Chapter 2
The Clinical Diagnosis of Bipolar Depression

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Abstract This chapter overviews considerations as to the nature of bipolar depression, an issue of some importance because of potential treatment implications. Representative studies indicate that those with a bipolar I disorder (BD-I) are somewhat likely to experience psychotic depression during depressive episodes, while for the remainder, a melancholic depressive state is most likely to be experienced. In contrast, for those with a bipolar II disorder (BD-II), episodes of psychotic depression are extremely rare, and most are more likely to experience melancholic depressive episodes. For both BD subtypes, 'bipolar depression' is rarely non-melancholic in nature, although as non-melancholic depressive episodes can be experienced by any individual as a consequence of life stressors, those with BD are also likely to acknowledge such episodes as well. Identification of the bipolar depressive subtype is therefore best addressed in relation to the individual's prototypic episodes. The high rates of nonpsychotic and psychotic melancholic depression in those with BD invite consideration as to whether such episodes differ from similar states experienced by those with equivalent unipolar states. Several studies indicate that certain symptoms, such as the 'atypical features' of hypersomnia and hyperphagia, may be more frequent in bipolar than unipolar melancholia, but the general conclusion is more one of similarity than of differences in symptom patterns. As bipolar depression is principally of the 'melancholic' type, clinical features weighting a diagnosis of melancholia are considered in some detail. Finally, several management nuances in managing bipolar depression are briefly noted.

Keywords Bipolar disorder • Bipolar depression • Melancholia

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2.1 Introduction

The bipolar disorders (both bipolar I (BD-I) and bipolar II (BD-II)) are mood disorders principally marked by oscillations in mood and energy across the hypo/manic and depressive phases. How features of the depressed phase (i.e. bipolar depression) differ from unipolar depression is not simply of definitional interest but should assist diagnosis and, as a consequence, management too.

A number of studies (reviewed shortly) have considered how the depressed phases experienced by those with BD differ from 'unipolar depression'. On theoretical grounds, such a question is unlikely to able to be answered with any precision when unipolar depression is a dimensional construct encompassing quite heterogeneous depressive states. If a dimensional model is applied, unipolar depression includes major and minor clinical depressive conditions (also very heterogeneous constructs). If a subtyping approach is adopted, candidate unipolar depressive conditions include psychotic depression, melancholic depression, and a heterogeneous mix of residual non-melancholic conditions. Thus, rather than question how bipolar depression differs from unipolar depression, a more productive question is how bipolar depression may correspond to or differ from distinctive unipolar depression subtypes. In essence, does bipolar depression correspond most closely to psychotic depression, melancholic depression, or the residual category of unipolar non-melancholic depression?

In this chapter, I will first overview previous studies that have explored the nature of bipolar depression, and that suggest that 'bipolar depression' corresponds most closely to unipolar melancholic and psychotic depression. I will then detail features that distinguish those depressive subtypes and make some brief comments about management models that respect such findings.

2.2 Previous Studies

Goodwin and Jamison (2007) tabulated relevant studies published over the preceding 50 years. They noted that most studies compared unipolar and BD-I patients and observed that bipolar-unipolar differences appear clearer when the BD-II group was excluded from such examinations. They concluded that the most widely replicated findings were that BD-I (compared to unipolar) depressed patients were more likely to show mood lability, psychotic features, and psychomotor retardation and to report more comorbid substance abuse; in contrast, 'typical unipolar patients in these studies had more anxiety, agitation, insomnia, physical complaints, anorexia and weight loss' (p. 17). They also noted that so-called atypical features (i.e. hypersomnia, increased weight, and appetite) were more likely to be reported in BD-II than in unipolar depressed patients. They too emphasised that heterogeneity in samples of unipolar patients provided a source of diverse findings, while differences between BD-I depressive and BD-II depressive states needed to be

identified in any study examining for clinical differences. In their synthesis, they judged that those with BD-II (1) were more likely to be female, (2) were more likely to experience comorbid anxiety and alcohol abuse, (3) had less severe but more frequent and chronic depressions, and (4) had shorter inter-episode intervals. In contrast, the BD-I patients were more likely to have severe and prolonged episodes and higher rates of psychosis and hospitalizations.

A number of studies undertaken by our group will now be reviewed as they consider the nature of the diagnostic subtype(s) in bipolar depression rather than differences in clinical features.

Parker and colleagues (2000) reported a study of patients attending a tertiary referral mood disorder unit, with the sample comprising 83 bipolar and 904 unipolar depressive patients. DSM diagnoses established a higher rate of psychotic depression (19.3 % vs. 10.4 %) as well as of melancholic depression (68.7 % vs. 36.9 %) in the BD participants and therefore a distinctly lower rate of non-melancholic depression (12.0 % vs. 52.7 %) when compared to the unipolar participants. Examining symptoms reported during the depressed phase in the two groups (which, importantly, did not differ significantly in terms of age or gender) established that those in the BD group were more likely when depressed to report appetite loss, slowed thinking, indecision, being slowed physically, a loss of interest, anticipatory anhedonia, non-reactivity to both friends and events, a non-variable mood, pathological guilt, and psychotic features. These features are historically weighted to melancholic and—in relation to delusions—to psychotic depression. Another study nuance was that decisions in regard to melancholic or non-melancholic depression status were made by three differing diagnostic strategies. Across all three definitions of melancholia, it was established that bipolar depression was distinctly more likely to be 'melancholic' in terms of its clinical features, while those with bipolar depression were also somewhat more likely to have psychotic depression.

Another study (Parker et al. 2006) that explored differences between bipolar and unipolar depression examined BD-I and BD-II subjects separately (and not as an overall 'bipolar' group) in comparison with a residual set of unipolar depressed patients. Study findings allowed the generation of an 'isomer model' for differentiating BD-I and BD-II from each other. Such differentiation is important because recent DSM manuals (including DSM-5) define mania and hypomania (and thus BD-I and BD-II) with very similar criteria sets. In essence, DSM symptoms are identical for both mania and hypomania—as is the cut-off score for their presence—so that the two conditions are essentially only differentiated across duration, severity, and hospitalisation parameters. The study involved comparing those who were assigned a BD-I diagnosis, respecting DSM-IV decision rules for mania (other than imposing any duration criterion), but required manic episodes to be associated with either (1) distinct impairment, (2) psychotic features at any time, or (3) hospitalisation during a high. A BD-II diagnosis was assigned to those who met DSM-IV decision rules for hypomania (again ignoring any duration criterion) but did not meet criteria on any of the three BD-I defining features listed in the previous sentence. Consecutive recruitment of 157 patients attending the clinic assigned 49 as having BD-I, 52 as having a BD-II, and 56 as having a unipolar

depressive disorder. The groups did not differ significantly by age or gender, nor did they differ in terms of social class, family history of BD, or age of onset at either their initial hypo/manic episode or initial depressive episode. By diagnostic assignment rules, none of the BD-II subjects had experienced psychotic features or been hospitalised when high, while two-thirds of the BD-I subjects reported psychotic features when high, and one-third had required hospitalisation. Importantly, 41 % of the BD-I subjects had experienced psychotic features when depressed compared to 0 % of the BD-II subjects, a finding that generated the 'isomer model' (described shortly) as a consequence of the specificity of psychotic features to BD-I in both hypo/manic and depressed moods.

In this study, several sets of analyses failed to establish any significant differences between the severity of manic and hypomanic symptoms, suggesting that the nature and severity of the 'core' mood/energy increase in hypomanic and manic states differs only marginally. Thus, levels of mood and energy are not clearly helpful in differentiating BD-I and BD-II states. We concluded that both disorders are unlikely to be successfully modelled or measured by any strategy that merely assesses the core construct of increased mood/energy and therefore proposed an 'isomer model'. This model assumes that the elevated mood/energy state is the 'core' construct to BD, being shared across BD-I and BD-II states, but is somewhat more severe in BD-I conditions. Mood and energy decreases are viewed as the core construct for melancholic and psychotic depressive states, with that core component being somewhat more severe in psychotic depression than in melancholic depression. In the same way, the model assumes that the presence of psychotic features provides a psychotic 'mantle' distinguishing BD-I from BD-II.

The principal advantage of the model is that it argues that 'mania' is reserved simply for those BD individuals who experience psychotic features during an elevated mood state (at some period in their lifetime). In contrast, those who have never been psychotic at such times are assigned to a BD-II category. The model is underpinned by the empirical data embedded in this paper and that goes to the thrust of this chapter—that those who have BD and have had psychotic features when high (BD-I according to the model) are moderately likely to have psychotic features when depressed (41 % in this study). In contrast, those who have never experienced psychotic features when high (and had been assigned a BD-II diagnosis) are unlikely to have experienced psychotic features when depressed (quantified as 0 % in this study). In essence, a mood/energy construct forms the core construct for the oscillations (and is not in and of itself differentiating), while the presence or absence of a 'mantle' of psychotic features provides categorical differentiation of BD-I and BD-II, respectively. In relation to the focus of this chapter, the message is that BD-I depression is likely to be psychotic or melancholic in its nature, while BD-II depression is virtually never psychotic in nature but likely to be melancholic in its type. This study further underlines the earlier point about the need to study BD-I and BD-II separately (rather than simply examining amalgamated samples of BD-I and BD-II subjects) when studying the nature of bipolar depression.

Parker and Fletcher (2009) focused on patterns of depression in BD-II patients only and when compared to unipolar depressed patients. They studied a consecutive

group of those attending a tertiary referral centre and reported data returned by 119 BD-II and 275 unipolar depressed patients. No significant differences were found between the groups in terms of gender or state depression severity scores, but the BD-II subjects were significantly younger. Comparison of depressive symptoms experienced during depressed phases identified only two differences: the BD-II subjects were more likely to report their thinking as slowed and felt less 'need to be close to people'. In a refined analysis after the groups had been matched for age, the groups showed minimal differences in depressive patterns. In further analyses, depressive symptoms in the BD-II group were compared with subsets of those with a unipolar melancholic and those with a unipolar non-melancholic depression to determine whether the clinical depressive pattern for those with BD-II approximated more to a melancholic or to a non-melancholic pattern of depressive features. The unipolar melancholic subjects were more likely to return higher scores on classical melancholic symptoms (e.g. anticipatory and consummatory anhedonia, mood non-reactivity, psychomotor slowing, and weight loss), supporting their diagnostic subtype assignment and thus allowing the secondary analyses to proceed. Those analyses showed that the depressive pattern in the BD subjects approximated more to the unipolar melancholic than to the unipolar non-melancholic subset, specifically in terms of psychomotor and cognitive slowing. The study also examined the impact of age on symptom ratings and established a number of trends, one of which was significant. This nuance is important in suggesting that studies seeking to determine differences between bipolar and unipolar depression should control for the age of participants when making comparisons.

Parker and colleagues (2013) employed the SMPI (Sydney Melancholia Prototype Index) in another comparative study. The SMPI provides 12 prototypic features of melancholic depression and 12 features of non-melancholic depression. These 'features' include symptoms and illness correlates—including premorbid functioning, personality factors, distal and proximal stressors, and ongoing emotional dysregulation—all of which capture historical differences between melancholic and non-melancholic depression. This study used both the self-report and the clinician-rated SMPI measure to investigate whether bipolar depression is prototypically closer to melancholic than non-melancholic depression. The sample comprised 901 subjects, with 468 having a BD condition (46 BD-I and 422 BD-II) and 433 having a unipolar longitudinal pattern. The composite group of BD patients was more likely to be female, have a younger onset of their depression, be older at initial assessment, more likely to have an illicit drug problem, and more likely to have a lifetime anxiety disorder in comparison to both unipolar melancholic and non-melancholic patients. Comparison of the BD and composite unipolar groups on the 12 SMPI prototypic melancholic clinical features (as rated by clinicians) indicated higher prevalences in the BD group for most items; five were significant for the self-report measure, and nine of the 12 were significant for the clinician-rated measure. A converse pattern was suggested for the 12 SMPI non-melancholic prototypic features, with the BD group reporting significantly lower prevalences for eight of the 12 items.

In essence, the BD patients were more likely than the comparator unipolar patients to report their depression as being disproportionately severe compared to their circumstances, for depression to be less consistent with circumstances, for there to be less likelihood of a clear cause for their depression, and for their depressed mood to be less reactive to positive events and to support. They were also more likely to report anergia, anhedonia, physical slowing, impaired concentration, and for their depression to be more likely to come 'out of the blue'. In essence, BD participants were distinctly more likely to report prototypic melancholic clinical features and a more endogenous onset, again supporting a conclusion that bipolar depression is more likely to be melancholic in nature. Additional analyses compared item prevalences in the BD group with those in the unipolar melancholic and non-melancholic depressive subtypes to determine whether the prototypic pattern for bipolar depression corresponded to either pattern. The bipolar depressed group differed distinctly from the non-melancholic unipolar subset on 22 of the 24 comparisons but less distinctly from the melancholic subjects (with only 11 of 24 being significant), indicating again that bipolar depression was phenotypically closer to melancholic than to non-melancholic depression. Differentiation using this prototypic measure appeared more distinctive than findings from previous studies examining differences on the basis of symptoms only.

A self-report depression severity measure included in this study also allowed consideration as to whether atypical features of hypersomnia and hyperphagia were over-represented in those with bipolar depression as had been suggested from clinical observations. The BD patients were more likely than the unipolar to affirm hyperphagia (46.9 % vs. 39.2 %) and hypersomnia (56.8 % vs. 38.2 %). However, while such atypical features are relatively common in BD patients, they appear to also be common in those with a unipolar depressive condition, with rates in this study suggesting a relatively similar prevalence of such symptoms in the melancholic and non-melancholic subsets. In an earlier paper considering the nature of 'atypical depression' (Parker et al. 2002), we proposed that such atypical features may be better conceptualised as reflecting a homeostatic mechanism seeking to reset the depressed individual's level of emotional dysregulation. Such data suggest that—whether homeostatic or not—they are not specific to any depressive type per se but that they are likely to be more prevalent in bipolar than unipolar depressive states.

Frankland and colleagues (2015) compared 202 patients with a DSM-IV diagnosis of BD-I, 44 patients with BD-II, and 120 patients with a unipolar major depressive disorder diagnosis. In comparison with the unipolar depressive group, the BD-I patients were significantly more likely to report terminal insomnia, hypersomnia, psychomotor retardation, difficulty thinking, morning worsening, and psychotic features (indicating a depressive pattern suggestive of psychotic and melancholic depression). Compared to the unipolar group, the BD-II patients were more likely to report initial insomnia, excessive guilt, difficulty thinking, and morning worsening (suggestive of a melancholic pattern) and also to report more 'mixed' features. This study had the advantage of comparing both BD-I and BD-II subsets against those with a unipolar depression and effectively reported that while melancholic and psychotic depressive patterns were more likely in the BD-I

participants, only melancholic features were more common in the BD-II participants.

2.3 Differences Between Unipolar and Bipolar Melancholic Patients

Such studies—indicating that bipolar depression is likely to be more melancholic than non-melancholic in type—allow that conclusion to be pursued by comparing unipolar and BD patients who are judged to experience melancholic depressive episodes. Mitchell and colleagues (1992) recruited depressed patients who met three differing criterion measures (DSM-III, RDC, and CORE) for a diagnosis of melancholia. Of the 138 patients, 27 were rated as having BD (17 manic, 10 hypomanic); after matching for age and gender, this group was compared with 27 unipolar 'melancholic' subjects (i.e. given a melancholia diagnosis by all three measures). Age of onset was similar. The BD patients reported significantly briefer depressive episodes, but the two groups did not differ on either self-reported or clinician-rated depression severity measures, while similar percentages (15 % BD vs. 22 % unipolar) were judged to have a clinical diagnosis of psychotic melancholia. In terms of mental state signs, there was a general trend for BD patients to be rated as showing more psychomotor agitation and less psychomotor retardation, to show a greater loss of appetite, and to be more likely to report subjective agitation and more 'vegetative' abnormalities such as early morning wakening, and diurnal variation with mood and energy being worse in the morning.

In a replication study, Mitchell and Sengoz (1996) adopted a similar methodology and compared 25 DSM-III-R-defined bipolar melancholic patients with a similar number of unipolar melancholic patients, with the groups matched by age and gender. The groups did not differ by age of onset of the first episode of depression, but there were trends for the duration of the current episode of depression to be briefer in the BD subjects and for them to have had more previous episodes. The two groups did not differ by depression severity nor by prevalence of psychotic features, but there was a trend for BD patients to be more likely to be psychotic during a previous episode. In terms of mental state signs, the only formal difference was for the bipolar melancholic patients to demonstrate shortened verbal responses (suggesting psychomotor retardation). When compared across 18 symptoms, the BD patients were less likely to report initial insomnia and suicidal thoughts but more likely to report hypersomnia. Mitchell and Sengoz concluded (p. 178) that analyses across the two studies indicated that there were more similarities than differences between the BD and unipolar patients in terms of cross-sectional clinical features and that the close phenotypic resemblance argued for 'a commonality of biological dysfunction at some level'.

The studies reviewed in the first two sections suggest that those with BD-I are likely to have a psychotic or melancholic depressive pattern during depressed

phases while those with BD-II are unlikely, when depressed, to have a psychotic depressive pattern. They are, however, likely to have melancholic depression; consequently 'bipolar depression' overall rarely evidences a non-melancholic depressive pattern. The lack of absolute specificity is likely to reflect two key factors (apart from measurement error). First, even if BD patients are most likely to experience (psychotic or nonpsychotic) melancholic depression as their prototypic depressive pattern, this does not mean they are not vulnerable to non-melancholic depressive episodes as might be experienced by any individual in response to some major stressors. Second, it may well be that a percentage of BD patients do experience episodes of non-melancholic depression as their standard depressive phenotype, but how common or rare this is remains unclear. Thus, if bipolar depression is principally melancholic or psychotic depression, what might be the best 'signals' for identifying such depressive subtypes?

2.4 Clinical Features Indicative of a Melancholic or Psychotic Depression

If BD patients are most likely to experience episodes of depression marked by melancholic features, it is important to be able to identify melancholia on the basis of clinical symptoms. Historically, a number of so-called endogeneity symptoms (e.g. anhedonia, mood non-reactivity) and vegetative symptoms (e.g. appetite loss, terminal insomnia) have been weighted. In our own studies, we have found that, while a number of such symptoms are common in melancholic depression, they are also common in those with non-melancholic depression. I therefore now detail features that we find clinically—as well as in our research studies—to be distinctly more common in melancholic than in non-melancholic depression; a number are included in the SMPI measure detailed earlier.

2.4.1 Psychomotor Disturbance

Historically (see Jackson 1986; Parker and Hadzi-Pavlovic 1996; Taylor and Fink 2006), melancholia was viewed more as a disorder of movement than of mood, with motor components including retardation and/or agitation. Retardation may be evidenced by a slowing of walking and talking, as well as facial immobility, postural slumping, a monotonous voice, scarcity of speech, and a loss of light in the eyes. Agitation can often be seen physically or mentally, with the patient often speaking in sharp and abrupt sentences, appearing preoccupied and unable to settle, experiencing multiple worrying thoughts, or having physical symptoms such as churning in the stomach and a fairly characteristic importuning refrain (i.e. 'What's going to become of me'). In both the retarded and agitated expressions, concentration

is likely to be significantly impaired (with 'foggy thinking' and fewer thoughts). An impaired capacity to absorb information occurs in both those with retardation and agitation often due to the scarcity and slowness of thought in retardation and multiple racing thoughts in those with agitation. Those with the 'retarded' form of melancholia tend to show such features consistently (although there may be a diurnal variation with retardation improving in late mornings), while those with the 'agitated' form of melancholia tend to have a base of retardation and superimposed epochs of agitation, with agitation also generally worse in the mornings. Psychomotor disturbance is generally more distinctive in older subjects with melancholia and may be one of the most distinctive phenomenological features in psychiatry in terms of its specificity to melancholia, but it is only distinctive in a small percentage of younger patients (i.e. those under the age of 40). In essence, when distinctive, it strongly supports a diagnosis of melancholia; however, as melancholia can present without substantive psychomotor disturbance, its absence does not reject a diagnosis of melancholia. Such an age impact on this phenotypic disturbance may reflect those with melancholia progressively recruiting more monoaminergic circuits (especially dopaminergic ones). As those with melancholia grow older, this age-related change in phenotype may perhaps also explain why those with melancholia tend to report a progressive lack of response to narrow-action antidepressants over the years. The 'psycho' component of psychomotor disturbance is considered next.

2.4.1.1 Impaired Concentration

Many measures of melancholia weight the presence of distractible thoughts and poor concentration. However, these constructs need to be assessed carefully as impaired concentration is actually common in melancholia and non-melancholic depression. However, those with a non-melancholic depression tend to report lots of racing and/or worrying thoughts that impair their concentration and make them distractible. In melancholia, the individual is much more likely to report their thinking as 'foggy' with fewer and foggier thoughts as well as difficulty absorbing information, so that reading a book or preparing for an examination can become distinctly compromised.

2.4.1.2 Anergia

I view it as important to distinguish between anergia, fatigue, and a lack of motivation. While fatigue and amotivation are common in those with melancholia, they are also common in non-melancholic depression; in contrast, anergia (or lack of physical energy) is far more distinctive in melancholic patients. As a consequence, rather than asking about fatigue or amotivation, I ask 'Do you find it difficult to get out of bed in the morning and to get going? Possibly even failing to have a bath or shower'? Those with distinct anergia will generally affirm this

probe question, detailing that they may stay in bed for many hours or, if they get out of bed, they may only move to the lounge, without bathing or washing for days or even weeks.

2.4.1.3 Anhedonic and Non-reactive Mood

Earlier studies suggested that those with melancholia were more likely to differ from those with a non-melancholic depression in reporting anticipatory rather than consummatory anhedonia, but our studies have not found support for any such differential; as a consequence, we tend to judge anhedonia as an overall construct. Thus, we ask the extent to which the patient finds a lack of pleasure in daily activities or in those activities which might generally give them pleasure, while a non-reactive mood is defined by an inability to be cheered up in social circumstances or when experiencing a pleasant life event. While both are over-represented in melancholic patients, they are difficult to quantify for several reasons. First, it is extremely rare to find a melancholic individual who describes such features as absolutely categorically present. For example, a melancholic patient may acknowledge that they are not getting any pleasure out of anything but, when pressed, note that when they see their grandchild, they may be cheered up briefly or superficially. Thus, such features are extremely helpful when they are absolute or clear-cut but, at minor levels, their specificity to melancholia tends to be low.

2.4.1.4 Diurnal Variation of Mood and Energy

Most individuals with a melancholic depression will report a diurnal variation, with their mood and energy levels being worst in the morning, and that they improve later in the morning or early afternoon. There is also a small percentage of those with seeming true melancholia who report mood and energy dropping late in the day (and usually when the sun is setting). The former is worth weighting, but the latter is only modestly differentiating.

2.4.2 Appetite and/or Weight Loss

While both are relatively common in melancholic depression, they are also commonly reported by patients with non-melancholic depression. Conversely, a percentage of both will experience food cravings and therefore report appetite increase (usually for specific foods such as carbohydrates and chocolates) and weight gain. As many depressed patients are taking weight-gaining medications when assessed, this can compromise the assessment of these constructs.

2.4.3 Insomnia

Those with melancholic depression commonly report early morning wakening with the classic time being around 3 AM. However, early morning wakening is a common feature in any anxiety or depressive condition marked with physiological arousal, so that early morning wakening may be quite common in those with mixed anxiety/depression and with grief states as well as in those with other expressions of non-melancholic depression.

2.4.4 Psychotic Features

The nature of psychotic depression remains somewhat unclear, with the two commonest models viewing it either as a more severe form of melancholia or as melancholia with superimposed (and categorical) features of delusions and/or hallucinations. Such psychotic features may be 'mood congruent' (e.g. feeling that the world is so bleak that the individual would be better off dead, viewing themselves as facing penury) or 'mood incongruent' (i.e. without any seeming depressive overtone or theme) with both expressions almost equally likely (Parker et al. 1996). If the patient does not volunteer such symptoms, they can generally be best elicited by pursuing any sense of guilt or shame directly or via the individual feeling that they 'deserve to be punished'.

2.4.5 Insular and Asocial Behaviours

While this is a relatively vague construct and territory, it is part of the melancholic terrain, although not specific to melancholia. It can be particularly useful in judging whether melancholia exists or not in an adolescent or young adult. Those with melancholia tend to become quite asocial, going or staying in their room, not phoning or returning telephone calls, and retreating from those around them.

2.4.6 Impairment

While those with a non-melancholic depression can clearly be impaired, impairment tends to be more severe in those with a melancholic depression—where patients are much more likely to report that their depression makes it a struggle to get to work, physically get out of bed, engage in normal exercise, relate to a partner, keep up hygiene, and maintain work performance.

2.4.7 Relationship to Stress

While melancholic depression was long described as 'endogenous depression' (i.e. it appeared to come from within rather than being caused by external factors or stressors), empirical research (e.g. Brown et al. 1994) indicated that both melancholic and non-melancholic depressive disorders were commonly preceded by a stressor, a finding that challenged the very construct of 'endogeneity'. Nevertheless, the role of stressors has a number of important diagnostic nuances. The first episode of a melancholic depression is commonly preceded by a stressor. Over time, the illness tends to become more autonomous, with the individual experiencing episodes of melancholic depression without stressors or in response to only minor stressors. More importantly, those with melancholia generally judge the depressive condition as more 'severe' than warranted by any antecedent stressor and, additionally, that it tends to persist far longer than might be expected for the stressor or persist when the stressor is no longer present or operative.

2.4.8 Disease-Like

In one of our studies (Parker et al. 2015), we quantified that some 70 % of those with a melancholic depression and less than 30 % of those with a non-melancholic depression were likely to judge their depression as akin to a 'disease'. Further, when asked to assign the predominant cause (as either biological, psychological, and/or environmental), they were likely to weight a biological contribution, whereas the non-melancholic subjects were distinctly more likely to view their depression as almost entirely environmental.

2.4.9 Family History

Those with a melancholic depression (unipolar or bipolar) are likely to report a family history of depression. In those with BD, they are also more likely to report a family history of depression, BD, and/or suicide in a first-degree or second-degree relative.

The clinical diagnosis of bipolar depression simply requires that the patient has BD and that they are currently distinctly depressed. We judge, however, that it is important to determine the depressive subtype during such states, as management is likely to be influenced by whether the patient is experiencing a psychotic, melancholic, or non-melancholic depressive episode.

2.5 Some Management Nuances

As management options are considered extensively in treatment guidelines for BD and in other chapters of this book, only some brief observations are provided here in relation to managing bipolar depression, but which build on our 'core and mantle' (or 'isomer') model for differentiating BD-I and BD-II and on the depressive subtype experienced by the patient.

My personal view (Parker 2012) is that the management of BD-II (including its depressive phase) should differ from the management of BD-I, in part reflecting the respective nonpsychotic and psychotic status of those two conditions. In managing a patient who presents with significant clinical depression and who has BD, as recommended in most treatment guidelines, I will initiate a mood stabiliser. However, the choice of the mood stabiliser varies considerably between BD-I and BD-II diagnoses. For BD-II, I will generally trial lamotrigine, and only if this failed would I consider other mood stabilisers such as lithium or valproate. For BD-I, I favour lithium, and if this is unsuccessful, I will try valproate next and tend not to find lamotrigine as likely to be effective. As most patients with BD present during an acute episode—and almost invariably the depressed phase—I will seek to address that state (as covered below) and not simply rely on a mood stabiliser.

The use of antidepressant medication in a patient who presents with a distinct episode of bipolar depression is controversial. Most treatment guidelines argue against the use of antidepressant medication on the basis that antidepressants can cause switching (into highs) and mixed states (where the patient is sometimes experiencing a mix of hypo/manic and depressive features or, equally commonly, experiencing a state of agitation not unlike a serotoninergic reaction) or worsen the course of the illness. Each of these propositions has been considered by a number of commentators (see Parker 2012), while the International Society for Bipolar Disorders (ISBD) has reviewed the benefits and concerns about the use of antidepressants in managing an individual with BD (Pacchiarotti et al. 2013); that review was more sanguine about the use of antidepressants. My personal practice is to introduce an antidepressant together with a mood stabiliser in a patient who presents with a significant episode of (bipolar) melancholic depression, but I continue to find the choice a difficult issue. Selective serotonin reuptake inhibitors (SSRIs) tend not to be particularly effective, dual-action antidepressants are more effective but are most likely to cause switching, tricyclics are commonly effective but have also been incriminated as causing switching, and monoamine oxidase inhibitors (MAOIs, long used in the management of bipolar depression) require judicious use in BD patients in light of the need to avoid certain foods. Surprisingly, psychostimulants such as methylphenidate can be useful in managing those with bipolar depression as we reported (Parker and Brotchie 2010) in a clinical case study, either as a single antidepressant agent or augmenting a more orthodox agent. The risk of such a stimulant switching the patient into a high has to be conceded but, as quantified in our report, was a relatively rare event. If the patient with a bipolar melancholic depression has not improved in the next week, I tend to introduce a low-dose

atypical antipsychotic medication as an augmenting strategy—and then try to cease it when the depression has been brought under control. In managing an individual with a (bipolar) psychotic episode, I would favour the immediate use of an antipsychotic in conjunction with the introduction of a mood stabiliser and possibly an antidepressant. If the individual is experiencing a (bipolar) non-melancholic depressive episode, I would introduce a mood stabiliser for the bipolar condition and weight a nondrug strategy initially to determine if this assisted their depressive episode. Management of the bipolar depressive episode is therefore somewhat contingent on identifying the bipolar subtype (I or II) and the depressive subtype (i.e. psychotic, melancholic, or non-melancholic). In essence, the subtyping model—and particularly the nature of the bipolar depressive condition—shapes management priorities.

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