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Review

Unipolar mania: A distinct entity?

Olcay Yazıcı *

Istanbul University, Istanbul Medical School, Psychiatry Department, Istanbul 34357, Turkey

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ABSTRACT

Background: Whether or not unipolar mania is a separate nosological entity remains a subject of dispute. This review discusses that question in light of recent data.
Methods: Unipolar mania studies in the PUBMED database and relevant publications and cross-references were searched.
Results: There seems to be a bipolar subgroup with a stable, unipolar recurrent manic course, and that 15–20% of bipolar patients may be unipolar manic. Unipolar mania may be more common in females. It seems to have a slightly earlier age of illness onset, more grandiosity, psychotic symptoms, hyperthymic temperament, but less rapid-cycling, suicidality and comorbid anxiety disorders. It seems to have a better course of illness with better social and professional adjustment. However, its response to lithium prophylaxis seems to be worse, although its response to valproate is the same when compared to that of classical bipolar.
Limitations: The few studies on the subject are mainly retrospective, and the primary methodological criticism is the uncertainty of the diagnostic criteria for unipolar mania.
Conclusions: The results indicate that unipolar mania displays some different clinical characteristics from those of classical bipolar disorder. However, whether or not it is a separate nosological entity has not been determined due to the insufficiency of relevant data. Further studies with standardized diagnostic criteria are needed. Considering unipolar mania as a course specifier of bipolar disorder could be an important step in this respect.

Contents

1. Introduction

Within the subtypes of bipolar disorders, the existence of a manic disorder with a unipolar course remains a controversial subject. If its existence as a distinct entity were confirmed, then reliable diagnostic criteria could be established, and diagnoses according to those criteria would be stable over time. Once established, those criteria

* Tel./fax: +90 212 2464121.
E-mail address: olcayyazicidr@gmail.com

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Table 1
Is unipolar mania rare?

1. Leonhard (1957): **9%** BD patients
2. Perris (1966): **4.5%** BD patients
3. Abrams and Taylor (1974): **28%** BD-I patients
4. Abrams et al. (1979): **18%** BD patients
5. Nurnberger et al. (1979): **15.7%** BD-I patients
6. Perris (1982): **1.1%** BD patients
7. Pfohl et al. (1982): **35.2%** BD patients (hospitalized)
8. Venkoba Rao and Madhavan (1983): **12%** BD patients (onset age 60)
9. Makanjuola (1985): **53%** BD-I patients
10. Srinivasan et al. (1985): **40%** BD patients (hospitalized)
11. Margoob and Dutta (1988): **42%** BD patients
12. Khanna et al. (1992): **44%** BD patients (hospitalized)
13. Shulman and Tohen (1994): **12%** BD-I patients (hospitalized, age > 65)
14. Avasthi et al. (1996): **6.45%** affective disorders patients
15. Aghanwa (2001): **47.2%** BD patients
16. Yazıcı et al. (2002): **16.3%** BD-I patients
17. Solomon et al. (2003): **26%** BD patients
18. Perugi et al. (2007): **21.8%** BD-I patients (hospitalized)
19. Dakhlaui et al. (2008): **65.3%** BD-I patients
20. Andrade-Nascimento et al. (2011): **5.6%** BD-I patients

would be able to help clarify the prevalence of the disorder and be of great help in improving the methodological problems in studies on unipolar mania (UM).

According to the current criteria, mania signifies bipolarity; namely, the presence of a manic episode predicts the presence of a depressive episode as well. This, however, can be seen as counter-intuitive, since mania and depression are entirely different, more or less opposite syndromes; accordingly, it would have been difficult to first conceive of them as parts of the same illness. Still, as can be seen in the comprehensive review of Angst and Marneros (2001), Aretaeus of Cappadocia (1847) was the first to say that they were two different aspects of the same illness. In 1851, Falret (1851) described an entity that he termed *folie circulaire*, which was characterized by a continuous cycle of depression, mania, and free interval. With that, he defined the basics of the modern concept of bipolar disorder (BD). Subsequently, came the dichotomization of endogenous psychoses into manic-depressive insanity and dementia praecox by Kraepelin (1899). He was also the first to describe some cases of recurrent manic episodes without depression, which he referred to as periodic mania. Kraepelin's unification grouped all affective disorders (with a unipolar and bipolar course) under one umbrella.

In 1900, Wernicke (1990), continuing Falret's concept, claimed that since both mania and depression were mandatory for a diagnosis of manic-depressive insanity, recurrent episodes of singular mania or depression should be viewed as distinct disorders. Similarly, Kleist (1911, 1953) and Leonhard (1957) differentiated between unipolar and bipolar disorders. Whereas pure mania and pure melancholia were classified under the rubric of pure phasic psychoses, manic-depressive illness was classified as a polimorphous phasic psychosis (Leonhard, 1957).

Later, Angst (1966) and Perris (1966) showed that unipolar depression was indeed a different entity from BD with respect to various aspects such as gender, genetics, course, premorbid personality, and age of onset, thus confirming the aforementioned assumption for unipolar depression. However, the authors concluded that unipolar mania was related closely, clinically, and genetically to BD, and therefore should be regarded as an artefact of it (Angst and Perris, 1968). This conclusion was accepted univocally, resulting in general quiescence on the subject for the last 50 years, as reflected by the strikingly few number of studies on UM during this time. Another reason for this scarcity of studies could be the assumption that UM is a rare condition.

2. Methodology

The PUBMED database between 1960 and 2013 was searched using the following key words: unipolar mania, recurrent mania, periodic mania, and pure mania. Relevant publications and cross references were searched manually.

3. The prevalence of unipolar mania

Leonhard (1957) reported the percentage of UM in BD as 9%. As can be seen in Table 1, this percentage varies between 1.1% and 47.2% in BD patients, 5.6% and 65.3% in Bipolar Disorder I (BD-I) patients, and 35% and 44% in hospitalized BD patients. The variance in these findings may be due to methodological problems or cultural differences.

4. Methodological problems

Methodological problems can be divided into three groups: retrospective, present, and prospective errors.

Regarding retrospective problems, since a UM diagnosis generally is made retrospectively, some earlier episodes of mild depression may remain unreported or overlooked. In this respect, studies from a specialized mood disorders center, and those using re-interview with the patient and the family about past episodes instead of just a chart review, would increase the reliability of their results.

Regarding current errors, the major problem is the lack of consensus on the defining criteria for UM. The basic questions concern the criteria for the minimum number of manic episodes, the minimum duration of follow-up, and criteria for exclusion. Shulman and Tohen (1994), for example, have suggested that at least three manic episodes and a follow-up between 3 and 10 years are needed for a reliable diagnosis of UM.

Almost all UM studies base the diagnosis on the absence of a major depressive episode (Table 2). In previous studies, the minimum number of manic episodes was one or two, whereas it has become three or four in more recent ones. These studies generally were carried out utilizing retrospective chart review. There have been two prospective studies with 5 and 20-year follow-up (Makanjuola, 1985; Solomon et al., 2003). In recent studies, a minimum 4 or 5 years of follow-up (Aghanwa, 2001; Yazici et al., 2002; Dakhlaui et al., 2008) or at least 10 years of illness duration (Perugi et al., 2007; Andrade-Nascimento et al., 2011) have been included. Additionally, two studies have emphasized the exclusion of cases with mixed episodes (Yazici et al., 2002; Andrade-Nascimento et al., 2011).

In conclusion, a consensus seems to have been reached on the requirement of the presence of at least three or four manic episodes without any intervening depressive episodes for a diagnosis of UM. Currently, a minimum four-year follow-up duration and the exclusion of cases with mixed episodes are being suggested as a diagnostic criterion. However, questions remain about the stability of the diagnosis when these criteria are applied.

The main issue with prospective error is the likelihood of depressive episodes that have not been recorded due to insufficient follow-up duration. Therefore, it seems the inclusion of a sufficient time period in the criteria as a required minimum duration of illness or follow-up is important. Still, the fact remains that even in the presence of a long follow-up and any number of manic episodes, the possibility of a future depressive episode cannot be excluded. However, the same criticism and limitations are also valid for a number of disorders, including unipolar depression.