Is Bipolar Affective Disorder Underdiagnosed?

Shokoufa Kashani1, Eva Bongards2,3, Mark Agius1,4,5
1South Essex University Partnership Foundation Trust, UK
2School of Clinical Medicine, University of Cambridge, UK
3Christ's College, University of Cambridge, UK
4Department of Psychiatry, University of Cambridge, UK
5Clare College, University of Cambridge, UK

Abstract

This article reviews the epidemiological evidence that bipolar affective disorder is often underdiagnosed and hence ineffectively treated. In order to mitigate this problem, all patients with depression should be systematically assessed using a full longitudinal history in order to detect hypomanic symptoms, as well as a family history. This is expected to lead to more appropriate diagnosis, and consequently treatment, of bipolar affective disorder.
Key words: bipolar affective disorder, unipolar depression, underdiagnosis, misdiagnosis.

Introduction

There has been much discussion as to whether or not bipolar affective disorder is underdiagnosed. In this review, the term 'underdiagnosis' will be used as referring to patients who actually have bipolar affective disorder but are not identified when the DSM-IV (1) or ICD-10 (2) criteria are applied. According to the DSM-IV criteria, bipolar affective disorder is defined as episodes of low mood interspersed with episodes of high mood, which are further characterised: in bipolar I disorder, the high moods consist of full mania lasting at least one week, while in bipolar II disorder, high moods consist of hypomania lasting for a minimum of four days. It is vital to realise that this definition is arbitrary, and that many patients have shorter symptomatic episodes, for example, hypomania lasting two days. Such patients are, at present, not considered to fulfil the full criteria for bipolar affective disorder and are therefore referred to as 'subsyndromal' for this condition. In line with the proposed arbitrary nature of the existing criteria, a study conducted by Angst (3) demonstrated that they are indeed artificial and hence potentially changeable parameters. He showed that the proportion of bipolar patients in a population of depressed patients could vary depending on the criteria. Additionally, many others have argued that bipolar affective disorder is underdiagnosed (4) (5) (6) (7).

Bipolar disorder is often misdiagnosed and underdiagnosed

Initial reports of underdiagnosis of bipolar affective disorder by Knutsen (4) and Schwartz (5) focused on the relatively easy misdiagnosis of bipolar I disorder as schizophrenia. The diagnosis of bipolar I disorder or schizoaffective disorder following a prior diagnosis of schizophrenia usually occurs as a result of a change in symptom patterns due to the natural evolution of the disorder (5). On the other hand, the diagnosis of bipolar affective disorder following prior diagnosis of unipolar depression is often far more difficult to achieve; this can be due to inadequate history taking and assessment of the patient (6).

Ghaemi et al. have shown that the time from initial presentation to diagnosis of bipolar affective disorder can be, on average, up to nine years for all bipolar patients. This figure is derived from the six years it can take for bipolar I disorder to be diagnosed, the eleven years it can take for bipolar II disorder, and the 12 years it can take for conditions at the 'softer end of the bipolar spectrum', also often described as 'bipolar affective disorder not otherwise specified', to be diagnosed (17).
Hirschfeld et al. (7) presented the results of a survey carried out by the National Depressive and Manic-Depressive Association of a large group of patients who had been diagnosed with bipolar affective disorder. Over one third of respondents stated that they had sought professional help within one year of onset of symptoms. It was reported that 69% of bipolar patients had initially been misdiagnosed

with a different condition and that the most frequent misdiagnosis had been unipolar depression. In addition, over one third of respondents stated that they had waited ten years or more before being accurately diagnosed. Furthermore, the results showed that those who had been misdiagnosed had consulted a mean of four physicians prior to receiving the correct diagnosis. Despite often under-reporting manic symptoms, more than half of the patients believed that it was the lack of understanding that their physician had of bipolar affective disorder which had delayed the diagnosis. Moreover, bipolar affective disorder was reported to have a profound negative impact on the patients and their families, in terms of social relationships, employment and careers. Patients stated that although the illness had manifested early in life, several years had passed before an accurate diagnosis was achieved.

Another important report of underdiagnosis of bipolar affective disorder is the GAMIAN-Europe/BEAM survey I of self-help groups, which showed that many patients who have bipolar affective disorder describe long durations of untreated illness (DUI) before diagnosis (8). Patients gave details of the following effects of this: worse clinical response, reduction of the effect of lithium treatment, poorer social adjustment, higher numbers of hospitalisations, increased risk of suicide and increased development of co-morbidities. Vazquez-Barquero et al. also report long DUI in bipolar affective disorder (9). According to Judd et al. (10) (11), the main reason for this, i.e. long DUI and misdiagnosis, is that on average, bipolar patients experience manic symptoms and symptoms of mixed states only 9% and 6% of their lifetime, respectively, while they are depressed 32% of the time, i.e. the vast majority of their symptomatic lives. Furthermore, the Stanley Foundation Bipolar Treatment Outcome Network reported that the first symptom in approximately half of the patients with bipolar affective disorder is depression (12). Bearing the above in mind, as well as the common clinical experience that many patients consider episodes of hypomania to be pleasant days, it is not surprising that bipolar affective disorder is often mistaken for unipolar depression, particularly at initial presentation.

Several ways of identifying more patients with bipolar affective disorder have been described

In order to screen for bipolar affective disorder in the community in 85,358 US citizens over the age of 18, Hirschfeld et al. developed the 'Mood Disorder Questionnaire' (13). They found the prevalence of bipolar I and bipolar II disorders to be 3.7%. Of all the patients thus diagnosed with bipolar affective disorder, only 19.8% had previously been identified to have the condition, 31.2% had been misdiagnosed with unipolar depression, and 49.0% had not received a diagnosis of either bipolar affective disorder or unipolar depression.

Benazzi (14) described another method of diagnosing bipolar II disorder. 111 outpatients with depression were interviewed for a history of hypomania and hypomanic symptoms using the Structured Clinical Interview for DSM-IV (SCID), modified by Benazzi and Akiskal. Bipolar I patients were excluded from the analysis, since their diagnosis was considered definitive. Benazzi then systematically assessed all past hypomanic symptoms, especially overactivity (14). The modification which he introduced was that the wording of the questions could be changed to increase understanding, and subsyndromal hypomania was defined as an episode of overactivity (increased goal-directed activity) plus at least two hypomanic symptoms (14).
Benazzi's results showed that 68 of the 111 patients (61.2%) HAD bipolar II disorder, while only 43 patients had 'true' major depressive disorder. Of the latter group of patients, 39.5% (15.3% of the entire sample) showed evidence of subsyndromal hypomania (14). Those patients who were diagnosed with major depressive disorder but had subsyndromal hypomania had a median of four symptoms; the most common hypomanic symptom being overactivity. Overall, 76.5% of the patients were shown to have a bipolar spectrum disorder. Furthermore, it was noted that overactivity had higher sensitivity than elevated mood for predicting a diagnosis of bipolar II disorder.

Similar results were obtained by Tavormina et al. (15). They assessed 300 consecutive new patients presenting to an Italian private practice, by taking a full longitudinal history and a family history. Of the 300 patients who were assessed, 238 were found to lie on the bipolar spectrum. However, none of them were diagnosed with bipolar I disorder. 26% of their patients had bipolar II disorder, 21%

cyclothymia, 4% irritable cyclothymia, 3% were said to have a cyclothymic temperament, 5% had mixed dysphoria and 28% had agitated depression. However, only 9% were diagnosed with unipolar recurrent depression and 4% with a major depressive episode.
Based on this evidence, Agius et al. (16) decided to reassess patients registered with a community mental health team (CMHT) in Bedford, United Kingdom. They reassessed all patients with unipolar depression and recurrent depressive disorder, 456 patients in total, by taking a full longitudinal history and a family history. If this was indicative of bipolar affective disorder, they also used the Mood Disorder Questionnaire to validate their results. They found that whereas in November 2006 the CMHT had had 41 bipolar patients (8.9% of patients), 63 with recurrent depressive disorder (13.8% of patients) and 73 with one or more depressive episodes (16.0% of patients), by September 2007, there were 65 bipolar patients (14.3% of patients in the CMHT), 64 with recurrent depressive disorder (14.1% of patients) and 74 with one or more depressive episodes (16.3% of patients). Thus, over a period of ten months, the percentage of bipolar patients in the team increased by 5.4%, but the proportion of patients with unipolar depressive disorder in the CMHT did not change significantly. The conclusion reached was that if one were to screen patients systematically for bipolar affective disorder, the proportion of bipolar patients in a secondary care outpatient sample would increase.

Effects of underdiagnosis on treatment

The concept of bipolar affective disorder is often misinterpreted, leading to inconsistent diagnosis and treatment. In order to determine the consequences of underdiagnosis of bipolar affective disorder, Ghaemi et al. (17) assessed the records of 85 patients seen in an outpatient clinic within one year, who had diagnoses of affective disorders. Past diagnostic and treatment information was obtained by taking systematic psychiatric histories from the patients. The diagnosis of bipolar affective disorder was based on the DSM-IV criteria. A SCID-based interview was used to assess patients. The authors found that bipolar affective disorder was misdiagnosed as unipolar depression in 37% of patients on initial presentation to a mental health professional after their first (hypo)manic episode. Therefore, antidepressants were used earlier and more frequently than mood stabilizers, leading to likely overuse of the former and under-use of the latter. As a result, 23% of this sample of initially misdiagnosed patients experienced a worse, rapid-cycling, bipolar course, which was attributed to antidepressant use. Ghaemi et al. concluded that bipolar affective disorder tended to be misdiagnosed as unipolar major depressive disorder and that use of antidepressants in bipolar affective disorder was associated with a worse course of the illness (17). They also suggested several possible reasons for the observed underdiagnosis of bipolar affective disorder, such as patients' poor insight into and recognition of (hypo)mania, failure of clinicians to take into account family members' views when making the diagnosis, and physicians' lack of understanding and therefore inadequate detection of (hypo)manic symptoms (6) (18) (19). Since Ghaemi et al. felt that the difference between the number of patients who had bipolar affective disorder and the number of patients diagnosed with it may also reflect disagreement among clinicians about the breadth of the bipolar spectrum; they suggested using the term "bipolar spectrum disorder" as a substitute for a more specific, more excluding diagnosis (6). The term is envisaged to place more emphasis on antidepressant-induced manic symptoms and family history, and also includes forms of bipolar illness that are not type I or II. In line with what is discussed above, Ghaemi et al. furthermore recommended more aggressive use of mood stabilizers and decreased use of antidepressants (17) (18) (19).

Can using self-report questionnaires alone lead to overdiagnosis of bipolar affective disorder?

Despite the convincing results just presented, difficulties have been encountered when basing diagnosis of bipolar affective disorder on self-report questionnaires alone. Zimmerman et al. (20) interviewed 700 psychiatric outpatients using the SCID. The patients also completed a self-report questionnaire, which asked whether they had previously been diagnosed with bipolar affective disorder by a healthcare professional. Furthermore, every patient's first-degree family history was sought. Less than half of those respondents who reported previously to have been diagnosed with bipolar affective disorder received a diagnosis of bipolar affective disorder based on the SCID.

Furthermore, patients diagnosed with bipolar affective disorder based on the SCID had a significantly higher risk of having suicidal thoughts than patients who reported a previous diagnosis of bipolar affective disorder that was not confirmed by the SCID. Patients who reported a previous diagnosis of bipolar affective disorder that was not confirmed by the SCID did not have a significantly higher risk of having suicidal thoughts than those patients who were negative for bipolar affective disorder by self-report as well as the SCID. Zimmerman et al. concluded that, although underdiagnosing bipolar affective disorder was a problem, using a screening tool as the sole method of assessing patients may lead to overdiagnosis of the condition. In other words, they argued that the SCID was a more accurate method of identifying bipolar affective disorder. Self-report questionnaires could lead to overdiagnosis, and those patients who were identified as having bipolar affective disorder by the self-report questionnaires but not by the SCID did not have a higher risk of having suicidal thoughts, despite being identified by the self-administered questionnaires, so that there was no advantage in identifying them as bipolar.

Can broadening of the term 'bipolar affective disorder' to 'bipolar spectrum disorder' lead to overdiagnosis?

Concerns have, indeed, been raised more generally regarding overdiagnosis of bipolar affective disorder. One argument is that overdiagnosis may stem from the "promulgation of the concept of the soft bipolar spectrum disorder" (21) (22) (23). Regardless, we need to emphasize that this is not the issue we are addressing in this review. We refer to underdiagnosis of bipolar affective disorder as misdiagnosis or complete lack of diagnosis of patients who meet the present DSM-IV or ICD-10 criteria for bipolar affective disorder. Indeed, we concur with Zimmerman (24) (25) and others, such as Iordache (26), that it is necessary for patients to fit the current DSM or ICD criteria to be able to be diagnosed with bipolar affective disorder, a) in order for the condition not to be overdiagnosed and b) for epidemiological data to give an accurate representation of the prevalence and incidence of the disorder. We are also conscious of Zimmerman's notable finding that many patients who are inappropriately diagnosed with bipolar affective disorder in fact have other important mental health conditions (24) (25).

Conclusion

Clearly, accurate diagnosis of bipolar affective disorder is a central issue in psychiatry. Only if we diagnose the condition accurately will we be able to devise the best possible management plans to reduce morbidity, as well as, importantly, mortality by suicide. Only then shall we be able to explain a diagnosis to our patients that finally makes sense to them, and support them in achieving their career- and other goals. As argued in this review, accurate diagnosis can only be achieved through thorough patient assessment and appropriate application of existing diagnostic criteria, which will also help us finally to treat some of those patients who were incorrectly diagnosed with resistant depression more effectively.

GP Comment

What have I learned from this paper?

I was surprised by the large number of patients who receive a diagnosis of unipolar depression, who may in fact have bipolar II disorder. When patients with depression present to primary care, there is a huge amount of ground to cover in the short consultation to assess current symptoms, risks, offer support and discuss treatments; asking about previous hypomanic episodes might be overlooked. However, as we follow these patients up at regular intervals we have the ideal opportunity to revisit the history and try to elicit any history of possible hypomanic-sounding episodes. The PHQ9 questionnaire, which is often used to screen for depression in primary care, does not include questions about manic symptoms so perhaps these could be incorporated.

Abigail Davis, GP Trainee.

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