PTSD DEPRESSION REVIEW OF STUDIES DONE IN SUB SAHARA ARICA

BY

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DECLARATION

I, Dr Abdulkadir Hussein Warsame do hereby declare that this is my original postgraduate diploma in clinical psychiatry work and that I have not presented the same to any other university

Signed _____ Date 14th Nov 2021

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Abbreviations

PTSD: post traumatic stress disorder

MDD: major depressive disorder

IPV: intimate partner violence

LMICs: low and medium income countries

IDP: internally displaced people

DSM: diagnostic and statistic manual

POW: prisoner of war

WHO: world health organization

ICD: international classification of diseases

USA: United States of America

CIDI: composite diagnostic intermittent interview

TS: traumatic stressors

HIC: high income countries

ECA: epidemiological catchment area

PTSD, DEPRESSION: A REVIEW OF STUDIES DONE IN SUB-SAHARAN AFRICA

Definition of Post-Traumatic Stress Disorder (PTSD)

Posttraumatic stress disorder (PTSD) is the most common psychiatric disorder that can develop after a person is exposed to a traumatic event, such as sexual assault, warfare, traffic collisions, child abuse, or other threats on a person's life. Symptoms may include disturbing thoughts, feelings, or dreams related to the events, mental or physical distress to trauma-related cues, attempts to avoid trauma-related cues, alterations in how a person thinks and feels, and an increase in the fight-or-flight response. These symptoms last for more than a month after the event. Young children are less likely to show distress, but instead may express their memories through play.

Definition of Depression

Depression is a mood disorder that causes a persistent feeling of sadness and loss of interest. Also called major depressive disorder or clinical depression, it affects how you feel, think and behave and can lead to a variety of emotional and physical problems. You may have trouble doing normal day-to-day activities, and sometimes you may feel as if life isn't worth living.

SUMMARY

Approximately half of people with post-traumatic stress disorder (PTSD) also suffer from depression which is a Major Depressive Disorder (MDD). The current paper examines evidence for two explanations of this comorbidity. First, that the comorbidity reflects overlapping symptoms in the two disorders. Second, that the co-occurrence of PTSD and MDD is not an artifact, but represents a trauma-related phenotype, possibly a subtype of

PTSD. Support for the latter explanation is inferred from literature that examines risk and biological correlates of PTSD and MDD, including molecular processes. Treatment implications of the comorbidity are considered.

Posttraumatic stress disorder (PTSD) and depression comorbidity is highly common. Many hypotheses concerning this relation have been raised but the pertinent issues, including the wide clinical picture of this comorbidity, are still not clear. They are also arguably the most common psychiatric disorders such as depression to arise after exposure to a traumatic event. Approximately half of people with post-traumatic stress disorder (PTSD) also suffer from Major Depressive Disorder (MDD). Although there are many factors associated with symptom severity, including PTSD and depression comorbidity, there is no agreement in the literature on the generalizability of these factors across different populations. Therefore, the knowledge of population-specific findings would be more appropriate and helpful to address the clinical difficulties associated with PTSD and depression comorbidity in different populations.

INTRODUCTION

Comorbidity between post-traumatic stress disorder (PTSD) and major depressive disorder is common, with approximately half of people with PTSD also having a diagnosis of major depressive disorder (MDD) across diverse epidemiological samples [1-4]. An alternative view is that the co-occurrence of PTSD and MDD represents a trauma-related phenotype that is distinct from MDD and reflects a fundamental dimension of risk for psychopathology following trauma exposure. Support for this explanation is less straightforward, but can be inferred from the research literature examining risk factors and biological correlates for the individual disorders, and where possible, for the comorbidity.

STUDIES ON TRAUMA

Suffering a traumatic event is very common in the societies, as suggested by many previous studies [1–4]. Among the most commonly identified sequelae of traumatic events are depression and post-traumatic stress disorder (PTSD). Approximately 50–90% of people experience a traumatic event in their lifetime; however, only 8–12% of people will go on to develop PTSD [3, 5]. In the majority of cases (74%), PTSD persists longer than 6 months, and women have been found to suffer from PTSD symptoms longer than men [5]. An individual's vulnerability to PTSD depends upon the severity of the trauma [6], childhood experiences, biological diathesis and co-morbid factors such as personality disorders, substance abuse, medical illness or depression [7]. Vasterling et al. demonstrated that the clinical impact of PTSD extends well beyond the defined PTSD symptomatology boundary and has been associated with a higher risk of somatic symptoms and medical illnesses [8]. Thus, PTSD has a negative impact on an individual's occupational and psychosocial functioning. Also, the presence of PTSD predisposes individuals to comorbid depression [9, 10].

Depression is a common mental illness that affects more than 20% of Americans at some point in their lifetime. Despite its high prevalence in the general population, depression still remains misunderstood, under-reported and largely untreated [11]. The direct and indirect impact of depression accounts for more than US$ 100 billion per year, which is ranked second only to cancer [12]. Depression has been linked to multiple physical symptoms, unsatisfactory health status and functioning, poor prognosis, and increased medical utilization and costs [12, 13]. PTSD with depression is very common in those who have been exposed to war [15], disaster [15] and intimate partner violence (IPV) [16], when compared with the general population [27].

Over 80% of PTSD cases are comorbid with other mental disorders or medical illnesses [18]. The most commonly reported PTSD comorbidities are anxiety, personality disorders, substance abuse, medical illness and depression [19]. The relationship between symptom severity and a dual diagnosis of PTSD and depression has been frequently studied in diverse populations such as the military, war victims, prisoners, teachers, victims of domestic violence and those affected by a natural disaster [20, 21]; in particular, the impact of PTSD and depression comorbidity on symptom severity [2,22, 23] . Although many previous studies conducted with traumatized populations have indicated adverse consequences of PTSD and depression comorbidity, including an increase in symptom severity, studies are not consistent about the impact of PTSD and depression comorbidity on symptom severity, especially across different populations [24]. Beside PTSD and depression comorbidity, other factors associated with symptom severity are the type of trauma suffered, severity of trauma, number of traumatic events, past psychiatric history, post-trauma social support, peri-traumatic emotional responses and peri-traumatic dissociation [25].

Mental disorders are a leading cause of disability globally [26 1], largely driven by depression and PTSD [27]. Most of the disease burden is in Low and Middle Income Countries (LMICs), where 75% of adults with mental disorders have no service access [28]. Despite nearly 15 years of efficacy research showing that local non-specialists can provide evidence-based care for depression and anxiety in LMICs [29], few studies have advanced to the critical next step and morbidity from mental disorders continues to escalate [30]. It is vital that global mental health treatment researchers now focus on implementation science to inform scale-up of evidence-based care to lower mental health burden. As emphasized by a recent World Health Organization (WHO) initiative [31], integration of mental health treatment into existing systems of care is critical to achieving public health impact.

With high prevalence of Major Depressive (MDD) (26% [32] and Posttraumatic Stress Disorder (PTSD) (35%) [33] in primary care populations, treatment for depression and PTSD are leading concerns for Kenyan mental health policy makers. Implementation knowledge gaps thwart efforts to scale up care for depression and trauma-related disorders. Kenyan healthcare providers and policy-makers launched a government-funded initiative to scale-up treatment for mental disorders in primary healthcare [34]. Yet, they lack an evidence base to guide programs for two essential treatments: psychotherapy and second generation antidepressants [35] without which Kenyan care scale-up will fall short of its potential [36]. The study described here responds to this need.

Implementation research on depression and PTSD treatment within existing LMIC health care systems must consider not only individual treatment benefits in culturally distinct populations, but also barriers affecting access to care, healthcare system capacities, and budget. Hence, we are partnering with local, national and regional mental health stakeholders to evaluate: 1) non-specialist delivery of evidence-based depression and PTSD treatment integrated within existing healthcare centers in regards to clinical effectiveness and implementation parameters; including 2) costs and cost-benefit ratios.

MDD and PTSD are frequently co-morbid—approximately 50% of those with PTSD also have MDD [37] and 30–40% of those with MDD also have PTSD [38]. Given our goal of investigating sustainable and scale-able interventions for use in "real-world" practice settings, we have intentionally selected permissive study eligibility criteria that will allow us to include participants with MDD, PTSD and both – the combinations that providers are likely to encounter in practice.

In literature search, depression is a major cause of morbidity worldwide [39]. One of the risk factors that is associated with the development of this illness and its increased clinical severity is the exposure to early traumatic events [40].

Standardized clinical classifications such as the Diagnostic and Statistical Manual of Mental Disorders (DSM) and the International Classification Disease (ICD) have postulated a single unipolar depression [41]. Nevertheless, there is clinical and neurobiological evidence that suggests a distinguishable subtype of depression as a function of childhood trauma that ought to require specialized treatments [42].

Most of the approaches related to trauma have considered Posttraumatic stress disorder (PTSD) as the main diagnosis [43]. However, depression is two times more prevalent than PTSD in the general population [44]. Even though both pathologies are very often present in comorbidity [45], the study of depression as a result of trauma exposure is scarce. This area needs more attention, not only in trauma research but also in public mental health policies.

During the past decade, international studies showed that over 50% of the general population has been exposed to psychological trauma [46]. In USA, 61% of men and 51% of women have been exposed to potentially traumatizing events [46, 47]. In Chile, 41.7% of men and 33.2% of women have had this previous reference [48].

While men are more exposed to non-interpersonal PTSD, women are seriously affected by interpersonal trauma, of which physical and sexual events are the most common [46, 48]. In these cases, poly-traumas are more frequent than single trauma [48]. Despite the high prevalence of PTSD in the general population, not all exposed persons develop a mental disorder such as depression related to the trauma [46]. Female gender, interpersonal trauma and childhood trauma constitute risk factors associated with the further development of psychopathology [49].

A series of epidemiological studies has demonstrated that childhood abuse is associated with a range of depression disorders in adulthood that includes mood, anxiety, and substance abuse disorders [50, 51]. PTSD is the most studied diagnosis as a result of trauma, including early PTSD experiences [49]. However, there is strong evidence demonstrating that emotional neglect as well as physical and sexual abuse during childhood constitutes risk factors in the development of depression in adulthood [45] not only in one depressive episode but in its recurrence [52].

Depression is two times more prevalent than PTSD in the general population, being a major cause of morbidity worldwide. In most countries, the number of people who will suffer from depression during their lives falls within an 8%–12% range [39]. According to the World Health Organization, in 2004 unipolar depressive disorders were ranked as the third leading cause of the global burden of disease and they will move to the first place by 2030 [53].

In the past decade, in Chile, according to an epidemiologic study, using the Composite Diagnostic International Interview (CIDI), the prevalence of major depression and PTSD was 9% and 4.4%, respectively [54]. Both pathologies were affecting twice the number of women than men. Recent studies have found that 17.7% of the general population has had depressive symptoms in the last year, with 25.5% occurring just in women [55].

In 2001, when the national program to treat depression had been promoted, the study conducted by Alvarado found that risk factors associated with depression among women being treated by primary care in Santiago of Chile were one previous depressive episode, social isolation and low social support, severe family dysfunction, and a family history of suicide or attempts of suicide. Of them, low social support and suicide among relatives were statistically associated with more severity [56]. Nevertheless, in this study, record of childhood trauma was not investigated as a risk factor for developing depression.

Since 2002, in Región del Maule, we have focused our research on the prevalence of early PTSD in adult patients with depression which in treatment at the primary care and secondary specialized care [57, 58]. All these studies have used the Marshall scale [59]. This scale is a screening that inquires whether an individual has memories of having one or more of the following traumatic experiences before the age of 15: traumatic separation from a parent or caregiver, alcohol or drug abuse by a family member, physical violence between parents or caregivers, systematic punishment by parent or caregiver, physical injury associated with punishment, and/or forced sexual contact with a relative or a nonrelative. In these studies, which were conducted in different clinical samples, we founded a range of prevalence between 52.1% and 87.5% of psychiatric patients who recalled at least one of the childhood traumatic events [57, 58].

Worldwide there are over 19 million refugees, most of whom were displaced because of war and other organized violence [60]. The majority of refugees stay in the recipient countries for years or even decades. It is estimated that by the end of 2014 nearly a half of the world's refugees will have lived in protracted refugee situations, which means that they have been in exile for 5 years or longer without immediate prospects for durable solutions. On average, however, a refugee spends more than 20 years in exile before he or she can go back home or find another solution [60]. Refugees' mental health often presents a challenge to clinicians and policy makers of the recipient countries.

Evidence from community studies amongst recently resettled refugees suggests that refugees have higher rates of mental disorders, in particular depression, PTSD and other anxiety disorders, than those usually found in the non-war affected general population [61]. Several longitudinal studies amongst recently resettled refugees have indicated that post-traumatic stress reactions may persist and even increase over time [62], at least during the immediate

period after war trauma and resettlement. This increased vulnerability has been linked to both pre-migration experiences, in particular exposure to war trauma [63], and post-migration conditions and stressors refugees often face in a new country, including separation from family, difficulties with asylum procedure or even detention, unemployment, inadequate housing, and issues related to acculturation [64].

Whether the refugees' increased risk of adverse mental health persists after the initial period of resettlement is unclear since there is a paucity of comparable data for long-settled refugees and the few studies that have been undertaken present an inconsistent picture. Whilst some studies reported a gradual improvement in symptoms over a period of a decade, to the point where prevalence rates of mental disorders were lower than in the general population of the host country [65], other studies found prevalence rates substantially higher than those in the general population [66]. Previous systematic reviews and meta-analyses evaluating mental health of refugees (including those recently resettled) have all indicated a reduction in risk for mental disorders as the length of time since displacement increases [63, 64]. However, these reviews did not specifically report findings for refugees with a longer duration of displacement [63, 64, 67], mostly assessed studies of recently resettled refugees [64,67] where rates would be expected to be higher, focused only on refugees in Western countries [63], and confined their findings to PTSD, depression or a generic effect size index of psychological distress derived from heterogeneous outcome measures across studies [63, 64, 66, 68] Thus, a systematic review focusing specifically on long-term mental health outcomes of war refugees worldwide is warranted. Understanding the long-term mental health of refugees is essential for guiding the health policies of recipient countries aimed at promoting long-term mental health of refugees [66, 67, 69].

The current review investigated whether mental disorders in war refugees persist beyond the immediate period after war trauma and resettlement by focusing on studies assessing mental disorders and factors associated with these disorders among long-settled war refugees, including those residing outside Western countries.

Humans are developing in a co-constructive way whereby the biological-genetic interface interacts with the cultural setting to form mind and brain and with it the potential for mental malfunctioning. Traumatic stressors (TS) evoke an alarm response, i.e., activate stages in a genetically prepared biological defence mechanism that thus appears in any culture. Research into the neurobiological foundations of PTSD experiences [70] and data reporting similarity in trauma-related symptom profiles across different cultural settings [71] suggest that PTSD and depression are possible ways of conceptualizing mental suffering in response to traumatic stress experiences. Thereby, the cumulative exposure to PTSD experiences, especially when event types vary, seems to have a potentially devastating consequence for mental health, [72, 73], probably because the exposure to varying types of stressors is particularly powerful to enlarge the fear network [74]. In the age of "new wars" [75], even civilians living in crisis regions are affected by organised violence and human rights violations and often have experienced and witnessed a whole trauma package. Data of Neuner and colleagues [76] for instance, indicate that a two-dozen of traumatic experiences is sufficient to traumatise 100% of any exposed sample.

A cross-sectional epidemiological study done by Roberts [77] among adults living in IDP-camps in Northern Uganda show a high exposure to traumatic war experiences resulting in 54% of PTSD and 67% depression, even with a higher risk among women. Correlating data of Klasen et. al [78] of a strong relationship between PTSD exposure and depression as a mental health outcomes could also be found among formerly abducted children.

Judith L. Herman [79] had defined complex PTSD exposure as being severe in its nature, continuing repeatedly over a long period of time and with an onset during the person's childhood. All of these criteria obviously apply to the experiences of formerly abducted children and young adults. In the present investigation we wanted to further study the severity and frequency of trauma-related mental suffering, particularly of those who have been abducted and specify the relationship between length of abduction as a measure of cumulative trauma exposure and mental health.

Many wars continue to engulf Africa, from east to west and from north to south, leaving many Africans severely traumatized [80]. Musisi [81], in his chapter in the recently published volume "Essentials of clinical psychiatry for sub- Saharan Africa", reports significant physical and psychological war-related trauma inflicted to the Ugandans in their homes, at military checkpoints and in detention. The most commonly encountered mental disorders were found to be post-traumatic stress disorder (PTSD) at 39.9%, depression at 52%, anxiety at 60% and somatization disorder at 72.2%. The prevalence of suicidal behavior was recorded as 22.7% and that of alcohol abuse as 18.2%.

These incredibly high figures for mental disorders in war-affected Ugandans are reflected by another recent study among internally displaced Kenyans following ethnic clashes in parts of the country. Njau [82] found, in this highly traumatized population, a prevalence rate of 80.2% of PTSD amongst the heads of households. Neuner et al [83] studied a random sample of 3,339 refugees in the west Nile region, including Ugandans and Sudanese, and found that 31.6% of the male and 40.1% of the female respondents fulfilled the criteria for a DSM-IV PTSD diagnosis. He also found a near linear rise of psychological strain with the increasing number of traumatic events, ranging from a 23% prevalence of PTSD in those who reported three or fewer pre-defined traumatizing experiences to a 100% prevalence in those who

reported 28 or more traumatic events. In a recent study, Pham et al [84] found that, among the 2091 participants who survived the 1994 genocide in Rwanda, 24.8% met the symptom criteria for PTSD.

In the DSM-III in 1980, knowledge has grown significantly regarding its causes, maintaining mechanisms and treatments. Despite this increased understanding, however, the actual definition of the disorder remains controversial. The DSM-5 and ICD-11 define the disorder differently, reflecting disagreements in the field about whether the construct of PTSD should encompass a broad array of psychological manifestations that arise after trauma or should be focused more specifically on trauma memory phenomena. This controversy over clarifying the phenotype of PTSD has limited the capacity to identify biomarkers and specific mechanisms of traumatic stress. This review provides an up-to-date outline of the current definitions of PTSD, its known prevalence and risk factors, the main models to explain the disorder, and evidence-supported treatments. A major conclusion is that, although trauma-focused.

The relationship between PTSD and depression has been a focus of trauma research over the past 20 years. Co-morbid depression has been documented at exceptionally high rates among numerous populations including American and Israeli veterans with PTSD, reaching 67%-82% [85]. Similarly, the prevalence of co-morbid PTSD among veterans suffering from depression is also high, ranging between 36%-73% [86]. Although this comorbidity has been studied both empirically and theoretically, the relationship between these disorders, including its causal effects and symptomatology, is still not fully clear [87].

War captivity is a pathogenic experience as it involves extreme situations in which one's life is being threatened in a prolonged and repeated nature. Ex-POWs suffer from a wide

range of psychiatric disorders, most common among them being PTSD and depression. Comorbidity of these disorders was found to be highly prevalent among ex-POWs when compared to other combatants in a previous study conducted by our research group [88].

Recent studies suggest that PTSD and depression represent a range of symptomatic expressions of the same latent traumatic response, calling into question the theoretical distinction between PTSD and mood/anxiety disorders among individuals who have experienced trauma. Neurobiological studies show that the comorbidity of PTSD and depression differs clinically and biologically from each of these disorders, supporting the need to better explain and elucidate the PTSD-depression comorbidity [89].

Most studies of PTSD and depression are cross-sectional in nature and relatively few studies have explored the longitudinal relationship between these two disorders. Studies conducted among both U.S. Gulf War veterans [90] and Israeli ex-prisoners of war (ex-POWs), [88] showed a bi-directional connection between the disorders, with PTSD predicting depression and vice versa. Similarly, Breslau et al. [91] found that the probability for depression to precede PTSD was as strong as the probability of PTSD to precede depression among young women. Recently, Ginzburg, Solomon, & Ein-Dor [92] found that, among Israeli 1982 Lebanon War veterans, early onset of PTSD predicts later depression and later PTSD/depression comorbidity, but not the other way around. These studies' inconsistent results concerning the course of these disorders further highlight the complexity of the connection between the two disorders and call into question their distinction as separate constructs.

Research suggests that one of the major concerns that comorbidity entails is its clinical severity and subsequent impairment. The outcome and correlates of the PTSD/depression comorbidity seem to differ from individual disorders, with the comorbid disorder

presenting worse psychosocial functioning [92] higher suicidality, and poorer prognosis than PTSD alone [86]

PTSD and depression, especially when observed after a traumatic experience, both indicate a decreased ability to regulate and modify affect, thoughts and experiences [93] which can be manifested in somatization and dissociation [94] as well as a tendency for self-destructiveness . To date, most studies connecting trauma and depression to these related outcomes were conducted with early trauma samples such as childhood maltreatment and sexual abuse. The literature on the relationship between comorbid PTSD/depression and the above outcomes and correlates is limited among adults, especially with respect to individuals who underwent severe trauma in adulthood, such as the military population.

The high levels of PTSD/depression joint expression and related outcomes and correlates over time merit further attention. The goal of the present study is to cast light on the characteristics of PTSD/depression and their comorbidity, 35 years after exposure to a war experience. Specifically, the focus will be on the relationship between these disorders over time with affect regulation and self-destructive manifestations (i.e., dissociation, somatization, self-destructive behaviors and suicidality) in two different veterans groups; ex-POWs and controls. This will be employed using a prospective design which will allow for assessments of the temporal changes in clinical manifestations.

Global mental health is about addressing inequities, namely the “treatment gap” for people with mental health conditions such as depression and PTSD [95] the ethical imperative to provide access to scientifically evidence-based treatment for mental disorders, regardless of the socioeconomic context in which people live [96]. Although studies suggest that the prevalence of depression in Low and Middle Income Countries (LMIC) and Sub-Saharan

African (SSA) countries is comparable to that found in High Income Countries (HIC), at around 10–20 percent of the population at any one time; most people living with depression go untreated [97]. Despite research carried out in primary healthcare settings indicating a high prevalence of depression among facility attendees, particularly in the context of co-morbid chronic disease [98] detection rates remain low, including in contexts where clinicians have received training in detection and treatment of common mental disorders [97]. Thus, a key objective for global mental health is to make sense of these discrepant findings. Critics of global mental health have suggested that psychiatric diagnostic criteria and accompanying standardized instruments, originated, developed and tested in the West are the source of art-factual findings related to the prevalence of depression in different cultural settings, and that the etic approach is invalid, given the role of the social and the cultural context in shaping the life world [99]. Nonetheless, there is a range of evidence that indicates the credibility of common underlying concepts of mental sickness [100], with explanatory models indicating that around the world people experience depression through the body as well as the mind [99]. For example, in systematic review of qualitative evidence, Haroz et al. found that depressed mood/sadness; fatigue/loss of energy and problems with sleep were the three most common features of depression mentioned by participants in studies carried out among non-Western populations and Western populations [101].

All these studies support the fact of the existence of recognizable PTSD within African populations. This reality, however, is in contrast to that held by some experts [102] who state that PTSD in Africa is a pseudo-diagnosis by Western agencies who medicalize understandable social consequences of war and who bring about Western models of management that are inappropriate. It is precisely this type of misconception that sets Africa aside and apart from the rest of the world when it comes to the conceptualization of PTSD. There is ample evidence in support of the fact that Western conceptualizations of PTSD have

validity in Africans, and that war survivors in Africa can and do show symptoms of PTSD [103]. It is expected that this Forum will stimulate thinking and action not only among African academics but also among aid agencies. These ought to wake up to the reality that the prevalence of mental disorders in Africa is likely to be extremely high, as a direct result of the wars that have caused many to lead lives as refugees.

On the other hand, PTSD and depression (Major Depressive Disorder (MDD) is common, with approximately half of people with PTSD also having a diagnosis of (major depressive disorder (MDD) across diverse epidemiological samples [104]. There are two competing explanations for this comorbidity. The first is that the comorbidity reflects imprecision in symptom classification into the two discrete categorical diagnoses. Support for this explanation would come from variability in comorbidity rates based on different versions of the *Diagnostic and Statistical Manual of Mental Disorders (DSM),* as there have been changes to the number of symptoms required for diagnosis of PTSD, but not MDD. An alternative view is that the co-occurrence of PTSD and MDD represents a trauma-related phenotype that is distinct from MDD and reflects a fundamental dimension of risk for psychopathology following trauma exposure. Support for this explanation is less straightforward, but can be inferred from the research literature examining risk factors and biological correlates for the individual disorders, and where possible, for the comorbidity. The study review evidence for both views. It is critical to then consider treatment implications in order to determine whether existing treatments for PTSD can be effective in treating people who present with symptoms of both disorders, or rather, whether the presence of both conditions requires an altogether different approach.

The changes to the diagnostic criteria for PTSD over time, with the corresponding absence of change in MDD criteria presents the opportunity to examine whether and how rates of comorbidity between the disorders change over the same time period. If the rates change

substantively over the different versions, this would suggest that the comorbidity is an artifact of nosology. Only a few epidemiological studies have been reported that examined comorbidity rates of *DSM-III* diagnoses of PTSD and MDD and the rates vary considerably. In the North Carolina catchment area study of the Epidemiological Catchment Area (ECA) program, the rate of *DSM-III* depression in people with PTSD was only 4% [105].

In the late 1980s and early 90s, large-scale and comprehensive epidemiological studies of PTSD were launched (e.g., the Detroit Area Survey of Trauma [106]. In addition, the National Comorbidity Survey was initiated in 1990. This effort assessed a broad range of current and lifetime *DSM-III-R* diagnoses in a nationally representative sample. Kessler and colleagues [107] reported that 47.9% of men and 48.5% of women with PTSD also had depression, consistent with the rate reported in the Detroit Area Survey of Trauma [108]. It will be of great interest to see whether the rate of comorbidity between PTSD and depression will change with the advent of *DSM-5,* as no studies to date have reported comorbidity rates of PTSD and depression using *DSM-5* criteria. However, in a multinational study of PTSD prevalence rates using varying criteria, the odds ratios associated with meeting criteria for a distress disorder (including major depression in response to a traumatic exposure that also lead to PTSD, declined from 11.1 using *DSM-TV* to 7.8 using *DSM-5* criteria [109]. The comorbidity rate between *DSM-5* PTSD and the distress disorders in this study was low (5.5%) because only cases with first onset in conjunction with the focal trauma exposure were considered in the comorbidity percentage.

In sum, there is little evidence to suggest that changes in the way that PTSD has been conceptualized in *DSM* has appreciably affected the comorbidity rates over time, as the comorbidity rate from *DSM-III-R* to *DSMIV-TR* has remained at about 50% in epidemiological samples. This is probably due to the fact that two of the three items that overlap (sleep disturbance and concentration difficulties) have stayed within the same cluster.

Of note, most investigations consider lifetime diagnoses, rather than comorbidity based on exposure to the same traumatic experience. Several investigations have also demonstrated that eliminating the common symptoms between PTSD and mood and anxiety disorders using *DSM-IV* criteria does not appreciably change the prevalence of PTSD [110].

Research on the latent structure of PTSD comorbidity shows that people with PTSD who report high negative affectivity and low positive affectivity are more likely to have a comorbid diagnosis of depression [111]. Thus, when PTSD and MDD co-occur this may be a manifestation of the underlying vulnerability to respond to trauma with the behavioral, affective, and cognitive symptoms that reflect the internalizing dimension. That is, people who report high levels of neuroticism are prone to react to everyday stressors and challenges with anxiety, worry, irritability, and sadness (i.e, negative affect). This style is particularly invoked when the challenge involves loss, threat, or frustration [112 and reflects a long-standing personality dimension. Coupled with low extraversion, which refers to a tendency to seek out and enjoy social activities, the individual is less likely to ask for support from others when frustrated or upset and/or less capable of seeking novel and stimulating experiences that might be mood brightening.

Thus, when exposed to a traumatic experience, the person who develops PTSD and has an internalizing personality style is vulnerable to developing depression. In support of this view, Spinhoven et al [113] examined the influence of neuroticism and extraversion on rates of PTSD and depression in a longitudinal study of more than 2400 adults. The results showed that high neuroticism and low extraversion assessed at baseline were associated with development of comorbid PTSD and depression 4 years later. Interestingly, the traits were not associated with new-onset cases of either disorder by itself, suggesting that it is the combination of high neuroticism and low extraversion that leads to the comorbidity. In contrast, the person who develops PTSD but has the externalizing personality style

characterized by impulsive thoughts and behaviors is not likely to develop depression. In this instance, PTSD is more likely to be accompanied by substance abuse and aggression. Longitudinal research is needed to better understand the structure and etiology of PTSD epidemiology.

A prominent risk factor for both PTSD and depression is childhood adversity and abuse [114] and in the study described above, Spinhoven et al [113] reported that the relationship between the high neuroticism/low extraversion and subsequent development of comorbid PTSD and depression was fully accounted for by retrospective reports of childhood sexual and physical abuse in multivariate analyses. A similar result was reported by Hovens et al [115] who found strong support for an association between retrospective reports of physical childhood abuse and comorbid mood and anxiety disorders in a large adult sample. In contrast, people with only a depression diagnosis were more likely to report emotional neglect and psychological abuse in childhood. Thus, childhood maltreatment, especially physical abuse, may mediate the association between the internalizing dimension and development of depression and PTSD. Other types of abuse may be associated with different adulthood outcomes.

HIGHLIGHTS

Co-occurrence of PTSD and depression is highly prevalent, expressing rapidly after the traumatic event. According to the literature review the comorbidity seems to have a worrisome chronic course continuing decades after the war. Related affect regulation and self-destructive symptoms (i.e., dissociation, somatization, self- destructive behavior and suicidality) are significantly higher among patients with a comorbidity diagnosis, yet these important sequelae may be lost in the current nosology. Depression is not explicitly anchored to a traumatic event, therefore symptom checklists and other diagnostic tools are not anchored in this manner, which may affect a patient's response [103]. Classification

systems should consider the growing evidence in the literature, including the current study, concerning the wider picture of human experience and symptoms after exposure to trauma.

Moreover, the complex time dynamics and high rate of comorbidity between PTSD, depression and other psychopathologies shown in this study suggests that the current emphasis in policy and clinical practice that considers PTSD as the main traumatic response may be short- sighted, Clinicians must regularly revisit all possible symptomatic and temporal expressions and dynamically update patients' diagnoses. Therapy for these individuals has to take into consideration the experience unique to each patient, which may be comprised of a larger range of symptoms than expected. These co-occurring symptoms may have concrete implications on the therapy plan [116]. Current diagnostic methods and tools may easily miss the comorbidity, especially given findings that it tends to present years after the initial PTSD diagnosis.

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