothalamic-pituitary-adrenal axis (the stress-response system) and reduces the frequency of mood episodes. Clinical studies show that people who keep regular sleep-wake times have up to 50% fewer relapses. A single night of missed sleep can precipitate mania in someone with bipolar disorder.
5. Psychoeducation: teach the patient to identify their personal early warning signs (such as needing less sleep, increased spending, social withdrawal), understand bipolar disorder as a chronic medical condition like diabetes, and recognize the importance of medication adherence → When people recognize the early signs of a developing episode — called early-warning (prodromal) symptoms — such as sleeping only 3 hours without feeling tired, suddenly losing interest in activities they love, or feeling irritable over small things, they can contact their provider before the episode becomes severe. Early intervention with medication adjustment (raising a dose, adding a short-term medication like a benzodiazepine to restore sleep) can prevent hospitalization and shorten episode duration. Studies show that psychoeducation reduces relapse rates by up to 40%. It also reduces the stigma and shame people feel, which improves adherence (sticking with the treatment plan).

Your top priorities at the bedside

1. Screen for suicide risk every shift using a validated tool and ask directly about intent, plan, and access to means; escalate immediately if any positive answer — why: Bipolar disorder carries 20 to 30 times higher suicide risk than the general population, peaking during mixed episodes, depressive phases, and the first weeks after starting treatment when energy returns before mood lifts, giving the patient the drive to act on suicidal thoughts
2. Monitor lithium level, creatinine (kidney function test), and thyroid-stimulating hormone (TSH, a measure of thyroid gland activity) per protocol—typically every 3 to 6 months for stable patients or sooner if vomiting, diarrhea, fever, or new medications — why: Lithium is cleared only by the kidneys and even small changes in hydration, kidney function, or salt balance can push levels from therapeutic to toxic; lithium also damages the thyroid gland over time, causing hypothyroidism (low thyroid hormone) in up to 20 percent of patients, which worsens depression
3. Enforce a fixed sleep-wake schedule with the same bedtime and wake time every day, even on weekends, and limit daytime naps to 20 minutes or less — why: The brain circuits that control circadian rhythm (the body's 24-hour clock) and mood regulation overlap heavily; even one night of sleep loss can trigger mania in vulnerable patients, and irregular sleep is one of the most common triggers for both manic and depressive episodes