

# Comorbidity of Psychiatric Disorders and Posttraumatic Stress Disorder

Kathleen T. Brady, M.D., Ph.D.; Therese K. Killeen, R.N., Ph.D.;  
Tim Brewerton, M.D.; and Sylvia Lucerini, M.D.

Posttraumatic stress disorder (PTSD) commonly co-occurs with other psychiatric disorders. Data from epidemiologic surveys indicate that the vast majority of individuals with PTSD meet criteria for at least one other psychiatric disorder, and a substantial percentage have 3 or more other psychiatric diagnoses. A number of different hypothetical constructs have been posited to explain this high comorbidity; for example, the self-medication hypothesis has often been applied to understand the relationship between PTSD and substance use disorders. There is a substantial amount of symptom overlap between PTSD and a number of other psychiatric diagnoses, particularly major depressive disorder. It has been suggested that high rates of comorbidity may be simply an epiphenomenon of the diagnostic criteria used. In any case, this high degree of symptom overlap can contribute to diagnostic confusion and, in particular, to the underdiagnosis of PTSD when trauma histories are not specifically obtained. The most common comorbid diagnoses are depressive disorders, substance use disorders, and other anxiety disorders. The comorbidity of PTSD and depressive disorders is of particular interest. Across a number of studies, these are the disorders most likely to co-occur with PTSD. It is also clear that depressive disorder can be a common and independent sequela of exposure to trauma and having a previous depressive disorder is a risk factor for the development of PTSD once exposure to a trauma occurs. The comorbidity of PTSD with substance use disorders is complex because while a substance use disorder may often develop as an attempt to self-medicate the painful symptoms of PTSD, withdrawal states exacerbate these symptoms. Appropriate treatment of PTSD in substance abusers is a controversial issue because of the belief that addressing issues related to the trauma in early recovery can precipitate relapse. In conclusion, comorbidity in PTSD is the rule rather than the exception. This area warrants much further study since comorbid conditions may provide a rationale for the subtyping of individuals with PTSD to optimize treatment outcomes. (*J Clin Psychiatry* 2000;61[suppl 7]:22-32)

Posttraumatic stress disorder (PTSD) is commonly comorbid with other psychiatric disorders. Data from epidemiologic surveys as well as studies in treatment-seeking samples are converging to strongly support the idea that in individuals with PTSD, the presence of other psychiatric disorders is the rule rather than the exception. The high prevalence of comorbidity has an important impact on the presentation and differential diagnosis of PTSD and has important treatment implications. In this article, the most common Axis I disorders that coexist with PTSD are reviewed. For each class of disorders, available prevalence data from epidemiologic and treatment-seeking samples are presented and treatment implications discussed.

From the Institute of Psychiatry, Medical University of South Carolina, Charleston.

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Reprint requests to: Kathleen T. Brady, M.D., Ph.D., Medical University of South Carolina, 67 President St., Charleston, SC 29425.

## COMORBIDITY IN PTSD

### Prevalence

Some of the most enlightening data on the epidemiology of PTSD and the comorbidity of PTSD with other psychiatric disorders come from the National Comorbidity Survey (NCS).<sup>1</sup> This is the largest epidemiologic survey to date examining psychiatric disorders in the general population of the United States. As can be seen in Table 1, 59% of men with PTSD and 44% of women with PTSD meet criteria for 3 or more other psychiatric diagnoses. The most common comorbid diagnoses are affective disorders (particularly depression), other anxiety disorders, and substance use disorders. In the Vietnam Experience Study,<sup>2</sup> among those who met current criteria for PTSD, 66% also met criteria for another anxiety or affective disorder and 39% had current alcohol abuse or dependence. In another large study of Vietnam veterans, Kulka and colleagues<sup>3</sup> found that 98.9% of those diagnosed with PTSD met criteria for at least one other psychiatric diagnosis. The most prevalent comorbid disorders were substance use disorders (73%), antisocial personality disorder (31%), and major depression (28%). Survey studies of women with

**Table 1. Comorbidity of Posttraumatic Stress Disorder (PTSD) With Other Disorders in the National Comorbidity Survey (NCS)<sup>a</sup>**

Psychiatric Diagnosis	Women	Odds Ratio	Men	Odds Ratio
No other disorder	21%	0.2	12%	0.2
1 diagnosis	17%	2.2	15%	2.4
2 diagnoses	18%	4.0	14%	3.8
3 or more diagnoses	44%	7.9	59%	14.5

<sup>a</sup>Data from Kessler et al.<sup>1</sup>

PTSD and treatment-seeking samples of civilians with PTSD<sup>3</sup> have reported similar findings. Cashman and colleagues<sup>4</sup> studied 277 female victims of assault and found that 60% had comorbid major depression, 25% had a comorbid substance use disorder, and there were high rates of borderline, avoidant, and paranoid personality disorders.

### Causal Pathways of Comorbidity

A number of different hypotheses have been put forth to explain the high levels of comorbidity of PTSD with other psychiatric disorders. These differing hypothetical constructs vary in the extent to which they fit various comorbidities, and it is likely that, in the clinical setting, one or more of these explanations may appropriately apply to individual cases depending on the specific comorbidity in question. The self-medication hypothesis has often been used to explain the connection between PTSD and substance use disorders. Specifically, it is posited that some individuals with PTSD turn to drugs and alcohol as a way of alleviating painful symptoms of PTSD such as sleep disturbance, intrusive thoughts, or hypervigilance. The short-term relief given by substances of abuse is often followed by a withdrawal state in which the symptoms of PTSD are exaggerated.

There is considerable symptom overlap between PTSD and a number of other psychiatric disorders, most notably depression (i.e., sleep disturbance, poor concentration, and guilt) and other anxiety disorders (i.e., panic attacks and avoidance). It has been suggested that the high rates of comorbidity in PTSD are simply an epiphenomenon of the diagnostic criteria used for all of these disorders.<sup>5</sup> Van der Kolk and colleagues<sup>6</sup> have suggested that PTSD and its comorbid conditions should not be seen as separate disorders, but as "complex somatic, cognitive, affective and behavioral effects of psychological trauma."<sup>(p291)</sup>

Another hypothesis, supported by a study conducted by Hyer et al.,<sup>7</sup> is that individuals with PTSD tend to report higher levels of symptoms when compared with individuals with other psychiatric disorders. As such, the high level of comorbidity might be partially explained by symptom overreporting and the high levels of global distress often experienced by individuals with PTSD.

Finally, the high levels of comorbidity may be partly explained by the fact that the presence of certain psychiat-

ric disorders (e.g., major depression) is actually a risk factor for the development of PTSD, and they may have been present prior to the trauma. Regardless of the conceptual framework used to understand the complex and heterogeneous presentations of PTSD, patient evaluation must include assessment of a wide range of psychological as well as somatic symptom areas.

### Comorbidity and Differential Diagnosis

PTSD is a heterogeneous disorder that can present with a number of different symptom constellations. The symptom overlap, as mentioned above, can make diagnosis particularly difficult. Diminished interest, restricted range of affect, and sleep difficulties are all core symptoms of both PTSD and major depressive disorder (MDD). Irritability, hypervigilance, and increased startle reflex are symptoms of PTSD that overlap with generalized anxiety disorder (GAD). Individuals with PTSD often have panic attacks upon exposure to reminders of their trauma. Because traumatic events are disturbingly common and PTSD has such heterogeneous presentations, routine screening for trauma is important in all psychiatric evaluations and in individuals with psychiatric or unexplained physical complaints in the primary care setting. It is important that the clinician ask specifically about traumatic events since patients often will not volunteer this information because they find it painful to talk about or feel that the trauma has no bearing on the present complaints. Making an accurate diagnosis of PTSD, rather than a long list of potential diagnoses to explain various symptoms, depends on the appropriate and thorough assessment of trauma history. Several brief screening assessments for traumatic events that might be ideal for use in the primary care setting are currently under investigation.<sup>8,9</sup>

### Comorbidity and Course of Illness

Data from a number of sources indicate that PTSD is often a chronic disorder. One third of individuals with PTSD have symptoms that fail to remit after 6 or more years regardless of treatment status.<sup>1</sup> It appears that comorbidity is related to chronicity of illness. Breslau et al.,<sup>10</sup> in a study of young urban adults, found that individuals with chronic PTSD were more likely to have one or more additional anxiety or affective disorder diagnoses when compared with subjects with nonchronic PTSD. In other studies,<sup>11</sup> both depression and substance abuse have been associated with prolonged episodes of PTSD. In a recent study of the course of PTSD in 54 individuals with at least one other anxiety disorder,<sup>12</sup> a history of alcohol abuse and childhood trauma were associated with a longer time until symptom remission. There are several potential explanations for these findings. Comorbidity in general may make individuals more resistant to both pharmacologic and psychotherapeutic interventions. Although this hypothesis has intuitive appeal, it has not been empirically

**Table 2. Comorbidity of PTSD and Affective Disorders in the NCS<sup>a</sup>**

Affective Disorder	Women	Odds Ratio	Men	Odds Ratio
Major depressive disorder	49%	4.1	48%	6.9
Dysthymia	23%	4.1	21%	6.0
Mania	5.7%	4.5	11.7%	10.4

<sup>a</sup>Data from Kessler et al.<sup>1</sup>

tested. In the case of the substance use disorders, substance use may interfere with the normal psychological processes responsible for the individual's ability to come to a healthy resolution of trauma. It is also possible that similarities in neuronal mechanisms involved in substance withdrawal and those involved in the pathophysiology of PTSD may actually lead to an exacerbation of PTSD, with repeated substance use and withdrawal contributing to chronicity of illness.

## PTSD AND AFFECTIVE DISORDERS

Across a number of studies, MDD and dysthymia are the psychiatric disorders most likely to co-occur with PTSD. As can be seen in Table 2, in the NCS, 48% of men and 49% of women with PTSD had lifetime MDD, making it the most common co-occurring disorder in the study. The relationship between PTSD and MDD is particularly complex because there are many overlapping symptoms, making differential diagnosis complicated. There is also evidence accumulating to indicate that PTSD and depression may be independent and common sequelae of exposure to a trauma.

### Symptom Overlap

The overlap of symptoms between PTSD and depressive disorders is substantial. Key features of both disorders include sleep disturbance, decreased concentration, avoidance and withdrawal, lack of interest and pleasure in activities, and a sense of isolation and distance from others. A key differentiation in PTSD should be that these problems began after the trauma experience, but in individuals who have experienced childhood trauma or multiple traumas, the timing of symptom onset relative to the trauma may be difficult to distinguish. Further complicating the issue, PTSD and depressive disorders commonly coexist. Keane and colleagues<sup>13</sup> asked 340 experienced clinicians to rate the extent to which 90 symptom items characterized PTSD, MDD, or GAD. They found that the raters were able to readily distinguish the disorders and situation-specific items, such as re-experiencing, hyperarousal, and avoidance specifically tied to trauma-related cues. Evaluating symptoms is the best way to distinguish these disorders from each other. In another study, Blanchard and colleagues<sup>14</sup> explored the notion that because of symptom overlap, the threshold for diagnosing

depression should be increased in individuals with PTSD (5–6 vs. 7–9 symptoms). They found that changing the threshold had no important effects on any indicators of "caseness," again supporting the idea that these disorders commonly coexist and can reliably be distinguished in spite of symptom overlap.

### Independent Sequelae

In addition to the symptom overlap between PTSD and depressive disorders, other explanations for the common co-occurrence of these disorders include the idea of sequential causation, in which depression is considered to be secondary to prolonged PTSD. In the NCS,<sup>1</sup> 78.4% of the individuals with comorbid MDD and PTSD reported that the onset of the affective disorder followed that of PTSD. On the other hand, a history of MDD is a predictor of the development of PTSD following exposure to a traumatic event. A number of recent studies support the fact that depression and PTSD are 2 common, sometimes related, but often independent responses of an individual to trauma. Shalev and colleagues<sup>15</sup> followed a group of trauma survivors recruited from an emergency room, with assessments at 1 week, 1 month, and 4 months. At the 4-month assessment timepoint, 17.5% met criteria for PTSD, 14.2% met criteria for MDD, and 43.2% met criteria for comorbid depression and PTSD. Individuals with comorbidity had greater symptom severity and a lower level of functioning. Prior MDD predicted a higher level of posttrauma depression. Survivors with PTSD had higher heart rates in the emergency room, more intrusions and exaggerated startle, and more peritraumatic dissociation. In a similar study,<sup>14</sup> 107 motor vehicle accident victims were examined, and results showed that 62 met criteria for PTSD and 33 met criteria for both PTSD and MDD 1 to 3 months postaccident. Analysis indicated that PTSD and MDD were correlated but independent responses to trauma. Again, those with both disorders were more distressed, had more major role impairment, and were less likely to experience symptom remission during the 6-month follow-up period. In sum, it appears that PTSD and depressive disorders are closely related, but the nature of this relationship is complex and variable and must be examined on a case-by-case basis.

### Neurobiological Connections

Both PTSD and MDD are characterized by dysregulation of the hypothalamic-pituitary-adrenal (HPA) axis, one of the major neurohormonal systems involved in the stress response. In both disorders, there is increased corticotropin-releasing factor (CRF) release, but the response at the level of the pituitary and below differs. In PTSD, there are lower circulating levels of cortisol in spite of increased CRF. This is thought to be because of stronger-than-normal negative feedback of cortisol on the HPA axis. In depression, there is an increase in circulating

cortisol and weaker negative feedback inhibition from cortisol on HPA function. HPA axis function in individuals with comorbid PTSD and MDD has not been well characterized, but would be of interest because of the discrete findings with each of these disorders.

In a recent study, Maes and colleagues<sup>16</sup> explored both serotonergic and noradrenergic markers in a group of individuals with PTSD with and without MDD. They found that PTSD was associated with lower paroxetine binding sites, suggesting defects in the serotonin (5-HT) system, whereas PTSD accompanied by MDD was associated with catecholaminergic dysfunction, suggesting that a neurobiological dissection of PTSD with and without MDD might be possible. This type of neurobiological specificity could have important treatment implications for comorbid populations.

### Treatment Issues

While the prevalence of comorbid affective disorder and PTSD is impressive and it is clear that comorbidity has a negative impact on prognosis and course of illness, there has been little investigation of the treatment of comorbid PTSD and MDD or dysthymia. Fortunately, most of the agents that have demonstrated efficacy in the treatment of PTSD are also antidepressant agents. Their efficacy in the treatment of PTSD, however, is not likely to be simply due to the treatment of depression, because symptoms that are characteristic of PTSD and not depression, such as the intrusive symptoms, are improved by antidepressant treatment. Because of the negative impact of depression on the course of PTSD and the presence of pharmacotherapeutic treatments with demonstrated efficacy, it seems intuitive that the threshold for treating these comorbid individuals with antidepressant agents should be low.

In spite of the fact that psychotherapy, particularly cognitive therapy, exposure therapy, and anxiety management techniques, can be extremely effective in the treatment of PTSD (Hembree and Foa,<sup>17</sup> this supplement), the use of these therapies in comorbid populations has not been systematically explored. Specifically, how well depressed individuals tolerate exposure therapy and whether cognitive-behavioral therapies specifically tailored to contain elements of treatment for both PTSD and depressive symptoms would improve treatment outcome remains to be seen.

### Bipolar Disorder

As can be seen in Table 2, the odds ratio for comorbid PTSD and mania in the general population is high (10.4 for men; 4.5 for women). Childhood mania has been found to be a risk factor for trauma exposure and PTSD.<sup>18</sup> It may be that individuals with bipolar disorder place themselves at particular risk for exposure to trauma during manic episodes, but this has never been systematically explored. In terms of treatment for this comorbid population, stabilization of mood and training in risk-reduction strategies

**Table 3. Comorbid Anxiety Disorder and PTSD in the NCS<sup>a</sup>**

Disorder	Women	Odds Ratio	Men	Odds Ratio
Generalized anxiety disorder	15.0%	5.9	16.8%	2.8
Panic disorder	12.6%	4.1	7.3%	3.2
Simple phobia	29.0%	7.1	31.4%	2.4
Social phobia	28.4%	3.0	27.6%	2.4
Agoraphobia	22.4%	4.5	16.1%	3.4

<sup>a</sup>Data from Kessler et al.<sup>1</sup> The Kessler et al. study did not capture or characterize obsessive-compulsive disorder.

would be essential. Interestingly, there is some evidence that anticonvulsant mood-stabilizing agents, which are useful in the treatment of bipolar disorder, can be useful in the treatment of PTSD (Friedman,<sup>19</sup> this supplement), but more investigation of these intriguing findings is necessary.

### Suicidality

PTSD, with or without major depression, appears to be an important risk factor for suicidality. In a study of over 3000 young adults, Wonderlich and colleagues<sup>20</sup> found that 91% of all suicide attempts had at least one psychiatric diagnosis, and the highest risk for suicide attempt was among those individuals with PTSD. In another study of refugees exposed to severe trauma,<sup>21</sup> the presence of suicidal behavior was found to be most frequent in individuals with the primary diagnosis of PTSD compared with all other diagnoses. Interestingly, PTSD patients with comorbid depression reported more suicidal ideation than those nondepressed individuals with PTSD.

## PTSD AND COMORBID ANXIETY DISORDERS

### Prevalence

The diagnostic confusion and symptom overlap between PTSD and other anxiety disorders is considerable. Physiologic symptoms of increased autonomic arousal, intense psychological distress, derealization or depersonalization, and fear of losing control are all characteristic of both PTSD and panic disorder. Social phobia, specific phobia, agoraphobia, and PTSD all share avoidance symptoms. Sleep disturbance, difficulty concentrating, and restlessness are common to all anxiety disorders.

As can be seen in Table 3, in the NCS,<sup>1</sup> the odds ratio for a coexisting anxiety disorder in individuals with PTSD ranges from 2.4 to 7.1. Simple and social phobia were the most common coexisting anxiety disorders (the study did not capture obsessive-compulsive disorder). In this study, men with PTSD appeared to have a greater relative risk for another coexisting anxiety disorder compared with women. Breslau et al.<sup>22</sup> found a 55% prevalence of other anxiety disorders in a sample of 801 women with PTSD. Again, simple and social phobia were the most common co-occurring anxiety disorders in this sample. Orsillo and colleagues<sup>23</sup> found a 46% prevalence of other anxiety dis-

orders in a sample of 311 male combat veterans. In this sample, panic was the most common co-occurring anxiety disorder.

### **PTSD and Panic Disorder**

Falsetti and Resnick<sup>24</sup> found that 69% of treatment-seeking patients with trauma histories reported experiencing panic attacks. They found no indication that panic disorder was related to type of traumatic experience. The panic symptoms most frequently reported in this study were rapid heart rate or palpitations and fear of going crazy or losing control. Deering and colleagues<sup>25</sup> found that panic disorder seemed to be more common in individuals with PTSD who had experienced a trauma that included extreme autonomic arousal, hypervigilance, and unpredictability (e.g., threat of murder during rape, high-risk war assignments, massive and uncontrollable fires). They suggest that panic and PTSD are not comorbid but rather interwoven disorders. In a comorbid sample of 140 veterans with combat-related current or lifetime PTSD, panic disorder was the most strongly associated comorbid psychiatric disorder (odds ratio = 13.7 and 15.6, respectively). For the most part, the panic disorder began after the onset of the PTSD.<sup>26</sup>

In differential diagnosis, it is helpful to keep in mind that in panic disorder, fear and avoidance have more to do with the physical symptoms associated with panic attacks (e.g., palpitations, sweating, chest pains, fear of having a heart attack), whereas in PTSD, fear and avoidance are specifically related to trauma-related memories and cues. Michelson et al.<sup>27</sup> stress the importance of differentiating panic with agoraphobia from PTSD for treatment purposes. In a study of patients with panic disorder treated with cognitive-behavioral therapy, exposure therapy, relaxation therapy, or a combination of techniques, a history of traumatic experiences and higher levels of dissociation were related to higher levels of psychopathology and poorer treatment outcomes. Specifically, higher levels of traumatic experiences and higher levels of dissociation were associated with greater agoraphobia at 1-year follow-up. This suggests that individuals with comorbid panic disorder and agoraphobia complicated by PTSD may need specifically tailored psychotherapies. If these patients are treated with therapy targeting panic and agoraphobia while trauma-related symptoms are not addressed, untreated PTSD may account for poorer outcomes. It is also possible that the dissociation sometimes associated with PTSD inhibits patients from retaining information from therapy sessions.

### **Social Phobia and PTSD**

The association between social phobia and PTSD has only recently been appreciated. Orsillo et al.<sup>23</sup> found that 72% of Vietnam veterans who met criteria for PTSD also met criteria for social phobia. Significantly more veterans

with PTSD met criteria for social phobia compared with a group of veterans without PTSD. Current social anxiety was associated with premilitary anxiety, shame, and homecoming adversity. It was postulated that fear of disapproval and lack of a supportive posttrauma environment contributed to social anxiety. Crowson et al.<sup>28</sup> found significant correlations between scores on the social phobia and agoraphobia subscales of the Social Phobia and Anxiety Inventory and PTSD severity. This effect appeared to be mediated through a depressed mood or negative affect. As previously discussed for panic disorder, this comorbidity has important treatment implications. Clearly, both disorders need to be addressed to optimize treatment outcomes.

### **Comorbidity and Order of Onset**

Several investigators have studied the time line for onset of PTSD relative to other anxiety disorders. Order of onset may be difficult to detect retrospectively because some individuals have difficulty recalling previous symptoms or minimize preexisting disorders relative to their current PTSD. Most of the evidence supports the notion that preexisting anxiety disorders increase the vulnerability to develop PTSD and have an adverse impact on severity, chronicity, and course of PTSD, as well as treatment outcome.<sup>5,25,27</sup> In looking at the relative order of onset of PTSD and other anxiety disorders in the NCS, unlike the situation with depressive disorders,<sup>1</sup> PTSD was more likely to occur after the onset of other anxiety disorders, suggesting that symptoms of arousal and avoidance, which are common to both PTSD and many other anxiety disorders, may develop subsequent to the trauma experience as a coping mechanism. Using data from the NCS, Bromet and colleagues<sup>29</sup> determined that, after controlling for trauma type, the odds ratio for developing PTSD in individuals with a preexisting anxiety disorder was high (2.4 for men, 1.3 for women).

### **Treatment of Comorbid PTSD and Other Anxiety Disorders**

As is the case with the treatment of comorbid depressive disorders and PTSD, in spite of the fact that the comorbidity is prevalent and has a negative impact on the course of illness, there is a lack of systematic study concerning the best treatment approach for individuals with comorbid PTSD and any other anxiety disorder. As we develop a greater number of specific psychotherapies for different anxiety disorders, studies exploring combined psychotherapies to specifically target comorbid populations will be extremely important. As is the case with depressive disorders, many of the pharmacologic agents known to be efficacious in the treatment of PTSD are also efficacious in the treatment of anxiety disorders. Specific investigation of pharmacotherapeutic interventions in comorbid populations will be critical in optimizing patient outcomes.

## PTSD AND SUBSTANCE USE DISORDERS

### Prevalence

A number of studies have documented the common co-occurrence of PTSD, victimization, and substance use disorders. In the National Vietnam Veterans Readjustment Study,<sup>3</sup> male veterans with PTSD were twice as likely and female veterans with PTSD were 5 times as likely as those without PTSD to have a substance use disorder. In the NCS, the odds ratio for a substance use disorder in individuals with PTSD varied from 2.0 to 4.5. Using data from another epidemiologic survey, Cottler and colleagues<sup>30</sup> found that cocaine/opiate users were the diagnostic group at highest risk for comorbid PTSD and that the overall rate of PTSD in these individuals was 10 times higher than comparison subjects. Data from treatment-seeking samples indicate similarly high rates of comorbidity. In general, a number of studies estimate that 30% to 60% of individuals in treatment for substance use disorders have lifetime PTSD.<sup>31,32</sup>

### Causal Pathways

As previously mentioned, the relationship between PTSD and substance use disorders has been the focus of much speculation and some investigation. Three major causal pathways have been hypothesized. The self-medication hypothesis is discussed above. Another hypothetical explanation of the relationship between these disorders is that substance users, because of their high-risk lifestyles, place themselves at risk for exposure to trauma and for that reason are more likely to develop PTSD. Another potential explanation for the high comorbidity is that individuals with substance use disorders are more likely to develop PTSD after exposure to trauma. This increased susceptibility could stem from poor coping strategies and/or changes in brain neurochemistry that might enhance susceptibility and worsen the course of PTSD.

Chilcoat and Breslau<sup>33</sup> examined the development of PTSD and substance use disorders in a prospective study of young adults in Michigan. After an initial assessment of psychiatric disorder using the Diagnostic Interview Schedule, follow-up assessments were conducted at 3 and 5 years. The investigators found that PTSD signaled an increased risk for the development of a substance use disorder (hazards ratio = 4.5), but there was no evidence that preexisting substance use increased the risk of subsequent exposure to a traumatic event or the risk of developing PTSD after exposure to a traumatic event. While this study supports the self-medication pathway to comorbid PTSD and substance use rather than substance use as a risk for the development of PTSD, the possibility of shared vulnerability remains. McFarlane<sup>34</sup> recently examined data from a number of epidemiologic studies of PTSD and substance use disorders using the Bradford Hill criteria for assessing causal associations. McFarlane<sup>34</sup> concluded that

the data supported the causal nature of the relationship between these disorders.

In conclusion, the relationship between PTSD and substance use disorders is complex, but it is likely that in many cases, the substance use disorder may develop as an attempt to self-medicate painful symptoms of PTSD. In any individual case, the relationship between these disorders, both in order of onset and symptom exacerbation and presentation, should be explored to provide individually tailored treatment.

### Course of Illness

As is the case with major depression, there is evidence that substance use disorders have a negative impact on the course and outcome of treatment for individuals with PTSD. Brown and colleagues<sup>35</sup> compared substance-dependent women with and without PTSD in substance abuse treatment outcomes and found that comorbid individuals relapsed more quickly and that PTSD was a significant predictor of relapse. In another study,<sup>36</sup> individuals with comorbid PTSD and substance dependence were found to benefit less from substance abuse treatment than those with a substance use disorder only. Finally, Brown and Stout<sup>37</sup> compared a group of individuals with alcohol dependence and symptomatic PTSD with an alcohol-dependent group who had PTSD in remission. They found that the symptomatic group had significantly more drinks per drinking day and a higher percentage of days of heavy drinking during a 6-month follow-up period.

### Treatment

Most individuals working with patients with both PTSD and substance dependence agree that for optimal treatment outcomes, the PTSD and substance use disorder must be treated concurrently. Unfortunately, the best approach to this concurrent treatment has not been clarified, but there have been recent promising although preliminary developments. The effectiveness of cognitive-behavioral therapy, including exposure treatment, specifically designed to target both PTSD and substance use has shown promise in decreasing both substance use and PTSD symptoms in a preliminary, noncontrolled investigation.<sup>38</sup> Najavits et al.<sup>39</sup> also reported that a specially designed 24-session cognitive-behavioral therapy showed preliminary efficacy in decreasing substance use but not PTSD symptoms in a group of 17 women with PTSD and cocaine dependence. Abueg and Fairbank<sup>40</sup> found that 42 individuals with comorbid PTSD and substance dependence who received relapse prevention training in addition to PTSD treatment had less alcohol use at a 6-month follow-up assessment when compared with a group who received PTSD treatment only.

Finally, the use of pharmacotherapy in comorbid individuals needs further investigation. Because of the possibility of toxic interaction and overdose, the use of any pharmacotherapeutic agent is somewhat more risky in the

substance-using population. This has led to a reluctance to use medication to treat individuals with substance use disorders. Fortunately, with the advent of the serotonin reuptake inhibitors and other new antidepressant agents that have a better safety profile, there has been more investigation of pharmacotherapeutic treatments of comorbid conditions in substance users. In a preliminary, noncontrolled study, Brady and colleagues<sup>41</sup> found significant decreases in PTSD, depression, and substance use during a 12-week period of treatment with sertraline in patients with comorbid substance dependence and PTSD. This promising finding is now being explored in a double-blind, placebo-controlled trial.

## COMORBID PSYCHOTIC DISORDERS

### Prevalence and Presentation

The comorbidity of PTSD and psychotic disorders is a relatively unexplored area, but probably occurs more commonly than expected. During acute hospitalization for psychotic individuals, treatment interventions focus on the stabilization of psychoses and improvement of cognitive disorganization, often leaving PTSD symptoms unrecognized and untreated. In a study of 275 patients with severe chronic mental illness, Mueser and colleagues<sup>42</sup> found that 43% met current criteria for PTSD, yet only 2% of these cases were diagnosed in the clinical chart. Nearly all (98%) of the patients in this sample reported exposure to at least one type of trauma. The number of traumatic experiences and childhood sexual assaults were strongly related to PTSD in both men and women. Other types of trauma were related to a lesser extent to the occurrence of PTSD in this sample. Chronically mentally ill patients are likely to be a particularly vulnerable population at high risk for trauma and subsequent PTSD due to their poor cognitive status, unstable living conditions (e.g., state hospitals, shelters, jails), and poor interpersonal skills.

Sautter et al.<sup>43</sup> found that patients with both PTSD and psychotic disorders had more psychotic symptoms, paranoia, violence potential, and general psychopathology when compared with patients with either psychotic disorders or PTSD occurring alone. Shaw and colleagues<sup>44</sup> found a 52% prevalence of postpsychosis PTSD in a sample of inpatients who were recovering from chronic psychotic disorders. The most distressing psychotic symptoms that were perceived as traumatizing and distinguished those with PTSD were persecutory delusions, ideas of being controlled, thought insertion, thought withdrawal, and visual hallucinations. Impact of event severity, avoidance, and intrusion psychotic symptoms were significantly more prevalent in the PTSD versus the non-PTSD group.

### Psychotic Symptoms in Individuals With PTSD

Several investigators have studied the presence of psychotic symptoms in individuals with PTSD. David et al.<sup>45</sup>

found 40% of veterans consecutively admitted to a PTSD inpatient rehabilitation unit reported psychotic symptoms. These psychotic symptoms included auditory hallucinations, visual hallucinations, and delusions. The hallucinations were nonbizarre and consisted of trauma-related themes. These veterans had no formal thought disorders. Eighty-one percent of the chronic PTSD veterans met criteria for current major depression, suggesting the psychotic symptoms were associated with major depression. There was no difference in measures of dissociation or alcohol and drug use between the psychotic and nonpsychotic PTSD groups.

Hamner and colleagues<sup>46</sup> found a strong positive relationship between the severity of PTSD symptoms and the presence of psychotic symptoms in a group of patients with PTSD. Comorbid major depression was also associated with more severe PTSD, and avoidance symptoms were more predominant in those individuals who had psychotic symptoms compared with those without psychotic symptoms. The authors suggest that PTSD with psychotic features may be a subtype of PTSD, a distinction that may have treatment implications. To further validate this subtype hypothesis, Hamner and Gold<sup>47</sup> found a significant elevation of dopamine  $\beta$ -hydroxylase (DBH) in psychotic versus nonpsychotic PTSD patients and normal controls, suggesting a biological marker for PTSD with psychoses. Plasma DBH is an enzyme responsible for the conversion of dopamine to norepinephrine and is also elevated in bipolar affective disorder with psychoses, but is reduced in psychotic depression. Altered DBH may serve as a marker to detect vulnerability to develop psychotic features in the context of trauma. The investigators suggest that the psychosis in PTSD may be associated with noradrenergic rather than dopaminergic activation.

### Treatment

There has been little investigation of the treatment of comorbid psychosis and PTSD. For those individuals who are not chronically mentally ill, but experience psychosis as a part of PTSD symptomatology, the use of antipsychotic agents has been successful in noncontrolled trials, but has not been explored systematically. There have been no trials investigating the treatment of PTSD in the chronically mentally ill. Specifically, questions concerning the ability of these patients to tolerate exposure therapy and to benefit from cognitive-behavioral therapy are obvious. Pharmacotherapeutic strategies for this population also remain unexplored.

## EATING DISORDERS

The relationship between PTSD and eating disorders has only recently become a focus of attention. Initial studies centered on the role of childhood sexual abuse in the etiology of eating disorders, and in a recent critical review

of available studies, Wunderlich<sup>48</sup> concluded that childhood sexual abuse was indeed a nonspecific risk factor for the development of bulimia nervosa but not anorexia nervosa. In addition, childhood sexual abuse predicted significantly greater comorbidity of other psychiatric disorders with bulimia nervosa, including major depression, anxiety disorders, substance abuse or dependence, and personality disorders.

In the only study to examine eating disorders and PTSD in a nonclinical, representative sample of United States adult women (the National Women's Study), Dansky and colleagues<sup>49</sup> reported higher lifetime (37%) and current (21%) PTSD prevalence rates in respondents with bulimia nervosa compared with the nonbulimic respondents (12% and 4%, respectively). Respondents with bulimia nervosa also had higher current but not lifetime PTSD rates compared with binge-eating disorder respondents. Respondents who met DSM-IV criteria for binge-eating disorder had higher lifetime but not current PTSD prevalence rates compared with controls.

In a clinical sample of 294 women with eating disorders (including bulimia nervosa, anorexia nervosa, and eating disorder not otherwise specified),<sup>50</sup> 52% reported symptoms consistent with PTSD. Although PTSD symptoms were not correlated with eating disorder symptoms, there was a significant association with measures of depression, anxiety, and dissociation.<sup>50</sup> In a study of 74 adolescent inpatients, boys with PTSD had higher rates of eating disorders than psychiatric controls without PTSD.<sup>51</sup>

Rorty and Yager<sup>52</sup> have described in detail how eating disorder pathology can represent a desperate attempt for a traumatized patient to regulate overwhelming affective states and construct a coherent sense of self and meaning within a sociocultural context preoccupied with thinness and beauty. This is not unlike the relationship between substance abuse and PTSD described earlier, except that bingeing and purging may be used instead of alcohol or illicit substances in an attempt to control PTSD symptomatology. In the National Women's Study, traumatic events preceded the first binge in 84% of cases,<sup>53</sup> thereby supporting this hypothesis.

As is the case with many of the other comorbidities discussed so far, there have been no controlled studies specifically addressing the treatment of individuals with PTSD and eating disorders. The selective serotonin reuptake inhibitors have been shown to be useful in the treatment of bulimia nervosa and in the treatment of PTSD, so these would be an obvious choice for individuals with comorbidity, but systematic exploration of this has not been carried out. Exploration of psychotherapies specifically tailored to address both conditions would also be of interest.

## SOMATOFORM DISORDERS

Relationships between trauma, PTSD, and somatoform disorders have also been reported in the literature. Investi-

gators first observed links between somatization and trauma starting with Freud,<sup>54</sup> who hypothesized that the conversion symptoms of hysteria, now classified as somatoform conversion disorder, were linked to earlier forms of trauma. Subsequent reports have confirmed that patients with somatoform disorders have higher prevalence rates of childhood abuse and other trauma. However, the notion of a direct link to PTSD was not investigated until recently.

Andreski et al.<sup>55</sup> reported that patients with DSM-III-R-defined PTSD are more likely to report symptoms of somatization than patients with other psychiatric disorders. Especially notable were increases over 2-fold in both pain and conversion symptoms. These results are similar to previous reports of somatization symptoms in PTSD patients.<sup>55</sup> For example, in a study by Beckham et al.,<sup>56</sup> 80% of combat veterans with PTSD reported chronic pain. Reports of the actual prevalence of somatoform disorders in PTSD patients are lacking; however, in one study by Lipschitz<sup>51</sup> of 74 adolescent inpatients, boys with PTSD had higher rates of somatization disorder than psychiatric controls.

Interestingly, recent studies on the health status of traumatized individuals with PTSD indicate higher rates of a variety of bona fide health problems as well as altered immune function.<sup>57-60</sup> Therefore, it is important to make the diagnosis of somatoform disorder only after a thorough medical evaluation.

In one study of 654 subjects with anxiety disorders, 5.5% of subjects had a past or current history of somatoform disorder.<sup>61</sup> Of those with somatoform disorder, 22% had PTSD versus 8% who did not have PTSD, a statistically significant difference ( $p < .01$ ). In a study of 45 patients with pseudoseizures (98% of whom had a DSM-III-R-defined somatoform disorder), 49% were found to meet DSM-III-R criteria for PTSD.<sup>62</sup> In patients with chronic pelvic pain and negative laparoscopy results, most of whom have somatoform pain disorder,<sup>58</sup> rates of PTSD have been found to be higher than in pain-free infertile controls.<sup>63</sup>

## DISSOCIATIVE DISORDERS

Like depression, anxiety, and somatization, dissociation can be either a symptom or a disorder unto itself. Dissociative symptoms have most commonly been reported to be associated with PTSD, particularly in more severe cases involving childhood,<sup>64-68</sup> but they can also clearly manifest without any overt PTSD symptoms in a variety of ways involving altered memory and/or identity. Aside from PTSD, dissociative disorders are the psychiatric disorders most closely linked to severely traumatic experiences, particularly when occurring during childhood.<sup>69</sup> Most experts see dissociation on a continuum, with dissociative symptoms being associated with greater and earlier trauma and PTSD severity.

Although the diagnosis of dissociative identity disorder (DID) has been controversial, several large case series confirm its existence in individuals with extremely high rates of severe childhood abuse or exposure to trauma (approximately 97%).<sup>70</sup> Controlled studies of PTSD prevalence rates in DID patients are lacking, but clinical reports indicate overt PTSD symptomatology at various points during the course of illness.<sup>6,65</sup> However, Bremner and Marmar<sup>69</sup> recently reported that 86% of 35 PTSD patients met criteria for one or more dissociative disorders using the Structured Clinical Interview for DSM-IV, Dissociative Disorders version.

There is a wealth of data linking trauma and PTSD with psychogenic or dissociative amnesia.<sup>71,72</sup> In the National Women's Study, Brewerton et al.<sup>53</sup> reported psychogenic amnesia in 41% of a representative, nonclinical sample of women with PTSD in comparison with 7% of women without PTSD. PTSD in women with psychogenic amnesia was associated with significantly higher rates of rape, childhood rape, molestation, aggravated assault, major depression, and eating disorder pathology than in those without psychogenic amnesia.

Peritraumatic dissociation, the presence of dissociative symptoms at the time of the traumatic event(s), has been reported to be a robust prognostic predictor of subsequent PTSD development and severity.<sup>73-76</sup> A subsample of PTSD patients with peritraumatic dissociation appears to have diminished rather than enhanced physiologic reactivity,<sup>77</sup> a finding that may eventually be shown to have important treatment implications.

## CONCLUSIONS

Evidence from a number of studies suggests that PTSD commonly co-occurs with other psychiatric disorders. The relationship between PTSD and these comorbid conditions is complex. For some psychiatric disorders, it appears that PTSD may have a causal role in the development of the comorbid condition. The existence of other psychiatric disorders appears to increase vulnerability to the development of PTSD after trauma exposure. The symptom overlap between PTSD and affective and anxiety disorders is pronounced and can make differential diagnosis difficult. In this regard, the biggest problem is likely to be an underdiagnosis of PTSD because of inadequate assessment of trauma history. Much work needs to be done in further exploration of the relationship of PTSD to its many comorbid conditions and in improvement of diagnostic techniques.

Finally, the treatment of PTSD complicated by other psychiatric disorders and symptoms is an area ripe for investigation. The development of a number of efficacious pharmacotherapeutic and psychotherapeutic strategies for the treatment of PTSD and for the treatment of other psychiatric disorders in the past 10 years is extremely encour-

aging. Blending these therapies in the treatment of comorbid conditions will be the next step. In the case of PTSD, comorbid conditions may provide a rationale for the subtyping of individuals with the disorder to optimize treatment outcomes.

*Drug names:* paroxetine (Paxil), sertraline (Zoloft).

*Disclosure of off-label usage:* The authors have determined that, to the best of their knowledge, no investigational information about pharmaceutical agents has been presented in this article that is outside U.S. Food and Drug Administration-approved labeling.

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