Comorbid Psychiatric Disorders in PTSD

Implications for Research

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Problems associated with high rates of comorbidity in posttraumatic stress disorder (PTSD) were initially identified by Fairbank *et al.*[1] who conducted an empirical study of the psychological characteristics of Vietnam veterans with PTSD, comparing them to veterans with other psychiatric disorders and veterans who were well adjusted. High rates of depression and anxiety were found to be associated with a clinician's diagnosis of PTSD. The authors recognized the importance of elevations in concurrent psychiatric conditions for both research and treatment in the area of PTSD and suggested that future research should specify the precise nature of comorbidity among individuals with PTSD.

In a subsequent study, Keane *et al.*[2] identified high rates of substance abuse among individuals with PTSD. Veterans with PTSD reported problems with alcohol and drug abuse and also high rates of intake of nicotine and caffeine. These projects were among the first to collect objective data using diagnostic interviews on the problem of comorbidity in PTSD.

This paper organizes the extant information on the high rates of comorbidity observed in PTSD. We evaluate the extent to which the high rates of comorbidity are a function solely of concurrent problems in military veterans or if they are a more pervasive finding, and we suggest methodological strategies that may improve and enhance the quality of biological and psychological research conducted in this area.

LITERATURE REVIEW ON COMORBIDITY

Clinical Studies

In addition to the studies conducted in our laboratory, other groups were noticing the same trend of high rates of comorbidity in veterans with PTSD. Sierles *et al.*[3] examined a group of 25 inpatients with PTSD at the North Chicago VA Medical Center and learned that 84% of these patients met criteria for another disorder. Using the schedule for affective disorders and schizophrenia (SADS) they found that patients with PTSD frequently met criteria for alcoholism (64%) and antisocial personality

disorder (48%). In addition, 72% of the patients reported a history of depression, although they did not meet criteria for formal diagnosis at the time of the study. Unfortunately, no comparison group was included in this study and so it was impossible to determine if the rates of comorbidity observed among veterans were greater for PTSD than for any other psychological disorder. Nonetheless, this was the first study to employ a comprehensive structured diagnostic interview for measuring both PTSD and the collateral disorders.

In a follow-up study, Sierles *et al.*[4] employed the same method with a sample of 25 PTSD outpatients. Their findings, also utilizing the SADS, indicated that 76% of these patients met criteria for alcoholism, 64% for an antisocial personality disorder, and 84% for at least one other disorder in addition to PTSD. Major affective disorder was found in 84% of the patients either at the current time or throughout lifetime. Again, the absence of a specific comparison group of patients with disorders other than PTSD limited the conclusions drawn in this study; however, clearly these investigations solidified the evidentiary base upon which future studies examining comorbidity were conducted.

Using the NIMH-Diagnostic Interview Schedule (DIS; Robins *et al.*[5]), Escobar and his colleagues[6] examined Hispanic veterans receiving care at the Los Angeles VA Outpatient Clinic. Studying 20 patients, all of whom were clinically diagnosed with PTSD, they found that PTSD patients had an average of 3.5 DSM-III lifetime diagnoses. The leading comorbid diagnosis was alcohol dependence (65%), followed by social phobia (50%), drug dependence (40%), major depression (35%), and schizophrenia (35%). While this study found high rates of comorbidity in patients with PTSD, the use of the DIS in clinical settings may present problems of reliability and validity. This is particularly problematic for diagnoses such as PTSD and schizophrenia where many symptoms appear to be overlapping and further intensive follow-up questioning is not possible. Yet these data are consistent with findings from other studies that used different diagnostic instruments. The high rates of comorbid schizophrenia are a likely result of the use of the DIS.

In a study designed to examine the interrelationship of substance abuse and PTSD, Keane *et al.*[7] interviewed 25 Vietnam veterans seeking treatment at the Boston VA Medical Center using a multimethod procedure that included clinician interviews, psychological tests, and psychophysiological assessment (cf, Keane *et al.*[8]; Malloy *et al.*[9]). Doctoral level clinicians using the Structured Clinical Interview for the DSM-III-R (SCID; Spitzer and Williams[10]) observed that 44% of PTSD patients met current diagnostic criteria for either drug abuse or drug dependence. In addition, 64% met criteria for alcohol abuse or dependence, and a total of 80% of the sample met diagnostic criteria for some form of substance abuse or dependence at the time that they sought treatment. Unfortunately, the focus of this study was on substance abuse and did not, therefore, include a more comprehensive range of psychiatric diagnoses.

Keane and Wolfe[11] selected randomly 50 outpatients seeking psychological treatment for PTSD. In this study, SCIDs were administered to all subjects so that a more complete view of comorbidity rates among help-seeking veterans with PTSD could be determined. This study found high rates of alcoholism (84%), drug abuse (42%), depression (68%), dysthymia (34%), and personality disorders, typically antisocial personality disorder (26%). The mean number of diagnoses in this sample was 3.8 including the PTSD diagnosis. The findings regarding the presence of personality

disorders were replicated and extended by Southwick *et al.*[12] who found extensive evidence for borderline personality disorder in their patients. While these studies replicated the findings of Sierles and his colleagues[3,4] who found high rates of comorbidity among samples of veterans with PTSD, they still did not provide any comparative information on comorbidity across diagnoses other than PTSD. The strengths of these studies clearly were in the use of structured diagnostic clinician-administered interviews for determining both the PTSD diagnosis and the rates of comorbidity.

Evidence for high rates of comorbidity also comes from Keane *et al.*[13] who examined 1,328 outpatient Vietnam theater help-seeking veterans using the SCID. This project also confirmed the high rates of comorbidity in PTSD and, importantly, these rates were found across 15 different medical centers in the United States employing nearly 30 different doctoral level diagnosticians. In this study, rates of major depressive disorder were high (36%) as were those of alcoholism (24%), drug abuse (12%), borderline personality disorder (18%), and antisocial personality disorder (ASPD) (11%).

It is clear from these preliminary studies that at least among patients who are seeking treatment for PTSD, the overwhelming majority of them present with a wide range of symptoms other than those directly associated with PTSD criteria. In fact, these individuals, who are primarily Vietnam veterans with PTSD, meet criteria for an additional three DSM diagnostic categories. The data, however, are limited by the fact that they have included only male, combat-related PTSD patients who are seeking help. Naturally, these characteristics might potentially yield biased conclusions that differ in important ways from PTSD secondary to other traumatic events and PTSD in women. Even more fundamentally, veterans with combat-related PTSD, but who are not help seeking at VA medical centers, may also present a different diagnostic picture from that of veterans seeking treatment.

Field Survey Studies

Data from population-based surveys might provide important new information to assist us in determining the true rates of comorbidity among individuals with PTSD. Given that all the preceding studies involved subjects obtaining treatment, field surveys may provide important new and different information regarding comorbidity. Perhaps those subjects who are seeking help differ fundamentally from those with the disorder, but who are not seeking help.

The Vietnam Experience Study[14] evaluated the psychological characteristics of 2,490 Vietnam Army veterans and 1,972 Vietnam era veterans using the DIS. Among Vietnam veterans, 15% had a lifetime diagnosis of PTSD and 2.2% had the disorder within 1 month of the interview. Among those who met criteria for PTSD during the last month, 66% also met criteria for another anxiety or depressive disorder and 39% fulfilled criteria for alcohol abuse or dependence. Thus, in a community-based sample of veterans, PTSD is frequently associated with anxiety, depression, and substance abuse. Although this particular study relied on the DIS for diagnosing PTSD, its findings still supported the concept of high rates of comorbidity among non-help-seeking Vietnam veterans with PTSD.

In possibly the most comprehensive and thorough psychiatric epidemiological study conducted to date of Vietnam veterans' psychological adjustment, Kulka *et*

al.[15] evaluated 3,016 Vietnam veterans, Vietnam era veterans, and civilian controls. Veterans were randomly selected from military records with women, blacks, Hispanics, and physically disabled veterans oversampled intentionally. High rates of comorbidity were observed among those veterans with PTSD. Substance abuse (73%) was easily the most prevalent accompanying disorder, with antisocial personality disorder (31%) and major depression (28%) also co-occurring with some frequency. Most impressive was the finding that 98.9% of all those diagnosed with PTSD met criteria for at least one other diagnosis. These findings from a field study confirm the high rates of comorbidity of PTSD with other conditions in combat-related PTSD.

Clearly, PTSD in Vietnam theater veterans is associated with meeting criteria for other disorders whether the samples were drawn from the clinic or the community or when comprehensive diagnostic interviews were used to evaluate veterans. Studies of clinical patients and community subjects also found a consistent association of PTSD with alcohol and drug abuse, major depressive disorder, dysthymia, and ASPD. Information regarding comorbidity rates needs to be obtained from other samples of traumatized patients and, in particular, from women with PTSD.

Studies of Female Subjects

In a study of 277 female victims of a recent sexual or nonsexual assault, Cashman *et al.*[18] presented information on the high rates of comorbidity among those subjects who developed acute PTSD as well as those subjects who developed a chronic form of the condition. With respect to Axis I disorders, both the acute and chronic cases of PTSD developed high rates of major depressive disorder (approximately 60% of the cases). In addition, substance abuse was present in approximately 25% of the cases and was represented equally in both the acute and chronic forms of PTSD. In terms of Axis 2 personality disorders, Cashman *et al.*[16] found high rates of paranoid personality disorder nearing 30% in both the acute and chronic forms of PTSD. Rates of borderline personality disorder and avoidant personality disorder were nearly 15% in the chronic cases of PTSD, findings that distinguished the acute and chronic forms of the condition.

Similarly, Resick *et al.*[17] presented comorbidity rates in women who developed rape-related PTSD. Among this outpatient help-seeking sample, 58% met diagnostic criteria for major depressive disorder, 39% for a substance abuse disorder, 12% for panic disorder, 12% for simple phobia, and 12% for social phobia. Data from these two research laboratories studying female victims of violent crimes indicate that rates of comorbidity, while not of the same magnitude as those found in veterans, are nonetheless quite high. In addition, the disorders typically associated with combat veterans also appear at high rates in assault victims with PTSD (i.e., depression, substance abuse, anxiety disorders). In the Resick *et al.*[17] study, 76% of female sexual assault victims with PTSD carried a current comorbid psychiatric condition, whereas only 24% of those who had been sexually assaulted but who did not develop PTSD carried a current comorbid condition.

Studies of PTSD and Trauma in Substance Abusers

Further information on the interrelationship of substance abuse and PTSD in women comes from studies of prevalence rates of PTSD among substance abusers

seeking treatment. Brown *et al.*[18] examined the prevalence of PTSD among a sample of treatment-seeking, substance-abusing males and females. Approximately one quarter of the sample presented with significant PTSD symptoms. Women had histories of physical and sexual abuse and they also reported experiencing more traumatic life events. These trauma-exposed women, compared to the men, were more likely to have been diagnosed with possible PTSD. In addition, the PTSD group reported more hospitalizations and greater utilization of services than did the non-PTSD cohort.

Similarly, Fullilove *et al.*[19] examined the association of violent events, trauma, and PTSD among female drug users. Of 105 women in the sample, 104 subjects reported one traumatic event or more and 59% of these reported symptoms consistent with the diagnosis of PTSD. Violent assault including sexual and physical assault was the most common precipitant to the development of PTSD. The more traumatic events to which a woman was exposed, the more likely she was to develop PTSD in this substance-abusing population.

National Comorbidity Study

In the National Comorbidity Study, Kessler *et al.*[20] found that, among males, rates of comorbidity with PTSD were approximately 88%, with alcoholism (52%) depression (48%), conduct disorder (43%), drug abuse (35%), and simple phobias (31%) representing the bulk of the concurrent disorders observed. In this premier study, 59% of the PTSD subjects had more than three diagnoses. In contrast, for female subjects Kessler *et al.*[20] found that 79% had an accompanying disorder of one type or another including depression (49%), alcoholism (30%), drug abuse (27%), phobia (29%), and conduct disorder (15%). Among women, 44% had more than three diagnoses associated with PTSD. Interestingly, the Kessler *et al.*[20] epidemiological data suggest that at least among women the occurrence of trauma was more likely to precede the development of substance abuse. This particular finding is supportive of a self-medication model for the comorbidity of substance abuse (alcohol and drug abuse) and PTSD. Yet other studies have not found this particular temporal relationship.

Davidson *et al.*[21] and Bremner *et al.*[22] suggest that PTSD and substance abuse in their samples of combat veterans are initiated concurrently. In addition, it appears from the Bremner *et al.*[22] study that PTSD symptoms and substance abuse track each other in a parallel course (i.e., waxing and waning) over the measurement time period employed in the study.

Interestingly, in a reanalysis of the Epidemiologic Catchment Area study data from St. Louis, Cottler *et al.*[23] found that drug and alcohol abuse preceded the development of PTSD symptoms and presumably the traumatic events; however, the findings of this study are not conclusive because of the way in which data on temporal parameters were collected. This particular study, however, does support the notion that alcohol and drug use can be risk factors for exposure to traumatic events as well as for the development of PTSD, clearly a logical and viable hypothesis.

Summary of Literature Findings

From the foregoing review of the literature on comorbidity in PTSD it seems eminently reasonable to conclude that high rates of comorbidity have been found

with respect to PTSD across populations (i.e., males, females, veterans, sexual assault victims, criminal assault victims, and the general population), stressors (i.e., military combat, rape, physical assault, childhood sexual abuse, and violence), patient and nonpatient status (help-seeking patients vs community-residing subjects), diagnostic measures (i.e., SCID, DIS, and self-report measures), and the level of interviewer training (lay interviewers vs doctoral level clinicians). These high rates of comorbidity appear to be most salient in the following disorders: (a) alcohol abuse, (b) drug abuse, (c) depression, (d) anxiety disorders (e.g., phobias and panic disorders), and (e) personality disorders, especially antisocial and borderline.

To explain these levels of comorbidity, clinicians and researchers have relied on various hypotheses including the self-medication hypothesis wherein individuals who develop PTSD on exposure to traumatic events ultimately begin to use substances to alleviate their emotional pain (e.g., Conger[24]). This self-medication or negative reinforcement model of comorbidity clearly explains some of the variance in predicting the rates of substance abuse in PTSD. Given that PTSD is characterized by elevations in arousal, reactivity, and sleep problems, it is not surprising that for a subsection of the PTSD population alcohol and drug use may provide immediate short-term relief from their symptoms.

Others have hypothesized different reasons for the great amount of comorbidity observed in PTSD. Keane and Wolfe[11] pointed out that there is considerable symptom overlap between PTSD and major depression and that symptoms such as arousal, reactivity, and avoidance are often associated with several other key disorders frequently observed in PTSD patients. This high degree of symptom overlap may in fact be responsible for some of the comorbidity observed. Further, Saladin *et al.*[25] found that symptoms of withdrawal from alcohol and drugs can mimic symptoms of PTSD which may contribute to the overwhelming evidence of comorbidity between these two problems. Furthermore, some researchers have proposed that the belief that alcohol and drugs will alleviate stress or tension (i.e., expectancies) is actually the operative variable in the high levels of alcohol and drug use in PTSD patients (e.g., Brown[26]). Thus, the question raised is whether the high levels of comorbidity observed in epidemiological and clinical studies may simply be an epiphenomenon of the diagnostic criteria employed for all these disorders.

A second possible explanation for high levels of comorbidity was offered by Hyer *et al.*[27] who found consistently that individuals with PTSD tend to report higher levels of symptoms than do individuals with other disorders. Is this high level of comorbidity between PTSD and other diagnostic categories simply a function of symptom overreporting? Or is it a function of global levels of distress that are apparent in PTSD? The extent to which these factors are responsible for or contribute to the levels of comorbidity in PTSD has not been addressed to date. It is clearly worthy of empirical testing.

Others have promoted the idea that the high levels of comorbidity in PTSD patients are actually a risk factor for the development of PTSD and that these disorders were present prior to trauma exposure. Indeed, the Kessler *et al.*[20] study provided some evidence that the substance abuse diagnoses appear to follow in a systematic way exposure to trauma and the development of PTSD. However, it is also clear from many studies in the literature that individuals who have a history of psychological or behavioral problems are at elevated risk for the development of PTSD (e.g., Kulka

et al.[15]). Undoubtedly, a subsection of individuals carry either genetic, social, or familial vulnerabilities that are risk factors for the development of major psychiatric disorders following exposure to high magnitude stressors. It is also, indeed, likely that many individuals who develop PTSD on exposure to one or more traumatic events are inclined to have used alcohol simply because of its availability, the expectancies associated with alcohol and drug use, and the immediate short-term relief often experienced upon intoxication.

Other studies have challenged the relationship of PTSD and substance abuse by relying on measures of early childhood conduct problems and adolescent drug abuse to predict the development of long-term drug and alcohol problems. Reifman and Windle,[28] reexamining the Vietnam Experience Study, found that drug use in the Army was the single best predictor of current levels of drug use. Similarly, Boscarino[29] failed to find any relation between combat exposure and drug use. Premorbid variables such as conduct disorder and juvenile delinquency emerged as the strongest predictors of current alcohol and drug use. Clearly more research is needed to untangle these close interrelationships, but it should be clear to clinicians and researchers alike that there is a subpopulation of individuals with PTSD who have major psychological problems or predispositions prior to exposure to traumatic events which make it likely that they will subsequently develop PTSD. It should also be clear that for at least some individuals with one or multiple traumatic events and with serious psychological sequelae attendant to these events, these factors can unleash a cascade of psychological and social problems that continue to complicate their lives over time.

RESEARCH IMPLICATIONS OF HIGH LEVELS OF COMORBIDITY

With the relative explosion of research in the area of PTSD, several caveats must be highlighted to alert researchers to possible problems in the interpretation of findings. One primary concern that is particularly relevant for biological and psychosocial research is that PTSD may in fact be a marker variable for other ongoing factors that are more directly responsible for findings on various objective indices. For example, several research studies have found that PTSD is associated with elevations in risk factors for a variety of health-related behavioral problems. Litz *et al.*[30] found differences between PTSD and non-PTSD subjects on a wide range of health risk behaviors. These differences included items such as (a) nutritional differences, (b) differences in exercise regimens practiced, (c) elevated smoking rates, (d) elevated caffeine intake, (e) distinctions in available housing and homelessness, and, of course, (f) high rates of alcohol and drug use.

Each of these factors individually or collectively may directly influence findings in biological and psychological research. Efforts to rule out the contributions of each of these variables may help us to understand what is uniquely a function of PTSD and what is a function of disorganized life styles and addictive practices. Future research should consider measuring as many of these variables as possible in order to covary the relationships of these confounding factors from the objective measures of interest (e.g., Keane *et al.*[13]).

There are additional research implications of finding high rates of comorbidity among PTSD patients. Clearly, the PTSD population is relatively heterogeneous.

Patients with four diagnoses differ from patients with solely the PTSD diagnosis probably on multiple variables of importance and interest in research. Clearly these differences could be the result of greater symptom severity or else the presence of preexisting risk factors for developing the disorder once an individual is exposed to a traumatic event. In either case, PTSD appears to be a heterogeneous disorder with multiple subpopulations. Examining these subtypes of patients in biological or psychological studies without identifying them in data analyses may lead to erroneous conclusions. Rejecting the null hypothesis when it should not be rejected (a Type I error) is one possibility, but probably more likely is accepting the null hypothesis when in fact differences do exist but they are clouded by population heterogeneity. It seems reasonable to conclude that the biology of PTSD may vary if one has a single psychological disorder rather than multiple psychological conditions. It also seems likely that the biology of PTSD might vary if one is traumatized when these already are existing psychological conditions (e.g., major depressive disorder). Identifying, labeling, and analyzing for these differences may promote a more coherent understanding of the biological and psychological factors associated with PTSD.

The findings of high rates of comorbidity in PTSD lead us to make several discrete recommendations for research on biological and psychological factors and the evaluations of treatment interventions. First, and perhaps foremost, is the need for the use of critical or key comparison groups. Employing groups of subjects that carry only the PTSD diagnosis and comparing them to groups of subjects with PTSD and a major depressive disorder, for instance, may help us to disentangle any confounding effects of the presence of major depression, a commonly associated condition. Similarly, comparing subjects with comorbid substance abuse and PTSD to a PTSD only group will help us to understand the contribution of substance abuse to any findings observed. This type of design may complement the more typical studies that look at PTSD groups versus trauma exposure without PTSD versus individuals with other psychological traumas versus groups with no trauma exposure at all. Simply comparing PTSD to normal controls will not help us to disentangle the effects of the high rates of comorbidity and may further contribute to false leads in our understanding of PTSD.

An additional strategy to be employed in research is to ensure that levels of comorbidity are known and measured for both presence and absence of comorbid conditions, but perhaps even more importantly in terms of overall severity. This will provide key information for employing statistical methods such as covariance to control for the contributions of these concurrent conditions. To use statistical control has a long history in psychological research and is now being introduced more frequently in biological research in mental health. This trend needs to be supported and continued particularly as it applies to the study of PTSD.

A third recommendation is to employ psychometric methods in efforts to understand what is associated with PTSD and what is associated with other existing conditions. The use of methods developed for convergent and discriminant validity may help in this regard. Convergent validity recommends the use of multiple measures that should agree with one another when certain constructs are measured. Discriminant validity methods also use multiple measurement tools that should diverge when certain known conditions are met. The use of convergent and discriminant validity

will assist in understanding what factors are due to PTSD predominantly and what factors might be a function of the levels of comorbidity in a given group of patients.

One final strategy that may help us to understand the role of comorbidity is to insure the measurement of functioning for all subject groups contained within a particular study. Utilizing a measure such as the Global Assessment of Functioning from Axis 5 of the DSM-IV may provide one index upon which subjects differing in levels of comorbidity are compared. In this way various biological or psychological variables found to be different in a particular research study can, through statistical means, be attributed to factors other than differences in overall levels of functioning.

SUMMARY

It is clear from the existing data that PTSD often occurs in the context of other major psychological conditions. Evidence to support this comes from clinical studies, epidemiological studies, and studies of PTSD among substance abusers. Clearly, probably several different subgroups of PTSD patients exist including those who had psychological or behavioral problems before exposure to traumatic events (e.g., substance abuse), those who developed other problems concurrent with exposure to the traumatic events, and those who developed problems secondary to the development of PTSD, perhaps in efforts to cope with the intensely debilitating symptoms of PTSD.

With this knowledge, research on PTSD must begin to contend with the comorbidity issue in systematic ways. The use of comparison groups that are carefully selected is one key way in which conclusions about PTSD can be most conservatively drawn. The use of statistical procedures to control for difference in levels of comorbidity is another responsible way in which to approach the problem. Finally, efforts to employ global measures of functioning such as the Global Assessment of Functioning to equate subjects within a study on minimally this characteristic may be the most economical method for trying to rule out the role of comorbidity and severity of condition in conclusions drawn in research studies. All these solutions presuppose the careful measurement of comorbidity in studies of PTSD, a recommendation that requires serious consideration for researchers operating in this field.

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