

# Comorbid mood and anxiety disorders in victims of violence with posttraumatic stress disorder

## Transtornos de humor e de ansiedade comórbidos em vítimas de violência com transtorno do estresse pós-traumático

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### Abstract

**Objective:** To review studies that have evaluated the comorbidity between posttraumatic stress disorder and mood disorders, as well as between posttraumatic stress disorder and other anxiety disorders. **Method:** We searched Medline for studies, published in English through April, 2009, using the following keywords: "posttraumatic stress disorder", "PTSD", "mood disorder", "major depressive disorder", "major depression", "bipolar disorder", "dysthymia", "anxiety disorder", "generalized anxiety disorder", "agoraphobia", "obsessive-compulsive disorder", "panic disorder", "social phobia", and "comorbidity". **Results:** Major depression is one of the most frequent comorbid conditions in posttraumatic stress disorder individuals, but individuals with posttraumatic stress disorder are also more likely to present with bipolar disorder, other anxiety disorders and suicidal behaviors. These comorbid conditions are associated with greater clinical severity, functional impairment, and impaired quality of life in already compromised individuals with posttraumatic stress disorder. Depression symptoms also mediate the association between posttraumatic stress disorder and severity of pain among patients with chronic pain. **Conclusion:** Available studies suggest that individuals with posttraumatic stress disorder are at increased risk of developing affective disorders compared with trauma-exposed individuals who do not develop posttraumatic stress disorder. Conversely, pre-existing affective disorders increase a person's vulnerability to the posttraumatic stress disorder--inducing effects of traumatic events. Also, common genetic vulnerabilities can help to explain these comorbidity patterns. However, because the studies addressing this issue are few in number, heterogeneous and based on a limited sample, more studies are needed in order to adequately evaluate these comorbidities, as well as their clinical and therapeutic implications.

**Descriptors:** Comorbidity; Stress disorders, post-traumatic; Anxiety disorders; Mood disorders; Violence

### Resumo

**Objetivo:** Buscar estudos que avaliem a comorbidade entre transtorno de estresse pós-traumático e transtornos do humor, bem como entre transtorno de estresse pós-traumático e outros transtornos de ansiedade. **Método:** Revisamos a base de dados do Medline em busca de estudos publicados em inglês até abril de 2009, com as seguintes palavras-chave: "transtorno de estresse pós-traumático", "TEPT", "transtorno de humor", "transtorno depressivo maior", "depressão maior", "transtorno bipolar", "distímia", "transtorno de ansiedade", "transtorno de ansiedade generalizada", agorafobia, "transtorno obsessivo-compulsivo", "transtorno de pânico", "fobia social" e "comorbidade". **Resultados:** Depressão maior é uma das condições comórbidas mais frequentes em indivíduos com transtorno de estresse pós-traumático, mas eles também apresentam transtorno bipolar e outros transtornos ansiosos. Essas comorbidades impõem um prejuízo clínico adicional e comprometem a qualidade de vida desses indivíduos. Comportamento suicida em pacientes com transtorno de estresse pós-traumático, com ou sem depressão maior comórbida, é também uma questão relevante, e sintomas depressivos mediam a gravidade da dor em sujeitos com transtorno de estresse pós-traumático e dor crônica. **Conclusão:** Os estudos disponíveis sugerem que pacientes com transtorno de estresse pós-traumático têm um risco maior de desenvolver transtornos afetivos e, por outro lado, transtornos afetivos pré-existent aumentam a propensão ao transtorno de estresse pós-traumático após eventos traumáticos. Além disso, vulnerabilidades genéticas em comum podem ajudar a explicar esse padrão de comorbidades. No entanto, diante dos poucos estudos encontrados, mais trabalhos são necessários para avaliar adequadamente essas comorbidades e suas implicações clínicas e terapêuticas.

**Descritores:** Comorbidade; Transtorno de estresse pós-traumático; Transtornos de ansiedade; Transtornos do humor; Violência

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## Introduction

Victims of violence commonly develop posttraumatic stress disorder (PTSD), an often chronic condition, associated with severe morbidity and psychosocial impairment. The description of PTSD in DSM-III and in subsequent DSM editions (American Psychiatric Association 1980, 1987, 1994) defines a syndrome that develops in response to a specific class of stressors, which is catastrophic or traumatic events which are distinguished from normal stressful life events, such as loss of job or marital discord. On the other hand, any psychological stressors, either those that meet the requirements for the definition of PTSD and those that do not, might precipitate major depression. Additionally, unlike PTSD, a major depression can occur regardless of stressors, and does not require an etiologic event as an essential factor.<sup>1</sup>

Data from the National Comorbidity Survey in the United States of America<sup>2</sup> have demonstrated that PTSD is associated with unemployment or educational impairment, and commonly co-occurs with other psychiatric disorders, pointing out that 88.3% of men and 79.0% of women with PTSD also meet criteria for at least one other psychiatric diagnosis. For example, comorbid major depressions have been reported in 30% to 50% of people diagnosed with PTSD.<sup>2-4</sup> In addition, PTSD is not the only psychopathological consequence of violence. Dutra et al. have reported that childhood abuse and chronic interpersonal trauma have frequently been associated with a risk of developing a wide range of psychiatric disorders, including mood, dissociative, addictive, eating and personality disorders.<sup>5</sup> According to Brady, PTSD is especially likely to overlap with mood disorders, other anxiety disorders, somatization, substance abuse and dissociative disorders, and she concluded that individuals with PTSD should always be screened for psychiatric comorbidity.<sup>6</sup>

A longitudinal study examining the developmental mental health histories of adults with PTSD has observed that almost all the adults diagnosed with PTSD were diagnosed previously with another mental disorder. Most of these PTSD individuals had received another mental-disorder diagnosis by the age of 15 and these rates of lifetime comorbidity were higher than those observed for many other common mental disorders.<sup>7</sup> Besides common environmental risk factors, genetic influences on PTSD overlap with those on other psychiatric disorders.<sup>8</sup> The limited data available suggest that the majority of genes that affect risk for PTSD are also associated with other psychiatric disorders.

It is common knowledge that overlapping psychiatric disorders may be associated with additional social and occupational disability. In fact, Olfson et al. have carried out a cross-sectional study to assess disability associated with several mental disorders in outpatients, and have shown that, compared with patients who had a single mental disorder, patients with co-occurring disorders reported significantly more disability in social and occupational functioning.<sup>9</sup> It is still controversial whether PTSD has a single effect on disability and quality of life after adjusting for other common mental disorders. Nevertheless, Sareen et al., studying the impact of PTSD on comorbidity, disability, and suicidality in a large sample of the general population, concluded that PTSD was not only associated with significant comorbidity with mental and physical health conditions but was also related to higher disability and suicidality, even when the influence of comorbidities was controlled.<sup>10</sup>

This paper aims to conduct a review of studies which evaluated comorbidity between PTSD and mood disorders (major depressive disorder and bipolar disorder), as well as between PTSD and anxiety disorders.

## Method

We conducted a bibliographic research study of articles investigating mood and anxiety disorder comorbidity in victims of violence with PTSD, published in English up to April 2009 (excluding specific phobias). Articles were searched on Medline databases, with the following keywords: "posttraumatic stress disorder," "PTSD," "mood disorder," "major depressive disorder," "major depression," "bipolar disorder," "dysthymia," "anxiety disorder," "generalized anxiety disorder," "agoraphobia," "obsessive-compulsive disorder," "panic disorder," "social phobia" and "comorbidity." Relevant studies in the references of the articles were also obtained.

## Results

To examine the comorbidity between PTSD and depression and, PTSD and anxiety disorders in victims of violence, we summarized the literature (26 articles).

### 1. Comorbid PTSD with mood disorders

#### 1) Major depressive disorder

Although some stressors might precipitate major depressive disorder (MDD), this affective disorder occurs in the absence of stressors and, unlike PTSD, does not demand an etiologic event as an essential factor.<sup>1</sup> Depression is one of the most common comorbid conditions associated with PTSD, and is typically present in 30-50% of PTSD cases. Individuals with both PTSD and comorbid depression usually have worse outcomes following treatment than individuals without PTSD.<sup>2,11-17</sup>

Salcioglu et al. achieved a reasonably clear separation between PTSD and depression symptoms, except for the symptoms shared by both disorders (loss of interest, memory and concentration problems, irritability and sleep disturbance).<sup>18</sup> The compositions of the two groups of symptoms were very similar to those observed in previous studies.<sup>19-21</sup> The authors grouped together the symptoms of re-experiencing, cognitive and behavioral avoidance, and hypervigilance, whereas the numbing and depressive symptoms were loaded on a separate factor, together with emotional numbing, detachment, sense of a foreshortened future, sleep difficulties, irritability, and memory and concentration difficulties. These symptoms are very reminiscent of depression, and based on studies with other trauma populations,<sup>22-24</sup> Salcioglu et al. suggested that numbing symptoms should not be classified with avoidance symptoms in DSM-V.<sup>18</sup>

Enduring grief-related reactions (Complicated Grief - CG) are a controversial and multidimensional disorder that has been conceptualized as a more involved combination of depression and PTSD,<sup>25,26</sup> especially when bereavement follows a violent death, such as by homicide or terrorist attack. In the current edition of the Diagnostic and Statistical Manual of Mental Disorders (2000), grief-related reactions are diagnosed as depression, posttraumatic stress disorder, or another anxiety disorder.<sup>27</sup>

In sharp contrast to this view, there is a growing movement among some bereavement researchers and theorists to elevate CG to a separate

and unique diagnostic entity,<sup>28,29</sup> arguing that existing treatments for either depression or PTSD are not efficacious for cases of severe, lasting grief reactions,<sup>30</sup> and that, in general, CG and PTSD symptoms exhibited opposite reactions to heart rate and autonomic reactivity response:<sup>31</sup> PTSD heightened autonomic response to cues that served as reminders of the traumatic event, whereas intense grief reactions were associated with reduced autonomic reactivity to cues of the loss.<sup>32</sup>

Animal studies have shown that infants separated from their mother exhibit an initial spike in arousal followed by a similar prolonged pattern of cardiovascular inhibition.<sup>33,34</sup> The same type of autonomic pattern appears to characterize human separation responses.<sup>35,36</sup> Pairing this response with CG symptoms may suggest that the absence of cardiovascular responsiveness could be a consequence of acute separation distress and preoccupation with the loss.<sup>32,37</sup> Instead of being an opposite reaction, the lack of cardiovascular responsiveness could be understood as an effect of a chronic and cumulative autonomic stress.<sup>38</sup>

In an experiment with Norway rats, Richter observed that the first response to stress was an increased heart rate, followed by slowing of heart rate and death, due to intense vagal discharge, when the stress situation was sustained.<sup>39</sup>

There was no agreement in the reviewed literature as to the best explanation for the association between PTSD and MDD. Prospective studies have supported several alternative explanations: 1) pre-existing MDD increases a person's propensity to the PTSD-inducing effects of traumatic events;<sup>40,41</sup> 2) PTSD increases the risk of the first onset of MDD;<sup>2,40</sup> 3) MDD increases the risk of exposure to traumatic events,<sup>40</sup> as it does for exposure to ordinary stressful life events;<sup>42</sup> 4) PTSD and MDD share genetic or environmental vulnerabilities.

Regarding environmental shared vulnerabilities, traumatic events leading to PTSD might also amplify the risk for major depression.<sup>4</sup> In addition to traumatic events, other factors have been associated with increased risk of both PTSD and MDD. For example, psychological aggression has been significantly related to depressive symptoms.<sup>14,43-45</sup> PTSD is highly prevalent in women exposed to intimate partner violence (IPV). This condition is associated with dysfunction resulting in problems in self maintenance, and difficulty in leaving home. Astin et al. reported prevalence rates of PTSD among battered women of up to 58%.<sup>46</sup> Johnson et al. have conducted a cross-sectional study with a sample of 177 battered women from a refuge to investigate the contribution of IPV severity and IPV-related PTSD severity on these women's psychiatric morbidity (i.e., comorbidity and psychiatric severity) and social damage. Their results were consistent with other studies, and IPV severity was related to several indices of impairment as well as to PTSD severity. However, when controlling for IPV severity, PTSD severity was significantly related to a higher degree of psychiatric morbidity and higher levels of social dysfunction. PTSD severity also significantly mediated the relationship between IPV severity and the severity of psychiatric disorders, as well as loss of resources.<sup>47</sup>

This finding is not surprising, given the probable effect of psychological aggression on an individual's sense of self, particularly on beliefs regarding self-esteem, competence, and worth. Intense threat or fear-provoking language may create intense and immobilizing shame, with a consequent schema that undermines the use of social networks and support to ameliorate psychological pain. Nixon et al. support the belief that cognitions and schemata may play an important role in understanding why depression that

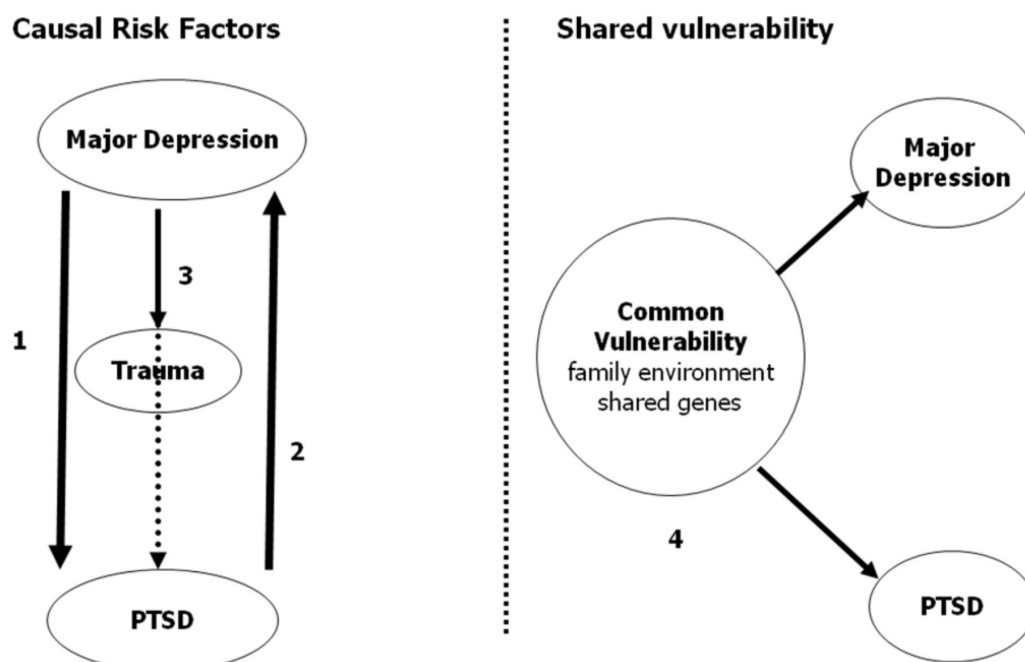


Figure 1 - The Association Between PTSD and Major Depression

develops in the context of PTSD is more critical than a general negative cognitive style, since it is directly related to trauma.<sup>14</sup> Dunmore et al. suggest that depression precedes dysfunctional schemata, as a cognitive vulnerability that is manifested through maladaptive interpretation,<sup>48</sup> sometimes evidenced even before the onset of depression.<sup>49</sup> This creates a sense of helplessness that accounts for the higher scores on depression and somatic symptom scales.

Individuals with comorbid PTSD and MDD seem to have more maladaptive depressogenic cognitive styles than individuals with PTSD alone.<sup>14</sup> Trauma-related guilt, particularly observed in the context of rape victims,<sup>50,51</sup> Vietnam veterans<sup>52</sup> and victims of intimate partner violence,<sup>53</sup> has been observed to be more strongly associated with depressive symptomatology than is PTSD, and excessive or inappropriate guilt is a symptom of depression.<sup>54</sup> Andrews suggests that shame brings about abusive experiences, then guilt and later, depression.<sup>55</sup>

The findings of Vranceanu et al., in a sample of children suffering multiple forms of abuse and neglect, suggest again that MDD and PTSD may have two different developmental mechanisms, where stress plays a central role in the development of depression, as the lack of social support does in the development of PTSD.<sup>56</sup> Nonetheless, there is a high correlation between stress and social support, which highlights the vulnerability that one disorder creates, allowing the development of the other. People with a history of childhood maltreatment are more susceptible to the effects of daily stressors,<sup>57</sup> and these individuals report more stress when compared to their non-maltreated counterparts.<sup>58</sup> Moreover, survivors of maltreatment may perceive life events as more stressful because of their predisposition to a pervasive sense of helplessness<sup>59</sup> and to decreased coping resources.<sup>60,61</sup> Usually they have smaller support networks, which they find unsatisfactory.<sup>58,62</sup> One potential explanation for these effects is that maltreatment causes distortions in children's cognitions regarding themselves and others. These distortions become internalized, leading to unhealthy adult relationships.<sup>63</sup> It is also likely that maltreated children have less actual support in adulthood because their potential family support is limited; their parents and siblings may have been the perpetrators, or may themselves have suffered maltreatment experiences,<sup>64</sup> and thus may be ineffectual as support providers.<sup>65</sup> In addition, often children who have been maltreated grew up in dysfunctional family environments, and may have poor scripts for healthy adult relationships.<sup>64</sup>

The role of social resources in psychological adjustment to trauma/stressful events/bereavement is further demonstrated by Holohan et al. via two longitudinal studies conducted on victims of natural disasters. They found that losses of interpersonal and personality resources were directly predictive of depressive symptoms over the course of an extended period of years.<sup>66,67</sup> Basoglu, Salcioglu and Livanou showed that a behavioral intervention designed to enhance a sense of control over fear reduces both PTSD and depressive symptoms.<sup>68</sup> However, depression resulting from resource loss might require social support and compensation for losses before there is any improvement.

Livanou et al. amplify the connection between loss and depression, postulating that, while depression might be due to bereavement,

it might be secondary to PTSD in other stressful events.<sup>20</sup> The fact that 24% of non-bereaved individuals in the traumatized sample of Salcioglu et al. had depression supports this hypothesis.<sup>18</sup> From this perspective, secondary depression might be related to helplessness generated by symptoms of chronic PTSD, exposure to numerous unpredictable and uncontrollable aftershocks, and anticipatory fear of a future traumatic experience,<sup>69</sup> which creates the sense of losing management and control.

Imported data from natural-disaster studies can help to clarify the relationship between trauma and depression. Salcioglu et al., in their study of earthquake survivors in Turkey, showed through linear regression analyses that depression was especially related to loss (of family members), while PTSD was strongly related to fear during the earthquake.<sup>18</sup>

As we can see, social support and stress are inversely correlated. This would suggest that victims of maltreatment may not only suffer impairment in their ability to develop basic social support structures, but also may become more vulnerable to stressors and additional losses (e.g., material or personal losses).

Besides the environmental vulnerabilities shared by PTSD and MDD, data from the Vietnam Era Twin Registry suggests that MDD is the psychiatric disorder with the largest overlap with genetic influences associated with PTSD. Genetic influences on major depression account for 100% of the genetic variance in PTSD.<sup>70</sup> The serotonin transporter promoter S/S polymorphism is implicated in both disorders.<sup>71</sup> Polymorphisms in FKBP5, a glucocorticoid-regulating cochaperone of stress proteins, which were associated with recurrence of major depressive episodes and response to antidepressant treatment<sup>72</sup> have also been associated with peritraumatic dissociation<sup>73</sup> (a risk factor for PTSD) and depression in medically injured children.

#### 2) PTSD, depression and chronic pain

Depression as a possible mediator for chronic pain in PTSD was the focus of the Poundja et al. study with male veterans.<sup>74</sup> High co-occurrence rates of pain and PTSD have been found in samples of war veterans treated in PTSD clinics,<sup>75,76</sup> with a striking 80% rate of chronic pain, and the Poundja et al. study suggests that 89.5% of the effect of PTSD on pain is mediated by depression.<sup>74</sup>

#### 3) Suicidal behavior

Both PTSD and major depressive episodes are individually associated with a risk of suicidal behavior. Lifetime prevalence of suicide attempts in a sample with major depressive episodes is approximately 16%.<sup>77</sup> In a community survey, patients with PTSD were 14.9 times more likely to attempt suicide than subjects without PTSD.<sup>3,78</sup> There is no study evaluating the prevalence of suicidal behaviors in a sample with comorbid PTSD and MDD. PTSD Individuals with comorbid BD also present an additional risk, and must be carefully evaluated for suicide risk by mental health professionals.<sup>79,80</sup>

#### 4) Bipolar disorder

Several studies have shown that bipolar disorder (BD) subjects are at high risk for experiencing traumatic events. This may be due to disruptive behavior during mania or to increased childhood trauma history.<sup>81-83</sup> As a result, BD patients usually report high rates of lifetime PTSD ranging from 16% to 39% in BD-I patients evaluated in the National Comorbidity Survey-Replication<sup>84,85</sup>



Moreover, if the traumatic event occurs during manic or hypomanic phases, there is a higher probability of PTSD symptoms developing afterwards.<sup>86</sup> Recent studies suggested that a history of trauma may be related to BD's etiology and prognosis.<sup>84</sup> For example, early parental loss has been identified as a risk factor for BD.<sup>87</sup> High-impact trauma has been associated with poor BD prognosis.<sup>88</sup>

Little is known about the quality of life (QoL) impairment and clinical consequences imposed by PTSD on bipolar patients. It is hypothesized that characteristics of PTSD have a substantial impact on the course of BD due to its nature, which contributes to raising the emotional instability in BD patients' lives.<sup>84</sup> At the baseline evaluation for a study, bipolar patients with comorbid PTSD were less likely to be found in recovery (relative euthymia).<sup>89</sup> Also, BD patients with PTSD frequently have sleep impairment, with consequent chronic over-arousal. It has a direct impact on the course of BD,<sup>82</sup> and is indicative of poorer coping with PTSD symptoms.<sup>90</sup>

Higher rates of comorbidity with anxiety disorders, specifically with PTSD,<sup>89,91</sup> have been found to be an important factor associated with poorer QoL among BD patients.<sup>92</sup> Overall, the magnitude of BD's impact on QoL seems to be similar to the impact of chronic diseases (e.g., chronic renal disease or rheumatoid arthritis).<sup>93</sup> Despite the fact that lower QoL scores are likely to be found during the depressive phase in BD patients,<sup>94-97</sup> some factors such as manic symptoms,<sup>98</sup> being of the female gender,<sup>99</sup> and affective conditions such as cyclothymia,<sup>100</sup> can influence the self-perception of QoL. Additionally, even BD patients in remission show impaired self-reporting of QoL,<sup>101-103</sup> indicating that other factors besides mood symptoms may influence QoL in BD patients.<sup>97</sup>

## 2. Comorbid PTSD with other anxiety disorders

Following the same lines as for MDD comorbidity, the explanation for the comorbidity between PTSD and other anxiety disorders is still unclear. Traumatic events can be a shared environmental trigger for other anxiety disorders besides PTSD. Brady has reported that exposure to family violence is associated with symptoms of posttraumatic stress and anxiety among youth.<sup>104</sup> Kar and Bastia have conducted a study aimed at finding the prevalence of post-traumatic psychiatric disorders such as PTSD, major depressive disorder, generalized anxiety disorder and possible comorbidities in a group of adolescent students in rural areas, 14 months after a natural disaster. They also studied the association of these morbidities with sociodemographic factors, and their impact on school performance. The study demonstrated that adolescents exposed to a natural disaster exhibited a mix of PTSD, depression and anxiety symptoms and high comorbidity of diagnoses. Nevertheless, Kar and Bastia did not succeed in proving any association between these morbidities and impairment of performance in school.<sup>105</sup>

Moreover, genetic influences common to generalized anxiety disorder and panic disorder symptoms account for approximately 60% of the genetic variance in PTSD.<sup>106</sup>

It is also possible that pre-existent anxiety disorders increase the risk for trauma exposure, and subsequently, PTSD. Silver et al. carried out a study to examine the association between victimization of people with and without a mental disorder. Compared with people with no mental disorder, people with anxiety disorders experienced more sexual assaults.<sup>107</sup> These findings were controlled

for psychiatric comorbidity, demographic characteristics, and for participants showing violent behavior.

On the other hand, Marshall et al. conducted a study with the National Screening Day for Anxiety Disorders sample to investigate the relationship between PTSD symptoms, level of disability, and comorbid anxiety or depressive disorders. They observed that functional impairment, number of anxiety disorders, rates of comorbid major depressive disorder, and current suicidal ideation increased linearly and significantly with a higher number of subthreshold PTSD symptoms.<sup>108</sup>

## Discussion

There is a high comorbidity rate between PTSD and other anxiety or mood disorders.

An explanation for the link between PTSD and unipolar MDD/ other anxiety disorders may be related to gender. Many studies have demonstrated that female gender is an important risk factor for the development of PTSD.<sup>109</sup> Data from the National Comorbidity Survey<sup>2</sup> have shown that lifetime prevalence of PTSD is more than double in women in comparison with men (10.4% vs. 5.0%;  $p < 0.05$ ).

Complementarily, some arguments focus on differences in types of exposure. When the violence is performed by the intimate partner, it contributes significantly to the emergence of PTSD in the female population.<sup>110</sup> Edwards et al. found that lower scores on the mental health domain of the SF-36 quality of life questionnaire were associated with more categories of abuse (sexual, physical and emotional abuse), which is exactly the type of traumatic experience most frequently found in women.<sup>111</sup> Oquendo et al. found that among 156 inpatients with major depression, those with comorbid lifetime PTSD were more likely to have attempted suicide than those without comorbid PTSD (75% vs. 54%;  $p \leq 0.01$ ), and among the group with PTSD, the risk of a suicide attempt was higher among women.<sup>112</sup>

Besides this, pre-existing MDD or another anxiety disorder was found to predict trauma exposure.<sup>113</sup> The likelihood of developing PTSD after traumatic exposure also seems to be significantly higher in this population.<sup>114</sup>

Psychiatric disorders also have been understood as a vulnerability factor for developing another psychiatric disorder after exposure to violence. Several studies were conducted aimed at identifying risk factors for trauma vulnerability and developing psychiatric disorders. Breslau reviewed epidemiological studies of PTSD in the general population and identified pre-existing psychiatric disorders, family history of disorders and childhood abuse as risk factors for PTSD in adults.<sup>115</sup> Gabriel et al. carried out a cross-sectional study to assess the prevalence of PTSD, major depression and other anxiety disorders after a terrorist attack, among three groups with different levels of exposure: people injured in the attacks, city residents not injured, and police officers involved in the rescue effort. The proportion of patients who had a current psychiatric disorder was: 5% among the injured and 9% among the non-injured individuals. Those who had a comorbid mental disorder were 8% among the injured group, and 22% among the non-injured group. The most frequent comorbid mental disorder with PTSD was depression, followed by agoraphobia. After multivariate analyses, the use

**Table 1 - Mood and anxiety disorders comorbidity in victims of violence with PTSD**

Study	Study profile	Study population	Main data
Bonanno et al. (2007)	1st study: longitudinal, and the 2nd study: cross-sectional	Bereaved participants living in the Washington, DC	Traumatic events heightens autonomic reactivity response, and losses reduce autonomic reactivity
Fedovsky et al. (2007)	Cross-sectional	Latino immigrant women assessed at a primary care	Patients meeting PTSD criteria have 10 times more likelihood in reporting MDD as well
Nishith et al. (2005)	Prospective	Female rape victims	Trauma-related guilt has been more associated with MDD symptomatology than with PTSD
Nixon et al. (2004)	Cross-sectional	Physically abused women recruited from local domestic violence assistance agencies and shelters	MDD is typically present in 30-50% of PTSD cases, resulting in poorer treatment outcome than individuals with PTSD alone
Oquendo et al. (2005)	Retrospective, cross-sectional	Subjects with lifetime history of MDD and MDD comorbid with PTSD	Patients with MDD and PTSD are 14.9 times more likely to attempt suicide than those having MDD without PTSD
Poundja et al. (2006)	Cross-sectional	French-Canadian male veterans assessed at an outpatient clinic	Depression was a possible mediator for chronic pain in patients with PTSD
Varma et al. (2007)	Cross-sectional study	Pregnant women attending an antenatal clinic in a public hospital	Psychological aggression was significantly related to MDD symptoms
Vranceanua et al. (2007)	Retrospective, cross-sectional	Women recruited from a gynecological treatment center for low-income women located in the inner city of a mid-sized city	Stress appeared central in the development of depression, as did social support in the development of PTSD
Kessler et al. (1995)	Cross-sectional	General population	The estimated lifetime prevalence of PTSD is 7.8
Dutra et al. (2008)	Cross-sectional	Outpatients at a treatment program for trauma survivors of a community hospital	Significant correlations were found between Young Schema Questionnaire scales and the post-traumatic diagnostic scale
Koenen et al. (2008)	Cohort	Children Born during a 1-year period in 1972-73 in Dunedin, New Zealand	PTSD almost always develops in the context of previous mental disorders
Olfson et al. (1997)	Cross-sectional	Primary care patients	Compared with patients who had a single mental disorder, patients with co-occurring PTSD and other disorders reported significantly more disability in social and occupational functioning
Sareen et al. (2007)	Cross-sectional	Canadian Community Health Survey	PTSD was found to have a unique impact on several measures of short- and long-term disability, overall well-being, and suicide attempts
Marshall et al. (2001)	Cross-sectional	Individuals screened for affective and anxiety disorders at 1,521 sites across the United States	Impairment, number of comorbid disorders, rates of comorbid major depressive disorder, and current suicidal ideation increased linearly and significantly with each increasing number of subthreshold PTSD symptoms
Johnson et al. (2008)	Cross-sectional	Residents of a battered women's shelter	PTSD severity was associated with considerable psychiatric morbidity, social maladjustment, and personal and social resource loss
Brady (2008)	Cross-sectional	University students	Depression and anxiety may play a role in the development and maintenance of eating disorder subsequent to repeated incidents of family violence exposure
Floen and Elklit (2007)	Cross-sectional	Patients in a psychiatric hospital	Ninety-one percent had been exposed to at least one Trauma; 69 percent had been repeatedly exposed to trauma for longer periods of time
Kar et al. (2006)	Cross-sectional	All the students studying in standard nine and ten of two high schools	The prevalences of PTSD, major depressive disorder and generalised anxiety disorder were 26.9%, 17.6% and 12.0% respectively
Gabriel et al. (2007)	Cross-sectional	Three groups of persons with different exposure to the March 11, 2004 terrorist attacks in Madrid	The use of psychoactive medication was consistently the main predictor of PTSD and major depression among those injured and of major depression and anxiety disorders others than PTSD
Silver et al. (2005)	Cohort	Study participants were born in Dunedin, New Zealand, between April 1972 and March 1973	Mentally disordered young adults tend to experience more violent victimization in the community than those without a mental disorder
Dean et al (2007)	Cross-sectional	Individuals with chronic psychosis living in the community in four urban UK centres	The 2-year prevalence of violent victimization in the sample was 23%. Factors were found to be predictive of victimization: history of victimization, less than daily family contact, young age at illness onset and the presence of co-morbid Cluster B personality disorder
Kessler et al. (1997)	Cross-sectional	General population	Respondents with bipolar I characterized by euphoria, grandiosity, and excessive energy
Mueser et al. (1998)	Cross-sectional	Inpatient and outpatient bipolar patients	PTSD Checklist, administered in an interview format might be considered less valid than those obtained from structured interviews
Neria et al. (2002)	Cross-sectional	Bipolar patients: first admission for psychosis	The findings highlight the importance of systematically ascertaining trauma histories in patients with psychotic disorders
Neria et al. (2008)	Cross-sectional	A systematic sample of adult primary care patients from an urban general medicine practice	Trauma exposure was related to bipolar disorder, and the frequency of PTSD among Patients with bipolar disorder appears to be common and clinically significant
Simon et al. (2003)	Cross-sectional	Bipolar I and II, treatment-seeking outpatients in the Systematic Treatment Enhancement Program for bipolar disorder	An independent association of comorbid anxiety with greater severity and impairment in bipolar disorder patients was demonstrated

of psychoactive medications before the attack was a significant predictor of PTSD and depression among the injured individuals; history of psychiatric disorder and female gender, among the non-injured ones.<sup>116</sup> The Gabriel et al. study provides strong evidence of an association between previous psychiatric disorder (major depression and anxiety disorder), or previous use of psychoactive medications, and subsequent psychopathology.

On the other hand, traumatic experiences and PTSD may have a higher impact on the development and course of other psychiatric disorders. A case report describes how a patient with no psychiatric history developed PTSD, depression and obsessive-compulsive disorder (OCD) after a serious work accident.<sup>117</sup> Additionally, according to McFarlane & Bookless, patients with a lifetime history of PTSD have eight times the risk for anxiety disorders compared to those without such history.<sup>118</sup> The question of whether traumatic events increase the risk for MDD, independently of their PTSD effects, would be clarified if a significantly higher incidence were found of major depression in individuals who were exposed to trauma but did not develop PTSD, as compared with people who were not exposed. Such evidence would suggest that the depressive consequence of traumatic events might have a distinct pathway, separate from that of PTSD.

On the other hand, evidence of an increased risk of the subsequent onset of MDD 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.<sup>1</sup>

Are those two risk factors for PTSD (female gender and preexistent anxiety/depression disorder) related? Kessler et al. found, in the data from the National Comorbidity Survey, that while men showed a predominance of alcohol or substance abuse/dependence in comorbidity with PTSD, women presented a predominance of comorbid anxiety disorders.<sup>2</sup>

PTSD also shares genetic vulnerabilities with other anxiety disorders and MDD. A family history of psychiatric disorders is a consistent risk factor for developing PTSD.<sup>115</sup> Pre-existing psychiatric disorders, particularly conduct disorders, major depression and nicotine dependence, also increase PTSD risk.<sup>119</sup> At the same time, PTSD increases the risk of first-onset major depression<sup>1</sup> as well as alcohol, drug, and nicotine dependence.<sup>115</sup> The incidence of other psychiatric disorders is no higher in individuals who experience trauma but do not develop PTSD. This fact has led to the suggestion that PTSD represents a generalized vulnerability to psychopathology following trauma.<sup>115</sup>

Finally, in terms of screening, preventive approaches through the assessment of the personal history of trauma in high-risk populations is fundamental to the investigation of the impact of violence on children's neurodevelopment and the profound negative functional consequences of trauma in the child's brain. Since violence can permanently alter neurogenesis, migration synaptogenesis, and neurochemical differentiation, the course of development of the brain over time is the key to grasping the relationship between exposure to violence in infancy and the emergence of the symptoms. This fact has implications for psychopathological outcomes, clinical assessment, research, intervention and prevention. Therefore, more research is needed into designing new treatment interventions,<sup>120</sup>

not only focused on treating symptoms but also on restoring the child's mental health during puberty, when the brain still has a degree of plasticity.<sup>121</sup>

### Conclusion

Available studies suggest that PTSD patients have a higher risk of developing affective disorders and, conversely, that pre-existing affective disorders increase a person's propensity to the PTSD-inducing effects of traumatic events. Considering the broad variety of disorders related to PTSD and its high rates of co-occurrence, one question arises about whether they constitute a single wide phenotype with the same etiology or whether there are different classes of disorders with different etiologies. However, there are only a few studies addressing this issue, and most of them have worked with small sample sizes and different methodologies, which may limit the generalizability of the results.

## Disclosures

Writing group member	Employment	Research grant <sup>1</sup>	Other research grant or medical continuous education <sup>2</sup>	Speaker's honoraria	Ownership interest	Consultant/ Advisory Board	Other <sup>3</sup>
Lucas C. Quarantini	UFBA	-	-	-	-	-	-
Liana R. Netto	Private practice	-	-	-	-	-	-
Monica Andrade-Nascimento	UEFS	-	-	-	-	-	-
Amanda Galvão-de Almeida	Private practice	-	-	-	-	-	-
Aline S. Sampaio	USP	-	-	-	-	-	-
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\*Modest

\*\* Significant

\*\*\* Significant. Amounts given to the author's and institution or to a colleague for research in which the author has participation, not directly to the author.

Note: UFBA = Universidade Federal da Bahia; UEFS = Universidade Estadual de Feira de Santana; USP = Universidade de São Paulo; UNIFESP = Universidade Federal de São Paulo; CNPq = Conselho Nacional de Desenvolvimento Científico e Tecnológico; FAPESP = Fundação de Amparo à Pesquisa do Estado de São Paulo; NIMH = National Institute of Mental Health.

For more information, see Instructions for authors.

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