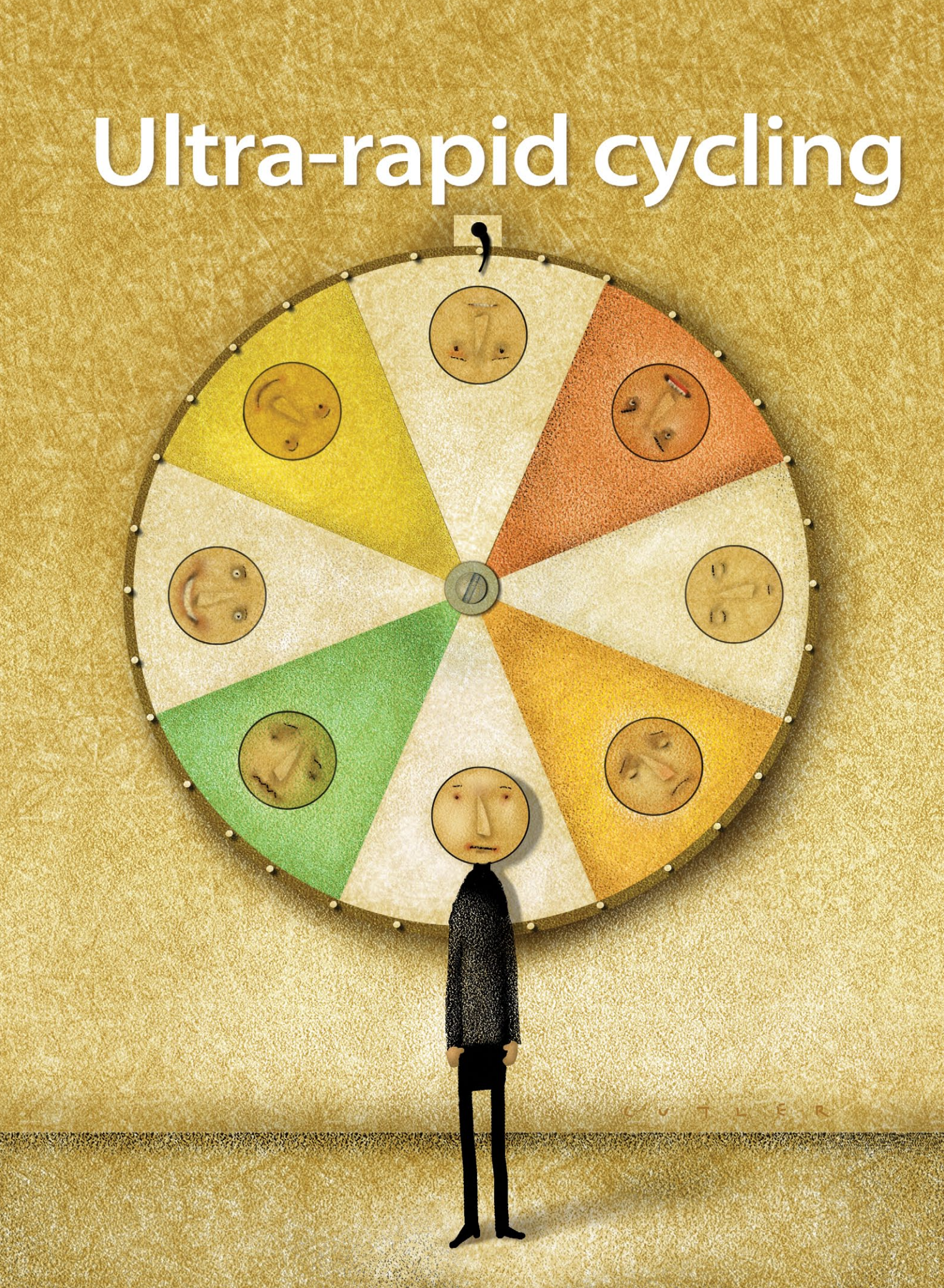
Ultra-rapid cycling



Web audio at CurrentPsychiatry.com
Dr. Goldberg: Treating patients with suspected ultra-rapid cycling bipolar disorder

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bipolar disorder: A critical look

Key factors help differentiate mood shifts in BD from other types of affective lability

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Ultra-rapid cycling (URC) entered the psychiatric lexicon in the 1990s as a proposed descriptor for manic/hypomanic, mixed, or depressed episodes of bipolar disorder (BD) that occur every few days or weeks. DSM-IV-TR incorporates rapid cycling (RC)—but not URC—as a course specifier that occurs in 10% to 15% of patients with BD who have ≥4 distinct affective episodes per year, each fulfilling duration criteria and separated by identifiable recovery periods (unless an episode directly changes polarity). Since then, the terms RC and URC have seemingly metamorphosed into imprecise, popular colloquialisms meant to loosely describe frequent mood changes rather than distinct episodes over extended time periods, with little regard for the associated signs that define manic or hypomanic episodes.

This article examines the meaning and validity of URC in BD, its relevance and differentiation from rapid mood shifts in patients without BD, and concepts relevant to treatment extrapolated from studies of RC BD.

Imprecise nomenclature

Post et al[1] coined the terms "ultra-rapid cycling" and "ultra-ultra-rapid cycling" (also called "ultradian cycling") to describe mood episodes that occur monthly (URC) or over the course of as little as 1 day (ultradian cycling). These constructs are controversial because they lack demonstrated content validity and discriminant validity relative to other disorders. ("Content validity" refers to whether the features thought to comprise an entity of interest accurately and meaningfully do so; "discriminant validity" tells researchers and clinicians whether the proposed description of a clinical entity uniquely differentiates it from other disorders—avoiding

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Ultra-rapid cycling

Clinical Point

Rapid cycling is neither a diagnosis in itself nor a criterion for diagnosing bipolar disorder

Table 1

Differential diagnosis in suspected URC

Phenomenon	Considerations for assessment
Mixed episodes in bipolar I disorder, or mixed depressive episodes in bipolar II disorder	DSM-IV-TR mixed episodes entail the co-occurrence of manic and depressive symptoms during the same episode without an intervening period of recovery. ICD-10 includes "rapid alternation of manic, hypomanic or depressive symptoms…from day to day or even hour to hour" in its definition of a mixed episode
Distress responses to acute environmental adversities (eg, adjustment disorders with mixed disturbance of emotions and conduct)	One would expect an absence of corresponding sleep-wake cycle changes or speech-language and psychomotor disturbances
Intoxication/withdrawal from psychoactive substances or drug-induced mental status changes (eg, corticosteroids, amphetamine, cocaine); a history of substance abuse also may be associated with development of URC in BD patients[4]	Substance-induced mood fluctuations caused by intoxication/withdrawal can mimic affective cycling
Disinhibition states and frontal lobe syndromes as seen in traumatic brain injury and other CNS disorders, such as multiple sclerosis	Assess for signs of perseveration and history of head trauma or neurologic damage from cumulative toxic-metabolic insults (eg, chronic alcoholism)
Autonomic hyperarousal, emotional volatility, and hyperreactivity to environmental stresses, suggestive of PTSD	Determine the presence of a trauma history and review whether DSM-IV-TR symptoms and associated features of PTSD exist, including re-experiencing/reliving and avoidance, as well as paranoid thinking, dissociation, and nightmares
Recurrent mood shifts related to premenstrual dysphoric disorder may mimic URC. Other endocrine dysfunctions also may present with URC (eg, thyroid or ovarian malignancies)	Affirm the independent presence of BD before inferring its manifestations solely from premenstrual mood changes
Trait affective instability associated with borderline personality disorder	Trait mood instability is more chronic and enduring than episodic, and would not be expected to occur in tandem with signs of psychomotor activation that define mania/hypomania

BD: bipolar disorder; ICD-10: International Statistical Classification of Diseases and Related Health Problems, 10th revision; PTSD: posttraumatic stress disorder; URC: ultra-rapid cycling

"false-positive" suspected cases.) Clinicians therefore must pay careful attention to non-bipolar psychiatric problems that can present with rapid mood changes but without the psychomotor and related signs that define bipolar mood episodes. In their looser, nontechnical meanings, "rapid cycling" or "ultra-rapid cycling" may be synonymous with affective lability. RC is neither a diagnosis in itself nor a criterion for diagnosing BD. Rather, it is a course specifier to describe episode frequency in patients with past unambiguous manic or hypomanic episodes.

In children and adolescents, whose presentations often are atypical and can be hard to differentiate from other forms of behavioral or temperamental dysregulation, severe non-episodic mood dysregulation without signs of mania or hypomania may indicate a phenomenon separate from BD.[2] Geller and colleagues[3] proposed using the term "episodes" to frame the duration of a DSM-IV-defined syndrome of mania/hypomania or depression, while reserving the term "cycling" to connote patterns of mood alternation within a given episode. It is not clear whether this concept of "cycling" differs qualitatively from mood lability that arises during a mood episode in children or adults, and notably, this perspective does not account for changes in psychomotor signs in conjunction with changes in mood.

Clinicians also sometimes blur the concept of "mixed episodes" with RC or URC. DSM-IV-TR defines mixed episodes within bipolar I disorder (BD I) based on criteria

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for a simultaneous manic and depressive episode, rather than on frequent oscillations between affective poles. These and other differential diagnostic considerations for suspected URC are summarized in ***Table 1***.[4]

A further concern regarding nomenclature involves the distinction between *cyclicity* (ie, successive episodes regardless of pole direction) and changes in *polarity* (ie, switches from depression to mania/hypomania or vice versa). Some mood disorder patients may have rapid oscillations from euthymia to depression while never changing polarity to mania/hypomania and may be best described as having recurrent brief depression.

Duration criteria

Clinicians and researchers have debated the minimum duration criteria for identifying manic or hypomanic episodes, and the extent to which suspected hypomanic periods of short duration constitute distinct illness phases. Although DSM-IV-TR designates 4 days as a minimum time for classifying an episode of hypomania, empirical studies suggest that mood symptoms lasting as few as 2 days may comprise a valid and reliably distinct entity relevant to RC.[5] More limited data (mainly case observations) identify "affective oscillations" and "mood shifts" occurring faster than once per 24 hours in BD patients without comorbid personality disorders.[6] Phenomenologic studies that have focused on 24- to 48-hour switch cycles have described new-onset URC arising spontaneously or following closed head injuries.[7] In children and younger adolescents, reports have identified long index manic episodes (mean durations as long as 80 weeks)[8] that involve continual (ultradian) mood cycling in as many as 80% of cases.[9]

Is URC a valid construct?

A central controversy surrounding the validity and meaningfulness of URC as a BD subtype involves its sole focus on mood variation rather than the fuller constellation of associated signs and symptoms that define episodes of mania/hypomania or depression. Abrupt, sudden, drastic, or dramatic mood shifts from one moment to the next are nowhere to be found in the DSM-IV-TR definition of BD, and the construct of mood lability or affective instability is neither a cardinal nor defining element of BD. Although individuals with BD I or bipolar II disorder (BD II) may have periods of affective lability, rapid shifts in mood are neither necessary nor sufficient for a BD diagnosis, and may indicate other types of psychopathology when affective instability occurs in the absence of a history of discernible manic or hypomanic episodes.

Studies by our group[10] and others[11] have shown that overattention to mood variation without considering associated cognitive, speech-language, chronobiologic, and motor signs of mania/hypomania accounts for substantial overdiagnosis of BD in patients with non-specific mood disturbances, particularly in those with active substance abuse or borderline personality disorder (BPD). Whereas the construct of RC BD attempts to account for changes in energy and psychomotor function as part of recurrent syndromes of mania/hypomania, existing literature on URC does not. Assessing mood changes in <24 hours also precludes assessing associated phenomena that occur over longer periods, such as changes in the sleep-wake cycle.

A rigorous, systematic approach to differential diagnosis for patients with affective instability is essential.

Borderline personality disorder

A common diagnostic debate regarding URC involves how to differentiate it from the chronic mood instability and reactivity inherent to BPD. Although some authors have suggested that RC BD and affective instability in BPD may be the same entity,[12] others object to unifying the 2 conditions without considering their phenomenologic and other clinical differences. For example, affective instability arising from borderline character organization is thought to reflect a patient's impaired capacity to self-regulate his or her internal state and emotional responses to interpersonal and other environmental stresses, or difficulty managing impulses. By contrast, manic or depressive phases of BD tend not to be "triggered" by interper-

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Clinical Point

Overattention to mood variation without considering associated signs of mania accounts for overdiagnosis of bipolar disorder

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sonal conflicts or frustrations. Furthermore, reframing intense mood reactions to the environment as bipolar variants carries several pitfalls: doing so wrongly accords patients a passive role in their reactions to life events, inaccurately reinforces a sense of victimization in response to stress, and diverts inquiry away from a patient's active role in life decisions and circumstances that may be unsatisfying, self-defeating, or volatile.

Two key considerations may be helpful in discriminating rapid mood changes in BD vs BPD. First, some longitudinal studies indicate that RC often is a transient, rather than enduring, phenomenon in BD,[13] in contrast to the nonvarying, trait feature of affective instability in persons with BPD. It is unknown whether URC is more enduring than transient. Notably, whereas bipolar mood episodes constitute deviations from a baseline state, affective instability in BPD is a *baseline characteristic*, rather than a deviation from it. Second, by definition, a BPD diagnosis hinges on additional elements unrelated to mood disturbances, such as interpersonal styles or defense mechanisms that involve splitting, projection, and projective identification, feelings of numbness, boredom, or emptiness, identity diffusion, fears of abandonment, and proclivities toward self-mutilation or other self-injurious behaviors as a means to alleviate tension and stress. These characteristics do not overlap with the core elements of BD.

Affective lability in patients with BPD entails prominent oscillations between anger and anxiety, or depression and anxiety, but not depression and elation[14]; by contrast, affective instability in BD has been linked with greater oscillations between euthymia and depression, and euthymia and elation, but not euthymia and anger.[15] Moreover, daily mood fluctuations in patients with BD appear to occur in a relatively random fashion,[16] whereas in BPD mood fluctuations are reactions that appear intimately linked to distressing interpersonal experiences.

Visit this article at CurrentPsychiatry.com for a table comparing the phenomenology of RC and URC and a discussion of studies that explored genetic markers or family patterns that may be related to RC or URC.

Treatment considerations

No systematic studies exist for treating URC. Because most clinical trials of BD focus on treatment or prevention of a single episode rather than changes of mood over time, it is difficult to draw inferences about the ability of any treatment to attenuate marked, day-to-day mood variations. Some antimanic drugs, such as carbamazepine, have been suggested to offer better prophylactic efficacy compared with lithium for "non-classical" BD presentations, although the efficacy of carbamazepine has not been studied in URC.

Broadly speaking, treatment for URC, similar to RC, pragmatically involves:

- identifying and eliminating sources of mood destabilization (eg, substance abuse, erratic sleep patterns)
- treating medical comorbidities such as hypothyroidism
- optimizing treatment with mood stabilizing agents
- exercising caution when using antidepressants (see below).

Interestingly, despite frequent allusion to certain medications as "mood stabilizers," no controlled study has examined mood instability on a day-to-day basis as a primary outcome measure in BD treatment, which limits the ability to surmise that any drug could be expected to diminish mood oscillations that occur over the course of days, or within a single day. However, a post hoc analysis by our group[17] compared randomized treatment with lamotrigine or placebo over 6 months in RC BD I or BD II. Using prospective life charting, we found patients who received lamotrigine were almost twice as likely as those receiving placebo to achieve euthymia from one week to the next, which suggests the possibility that lamotrigine may offer benefit for affective instability in BD I or BD II patients, in addition to preventing discrete mood episodes.

Antidepressant controversy. Concerns that antidepressants might acutely induce mania or accelerate cycling frequency over long time periods have led to a contentious, long-standing debate within psychopharmacology. As noted in the table at CurrentPsychiatry.com, several long-term naturalistic follow-up studies have

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Clinical Point

Affective instability in BD has been linked with oscillations between euthymia and depression, and euthymia and elation

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Visit this article at CurrentPsychiatry.com for a table comparing phenomenology of RC and URC

Ultra-rapid cycling

Clinical Point

Lamotrigine may offer benefit for affective instability in BD I or BD II, in addition to preventing discrete mood episodes

Table 2

Evidence-based treatments for ultra-rapid cycling BD

Intervention	Strength of evidence	Comment
Antidepressant elimination	Cycling frequency may lengthen during antidepressant-free periods among patients with RC[20]; long-term (up to 1 year) antidepressant use in RC patients may increase the likelihood of depressive recurrences[19]	Findings based mostly on small sample sizes; no controlled trials of antidepressant cessation as an intervention specifically for URC
Lithium	Single case report of ECT-induced URC resolved by lithium augmentation during continued ECT[22]	No large-scale or randomized trials
Carbamazepine	No controlled trials or case reports	Possible anti-cycling benefits relevant for URC could be inferred from post hoc studies among patients with RC
Divalproex	Single case report describing resolution of a 48-hour cycle after augmentation of lithium with divalproex[23]	No large-scale or randomized trials
Lamotrigine	Single case report of 100 mg/d lamotrigine augmentation to divalproex yielded 8 months of remission in a 25-year-old man with BD II and a long-standing pattern of 3 days of hypomania followed by 5 days of depression[24]	No large-scale or randomized trials
Topiramate	Single case report in URC describing reduction of cycling frequency over 3 years[25]	Multiple large scale placebo-controlled studies in bipolar mania have been negative
Second-generation antipsychotics	No controlled trials or case reports	Possible anti-cycling benefits relevant for URC could be inferred from post hoc studies in RC
Combinations of ≥2 mood stabilizing drugs	No controlled trials or case reports	Combining multiple anti-cycling agents is intuitively logical but largely unstudied
Nimodipine	1 unipolar and 11 BD patients treated in randomized, off-on-off-on fashion (begun at 90 mg/d, increased up to 720 mg/d, mean duration of 12 weeks on active drug)[26]	Response in 5 of 9 completers. Findings await replication with larger sample sizes
Hypermetabolic thyroid hormone (levothyroxine)	Findings from a small (N = 11) study of adjunctive high-dose levothyroxine (0.15 to 0.4 mg/d, with dosages increased by 0.05 to 0.1 mg/d every 1 to 2 weeks); an unspecified subgroup had "a very rapid cycling pattern" (reviewed by Bauer et al[21])	10 of 11 RC patients had reductions in depressive symptoms, 5 of 7 had improvement from baseline manic symptoms (observation period ≥60 days)
ECT	Case reports of improvement with ECT in refractory RC that was presumed secondary to tricyclic antidepressants	Reports of induction of URC by ECT[22]; whether or not ECT would more likely improve or exacerbate cyclicity for a given patient may require empirical determination

BD: bipolar disorder; BD II: bipolar II disorder; ECT: electroconvulsive therapy; RC: rapid cycling; URC: ultra-rapid cycling

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Visit this article at CurrentPsychiatry.com for a discussion of genetic markers related to RC or URC

reported RC as a perceived consequence of antidepressants in most RC patients, although efforts to differentiate cycle acceleration caused by antidepressants (or other iatrogenic factors) from the natural course of illness remains exceedingly difficult without prospective randomized trials. (Antidepressants might cause more affective recurrences, but having multiple episodes may also cause more antidepressant prescriptions.) Some researchers (eg, Schneck et al[18]) have reported more frequent episodes among patients taking antidepressants but did not consider that patients with

Table 3

Tips for managing suspected ultra-rapid cycling BD

Do's	Don'ts
Ascertain a history of ≥1 lifetime manic or hypomanic episode to diagnose BD	Diagnose BD solely on the presence of rapid mood fluctuations
Determine the presence of changes in sleep, energy, speech-language, and related behavior as correlates of mood to differentiate syndromes from isolated variation in mood	Ignore constellations of associated signs and symptoms of mania/hypomania
Obtain patient history to assess for head trauma or other medical and neurologic events that could have affective or other psychiatric manifestations	Disregard possible medical etiologies for new-onset affective dysregulation
Ascertain the resolution of 1 episode before counting the resurgence of symptoms as constituting a new episode; a waxing and waning course may reflect illness chronicity with incomplete recovery rather than true cyclicity	Misidentify incomplete recovery from an existing episode as the occurrence of new multiple episodes, which would inflate false-positive cases of RC or URC
Advise patients to refrain from alcohol or illicit substances that could destabilize mood	Assume that comorbid alcohol or illicit substance abuse will remit only after mood stabilization has been achieved, rather than the reverse
Monitor changes in sleep-wake cycles and the effects of erratic sleep or sleep deprivation on mood	Ignore the effects of poor sleep hygiene on mood
Minimize antidepressant exposure in patients with RC or URC	Continue long-term antidepressant maintenance therapy in patients with manic or mixed features or ongoing oscillations between mania/hypomania and depression
Assure euthyroid status and consider the potential utility of hypermetabolic levothyroxine	Assume that RC or URC will resolve solely by normalizing or optimizing thyroid function
Use rational, pharmacodynamically nonredundant anti-cycling drugs	Ignore the cumulative burden of adverse effects of multiple drugs
Consider the potential role for ECT as a strategy to arrest URC during any phase of BD	Assume ECT has value only during acute depressive phases of BD
Use prospective mood charting to document the evolution of mood changes over time, particularly when gauging treatment efficacy	Rely solely on impressionistic recall of mood states or polarity changes as reflecting distinct phasic changes

BD: bipolar disorder; ECT: electroconvulsive therapy; RC: rapid cycling; URC: ultra-rapid cycling

Clinical Point

Minimize antidepressant exposure in BD patients with rapid cycling or ultra-rapid cycling

multiple episodes may be more likely to receive antidepressants, which fail to ameliorate acute or recurrent affective episodes. Importantly, a recent multi-site randomized trial by Ghaemi et al[19] found that after a favorable acute response to antidepressants plus mood stabilizers, patients with pre-existing RC who were randomized to continue antidepressants for up to 1 year had a 3-fold increased likelihood of developing a new depressive episode, which affirms suggestions that antidepressants do not help—but may exacerbate—cycling in patients with RC. No studies in BD have examined whether URC is more likely to arise as a consequence of antidepressant use.

Mood stabilizers and other biologic therapies. A small body of literature specifically addresses pharmacotherapy of URC in patients with BD (***Table 2***).[19-26] A limitation of most existing literature is its focus on case reports, small open trials, or anecdotal observations rather than large, randomized controlled trials using systematic outcome measures. Extrapolation from reports focusing on patients with DSM-IV-TR RC is limited because it is uncertain whether URC differs fundamentally from RC and studies of DSM-IV-TR RC typically examine acute response during an index episode or time until relapse during maintenance therapy, rather than impact on mood changes over time.

continued

Ultra-rapid cycling

Related Resources

- American Psychiatric Association practice guideline for the treatment of patients with bipolar disorder (revision). Am J Psychiatry. 2002;159(4 suppl):1-50.
- Massachusetts General Hospital Bipolar Clinic and Research Program. Sample mood chart (downloadable). www.manicdepressive.org/moodchart.html.

Drug Brand Names

Carbamazepine • Equetro, Tegretol
Divalproex • Depakote
Lamotrigine • Lamictal
Levothyroxine • Synthroid
Lithium • Lithobid
Nimodipine • Nimotop
Topiramate • Topamax

Disclosure

Dr. Goldberg is on the speakers' bureaus for AstraZeneca, Dey Pharmaceuticals, Eli Lilly and Company, Merck, and Sunovion and is a consultant for Axon Advisors, Dey Pharmaceuticals, Eli Lilly and Company, and Grünenthal Group.

Acknowledgment

The author wishes to thank David L. Dunner, MD, for his helpful comments regarding this article.

Clinical Point

Prospective life charting helps clinicians determine whether meaningful changes are occurring in cyclicity

Psychotherapy. A limited database on the efficacy of adjunctive cognitive-behavioral therapy (CBT) in RC BD describes improvement in depressive symptoms over short-term follow-up.[27] No long-term studies of CBT or other structured psychotherapies have focused on RC or URC. Intuitively, one might expect that psychoeducation targeting sleep hygiene, substance use, stress management and coping skills, medication adherence, and prodrome recognition would be of value to patients with BD who experience frequent mood episodes, especially in those who may be unaware of or unfamiliar with basic concepts related to BD. In addition, relevant concepts from dialectical behavior therapy may be beneficial for BD patients with possible URC, such as skills to enhance emotional regulation, distress tolerance, mindfulness, and interpersonal effectiveness.

Treatment monitoring. Prospective life charting allows patients to systematically record manic/hypomanic and depressive symptoms day-to-day and week-to-week, thus creating a measure that may be particularly relevant for patients whose moods change rapidly. Simple mood charts (see ***Related Resources***) typically take into account the severity of symptoms of either polarity with ratings of mild, moderate, or severe. Such visual records permit simple calculations over the course of a given interval (eg, week-by-week or across months) of several important parameters, including:

- number of days euthymic
- number of days with depression
- number of days with abnormal mood elevation
- number of occasions in which moods of both polarities occur on the same day.

Tracking these parameters during a treatment allows clinicians to make quantitative comparisons over time as a method of determining whether or not meaningful changes are occurring in cyclicity. Visit this article at CurrentPsychiatry.com for an example of a completed mood chart and its interpretation.

Additional recommendations for assessing and managing cyclicity in BD are summarized in ***Table 3*** (***page 51***).

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Visit this article at CurrentPsychiatry.com for an example of a completed mood chart and its interpretation

Bottom Line

Ultra-rapid cycling (URC) has not been validated as a distinct clinical entity, and frequent mood swings should not be used as a criterion for diagnosing bipolar disorder. Careful evaluation of mood fluctuations over hours or days requires rigorous attention to psychomotor signs of mania or depression to differentiate URC from affective lability seen in other conditions. Proper management involves identifying underlying etiologies, minimizing factors that destabilize mood, optimizing mood stabilizing agents, and minimizing antidepressant use.

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Table

Rapid cycling and ultra-rapid cycling BD: A comparison

Construct	Rapid cycling	Ultra-rapid cycling
Bipolar I vs II	Predominantly BD II[a]	No systematic data
Sex	Predominantly women	No systematic data
Longitudinal course	May be a transient phenomenon that can occur at any time[b] or an enduring phenomenon that may persist for years[c]	Ultradian patterns may be more common across the first several episodes among pediatric BD patients[d]
Age at onset	Associated with younger age at onset[e]	May be more evident in prepubescent onset mood disorders[d]; ultradian cycling more likely when onset occurs before age 13 than in adulthood[e]
Diurnal variation in mood	Morning-to-evening mood switches usually involve depression to mania/hypomania, with the opposite typifying evening-to-morning mood switches[f]	Not reported
Relationship to environmental stresses	Life stresses may precede initial affective episodes but may be less important as subsequent episodes arise with increasing automaticity	No systematic data
Relationship to menstrual cycle	Despite case reports and self-reported links between RC and menstrual mood exacerbations, prospective data do not identify associations between RC and menstrual patterns[g,h]	No systematic data
Subclinical hypothyroidism	Bauer and Whybrow identified hypothyroidism independent of lithium use in 60% of 30 rapidly cycling BD patients, with evidence of improvement in a separate study of 11 RC patients given suprametabolic levothyroxine (reviewed by Bauer et al[i])	No systematic data
Relationship to psychosis	None[a]	No systematic data
Relationship to antidepressant use	Naturalistic observations suggest RC may occur later in the illness course as a result of antidepressant use.[c] Small open case series data suggest shorter intermorbid intervals on antidepressants with longer intervals off antidepressants.[j] RC patients often receive antidepressants, but causal relationships are not well-documented.[k] Some case-control data dispute links between antidepressant use and RC[l]	No specific published cases
Considerations for suicide risk	RC linked with more serious suicide attempts[l]	Suicide attempts may be associated with cycling within an episode[m] or rapid shifting in mood[n]
Time course for judging treatment efficacy	Efforts to diminish acute affective instability may be measured over the course of days to weeks	By definition, treatment of RC involves relapse prevention over the course of 1 year

BD: bipolar disorder; RC: rapid cycling

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continued

Ultra-rapid cycling

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Box

Biologic correlates of ultra-rapid cycling

From a biologic perspective, a handful of preliminary studies have examined genetic markers or familial patterns that might be related to rapid cycling (RC) or ultra-rapid cycling (URC). These include a reported link between URC and the low activity variant of the catechol-o-methyltransferase gene polymorphism in a small group of patients with velo-cardio-facial syndrome,[a] although this finding was not replicated in a larger sample.[a] Other preliminary reports on RC have implicated both the long (l) and short (s) allelic variants of the serotonin transporter gene (SLC6A4), the val66met variant of the brain-derived neurotrophic factor gene, and the circadian cryptochrome 2 (CRY2) gene (reviewed by Bauer et al[b]). These candidate loci have been examined in RC but not URC.

URC has not been examined as a familial entity, although in the National Institute of Mental Health Collaborative Depression Study, DSM-IV-TR RC did not occur with elevated frequency in bipolar pedigrees.[c] Rapid mood switches—abrupt rather than gradual transitions from one affective pole to another—appear to be only slightly, nonsignificantly more common in first-degree bipolar relatives of BD patients who themselves have rapid rather than gradual transitions from one affective pole to the other.[d]

Neuroimaging studies in BD seldom focus on subpopulations with RC or URC, and have been confined mainly to case reports that have yielded limited, non-generalizable observations, such as state-dependent variations in prefrontal activity during tasks of facial recognition (reviewed by Bauer et al[b]).

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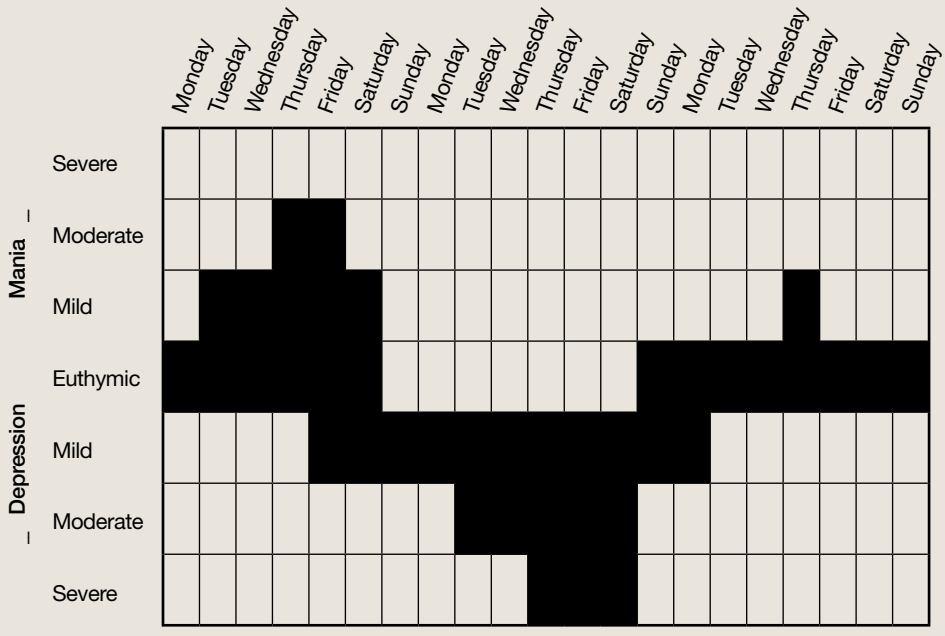
Figure

Example of prospective mood charting to document changes in manic/hypomanic and depressive symptoms across time



In the above example, the prevalence and severity of mood symptoms are identified over 21 days. Note the distinctly separate phases of mood elevation followed by depression, whereas euthymia was present only 6 of 21 days (29% of the time). Symptoms of at least moderate severity were more prominently depressive (5 of 21 days, or 24% of the time) than manic/hypomanic (2 of 21 days, or approximately 10% of the time). Mood charting does not capture associate DSM-IV-TR criteria for a mood episode but instead focuses solely on longitudinal changes in mood elevation or depression