
A Second Look at Comorbidity in Victims of Trauma: The Posttraumatic Stress Disorder–Major Depression Connection

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Background: *We examine whether traumatic events increase the risk for major depression independent of their effects on posttraumatic stress disorder (PTSD).*

Methods: *Data come from the Epidemiologic Study of Young Adults in southeast Michigan (N = 1007). Retrospective and prospective data were used to estimate the risk of major depression in persons with PTSD and persons exposed to trauma with no PTSD, compared with persons who did not experience a trauma. National Comorbidity Survey data were used to evaluate the influence of trauma type.*

Results: *In the retrospective lifetime data, hazard ratios were, for first-onset major depression in exposed persons with PTSD, 2.8 and, in exposed persons with no PTSD, 1.3 (not significant), as compared with persons who were not exposed. Corresponding estimates from the prospective data were 11.7 and 1.4 (not significant). The difference in the risk for depression associated with PTSD versus exposure without PTSD is unlikely to be due to differences in trauma type.*

Conclusions: *The findings of a markedly increased risk for major depression in persons with PTSD, but not in exposed persons without PTSD, do not support the hypothesis that PTSD and major depression in trauma victims are influenced by separate vulnerabilities.* Biol Psychiatry 2000;48:902–909 © 2000 Society of Biological Psychiatry

Key Words: Comorbidity, posttraumatic stress disorder, major depression, vulnerability, epidemiology, prospective study

Introduction

The definition of posttraumatic stress disorder (PTSD) in DSM-III and in subsequent DSM editions (American Psychiatric Association 1980, 1987, 1994) links a specific syndrome with a specific class of stressors, catastrophic or traumatic events that are distinguished from ordinary stressful life events, such as loss of job or marital discord. Although stressors, those that qualify for the definition of PTSD and those that do not, might precipitate major depression, major depression occurs independent of stressors and, unlike PTSD, does not require an etiologic event as an essential part of its definition. High rates of comorbid major depression in persons diagnosed with PTSD have been reported (Breslau et al 1991; Davidson et al 1991; Green et al 1992; Helzer et al 1987; Keane and Wolfe 1990; Kessler et al 1995; McFarlane and Papay 1992). Studies that examined the temporal order in PTSD and major depression have suggested that the lifetime association of the two disorders might be explained by several causal pathways. First, pre-existing major depression increases a person's susceptibility to the PTSD-inducing effects of traumatic events (Breslau et al 1997; Bromet et al 1998; Connor and Davidson 1997). Second, PTSD increases the risk for the first onset of major depression (Breslau et al 1997; Kessler et al 1995). There is also evidence that major depression increases the risk for exposure to traumatic events (Breslau et al 1997), as it does for exposure to ordinary stressful life events (Kendler et al 1993, 1999). The finding that PTSD increases the risk for major depression, taken together with the evidence that major depression increases the risk for PTSD following trauma, suggests the possibility of a shared diathesis, an underlying vulnerability to both PTSD and major depression (Breslau et al 1997). That personal vulnerabilities play a critical role in the PTSD and the depressive effects of stressors is clear, for only a minority of persons who report the occurrence of a trauma or a stressful event develop PTSD or become depressed, respectively (Breslau and Davis 1987; Breslau et al 1991; Kendler et al 1995; Kessler 1997; Yehuda and McFarlane 1995).

An alternative explanation that might account for the

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Received February 3, 2000; revised May 5, 2000; accepted May 16, 2000.

PTSD–major depression comorbidity is that the traumatic events that lead to PTSD might also increase the risk for major depression (McFarlane and Papay 1992). The hypothesis that traumatic events increase the risk for major depression, independent of their PTSD effects, would be supported if we found a significantly higher incidence of major depression in persons exposed to trauma who did not develop PTSD, as compared with persons who were not exposed. Such evidence would suggest that the depressive effects of traumatic events might have a distinct pathway, separate from that of PTSD. Conversely, evidence of an increased risk for the subsequent onset of major depression in exposed persons with PTSD, but not in exposed persons who did not develop PTSD, would suggest that PTSD might cause major depression or that the two disorders share a common underlying vulnerability.

In this study we examine this hypothesis using data from the Epidemiologic Study of Young Adults in southeast Michigan (Breslau et al 1991). We estimate the risk for first-onset major depression in persons with PTSD and in persons exposed to traumatic events with no PTSD sequelae, with persons who were not exposed to traumatic events serving as a reference. In addition, we examine data from the National Comorbidity Survey (NCS; Kessler et al 1995) to address the concern that traumatic events might vary in their potential for inducing major depression, just as they vary in their potential for inducing PTSD. It might be argued that the traumas experienced by persons who developed PTSD are different from those experienced by exposed persons who did not, and that it is the differences in the types of traumas that might account for any observed differences in the risk for major depression in persons with PTSD versus exposed persons without PTSD. The larger sample of the NCS, as compared with the sample of the Epidemiologic Study of Young Adults, offers an opportunity to estimate the risk for major depression by history of exposure and PTSD, holding constant trauma type. The structured diagnostic interviews used in these studies do not measure severity of trauma within the same type of trauma; however, it should be emphasized that the consistent evidence of differences in the risk of PTSD across trauma types (e.g., Breslau et al 1998a; Kessler et al 1995; Norris 1992) indicates that the classification of traumas by type is an important index of the potential to induce PTSD.

Methods and Materials

Samples and Data

THE EPIDEMIOLOGIC STUDY OF YOUNG ADULTS. A sample of 1200 persons was randomly selected from all 21- to 30-year-old members of a large health maintenance organization

in southeast Michigan. Personal interviews were conducted in 1989 with 1007 (84%), and follow-up interviews were conducted in 1990, 1992, and 1994. Complete follow-up data are available on 974 persons (97%). At baseline the sample was 62% female, 80% white, 45% married, and 29% college educated. (Detailed information on the sample has been previously reported—e.g., Breslau et al 1991, 1998b.) We used the National Institute of Mental Health Diagnostic Interview Schedule (NIMH DIS; Robins et al 1989), revised according to DSM-III-R. The PTSD section of the revised NIMH DIS opens with a listing of typical PTSD events, and respondents are asked whether any of these events have ever happened to them. The description of traumatic events follows the DSM-III-R text closely, using the examples listed in the text. A respondent's report of an event that does not fit the DSM-III-R stressor definition (e.g., severe illness, divorce, loss of job) is excluded from further inquiry, and the respondent is asked whether he or she has experienced another event of the sort described in the question. A report of a qualifying stressor is followed by questions about the occurrence of PTSD symptoms after the event. The inquiry begins with the worst event and continues up to three events and their PTSD sequelae. For each event information is elicited on age at exposure and time of onset of symptoms. In persons with two or three events, we used the worst event but replaced it with the event that caused PTSD in persons with PTSD from an event other than the worst.

Lifetime history of psychiatric disorders was measured at baseline, and interval history, covering the period since the last assessment, was gathered at each follow-up interview. Data from the three follow-up interviews were combined to provide information on new exposure and new onset of disorders occurring during the 5-year interval since baseline.

THE NATIONAL COMORBIDITY SURVEY. The NCS is based on a stratified, multistage area probability sample of persons 15 to 54 years of age in the United States (Kessler et al 1995). The diagnostic interview was a modified version of the Composite International Diagnostic Interview (CIDI), which also yields DSM-III-R diagnoses (World Health Organization 1997). The CIDI PTSD section is modeled after the NIMH DIS. Data on PTSD were gathered on a subset of 5877 respondents. Posttraumatic stress disorder was measured in connection with the worst event. On three event types (combat, physical abuse in childhood, and serious neglect in childhood) age of exposure was not elicited. Persons whose worst event was one of these three types were excluded from the analysis. The analysis was conducted on 5014 respondents.

Analytic Strategy

The diagnosis of DSM-III-R PTSD is made by inquiring whether the respondent experienced the defining symptoms of the disorder in connection with a specific traumatic event. Because PTSD, by definition, cannot occur without exposure to a qualifying stressor, the risk for PTSD is not a relative risk, which compares exposed persons to a reference group of unexposed persons. Instead, the risk for PTSD following exposure is a measure of conditional probability, which can range from 0 to 1. In contrast, the risk for major depression associated with prior exposure is

estimated by comparing exposed persons with a reference group of unexposed persons. The evaluation of the risk for major depression associated with trauma is not different from the evaluation of the risk for major depression associated with any other risk factor of interest. The DSM-III-R diagnosis of major depression does not require a connection with a traumatic event; therefore it is not necessary to inquire whether or not an exposed person experienced depressive symptoms due to or following the exposure. In fact, relying on respondents' accounts on whether or not they developed depressive symptoms due to or following exposure is methodologically flawed: it introduces a reporting bias and precludes any hope for testing whether the risk for major depression following exposure is in fact increased beyond what would have occurred in the absence of exposure.

Comorbidity of PTSD and major depression refers to the co-occurrence of the two disorders in lifetime, either concurrently or in separate episodes. There are no hierarchical rules in DSM-III-R that exclude the diagnosis of major depression when it is contemporaneous with PTSD. First onset of major depression in persons with PTSD is estimated in all persons with onset of PTSD preceding the onset of major depression, regardless of whether symptoms of either disorder are active or have remitted.

Statistical Analysis

We used Cox proportional hazards models for censored survival data (Breslow 1974; Cox 1972, 1975) with time-dependent variables to calculate the hazards ratio (HR) of the first occurrence of major depression associated with prior PTSD and with prior exposure to traumatic events with no PTSD. In analyses of the retrospective data from the Epidemiologic Study of Young Adults (gathered at baseline), time was defined as chronologic age. Persons who had not experienced major depression by the time of the baseline interview were censored. Two time-dependent covariates were used, representing the three strata of the independent variable (i.e., exposed-PTSD, and exposed-no PTSD, with not exposed as the reference). This model yields estimates of the risk for major depression in persons who experienced PTSD following a trauma and in persons who experienced a trauma with no PTSD, compared with persons who did not experience a trauma. The parameter estimate (β) in the Cox proportional hazards model is a regression coefficient from which the HR can be obtained by taking the antilogarithm of the parameter estimate. Hazards ratios with 95% confidence intervals (CIs) that do not include the null value of 1 are statistically significant at $\alpha < .05$ (two tailed). We used the SAS procedure for proportional hazards regression, with the logit link to address the interval censored data (SAS Institute Inc. 1991). Proportionality assumptions were tested with graphic techniques (Kalbfleisch and Prentice 1980). All models included sex, race, and education as covariates. Sex interactions with exposure and PTSD were tested, but none were detected at $\alpha < .15$.

In the analysis of the *prospective data* from the Epidemiologic Study of Young Adults, time was defined as number of years since baseline. Persons who experienced major depression by the time of the baseline interview were excluded and the analysis was conducted only on the subset at risk for first-time occurrence of major depression. The Cox proportional hazards model

Table 1. HRs of Exposure to Traumatic Events and PTSD by Pre-Existing MDD: Results from Two Analyses of Data from the Epidemiologic Study of Young Adults (Baseline Interview)

	Exposure in total sample (N = 1,007)		PTSD in exposed sample (N = 399)	
	HR	(95% CI)	HR	(95% CI)
Prior major depression	2.12	(1.39, 3.25)	3.69	(2.00, 6.81)
Sex (female)	0.76	(0.61, 0.93)	2.28	(1.41, 3.69)
Race (white)	0.89	(0.70, 1.15)	1.22	(0.71, 2.11)
Education (\geq college)	0.70	(0.55, 0.89)	0.68	(0.40, 1.17)

Estimated in Cox proportional hazards models with major depression (MDD) as a time-dependent covariate. Analysis of posttraumatic stress disorder (PTSD) is based on the subset reporting exposure to traumatic events. HR, hazards ratio; CI, confidence interval.

included two components: 1) baseline history of PTSD and history of exposure with no PTSD and 2) time-dependent covariates for PTSD and for exposure with no PTSD occurring during the 5-year follow-up interval. The historical component (fixed covariates) estimates the risk for first-onset major depression during the follow-up that is associated with baseline status. The time-dependent component estimates that risk due to more recent experiences occurring during the 5-year interval since baseline. Each component is estimated controlling for the other. The proportional hazards model with two fixed and two time-dependent covariates is as follows:

$$h_i(t) = e^{\alpha W_i + \beta X_i + \gamma Y_i(t) + \delta Z_i(t)} h_o(t),$$

where $W_i = 1$ if history of PTSD occurred before baseline and 0 if not, $X_i = 1$ if history of exposure only occurred before baseline and 0 if not, $Y_i(t) = 1$ if PTSD occurred before time t during follow-up and 0 if not, and $Z_i(t) = 1$ if exposure only occurred before time t during follow-up and 0 if not; α , β , γ , and δ are the corresponding coefficients of risk for first-onset major depression for these variables.

The analysis of NCS data applied the same approach used in the analysis of our baseline data, described above, except that the number of time-dependent covariates was higher, representing specific types of trauma with and without subsequent PTSD.

Cases in which the onset of major depression and exposure to trauma or PTSD occurred in the same year were censored just before the year in which they occurred, since no information was available about their temporal sequence. This procedure avoids imposing a temporal sequence based on *a priori* assumptions. An assumption that in these cases major depression followed the trauma would fly in the face of evidence that major depression predisposes to traumatic events and increases the vulnerability to their PTSD effects (Breslau et al 1991; Kendler et al 1995, 1999).

Results

We first summarize results on pre-existing major depression, to provide a more complete picture of the relationship of major depression with exposure to trauma and PTSD (Table 1). Calculating with Cox proportional hazards models with time-dependent covariates, we found that

Table 2. HRs of MDD Associated with Prior PTSD and Exposure/No PTSD: Results from the Epidemiologic Study of Young Adults (Baseline Interview)

	HR	(95% CI)
PTSD	2.81	(1.57, 5.04)
Exposure/no PTSD	1.34	(0.82, 2.18)
Sex (female)	1.69	(1.13, 2.54)
Race (white)	1.00	(0.65, 1.57)
Education (\geq college)	0.69	(0.45, 1.06)

N = 1,007. Estimated in a Cox proportional hazards model with posttraumatic stress disorder (PTSD) and exposure/no PTSD as time-dependent covariates. HR, hazards ratio; MDD, major depression; CI, confidence interval.

the adjusted HR of exposure to trauma was higher in persons with pre-existing major depression, as compared with persons with no pre-existing major depression (HR = 2.12; 95% CI 1.39, 3.25). In the subset of exposed persons, those with pre-existing major depression had a higher risk for PTSD than those without (HR = 3.69; 95% CI, 2.00, 6.81). The results also show that female subjects were less likely to be exposed to traumatic events but more likely to develop PTSD if exposed. Race was not significantly related to either exposure to traumatic events or to PTSD. Education was not significantly related to PTSD but was significantly associated with a risk for exposure, with persons with college education at a lower risk than those without.

Major Depression following Exposure to Trauma and PTSD: Lifetime Data at Baseline

Descriptive analysis of lifetime data gathered at baseline show that, of all persons exposed to a traumatic event (*N* = 394), 23.6% experienced PTSD. In most cases, the onset of PTSD occurred within days of exposure, and in all cases within 1 year. Table 2 presents estimates from a Cox proportional hazards model of the risk for first-onset major depression associated with prior PTSD and with prior exposure to trauma without PTSD based on these lifetime data. The adjusted HRs were 2.81 (95% CI, 1.57, 5.04) for major depression in persons with prior PTSD and 1.34 (95% CI 0.82, 2.18) in persons who were exposed to trauma but did not develop PTSD, as compared with persons who were not exposed. The difference between the two estimates is statistically significant (*p* = .034).

Major Depression following PTSD and Exposure with No PTSD: Prospective Data

Analysis of the risk of first-onset major depression occurring during the 5-year interval since baseline was conducted on persons with no history of major depression at baseline who were at risk for the first onset of major depression (*N* = 872). Of this subset, 231 (26.5%) were exposed to a traumatic event during the follow-up period, and of those exposed, 21 (9.1%) developed PTSD.

Table 3. HRs for MDD during 5-Year Interval Associated with Prior PTSD and Exposure: Results from the Epidemiologic Study of Young Adults (Prospective Data)

	HR	(95% CI)
New PTSD ^a	11.71	(3.97, 34.58)
New exposure/no PTSD ^a	1.44	(0.67, 3.11)
Baseline history of PTSD	3.12	(1.61, 6.05)
Baseline history of exposure/no PTSD	1.45	(0.86, 2.43)
Sex (female)	2.16	(1.26, 3.78)

N = 872. Estimated in a Cox proportional hazards model; persons with history of major depression (MDD) at baseline were excluded. HR, hazards ratio; PTSD, posttraumatic stress disorder; CI, confidence interval.

^aTime-dependent covariates.

Table 3 presents results from a Cox proportional hazards model of the prospective data. To estimate the risk for first-onset major depression, two time-dependent covariates were used, representing PTSD during the follow-up period (new exposure/PTSD) and exposure to trauma that did not culminate in PTSD during that period (new exposure/no PTSD). Lifetime history of PTSD and of exposure with no PTSD ascertained at baseline were included as fixed covariates. Compared with persons who did not experience a new trauma during the 5-year interval, persons with PTSD due to a trauma occurring during that period were at a considerably increased risk of first-onset major depression (HR = 11.7; 95% CI, 4.0, 34.6). In contrast, persons who experienced a trauma during the 5-year interval but did not develop PTSD were at a modestly and not significantly increased risk of first-onset major depression (HR = 1.4; 95% CI, 0.7, 3.1). The difference between the two HRs is statistically significant (*p* = .0007). Lifetime history of PTSD up to the baseline interview also increased the risk for first-onset major depression during the 5-year follow-up (HR = 3.1; 95% CI, 1.6, 6.1), whereas baseline history of exposure only with no PTSD had little effect.

Major Depression following Traumatic Events Stratified by Event Type in the NCS

Table 4 presents NCS data on sex-adjusted HRs for major depression associated with PTSD due to seven types of trauma, and with exposure only with no PTSD by eight types (the seven that are listed for PTSD plus "disaster," an event type with few PTSD cases and no cases of major depression following PTSD). Except for serious physical attack, the increase in the risk for major depression in persons with PTSD (as compared with persons who were not exposed) was at least twofold higher than in persons who were only exposed with no PTSD across all event types. On three comparisons—life-threatening accidents, witnessing violence to others, and sexual molestation—the differences between PTSD and exposed-only were statis-

Table 4. HRs for First MDD Associated with Prior PTSD and Exposure to Trauma with No PTSD, by Trauma Type: NCS Data

	HR	(95% CI)
PTSD		
Life-threatening accidents	5.79	(3.21, 10.43)
Witnessing violence to others	2.42	(1.46, 4.02)
Rape	2.59	(1.74, 3.87)
Sexual molestation	3.18	(2.24, 4.50)
Serious physical attack	1.11	(0.35, 3.48)
Kidnapping, threatened with weapon	3.80	(1.39, 10.36)
Trauma to a loved one	3.15	(1.54, 6.42)
Exposed/no PTSD		
Life-threatening accidents	1.39	(1.02, 1.88)
Disaster	1.18	(0.85, 1.63)
Witnessing violence to others	1.44	(1.14, 1.83)
Rape	1.82	(1.13, 2.94)
Sexual molestation	1.65	(1.24, 2.18)
Serious physical attack	1.58	(1.00, 2.46)
Kidnapping, threatend with weapon	1.89	(1.32, 2.71)
Trauma to a loved one	1.82	(1.32, 2.71)

N = 5,014. Estimated in a Cox proportional hazards model with multiple time-dependent covariates, controlling for sex. HR, hazards ratio; MDD, major depression; PTSD, posttraumatic stress disorder; NCS, National Comorbidity Survey; CI, Confidence interval.

tically significant. Separate analyses in males and females yielded similar results.

Discussion

Analysis of lifetime data gathered at baseline indicates that pre-existing major depression increased the risk for subsequent exposure to traumatic events twofold and increased the risk for PTSD among exposed persons more than threefold. With respect to our key question (do traumatic events increase the risk for major depression independent of their PTSD effects?), we found that the risk for major depression was 2.8 times higher (relative to persons who were not exposed) in exposed persons who developed PTSD, but only slightly and not significantly increased in exposed persons who did not develop PTSD. These findings do not support the hypothesis that the depressive effects of traumatic events are independent of the PTSD-inducing effects of traumatic events.

Further and clearer support of these findings comes from the analysis of the *prospective* data, in which we estimated the risk for major depression during a 5-year follow-up interval among persons with no history of major depression at the beginning of that period. Exposure to a trauma during the follow-up period increased considerably the risk for first-onset major depression in persons who developed PTSD, but not in persons who did not develop PTSD. Analysis of data from the NCS provides evidence that the higher rate of comorbid major depression in exposed persons with PTSD versus exposed persons with

no PTSD is unlikely to be due to differences in trauma types.

We focused on major depression rather than on other comorbid disorders, because the PTSD–major depression relationship in victims of trauma has been a topic of growing interest in psychiatric research. Analysis of the relationship of PTSD and exposure to trauma without PTSD with anxiety disorders or substance use disorders has yielded similar results (e.g., Chilcoat and Breslau 1998).

The results should be interpreted in light of the following considerations. First, data generated by the NIMH DIS and the CIDI date events by *year* of occurrence. These data include cases in which the onset of major depression occurred in the same time span as exposure to trauma or PTSD. These cases provide no information on the temporal sequence of exposure and onset of major depression. Our approach, outlined in Statistical Analysis, was to censor these cases just before the year they occurred. A more precise dating of events would have reduced the need for this solution; however, it should be noted that relatively few cases fell within this category (in the prospective analysis, only three cases were censored) and they were approximately evenly divided between PTSD and exposure with no PTSD. Second, in the analysis of the NCS we excluded approximately 25% of exposed persons, due to the lack of information about the time of occurrence of some event types. There is no reason to suspect that this exclusion biased the results of the analysis on the risk for major depression by event type.

Lastly, the prospective analysis is based on a relatively small number of PTSD cases occurring during the follow-up interval, yielding an estimate of the relative risk of first-onset major depression in these cases with a wide CI. Nonetheless, the lower limit of the 95% CI of that estimate was well above the null value of 1. The methodological advantages of the prospective analysis are considerable, despite the limited number of persons at risk for depression by virtue of experiencing PTSD due to exposure during the follow-up period. One advantage that deserves note is that, by controlling for baseline reports of PTSD and exposure to trauma and by excluding persons with history of depression at baseline, we control for persons' propensities to report adverse histories. Associations between exposure to traumatic events and depression based on retrospective data are likely to be upwardly biased, compromising our ability to draw causal inferences (Kessler 1997).

Despite the general deference to clinical diagnoses, the use of structured diagnostic interviews in the Epidemiologic Study of Young Adults and the NCS offers a clear advantage in testing causal pathways between our postulated risk factors and major depression. A clinician's

diagnosis of major depression might be tainted by information the clinician elicits about the subject's history, including prior traumatic experiences and their sequelae. A contamination of diagnostic data by other biographic information is far less likely to occur when a methodology represented by the DIS is used.

The findings that the increased risk for major depression in persons exposed to trauma was confined chiefly to the subset of persons who developed PTSD and that exposure with no PTSD did not increase significantly the risk for major depression replicate our previous report based on a study of a sample of women (Breslau et al 1997). A similar pattern can be discerned in other epidemiologic reports on PTSD and a variety of comorbid disorders, including alcohol and drug use disorders, major depression, and anxiety disorders (Chilcoat and Breslau 1998; Kulka et al 1990; North et al 1999). For example, in a survey of psychiatric disorders among survivors of the Oklahoma city bombing, North et al (1999) found that the prevalence of postdisaster comorbid disorders (major depression, panic disorder, generalized anxiety disorder, and alcohol and drug use disorders) in exposed persons who developed PTSD was 63%, but in the absence of PTSD it was only 9%. The percentage of postdisaster major depression in persons with PTSD was 55%; the corresponding estimate in persons with no PTSD was not reported, although it must have been less than 9%. This pattern also can be observed in data from the large-scale National Vietnam Veterans Readjustment Study (Kulka et al 1990). Examination of the report from that study reveals that it is only among veterans with PTSD, rather than the entire subset of veterans exposed to high war zone stress (from which most PTSD cases came), that the prevalence of comorbid disorders reached a markedly high level, as compared with the overall rate in Vietnam veterans.

A report from a clinical sample of trauma victims recruited from an emergency room displayed the same pattern (Shalev et al 1998). The prevalence of major depression in trauma victims with PTSD, diagnosed 1-4 months after the trauma, was much higher than in those without PTSD (57.7% [41/71] vs. 12.1% [17/140], respectively). These figures include cases with onset before the trauma; the incidence of first-onset major depression after the trauma was not reported. The absence of a control group of unexposed persons makes it difficult to assess the extent to which the prevalence of depression among trauma victims with no PTSD was increased as a result of the trauma. A comparison with estimates from general population surveys should take into account that the closely timed, repeated posttrauma diagnostic assessments are likely to have contributed to high rates of major depression in that study, as compared with rates observed in a one-time general population survey.

Our findings do not support the notion of separate and distinct vulnerabilities for PTSD and major depression. They suggest that PTSD might lead to major depression. In view of the additional evidence that pre-existing major depression increases the risk for PTSD, these results also suggest that PTSD and major depression in trauma victims might be influenced by overlapping or common vulnerabilities, and that it might be a mistake to regard PTSD and major depression in "comorbid" cases as being separate and distinct. This inference is in accord with reports that suspected risk factors for PTSD, including female sex, neuroticism, family history of major depression, history of childhood trauma, and pre-existing anxiety and depressive disorders, overlap with risk factors for major depression (Boyce et al 1991; Bremner et al 1993; Breslau et al 1991, 1997; Bromet et al 1998; Connor and Davidson 1997; Davidson et al 1985, 1991; Helzer et al 1987; Kessler and Magee 1993; Kessler et al 1995; McFarlane 1989; Weiss et al 1999; Zaidi and Foy 1994). Psychiatric research in general has had limited success in identifying disorder-specific risk factors. The results of this study go a step further. They suggest that the emergence of PTSD might identify a vulnerable subset among people who experienced traumatic events, and that the subsequent development of depression in this subset might result from the pre-existing vulnerabilities that are exposed and possibly exacerbated by the trauma.

This conclusion is in contrast with the model advanced by Yehuda et al (1998) that exposure to trauma causes PTSD in some persons and major depression in others, depending on the subjects' distinct biological predispositions. These authors cited a study that attempted to capture subjects' predispositions to PTSD versus depression by comparing cortisol levels in the acute state (McFarlane et al 1997). Cortisol levels were measured immediately after the trauma. Three diagnostic groups were identified 6 months later: PTSD, major depression, and no psychiatric disorders. An overall significant difference in initial cortisol across the three groups was reported. Posttraumatic stress disorder cases showed a lower mean cortisol level than cases of major depression, but the difference was no longer significant when methodological factors were controlled, according to the report. Further, the PTSD group did not differ significantly from the no-disorder control group. These findings do not support the claim by Yehuda et al (1998) that in the acute state PTSD cases manifested a discernable and distinct cortisol abnormality. An earlier study of rape victims, cited by Yehuda et al (1998), also failed to find a relationship between acute cortisol right after the trauma and the diagnosis of PTSD 4 months later (Resnick et al 1995). In that study, persons with a history of previous assault had a lower mean acute cortisol level and a higher risk for PTSD due to the current trauma;

however, the possibility that acute cortisol level was the mediating variable that could explain the association between assault history and PTSD due to the current trauma was ruled out: the association was observed when acute cortisol level was controlled in a multivariable model, and acute cortisol level proper was unrelated to PTSD following the current rape.

There is sound evidence that the effects of stressful life events on major depression is likely to be influenced by genetic factors that control the sensitivity to the depressogenic effects of exposure. A similar mechanism helps to account for the onset of depression in victims of trauma. The epidemiologic data suggest that the diagnosis of PTSD among trauma victims might be a marker of a more generalized susceptibility, including the susceptibility to depression, possibly other disorders, and functional impairment. Future studies, especially those that use the methods of genetic epidemiology, could shed further light on this question.

Supported by Grant No. MH 48802 from the National Institute of Mental Health, Bethesda, Maryland (NB).

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