Post Traumatic Stress Disorder Comorbid with Major Depression: Factors Mediating the Association with Suicidal Behavior

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Abstract:

Objective: To determine if patients with a history of major depressive episode (MDE) and comorbid post traumatic stress disorder (PTSD) have a higher risk for suicide attempt and differ in other measures of suicidal behavior from MDE patients with no PTSD. We also explore how PTSD comorbidity might increase risk suicidal behavior in MDE by investigating the relationship between PTSD, cluster B personality disorder (CBPD), childhood sexual or physical abuse, and aggression/impulsivity.

Methods: We enrolled 230 subjects with a lifetime history of MDE; 59 also had lifetime comorbid PTSD. The demographic and clinical characteristics of those with and without PTSD were compared. The relationship between suicidality and comorbid PTSD was assessed in a univariate fashion, and also after adjusting for factors that differentiated those subjects with PTSD as well as clinical variables known to be associated with suicidal behavior.

Results:

Lifetime PTSD patients were significantly more likely to have made a suicide attempt. There was no difference between the groups with respect to suicidal ideation or intent, number of attempts made or maximum lethality of attempts. The PTSD group had higher objective depression, impulsivity and hostility scores, and higher rates of comorbid CBPD and reported childhood history of abuse. Cluster B personality disorder was the only independent variable related to lifetime suicide attempt in a multiple regression model.

Conclusions: Post Traumatic Stress Disorder is frequently comorbid with MDE and their co-occurrence enhances the risk for suicidal behavior. Higher rates of comorbid CBPD appear to be a salient factor contributing to greater risk for suicidal acts in MDE patients who also have PTSD compared to those with MDE alone.

Introduction:

In the US, the annual prevalence of Major Depressive Episode (MDE) is about 17% (1) and 1.3% of adults aged 18 to 54 suffer Posttraumatic Stress Disorder (PTSD) during the course of a year (2). Between 14% and 25% of individuals exposed to catastrophic trauma develop PTSD (3-5) and as many as half of them have at least one additional Axis I diagnosis. In 26%, the additional diagnosis is MDE (6). Indeed, within 8 months of a traumatic event, 23% of exposed adults develop MDE with or without PTSD, often within days of the event (7).

Preexisting Major Depression increases susceptibility to the effects of traumatic events as well as ordinary stressful life events (8). At the same time, PTSD increases the risk for the first onset of Major Depression (9,10). Thus, these two disorders are common, often comorbid and the presence of one diagnosis compounds risk for the development of the other.

Both PTSD and MDE are associated with risk for suicidal behavior. Lifetime prevalence of suicide attempts in MDE is approximately 16% (11). In a community survey, patients with PTSD were 14.9 times more likely to attempt suicide than non-PTSD subjects (12). Although suicide rates are higher in Vietnam Veterans than the general population, studies of these veterans have yielded conflicting results regarding the degree of increased risk of suicide attempts and suicidal ideation in trauma victims. Some report that the increased risk of suicidal behavior in PTSD, while greater than that of non-veterans, has been overestimated, however, others find that specific symptoms within PTSD, such as guilt or anxiety, are responsible for the increase in risk, not the presence of PTSD in general (13-17).

Some (18-20) but not all (21) studies of suicidality when PTSD and MDE are comorbid found that PTSD and MDE interact to increase suicidal ideation and behavior over that of those suffering from PTSD or MDE alone. However, the relationship between MDE, PTSD and suicidal behavior is likely to be influenced by other factors. For example, child abuse increases risk for PTSD, major depression, and suicidal behavior. About one third of those who have been abused or neglected during childhood develop PTSD (22) and a history of childhood abuse more than doubles the odds of developing MDE (23). Early childhood trauma, including abuse, has been associated with self destructive and suicidal behavior later in life (24,25).

Both suicidal behavior and childhood history of abuse and trauma are also associated with borderline personality disorder (BPD)(26,27) and some conceptualize BPD as a form of chronic PTSD (28). In addition, BPD is often also comorbid with major depression (29). Thus, the influence of PTSD on suicidality requires attention to a constellation of risk factors including MDE, personality disorder, and childhood history of abuse, as well as concomitant traits such as impulsivity and aggression that are often part of the clinical picture in cluster B personality disorders and associated with suicidal acts.

We recently reported that patients presenting for treatment of major depression who had PTSD were more likely to have exhibited suicidal behavior and that the effect of PTSD was independent of the presence of cluster B personality disorders, childhood history of abuse, and aggressive behavior (19). We sought to replicate these findings and in this study we examine the relationship between suicidal behavior and PTSD taking into account known risk factors for suicidal behavior including cluster B personality

disorders, childhood sexual or physical abuse, and history of aggression/impulsivity. We report the findings from this larger, mostly independent sample of adults with a history of a Major Depressive Episode (MDE). We hypothesize that in patients with a history of MDE, those who have PTSD will be more likely to be suicide attempters and will differ in other measures of suicidal behavior.

Methods:

Sample

Samples were recruited from inpatient units in New York (New York State Psychiatric Institute and Payne Whitney Clinic) and in Pittsburgh (Western Psychiatric Institute and Clinic and St. Francis Hospital) and in both cities by advertisement. About half of the subjects were inpatients at the time of assessment (n=108, 49%). Subjects (N=230) with a current or past Major Depressive Episode (MDE) were entered into the study after giving written informed consent. Thirty one (n=31) of the subjects with a lifetime history of MDE in this sample had been included in a previous analysis (total n=156) (19), of which 6 had a history of lifetime PTSD.

Assessment

Subjects were assessed for the presence of lifetime and current DSM-IV psychiatric disorder using the Structured Clinical Interview for DSM-IV (SCID-I)(30). Patients were assessed for severity of depressive symptoms by a research clinician using the Hamilton Depression Rating Scale (31), and via patient self-report with the Beck Depression Inventory (32). Suicide attempts were defined as self-inflicted injury with intent to end one's life. Lifetime history of suicidal behavior was gathered on the

Columbia University Suicide History form (33). Degree of medical injury from suicide attempts was measured with the Lethality Rating Scale (LRS)(34). Suicidal intent and ideation were measured using the Suicide Intent Scale (SIS)(34) and the Scale for Suicidal Ideation (SSI)(35), respectively. Hopelessness was assessed with the Beck Hopelessness Scale (BHI)(36). Lifetime aggression was measured using the Brown Goodwin Aggression History form (BGA)(37), hostility with the Buss Durkee Hostility Inventory (BDHI)(38), and impulsivity with the Barratt Impulsivity Scale (BIS)(39). Axis II disorders were diagnosed by the Structured Clinical Interview for DSM-IV Personality Disorders (40). A history of physical and sexual abuse during childhood were assessed from a series of screening questions in our demographic questionnaire.

Diagnostic Procedure

All interviewers were Master's or PhD level clinicians or psychiatric nurses who received extensive training in the administration of semi-structured interviews. Best-estimate diagnoses were made by consensus and used all available data sources in diagnostic consensus conferences. Within and cross-site reliability on the SCID-I and SCID–II, suicide history, and the BGA were high (ICCs = 0.82-0.98, κs = 0.86-0.95).

Statistical Analysis:

Frequencies and associations between variables were examined. Demographic and clinical variables were compared in subjects with and without a lifetime history of PTSD using a Student's t for continuous variables and Chi Square statistic or Fisher's Exact test for categorical variables. Because not all subjects were in a MDE at the time of assessment, state dependent clinical variables were compared by ANOVA controlling for Hamilton scores. We compared the age of onset of PTSD and the age of first suicide

attempt in all suicide attempters with a history of PTSD. Then, a step-wise backward logistic regression was constructed with lifetime suicide attempter status as the dependent variable and lifetime PTSD, childhood history of abuse, CBPD, impulsivity and aggression as the independent variables.

Results:

Demographics: Fifty-nine subjects (n=59, 25%) had a lifetime history of Post Traumatic Stress Disorder. Lifetime PTSD subjects and non-PTSD subjects did not differ significantly in age or income. Lifetime PTSD subjects were significantly more likely to be female, non-white, unmarried and to have fewer years of education (See Table 1).

Severity of acute psychopathology: The lifetime PTSD group had significantly higher objective depression ratings (HDRS) compared to the group with no history of PTSD (See Table 2). There were no significant differences between the groups in the level of subjective depression (BDI), hopelessness (BHS) or in presence of a current depressive episode (See Table 2).

Comorbid conditions and character traits: Lifetime PTSD subjects had significantly higher rates of comorbid cluster B personality disorders but not substance abuse or head injury (See Table 2). Higher Impulsivity (BIS) and hostility scores (BDHI) but not higher lifetime aggression (BGA) were found in the lifetime PTSD group.

Suicidal Behavior: Lifetime PTSD patients were significantly more likely to have made a suicide attempt. However, there was no difference between the groups in suicide ideation adjusted for depression severity or suicidal intent at the time of the most lethal attempt. Among subjects with a history of suicide attempt there was no difference between the lifetime PTSD group and non PTSD group in the number of attempts made or maximum

lethality of suicide attempts. The first suicide attempt for attempters with PTSD occurred at an earlier age than for attempters with no PTSD, but the difference did not reach statistical significance (see table 2).

Trauma History: A significantly greater number of lifetime PTSD subjects than non PTSD subjects reported a childhood history of abuse. Lifetime PTSD subjects were more likely to have experienced sexual abuse including intercourse before the age of 16, physical abuse before the age of 16, severe physical abuse before the age of 16 and rape as an adult (See Table 2).

Age of onset PTSD: For subjects with comorbid PTSD, the mean age of onset was 19.2 ± 14.2 years for PTSD. Subjects with PTSD who attempted suicide were 26 ± 14 years at the time of first attempt. For the most part, PTSD preceded the first suicide attempt (24/33, 72%) and the age of onset of PTSD and of first suicide attempt showed a positive correlation (Pearson's r = 0.52, p<.002, n=33).

Multivariate Analysis: A step-wise backward logistic regression with lifetime suicide attempter status as the dependent variable and lifetime PTSD, childhood history of abuse, CBPD, impulsivity and aggression as the independent variables resulted in only CBPD being significantly associated with suicide attempt (C.I.=95%, O.R.=8.192, df=1, Chi-square=22.06, p<.0001). Presence of a history of childhood abuse approached statistical significance (df=1, chi-square=2.91, p=0.088)(see Table 3).

Discussion:

PTSD, MDE and Suicidal Behavior

We (19) and others (18) have reported that when comorbid with MDE, PTSD is associated with higher rates of suicidal acts. In this larger sample of subjects with MDE,

those with a lifetime history of PTSD were also significantly more likely to be suicide attempters. As in our previous study, we detected no differences in the suicidal behavior exhibited by suicide attempters whether they had a lifetime history of PTSD or not, in terms of suicidal intent, number of previous attempts, age of first suicide attempt and lethality of previous attempts.

Our previous study reported that currently depressed subjects whose PTSD had resolved did not report more suicidal ideation, but that those currently suffering PTSD had more suicidal ideation than those with no current or past PTSD. This study considered only lifetime PTSD and MDE and detected no difference in suicidal ideation as well. Perhaps suicidal ideation is heightened only while depressed patients are suffering from PTSD and ideation lessens once PTSD remits. Indeed, Marshall et al (20) report that, in those with symptoms of PTSD, for each additional symptom present suicidal ideation was likely to be present in a larger proportion of the sample, even when controlling for the presence of Major Depression. However, not all studies agree. For example, Shalev et al (21) found no difference in suicidal ideation in patients with PTSD and MDE compared to MDE only, although the sample was recruited from emergency services after experiencing trauma possibly representing more acutely ill individuals. Thus, whether suicidal ideation increases with PTSD over and above the risk conferred by depression requires further study.

Consistent with the lack of difference in suicidal ideation in the two groups, there were no significant differences between lifetime PTSD subjects and no PTSD subjects in levels of subjective depression or hopelessness. Both groups had a similar proportion of subjects with a current depressive episode, however PTSD subjects showed significantly

higher objective depression ratings compared to subjects with no history of PTSD. Although Golier et al (41) have suggested that comorbidity with PTSD does not result in increased severity of depressive episode but instead is associated with greater pronounced variability in mood, Shalev (21) noted about twice the severity of depressive symptoms in those with PTSD and MDE compared to those with MDE alone. Moreover, Freeman et al (18) have reported more depressive symptoms in those with PTSD and suicidal behavior, although comorbidity with depression was not established in that study. PTSD and MDE share a number of symptoms including sleep disturbance, poor concentration, guilt, restricted affect and suicidal ideation, all of which, with the exception of restricted affect, are measured by the Hamilton Depression Rating Scale (HDRS). We did not measure severity of PTSD symptoms and thus cannot assess the relationship of severity of PTSD and objective severity of depression. However, given that some of the subjects with a lifetime history of PTSD still had ongoing symptoms of PTSD (n=37/59, 62%), it is not surprising that a history of these two disorders leads to higher ratings of depression on the HDRS.

PTSD, aggression, hostility and impulsivity.

Aggression, hostility, and impulsivity have been associated with elevated risk for suicidal behavior in borderline personality disorder (42), major depression (43) and PTSD (18,18,44-46). In this sample, lifetime aggression was not higher in lifetime PTSD subjects suggesting that the presence of MDE and PTSD do not have an additive effect on aggression. That impulsivity and hostility were higher in the group with lifetime PTSD while aggression was not is notable. We (19) and others (7) have suggested that females may be more vulnerable to PTSD than males. Most studies of the relationship

between PTSD and aggression have been conducted in predominantly male cohorts of veterans (18,45,46). Perhaps in this mostly female sample of depressed subjects with lifetime PTSD, the presence of elevated impulsivity and hostility is related to the high co-occurrence of cluster B personality disorder and childhood history of abuse. The absence of an effect on aggression may be related to the low numbers of males in the group, since only 3 of the 59 subjects with lifetime PTSD and major depression were male.

Trauma History, PTSD and Cluster B Personality Disorders.

A history of childhood sexual or physical abuse is associated with suicidal behavior in BPD (47), in the offspring of depressed parents (48), and with elevated rates of self-destructive behaviors in adults with a history of sexual abuse (49). Thus, abuse during childhood may create a later predisposition to self-mutilation and suicidal behavior (47,49). Childhood sexual or physical abuse has also been thought to have long term sequelae in terms of other psychological as well as biological effects (see Heim and Nemeroff (50) for a review). Indeed, some (51) have characterized BPD as a chronic form of PTSD stemming from early childhood abuse. Other studies suggest significant, but not complete overlap of these two disorders and report that over half (55%) of borderline personality disorder patients carry a diagnosis of PTSD (52). In our sample, 35% of the depressed patients with lifetime PTSD had comorbid CBPD compared to 20% with MDE and no PTSD. However, in addition to greater comorbidity with CBPD, the patients with comorbid PTSD were also significantly more likely to report a history of childhood physical or sexual abuse.

As is the case for childhood physical or sexual abuse, cluster B personality disorders, specifically borderline personality disorder, are a risk factor for suicidal

behavior in depressed patients (47,53,54), even when patients do no satisfy full criteria for CBPD (55). Moreover, BPD has been reported to have an additive effect with respect to suicidal behavior when comorbid with PTSD. In a non depressed sample, Zlotnick et al (56) found that patients with BPD or BPD and PTSD scored higher on suicide proneness than those with PTSD only . In contrast, women with PTSD, irrespective of the presence of comorbid BPD had higher levels of childhood trauma than women with BPD only, suggesting that childhood trauma is more influential in the development of PTSD than BPD. This notion is also supported by another report in which childhood trauma emerged as a risk factor for PTSD, independent of the type of comorbid personality disorder (41). Perhaps childhood abuse increases liability for PTSD in the face of later traumatic events, but it is comorbidity with BPD that elevates risk of suicidal behavior in those with PTSD. This is in keeping with the results of our multivariate analysis in which cluster B personality disorder is a significant contributor to suicide attempt status but PTSD is not. Indeed, Heffernan and Cloitre (57) studied women with a history of childhood abuse and found that women with both PTSD and BPD were more likely to engage in suicidal behavior than those with PTSD alone. In the current study, lifetime PTSD subjects were more likely to have a history of physical and sexual abuse both in childhood and as adults. Our design did not permit tracking the patterns and timing of onset of comorbid disorders and MDE, however it did show that, generally, the onset of PTSD antedated first suicide attempt, and both occurred later than reported childhood abuse. Nevertheless, that PTSD did not emerge as an independent predictor of suicide attempt status in our backward regression model suggests a more complex causal pathway. One possible explanation for our findings is that childhood history of abuse

leads to both PTSD and CBPD and that this latter condition is associated with suicidal behaviors. To dissect this relationship, prospective studies which attend to sequence of onset of disorders would be instructive.

Summary

Post traumatic stress disorder is a frequent comorbidity in MDD and when they co-occur the risk for suicidal behavior is enhanced. The relationship between PTSD and suicidal behavior appears to be mediated by the presence of CBPD, with both PTSD and CBPD arising as a result of earlier traumatic experiences. The assessment and treatment of comorbid conditions such as PTSD and CBPD in the context of MDD is likely to be contributory to the reduction of suicide risk in this vulnerable population.

Table 1. Demographics of MDE Patients with and without Lifetime PTSD					
	No PTSD N=162 Mean ± SD (%) Median (range)	**PTSD N=59 Mean ± SD (%) Median (range)**	t(z) x^2	df	p
Age	45.24±11. 29 43(26-79)	41.66±10.56 42(25-76)	2.12	219	**0.035**
Sex (Female)	(124/162) 76.5%	(56/59) 94.9%	9.66	1	**0.002**
Race (White)	(116/161) 72.1%	(29/59) 50%	10.07	1	**0.002**
Married (%)	(87/162) 53.7%	(16/59) 27.1%	12.28	1	**0.001**
Education (years)	14.68±3.29 14(5-24)	13.27±2.71 13(4-20)	2.95	218	**0.003**
Income	22101±26997 12500(0-200000)	14835±13283 9000 (0-50000)	(1.334)	226	0.184

Table 2. Clinical Characteristics of MDD Patients with and without Lifetime PTSD.

	No PTSD Mean ± SD(%) Median (range)	PTSD Mean ± SD (%) Median (range)	t (z) x^2	df	P
Hamilton Depression Rating Scale	11.96±7.59 12(0-31)	14.45±7.25 13(4-20)	-2.19	217	**0.035**
Beck Depression Inventory*	21.31±12.49 20(0-51)	26.07±13.65 25(1-58)	F=1.61	2,214	0.205
Beck Hopelessness Scale*	9.81±6.08 9(0-20)	11.09±6.13 11(0-20)	F=0.17	2,212	0.678
Current Depression	(103/162)63.6%	(43/59)72.9%	1.669	1	0.196
Cluster B Personality Disorder	(31/154)20.1%	(20/57) 35.1%	5.078	1	**0.024**
Substance Abuse	(73/162)45.1%	(33/59) 55.9%	2.048	1	0.152
Head Injury	(34/158) 21.5%	(17/58) 29.3%	1.428	1	0.232
Barratt Impulsivity Scale	54.09±18.89 52(12-99)	61.05±17.70 62.5(24-104)	-2.43	211	**0.016**
Buss Durkee Hostility Inventory	34.55±12.96 33(7-62)	40.42±14.92 40(12-99)	-2.74	196	**0.007**
Brow Goodwin Aggression History	19.51±6.06 19(10-37)	20.56±6.00 21(11-34)	-1.01	185	0.315
Suicide Attempt	(78/161) 48.5%	(39/59) 65.0%	5.405	1	**0.020**
Age at first attempt	30.31±13.42 31(8-64)	25.58±13.78 21(7-56)	1.798	116	0.075
Suicidal Ideation*	8.69±9.89 5(0-34)	9.38±12.00 3(0-32)	F=0.00	2,200	0.956
Suicide Intent Scale**	15.47±5.38 15(3-27)	16.55±5.14 17(4-28)	-1.10	115	0.297

Number of Suicide Attempts**	2.19±1.98 2(1-14)	2.69±1.79 2(1-7)	(-1.79)	115	0.073
Maximum Lethality**	3.26±1.89 3(0-7)	3.41±1.52 3(0-6)	-0.45	113	0.675
Childhood history of abuse	(47/162)29.0%	(42/59) 71.2%	31.981	1	**0.000**
Rape as an Adult	(17/81) 21.0%	(10/21) 47.6%	6.077	1	**0.014**
Sex Abuse before age 16	(14/81) 17.3%	(14/21) 66.7%	20.420	1	**0.000**
Sexual Intercourse before age 16	(8/80) 10.0%	(11/21) 54.55%	19.562	1	**0.000**
Physical Abuse before age 16	(26/81) 32.1%	(12/21) 57.1%	4.475	1	**0.034**
Severe Physical Abuse before age 16	(11/81) 13.6%	(9/21) 42.9%	9.068	1	**0.003**

** adjusted for depression (Hamilton scale).*
** attempters only

Table 3: Results of logistic backward regression with suicide attempt as dependent variable.

Variable	OR	Df	Chi-square	P
Lifetime PTSD	0.938	1	0.0233	0.879
Impulsivity	0.995	1	0.1410	0.707
Aggression	1.014	1	0.1690	0.681
Childhood Abuse	1.709	1	2.9097	0.088
Cluster B PD	7.751	1	22.0597	**<.0001**

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