02 - 8.2 Dysthymia and Cyclothymia

8.2 Dysthymia and Cyclothymia

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compared to usual psychiatric treatment for bipolar disorders. Int J Neuropsychopharmacol. 2007;10:123. 8.2 Dysthymia and Cyclothymia DYSTHYMIA The most typical features of dysthymia, also known as persistent depressive disorder, is the presence of a depressed mood that lasts most of the day and is present almost continuously. There are associated feelings of inadequacy, guilt, irritability, and anger; withdrawal from society; loss of interest; and inactivity and lack of productivity. The term dysthymia, which means “ill humored,” was introduced in 1980. Before that time, most patients now classified as having dysthymia were classified as having depressive neurosis (also called neurotic depression). Dysthymia is distinguished from major depressive disorder by the fact that patients complain that they have always been depressed. Thus, most cases are of early onset, beginning in childhood or adolescence and certainly occurring by the time patients

reach their 20s. A late-onset subtype, much less prevalent and not well characterized clinically, has been identified among middle-aged and geriatric populations, largely through epidemiological studies in the community. Although dysthymia can occur as a secondary complication of other psychiatric disorders, the core concept of dysthymia refers to a subaffective or subclinical depressive disorder with (1) low-grade chronicity for at least 2 years; (2) insidious onset, with origin often in childhood or adolescence; and (3) a persistent or intermittent course. The family history of patients with dysthymia is typically replete with both depressive and bipolar disorders, which is one of the more robust findings supporting its link to primary mood disorder. Epidemiology Dysthymia is common among the general population and affects 5 to 6 percent of all persons. It is seen among patients in general psychiatric clinics, where it affects between half and one-third of all patients. No gender differences are seen for incidence rates. The disorder is more common in women younger than 64 years of age than in men of any age and is more common among unmarried and young persons and in those with low incomes. Dysthymia frequently coexists with other mental disorders, particularly major depressive disorder, and in persons with major depressive disorder, there is less likelihood of full remission between episodes. The patients may also have coexisting anxiety disorders (especially panic disorder), substance abuse, and borderline personality disorder. The disorder is more common among those with first-degree relatives with major depressive disorder. Patients with dysthymia are likely to be taking a wide range of psychiatric medications, including antidepressants, antimanic agents such as lithium (Eskalith) and carbamazepine (Tegretol), and sedative-hypnotics. Etiology Biological Factors. The biological basis for the symptoms of dysthymia and major depressive disorder are similar, but the biological bases for the underlying pathophysiology in the two disorders differ. SLEEP STUDIES. Decreased rapid eye movement (REM) latency and increased REM density are two state markers of depression in major depressive disorder that also occur in a significant proportion of patients with dysthymia. NEUROENDOCRINE STUDIES. The two most studied neuroendocrine axes in major depressive disorder and dysthymia are the adrenal axis and the thyroid axis, which have been tested by using the dexamethasone-suppression test (DST) and the thyrotropin-releasing hormone (TRH)-stimulation test, respectively. Although the results of studies are not absolutely consistent, most indicate that patients with dysthymia are less likely to have abnormal results on a DST than are patients with major depressive disorder.

Psychosocial Factors. Psychodynamic theories about the development of dysthymia posit that the disorder results from personality and ego development and culminates in difficulty adapting to adolescence and young adulthood. Karl Abraham, for example, thought that the conflicts of

depression center on oral- and anal-sadistic traits. Anal traits include excessive orderliness, guilt, and concern for others; they are postulated to be a defense against preoccupation with anal matter and with disorganization, hostility, and self-preoccupation. A major defense mechanism used is reaction formation. Low self-esteem, anhedonia, and introversion are often associated with the depressive character. FREUD. In Mourning and Melancholia, Sigmund Freud asserted that an interpersonal disappointment early in life can cause a vulnerability to depression that leads to ambivalent love relationships as an adult; real or threatened losses in adult life then trigger depression. Persons susceptible to depression are orally dependent and require constant narcissistic gratification. When deprived of love, affection, and care, they become clinically depressed; when they experience a real loss, they internalize or introject the lost object and turn their anger on it and thus on themselves. COGNITIVE THEORY. The cognitive theory of depression also applies to dysthymia. It holds that a disparity between actual and fantasized situations leads to diminished self-esteem and a sense of helplessness. The success of cognitive therapy in the treatment of some patients with dysthymia may provide some support for the theoretical model. Diagnosis and Clinical Features The DSM-5 diagnosis criteria for dysthymia (Table 8.2-1) stipulate the presence of a depressed mood most of the time for at least 2 years (or 1 year for children and adolescents). To meet the diagnostic criteria, a patient should not have symptoms that are better accounted for as major depressive disorder and should never have had a manic or hypomanic episode. DSM-5 allows clinicians to specify whether the onset was early (before age 21 years) or late (age 21 years or older). DSM-5 also allows specification of atypical features in dysthymia. Table 8.2-1 DSM-5 Diagnostic Criteria for Dysthymia

The profile of dysthymia overlaps with that of major depressive disorder but differs from it in that symptoms tend to outnumber signs (more subjective than objective depression). This means that disturbances in appetite and libido are uncharacteristic, and psychomotor agitation or retardation is not observed. This all translates into a depression with attenuated symptomatology. Subtle endogenous features are observed, however, including inertia, lethargy, and anhedonia that are characteristically worse in

the morning. Because patients presenting clinically often fluctuate in and out of a major depression, the core DSM-5 criteria for dysthymia tend to emphasize vegetative dysfunction; however, cognitive symptoms are often present. Dysthymia is quite heterogeneous. Anxiety is not a necessary part of its clinical picture, yet dysthymia is often diagnosed in patients with anxiety and phobic disorders. That clinical situation is sometimes diagnosed as mixed anxiety depressive disorder. For greater operational clarity, it is best to restrict dysthymia to a primary disorder, one that cannot be explained by another psychiatric disorder. The essential features of such primary dysthymia include habitual gloom, brooding, lack of joy in life, and preoccupation with inadequacy. Dysthymia then is best characterized as long-standing, fluctuating, low-grade depression, experienced as part of the habitual self and representing an accentuation of traits observed in the depressive temperament (Table 8.2-2). The clinical picture of dysthymia is varied, with some patients proceeding to major depression and others manifesting the pathology largely at the personality level. Table 8.2-2 Attributes, Assets, and Liabilities of Depressive and Hyperthymic Temperaments A 27-year-old male grade-school teacher presented with the chief complaint that life was a painful duty that had always lacked luster for him. He said that he felt “enveloped by a sense of gloom” that was nearly always with him. Although he was respected by his peers, he felt “like a grotesque failure, a self-concept I have had since childhood.” He stated that he merely

performed his responsibilities as a teacher and that he had never derived any pleasure from anything he had done in life. He said

that he had never had any romantic feelings; sexual activity, in which he had engaged with two different women, had involved pleasureless orgasm. He said that he felt empty, going through life without any sense of direction, ambition, or passion, a realization that itself was tormenting. He had bought a pistol to put an end to what he called his “useless existence” but did not carry out suicide, believing that it would hurt his students and the small community in which he lived. (Courtesy of HS Akiskal, M.D.) Dysthymic Variants. Dysthymia is common in patients with chronically disabling physical disorders, particularly among elderly adults. Dysthymia-like, clinically significant, subthreshold depression lasting 6 or more months has also been described in neurological conditions, including stroke. According to a recent World Health Organization (WHO) conference, this condition aggravates the prognosis of the underlying neurological disease and therefore deserves pharmacotherapy. Prospective studies on children have revealed an episodic course of dysthymia with remissions, exacerbations, and eventual complications by major depressive episodes, 15 to 20 percent of which might even progress to hypomanic, manic, or mixed episodes postpuberty. Persons with dysthymia presenting clinically as adults tend to pursue a chronic unipolar course that may or may not be complicated by major depression. They rarely develop spontaneous hypomania or mania. When treated with antidepressants, however, some of them may develop brief hypomanic switches that typically disappear when the antidepressant dose is decreased. Differential Diagnosis The differential diagnosis for dysthymia is essentially identical to that for major depressive disorder. Many substances and medical illnesses can cause chronic depressive symptoms. Two disorders are particularly important to consider in the differential diagnosis of dysthymia—minor depressive disorder and recurrent brief depressive disorder. Minor Depressive Disorder. Minor depressive disorder (discussed in Section 8.1) is characterized by episodes of depressive symptoms that are less severe than those seen in major depressive disorder. The difference between dysthymia and minor depressive disorder is primarily the episodic nature of the symptoms in the latter. Between episodes, patients with minor depressive disorder have a euthymic mood, but patients with dysthymia have virtually no euthymic periods. Recurrent Brief Depressive Disorder. Recurrent brief depressive disorder (discussed in Section 8.1) is characterized by brief periods (less than 2 weeks) during which depressive episodes are present. Patients with the disorder would meet the diagnostic criteria for major depressive disorder if their episodes lasted longer. Patients

with recurrent brief depressive disorder differ from patients with dysthymia on two counts: They have an episodic disorder, and their symptoms are more severe. Double Depression. An estimated 40 percent of patients with major depressive disorder also meet the criteria for dysthymia, a combination often referred to as double depression. Available data support the conclusion that patients with double depression have a poorer prognosis than patients with only major depressive disorder. The treatment of patients with double depression should be directed toward both disorders because the resolution of the symptoms of major depressive episode still leaves these patients with significant psychiatric impairment. Alcohol and Substance Abuse. Patients with dysthymia commonly meet the diagnostic criteria for a substance-related disorder. This comorbidity can be logical; patients with dysthymia tend to develop coping methods for their chronically depressed state that involve substance abuse. Therefore, they are likely to use alcohol, stimulants such as cocaine, or marijuana, the choice perhaps depending primarily on a patient’s

social context. The presence of a comorbid diagnosis of substance abuse presents a diagnostic dilemma for clinicians; the long-term use of many substances can result in a symptom picture indistinguishable from that of dysthymia. Course and Prognosis About 50 percent of patients with dysthymia experience an insidious onset of symptoms before age 25 years. Despite the early onset, patients often suffer with the symptoms for a decade before seeking psychiatric help and may consider early-onset dysthymia simply part of life. Patients with an early onset of symptoms are at risk for either major depressive disorder or bipolar I disorder in the course of their disorder. Studies of patients with the diagnosis of dysthymia indicate that about 20 percent progressed to major depressive disorder, 15 percent to bipolar II disorder, and fewer than 5 percent to bipolar I disorder. The prognosis for patients with dysthymia varies. Antidepressive agents and specific types of psychotherapies (e.g., cognitive and behavior therapies) have positive effects on the course and prognosis of dysthymia. The available data about previously available treatments indicate that only 10 to 15 percent of patients are in remission 1 year after the initial diagnosis. About 25 percent of all patients with dysthymia never attain a complete recovery. Overall, however, the prognosis is good with treatment. Treatment Historically, patients with dysthymia either received no treatment or were seen as candidates for long-term, insight-oriented psychotherapy. Contemporary data offer the most objective support for cognitive therapy, behavior therapy, and pharmacotherapy. The combination of pharmacotherapy and some form of psychotherapy may be the most effective treatment for the disorder.

Cognitive Therapy. Cognitive therapy is a technique in which patients are taught new ways of thinking and behaving to replace faulty negative attitudes about themselves, the world, and the future. It is a short-term therapy program oriented toward current problems and their resolution. Behavior Therapy. Behavior therapy for depressive disorders is based on the theory that depression is caused by a loss of positive reinforcement as a result of separation, death, or sudden environmental change. The various treatment methods focus on specific goals to increase activity, to provide pleasant experiences, and to teach patients how to relax. Altering personal behavior in depressed patients is believed to be the most effective way to change the associated depressed thoughts and feelings. Behavior therapy is often used to treat the learned helplessness of some patients who seem to meet every life challenge with a sense of impotence. Insight-Oriented (Psychoanalytic) Psychotherapy. Individual insightoriented psychotherapy is the most common treatment method for dysthymia, and many clinicians consider it the treatment of choice. The psychotherapeutic approach attempts to relate the development and maintenance of depressive symptoms and maladaptive personality features to unresolved conflicts from early childhood. Insight into depressive equivalents (e.g., substance abuse) or into childhood disappointments as antecedents to adult depression can be gained through treatment. Ambivalent current relationships with parents, friends, and others in the patient’s current life are examined. Patients’ understanding of how they try to gratify an excessive need for outside approval to counter low self-esteem and a harsh superego is an important goal of this therapy. Interpersonal Therapy. In interpersonal therapy for depressive disorders, a patient’s current interpersonal experiences and ways of coping with stress are examined to reduce depressive symptoms and to improve self-esteem. Interpersonal therapy lasts for about 12 to 16 weekly sessions and can be combined with antidepressant medication. Family and Group Therapies. Family therapy may help both the patient and the patient’s family deal with the symptoms of the disorder, especially when a biologically based subaffective syndrome seems to be present. Group therapy may help withdrawn patients learn new ways to overcome their interpersonal problems in social situations. Pharmacotherapy.

Because of long-standing and commonly held theoretical beliefs that dysthymia is primarily a psychologically determined disorder, many clinicians avoid prescribing antidepressants for patients; however, many studies have shown therapeutic success with antidepressants. The data generally indicate that selective serotonin reuptake inhibitors (SSRIs) venlafaxine and bupropion are an effective treatment for patients with dysthymia. Monoamine oxidase inhibitors (MAOIs) are effective in a subgroup of patients with the disorder, a group who may also respond

to the judicious use of amphetamines. Hospitalization. Hospitalization is usually not indicated for patients with dysthymia, but particularly severe symptoms, marked social or professional incapacitation, the need for extensive diagnostic procedures, and suicidal ideation are all indications for hospitalization. CYCLOTHYMIC DISORDER Cyclothymic disorder is symptomatically a mild form of bipolar II disorder, characterized by episodes of hypomania and mild depression. In DSM-5, cyclothymic disorder is defined as a “chronic, fluctuating mood disturbance” with many periods of hypomania and of depression. The disorder is differentiated from bipolar II disorder, which is characterized by the presence of major (not minor) depressive and hypomanic episodes. As with dysthymia, the inclusion of cyclothymic disorder with the mood disorders implies a relation, probably biological, to bipolar I disorder. Some psychiatrists, however, consider cyclothymic disorder to have no biological component and to result from chaotic object relations early in life. Contemporary conceptualization of cyclothymic disorder is based to some extent on the observations of Emil Kraepelin and Kurt Schneider that one-third to two-thirds of patients with mood disorders exhibit personality disorders. Kraepelin described four types of personality disorders: depressive (gloomy), manic (cheerful and uninhibited), irritable (labile and explosive), and cyclothymic. He described the irritable personality as simultaneously depressive and manic and the cyclothymic personality as the alternation of the depressive and manic personalities. Epidemiology Patients with cyclothymic disorder may constitute from 3 to 5 percent of all psychiatric outpatients, perhaps particularly those with significant complaints about marital and interpersonal difficulties. In the general population, the lifetime prevalence of cyclothymic disorder is estimated to be about 1 percent. This figure is probably lower than the actual prevalence because, as with patients with bipolar I disorder, the patients may not be aware that they have a psychiatric problem. Cyclothymic disorder, as with dysthymia, frequently coexists with borderline personality disorder. An estimated 10 percent of outpatients and 20 percent of inpatients with borderline personality disorder have a coexisting diagnosis of cyclothymic disorder. The female-to-male ratio in cyclothymic disorder is about 3 to 2, and 50 to 75 percent of all patients have an onset between ages 15 and 25 years. Families of persons with cyclothymic disorder often contain members with substance-related disorder. Etiology As with dysthymia, controversy exists about whether cyclothymic disorder is related to

the mood disorders, either biologically or psychologically. Some researchers have postulated that cyclothymic disorder has a closer relation to borderline personality disorder than to the mood disorders. Despite these controversies, the preponderance of biological and genetic data favors the idea of cyclothymic disorder as a bona fide mood disorder. Biological Factors. About 30 percent of all patients with cyclothymic disorder have positive family histories for bipolar I disorder; this rate is similar to the rate for patients with bipolar I disorder. Moreover, the pedigrees of families with bipolar I disorder often contain generations of patients with bipolar I disorder linked by a generation with cyclothymic disorder. Conversely, the prevalence of cyclothymic disorder in the relatives of patients with bipolar I disorder is much higher than the prevalence of cyclothymic

disorder either in the relatives of patients with other mental disorders or in persons who are mentally healthy. The observations that about one-third of patients with cyclothymic disorder subsequently have major mood disorders, that they are particularly sensitive to antidepressant-induced hypomania, and that about 60 percent respond to lithium add further support to the idea of cyclothymic disorder as a mild or attenuated form of bipolar II disorder. Psychosocial Factors. Most psychodynamic theories postulate that the development of cyclothymic disorder lies in traumas and fixations during the oral stage of infant development. Freud hypothesized that the cyclothymic state is the ego's attempt to overcome a harsh and punitive superego. Hypomania is explained psychodynamically as the lack of self-criticism and an absence of inhibitions occurring when a depressed person throws off the burden of an overly harsh superego. The major defense mechanism in hypomania is denial, by which the patient avoids external problems and internal feelings of depression. Patients with cyclothymic disorder are characterized by periods of depression alternating with periods of hypomania. Psychoanalytic exploration reveals that such patients defend themselves against underlying depressive themes with their euphoric or hypomanic periods. Hypomania is frequently triggered by a profound interpersonal loss. The false euphoria generated in such instances is a patient's way to deny dependence on love objects and simultaneously disavowing any aggression or destructiveness that may have contributed to the loss of the loved person. Diagnosis and Clinical Features Although many patients seek psychiatric help for depression, their problems are often related to the chaos that their manic episodes have caused. Clinicians must consider a diagnosis of cyclothymic disorder when a patient appears with what may seem to be sociopathic behavioral problems. Marital difficulties and instability in relationships are common complaints because patients with cyclothymic disorder are often promiscuous and irritable while in manic and mixed states. Although there are anecdotal reports of

increased productivity and creativity when patients are hypomanic, most clinicians report that their patients become disorganized and ineffective in work and school during these periods. The DSM-5 diagnostic criteria for cyclothymic disorder stipulate that a patient has never met the criteria for a major depressive episode and did not meet the criteria for a manic episode during the first 2 years of the disturbance. The criteria also require the more or less constant presence of symptoms for 2 years (or 1 year for children and adolescents). Signs and Symptoms. The symptoms of cyclothymic disorder are identical to the symptoms of bipolar II disorder except that they are generally less severe. On occasion, however, the symptoms may be equally severe but of shorter duration than those seen in bipolar II disorder. About half of all patients with cyclothymic disorder have depression as their major symptom, and these patients are most likely to seek psychiatric help while depressed. Some patients with cyclothymic disorder have primarily hypomanic symptoms and are less likely to consult a psychiatrist than are primarily depressed patients. Almost all patients with cyclothymic disorder have periods of mixed symptoms with marked irritability. Most patients with cyclothymic disorder seen by psychiatrists have not succeeded in their professional and social lives as a result of their disorder, but a few have become high achievers who have worked especially long hours and have required little sleep. Some persons' ability to control the symptoms of the disorder successfully depends on multiple individual, social, and cultural attributes. The lives of most patients with cyclothymic disorder are difficult. The cycles of the disorder tend to be much shorter than those in bipolar I disorder. In cyclothymic disorder, the changes in mood are irregular and abrupt and sometimes occur within hours. The unpredictable nature of the mood changes produces great stress. Patients often feel that their moods are out of control. In irritable, mixed periods, they may become involved in unprovoked disagreements with

friends, family, and coworkers. Mr. B, a 25-year-old single man, came for evaluation due to irritability, insomnia, jumpiness, and excessive energy. He reported that such episodes lasted from a few days to a few weeks and alternated with longer periods of feeling hopeless, dejected, and worn out with thoughts of suicide. Mr. B reported having been this way for as long as he could remember. He had never been treated for his symptoms. He denied using drugs and said he had "only the occasional drink to relax." As a child, Mr. B went from one foster family to another and was an irresponsible and trouble-making child. He frequently ran away from home, was absent from school, and committed minor crimes. He ran away from his last foster family at the age of 16 years and drifted ever since, taking occasional odd jobs. When he became restless at one location or job, he quickly moved on to the next. He did not have close friends because he would form and end friendships quickly.

Substance Abuse. Alcohol abuse and other substance abuse are common in patients with cyclothymic disorder, who use substances either to self-medicate (with alcohol, benzodiazepines, and marijuana) or to achieve even further stimulation (with cocaine, amphetamines, and hallucinogens) when they are manic. About 5 to 10 percent of all patients with cyclothymic disorder have substance dependence. Persons with this disorder often have a history of multiple geographical moves, involvements in religious cults, and dilettantism. Differential Diagnosis When a diagnosis of cyclothymic disorder is under consideration, all the possible medical and substance-related causes of depression and mania, such as seizures and particular substances (cocaine, amphetamine, and steroids), must be considered. Borderline, antisocial, histrionic, and narcissistic personality disorders should also be considered in the differential diagnosis. Attention-deficit/hyperactivity disorder (ADHD) can be difficult to differentiate from cyclothymic disorder in children and adolescents. A trial of stimulants helps most patients with ADHD and exacerbates the symptoms of most patients with cyclothymic disorder. The diagnostic category of bipolar II disorder (discussed in Section 8.1) is characterized by the combination of major depressive and hypomanic episodes. Course and Prognosis Some patients with cyclothymic disorder are characterized as having been sensitive, hyperactive, or moody as young children. The onset of frank symptoms of cyclothymic disorder often occurs insidiously in the teens or early 20s. The emergence of symptoms at that time hinders a person's performance in school and the ability to establish friendships with peers. The reactions of patients to such a disorder vary; patients with adaptive coping strategies or ego defenses have better outcomes than patients with poor coping strategies. About one-third of all patients with cyclothymic disorder develop a major mood disorder, most often bipolar II disorder. Treatment Biological Therapy. The mood stabilizers and antimanic drugs are the first line of treatment for patients with cyclothymic disorder. Although the experimental data are limited to studies with lithium, other antimanic agents—for example, carbamazepine and valproate (Depakene)—are reported to be effective. Dosages and plasma concentrations of these agents should be the same as those in bipolar I disorder. Antidepressant treatment of depressed patients with cyclothymic disorder should be done with caution because these patients have increased susceptibility to antidepressantinduced hypomanic or manic episodes. About 40 to 50 percent of all patients with cyclothymic disorder who are treated with antidepressants experience such episodes.

Psychosocial Therapy. Psychotherapy for patients with cyclothymic disorder is best directed toward increasing patients' awareness of their condition and helping them develop coping mechanisms for their mood swings. Therapists usually need to help patients repair any damage, both work and family related, done during episodes of hypomania. Because of the long-term nature of cyclothymic

disorder, patients often require lifelong treatment. Family and group therapies may be supportive, educational, and therapeutic for patients and for those involved in their lives. The psychiatrist conducting psychotherapy is able to evaluate the degree of cyclothymia and so provide an early-warning system to prevent full-blown manic attacks before they occur. REFERENCES Epperson C. Premenstrual dysphoric disorder and the brain. Am J Psychiatry. 2013;170(3):248–252. Fava GA, Rafanelli C, Tomba E, Guidi J, Grandi S. The sequential combination of cognitive behavioral treatment and wellbeing therapy in cyclothymic disorder. Psychother Psychosom. 2011;80:136. Gitlin M, Frye MA. Maintenance therapies in bipolar disorders. Bipolar Disord. 2012;14(s2):51. Helseth V, Samet S, Johnsen J, Bramness JG, Waal H. Independent or substance-induced mental disorders? An investigation of comorbidity in an acute psychiatric unit. J Dual Diagn. 2013;9(1):78–86. Huprich SK, DeFife J, Westen D. Refining a complex diagnostic construct: Subtyping Dysthymia with the Shedler–Westen Assessment Procedure-II. J Affect Disord. 2014;152:186–192. Khazaal Y, Gex-Fabry M, Nallet A, et al. Affective temperaments in alcohol and opiate addictions. Psychiatr Q. 2013;84(4):429–438.. Mechri A, Kerkeni N, Touati I, Bacha M, Gassab L. Association between cyclothymic temperament and clinical predictors of bipolarity in recurrent depressive patients. J Affect Disord. 2011;132:285. Parker G, McCraw S, Fletcher K. Cyclothymia. Depress Anxiety. 2012;29:487. Perugi G, Popovic D. Practical management of cyclothymia. In: Young AH, Ferrier IN, Michalak EE, eds. Practical Management of Bipolar Disorders. New York: Cambridge University Press; 2010:139. Post RM, Altshuler LL. Mood disorders: Treatment of bipolar disorders. In: Sadock BJ, Sadock VA, Ruiz P, eds. Kaplan & Sadock’s Comprehensive Textbook of Psychiatry. 9th edition. Vol. 2. Philadelphia: Lippincott Williams & Wilkins; 2009:1743. Rubio JM, Olfson M, Villegas L, Perez-Fuentes G, Wang S, Blanco C. Quality of life following remission of mental disorders: Findings from the National Epidemiologic Survey on Alcohol and Related Conditions. J Clin Psychiatry. 2013;74(5):e445–e450. Serretti A, Chiesa A, Calati R, et al. Influence of family history of major depression, bipolar disorder, and suicide on clinical features in patients with major depression and bipolar disorder. Eur Arch Psychiatry Clin Neurosci. 2013;263(2):93–103. Tomba E, Rafanelli C, Grandi S, Guidi J, Fava GA. Clinical configuration of cyclothymic disturbances. J Affect Disord. 2012;139:244. Totterdell P, Kellett S, Mansell W. Cognitive behavioural therapy for cyclothymia: Cognitive regulatory control as a mediator of mood change. Behav Cogn Psychother. 2012;40:412. Vaingankar JA, Rekhi G, Subramaniam M, Abdin E, Chong SA. Age of onset of life-time mental disorders and treatment contact. Social Psychiatry and Psychiatric Epidemiology. 2013;48(5):835–843. Van Meter AR, Youngstrom EA, Findling RL. Cyclothymic disorder: A critical review. Clin Psychol Rev. 2012;32:229.

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