
Comorbidity of Depression and Other Diseases

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Abstract: This paper outlines the comorbidity of depression and other diseases that are frequently seen in the primary care of depression. Since the operational diagnostic criteria of the DSM-III-R (Diagnostic and Statistical Manual of Mental Disorders, revised 3rd edition) and the current DSM-IV (4th edition) were introduced to Japan from the U.S., Japanese psychiatrists have become active in assigning a single patient parallel or overlapping diagnoses of mental disorders. In patients with depression, the comorbidity of anxiety disorder (panic disorder, generalized anxiety disorder), obsessive-compulsive disorder, drug dependence, alcohol dependence, post-traumatic stress disorder, or personality disorder is an issue. When depression is comorbid with another mental disorder, both disorders are reported to be severer, more likely to be refractory, and more likely to be associated with a poor prognosis. Although the concept of comorbidity in the field of mental disorders is useful in understanding patients' symptoms and determining prognosis, it is also possible that the patient's pathological structure is too greatly simplified. The concept of comorbidity should be employed within the limits of its clinical usefulness, while maintaining full recognition of this possible simplification.

Key words: Comorbidity; Depression; Mental disorders; DSM-IV

Introduction

Comorbidity is a term that has become increasingly common during the past 10 years or so, particularly in the field of psychiatry as practiced in Europe and North America. This concept now represents a major theme in clinical psychiatry. Comorbidity means the state of being jointly (co-) morbid, and it is defined as "the presence of more than one disease in a single person during a certain

period of time". In Japanese, "comorbidity" is translated as "*heison*," "*heibyō*," or "*kyoson*," but the original, untranslated English word is often used in practice.

The assumption that a patient has comorbid mental disorders is often helpful in understanding his or her pathological condition and in formulating treatment policy and determining prognosis. General information on psychiatric comorbidity, including depression, has been the topic of several review articles that

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have been published in Japanese psychiatric journals.¹⁻³⁾ This paper outlines the comorbidity of depression and other diseases, focusing on those cases that frequently may be seen in the general clinical setting.

Historical Development

Although the concept of the coexistence of two or more diseases is not at all new, conventional clinical psychiatry has tended to avoid it. Traditional psychiatric diagnostic criteria have been presented as a stratified structure of independent disease classifications, and various symptoms have been subsumed under a single psychiatric disease. For example, if a patient had both depressive and compulsive symptoms, depression and obsessive-compulsive disorder were considered in the differential diagnosis, and the patient's condition was generally diagnosed as depression, a diagnosis that superseded obsessive-compulsive disorder. Until recently there had been no tendency to label a single patient with both of these diagnoses.

However, since the operational diagnostic criteria of the DSM-III-R (Diagnostic and Statistical Manual of Mental Disorders, revised 3rd edition) and the current DSM-IV (4th edition), which are based on multiaxial evaluation involving five axes,⁴⁾ were introduced from the U.S., the concept of psychiatric comorbidity has spread throughout clinical practice in Japan, allowing Japanese psychiatrists to give a single patient two or more diagnoses at the same time. Thus, a patient such as the one mentioned above would be regarded as having both depression and obsessive-compulsive disorder. The development of such parallel, overlapping diagnostic criteria in the U.S. seems to be grounded not only on progress in the area of operational diagnostic criteria but also on the finding that drug dependence is associated with various mental disorders.

Comorbidity of Depression

A large-scale national survey on the comorbidity of depression was carried out in the U.S. principally by the University of Michigan.⁵⁾ The results indicated that more than half of all patients with a DSM-III-R diagnosis of major depressive disorder were associated with a comorbid anxiety disorder, and that more than one-third of patients showed the comorbidity of drug or alcohol dependence. Thus it is safe to say that depression is often present together with other mental disorders. According to Kessler *et al.*,⁵⁾ patients with pure depression, i.e., without comorbidity, accounted for only one-fourth of all patients with that diagnosis. However, as approximately 20% of patients with depression have comorbid post-traumatic stress disorder (PTSD), diagnoses of these coexisting disorders are based simply on the fact the patient has met the requirements for more than one disease in the current operational diagnostic criteria. This is because the previous system of diagnosis was likely to adopt one diagnosis while deliberately or inadvertently excluding others; it does not mean that the comorbidity of mental disorders has increased particularly in recent years.

The presence of comorbidity brings several important issues to the surface. First, when depression coexists with another mental disorder, these disorders are reported to be severer than when either is present alone. The frequencies of admissions and suicide attempts are higher, and the prognosis worse, in patients with comorbid depression.⁵⁾ This trend is particularly prominent among young patients with depression. A second issue is the temporal relationship between depression and other comorbid mental disorders. There are three ways of considering the order of onset⁶⁾: 1) When depression precedes the other disorder, depression may serve as a causative factor for the subsequent disorder; 2) when the other disorder precedes depression, that disorder

may serve as a causative factor for depression; and 3) when depression and the other disorder occur simultaneously, the symptoms of these two diseases may be considered attributable to a different cause(s). In general, in patients with comorbid depression, the other mental disorder often precedes the initial episode of depression (secondary depression), and this is particularly so when the patient is male.⁵⁾

The comorbidity of depression and other mental disorders is outlined below in relation to individual common disorders.

1. Depression and anxiety disorder

Comorbid anxiety disorder is the disorder most frequently found in patients with depression. Many researchers have reported that more than 50% of patients with panic disorder, characterized by sudden episodes of strong anxiety, or generalized anxiety disorder, characterized by continuous anxiety, experience at least one episode of depression in their lifetimes.⁵⁾ Based on this high rate of comorbidity, some researchers consider anxiety disorder and depression to have a common hereditary predisposition and differences in clinical picture to result from differences in phenotype influenced by environmental factors.⁷⁾ Without going that far, it is clear that many patients, at least clinically, have symptoms of both depression and anxiety, and that the close relationship between the two disorders has been pointed out. In addition, the actions of anxiolytics and antidepressants are considered to affect both conditions. Further research on the comorbidity of these conditions, not only from the aspect of etiological studies and clinical evaluation, but also from the viewpoint of psychopharmacology, is awaited.

As mentioned in the previous section, both depression and anxiety are severe in patients with comorbid depression and anxiety disorder. Moreover, these patients are more likely to be resistant to tricyclic antidepressant drug

therapy, to have markedly decreased social function including occupational and marital problems, and to have a high incidence of attempted suicide, resulting in a poor prognosis.⁶⁾

2. Depression and obsessive-compulsive disorder

Obsessions (such as irrational adherence to certain ideas or repetitive thinking) or compulsions (such as compulsive rituals or ascertainment behavior) are known often to be concomitant with various mental disorders including schizophrenia, depression, and organic brain disease. As in cases of anxiety disorder, secondary depression is also common in cases of comorbid obsessive-compulsive disorder and depression, with depression developing during the course of preceding obsessive-compulsive symptoms. A survey of a large number of patients with obsessive-compulsive disorder showed that about one-third of them had comorbid depression at the time of the survey and inferred that about two-thirds of them would develop depression sometime in their lives.⁸⁾

There are biological markers common to depression and obsessive-compulsive disorder, and serotonin-related drugs, particularly selective serotonin reuptake inhibitors (SSRIs), are effective for both depression and obsession. These findings suggest a biological relationship between the two conditions. However, the responses of depression and obsession to antidepressants are not necessarily the same in patients with comorbidity. This is an issue that requires further investigation.

3. Depression and alcoholism

The association of depression and alcoholism has long been discussed. In a review of previous reports, Davidson *et al.*⁹⁾ found comorbidity between depression and alcoholism in 16–88% of patients. According to the previously mentioned report by Kessler *et al.*, comorbid alcohol dependence or abuse is

present in nearly 30% of patients with depression.⁵⁾ When depression precedes alcoholism, alcoholism may be a symptom of depression, or the patient's attempt to reduce depressive symptoms may result in alcoholism. It is understandable that a patient may succumb to alcoholism in trying to relieve depression or hostility. On the other hand, when alcoholism is present initially, the risk of developing depression is considered to be 2–3 times higher than that in the general population. Patients with alcoholism often fall into a depressive state when they lose control of drinking or are in a period of withdrawal. Therefore, caution is necessary when considering the nature of the comorbidity of depression and alcoholism. It is also possible in some cases that common risk factors and heredity are involved in the development of the two conditions.

4. Depression and personality disorder

It has been a firmly rooted belief that mood disorder is related to premorbid personality disorder, and, specifically among psychiatrists in this country, it is generally accepted that unipolar depression and melancholic personality are related. However, recent etiological studies of a large number of patients have resulted in negative findings, indicating the need for caution with regard to this issue.¹⁰⁾ There is an interesting finding from the aspect of comorbidity between depression and personality disorder. According to DSM-IV,⁴⁾ the original mental disorder is diagnosed on the first axis, and the accompanying personality disorder, if any, is coded on the second axis. In this sense, the multiaxial diagnosis of DSM-IV is based on the premise that comorbidity of personality disorder and other mental disorders exists. A recent review of patients with depression indicated that some type of personality disorder was present in 20–50% of inpatients and 50–85% of outpatients with depression.¹¹⁾ Among these patients, relatively frequent types of personality disorders were

borderline (10–30%), histrionic (2–20%), anti-social (0–10%), and obsessional (0–20%), showing a great deal of diversity. Although the comorbidity of depression and personality disorder is of clinical importance, it is not an uncomplicated problem. It needs to be borne in mind that the prognosis and treatment policy will vary according to the type of comorbid personality disorder.

5. Depression and physical or neurologic diseases

When depressive symptoms are present in association with organic brain disease or general physical diseases, as coded on axis III of DSM-IV, it is not particularly helpful to regard this as comorbidity of depression, as pointed out by Yoshimatsu.¹²⁾ It would be preferable to consider it a unified combination of the partial manifestations of underlying physical and organic disease or as a secondary response, if possible. For example, in clinics we often encounter patients with dementia in whom a depressive state has preceded dementia. However, it seems to be of greater significance from the aspects of both early diagnosis and integrated understanding of the pathological condition to regard the depressive state as the initial symptom of dementia rather than consider it to be a case of comorbidity of depression and dementia.

Conclusion

Comorbid conditions that are likely to be seen frequently in the clinical setting for primary care of depression have been outlined. The concept of comorbidity expressed through the names of multiple diseases that satisfy diagnostic criteria is rational from one point of view, conforming as it does to certain operational diagnostic criteria, and is helpful in understanding a patient's symptoms as well as in clarifying treatment and prognosis. However, there is also the possibility that the patient's pathological structure is too greatly

simplified into “a mosaic aggregate of a number of diseases” (Yoshimatsu¹²). The concept of comorbidity should be employed within the limits of its clinical usefulness, while maintaining full recognition of this possible simplification.

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