



Lifestyle Visions

Presents

Bipolar Disorder (Manic Depression)

Description and Treatment Protocol

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Research Report: Bipolar Disorder

What is Bipolar Disorder?

Bipolar disorder, also known as manic-depressive illness, is a common illness characterized by current episodes of mania and major depression. An affected person's mood can swing from excessive highs (mania) to profound hopelessness (depression), usually with periods of normal mood in between. Some individuals may exhibit mixed symptoms of both mania and depression at the same time, while others may have more moderate symptoms of mania (hypo mania).

The type, severity and duration of mood episodes experienced can vary. Some individuals may have a predominance of either mania or depression, whereas some sufferers may experience equal numbers of both. The mood episodes can last for a few days to as long as several months, particularly when left untreated or not treated effectively. Depressions tend to last longer than manic episodes. Typically, a person with bipolar disorder can expect an average of ten episodes of mania or depression in his or her lifetime but some sufferers experience much more frequent mood episodes. The frequency of episodes tends to increase with time and individuals who experience four or more episodes in a year are said to have rapid cycling.

Characteristics

Symptoms of Mania:

- * Increased energy, activity, restlessness, racing thoughts and rapid speech
- * Excessive euphoria, Extreme irritability and distractibility
- * Decreased sleep requirement
- * Uncharacteristically poor judgment, increased sexual drive
- * Denial that anything is wrong, Overspending, Risk-behavior

Symptoms of Depression:

- * Persistent sad, anxious or empty mood
- * Feelings of hopelessness, pessimism, guilt, worthlessness or helplessness
- * Loss of interest or pleasure in ordinary activities, including sex
- * Decreased energy, feelings of fatigue
- * Difficulty in concentrating, remembering or making decisions
- * Change in appetite or weight
- * Thoughts of death or suicide

Prevalence

Approximately 1-2% of adults and children suffer from the illness. It affects both male and female and there are striking similarities in between different countries and cultures. Between 13-20% of individuals diagnosed with bipolar disorder suffer from the rapid cycling form of the illness, which tends to be more common in women than in men.

Most people with the illness experience their first mood episode in their 20's but it can start later in life. Recognition of the illness, in particular the manic episodes, can often be difficult and it can often be mistaken for depression. This can lead to a delay in diagnosis and inappropriate treatment.



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Classifications

There are several types of bipolar disorder, depending on the nature of the illness. The main types are:

Bipolar I Disorder: Individuals have had at least one full manic or mixed mood episode, and may or may not suffer from episodes of depression.

Bipolar II Disorder: Individuals have at least one depressive episode and at least one hypo-manic episode, but never experience a full manic or mixed mood episode. Bipolar II can go unrecognized because the hypo-manic symptoms may not appear that unusual.

Cyclothymic Disorder: Individuals have suffered numerous hypo manic and depressive symptoms over at least 2 years that are not severe enough or not long enough in duration to meet the criteria for a mood episode.

Subtypes of bipolar disorder include:

Rapid cycling: Individuals who experience more frequent mood episodes (4 or more per year) are called rapid cyclers.

Ultra-Rapid Cycling: This is the same as rapid cycling, only the cycles are more frequent. (4 or more per week, and can cycle as rapidly as 4 or more per day).

Seasonal pattern: Some individuals have predictable seasonal patterns to the onset of their mood episodes.

Post-partum onset: When the mood disturbance occurs within 4 weeks of childbirth.

Abstract: Mania, abnormally elevated moods disorder, normally found in the context of bipolar or manic-depressive disorder, comes at a high personal cost. Symptoms range from abrupt alertness and grandiose plans to financial excess, delusions, and embarrassing behavior. Manic behavioral patterns lack predictability, rendering treatment only partially successful. Mild forms of mania benefit from lithium, while neuroleptics are faster acting in more severe cases. Alternative drugs are carbamazepine or valproate. Electroconvulsive treatment is indicated after routine drug therapy fails.

Mania is an abnormal condition of elevated mood which affects about 1% of the population, and which usually occurs in association with episodes of depression to constitute bipolar disorder or manic-depressive illness. It is a disorder with considerable implications for personal and social functioning where impairments can be severe and long lasting, even after sustained clinical recovery.

The Spectrum of Mania

Manic symptoms cover a spectrum of severity from cyclothymia to severe delusional mania. Cyclothymia, which usually starts in adolescence or early adulthood, describes fluctuations of mood between mild elation and depression. Although mild elation of this type may be associated with enhanced personal and social functioning, cyclothymia can also lead to considerable social or interpersonal difficulties because of its unpredictability. A proportion of cyclothymic individuals go on to develop mania. Bipolar disorder is characterized by clinically marked mood swings between mania and depression. The DSM classification further differentiates between bipolar I (BPI) and bipolar II (BPII) disorders. Mania is characteristic of BPI, while mild mania or hypomania (not



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requiring hospitalization) is characteristic of BPII. Unipolar mania describes recurrent episodes of mania in the absence of depressive illness. It is uncommon and otherwise resembles bipolar disorder. Secondary or induced mania describes manic symptoms or syndromes that are seen in various organic conditions. Finally, there are conditions, which lie between the schizophrenias and affective disorders, so-called schizoaffective disorders. When manic symptoms are the predominant mood component, these disorders tend to pursue a course similar to that of manic-depressive illness rather than schizophrenia.

Clinical Description and Diagnosis

An episode of mania may begin abruptly, over the space of a few hours or days, or gradually, over some weeks. The subjective experience of mania in its minor forms usually includes heightened feelings of well being with increased alertness and drive, inflated self-esteem, and expansive sociability. In addition to a general elevation of mood, instability is typical. Irritability may easily be evoked and other mood states such as anxiety or sadness, fleetingly but intensely expressed, may become apparent. In mixed mood states (also referred to as dysphoric mania), pronounced symptoms of both depression and mania either coexist or alternate during different periods of the day. As mania deepens, overactivity and overtalkativeness become more obvious. Grandiose ideas and plans, and grandiose delusions may develop. Overspending or socially embarrassing behavior can be a source of great distress to the family and the recovering patient. Up to two-thirds of patients experience psychotic symptoms at some time. Delusions occur more commonly than hallucinations, but ideas of reference or even experiences of possession or control, may also be seen. In most cases these symptoms are transient, their content reflects the underlying mood, and the diagnosis remains clear.

The differential diagnosis of mania includes schizophrenia, drug-induced states, and organic disorders. It is sometimes difficult to distinguish between mania and schizophrenia, especially if psychotic symptoms are prominent, incongruent with the underlying mood, or persist after the overactivity subsides. Such diagnostic difficulties are commonly found in cases presenting in adolescence. When affective and schizophrenic symptoms are evenly balanced and prominent enough such that a diagnosis of each can be made independently, then the term schizoaffective disorder is used. Kraepelin's original distinction between schizophrenic and affective diagnoses was founded on both cross-sectional data and longitudinal course, and the need to maintain this dual perspective remains. Quite frequently, it is only over a prolonged period of observation that the diagnosis can be established with reasonable certainty. Drug-induced states and organic conditions must also be included in the differential diagnosis. Steroids, stimulants, and antidepressants are known to induce manic symptoms and a large variety of other drugs have also been implicated. Secondary mania can occur due to a variety of neurological lesions and metabolic or other states affecting brain functioning. Although late-onset cases of mania do occur, the likelihood of organic causation should always be considered, especially in the absence of a past or a family history of affective disorder. Sometimes the delirium of severe mania can itself resemble that of an acute confusional state. Alcohol and other substance abuse are important co-morbid conditions, and their intake often escalates during acute episodes of mania, sometimes masking or clouding the presentation.

Epidemiology

The lifetime prevalence of mania (bipolar affective disorder) is approximately 1%. Onset is most common in late adolescence or early adulthood although new cases are seen in all decades. First occurrence in childhood or early adolescence is increasingly being recognized, when it is sometimes accompanied by hyperactivity disorders. A minority, about 10%, of people with major depression will subsequently develop mania, most within 5 years of onset. Prevalence rates do not differ between men and women. Rates may be raised among the unmarried and separated or divorced which may reflect the deleterious effect this disorder can have on relationships. Raised rates have been reported in urban dwellers and among the homeless. A number of studies



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have reported a raised prevalence in upper socio-economic groups although these findings may be due to diagnostic bias. A possibly related finding is the greater social and occupational attainment sometimes seen among the relatives of those with bipolar disorder. Seasonal effects on incidence have been reported, the most common being a spring-summer excess of elation. Secondary mania due to organic factors occurs sporadically and its overall incidence is unknown, but it is probably more common than believed and is possibly under-recognized. In general, drug-induced manic disturbances are more likely to occur in predisposed individuals (those with previous episodes of mania or depression or with a family history of mood disorders), while mania due to structural brain damage may show less association with prior vulnerability.

Aetiology

Mania shows greater inheritability than any of the other major disorders in psychiatry. Concordance rates for monozygotic twins are about 70% and the risk for mood disorders among first-degree relatives is about 20%, depression being more frequently reported than mania. Earlier reports of genetic linkage have not been replicated in wider populations, although large-scale studies are underway. Disturbances in monoamine neurotransmitter function have been studied much less extensively in mania than in depression.

In recent years attention has shifted towards the study of intracellular modulatory functions such as signal transduction mechanisms and second-messenger systems. Lithium may inhibit both the cAMP and phosphoinositol second-messenger generating systems, and also alter signal transduction through its effects on guanine nucleotide binding (G) proteins. This secondary regulation affects the functioning of multiple neurotransmitter systems, and may well provide hypotheses for elucidating neurochemical regulation of mood in addition to denoting possible molecular mechanisms underlying lithium's therapeutic actions. Computed tomographic and magnetic resonance imaging (MRI) findings include ventricular enlargement and increased sulcal prominence which are not specific to mania but are also seen in schizophrenia. Additional MRI findings of increased subcortical hyperintensities point to the presence of focal abnormalities of white matter and have been reported among young as well as older patients. Their occurrence in younger individuals shows some correlation with increased cognitive impairment and with positive family history. Electroencephalogram abnormalities have been reported in substantial minorities and paroxysmal abnormalities have sometimes been reported in association with suicidal and other behavioral disturbance. While a number of studies have suggested a possible role for stressful life events in precipitating mania, most have been retrospective and the evidence must be interpreted with caution. A considerable proportion of women with established bipolar disorder who have children will suffer a puerperal psychosis. For those with established bipolar disorder and a previous puerperal disturbance the risk for subsequent pregnancies rises to more than 50%. While metabolic and endocrine changes are likely to be of primary importance, it has also been suggested, somewhat speculatively, that sleep deprivation may underlie the often-noted manic response to such disparate events as childbirth, bereavement, and jet-lag associated with time-zone travel. Secondary mania has been observed in association with a variety of neurological conditions including multiple sclerosis, brain tumors, epilepsy, and brain trauma, and also in association with metabolic and endocrinological disorders such as hyperadrenocorticalism and hyperthyroidism. Some studies have suggested that midline or right-sided lesions in particular may give rise to manic syndromes. Drugs commonly noted to induce mania include corticosteroids and androgenic steroids, L-dopa and antidepressants.

Course and Outcome

Most manic episodes remit with treatment within a few months. However, the majority of patients will go on to have recurrences. Variability in outcome is considerable. While the length of episode does not show any consistent variation over time, some follow a pattern where the duration between the first few episodes seems to



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shorten progressively. Thereafter, it may level out and, later, may begin to lengthen again. In general, more depression and less mania is associated with advancing age. Chronicity, that is either unremitting illness or recovery of only a few weeks before the next episode, occurs in a small minority. Full occupational or social recovery lags behind clinical recovery, and many individuals show enduring difficulties in some areas of social adjustment.

Predicting the course of the disorder is difficult. Probably the best indication of future trends is the pattern of episodes in the past. Those with childhood or adolescent onset may follow a more severe course in early years but in the longer term often fare no worse. A positive family history of mania is predictive of more manic recurrences over time. Women tend to experience more depressive and mixed mood states and, conversely, fewer elations than men, and mixed states are associated with poor response to treatment in the short term. Women are also about three times more likely than men to experience rapid cycling, arbitrarily defined as the occurrence of four or more episodes in a year. In addition to occurring more frequently in women, rapid cycling is also associated with antidepressant use and possibly with hypothyroidism, although the evidence for the latter is less clear-cut. While rapid cycling, which occurs in up to 20% of cases, is predictive of a stormier course, it does not persist indefinitely but tends to be phasic over time. The association of mania with childbirth has already been mentioned. The observation of mild hypomania ("the highs") during the first week postnatally has been associated with a higher risk of depression in subsequent months.

The presence of comorbid illness can adversely affect the outlook for mania, being associated with increased dysphoria and mixed mood states and with treatment resistance. Commonly occurring comorbid illnesses include alcoholism and substance abuse. The alcoholism that accompanies bipolar disorder may be qualitatively different to that seen in other populations and have a high rate of remission. In one series of cases where alcoholism preceded the onset of mania, subsequent abstinence was associated with a reduced frequency of manic-depressive recurrences.

The possibility of suicide should not be forgotten in the management of manic states. Although it is relatively uncommon in pure or uncomplicated mania, the expression of suicidal thoughts occurs in more than 50% of those with mixed mood states. Furthermore, mania is often succeeded by depression, sometimes quite abruptly, and suicidal expression can be an important early emergent feature. Comorbidity, especially alcohol and drug abuse, increases risk of suicide considerably.

In BPII disorder, the degree of elation is mild and does not warrant admission to hospital. Because it is mild, it may not be spontaneously reported by the patient. It does however, mark a disorder which can sometimes be characterized by atypical and chronic depression with high levels of associated comorbid disturbance and psychosocial impairment and which is often resistant to treatment.

Management and Treatment

Mild mania may be managed at outpatient clinics but it is important to realize that progression to more severe mania can occur quite rapidly and unexpectedly. Outpatient management should include frequent clinical monitoring and a careful evaluation of the patient's support network. It is important to extend support to family members and to monitor their coping abilities. The possible consequences for both patient and family of disinhibited or socially embarrassing behavior may dictate a prudent policy in relation to hospital admission. If admission is indicated tactful persuasion, perhaps with help from family members, may be enough to encourage the patient's agreement. Often, however, the manic patient lacks sufficient insight and involuntary detention must be considered.



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Milder cases of mania may respond well to lithium, either alone or with benzodiazepines. Lithium, which has fewer side effects than neuroleptics, may also help prevent subsequent depressive relapse, a fairly common occurrence. Doses sufficient to maintain 12-hour serum concentrations of 1.0-1.2 mmol/L are usually required and a delay of about 7-10 days before onset of action may be expected. Benzodiazepines may be added for sedation and to restore sleep. In more severe cases, lithium alone is impractical, and it may then be combined with neuroleptics which have a faster onset of action. There is a trend towards lower doses and less frequent use of neuroleptics in mania because of tardive dyskinesia, neurotoxicity, neuroleptic malignant syndrome, and because of the possibility of cardiac conduction disturbances and sudden death with high doses. Some studies report adequate clinical response to moderately low-dose neuroleptic treatment (i.e., haloperidol 10 mg/day or equivalent) rather than higher doses. Although lithium remains the treatment of choice in mania, carbamazepine or valproate are increasingly being used as alternatives or, with lithium, in place of neuroleptics. Although some reports have suggested that they may be of particular benefit in mixed-mood states and rapid-cycling disorder, situations where lithium does not appear to be highly effective, no firm conclusions can be drawn because of the paucity of adequate controlled trials. Treatment of acute mania with anticonvulsants, as with lithium, usually requires the addition of other more sedative medication. Open trials with other drugs, including calcium-channel blockers such as verapamil, and new anticonvulsants suggest potential benefits from these agents. Electroconvulsive treatment continues to be an effective treatment with good response rates in those otherwise failing to respond to treatment and reported response rates of about 80% overall in mania. Secondary mania is treated similarly.

For prophylaxis, lithium is again the drug of first choice. The decision when to initiate lithium prophylaxis depends on the likelihood of early recurrence. Generally, if episodes recur every year or two then prophylactic treatment should be considered, but if bipolar disorder presents with a manic episode in an adolescent or young adult it should probably be used from the outset. Increasing awareness of limitations to lithium's effectiveness reflects less impressive responses noted from trials in the last two decades than earlier, and also a disparity between the results of case-control trials and follow-up studies. Possible explanations include that use of lithium has become more widespread and it may have been used for conditions other than bipolar disorders. The risk of rebound mania after stopping lithium may be considerably higher than the natural risk. There is some evidence, too, that reintroduction of lithium after discontinuation fails to restore mood stability to the same degree. Finally, studies of alternate day dosing strategies would appear to indicate that even minor degrees of noncompliance carry an increased risk of relapse. If lithium must be discontinued (or the patient wishes to discontinue it), gradual reduction over a few weeks is associated with a considerably lower risk of relapse than abrupt discontinuation. Some studies have shown that elevated mortality rates in those with bipolar disorder, mainly from suicide, can be reduced considerably among those on long-term lithium treatment. There is not enough evidence to advocate the more widespread use of anticonvulsants as first-line agents in prophylaxis. They may be considered in cases of non-response or intolerance to lithium. Although most studies have shown little advantage from prophylaxis with neuroleptics, those who relapse frequently on mood stabilizers are often maintained on neuroleptics.

The psychological and social consequences of mania can be considerable. While mood-stabilizing drugs remain the primary focus of intervention, psychotherapy is an essential adjunctive treatment. Studies of psychosocial interventions have been few and lack sufficient rigor. However, tentative evidence suggests some success in reducing recurrence and future research should focus on more systematic evaluation of these adjunctive therapies.