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372 *Current Neuropharmacology*, **2017**, *15*, **372-379**

REVIEW ARTICLE

Diagnosis and Treatment of Cyclothymia: The "Primacy" of Temperament

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Abstract: ***Background*:** Contrary to DSM-5 definition based on recurrence of low grade hypomanic and depressive symptoms, cyclothymia is better defined in a neurodevelopmental perspective as an exaggeration of cyclothymic temperament. Emotional dysregulation with extreme mood instability and reactivity is the core features of the complex symptomatology.

***Method*:** In the present article, we critically reviewed the literature on the diagnosis and treatment of cyclothymia, focusing on the temperamental and neurodevelopmental perspectives.

***Results*:** Current epidemiological and clinical research showed the high prevalence and the validity of cyclothymia as a distinct form of bipolarity, frequently associated with multiple comorbidities with anxiety, impulse control, substance use, and so called "personality" disorders. Many patients receive correct diagnosis and treatments after many years of illness, when the superposition of complications reduces the possibility of complete remission. A therapeutic model combining the focus on symptomatic presentations with a temperamental perspective seems to represent an effective approach for cyclothymic patients with complex clinical presentations.

***Conclusion*:** Cyclothymic mood instability is an understudied issue despite the evidence of its clinical relevance. Unresolved issues concern its diagnostic delimitation and the possible relationships with emotional dysregulation observed in other neurodevelopmental disorders. We need to confirm the specificity of the disorder and to improve its recognition in early phase of the life, especially in youth. Early recognition means avoiding unnecessary complications and establishing specific treatments and clinical management since the beginning.

ARTICLE HISTORY

Received: December 24, 2015
Revised: April 25, 2016
Accepted: May 24, 2016

DOI:
10.2174/1570159X14666160616120157

Keywords: Bipolar disorder, cyclothymia, DSM system, emotional dysregulation, mood, temperament.

INTRODUCTION

Cyclothymia is characterized by early onset, persistent, spontaneous and reactive mood fluctuations, associated with a variety of anxious and impulsive behaviors, resulting in a very rich and complex clinical presentation. Current diagnostic criteria for cyclothymic disorder (DSM-5 and ICD-10), emphasizing only episodic mood symptoms, may be misleading both from diagnostic and therapeutic point of views.

Temperamental mood reactivity and instability as well as most of their psychological, behavioral and interpersonal consequences should be considered the basic features of cyclothymia. DSM-5 criteria for cluster B and C personality disorders and ICD-10 definitions of emotionally unstable and histrionic personality disorders describe many of these characteristics from a different perspective [1-3]. As a consequence, the distinction from histrionic or borderline personality disorders (BPD) mainly stands in the clinician's eye, rather than depending on real clinical differences [4, 5].

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In the present article, we reviewed the literature on the diagnosis and treatment of cyclothymia, focusing on the temperamental and neurodevelopmental perspectives.

CYCLOTHYMIA AS A NEURODEVELOPMENTAL DISORDER

Emotional dysregulation, characterized by intense and rapid mood changes of both polarities and by the tendency to over-react to external stimuli, especially within the interpersonal field, represents the temperamental basis of cyclothymia.

Different degrees of emotional dysregulation, associated with changes of energy and motivation, are described in cluster B personality disorders and in all neurodevelopmental disorders. The fact that all these conditions share with cyclothymia a difficulty in modulating their behavior during emotional states suggests a plausible common neuro-physiological basis. The observation of structural and functional abnormalities in the neural network subserving emotional information, such as amygdala hyper-reactivity and regulatory deficits of the orbito-frontal and prefrontal cortex [6, 7], are consistent with the notion of reduced

1570-159X/17 $58.00+.00

emotional regulation in BPD subjects. Similar findings have been reported in patients with BD and mood instability (over-activation within the parahippocampus/amygdala and thalamus and reduced engagement within the ventrolateral prefrontal cortex [8]) clearly suggesting that emotional arousal may interfere with cognitive processing also in these patients. In other terms, some neurodevelopmental dysfunctions of amygdala and fronto-limbic circuitries may represent the common neurophysiological substrate of the emotional dysregulation involved in different and apparently separated clinical entities.

We suggested that the emotional dysregulation of cyclothymic type should be considered a neuro-developmental disorder. This hypothesis is empirically strengthened by the observation that such an emotional dysregulation is met more frequently than expected in a wide span of neurodevelopmental disorders including Attention Deficit Hyperactivity Disorder, Autistic Spectrum Disorders, Tourette's Syndrome and Intellectual Disability. As a consequence cyclothymic disposition should be understood in a developmental perspective as a result of very complex interactions between constitution and environment. Those interactions may produce different effects depending on the weight of genetic and environmental background in different subjects, but also the developmental period when they become apparent. This is the reason why "clinically, one may encounter patients in whom many or all the conditions associated with emotional dysregulation coexist, emerging in childhood and adolescence, or in less severe forms becoming recognizable a few years later in early adult life" [9].

In this perspective, it is easily understandable that the cyclothymic disposition might heavily influence the interaction between the subject and the environment. The exaggerated emotional over-reactivity in stressful situations and interpersonal relationships may favor a distorted perception of the "traumatic" experiences, resulting in personal histories characterized by high rates of emotional abuse, frequently in different contexts. On the other hand cyclothymic sensation seeking may be associated to the tendency to be involved in potentially risky situations that facilitates the occurrence of actual traumatic events. Finally, intense mood reactivity and instability are invariably associated with a series of psychological and behavioral consequences, which may represent the major complaints in many subjects. The detection of the cyclothymic nature of certain psychological faults and their behavioral consequences requires experience and careful clinical evaluation. In most cases mood fluctuations represent the habitual self of the patients, transient depressive symptoms can be misattributed to concomitant unpleasant events and sub-excitatory symptoms are usually related to a special character.

Increased mood reactivity is expressed with a peculiar kind of sensitivity to different environmental stimuli. Cyclothymic persons react to positive events by quickly becoming extremely joyful, enthusiastic and active, in some cases they briefly appear excessively euphoric and impulsive. They react to negative events (real or perceived) with disproportionally intense down-beating reactions. Even minor distress may precipitate a wide range of emotions and feelings, from unusual sadness to prostration, extreme fatigue, anguish, desperation, even to suicidal thoughts. When irritability and impulsivity are associated, those feelings may be complicated by uncontrolled crushing gestures. As "environment" we mean any sort of external stimuli: psychological (for example falling in love, romantic, scholastic and working failure), environmental "strictu senso" (*i.e.* meteorological, seasonal or time zone changes), physical (*i.e.* immobility vs. hyperactivity) or chemical (*i.e.* medications, alcohol, drugs).

Interpersonal sensitivity and emotional over-reactivity are strongly correlated each other, and they seem to represent the cognitive and affective aspects of the same psycho(patho)logical dimension [3, 10]. Rejection sensitivity is also related to marked fluctuations in self-esteem in a "vicious circle". Emotional reactivity and sensitivity make cyclothymic persons prone to feeling wounded also for minor critiques or imagined slights. Hostility and anger may trigger as an avalanche a variety of reactions against those who are supposed to be the originators of their sufferings. These reactions range from minor disputes up to rage explosions. When emotional reactivity is very intense, sensitivity may favor interpretation and overvalued ideas. Separation anxiety is strictly connected with cyclothymic mood instability and, sometimes, reactivity [11, 12]. Some studies in adults with anxiety and mood disorders reported a significant link between separation anxiety, interpersonal sensitivity and mood instability of cyclothymic type [10, 13]. The correlation between both childhood and/or adult separation anxiety and cyclothymic mood instability has been replicated in different clinical populations [12, 13].

Fear of being disapproved, rejected or turned away, and anxiety upon separation may lead to submissive behavior and persistent involvement in abusive relationships, as well as 'pathological altruism', described as a tendency to excessively please others. Pathological jealousy and propensity to test the limits in interpersonal relationships can be framed in this context. On the other hand, the extreme sensitivity to approval, compliments and positive rewards may determine a sort of addiction associated with histrionic behaviors. Excessive complacency alternating with anger-hostility frequently disrupt interpersonal relationships, family life or social functioning [14]. A stormy youth is traceable for many of these individuals reporting a history of tempestuous relationships [15].

The coexistence of conflicting and opposite temperamental attitudes (*e.g.* novelty seeking and harm avoidance) may represent another source of distress for some cyclothymic individuals [16]. Sensation-seeking and self-stimulating behavior can be associated with anxious reactions [15]. In some cases full-blown impulse control disorders may emerge such as pathological gambling and compulsive sexuality in men, or compulsive buying and binge eating in women [15, 17-19]. In this perspective, cyclothymia could represent a predisposing background for drug abuse and addiction because of a mix of sensation-seeking, impulsivity and high sensitivity to substances (including any sort of illicit drug and alcohol, but also hypnotics and sedatives) [20, 21].

Table 1. Endogenous versus Exogenous cyclicity in BD: Role of affective temperaments.

Basic Temperament	Stable – Hyperthymic	Unstable – Complex Cyclothymic
Sequence	MDI	DMI
Cyclicity	Endogenous	Exogenous
Evolution	Episodic, free intervals	Instability, tendency to rapid cycling
Reactivity to treatment	Prophylactic effect of lithium *via* attenuating hyperthymia	Worsening effect of antidepressants (formation of rapid cycling; chronic mixed state; mood switching)

MDI=mania-depression-interval, DMI=depression-mania-interval
Modified from [28] and [36].

CYCLOTHYMIC TEMPERAMENT AND BIPOLAR DISORDER

The relationship between cyclothymic temperament and BD are expressed at different levels. The temperamental disposition 1) can be considered a vulnerability factor for the onset of a full-blown BD episode and most comorbid conditions; 2) may influence the course of BD and the clinical expression of depressive, manic or mixed episodes; 3) requires a specific approach for the treatment and management of the concomitant mood disorder.

Both DSM-5 and ICD-10 recognizes that cyclothymic disorder is often observed in the relatives of BD patients and that some patients with cyclothymia eventually develop BD. The observation of cyclothymic temperament in children and adolescents with depression has been considered one of the strongest predictor for the further development of BD [22].

In adults, cyclothymic temperament is considered an expression of bipolar diathesis and has been associated with frequent depressive or mixed-depressive recurrences [23]. Cyclothymic temperamental features such as "mood lability", "energy activity", and "daydreaming" have been proved to be specific in identifying unipolar depressives who switched to hypomania [24].

A major part of Koukopoulos's legacy in the modern era of bipolarity was to clarify the clinical picture of bipolarity by integrating basic affective temperaments, the sequence of mood episodes, the phenomenology of cyclicity and the treatment responses [25]. According to Koukopoulos [28], there is little doubt about the importance of the temperaments in the formation and clinical expression of affective disorders. Table **1** illustrates the clinical approach of Koukopoulos where we can observe the intimate interactions between:

- Hyperthymic temperament, exogenous cyclicity, the MDI sequence (Mania–Depression-Interval cycle), and the good prophylactic action of lithium. In these cases the prevention of the new cycles is probably accomplished through the control of the hypomanic episodes and the hyperthymia levels during free intervals.
- Complex cyclothymic temperament (excitable and labile affective traits), endogenous cyclicity, prevalence of BP-II disorder, the DMI sequence, and rapid cycling. The main clinical problem is observed in many cases when rapid cyclicity persists beyond the first year of adequate treatment.

"Cyclothymic depression" is probably the most common manifestation of bipolarity, as it regards at least the 50% of depressed outpatients in psychiatric settings [26]. Similar findings have been reported in depressive patients in general medical practice [27]. Although Cyclothymia can be associated with BD I, it is more frequently observed in BD II patients. A large study conducted in France showed that 88% of major depressive patients with cyclothymic features belonged to the BD II subtype [26]. In the largest proportion of these subjects, cyclothymic temperament is present since childhood or adolescence, but clear clinical manifestations may be triggered by stressful life events later in life at any age. From this perspective cyclothymia is the temperamental foundation ("basic state") of many bipolar II depressions. Depressive phases usually dominate the clinical presentation or, anyway, cyclothymic patients only report depressive symptoms being scarcely aware of the hypomanic phases. Despite this, hypomania is very common [28] and mostly characterized by irritability, disinhibited and impulsive behavior, rather than elation or euphoria.

The "primacy" of cyclothymic temperament is also reflected by its influence on the BD course in terms of cyclicity, comorbidity and complications such as suicidality and drug resistance. Cyclothymia is associated with early onset of BD in childhood or adolescence and with extreme spontaneous or medication-induced mood cyclicity and instability [15, 28, 29]. Finally, emotional dysregulation associated with cyclothymic temperament and other neuro-developmental disorders seems to represent the most common substrate of the high comorbidity rates with anxiety, impulse control, and also with alcohol and substance use disorders [15, 19, 30] frequently observed in bipolar samples and in patients with neurodevelopmental disorders [31, 32].

As concerns the clinical presentation of the BD episodes, "cyclothymic depression" frequently shows atypical features such as hypersomnia, hyperphagia, inverse diurnal variations and marked fatigue ('leaden paralysis') [10, 33-35]. Atypical features are often accompanied by a variety of associated features strictly related to the underlying emotional dysregulation: mood reactivity, interpersonal sensitivity, separation anxiety, panic and phobic anxiety, obsessive-compulsive symptoms, somatizations, self-pity, subjective or overt anger, jealousy, suspiciousness, and overvalued ideas [24].

Suicidality is a reactive and sometime impulsive behavior, frequently triggered by real, perceived or delusional problems in different areas of life, usually interpersonal relationships, financial concerns, health problems. Cyclothymic mood instability associated with extreme emotional reactivity, impulsivity and rapid shift from inhibition to disinhibition, may play a major role in suicidal behaviors, providing the necessary energy and drive. The association between constitutional mood instability and suicidal behavior has been supported by several studies in different samples of mood disorder patients and in suicide attempters [36-39]. Significantly higher rates of suicidal ideation and violent and nonviolent attempts have been observed in subjects with cyclothymic temperament in comparison with those without.

Although there are few evidence-based data regarding the influence of co-existing cyclothymia on BD response to pharmacological treatment, it has been shown that a substantial proportion of bipolar patients showing scarce, excessive or anomalous response to usual treatments share a cyclothymic diathesis [40-42]. The current knowledge on this topic is mainly assigned to few naturalistic reports, clinical observations and expert opinions. Few studies showed a mild to moderate efficacy of mood stabilizers, especially lithium [43-45] but also valproate [46, 47] and lamotrigine [48], in the prevention of depressive episodes [42, 43, 49], as well as mood episodes of other polarities (*i.e*., mixed or hypomanic) [50]. Interestingly the response to lithium seems to be higher in patients with cyclothymic disposition than in other psychiatric conditions [51] and, by the contrary, the presence of cyclothymia should be considered a predictor of good response to lithium on a variety of conditions [52]. There are also evidences that antidepressant-resistant depressions responding to lithium frequently have a neglected cyclothymic background [53]. Not all the data on lithium are positive: cyclothymic bipolar patients seem to report a worse response to lithium compared to hyperthymics [45] and patients with cyclothymic disorder may show lower response than BD I and II [44].

The use of antidepressants is really debated. Tricyclic antidepressants account for some positive results in depressive patients [54, 55], whereas SSRIs have been associated not only with low response rates [42], but also with worsening of the illness [40]. In particular, cyclothymic patients resulted more sensitive to drugs and medications, showing high rates of antidepressant-induced hypomanic and mixed-manic switches and long-term mood instability, chronic course, rapid cycling and increased suicidality [40]. Some of these patients may also experience the "wear-off" phenomenon [41, 56], described as the emergence of recurrence or relapse during a previously effective maintenance treatment (something different from tachyphylaxis). Usually, this condition is not responsive to the switch to another antidepressant and has to be considered a sign of bipolarity.

Similar considerations could be done on the use of antipsychotics. In our experience cyclothymic patients are very sensitive to D2-antagonism, which may induce adverse effects such as depression, amotivational syndrome and extrapyramidal symptoms more frequently and at lower doses than in other mood disordered patients. The induction of depression may heavily contribute to the destabilization of the illness.

THE ROLE OF TEMPERAMENT IN THE TREATMENT OF CYCLOTHYMIA

Differently from classical bipolars, the treatment of cyclothymia requires a specific management of pharmacotherapy to be assorted with adapted psychoeducation, in order to facilitate acceptance of the disorder and to focus on the goals of the treatment. The main target of the pharmacological and psycho-educational interventions should be the basic mood dysregulation, underlying most of the psychological dysfunctions and behavioral problems of these patients.

A complete treatment strategy should include adapted psychoeducation and, eventually when required, psychotherapy. The psychoeducational approach, structured or not, should be adopted since the beginning differently from what recommended for BD patients. Psychoeducation is aimed at the achievement of acceptance of the illness, confidence in the doctor, adherence to medications and focusing on the behavioral and interpersonal consequences of the illness as objectives of the therapy.

Because of the temperamental nature of the disorder, psychoeducation should be an integral part of every single follow-up visit. The physician should give the patient a continuous feedback to circumscribe dysfunctional behavioral and interpersonal pathways. It is particularly important to assess periodically the psychological aspects of cyclothymia even after months since the therapy have been started.

It is important to keep in mind that most cyclothymic patients do not match with the psychoeducational approach proposed for "classic" BD forms [57]. Psychoeducational models for BD I cannot fit with the main psychological, behavioral and interpersonal features related to cyclothymia and may induce in cyclothymic patients the unpleasant feeling of not being understood. Hantouche and colleagues in the Anxiety and Mood Center team (Paris, France) [58] elaborated a psychoeducation group therapy specific for cyclothymia. The format consisted of six weekly 2-hour sessions. During the first session a clinical description of cyclothymia is provided together with a discussion regarding causes and medications. The second session focuses on monitoring of mood swings, assessment of warning signs, strategies to cope with early relapses and planning of 'positive' routines. Sessions 3 and 4 are dedicated to the assessment of psychological vulnerabilities such as emotional dependency, sensitivity to rejection, excessive need to please and other psychological faults. The cognitive processes strictly associated to the ups-and-downs are examined during the fifth session. Finally, the sixth session is focused on interpersonal conflicts [59]. Although systematic long-term follow-up data are unavailable, this approach obtained promising preliminary results in terms of better understanding of the nature of the illness, less opposition to medications and better adherence to treatments in general.

Three fundamental principles should guide decision-making for the pharmacotherapy of cyclothymia in clinical practice: 1. Establish the hierarchy of clinical priorities on

the basis of severity and functional impairment. 2. Draw principal objectives both in mid-term and long-term, actively involving and motivating the patient. 3. Follow the rule of "go slow and stay low", considering that these patients are abnormally sensitive to the effects of medications.

The hierarchical approach usually implies the treatment of the current acute episode, typically nonpsychotic depressive or mixed-depressive states, often chronic and with a history of multiple antidepressants failure. Managing the acute phase can require from few weeks to several months. The position of comorbidity in this hierarchy (as obsessive-compulsive disorder, panic, impulsivity, drug/alcohol abuse and bulimia) may vary on the basis of severity and impact on the individual functioning. For example, a severe alcohol or drug abuse may have the priority. Similarly, the presence of suicidal risk and self-harm behaviors need prompt intervention.

The mid-term objective of treatment aims to achieve in a period ranging from 6 months to one year a relative mood stability, meant as the decrease of amplitude and frequency of ups-and-downs, and a greater behavioral control. For the success of the treatment it is essential to establish a cooperative relationship with the patient, explaining with great details the length of the period of treatment, specific objectives in the different phases of the therapy and reminding these concepts throughout the entire treatment period. In fact, the scarce involvement of the patient may lead him/her to give up medications (especially mood stabilizers) in front of apparent ineffectiveness or too slow improvement. The patient has to be educated that medications are not like drugs that must push him/her up when he/she feels depressed and then sedate him when he/she feels too much hyperactive, anxious or nervous. The doctor is not the pusher. Once mood stabilization is achieved, the long-term aims of the therapeutic program should be the enhancement of functional adjustment and the modification of dysfunctional life schemas.

Always respecting the most important and fundamental rule of "go slow and stay low", in our clinical practice we sew up the treatment as tailors targeting specific dimensions on the basis of the peculiar clinical picture.

Some evidences suggest the value of mood stabilizer agents, including lithium and some anticonvulsants, both in the mid and long-term [60, 61]. The use of antidepressant or antipsychotic drugs should be considered to manage depressive, anxious or hypomanic symptoms but only for brief periods and after the failure of mood stabilizers.

When mixity and mood reactivity are dominant, cyclothymic patients would benefit from a small dose of valproate (300-600mg/die). When anxious–depressive polarity is dominant, Lamotrigine should be preferred, while lithium may be utilized in patients with marked cyclic course and affect intensity. Some patients may benefit from the combination of small dosages of lithium (200–400 mg/day) plus lamotrigine (25–100 mg/day) [62].

Although antidepressants are demonized and actually may represent a gun in some cases, in real-world practice almost all cyclothymic patients receive antidepressants and a correct diagnosis is frequently established in recurrent, difficult-to-treat, resistant "depression". Indeed, cyclothymic patients usually perceive greater distress linked to depression and anxiety, rather than hypomanic symptoms or emotional instability. For this reason, most patients seek treatments to manage depressive symptoms or anxious comorbidity and are treated with antidepressants and sedatives. Evidence regarding the efficacy and safety of antidepressants in these populations are substantially lacking but there is broad agreement among clinicians that the use of these drugs should be carefully monitored in order to minimize mood switches and long-term destabilization. Possible consequences of incautious use of antidepressants in cyclothymia range from the increase of highs and lows amplitude and frequency of cycling [61], induction of chronic treatment-resistant mixed-depressive states and increase of suicidal risk [63]. Finally, as cyclothymia may be a harbinger of full-blown bipolarity, antidepressants might be responsible for the onset of severe manic or mixed episodes in certain individuals.

It is likewise true that a selected subpopulation of cyclothymics may really benefit from low-doses of antidepressants. As a general rule, a gradual removal of the antidepressants and unnecessary drugs and the introduction of one or more specific mood stabilizers should be attempted when possible. As a rule, antidepressants should be avoided from the beginning and reserved as second or third-line choices only for long-lasting severe depressive or anxious symptomatology when combination therapy with different mood stabilizers had failed. A possible alternative option in mild depression with anxiety or irritability and sleep disturbances may be quetiapine [64], also demonstrated effective in acute bipolar depression. Doses should not exceed 100mg/day because these patients usually complain adverse effects at higher dosages, with subsequent increase of the risk of nonadherence. More in general, the use of antipsychotics should be limited in terms of both dosage and treatment duration. Cyclothymic patients are likely to develop in a short period psychomotor adverse effects such as motor impairment, blunted affect, loss of motivation and depression. Because of this heightened sensitivity, cyclothymia is also associated with an increased risk for the early development of tardive neuropsychiatric side effects. In this respect, the use of first generation antipsychotics or drugs with selective blockade of D_2 receptors should be avoided, unless strictly necessary. Other antipsychotics with different receptor profiles should be preferred and used at low doses. For example, 25-50 mg/day of quetiapine as well as 2,5-5 mg/day of olanzapine or 2-6 mg/day of perphenazine may be useful for the management of irritability, impulsivity and other excitatory phenomena during an acute hypomanic or mixed state.

The comorbidity with anxiety, impulse–control, eating and attention deficit hyperactivity disorders in youths is very common and represents another important treatment challenge. The selection of treatments for each comorbid condition is mostly based on open clinical experience [3, 65]. For instance, Valproate seems to be more effective than lithium in controlling anxiety, panic attacks and inner tension, very common in mixed depressive state and ultra-rapid cycling. When anxiety disorders, such as panic and social anxiety, or alcohol use disorder are present as

comorbid condition, Gabapentin seems to be helpful. Comorbid OCD is probably the most challenging condition to treat and usually requires complex combinations of different mood stabilizers with SSRIs [66, 67].

Mood disorders are accompanied by circadian rhythm deregulations, which are particularly common among cyclothymic patients. These latter frequently report abnormalities in sleep/wake cycles and show abnormal oscillating melatonin secretion and frequent delayed sleep phase disorder (DSPD) [68]. DSPD is a circadian rhythm disorder characterized by the inability to fall asleep and wake up until much later in the morning or in the early afternoon. Melatonin and agomelatine are known to have chronobiotic properties. In cyclothymic patients, the restoration of circadian rhythms through MT1 and MT2 agonism, increasing the sleep efficiency and reducing the intra-sleep awakening, may contribute to improve mood symptomatology, motivational aspects and psychosocial functioning. The efficacy of melatonin and agomelatine and the importance of resynchronization of circadian rhythms in the therapy of cyclothymia deserve further investigations.

Finally, cyclothymic patients should be considered at high risk of developing sedative misuse (particularly benzodiazepines). The long-term use of sedatives is a frequent complication in such patients: the most evident effect is the worsening of mood lability, irritability, impulsivity and cognitive functions. Thus, it seems very important to promote a gradual tapering down of sedatives according to adapted but rigid protocols, choosing long half-life medications to reduce withdrawal symptoms and craving.

In most cases, medications and adapted psychoeducation are sufficient to control acute symptomatology and to mitigate psychological dysfunction associated with cyclothymic temperament. For a minority of patients it might be useful to be part of an individual psychotherapy package. Research is not advanced in this field and at the moment there is no rigid or strict format for psychological therapy. Independently from the type of psychotherapy, the therapist should keep in mind the model according which mood swings and circularity are linked to neurodevelopmental and constitutional mood dysregulation.

CONCLUSION

Cyclothymic mood instability is an understudied issue despite the evidence that 30 to 50% of depressives, anxious, impulsive, borderline and other personality disorder patients may be affected by this condition. Many patients receive correct diagnosis and treatments after many years of illness, when the superposition of complications reduces the possibility of complete remission. Some major challenges concerning clinical, pharmacological, psychological and genetic researches are still open. There are a lot of issues concerning its diagnostic delimitation and the possible relationships with emotional dysregulation observed in other neurodevelopmental disorders. As cyclothymia tends to onset during childhood and adolescence, diagnostic identification and treatment interventions should be well-timed. In this perspective, the recognition of the disorder in early phase of the life should be improved.

A therapeutic model combining the focus on symptomatic presentations with a temperamental perspective seems to represent an effective approach for cyclothymic patients with complex clinical presentations characterized by mood instability, depression, excitement, anxiety, impulse control, substance use disorders. Establishing specific treatments and clinical management since the beginning prevents unnecessary complications and risks, especially those related to antidepressants exposure. Obviously, the influence of early detection and treatment on the longitudinal course of cyclothymia needs to be confirmed. In our experience, long-term prospective observation is in favor of persistent significant improvement, in particular when specific pharmacotherapy and psychoeducation are applied to patients never treated before.

CONFLICT OF INTEREST

The authors confirm that this article content has no conflict of interest.

ACKNOWLEDGEMENTS

Declared none.

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