Understanding Comorbid Depression and Anxiety

December 01, 2007 | Anxiety [1], Depression [2], Comorbidity In Psychiatry [3], Mood Disorders [4], Generalized Anxiety [5], Major Depressive Disorder [6], Dysthymia [7]
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Comorbidity of psychiatric syndromes is quite common—in a 12-month period, almost 50% of adults in the United States with any psychiatric disorder had 2 or more disorders.

The National Comorbidity Survey Replication\(^1\) reported that in a 12-month period, the prevalence for an anxiety disorder was about 18%, and for a mood disorder it was 9.5%. Lifetime prevalences for any anxiety disorder and MDD were approximately 29% and 16.6%, respectively.\(^4\) Assuming a (perhaps conservative) 50% comorbidity rate, between 5% and 9% of the adult population has comorbid depression-anxiety in a 12-month period.

The impact of comorbid depression and anxiety is substantial. As demonstrated by the Global Burden of Disease study, neuropsychiatric disorders accounted for more than 13% of all medical disability worldwide and for more than 27% of all noncommunicable disease in 2005.\(^5\) Depression alone produced 10% to 12% of all disability from noncommunicable disease and approximately 5% of all disability (noncommunicable, communicable, injury). Thus, comorbid anxiety and depression may account for as much as 2% to 4% of all medical disability worldwide. In addition, depression (and, thus, comorbid depression and anxiety) is associated with other psychiatric and nonpsychiatric medical conditions (eg, cardiovascular disease, diabetes, HIV/AIDS, maternal and reproductive-related syndromes, and psychosomatic illnesses), with their resulting socioeconomic costs.\(^5\)

Risk factors and prognoses

There has been little research on risk factors that predict the development of comorbid anxiety and depression compared with risk factors for either disorder alone. However, the high rate of comorbidity indicates that the simple occurrence of one disease state should be considered a predisposing factor for the development of the other. Psychosocial and situational difficulties also appear to be risk factors for the development of comorbid anxiety and depression.\(^6\) Familial/genetic studies reported different results, partly determined by the anxiety disorder under consideration.\(^6\) For example, MDD and GAD appear to be related to the same genetic factors, while MDD and PD are familially independent.\(^7-9\) Gender may also play a role, because women have a higher risk than men for both disorders.\(^4\)

Age is another consideration. Patients with anxiety disorders have a much earlier median age at onset than do those with mood disorders (age 11 years vs age 30 years).\(^4\) As would be expected, onset of anxiety usually predates onset of depression in patients with this comorbidity.\(^5,10\) However, the earlier onset of anxiety disorders does not necessarily infer causality. The expected prognosis for patients with comorbid anxiety and depressive disorders is poorer than that for either disorder alone. These patients have greater severity of symptoms, increased risk of suicidality, a more chronic and persistent course, and more functional impairment. This syndrome is also more difficult to treat, with longer time to remission and need for increased medication.\(^6,11,12\)

Biological studies

There are several possible explanations for this high rate of comorbidity.\(^13\) First, the present DSM-IV diagnostic criteria tend to overlap, raising the likelihood that a person meeting criteria for one disorder has an increased probability of having the other. For example, depressive ruminations are similar to the obsessional thinking/worry seen in GAD; poor sleep quality and difficulty in concentrating occur in both depression and posttraumatic stress disorder; and phobic avoidance can
be mistaken for depressive loss of energy or fatigue. A second possibility is that the disorders are etiologically different, but symptom episodes are provoked by related environmental events (ie, stressors), such as threat (anxiety) and loss (depression). The third possibility is that the underlying biologies of the disorders are the same or are highly overlapping; this is related to the first possible explanation. An understanding of the pathophysiology of depressive and anxiety disorders is necessary to address the first and third reasons.

A number of potential biological markers have been studied in people with comorbid depression and anxiety. Several markers have assessed noradrenergic or hypothalamic-pituitary-adrenocortical (HPA) axis function. Serotonergic (along with noradrenergic) function has also been of interest, because many medications with serotonergic and/or noradrenergic effects are beneficial for individuals with depression and/or anxiety. Other markers studied include sleep (which is abnormal in both types of disorders), thyroid axis activity (abnormal in depression), lactate infusion (abnormal in anxiety), and cardiovascular function (abnormal in both depression and anxiety). (Abnormality associated with sleep and cardiovascular functions presents differently in anxiety versus depression.)

Earlier studies have not included nonpathological controls, patients with depression only, patients with anxiety only, and patients with both disorders. Interpretation of results has been somewhat hampered by the lack of inclusion of all 4 groups. Therefore, we recently designed and completed a study of HPA axis function and CNS noradrenergic function that included these 4 groups.

In order to determine the roles of each disorder as well as the comorbid state, we compared "pure" participants —those with anxiety only (social anxiety disorder or PD) or MDD only—with individuals who had comorbidity; these participants were also matched with controls. We used the Trier Social Stress Test (a reliable activator of the HPA axis) and the growth hormone response to the $a_2$-adrenoreceptor agonist clonidine.

As can be seen in the Table, anxiety was associated with a noradrenergic abnormality; depression was associated with a disruption of the normal negative correlation between the 2 systems. Most notably, hyperactivity of the HPA axis was uniquely associated with the comorbid state, indicating that there is something qualitatively (not just quantitatively) distinctly biological about the comorbid state. In other words, comorbid anxiety and depression might be a distinct disorder.

<table>
<thead>
<tr>
<th>Diagnostic group</th>
<th>HPA axis</th>
<th>Noradrenergic function</th>
<th>Association of markers</th>
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</thead>
<tbody>
<tr>
<td>Anxiety</td>
<td></td>
<td>Blunted GH response*</td>
<td></td>
</tr>
<tr>
<td>Depression</td>
<td></td>
<td>No negative correlation‡</td>
<td></td>
</tr>
<tr>
<td>Comorbid†</td>
<td>Hyperactive</td>
<td>Blunted GH response*</td>
<td>No negative correlation‡</td>
</tr>
</tbody>
</table>

HPA, hypothalamic-pituitary-adrenocortical; GH, growth hormone.

*A blunted growth hormone response to clonidine. (Noradrenergic dysfunction was only abnormal in those who were comorbid and predominantly anxious.)

†An elevated adrenocorticotropic hormone response to the Trier Social Stress Test, with a similar trend for cortisol, seen only in patients who were both anxiety and depression.
depressed and anxious.

Control participants and those with anxiety showed negative correlations between the magnitudes of the HPA axis and growth hormone responses, which was not observed in depressed or comorbid groups.

References:


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